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3rd INTERNATIONAL CONFERENCE WITH STUDENT SESSION HEALTHY AGING 2026

Transforming Science into Impact

23-24 APRIL, 2026

DEPARTMENT OF REHABILITATION, MEDICAL UNIVERISTY OF LUBLIN

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Introduction

This issue of *Wiadomości Lekarskie /Medical Advances* results from the collaboration between the Medical University of Lublin (Poland) and Gulf Medical University (United Arab Emirates). These two esteemed institutions have been working together to bridge gaps in aging research, sharing expertise, and fostering international collaboration in medical advancements. We intentionally connect geriatrics, orthopedics, rehabilitation, public health, nutrition, and medical technologies because aging is not a process affecting a single organ or discipline. It is a process involving the whole person- biological, functional, and social.

It is therefore with genuine joy and a sense of responsibility that we also invite you to the next edition of the International Healthy Aging Conference, which on April 23–24, 2026, will once again bring physicians, researchers, physiotherapists, students, and clinicians from many countries to Lublin and to Ajman. This year's theme, "Transforming Science into Impact," reflects what modern medicine increasingly demands from us because knowledge alone is no longer enough. Scientific discovery must translate into real improvement in the lives of patients. Healthy Aging was meant to be the latter from the very beginning. When we first initiated this meeting, our intention was never to organize just another scientific event that ends with slides archived on computers and certificates placed in drawers. We wanted to create a space where people meet because they share a common conviction: aging is not merely a medical issue – it is one of the most important civilizational challenges of our time.

The year 2026 carries a particularly personal meaning for us. This edition coincides with the 60th Anniversary of the Department and Clinic of Rehabilitation at the Medical University of Lublin. Over six decades, thousands of patients have passed through our Clinic, generations of physicians and physiotherapists have trained within its walls, and countless students have taken their first steps in clinical medicine. Methods have changed, technologies have evolved, and the understanding of rehabilitation itself has transformed- yet one principle has remained constant: medicine does not end with diagnosis. True medicine begins when a person regains function, independence, and dignity.

This is an opportunity to reflect on a journey – from rehabilitation understood as recovery after injury to contemporary functional, preventive, and regenerative medicine. It is an opportunity to pause and ask ourselves where we stand today and where we are heading as clinicians, researchers, and healthcare systems.

Conference Healthy Aging has always been built on international collaboration. The partnership between the Medical University of Lublin and Gulf Medical University is not merely an organizational arrangement; it represents how modern science should function. Population aging does not recognize national borders. Whether in Poland, the United Arab Emirates, or elsewhere, patients face similar realities: multimorbidity, frailty, loss of mobility, and social isolation. The answers, therefore, must also be developed together.

The presence of young researchers is especially important to us. Every edition of Healthy Aging reminds us that the future of medicine does not emerge solely from textbooks but from conversations- often the first uncertain questions asked by students. For this reason, the student session is not an addition to the conference, it is its heart.

Lublin provides a meaningful setting for this dialogue. It is a city at a crossroads- geographically, historically, and intellectually- where tradition meets innovation. Here, discussions about the future of aging feel particularly appropriate, because healthy aging is not simply about living longer. It is about living as fully as possible.

We believe modern medicine is undergoing a fundamental shift. The central question is no longer only how to treat diseases of old age, but how to help people reach old age while maintaining function and independence. Rehabilitation, prevention, physical activity, nutrition, and supportive technologies are becoming as important as pharmacological treatment.

This publication is a record of ideas we hope to develop together. It does not aim to close a discussion- it aims to begin one.

We warmly invite you to be part of it.

With sincere regards,

Prof. Tatjana Ille, MD, MSc, PhD
Gulf Medical University, Ajman, United Arab Emirates

Prof. Tomasz Blicharski, MD, PhD, MBA
Medical University of Lublin, Lublin, Poland

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SIXTY YEARS OF REHABILITATION
A STORY ABOUT RETURNING TO LIFE

In most hospital departments success can be measured quickly. A wound heals, laboratory results normalize, a patient leaves the ward. Rehabilitation is different. Here progress is often quiet and slow. Sometimes it is a first step after weeks of immobility. Sometimes a hand that finally manages to hold a spoon, and sometimes it is simply a patient who no longer needs help to sit up in bed.

The 60th anniversary of the Clinical Department of Rehabilitation at the University Clinical Hospital No. 4 in Lublin is therefore not only a date. It is a reminder that medicine is not limited to saving lives. It is also about helping people return to them.

The beginnings were modest. In the 1960s a small ward was created for patients who, after surgery or neurological disease, could not simply be discharged home. Someone had to answer the practical question: what next? The answer was not a single procedure but a new way of thinking. Treatments does not end with the control of disease, it end's when the patients regained function. From the very start rehabilitation in Lublin grew between orthopaedics and neurology. This combination turned out to be crucial, as physicians quickly understood that the human body cannot be divided into separate specialties once a patient tries to stand, walk or dress independently. While function connects everything, it also forces cooperation, long before the term "interdyscyplinary care" became well known.

The early years were far from comfortable. Equipment was simple, the team small, and many solutions had to be invented in daily practice. Yet something important was created then: a specific professional culture. Everyone did a little more than their formal duties. Doctors exercised with patients, physiotherapists suggested treatment modifications, and nurses became the closest observers of real functional change. Rehabilitation was not a service added to treatment. It became its continuation.

With time the department became academic. Students began appearing on the ward, initially uncertain and often surprised. Rehabilitation looked different from what they had imagined. There were no spectacular procedures, but there was constant work and close contact with patients. Many of them discovered here for the first time that medicine is not only about diagnosing disease but about accompanying a person through recovery. Teaching, in turn, changed the staff as well practical experience had to be explained, named and organized. While daily practices turned into knowledge, scientific activity developed naturally from clinical questions; why some elderly patients are unable to tolerate physical strain. Additionally, why does functional improvement depend on bone quality? Can small intervention to a specific site support rehabilitation more effectively than extensive surgery? Observations from the ward became research topics, and research returned to the ward as better decisions. Rehabilitation began to be understood not only as exercise but as applied physiology.

A new chapter began in 2022 with a change of leadership. Importantly, it was not experienced as a new beginning but as a continuation. The clinic already had a strong identity built over decades, and the goal

was not to replace it but to strengthen it. Under Professor Tomasz Blicharski the development has been evolutionary: expanding neurological rehabilitation, organizing interdisciplinary cooperation and introducing modern technologies only where they genuinely improve patient outcomes.

One of the most visible changes has been the growing focus on neurological patients. Stroke survivors, patients with severe spasticity and individuals in disorders of consciousness require time, patience and coordinated care. Patients progress rarely appears in statistics, however it is very real in their life. The creation of a regional spasticity treatment program and systematic work with patients awakening from coma demonstrated that even difficult cases benefit from persistent, well-planned therapy.

Technology also entered the ward robotics, biofeedback and virtual-reality-supported exercises. Yet the lesson quickly became clear: devices themselves do not rehabilitate anyone, they only enhance what coordinated team efforts can achieve. When adequately used, it provided patients with ability to recovery. Perhaps the most important development has not been technological, however organizational. Modern rehabilitation requires constant communication. Physicians plan direction, physiotherapists observe functional change hour by hour, nurses notice fatigue and small improvements, and speech therapists restore communication and safe swallowing. With such cooperative efforts of rehabilitation the patients feels progression in physical well being. Many describe the department in simple terms: "everyone here knows what the others are doing."

Recognition came in 2024 with a national award for the best rehabilitation department in Poland. For the team it was less a triumph than confirmation that daily, often invisible work has value. Rehabilitation rarely produces dramatic moments, but it produces durable results: independence, mobility and dignity.

Looking back at sixty years, one conclusion becomes clear. Medicine advances through technology, but healing often advances through persistence. Rehabilitation encourage the act of patience not only to the patients, however to physicians, even thought progression may be slow, however it is meaningful. The goal is not to perfect radiography but the functioning person. In a hospital environment which focuses on procedures and efficiency, rehabilitation preserves something essential "it keeps medicine human-scaled". It requires time spent with the patient, attention to small changes and cooperation instead of individual achievement.

Anniversaries usually summarize the past. This one rather points toward the future. The experience gathered over decades shows that modern medicine needs rehabilitation more, not less. Populations age, survival after severe diseases improves and patients expect not only to live but to live independently. The story of this department therefore is not primarily about an institution. It is about a simple conviction repeated daily in clinical practice: recovery is possible, but it requires effort from both the patient and the medical team. And when it succeeds, even partially, it becomes one of the most satisfying outcomes medicine can offer.

After sixty years the message remains surprisingly contemporary. Saving life is the beginning. Helping someone return to it is the real completion of treatment.

ORIGINAL ARTICLE

CONTENTS

Clinico-epidemiological spectrum of chronic liver disease patients at a tertiary care center in Ajman, UAE – a descriptive 5 year data analysis

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ABSTRACT

Aim: To describe the clinico-epidemiological profile, metabolic risk factors, and treatment outcomes of patients with chronic liver disease (CLD) at a tertiary care center in Ajman, UAE.

Materials and Methods: 149 individuals with confirmed CLD were included in a descriptive five-year retrospective study. Descriptive statistics (frequencies and percentages) were utilized for analyzing demographic data, lifestyle variables, metabolic comorbidities, and clinical outcomes.

Results: The male-to-female ratio in the cohort was 3.7:1, with a significant male preponderance (78.5%; n=117). In particular, most patients (91.3%) were under 60, with those under 40 making up the biggest group (46.3%; n=69). The Eastern Mediterranean Region was the place of origin for more than half of the participants (55.7%). In terms of lifestyle risk factors, 32.9% of respondents smoked, and 24.2% reported drinking alcohol (14.1% now, 10.1% previously). Although only 8.1% were classified as obese (BMI ≥30 kg/m^2), 84.6% had abnormal BMI (overweight or obese). Fatty liver (41.6%), diabetes mellitus (38.9%), dyslipidaemia (37.6%), and hypertension (36.2%) were among the significant metabolic comorbidities. Nearly half (49.0%) of patients had incomplete or poor clinical outcomes to medications, whereas 51.0% had "good" results.

Conclusions: This tertiary-care cohort found a predominance of economically productive males who were affected by CLD, who also exhibited a high prevalence of metabolic risk factors. Origins of obesity and diabetes have highlighted the regional influence of metabolic (MAD) liver disease. To optimise the outcome of patients who have these diseases, there is an urgent need for early screening and comprehensive management of metabolic risk factors.

KEY WORDS: BMI, metabolic syndrome, lifestyle factors, cardiovascular risk, liver function, diabetes, public health, Middle East

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INTRODUCTION

Chronic liver disease (CLD) has risen as a dreadful public health challenge globally. It is characterised by progressive destruction of liver parenchyma that leads to fibrosis, cirrhosis, and potentially hepatocellular carcinoma [1,2]. Typically, viewed as a condition that mainly affects the elderly, recent epidemiological shifts show a rising incidence among younger adults, largely driven by the changing lifestyle patterns [3,4]. Globally, CLD was estimated to affect approximately 1.5 billion people in 2017, with metabolic-associated conditions accounting for nearly 60% of these cases [5,6]. The burden remains overwhelming, as of 2021, cirrhosis and other chronic liver pathologies contributed to over 1.4 million deaths and 46.4 million disability adjusted life years worldwide [7].

In the Middle East and North Africa (MENA) region, the clinical spectrum of CLD is going through a rapid transition. While the success of vaccination campaigns and antiviral therapies has led to a decline in viral hepatitis, there has been a significant surge in Metabolically Dysregulated Associated Steatotic Liver Disease (MASLD) [8]. In the MENA region, MASLD prevalence is estimated to be around 39.4% in the general adult population, rising to a concerning 68.7% among patients with type 2 diabetes [9,10]. In the last decade, the incidence of MASLD in this region increased by nearly 14%, with high fasting plasma glucose identified as the major contributing factor [11].

The United Arab Emirates (UAE) reflects these regional trends as well, where metabolic risk factors have become the main cause of CLD [12]. In the UAE, CLD is increasingly associated with the rising cases of obesity and type 2 Diabetes Mellitus [13]. This shift is critical as liver diseases are often asymptomatic in their early stages, complicating early detection and leading to worse clinical prognoses. For younger adults, this early onset leads to long-term metabolic complications, impaired quality of life, and a substantial socio-economic burden [14]. Clinical outcomes in CLD are often influenced by a complex interplay of comorbidities such as Hypertension, Hypercholesterolemia, and Diabetes Mellitus, which can accelerate disease progression [15]. Therefore, identifying specific predictors within the UAE is essential for promoting and achieving healthy ageing [16].

Research indicates that while age and gender are significant non-modifiable factors, men often show a higher risk and faster fibrosis progression [17, 18]. The modifiable lifestyle factors, too, like tobacco use, alcohol consumption, and dietary habits, play a vital role in the clinical epidemiological profile of these patients. These factors, along with abnormal body mass index (BMI), have proven to be predictors of CLD [19]. Understanding how these factors correlate with objective clinical markers such as Liver function tests (LFTs) is critical for early detection [20]. As these diseases undergo silent progression, characterising these variables within a tertiary care setting is vital for developing targeted screening and lifestyle-based preventive initiatives.

Despite the rising health concern, there remains a notable lack of awareness regarding liver disease risk, especially among the younger population. This study aims to provide a comprehensive five-year descriptive analysis of the clinical epidemiological spectrum of CLD at a tertiary care centre in Ajman, UAE. By examining demographic, lifestyle, and clinical variables, this research seeks to identify the key factors that can inform effective public health strategies to reduce the burden of liver disease and support the goal of healthy ageing within the UAE.

AIM

The primary aim of this study was to describe the clinico-epidemiological spectrum of chronic liver disease (CLD) among adult patients managed at a tertiary care center in Ajman, United Arab Emirates, over five years. Specifically, the study sought to characterize the demographic profile, lifestyle risk factors, metabolic comorbidities, anthropometric patterns, vaccination status, and clinical outcomes of patients diagnosed with CLD in order to provide a comprehensive overview of disease patterns within this population.

MATERIALS AND METHODS

STUDY DESIGN, SETTING, AND SAMPLING

A retrospective cross-sectional study was conducted to review the cases of chronic liver diseases reported to an Academic Healthcare Institution in Ajman, UAE. The electronic medical records of patients diagnosed with chronic liver disease from January 2020 to July 2025 were retrieved to assess the clinical and epidemiological spectrum. Cases were identified using ICD-10 codes, and records with missing key demographic or clinical information were excluded.

DATA COLLECTION AND VALIDATION

Information was retrieved from the hospital's electronic medical records using a structured data collection form developed from the standard clinical documentation practices adopted in the hospital. Extracted variables comprised sociodemographic characteristics, clinical features of Chronic liver diseases, medical conditions, prognosis, and lifestyle factors. To ensure data quality, a systematic validation and cleaning process was applied, including the identification and removal of duplicate entries using unique patient identifiers and the exclusion of records with missing key information. In cases where multiple records existed for the same patient, the most complete and diagnostically confirmed record was retained.

DIAGNOSTIC CRITERIA AND CLINICAL DOCUMENTATION

The diagnosis of chronic liver disease was based on documentation by the treating physician, supported by clinical evaluation and relevant investigations recorded in the electronic medical records. Diagnostic consisten-

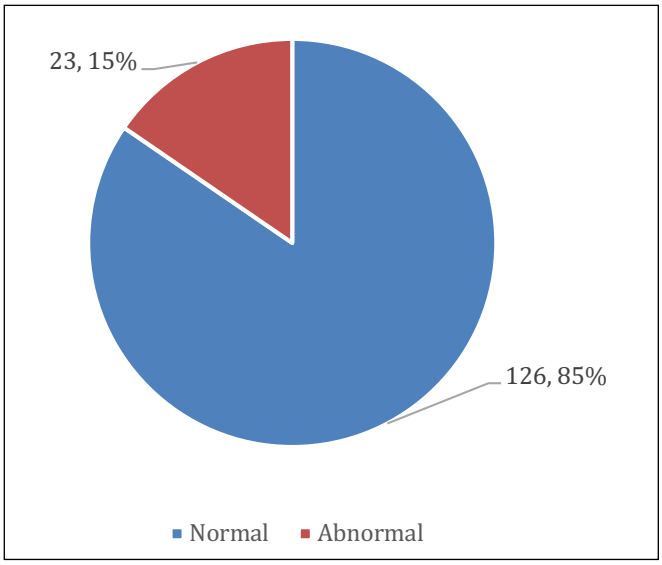

Fig. 1. Distribution of participants according to their anthropometric characteristics
Source: Own materials

cy was maintained through the hospital's standardized clinical documentation protocols.

ETHICAL APPROVAL

The study received approval from the Institutional Review Board of the Medical University (IRB Ref. no. IRB-COM-STD-119-Dec-2025), and permission to access records was granted by the University Hospital, Ajman. As the study used anonymized retrospective data, informed consent was waived. All procedures adhered to the ethical principles of the Declaration of Helsinki, ensuring participant confidentiality and anonymity.

DATA MANAGEMENT AND STATISTICAL ANALYSIS

After data cleaning, a total of 149 records of patients with chronic liver diseases were included in the final dataset. The dataset was verified in Microsoft Excel® and subsequently analyzed using IBM SPSS Statistics version 30. Descriptive statistics were used to summarize the study variables, with categorical data presented as frequencies and percentages.

RESULTS

During five years, a total of 149 patients with chronic liver disease (CLD) were identified for the study, which describes the characteristics of patients at a tertiary care hospital in Ajman, United Arab Emirates. Complete demographic, clinical, and risk factor data were collected from all included cases.

In terms of age (Table 1), 69 patients (46.3%) were under 40 years, 67 patients (45.0%) were between 40 and 60 years, and only 13 patients (8.7%) were over 60 years. In fact, more

Table 1. Distribution of participants according to sociodemographic characteristics

Variable	Category	Frequency [n]	Percent [%]
Age Group	Below 40 years	69	46.3
	40 years to 60 years	67	45.0
	Above 60	13	8.7
Gender	Male	117	78.5
	Female	32	21.5
Marital Status	Single	29	19.5
	Married	120	80.5
Nationality / WHO Region	EMR (Eastern Mediterranean Region)	83	55.7
	SEAR (South-East Asia Region)	53	35.6
	Others	13	8.7

Source: Own materials

Table 2. Distribution of participants according to their personal habits

Variable	Category	Frequency [n]	Percent [%]
Alcohol Use	Never	113	75.8
	Former Use	15	10.1
	Current Use	21	14.1
Smoking	Yes	49	32.9
	No	100	67.1

Source: Own materials

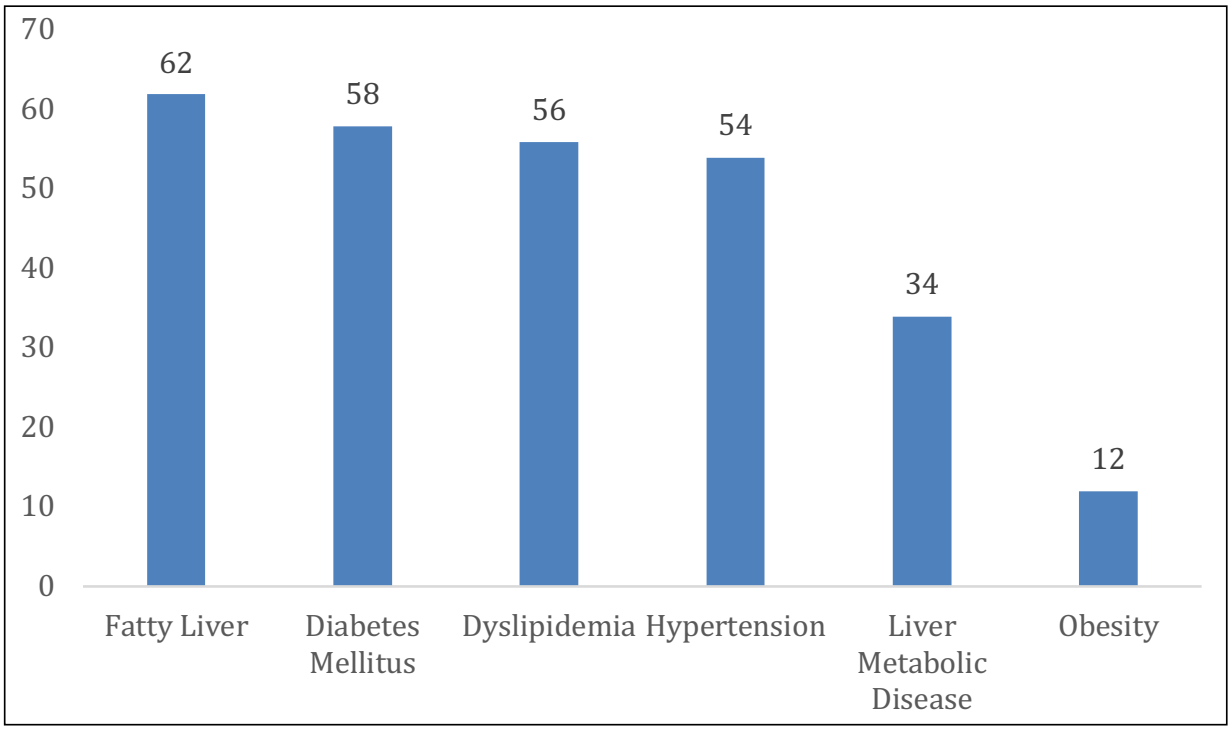

Fig. 2. Distribution of participants according to history of metabolic comorbidities
Source: Own materials

Table 3. Distribution of participants according to history of past surgeries and vaccination status

Variable	Category	Frequency [n]	Percent [%]
Surgical History	Yes	56	37.6
	No	93	62.4
Vaccination Status	Vaccinated – up to date	103	69.1
	Vaccinated – not up to date / incomplete	36	24.2
	Not vaccinated at all	6	4
	Not sure / don't know	4	2.7

Source: Own materials

Table 4. Distribution of participants according to clinical outcomes to medication

Variable	Category	Frequency [n]	Percent [%]
Treatment Outcome	Good	76	51.0
	Partial	31	20.8
	Poor	42	28.2

Source: Own materials

than 90% of the cohort (91.3%) was below 60 years of age, implying that CLD mostly impacted people who were economically productive. The male predominance in the study population was quite striking; there were 117 males (78.5%) and 32 females (21.5%), making the male-to-female ratio approximately 3.7:1.

Most of the patients were married (120; 80.5%), and the rest (29; 19.5%) were single. When the patients were classified according to the regional classification of the World Health Organization, 83 patients (55.7%) were from the Eastern Mediterranean Region, 53 patients (35.6%) were from the South, East Asia Region, and 13 patients (8.7%) were from other regions.

In terms of lifestyle-related risk factors (Table 2), out of 36 cases (24.2%) where alcohol consumption was present, 21 (14.1%) were still using alcohol, 15 (10.1%) were previously using alcohol, and 113 cases (75. 8%) were no alcohol consumers. out of the total cases, 41 patients (32.9%) were smokers, while the remaining 100 (67.1%) were non-smokers.

Anthropometric assessment (Fig. 1) showed that only 12 patients (8. 1%) were considered obese by the binary obesity variable; however, by BMI classification, 126

patients (84.6%) were in the abnormal BMI category, with only 23 patients (15.4%) having a normal BMI. Hence, the group under study was characterized by a high level of abnormal body mass.

Most of the study participants were metabolically unhealthy. Concurrent with other metabolic disorders, 58 (38.9%) of the patients had diabetes, 54 (36.2%) had hypertension, and 56 (37. 6%) had dyslipidemia. Fatty liver was found in 62 patients (41.6%) and 87 (58.4%) without fatty liver changes, while 34 (22.8%) were classified as NAFLD based on liver metabolic disease (Fig, 2).

A history of previous surgery was reported by 56 (37.6%) out of the total 149 patients, and 93 (62.4%) had no record of these surgeries. The vaccination status of hepatitis B was different among the groups. Based on the definition of the four categories in the methodology, there were 103 patients (69.1%) who were vaccinated up to date, 36 patients (24.2%) had not received their complete immunization series, 6 patients (4. 0%) who were not vaccinated at all, and 4 patients (2.7%) who were unsure of vaccination status (Table 3).

Clinical outcomes for patients who received treatment (Table 4) were divided into three groups: good, partial, and poor. Among the study participants, 76 patients (51.0%) had a good outcome, 31 patients (20.8%) had a partial outcome, and 42 patients (28.2%) had a poor outcome. Almost half of the study participants (49. 0%) had partial or poor clinical outcomes during the study period.

DISCUSSION

The present five-year descriptive study done in the UAE provides important insight into the evolving clinico-epidemiological spectrum of Chronic Liver Disease within the Gulf population. The key findings that emerged include insights into the gender predominances, regional distribution, age factors, and metabolic comorbidities.

The pronounced male predominance (78.5%) observed in the present study is consistent with the global epidemiological data. Several studies have emphasized persistent sex disparities in CLD incidence and outcomes, attributed to behavioral, hormonal, and metabolic differences [21]. The Global Burden of Disease analysis also demonstrated a higher age-standardized mortality and DALY rates from CLD among males compared to females [22].

The high proportion of patients under the age of 60 years is particularly striking. Although chronic liver disease tends to predominantly impact the older age groups, new information indicates that there is a rising burden among younger, economically productive populations due to metabolic disease and viral hepatitis patterns [23, 24].

According to a 2024 analysis in the MENA region, there is a reported rising CLD prevalence among young individuals due to obesity and other metabolic conditions [25]. Since more than 90% of our population was under the age of 60, the socioeconomic impact is quite significant, as CLD among the working age group can have a substantial effect on the healthcare systems and productivity [24, 26].

A significant percentage reported no alcohol use (75.8%), while 24.2% had current or prior exposure to alcohol. This low prevalence in Gulf countries can be attributed to the region's cultural and religious norms. However, the incidence of chronic liver disease has risen significantly, with alcohol use emerging as a notable contributor [27]. Therefore, the fact that there is still a significant proportion of alcohol consumers in our study is still an important consideration and remains clinically relevant.

The smoking prevalence of 32.9% in this study aligns with the clinical evidence indicating that cigarette smoking negatively impacts the incidence and severity of CLD at multiple levels: promoting hepatocarcinogenesis, hepatic fibrogenic stimulus, exacerbating metabolic fatty liver disease, and overall, negatively impacting liver-related outcomes [28, 29]. Southeast Asian regions are significantly reporting the risk of smoking as the leading cause of NAFLD [30].

A key finding of this study is the high metabolic risk profile of the population, with a significant population having an abnormal BMI (84.6%), diabetes mellitus (38.9%), hypertension (36.2%), and dyslipidemia (37.6%). These findings strongly support the global transition towards metabolic dysfunction associated with steatotic liver disease (MASLD) as a leading CLD etiology. This is further evidenced by MASLD becoming the most widespread CLD globally, affecting over 30% adults and increasingly recognized as a significant contributor to liver cirrhosis and failure [31, 32].

The pandemic levels of obesity and T2DM in the Gulf region, together with an aging population, suggest that NAFLD/NASH-associated advanced liver disease and mortality will increase in these countries [33]. Metabolic factors lead to hepatocyte injury and stress, contributing to mitochondrial dysfunction in MASLD. This leads to hepatocellular oxidative injury, inflammation, and accelerated fibrosis progression with worse prognosis [34]. The results of this study showed that most of the population was vaccinated against the hepatitis B virus. Hepatitis B vaccination programs have dramatically reduced the incidence of new chronic HBV infections globally, especially where infant immunization has been implemented [35, 36]. In GCC countries, including the

UAE, vaccination programs have significantly reduced HBV incidence.

However, in countries where adult vaccination coverage and catch-up campaigns are sub-optimal, like sub-Saharan Africa and East Asia, the burden of HBV infection remains, with approximately 296 million people affected by it [37]. Nearly half (49%) of the patients had partial or poor outcomes. This large proportion of adverse clinical courses is consistent with several global observational studies that have shown the persistence of morbidity in CLD despite the advances in therapy and supportive care [38]. Metabolic risk factors, which were highly prevalent in our population, have been well recognized as predictors of rapid fibrosis progression, decompensation, and liver-related mortality [34, 39]. Delayed presentation and advanced disease at the time of diagnosis may also underlie the high proportions of suboptimal outcomes.

These findings emphasize the need for proactive liver disease screening, structured follow-up, and integrated management plans. This study was conducted at a single tertiary care centre in the UAE, which may limit external validity as patient characteristics and disease patterns may vary across several healthcare settings within the country.

CONCLUSIONS

A thorough picture of the clinico- epidemiological range of chronic liver disease (CLD) in the area is given by this five-year descriptive study of patients with CLD who were seen at a tertiary care facility in Ajman, United Arab Emirates. The results show that middle-aged persons are mostly affected by CLD, and that men are more likely to be affected by patients with cirrhosis and associated consequences presented at advanced stages of the disease, indicating delayed diagnosis and inadequate early screening, according to the clinical profile.

The continuous epidemiological shift in the United Arab Emirates and the larger Gulf area is reflected in the etiological pattern. While viral hepatitis, especially hepatitis B and C, remains a significant but relatively declining cause, probably due to better vaccination and antiviral treatment strategies, metabolic dysfunction-associated steatotic liver disease (MASLD) and alcohol – related liver disease emerged as the leading contributors. The strong metabolic foundations of CLD in this group are highlighted by the coexistence of metabolic comorbidities such as obesity, type 2 diabetes mellitus, dyslipidaemia, and hypertension.

The prevalence of metabolic and lifestyle-related variables in the development of disease is further supported by biochemical and radiological data. Elevated liver enzymes, aberrant lipid profiles, and imaging indications of fatty infiltration of fibrosis were present in a significant percentage of individuals. The need to use an integrated, multidisciplinary approach to liver health is highlighted by the clustering of metabolic risk factors among CLD patients.

Overall, the study highlights that most of the risk variables identified, such as obesity, sedentary lifestyle, poor eating patterns, and alcohol intake, are controllable, even though other demographic characteristics, such as age and gender, cannot be changed. In Ajman, the growing role of metabolic aetiologies indicates a change in the causes of liver disease from communicable to non-communicable, requiring focused public health initiatives.

According to the study, frequent liver function testing and non-invasive fibrosis assessment should be used to improve early diagnosis of chronic liver disease, especially in high-risk populations like those with metabolic risk factors. In addition to alcohol harm reduction techniques, liver health should be incorporated into non-communicable disease programs with a focus on weight control, glycaemic management, and cholesterol regulation. To lower the disease burden and enhance outcomes, multidisciplinary care, community awareness campaigns, hepatitis B immunisation, hepatitis C screening, and the creation of a regional liver disease registry are crucial.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Clinico-epidemiological spectrum of constipation patients at a tertiary care center in Ajman, UAE – a descriptive 5 year data analysis

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ABSTRACT

Aim: This research aims to assess the clinical and epidemiological profile of elderly patients reported to a tertiary care centre in Ajman, UAE.

Materials and Methods: A retrospective cross-sectional review of electronic medical records was conducted for patients diagnosed with constipation between January 2020 and July 2025. Sociodemographic characteristics, anthropometric measures, functional status, lifestyle factors, comorbidities, gastrointestinal history, and treatment outcomes were extracted using a structured proforma. Descriptive statistics were applied.

Results: Eighty elderly patients were included, predominantly male (71.3%) and aged 60–69 years (78.8%). Abnormal BMI was present in 76.3%. Chronic symptoms were common, with 52.5% reporting constipation ≥3 months and 47.5% >6 months. Low fluid intake (66.3%), low dietary fiber intake (67.5%), and sedentary lifestyle (62.5%) were highly prevalent. Cardiometabolic comorbidities were frequent, including hypertension (68.8%), diabetes mellitus (65.0%), and hypercholesterolemia (63.7%). Only 38.8% achieved good therapeutic response, while 61.3% had poor or partial improvement.

Conclusions: Constipation in elderly patients at this tertiary center represents a persistent, multifactorial condition requiring comprehensive, individualized, and lifestyle-integrated management strategies to improve outcomes.

KEY WORDS: elderly, lifestyle factors, comorbidities, body mass index, treatment outcomes

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INTRODUCTION

Constipation is one of the most frequently faced gastrointestinal complaints in both primary care and tertiary healthcare settings. Although often perceived as a minor discomfort, it is a complex multisystemic issue that significantly impairs an individual's physical comfort, psychological well-being, and overall quality of life [1, 2]. Clinically, constipation is a heterogeneous symptom-based disorder defined by infrequent bowel movements, difficulty passing stools, hard consistency, excessive straining, or a sensation of incomplete evacuation [3]. The Rome IV criteria currently serve as the gold standard for clinical diagnosis, shifting the focus from simple stool frequency to a broader spectrum of sensory and oscillatory symptoms [4, 5].

Globally, the prevalence of chronic constipation is estimated between 10% and 20% in the adult population [6]. Epidemiological data consistently presented

a higher predilection among women, possibly due to hormonal influences on gut motility, and the elderly, where polypharmacy and age-related physiological decline play major roles [7,8]. Beyond the physical burden, the condition is a significant cause of healthcare utilization, contributing to millions of outpatient visits and billions in annual costs related to over-the-counter laxatives and diagnostic procedures [9]. If left unmanaged, chronic constipation can lead to debilitating complications such as hemorrhoids, anal fissures, rectal prolapse, and fecal impaction [10].

In the Middle East and North Africa (MENA) region, the clinical landscape of gastrointestinal health is undergoing a rapid shift. Rapid urbanization has led to a "nutritional transition" characterized by the increased consumption of processed foods, low fiber intake, and inadequate hydration [11]. Furthermore, the high regional prevalence of metabolic disorders, such as Diabetes Mellitus and Obesity, contributes to autonomic neuropathy and altered colonic transit times [12, 13]. Recent studies also highlight the importance of the gut-brain axis, where high stress levels and sedentary lifestyles, common in urbanized Gulf centers, exacerbate functional bowel disorders [14].

The United Arab Emirates (UAE) reflects these regional shifts, yet hospital-based data regarding the specific demographic and clinical characteristics of these patients remains sparse. In tertiary care settings, patients often present with constipation that is either idiopathic or secondary to other comorbidities. Identifying the interplay between lifestyle determinants (such as daily fluid and fiber intake) and objective clinical markers (such as BMI and existing comorbidities like Hypertension or Hypercholesterolemia) is essential for a holistic management approach [15].

Despite the rising incidence, public awareness regarding the modifiable risk factors of constipation remains limited in Ajman and the surrounding Northern Emirates. This study aims to provide a comprehensive five-year descriptive analysis of the clinical epidemiological spectrum of constipation patients at a tertiary care center in Ajman, UAE. By examining demographic trends, lifestyle habits, and associated medical conditions, this research seeks to provide the local evidence needed to optimize preventive strategies and promote healthy gastrointestinal aging within the UAE.

AIM

This research aims to assess the clinical and epidemiological profile of elderly patients with constipation reported to a tertiary care centre in Ajman, UAE.

MATERIALS AND METHODS

STUDY DESIGN, SETTING, AND SAMPLING

A retrospective cross-sectional study was conducted at a tertiary teaching hospital affiliated with a medical university in Ajman, reviewing archived electronic medical records of patients diagnosed with constipation between January 2020 and July 2025. All eligible records within the study period were included, representing a census of cases, irrespective of nationality or gender. Constipation cases were identified using the ICD-10 code from the hospital's EMR system. Records lacking essential demographic or clinical information were excluded.

DATA COLLECTION AND VALIDATION

Data were extracted from the electronic medical records using a structured proforma based on relevant literature and standard clinical documentation. Collected variables included sociodemographic details, constipation-related clinical features, comorbidities, and lifestyle factors. Data accuracy was ensured through systematic validation and cleaning, including the removal of duplicate entries using unique patient identifiers and the exclusion of records with missing essential information. When multiple records existed for a patient, the most complete and diagnostically confirmed entry was retained.

DIAGNOSTIC CRITERIA AND CLINICAL DOCUMENTATION

The diagnosis of constipation was based on documentation by the treating physician, supported by clinical assessment and relevant investigations as recorded in the EMR. Diagnostic consistency was ensured through standardized institutional clinical documentation practices.

ETHICAL APPROVAL

The study was approved by the Institutional Review Board of the Medical University (IRB-COM-STD-203-June-2025), with permission obtained from the University Hospital, Ajman. Informed consent was waived due to the retrospective use of anonymized data, and ethical principles of the Declaration of Helsinki were followed, ensuring confidentiality and anonymity.

DATA MANAGEMENT AND STATISTICAL ANALYSIS

After cleaning, 80 unique patient records were included in the final dataset, which was verified in Microsoft

Table 1. Sociodemographic and anthropometric characteristics of elderly patients with constipation

Variable	Category	Frequency (n)	Percent (%)
Age Group	60-69	63	78.8
	70-79	9	11.3
	≥ 80 years	8	10.0
Gender	Male	57	71.3
	Female	23	28.7
Marital Status	Single	2	2.5
	Married	78	97.5
Nationality / WHO Region	South East Asia Region	13	16.3
	Eastern Mediterranean Region	59	73.8
	Other regions	8	10.0
BMI level	Normal	19	23.8
	Abnormal	61	76.3

Source: Own materials

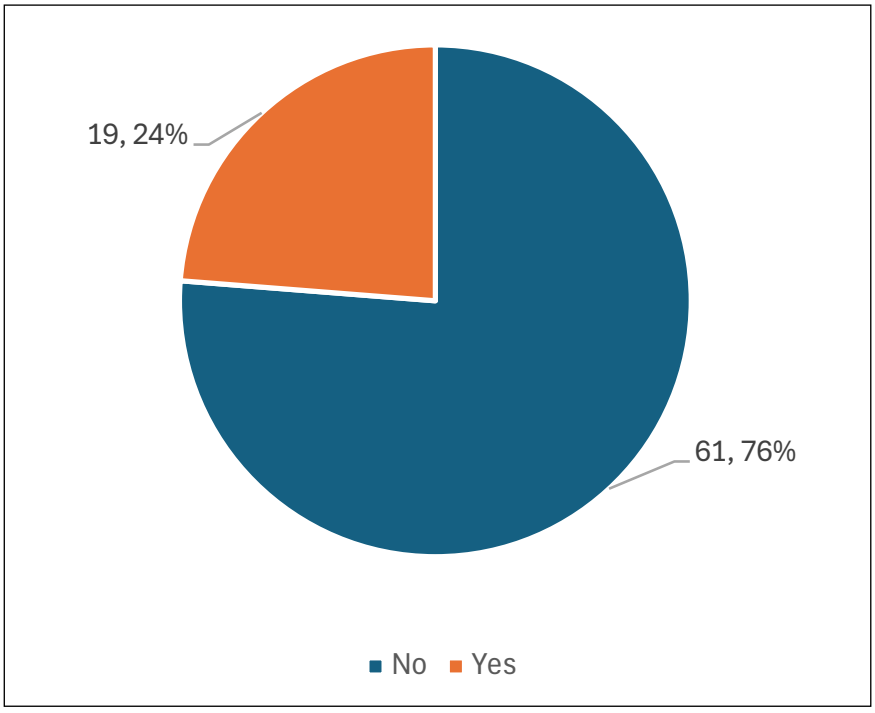

Fig. 1. Prevalence of cognitive impairment among elderly patients with constipation
Source: Own materials

Excel® and analyzed using IBM SPSS Statistics version 30. Descriptive statistics were used to summarize study variables, with categorical variables presented as frequencies and percentages. .

RESULTS

A description of baseline sociodemographic and anthropometric characteristics is essential to contextualize the study population. Accordingly, Table 1 presents the demographic distribution and BMI profile of the 80 elderly patients diagnosed with constipation. There was a clear predominance of male patients, who accounted for 71.3% (n = 57) of the cohort, while females constituted 28.7% (n = 23). Most participants belonged to the younger elderly age group, with 78.8% (n = 63) aged between 60–69 years, followed by 11.3% (n = 9) aged 70–79 years and 10.0% (n = 8) aged 80 years or older. The population was largely married, as 97.5% (n = 78) reported being married, whereas only 2.5% (n = 2) were single. With respect to geographical distribution based on WHO regional grouping, the majority originated from the Eastern Mediterranean Region (73.8%, n = 59), followed by the South-East Asia Region (16.3%, n = 13), while 10.0% (n = 8) were from other regions. Anthropometric assessment demonstrated a high prevalence of abnormal body mass index, observed in 76.3% (n = 61) of patients, whereas only 23.8% (n = 19) had BMI values within the normal range.

Table 2. Duration of symptoms among elderly patients with constipation

Variable	Category	Frequency (n)	Percent (%)
Constipation for more than 6 months	Yes	38	47.5
	No	42	52.5
Duration of constipation	<2 weeks	16	20.0
	2-4 weeks	10	12.5
	1-3 months	12	15.0
	≥ 3 months (chronic constipation)	42	52.5

Source: Own materials

Table 3. Prevalence of metabolic and endocrine comorbidities in elderly patients with constipation

Variable	Category	Frequency [n]	Percent [%]
Hypercholesterolemia	Yes	51	63.7
	No	29	36.3
Hypothyroidism	Yes	11	13.8
	No	69	86.3
Hypertension	Yes	55	68.8
	No	25	31.3
Diabetes Mellitus	Yes	52	65.0
	No	28	35.0

Source: Own materials

Table 4. Associated gastrointestinal conditions among elderly patients with constipation

Variable	Category	Frequency [n]	Percent [%]
Gastritis	Yes	23	28.7
	No	57	71.3
GERD	Yes	41	51.2
	No	39	48.8

Source: Own materials

Table 5. Lifestyle-related factors in elderly patients with constipation

Variable	Category	Frequency [n]	Percent [%]
Alcohol use	Never	72	90.0
	Occasionally	7	8.8
	Regular	1	1.3
Smoking	Never	51	63.7
	Former	21	26.3
	Current	8	10.0
Daily fluid intake	Low	53	66.3
	Moderate	22	27.5
	High	5	6.3
Daily fiber intake	Low	54	67.5
	Moderate	19	23.8
	High	7	8.8
Physical activity levels	Sedentary	50	62.5
	Moderate	20	25.0
	Vigorous	10	12.5

Source: Own materials

Table 6. Surgical history and structural conditions among elderly patients with constipation

Variable	Category	Frequency [n]	Percent [%]
History of abdominal and pelvic hernias (eg, umbilical and femoral hernia)	Yes	11	13.8
	No	69	86.3
Recent major abdominal or pelvic surgeries (last 3 months)	Yes	22	27.5
	No	58	72.5
History of anorectal surgery (e.g., hemorrhoidectomy, prolapse repair)	Yes	15	18.8
	No	65	81.3
History of bowel resection	No	100	100

Source: Own materials

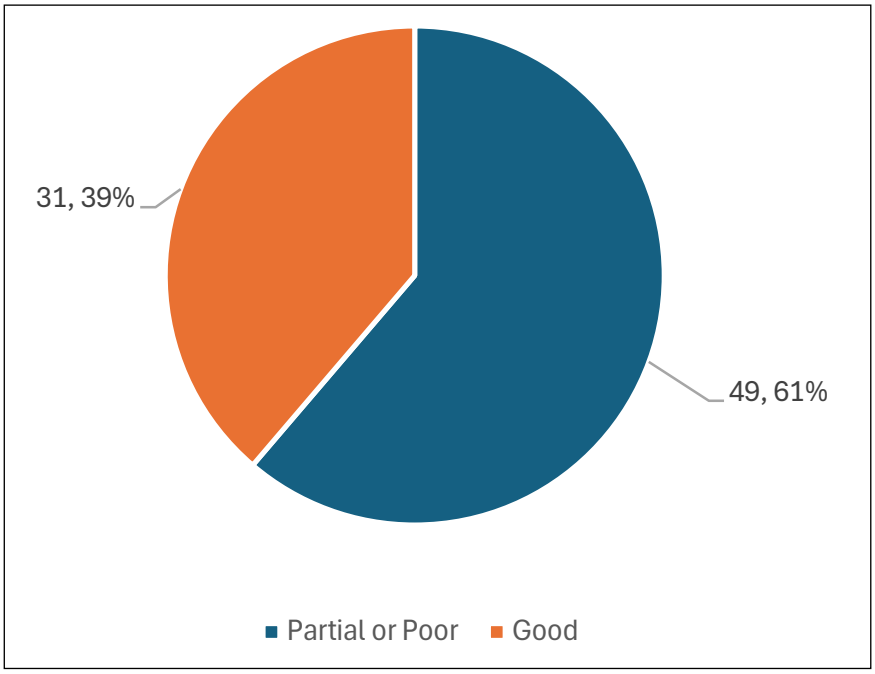

Fig. 2. Treatment outcomes in elderly patients with constipation
Source: Own materials

Cognitive impairment is a highly prevalent state among the elderly; many recent studies have also highlighted the potential influence of cognitive function on bowel habits. Therefore, cognitive impairment was assessed and is illustrated in Figure 1. Cognitive impairment was documented in 23.8% (n = 19) of patients, while 76.3% (n = 61) had no evidence of cognitive impairment.

The duration of constipation symptoms is an important variable of interest, since it helps determine if the condition is acute or chronic and therefore will also influence the management strategies, respectively. The findings of this symptom duration are summarized in Table 2. More than half of the patients (52.5%, n = 42) reported constipation lasting three months or longer, consistent with chronic constipation, while 47.5% (n = 38) had symptoms persisting for more than six months. Shorter symptom durations were less common, with 20.0% (n = 16) reporting symptoms for less than two weeks, 12.5% (n = 10) between two and four weeks, and 15.0% (n = 12) between one and three months.

Because constipation in the elderly frequently coexists with chronic systemic illnesses, the prevalence of major metabolic and endocrine comorbidities was assessed. As shown in Table 3, hypertension was present in 68.8% (n = 55) of patients, while diabetes mellitus was identified in 65.0% (n = 52). Hypercholesterolemia was reported in 63.7% (n = 51) of participants. Hypothyroidism, a condition known to influence gastrointestinal motility, was documented in 13.8% (n = 11) of the cohort.

In order to obtain a more comprehensive understanding of constipation, associated gastrointestinal conditions were also evaluated. These findings are presented in Table 4. Gastroesophageal reflux disease (GERD) was present in 51.2% (n = 41) of patients, whereas gastritis was identified in 28.7% (n = 23). Conversely, 48.8% (n = 39) had no history of GERD and 71.3% (n = 57) had no history of gastritis.

Lifestyle-related factors represent the modifiable contributors to constipation and were therefore systematically analyzed. Table 5 summarizes fluid intake, fiber intake,

physical activity levels, smoking status, and alcohol consumption. Low daily fluid intake was observed in 66.3% (n = 53) of individuals, while 27.5% (n = 22) reported moderate intake and only 6.3% (n = 5) reported high intake. Low dietary fiber intake was common, affecting 67.5% (n = 54) of patients, whereas 23.8% (n = 19) reported moderate intake and 8.8% (n = 7) reported high intake. Physical activity levels were predominantly low, with 62.5% (n = 50) classified as sedentary, 25.0% (n = 20) reporting moderate activity, and 12.5% (n = 10) engaging in vigorous activity. Regarding smoking status, 63.7% (n = 51) were never smokers, 26.3% (n = 21) were former smokers, and 10.0% (n = 8) were current smokers. Alcohol consumption was uncommon, with 90.0% (n = 72) reporting no alcohol use, 8.8% (n = 7) occasional use, and 1.3% (n = 1) regular use.

Finally, to evaluate the response to therapy among patients receiving treatment for constipation, treatment outcomes were analyzed and are presented in Figure 2. A good treatment outcome was observed in 38.8% (n = 31) of patients, whereas 61.3% (n = 49) demonstrated partial or poor response.

DISCUSSION

The study reveals a distinct clinico-epidemiological signature of constipation in the elderly population of Ajman. The findings show a high prevalence of male dominance, prevalence in early elderly (60-69 years), and high prevalence of cardiometabolic multimorbidity. The most important finding is the high prevalence of chronic symptoms (>3 months) and the "lifestyle triad" of low fluid, low fiber, and low physical activity. The most worrisome finding is that more than 60% of patients had suboptimal treatment outcomes, which indicates that the current management practices are not addressing the complex issue of geriatric constipation.

In contrast to the global trend, where the prevalence of constipation is more common in females because of the dynamics of the pelvic floor and hormonal changes, in this study, the predominance of males (71.3%) was found, which is contrary to most of the community-based studies that have shown a higher prevalence of constipation in females, especially in the older population living in the community. [16,17]. The prevalence of constipation in the older population has been estimated to range between 15% and 25% globally, with higher prevalence rates found in hospitalized and institutionalized patients. [17,18]. This "gender paradox" observed in the UAE may be due to the differences in the healthcare-seeking behavior of the population in this region, where the older males may have a tendency to seek tertiary care for their quality-of-life issues, while the females may have a preference for home remedies or traditional practices.

The age distribution in our cohort showed a preponderance of patients in the younger elderly subgroup (60-69 years), with 78.8% of patients in this subgroup. This is slightly at variance with the general epidemiological trend that the prevalence of chronic constipation increases with age, particularly in those aged ≥70-80 years, as reflected in recent systematic reviews and population studies [16,19]. For example, pooled data show that the prevalence of constipation increases substantially with age, with higher rates observed in those >70 years compared with the younger elderly subgroup [19,20]. There are several possible explanations for the underrepresentation of the oldest age subgroup in our tertiary care population. It is likely that patients aged ≥80 years have already developed bowel care practices in the community or long-term care facilities that reduce the need for tertiary care referral, or that they may be physically or cognitively impaired and lack access to tertiary care. In contrast, the "younger elderly" subgroup may be more likely to be mobile, health-seeking, or newly presenting with age-related bowel symptoms.

A striking observation was that 52.5% of patients with symptoms for ≥3 months, and almost half of patients with symptoms for >6 months, chronicity is the rule rather than the exception. Chronic constipation in the elderly indicates deferred healthcare-seeking, normalization of the passage of bowel changes with advancing age, and the presence of multifactorial contributing factors like decreased colonic motility, comorbidities, and polypharmacy. Chronic symptoms cause substantial impairment in the quality of life and functional mobility in the elderly. Chronic constipation also increases the risk of severe complications like fecal impaction, which is a frequent problem in the elderly population and is linked to high morbidity [21-24].

The prevalence of cardiometabolic comorbidities, namely hypertension (68.8%), diabetes mellitus (65.0%), and hypercholesterolemia (63.7%), reflects the international recognition that an ageing population is increasingly affected by multimorbidity. In the Middle Eastern hospital setting, there is also evidence of the frequent co-existence of diabetes and cardiometabolic risk factors with constipation and gastrointestinal symptoms, particularly in older or systemically ill patients [20,25]. Chronic non-communicable diseases may affect bowel motility either directly through autonomic neuropathy (diabetes) or indirectly through polypharmacy and reduced mobility [20]. Moreover, a study conducted in Saudi Arabia showed that nearly one-third of diabetic patients had symptoms of constipation, thus supporting the relationship between metabolic disease and bowel dysfunction in the local population [26].

Besides cardiometabolic disease, more than half of our patients also had gastrointestinal comorbidities like

GERD (51.2%) and gastritis (28.7%). While there is no direct literature to support the association of these gastrointestinal disorders with constipation, there is recent evidence in our region showing a significant overlap between reflux symptoms and functional constipation, implying a common pathophysiology of dysmotility or symptom complexes in gastrointestinal disorders [27]. Postoperative conditions were also prevalent, with 27.5% having recent major abdominal/pelvic surgery and 18.8% having anorectal surgery, both of which are known to increase the risk of delayed bowel function due to postoperative ileus and anorectal dysfunction [28]. None of our patients had bowel resection, thus ruling out resection-related dysmotility.

Constipation in the elderly population may also be a sign of overall health risks, including cognitive impairment. Recent studies have shown associations between constipation and mild cognitive impairment, possibly through the gut-brain axis, including microbiota changes and inflammation. In our study, 23.8% had cognitive impairment, consistent with the literature that suggests a neurological component in chronic constipation [17, 18,29].

In the present study, the sample revealed the following important modifiable risk factors for constipation: low fluid intake (66.3%), low dietary fiber (67.5%), and sedentary lifestyle (62.5%), which were all significant risk factors for constipation. Low fluid and fiber intake leads to decreased stool volume and slowed colonic transit times, thus contributing to the functional obstruction of the bowel, as evidenced in the elderly population [21, 30]. Recent studies also suggest that moderate to high levels of physical activity can reduce the risk of constipation by a significant margin, thus establishing the role of lifestyle modification as a treatment modality [31].

The large proportion of abnormal BMI (76.3%) in our population may also interact with the risk of constipation, since abnormal weight is a marker of underlying nutritional and metabolic disturbances that can negatively impact bowel function. Although BMI does not distinguish between adiposity and lean body mass, there is substantial evidence from large population databases that there is a strong association between indices of elevated body adiposity and the risk of constipation, with individuals who had higher BMI or indices of obesity being at increased risk of constipation in adjusted analyses, with nonlinear associations observed between BMI and the risk of constipation, especially above the threshold of excess weight [32,33]. Mechanistically, abnormal BMI is known to be associated with derangements in gastrointestinal motility, systemic inflammation, and alterations in gut microbiota, all of which have been shown to play a role in delayed colonic transit and constipation pathophysiology [33-35]. Moreover, underlying abnormal nutritional status, such as undernutrition or poor dietary intake, may also contribute to this interaction, especially in the elderly, in whom low nutrient intake and changes in eating habits are associated with an increased burden of constipation [35].

A critical finding was the suboptimal treatment outcome, with only 38.8% of patients obtaining good outcomes. This indicates that current management strategies may not adequately target the complex, multifactorial pathophysiology of constipation in older patients. Evidence suggests that individualized, multimodal strategies often provide better outcomes than current standard therapy alone, emphasizing the importance of comprehensive evaluation and individualized management that considers lifestyle, comorbidities, mobility, and medication burden [36, 37].

The study has the advantage of including a 5-year population and a comprehensive evaluation of clinical, lifestyle, and comorbid variables in a real-world tertiary population. Disadvantages include the descriptive nature of the study, which does not allow for causality, possible information bias due to self-reported dietary and activity data, and the lack of classification of constipation subtypes. Results may not be generalizable to older patients living in the community. Public health initiatives should emphasize high-fiber diets, adequate fluid intake, and regular physical activity in the elderly. Future studies should utilize longitudinal study designs, incorporate assessments of frailty and functional status, objectively assess lifestyle variables, and investigate structured, multidisciplinary treatment pathways to optimize constipation management and geriatric outcomes.

CONCLUSIONS

This five-year analysis demonstrates that constipation in older adults is a persistent and clinically relevant condition, with a high proportion experiencing chronic symptoms (≥3 months: 52.5%) and suboptimal therapeutic outcomes (poor/partial response: 61.3%), indicating that current management often remains insufficient. The coexistence of metabolic comorbidities such as hypertension (68.8%) and diabetes mellitus (65.0%), together with lifestyle-related risks, suggests a broader systemic context influencing bowel health. Future healthy-aging strategies should prioritize early lifestyle interventions, routine assessment of metabolic and functional factors, and stronger continuity of care, ensuring constipation is addressed proactively rather than as an afterthought, thereby reducing physical discomfort, psychological burden, and decline in quality of life among elderly populations.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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CONTENTS

Potential predictors of chronic liver disease among adults: Key determinants for promoting healthy aging

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ABSTRACT

Aim: This study aimed to find out predictors of chronic liver disease (CLD) in adults and evaluate key determinants that may influence healthy aging.

Materials and Methods: A case-control study was conducted among adults who were receiving care at a tertiary care center. Demographics, lifestyle factors, and clinical variables like BMI were collected. Statistical analysis was performed using chi-square testing for association and logistic regression analysis to identify independent factors that predict CLD, p-value of <0.05 was used to identify significance for all information collected.

Results: Significant links were found between CLD and several factors. Males were significantly more affected with CLD (78.5%, $p < 0.001$), making gender one of the factors that predict CLD. Similarly, age was a significant factor, with those aged 40-60 being the most affected (33%, $p = 0.039$). Abnormal BMI was strongly associated with CLD, found in 84.6% cases ($p = 0.008$). Alcohol consumption demonstrated a marked association with chronic liver disease ($p < 0.001$), with former and current alcohol use substantially more common among cases. After logistics regression analysis, male gender, abnormal BMI, and alcohol consumption are significant independent predictors of CLD.

Conclusions: The study highlights gender (male), age (40-60), abnormal BMI and alcohol consumption as significant predictors of CLD in the studied population. These findings emphasize the urgent need for targeted screening and lifestyle-based preventive interventions, particularly focusing on metabolic health and weight management, to mitigate the rising burden of liver disease and promote healthy aging.

KEY WORDS: liver fibrosis, case–control study, body mass index, alcohol use, sex differences, metabolic risk factors

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INTRODUCTION

Chronic liver disease is one of the most common disorders that causes significant morbidity and mortality, even among young adults. Although chronic liver disease was most associated with older individuals, today there is a significant shift in that trend, with even adolescents aged 15 years–21 years being affected, this is largely attributable to shifting trends in lifestyle and disease patterns [1]. CLD encompasses a spectrum of disorders, including Metabolic dysfunction associated with steatotic liver disease, chronic hepatitis caused by viral etiology, autoimmune hepatitis, and liver cirrhosis, which can ultimately lead to liver failure [2]. Previously, chronic hepatitis caused by viral etiology was known to be most commonly associated with chronic liver disease among young adults, but according to recent studies, it is observed that MASLD is seen more commonly than chronic hepatitis among the young population [2]. Alcohol-associated liver disease is also an increasing feature in adults, notably in populations where alcohol consumption is increasing, thus adding to the overall burden of CLD within this age spectrum [6].

Despite this rising trend of CLD among adults, especially the young population, there seems to be a lack of aware-

ness regarding the same. For instance, a study from the U.S focused on awareness of MAFLD in young adults showed that awareness regarding the same among young adults aged 18–29 was significantly low [3]. This is complicated by the fact that liver diseases are often asymptomatic, therefore making it significantly difficult to diagnose them and in turn leading to a delay in treatment and worse prognosis [4].

Beyond liver-related morbidity, affected young adults face metabolic complications, impaired quality of life, psychological distress, and reduced productivity, which together contribute to an increasing socio-economic and healthcare burden [5]. Early onset of the disease often goes undiagnosed due to its asymptomatic nature, delaying intervention and increasing the risk of progression to later liver cirrhosis, hepatocellular carcinoma, or requirement for liver transplantation [6].

Globally, CLD currently remains a very significant public health concern. It encompasses a wide spectrum of liver diseases, including non-alcoholic fatty liver disease, chronic viral hepatitis due to HBV and HCV, alcohol-related liver disease, autoimmune liver diseases, and cirrhosis. Worldwide, it is estimated that about 1.5 billion people were diagnosed with CLD in 2017; the highest burden for the mentioned year was from NAFLD (~59% of cases), followed by chronic hepatitis B (~29%) and hepatitis C (~9%) [7]. The results of the Global Burden of Disease study in 2021 estimated that there were 58.4 million incident cases of cirrhosis and other forms of chronic liver disease, leading to approximately 1.43 million deaths and 46.4 million Disability-adjusted life years (DALYs) [8]. Ensuring efficient vaccination campaigns and antiviral therapies in most developed and developing countries has led to a decrease in viral hepatitis in the past decade. However, metabolic-associated liver disease, particularly Metabolic dysfunction-associated steatohepatitis, has notably risen due to the increase in metabolic risk factors such as obesity, type 2 diabetes, and dyslipidemia [9]. Cirrhosis and other chronic liver diseases account for 2.46% of global mortality and 1.3% of total DALYs, indicating that despite progress in prevention and treatment, CLD remains an important contributor to global morbidity and mortality [9].

Chronic liver disease remains a major and increasing health burden for the entire MENA region, with metabolic dysfunction-associated steatotic liver disease being the leading cause. In a meta-analysis, MASLD was estimated to have a prevalence of about 39.4% among the general adult population and nearly 68.7% among the patients with type 2 diabetes in this setting [10]. Between 2010 and 2021, modelling based on Global Burden of Diseases (GBD) and other sources suggested that MASLD prevalence in MENA increased from 26.3% (~118 million people) to 27.7% (~164 million), with marked increases in adults aged ≥20 years, from 37.1% to 41.0%, and an APC for cirrhosis of ~2.2% yearly [11]. Another investigation from 1990 to 2021 shows a 13.8% increase in MASLD incidence and a 26.4% increase in age-standardized MASLD prevalence, with high fasting plasma glucose as a major contributing factor [12]. While incidence associated with MASLD rose, viral hepatitis and alcohol-related cases decreased, and incident CLD/cirrhosis more than doubled in the area of interest between 1990 and 2021 [13].

In the United Arab Emirates, metabolic risk factors are the primary cause of CLD, which has become a significant and expanding health concern. The major cause of CLD in the UAE includes metabolic dysfunction–associated steatotic liver disease [14,15,16]. It occurs in a relatively high percentage of patients with Type 2 Diabetes Mellitus, and it could be diagnosed non-invasively using FIB-4, NFS, liver ultrasonography, FibroScan, and the Hamachi ultrasound grading system [16]. Cases of HCC in the UAE number approximately 60–100 annually, and with the rising prevalence of obesity and diabetes, this number is expected to increase [15]. Liver transplantation for HCC in the UAE and the wider GCC follows the Milan criteria. Twenty-five liver transplants have been performed in the UAE for HCC, with very good short-term results, and 96% of the transplanted livers are functioning well with no recurrence of cancer reported [15]. The development of chronic liver disease is attributed to harmful alcohol consumption, obesity, viral hepatitis, and MASLD. In addition, genetic predisposition, lifestyle factors like smoking, diet, and lower physical activity levels are also strong contributors [17, 18]. This research will provide data that public health experts can utilize to develop strategies aimed at preventing chronic liver disease by identifying key risk factors linked to its onset in adults.

AIM

This study aimed to identify potential predictors of chronic liver disease among adults and to determine key demographic, clinical, and lifestyle factors associated with its occurrence to support strategies for promoting healthy aging.

MATERIALS AND METHODS

RESEARCH DESIGN AND STUDY POPULATION

This study employs a case–control design and is conducted among adults aged 18 years and above in the UAE. Cases include records of patients with confirmed liver disease, encompassing both genders and any nationalities, while records with incomplete data will be excluded. Controls

Table 1. Association between key determinants and chronic liver disease

Variables	Group	Cases		Controls		p-value
		N	[%]	[N]	[%]	
Age Group	Less than 40	69	46.3	175	58.3	0.039
	40 to 60	67	45.0	99	33.0	
	Above 60	13	8.7	26	8.7	
Gender	Male	117	78.5	154	51.3	<0.001
	Female	32	21.5	146	48.7	
Marital Status	Single	29	19.5	44	14.7	NS (0.195)
	Married	120	80.5	256	85.3	
Nationality	Eastern Mediterranean Region (EMRO)	83	55.7	180	60.2	NS (0.659)
	South-East Asia Region (SEARO)	53	35.6	95	31.8	
	Others	13	8.7	24	8.0	
BMI	Normal	23	15.4	80	26.7	0.008
	Abnormal	126	84.6	220	73.3	
Alcohol Consumption	Never	113	75.8	293	97.7	<0.001
	Former Use	15	10.1	6	2.0	
	Current Use	21	14.1	1	0.3	

Source: Own materials

consist of records of adults without liver disease, including both genders and any nationalities, with exclusion limited to records containing incomplete data.

SAMPLE SIZE

The prevalence of chronic liver disease, specifically non-alcoholic fatty liver disease (NAFLD), among adults in the United Arab Emirates was reported to be 25% [16]. High alcohol intake was associated with a twofold increased risk of developing chronic liver disease [19]. These estimates were used to determine the sample size for the study population. For this case–control study, the minimum required sample size for cases was calculated as 149, assuming a study power of 90% and a significance level of 0.05. With a case–control ratio of 1:2, approximately 300 control subjects were required. A convenience sampling technique was adopted to recruit participants.

METHODOLOGY

The study was conducted after obtaining approval from the Institutional Review Board (IRB). Permission to carry out the research and access the required data was granted by the University Hospital administration. All study procedures were performed in accordance with institutional ethical guidelines, and confidentiality of participant information was strictly maintained throughout the study. Relevant information, including demographic characteristics and details of presenting symptoms, was extracted from the charts. Strict confidentiality and data protection protocols were always followed, and no personal identifiers were included in the study dataset.

DATA ANALYSIS

After data collection, the data were downloaded into an Excel spreadsheet and subsequently transferred to SPSS (Version 30) for statistical analysis. Both descriptive and inferential statistics were performed. Descriptive results were expressed as frequencies and percentages where appropriate. Associations between dependent and independent variables were assessed using the Chi-square test. Binary and multivariable logistic regression analyses were conducted to identify predictors. Statistical significance was set at a p-value ≤ 0.05.

ETHICAL ASPECTS

Approval for the proposal was granted by the Institutional Review Board (IRB Ref. no. IRB-COM-STD-119-Dec-2025) of Gulf Medical University. No information revealing participants' identities was recorded to ensure anonymity. Data were analyzed in aggregate form, and access was restricted to the researchers, IRB members, and statisticians in accordance with Gulf Medical University research policies. The research was conducted according to the Helsinki Declaration.

RESULTS

The analysis outlines the distribution of sociodemographic and clinical characteristics among participants with chronic liver disease (cases) and those without

Table 2. Logistic regression for socioeconomic factors and chronic liver disease

Variables	Group	Chronic Liver Disease					
		Crude			Adjusted		
		OR	CI	p-value	OR	CI	p-value
Age Group	Less than 40	0.79	0.38 - 1.62	NS(0.519)	--	--	--
	40 to 60	1.35	0.65 - 2.82	NS(0.419)	--	--	--
	Above 60	1	--	--	--	--	--
Gender	Male	3.47	2.21 - 5.45	<0.001	3.03	1.88 - 4.90	<0.001
	Female	1	--	--	1	--	--
BMI	Normal	1	--	--	1	--	--
	Abnormal	1.99	1.19 - 3.33	0.008	2.33	1.30 - 4.20	0.005
Alcohol Consumption	Never	1	--	--	1	--	--
	Former Use	6.48	2.45 - 17.12	<0.001	5.62	2.07 - 15.26	<0.01
	Current Use	54.45	7.24 - 409.57	<0.001	53.35	6.87 - 414.15	<0.001

Source: Own materials

chronic liver disease (controls). Several variables illustrate key differences between these two groups, indicating potential patterns as seen in the study sample associated with chronic liver disease as seen in table 1.

For age group analysis, participants were stratified into three age groups: <40 years, 40-60 years, and ≥60 years. A greater percentage of participants under 40 years of age were controls (58.3% vs 46.3%). However, participants 40 to 60 years old were more often represented among cases, 45.0% of chronic liver disease and 33.0% of control participants. The number of participants over 60 years of age had a small percentage of representation in both the case and control groups (8.7%). Overall, the total chronic liver disease distribution across age categories was statistically significant (p=0.039), indicating variation in chronic liver disease occurrence across different age groups.

The two groups also exhibited a significant difference in gender distribution. Male participants made up a greater percentage of chronic liver disease cases (78.5%) than did males in the control group (51.3%). In contrast, females represented a much larger percentage of controls (48.7%) than did females in cases (21.5%). This disparity was statistically significant (p<0.001) and demonstrates a strong association of male gender with chronic liver disease.

Marital status showed no apparent statistically significant difference between the two groups. Married individuals comprised the majority of both cases (80.5%) and controls (85.3%), while single participants represented a smaller proportion within each group. The observed difference in marital status distribution was not statistically significant (p = 0.195), suggesting the relationship does not appear to be associated with chronic liver disease.

Similarly, chronic liver disease did not vary significantly across different nationalities. Participants from the Eastern Mediterranean Region formed the largest subgroup among both cases (55.7%) and controls (60.2%), followed by individuals from the South-East Asia Region and other regions, including the Western Pacific Region, African Region, Region of the Americas, and European Region. The distribution across nationality categories was comparable between cases and controls, and no statistically significant difference was observed (p = 0.659).

The level of Body Mass Index differed significantly between cases and controls. Abnormal BMI, including underweight, overweight, and obese classifications, was more prevalent among cases (84.6%) than controls (73.3%). In contrast, fewer populations without chronic liver disease were classified as having a normal body mass index (26.7%) compared to the number of patients with chronic liver disease (15.4%). Therefore, the association between abnormal body mass index and chronic liver disease was statistically significant (p = 0.008).

Alcohol consumption showed a strong and statistically significant association with chronic liver disease (p < 0.001). Never alcohol users constituted 75.8% of cases compared with 97.7% of controls. In contrast, former alcohol use was more common among cases (10.1%) than controls (2.0%), and current alcohol use was markedly overrepresented among cases (14.1%) compared with controls (0.3%). Details are given in Table 1.

Binary logistic regression analysis was used in order to determine independent factors that were associated with chronic liver disease (Table 2). In crude analysis, gender (male), abnormal body mass index, and alcohol consumption were significantly associated with chronic liver disease; however, there is no statistically significant association between age group, marital status, or nationality and the presence of chronic liver disease.

Male gender remained independently associated with chronic liver disease (adjusted OR = 3.03; 95% CI: 1.88–4.90;

$p < 0.001$), indicating approximately threefold higher odds of disease among males compared with females.

Abnormal BMI was also independently associated with chronic liver disease (adjusted OR = 2.33; 95% CI: 1.30–4.20; $p = 0.005$), suggesting more than twofold increased odds of disease among individuals with abnormal BMI relative to those with normal BMI.

Alcohol consumption emerged as the strongest independent predictor. Compared with never drinkers, former alcohol users had significantly higher odds of chronic liver disease (adjusted OR = 5.62; 95% CI: 2.07–15.26; $p < 0.01$), while current alcohol users demonstrated markedly elevated odds (adjusted OR = 53.35; 95% CI: 6.87–414.15; $p < 0.001$). Although the confidence interval for current alcohol use was wide, the association remained statistically significant.

In contrast, associations for age groups that were shown in univariate analyses became attenuated after multivariable adjustment and did not independently predict chronic liver disease. Similarly, marital status and nationality did not have independent associations with chronic liver disease when analyzed with the multivariate model, as indicated by confidence intervals crossing unity and non-significant p-values.

In summary, the analysis identified that male gender, abnormal BMI, and alcohol consumption are significant independent predictors of chronic liver disease in this tertiary care setting. independent associations with chronic liver disease when analyzed with the multivariate model, as indicated by confidence intervals crossing unity and non-significant p-values.

DISCUSSION

CLD is a significant health challenge that continues to garner considerable attention, especially in the middle-aged and elderly, as a result of the established association with lifestyle, comorbidity, and socio-economic factors. The current study evaluated the socio-demographic risk factors in CLD, focusing on patients within the socio-economic landscape of a tertiary healthcare center in Ajman, UAE.

Age has long been identified as a major risk factor for various chronic health complications. This includes chronic liver diseases. In the present study, patients between the ages of 40 and 60 showed a larger proportion of CLD. Patients less than 40 years of age showed a lower proportion of CLD. Although age was statistically significant in predicting CLD in the bivariate analysis, it was not significant in the logistic regression analysis. This implies that it could be lifestyle habits and comorbid conditions that are more associated with the occurrence of CLD rather than age. Global epidemiological data indicate that CLD incidence increases with age, peaking in middle-aged and elderly populations, although the pattern varies depending on the etiology [19–21]. Aging decreases hepatic regenerative capacity and alters drug metabolism, while increasing the burden of comorbid conditions like diabetes and hypertension. All these factors enhance the vulnerability to liver injury [22,23]. However, increasing metabolic disorders in younger adults have shifted some of the risk to middle-aged individuals [24,25]. It is vital to have early lifestyle modifications and metabolic control in this middle-aged group to prevent progression to advanced liver disease later in life [26]. In agreement with this, the present study suggests that prevention strategies must focus on early detection and management of risk factors throughout the course of adult life, especially in middle-aged individuals.

Gender differences in the levels of CLD burden and progression are well documented across the world. In the present study, it was found that men were more at risk of CLD than women, which is in agreement with the data obtained from the rest of the world. This association was maintained even after controlling for other variables, suggesting the strong influence of male gender in the risk of CLD. Across the world, in the context of CLD burden, the male population has more instances of CLD in terms of incidence, prevalence, and mortality due to diverse reasons, including viral infections, alcohol use, and NAFLD [27–29].

Biologically, estrogen exerts hepatoprotective action by influencing inflammation and fibrosis, while androgen-related mechanisms could potentially exacerbate liver damage in males [29]. Behavior-wise, males are more inclined to alcohol use, smoking, and an unhealthy diet, coupled with a reluctance to seek medical care promptly, which often results in a late-stage diagnosis in males [30]. Indeed, retrospective cohort studies showed faster fibrosis progression in males compared to females [30]. The values of these androgen and estrogen variations in the pathogenesis of liver fibrosis warrant active focus in prevention and screening, especially behavior-wise in males.

High BMI levels were strongly identified as independent determinants for CLD. Abnormal BMI was identified as associated with a high probability of CLD, as predicted in crude and adjusted models, which strongly supports studies of the association between obesity and NAFLD and the progression of CLD to hepatocellular carcinoma [31, 32, 39].

Cross-sectional studies using transient elastography support the findings, showing clearly that generalized as well as abdominal obesity play a major role in increasing the risk of NAFLD [32]. Longitudinal data have also shown that BMI patterns over a lifetime predict NAFLD, independent of age and metabolic status [31]. Even data from the Middle East show a high prevalence of obesity and metabolic syndrome, mirroring the rising burden of NAFLD [11, 33, 34, 36].

These findings also highlight the significance of emphasizing the prevention of obesity and metabolic risk for

the effective management of CLD. Considerable attention should be given to the screening of high BMI and metabolic disorders in clinical practices, especially for high-risk groups. Again, community-based interventions for healthy lifestyle habits and obesity prevention are considered significant for minimizing the increasing incidence of chronic liver diseases.

In this study, marital status and nationality were not independently associated with CLD after multivariable adjustment. While married participants were a larger group of cases and controls, it did not predict CLD in logistic regression. Similarly, participants from different WHO regions did not exhibit clinically significant risk for CLD differences, and thus, national or regional origin is not a determinant when other risk factors are accounted for. These findings are in line with hospital-based studies, which indicate that demographic factors like nationality or marital status have little independent impact on NAFLD or other CLD forms [37]. Though ethnicity or regional origin may influence the outcome of CLD due to genetic or dietary and lifestyle factors, the impact is most often mediated through metabolic risk rather than nationality per se [38]. The findings stress the primary role of metabolic and behavioral factors over merely nominal demographic categories, although cultural and social determinants should not be disregarded at the level of public health planning.

In our study, alcohol consumption demonstrated a strong and independent association with chronic liver disease, with both former and current use linked to higher odds of disease compared with abstainers. This observation is aligning with extensive epidemiological evidence demonstrating that alcohol is a major risk factor for chronic liver pathology; for instance, a systematic review and meta-analysis reported that heavier alcohol intake is associated with a progressively increased risk of liver cirrhosis and other chronic liver outcomes [39], additionally large prospective study from the China Kadoorie Biobank similarly found positive dose-response associations between regular alcohol consumption and various chronic liver diseases, including alcoholic liver disease and cirrhosis [40].

These finding is in agreement with epidemiological evidence showing that there is a well-documented dose-response relationship between alcohol exposure and liver disease, such that greater intake and longer duration increase the risk of fibrosis, cirrhosis, and related complications [41].

The markedly elevated adjusted odds ratio observed among current users should therefore be interpreted with caution, as the very wide confidence intervals likely reflect sparse data and limited statistical precision. The association among former users may partly represent reverse causation ("sick quitter" effect) [42]. While alcohol consumption is generally lower in Gulf settings, alcohol-related liver injury remains clinically relevant [43]. Emerging evidence further suggests that alcohol and elevated BMI may act synergistically, indicating a potentially high-risk combined phenotype that warrants longitudinal evaluation [44].

Together, these studies conclude that sustained alcohol exposure significantly contributes to the development of chronic liver disease, supporting the pattern observed in our analysis that alcohol use is a critical determinant of liver health.

Several limitations need to be mentioned with respect to this study. In this case-control study, it was conducted in one center and in a hospital-based setting, which may reduce generalizability. Lifestyle variables include alcohol intake assessed by self-report and could be subject to recall or social desirability bias. Although the multivariable regression is adjusted for many covariates, residual confounding by unmeasured factors, which might include but are not limited to genetics, environmental exposure, or comorbidities, cannot be excluded. Reliance on hospital records might also underestimate undiagnosed or asymptomatic CLD cases. Despite these limitations, the present study provides important baseline evidence of both modifiable and non-modifiable predictors of CLD in the UAE, informing future longitudinal studies and preventive strategies.

CONCLUSIONS

This study identifies critical preventable and inherent determinants of CLD within the adultpopulation of Ajman, UAE. The findings reveal that the male gender, middle age (40-60 years), an abnormal BMI and alcohol consumption are significantly associated with a higherrisk of developing CLD.

For the subjects studied here, alcohol was the strongest predictor of chronic liver disease. Independent associations between current and former alcohol use and developing chronicliver disease were statistically significant, but the effect of current alcohol use was strongerthan that of former alcohol use. Elevated BMI had a significant independent association withan increased risk for chronic liver disease, which suggests that there are metaboliccontributions to the disease. Even after controlling for both alcohol use and BMI, being male remained an independent predictor for having a chronic liver disease; thus, demographic factors may outlive behaviors.

The results of this study are compatible with the regional epidemiological transition ofmetabolic dysfunction- associated steatosis, which is developing into the primary cause ofchronic liver disease (CLD) and highlights the need for early identification of individuals atrisk. While age and gender are intrinsic characteristics

that cannot be changed, supported bytheir inherent biological characteristics, they are still valid and useful indicators to informtargeted screening and surveillance efforts. Alternatively, abnormal body mass index (BMI) and alcohol consumption is a significant and preventable risk factor, which then creates anopportunity for preventive intervention through lifestyle changes, weight management, andthe control of metabolic risk.

Therefore, this study supports the development of a preventive approach to supporting healthy aging with care by emphasizing the promotion of metabolic health in addition to theimplementation of a demographic risk-based approach to risk profiling. The concepts ofearly screening and patient education should be utilized both in public health and clinicalpractice. Community-based obesity prevention and optimizing habits among middle-aged.

Men should also be a priority area, as they are at higher risk than women. By addressing modifiable as well as non-modifiable determinants, substantial decreases in the burden of chronic liver disease can be accomplished, resulting in improved long-term outcomes for both the liver and the overall health of the population in the region.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Understanding constipation among the elderly: Determinants and relevance to healthy ageing in a tertiary care setting in Ajman, UAE

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ABSTRACT

Aim: The primary aim of this study was to identify and analyze the socio-demographic determinants of constipation among elderly individuals (≥60 years) attending a tertiary care hospital in Ajman, United Arab Emirates, in order to address an important gap in regional geriatric gastrointestinal research.

Materials and Methods: A record-based case–control study was conducted among patients aged 60 years and above attending a tertiary care hospital. The cases were elderly patients with documented constipation, while the controls were elderly patients without constipation, selected in a 1:2 ratio. Data were extracted using a structured and validated proforma. Descriptive statistics, chi-square tests, and binary logistic regression were performed to examine associations. Crude and adjusted odds ratios with 95% confidence intervals were calculated, and a p-value ≤0.05 was considered statistically significant.

Results: Constipation was more frequently observed among males and in specific age groups. Participants aged 60–69 years constituted the largest proportion of cases (78.8%), while those aged 70–79 years were more commonly represented among controls. A significant association was observed between age group and constipation ($p<0.01$). Male participants accounted for 71.3% of cases compared to 37.4% of controls ($p<0.01$). In adjusted analysis, male gender remained a strong predictor of constipation (AOR: 4.41; 95% CI: 2.40–8.11).

Conclusions: Male gender and age group were key socio-demographic determinants of constipation among elderly patients in this tertiary care setting. These findings highlight the need for targeted screening, early recognition, and preventive strategies for constipation as part of routine geriatric care.

KEY WORDS: socio-demographic factors, case–control studies, logistic regression, gastrointestinal motility, preventive geriatrics, quality of life

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INTRODUCTION

Constipation is one of the most common gastrointestinal disorders affecting the elderly population globally. It is characterized by lumpy or hard stools, excessive straining, difficulty in defecation, bloating, abdominal pain, and decreased frequency of defecation [1,2]. In general, constipation can be defined as a lack of satisfactory defecation, which incorporates various symptoms and may be either chronic or sporadic. Constipation has a major negative impact on the quality of life of individuals, affecting both their physical and emotional well-being. It also has a burden on the healthcare system due to increased costs, increased hospital visits, specialty referrals, and hospital admissions [3]. Constipation has substantially become more common with advancing age and is now recognized as an important geriatric problem. In the elderly, it can lead to several complications: anal pain, anal hemorrhoids, rectal bleeding, fecal impaction, bowel perforation, fecal incontinence, rectal prolapse, volvulus, and excessive perineal descent [1, 4]. Therefore, we can determine that constipation is a major global health concern.

Globally, constipation is a very prevalent gastrointestinal condition, specifically among the older population. This is clearly evident in a recent systematic review and meta-analysis of 36 studies. These studies included 58,405 older adults aged 60-93 years. The overall prevalence of constipation in older adults was found to be 18.9% (95% confidence interval [95% CI]: 14.7-23.9%) [5]. Similarly, in another study conducted in China, it was shown that constipation among adults aged ≥ 65 years had a prevalence of 14.8% (95% CI 14.6–15.0), with women (16.0%) having higher rates than men (14.1%) [6]. Furthermore, a community- and hospital-based study conducted in Spain of functional constipation in those over 70 years reported a prevalence of 26.8%, again significantly higher in women (32.4%) than men (21.8%) ($p = 0.019$) [7]. Another striking finding comes from a cross-sectional study conducted in Iran among 200 older adults, which showed that, according to the Rome III criteria, the prevalence of functional constipation was 45 percent, a very significant number among the older adult population [8]. Therefore, with the aid of these studies from different parts of the world, it is evident that constipation is a common and significant problem, particularly among the elderly, affecting their quality of life.

The recent epidemiological literature in the MENA region demonstrates that constipation is both common and under-recognised, with wide variability related to diagnostic criteria, comorbidities, dietary patterns, and healthcare-seeking behaviours. A 2023 prospective cohort study from Oman demonstrated that more than 40% of medically hospitalized older adults suffer from constipation, emphasizing the role of polypharmacy, immobility, and acute illness [2]. Community-based studies from Saudi Arabia also represent an increasing burden; a 2023 study in the Western Region recognized poor symptom recognition and limited complication awareness, which may indicate that prevalence is underestimated [9].

Emerging 2024 evidence reinforces the magnitude of constipation in older and high-risk groups. In Qassim, a study among diabetic adults, most of whom were elderly, reported a prevalence of 30.4%, with age, disease duration, coronary disease, and insulin therapy identified as significant contributors10. Another 2024 population-level study from Al-Ahsa documented a 40.7% prevalence using Rome III criteria, while physical inactivity, chronic disease, female sex, and medication use served as major associated factors [11]. These findings mirror global trends linking constipation in older adults to multimorbidity, reduced mobility, low-fibre diets, and use of medications such as opioids, anticholinergics, and calcium-channel blockers.

Taken together, the accumulating evidence from Oman and Saudi Arabia, and other MENA settings, suggests that constipation represents an important and emerging health issue among older individuals. Its consistently high prevalence, in particular among those with chronic illnesses, calls for analytic studies to determine region-specific risk factors and appropriate targeted prevention, early recognition, and geriatric care strategies [2, 5, 9–11].

From a clinical perspective, constipation is a highly significant gastroenterological condition in the UAE; however, there is a marked lack of data regarding its associated factors within the UAE population. This broader trend of limited epidemiological insight across a spectrum of gastrointestinal diseases was highlighted by a decade-long histopathological and epidemiological study conducted in tertiary hospitals in the UAE [12]. Within this same study, functional gastrointestinal disorders, such as chronic constipation, were excluded because functional conditions do not require histopathological confirmation [12]. Despite this exclusion, the study reported a substantial proportion of the population affected by lower gastrointestinal conditions such as hemorrhoids and anal fissures - disorders that commonly occur in association with constipation [12]. However, to date, there are no recent studies that specifically focus on constipation as a primary topic of investigation in the UAE.

Some studies have reported the prevalence of related disorders, such as irritable bowel syndrome (IBS), at 17.3% (n = 471), [13] but these findings do not provide specific data on constipation-predominant IBS, thereby highlighting a significant gap in the existing literature. Overall, constipation remains one of the most understudied gastrointestinal conditions in the UAE, with a notable lack of research examining its determinants. This research gap is also evident among the elderly population. Only a single study conducted in 2015 examined pelvic floor muscle weakness secondary to chronic constipation among elderly Emirati women [14]. Apart from this, no studies have specifically focused on constipation in elderly populations in the UAE, despite it being one of the most prevalent conditions in older adults. This underscores the need for targeted research exploring constipation as an independent condition, particularly among the elderly, to support the development of evidence-based care and improve clinical outcomes for this vulnerable population.

Constipation is a common and clinically important problem among elderly individuals, yet data on its determinants in the United Arab Emirates are limited. Existing regional evidence is limited and largely focuses on other gastrointestinal conditions, leaving a significant

gap in understanding constipation as a standalone issue in older adults. Therefore, this study was conducted to identify sociodemographic determinants of constipation among elderly patients attending a tertiary care hospital in Ajman, UAE, to support improved detection and targeted care. The study outcomes may enable care providers to formulate and implement targeted strategies for early identification of vulnerable populations and to advocate for preventive measures before the onset of symptoms, contributing to healthy aging.

AIM

The primary aim of this study was to examine and characterize the socio-demographic factors associated with constipation among elderly individuals aged 60 years and above attending a tertiary care hospital in Ajman, United Arab Emirates. By analyzing variations across age groups, gender, and other key demographic characteristics, this study seeks to address the existing gap in region-specific evidence on constipation in older adults and to contribute data that may support improved detection, risk stratification, and preventive geriatric care within the UAE healthcare setting.

MATERIALS AND METHODS

STUDY DESIGN, STUDY POPULATION, SAMPLE SIZE, AND SAMPLING

A record-based case–control study was conducted to examine determinants of constipation among elderly individuals attending a tertiary care hospital in Ajman, United Arab Emirates. The study population consisted of individuals aged 60 years and above whose medical records were available at a Tertiary care centre, Ajman, UAE. Cases were defined as elderly patients with confirmed documented cases of constipation, while controls were elderly patients without constipation. Records with incomplete data were excluded.

Based on a reported prevalence of constipation of 18.9% among older adults and evidence suggesting higher odds of constipation among advanced age groups, the minimum required sample size was calculated as 80 cases with a case-to-control ratio of 1:2, resulting in 161 controls. A convenience sampling method was adopted to retrieve the records of people with constipation and without constipation.

STUDY PROFORMA

A proforma was developed in accordance with the objectives of the study. It included information on constipation status; socio-demographic characteristics such as age, gender, nationality, and marital status; and anthropometric measurements, including height and weight, which were used to calculate body mass index (BMI). The proforma was refined through a pilot study conducted using five patient records with a diagnosis of constipation.

DATA COLLECTION PROCEDURE

Following approval from the Institutional Review Board of the Medical University, permission was obtained from the hospital administration to access medical records. Eligible patient charts were reviewed, and relevant data were extracted using a structured proforma. In this study, patients with a confirmed diagnosis of constipation were classified as cases, while patients without constipation and presenting with other conditions were classified as controls. No personal identifiers were collected, and all data were handled in strict accordance with the institution's research confidentiality and data protection policies.

DATA ANALYSIS

Data was entered into Microsoft Excel and subsequently analyzed using SPSS version 30. Descriptive statistics were computed and presented as frequencies and percentages. The association between constipation and socio-demographic variables was assessed using the chi-square test. Binary logistic regression analysis was performed to estimate crude and adjusted odds ratios with 95% confidence intervals. A p-value ≤0.05 was considered statistically significant

ETHICS STATEMENT

The study protocol was reviewed and approved by the Institutional Review Board of the Medical University (IRB Ref. no. IRB-COM-STD-104-Dec-2025). Approval obtained from the Hospital administration before retrieving the data. The study involved no invasive procedures or interventions and posed no risk. Confidentiality was maintained through secure data storage, and no personally identifying information, including email addresses, was collected to ensure anonymity.

RESULTS

A total of 241 adults participated in the study, with 80 classified as cases (diagnosed with constipation) and 161 as controls (without constipation). The sociodemographic predictors were analyzed. Socio-demographic characteristics play a fundamental role in shaping health patterns among older adults.

Table 1. Distribution of sociodemographic factors between patients with and without constipation

Variables	Group	Controls		Cases		p-value
		[N]	[%]	[N]	[%]	
Age Group	60-69	101	59.1	63	78.8	<0.01
	70 -79	56	32.7	9	11.3	
	>= 80	14	8.2	8	10.0	
Gender	Male	64	37.4	57	71.3	<0.01
	Female	107	62.6	23	28.7	
Marital Status	Single	3	1.8	2	2.5	NS (0.698)
	Married	167	98.2	78	97.5	
Nationality	Eastern Mediterranean Region	115	68.0	59	73.8	NS (0.656)
	South-Asian	33	19.5	13	16.3	
	Others	21	12.4	8	10.0	
BMI	Normal	27	15.9	19	23.8	NS (0.134)
	Abnormal	143	84.1	61	76.3	

Source: Own materials

Table 2. Logistic regression for sociodemographic predictors of constipation

Variables	Group	Constipation					
		Crude			Adjusted		
		OR	CI	p-value	OR	CI	p-value
Age Group	60-69	1	--	--	1	--	--
	70 -79	0.26	0.12 - 0.56	<0.001	0.25	0.11 – 0.55	0.001
	>= 80	0.92	0.36 - 2.31	NS (0.85)	1.06	0.40 - 2.83	NS (0.91)
Gender	Male	4.14	2.33 – 7.36	<0.001	4.30	2.38 - 7.78	<0.001
	Female	1	--	--	1	--	--

Source: Own materials

Table 1 presents the distribution of these socio-demographic characteristics between elderly patients with constipation (cases) and those without constipation (controls). Clear differences were observed in relation to age distribution and gender, highlighting important demographic patterns associated with constipation in this population.

Participants aged 60–69 years constituted the largest age group overall; however, they were disproportionately represented among cases compared with controls (78.8% *vs.* 59.1%). Conversely, individuals aged 70–79 years were more commonly observed in the control group (32.7%) than among cases (11.3%). Those aged ≥80 years formed a smaller but notable proportion in both groups, accounting for 10.0% of cases and 8.2% of controls. Collectively, these findings demonstrate a statistically significant variation in constipation prevalence across age categories ($p < 0.01$), suggesting that age-related patterns of risk exist within the elderly population.

A striking gender-based difference was identified. It revealed a pronounced male predominance among cases. Males represented 71.3% of constipation cases compared with 37.4% of controls, whereas females accounted for 28.7% of cases and 62.6% of controls ($p < 0.01$), therefore indicating a strong association between male gender and constipation.

Marital status did not differ significantly between the two groups. Most participants in both cases and controls were married (97.5% and 98.2%, respectively), with only a very small proportion being single. Similarly, nationality showed no statistically significant association with constipation. Participants from the Eastern Mediterranean Region constituted the largest subgroup in both cases (73.8%) and controls (68.0%), followed by South Asians and individuals from other regions.

With respect to nutritional status, abnormal BMI levels (overweight, obese, and underweight) were highly prevalent in both cases (76.3%) and controls (84.1%). Although a slightly higher proportion of cases had normal BMI levels compared with controls (23.8% vs. 15.9%), the overall distribution of BMI levels did not differ significantly between groups. This indicates that excess body weight is common among elderly patients, irrespective of constipation status in this population.

In order to identify which socio-demographic factors independently predict constipation after accounting for potential confounding influences, a multivariable logistic regression model was applied.

Table 2 presents the results of this adjusted logistic regression analysis, comparing the crude and adjusted odds ratios for various sociodemographic factors. Among which gender was the most significant determinant of constipation within the study population? In the adjusted model, male participants demonstrated a substantially higher risk, being 4.41 times more likely to have constipation compared to their female counterparts (AOR: 4.41; 95% CI: 2.40–8.11; p = < 0.01)

Additionally, age also played a significant role, particularly within the 70–79 age group, which exhibited a significantly lower risk of constipation compared to the reference group of individuals aged 80 and older (AOR: 0.25; 95% CI: 0.77–0.84; p = 0.02). In contrast, no significant difference in risk was found between the 60–69 age group and the reference group (AOR: 1.17; p = 0.76).

Other socio-demographic variables, including marital status, nationality, and BMI category, did not show statistically significant associations with constipation after adjustment. Married individuals did not differ significantly from single participants, and no meaningful differences were observed across nationality groups. Likewise, abnormal BMI was not significantly associated with constipation in crude (OR = 0.61; 95% CI: 0.31–1.17; p = 0.14) or adjusted models (adjusted OR = 0.58; 95% CI: 0.28–1.26; p = 0.15).

Overall, the adjusted analysis indicates that age group 70-79 years and male gender remain key socio-demographic determinants of constipation among elderly patients in this tertiary care setting.

The adjusted analysis indicates that the 70–79-year age group and male gender remain key socio-demographic determinants of constipation among elderly patients in this tertiary care setting. This association may reflect age-related physiological changes, including reduced gastrointestinal motility, increased comorbidity burden, polypharmacy, and decreased physical activity, which become more pronounced with advancing age. The higher prevalence observed among males may be related to gender-specific differences in lifestyle behaviors, dietary habits, health-seeking patterns, and comorbid conditions such as benign prostatic hyperplasia, which can indirectly influence bowel function. These findings highlight the need to incorporate age- and gender-specific risk stratification into routine geriatric assessments, with a focus on early identification and preventive management of constipation. Such targeted approaches are essential to support healthy aging, preserve functional independence, improve quality of life, and reduce preventable complications among older adults in tertiary care and community settings.

DISCUSSION

Constipation is a common public health condition and a clinically significant condition among older adults, adversely affecting quality of life, functional independence, and healthcare utilization. Identifying the determinants of constipation in the elderly is essential for informing appropriate healthcare planning and healthy aging strategies. Importantly, the findings also emphasize the need to initiate preventive strategies at an earlier age, as many risk factors for constipation, such as physical inactivity, inadequate dietary fiber intake, poor hydration, and long-term medication use, are modifiable and accumulate over the life course. Early adoption of healthy bowel habits and lifestyle interventions may reduce the burden of constipation in later life, support functional independence, and promote healthy aging. This case–control study, conducted in a tertiary care setting in Ajman, UAE, examined the socio-demographic predictors of constipation among elderly patients attending the healthcare facility.

The results underscore the influence of age and gender on constipation while highlighting its multifactorial etiology among older adults in tertiary care settings. Age was found to be associated with constipation, though in a non-linear manner, with individuals aged 60-69 years and those aged 70-79 years presenting with higher and lower odds, respectively, compared to the oldest age group, i.e., individuals aged 80 years or above with constipation. The evidence suggests that the risk among individuals may be influenced by interactions among various biological, behavioral, and healthcare factors with age. According to recent evidence, constipation among older individuals has been found to be influenced by factors such as decreased muscle mass, slow colonic transit, and weakness of the pelvic floor muscles associated with age [15]. According to a population-based cohort study, constipation among older individuals has been associated with sarcopenia, a major aspect associated with biological ageing, pointing towards the role of decreased muscle mass and strength in the onset of constipation [16]. In another study, constipation among older individuals has been associated with sarcopenia and slow gait speed, pointing towards other factors associated with constipation, other than aging, among older individuals [17]. Younger elderly groups may also have a higher exposure to potentially modifiable lifestyle-related risk factors, which include

lower dietary fiber, inadequate water intake leading to dehydration, or lack of exercise, particularly in the past. Older age groups may have a lower exposure to risks related to bowel care, given better surveillance or care systems, and other use of laxatives.

Wang et al. reported an age- and gender-adjusted prevalence of constipation of 14.8%, with higher rates observed among younger elderly individuals, indicating that constipation can occur early within the older adult population in community settings [6]. Moreover, Oztop et al. examined the association between constipation and functional status among community-dwelling older adults, finding that reduced lower-limb mobility and diminished quality of life were significantly associated with constipation, highlighting the impact of functional impairment independent of chronological age [18].

Male gender was a strong independent predictor of constipation. The odds were significantly higher among elderly men than women, which contrasts with many community-based studies reporting a higher prevalence among females [5, 19]. Sex-specific patterns may indeed be different in the case of the healthcare-seeking population, as pointed out by hospital-based studies [2, 20, 21]. In tertiary care facilities, men often present with higher burdens of cardiovascular disease, diabetes, and neurological disorders, commonly associated with secondary constipation [2]. Prescriptions of constipating drugs such as opioids, calcium channel blockers, and anticholinergics are also likely to be given more frequently to men. Cultural or behavioral factors, such as delayed symptom reporting until symptoms worsen, further affect the prevalence among hospitalized men [2]. These data emphasize the need for gender-specific screening, early recognition, and targeted prevention during geriatric management, especially in tertiary healthcare settings where constipation can be overlooked due to other clinical priorities.

Marital status was not significantly associated with clinically diagnosed constipation. Social relationships contribute to health outcomes for older people, including the perception of symptoms and functional health, as reported by Holt-Lunstad et al [22]. However, marital status alone may inadequately capture psychosocial determinants of bowel health. Lee et al. reported differences in constipation perception between married and never-married adults, but the study included a younger community sample, which may not reflect the older population in the hospital context [23].

Statistical insignificance was observed in nationality, although this study comprised people from different backgrounds, including the Eastern Mediterranean Region and South Asia, due to shared clinical exposures, care methods, and clinical management, which might reduce possible ethnic or cultural effects on constipation risks. This observation is also strengthened by recent findings indicating constipation risks vary across different regions, while in clinical settings, risk factors are standardized, leading to reduced effects of nationality on constipation risks [5]. Indeed, all this suggests the need to find out how refined indicators of social support and living arrangements, and cultural health behaviors, may be in relation to constipation risks among older people.

Levels of BMI were not significantly associated with constipation in this study. Recent evidence suggests that bowel function in older age is modulated by body composition factors-sarcopenia and obesity-wherein a sole measure of BMI will not suffice to understand these complex relationships [17,24]. Anthropometric measures of nutritional status alone cannot provide a functional representation of the determinants of constipation; therefore, assessment should not be limited to BMI but also needs to incorporate functional status, diet quality, and muscle mass.

Constipation among the elderly is associated with several adverse outcomes, which include prolonged hospitalization, delirium, and increased utilization of health care [25]. According to studies, structured assessments, routine reviews of medications, and non-pharmacologic approaches, such as dietary changes and physical activity, have the potential to reduce symptom burden and improve quality of life [26]. Recent evidence indicates that supplementation with dietary fiber in chronically constipated elderly subjects improves stool consistency, reduces laxative dependence, and promotes gut microbiota health [27]. On the other hand, according to a recent narrative review, the most common pitfalls of constipation among older adults are improper assessment and identification of underlying conditions and irrational use of medications [28].

The strengths of this study include a clinically diagnosed, hospital-based elderly population and the use of multivariable logistic regression to account for most of the key confounders, which strengthens the validity of the associations observed. However, several limitations should be declared. First, the case–control design precludes causal inference, and the hospital-based sample may limit generalizability to community-dwelling older adults. Second, data were extracted from medical records, which may underreport bowel symptoms, lifestyle factors, over-the-counter medication use, and adherence to prescribed regimens. Third, constipation severity, chronicity, dietary patterns, hydration status, physical activity, and psychosocial determinants such as stress, caregiver support, or living arrangements were not measured and might modify the association

observed [19,29]. Finally, residual confounding due to unmeasured clinical or behavioral factors cannot be entirely ruled out. Future studies should adopt a longitudinal and community-based design, a detailed assessment of lifestyle, functional status, and psychosocial determinants, and consideration of patient-reported outcomes in order to better elucidate the modifiable risk factors for constipation among older adults.

CONCLUSIONS

This study highlights the sociodemographic determinants of constipation among elderly patients attending a tertiary care center in Ajman, UAE. Elderly males were four times more likely to experience constipation than females, and individuals aged 70–79 years had a higher risk compared with those aged 80 and above, suggesting that constipation risk varies across age categories rather than increasing uniformly. These findings emphasize the importance of early preventive strategies, including adequate hydration, dietary fiber intake, physical activity, and careful medication monitoring, to reduce constipation burden and support healthy aging. Public health advocates and clinicians play complementary roles in this effort: advocates implement population-level education, community programs, and policies to promote prevention and early identification, while clinicians provide individualized assessment, management, and lifestyle guidance. Together, these approaches can reduce morbidity, preserve functional independence, and enhance healthy aging among older adults.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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ORIGINAL ARTICLE

CONTENTS

Adult perceptions and awareness of longevity in the elderly: Healthy aging from a public health perspective in Ajman, UAE

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ABSTRACT

Aim: This study aimed to assess adult perceptions and awareness of factors influencing longevity and healthy ageing in the UAE.

Materials and Methods: A cross-sectional study was conducted among 446 adults in the UAE using a self-administered, structured online questionnaire comprised of different domains. Data was analyzed using SPSS version 29. Descriptive statistics summarized perception levels, and Chi-square tests assessed associations between sociodemographic, cultural, lifestyle, and healthcare-related factors and perceptions of longevity. A p-value <0.05 was considered statistically significant.

Results: Most participants demonstrated good overall longevity perception (87.9%). Lifestyle-related factors, including healthy diet (84.5%), regular physical activity (83.6%), stress management (84.8%), non-smoking (79.8%), and limited alcohol consumption (82.7%), were widely recognized as important contributors to longevity. Access to quality healthcare (83.6%) and financial security (79.4%) were also strongly endorsed. Significant associations were observed between longevity perception and nationality (p=0.011), education level (p=0.007), occupation (p=0.002), marital status (p=0.025), and age group (p<0.001). Preventive health beliefs, particularly stress management, healthy diet, and regular medical check-ups (p<0.001), showed strong associations with positive longevity perception.

Conclusions: Adults exhibit high awareness of modifiable lifestyle and healthcare determinants of longevity. Perceptions are shaped primarily by preventive health beliefs rather than cultural or caregiving exposure alone. Strengthening public health education and preventive healthcare initiatives is essential to support national healthy-ageing strategies.

KEY WORDS: public perception, lifestyle factors, preventive health, United Arab Emirates

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INTRODUCTION

Global demographic shifts have created an unprecedented rise in life expectancy, making longevity critical to public health priorities. According to the World Health Organization (WHO), one in six people worldwide will be aged 60 years or older by 2030, a figure expected to nearly double by 2050 [1]. While increased longevity represents the triumph of modern medicine, it necessitates a focus on "health span," the period of life spent in good health [2]. In the Gulf Cooperation Council (GCC) and the UAE, these trends are particularly relevant; despite a currently young population, the region is aging rapidly due to improved healthcare and reduced fertility rates [6, 8].

Longevity is no longer viewed simply as extending lifespan. Research indicates that approximately 25% of individual longevity is genetically determined, while the remaining variation is shaped by behavioral, environmental, and social factors [2]. Scientific literature emphasizes that longevity is determined more by modifiable lifestyle choices than by genetics [3]. Key domains such as a healthy diet, regular exercise, adequate sleep, and social connectedness are critical to maintaining good health [4].

Despite this evidence, a significant "perceptual gap" persists between scientific understanding and public belief. Many adults still associate aging with inevitability or fate rather than with modifiable risk factors [5].

These perceptions are vital because they act as social determinants; adults who perceive aging positively are more likely to engage in preventive behaviors, whereas negative perceptions are linked to poorer health outcomes [9]. Furthermore, the WHO identifies ageism and societal stereotypes as key barriers to healthy aging, as they shape how individuals view their own aging process [1].

In the UAE, perceptions of aging are strongly influenced by cultural expectations and familial proximity. Emirati culture emphasizes family as the central pillar of support, reflecting deep intergenerational obligations and moral duty [7]. However, local evidence suggests that while younger adults hold generally positive views, they may have limited awareness of the physical and financial realities of aging [7]. As the UAE population aged 65 and over is estimated to reach 18% by 2050, bridging the gap between traditional values and evidence-based health practices becomes essential [6, 10].

This study aims to assess the adult perceptions and awareness of the factors affecting longevity and healthy aging in Ajman, UAE. By exploring how individuals conceptualize healthy aging, whether through biological, lifestyle, or familial lenses, policymakers can better design culturally grounded interventions. Aligning public perception with scientific insight is crucial for supporting the UAE's Vision 2031 and ensuring a dignified aging process for the population.

MATERIALS AND METHODS

STUDY DESIGN, STUDY SETTING, AND STUDY POPULATION

This cross-sectional study was conducted in Ajman, UAE, among 446 adults aged 18 years and above. The study targeted members of the general adult population residing in Ajman. Individuals who were below the age of 18 years and those who declined to participate were excluded from the study. Participation was entirely voluntary, and only respondents who provided informed consent were included in the final analysis.

The sample size was calculated using the standard formula for estimating a proportion in a population: $n = Z^2 \times p \times (1 - p) / d^2$, where Z represents the standard normal deviation at a 95% confidence level (1.96), p represents the estimated prevalence, and d represents the margin of error. In the absence of prior local data on adult perceptions regarding longevity, the prevalence was assumed to be 50% to yield the maximum sample size, and the margin of error was set at 5%. The minimum calculated sample size was approximately 384 participants. To compensate for possible non-response and incomplete questionnaires, the sample size was increased by 15-20%, resulting in a final sample of 446 participants. Participants were recruited by a convenience sampling method.

STUDY INSTRUMENT AND VALIDATION

The instrument used in this study was a self-administered questionnaire developed from a comprehensive review of the available literature. The questionnaire was structured into four domains: socio-demographic characteristics (age, gender, nationality, education level, employment/occupation, marital status, and contact or living arrangements with elderly family members); connection to the elderly (frequency of contact with elderly individuals, caregiving history, and type of relationship with elderly persons such as family member, friend, or community member); perceptions on factors affecting longevity (participants' views on the importance of genetics, diet, physical activity, stress management, social relationships, financial stability, and access to healthcare in promoting long life); and personal perceptions and attitudes (beliefs about the most important determinants of healthy aging and their observations of elderly lifestyle patterns within their community). A draft of the questionnaire was submitted to three experts for content validation to ensure relevance, clarity, and comprehensiveness. Content and face validity were established, and revisions were made based on expert feedback. A pilot study among adults who met the inclusion criteria of the target population was conducted to assess clarity, feasibility, and comprehension, after which the questionnaire was finalized.

DATA COLLECTION PROCEDURE

Data was collected using a self-administered questionnaire distributed via Google Forms. An informed consent statement was presented on the first page of the questionnaire, and participants were required to provide consent before proceeding. Participants' privacy, anonymity, and confidentiality were strictly maintained throughout the study. The questionnaire included sections on sociodemographic details, connection and caregiving experience, cultural and social determinants, lifestyle and health determinants, attitudes, awareness, and preventive perspectives, as well as perceptions regarding factors affecting longevity. Perceptions on longevity were assessed using a validated questionnaire consisting of 11 components, which included genetics and family history, quality of diet and nutrition, regular physical activity, stress management and mental well-being, strong social connections and

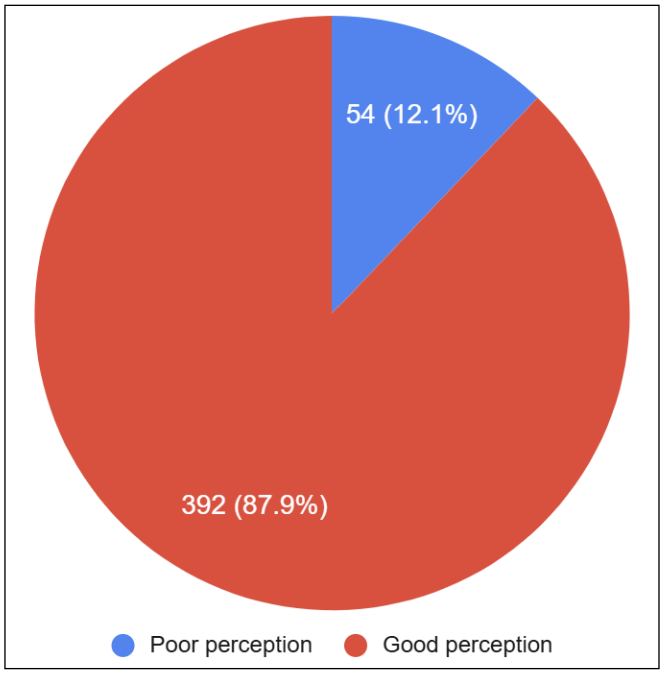

Fig. 1. Overall distribution of longevity perception among adults
Source: Own materials

relationships, access to quality healthcare, financial security and stability, having a sense of purpose in life, not smoking, limiting alcohol consumption, and a general statement-based perception component contributing to the overall score. Each component was measured through structured statements, and the Adult Perception Score was calculated by summing the scores of all 11 components. The total score ranged from 0 to 44, with scores from 0 to 22 categorized as poor perception of longevity and scores of 23 or higher categorized as good perception of longevity.

DATA ANALYSIS

Following data collection, the responses were downloaded into a Microsoft Excel spreadsheet and subsequently transferred to the Statistical Package for Social Sciences (SPSS) version 29 for analysis. Descriptive statistics were used to summarize sociodemographic characteristics and perception scores. The association between categorical variables and perception regarding longevity (poor vs. good perception) was assessed using the Chi-square test. A p-value of <0.05 was considered statistically significant.

ETHICAL CONSIDERATIONS

Approval for the research was obtained from the Institutional Review Board of the medical university in Ajman, United Arab Emirates (Ref. no. IRB-COM-STD-69-Nov-2025). The study was conducted in accordance with the Helsinki Ethical Guidelines. Participation was entirely voluntary, and informed consent was obtained from all participants before their involvement in the study. The confidentiality, privacy, and anonymity of the data were strictly maintained by restricting access to the research team and the Institutional Review Board with proper authorization. No identifying information was shared or included in any reports, presentations, or publications.

RESULTS

SOCIODEMOGRAPHIC CHARACTERISTICS OF THE STUDY PARTICIPANTS

A total of 446 respondents were included in the final analysis. The majority of participants were female (71.1%, n = 317), while males accounted for 28.9% (n = 129). Most respondents were from the South-East Asia Region (72.0%, n = 321), followed by those from other regions (16.1%, n = 72) and the Eastern Mediterranean Region (11.9%, n = 53). With regard to educational attainment, 39.7% (n = 177) held a bachelor's degree, and 24.9% (n = 111) possessed a master's degree. One-fifth of the participants (20.0%, n = 89) had completed secondary or high school education. Only a small proportion reported no formal education (0.7%, n = 3) or primary education (1.3%, n = 6). In terms of occupation, students (34.3%, n = 153) and full-time employees (32.3%, n = 144) represented the largest groups, followed by self-employed individuals (12.6%, n = 56) and part-time employees (10.3%, n = 46). Homemakers and retirees comprised 8.7% (n = 39) and 1.8% (n = 8) of the sample, respectively. Regarding marital status, more than half of the participants were single (50.7%, n = 226), while 41.9% (n = 187) were married. Divorced and widowed respondents accounted for 6.3% (n = 28) and 1.1% (n = 5), respectively.

Based on the overall longevity perception score, most participants were categorized as having good perception (87.9%, n = 392), while 12.1% (n = 54) demonstrated poor perception. This distribution suggests generally high awareness and positive attitudes toward factors influencing longevity and healthy ageing among the study population, as depicted in Figure 1.

Participants' perceptions of factors influencing longevity were assessed across multiple domains as described in Table 1. Overall, respondents demonstrated strong recognition of both biological and lifestyle-related determinants of healthy ageing. Genetics and family history were rated as very or extremely important by 68.2% (n = 304) of participants, while geographical location was similarly rated by 59.8% (n = 267). Life-

Table 1. Perceived importance of longevity-related components

Longevity Components	Groups	Frequency [n]	Percentage [%]
Genetics & family history	Not important	21	4.7
	Slightly important	42	9.4
	Moderately important	79	17.7
	Very important	131	29.4
	Extremely important	173	38.8
Geographical location	Not important	17	3.8
	Slightly important	62	13.9
	Moderately important	100	22.4
	Very important	130	29.1
	Extremely important	137	30.7
Quality of diet & nutrition	Not important	3	0.7
	Slightly important	23	5.2
	Moderately important	43	9.6
	Very important	121	27.1
	Extremely important	256	57.4
Regular physical activity	Not important	6	1.3
	Slightly important	24	5.4
	Moderately important	43	9.6
	Very important	154	34.5
	Extremely important	219	49.1
Stress management & mental well-being	Not important	6	1.3
	Slightly important	26	5.8
	Moderately important	36	8.1
	Very important	132	29.6
	Extremely important	246	55.2
Strong social relationships	Not important	6	1.3
	Slightly important	36	8.1
	Moderately important	63	14.1
	Very important	147	33.0
	Extremely important	194	43.5
Access to quality healthcare	Not important	5	1.1
	Slightly important	17	3.8
	Moderately important	51	11.4
	Very important	130	29.1
	Extremely important	243	54.5
Financial security	Not important	5	1.1
	Slightly important	22	4.9
	Moderately important	65	14.6
	Very important	144	32.3
	Extremely important	210	47.1
Sense of purpose in life	Not important	7	1.6
	Slightly important	26	5.8
	Moderately important	65	14.6
	Very important	136	30.5
	Extremely important	212	47.5
Not smoking	Not important	7	1.6
	Slightly important	26	5.8
	Moderately important	57	12.8
	Very important	105	23.5
	Extremely important	251	56.3
Limiting alcohol consumption	Not important	9	2.0
	Slightly important	23	5.2
	Moderately important	45	10.1
	Very important	116	26.0
	Extremely important	253	56.7

Source: Own materials

Table 2. Association between sociodemographic factors and longevity perception

Sociodemographic characteristics	Groups	Overall Longevity Perception Score				p-value
		Good Perception		Poor Perception		
		No.	[%]	No.	[%]	
Gender	Male	18	14.0	111	86.0	0.446
	Female	36	11.4	281	88.6	
Nationality	SEAR	35	10.9	286	89.1	0.011
	EMR	13	24.5	40	75.5	
	Others	6	8.3	66	91.7	
Level of education	Secondary/High school	21	23.6	68	76.4	0.007
	Bachelor's degree	19	10.7	158	89.3	
	Master's degree	7	6.3	104	93.7	
	Diploma	7	14.3	42	85.7	
	Doctorate or higher	0	0.0	11	100.0	
Occupation	Student	30	19.6	123	80.4	0.002
	Employed (full-time)	8	5.6	136	94.4	
	Employed (part-time)	7	15.2	39	84.8	
	Self-employed	6	10.7	50	89.3	
	Homemaker	1	2.6	38	97.4	
	Retired	2	25.0	6	75.0	
Marital status	Single	36	15.9	190	84.1	0.025
	Married	13	7.0	174	93.0	
	Divorced	5	17.9	23	82.1	
	Widow	0	0.0	5	100.0	
Age group	18–29 years	39	18.9	167	81.1	<0.001
	30–59 years	11	5.1	205	94.9	
	≥60 years	4	16.7	20	83.3	

Source: Own materials

style-related factors were particularly emphasized. Quality of diet and nutrition was considered very or extremely important by 84.5% (n = 377) of respondents, and regular physical activity by 83.6% (n = 373). Stress management and mental well-being were rated as highly important by 84.8% (n = 378).

Social and healthcare-related factors were also strongly endorsed. Strong social relationships were perceived as highly important by 76.5% (n = 341) of participants, while access to quality healthcare was rated as very or extremely important by 83.6% (n = 373). Financial security was similarly valued, with 79.4% (n = 354) rating it as highly important. A sense of purpose in life was considered very or extremely important by 78.0% (n = 348). Health-promoting behaviors were also widely recognized, as 79.8% (n = 356) and 82.7% (n = 369) of respondents rated not smoking and limiting alcohol consumption, respectively, as highly important. These findings indicate a comprehensive understanding among participants of the multifactorial nature of longevity.

Associations between sociodemographic variables and longevity perception were examined using chi-square tests, provided in Table 1. Gender was not significantly associated with perception grouping (p = 0.446). Both male and female participants exhibited comparable levels of good perception. In contrast, nationality was significantly associated with longevity perception (p = 0.011). Participants from the Eastern Mediterranean Region exhibited a higher proportion of poor perception (24.5%) compared with those from the South-East Asia Region (10.9%) and other regions (8.3%).

Educational level showed a significant association with longevity perception (p = 0.007). Respondents with secondary or high school education demonstrated the highest proportion of poor perception (23.6%), whereas those with higher academic qualifications, particularly master's and doctoral degrees, exhibited more favorable perception. Occupational status was also significantly related to perception grouping (p = 0.002). Students and retired participants showed rel-

Table 3. Influence of elderly exposure, cultural, lifestyle, and healthcare factors on longevity perception

Factors	Categories	Groups	Overall Longevity Perception Score				p-value
			Good Perception		Poor Perception		
			No	%	No	%	
Elderly exposure	Presence of elderly family members (≥65 years)	Yes	40	11.0	325	89.0	0.114
		No	14	17.3	67	82.7	
	Relationship to elderly family member	First-degree relative	29	9.4	278	90.6	0.064
		Second-degree relative	10	20.4	39	79.6	
		Third-degree relative	1	11.1	8	88.9	
	Frequency of contact with an elderly person	Daily	14	7.2	180	92.8	0.009
		Several times/week	17	23.3	56	76.7	
		Once/week	7	11.1	56	88.9	
		Few times/month	11	15.1	62	84.9	
		Rarely/Never	5	11.6	38	88.4	
Caregiving experience	Primary caregiver experience	Yes, currently	16	8.8	166	91.2	0.059
		Yes, in the past	21	17.9	96	82.1	
		No	17	11.6	130	88.4	
Cultural beliefs	Cultural beliefs influence longevity	Yes	45	12.7	308	87.3	0.419
		No	9	9.7	84	90.3	
	Respecting elders improves emotional well-being	Yes	45	11.0	365	89.0	0.013
		No	9	25.0	27	75.0	
Lifestyle–Healthcare Factors	Stress management contributes to longevity	Yes	45	10.6	378	89.4	<0.001
		No	9	39.1	14	60.9	
	Access to affordable healthcare promotes healthy ageing	Yes	45	10.8	373	89.2	0.001
		No	9	32.1	19	67.9	
	Healthy eating supports healthy ageing	Yes	44	10.3	383	89.7	<0.001
		No	10	52.6	9	47.4	
	Regular medical check-ups support healthy ageing	Yes	40	9.6	376	90.4	<0.001
		No	14	46.7	16	53.3	

Source: Own materials

atively higher proportions of poor perception (19.6% and 25.0%, respectively), while full-time employees demonstrated the lowest proportion (5.6%).

Marital status was significantly associated with longevity perception (p = 0.025). Single and divorced participants reported higher levels of poor perception compared with married respondents. Age group demonstrated a strong association with longevity perception (p < 0.001). Participants aged 18–29 years exhibited the highest proportion of poor perception (18.9%), whereas those aged 30–59 years showed the most favorable perception profile, with 94.9% classified as having good perception.

The relationship between exposure to elderly individuals, cultural beliefs, lifestyle practices, and healthcare-related factors and longevity perception was further examined. The presence of elderly family members was not significantly associated with perception grouping (p = 0.114), and no statistically significant association was observed for the degree of relationship to elderly individuals (p = 0.064). Similarly, primary caregiver experience was not significantly related to longevity perception (p = 0.059). Although the frequency of contact with elderly individuals demonstrated a statistically significant association (p = 0.009), with daily contact associated with lower proportions of poor perception, this finding was interpreted cautiously due to sparse cell counts across multiple categories, which limited the robustness of the analysis.

Cultural beliefs influencing longevity were not significantly associated with perception grouping (p = 0.419). While respect for elders was significantly asso-

ciated with perception of longevity ($p = 0.013$), more than 25% of the contingency table cells had small, expected counts, resulting in violations of chi-square test assumptions. Consequently, this association was considered statistically unreliable. In contrast, lifestyle and healthcare-related beliefs demonstrated strong statistical associations with longevity perception. Belief in the role of stress management in promoting longevity was significantly associated with good perception ($p < 0.001$). Likewise, participants who perceived access to affordable healthcare as supportive of healthy ageing were significantly more likely to demonstrate a favorable perception ($p = 0.001$). Healthy eating and regular medical check-ups were also strongly associated with positive longevity perception (both $p < 0.001$).

Despite these statistically significant findings, interpretation was approached with caution. The "No" response categories for several lifestyle and healthcare variables contained very small subgroup sizes, resulting in violations of chi-square assumptions. As a result, although these factors reached statistical significance, they could not be regarded as definitive predictors of longevity perception. Overall, while several elderly exposures, cultural, lifestyle, and healthcare-related factors appeared to be associated with longevity perception, none simultaneously satisfied both statistical significance and adequate cell distribution criteria, underscoring the need for cautious interpretation and further investigation using larger and more balanced samples.

DISCUSSION

Adult perceptions and awareness of longevity and healthy ageing have gained increasing attention over the past decade, with contemporary scientific literature conceptualizing longevity as a multidimensional outcome shaped by biological resilience, behavioral patterns, psychosocial factors, and healthcare environments rather than an inevitable biological decline [11].

In the present study conducted among 446 adults in the UAE, exposure to elderly individuals showed limited influence on perceptions of longevity, as the presence of elderly family members ($p = 0.114$) and the degree of relationship to elderly individuals ($p = 0.064$) were not significantly associated with perception grouping. These findings align with cross-cultural evidence demonstrating that perceptions of ageing are shaped more by societal values and the quality of intergenerational engagement than by household proximity alone (12). Although the frequency of contact with elderly individuals demonstrated a statistically significant association with perception of longevity ($p = 0.009$), this finding was interpreted cautiously due to sparse subgroup sizes, suggesting that contact frequency alone may be insufficient to produce stable shifts in ageing perceptions. This interpretation is consistent with behavioural and psychosocial literature emphasising that attitudes toward ageing are influenced by broader psychological and social contexts rather than contact alone [13].

Furthermore, primary caregiver experience was not significantly associated with perceptions of longevity ($p = 0.059$) in the present study, despite professional guidance highlighting that caregiving roles may enhance ageing awareness when embedded within structured psychological and healthcare frameworks (14). Notably, cultural beliefs regarding longevity did not demonstrate a statistically significant association with perception grouping ($p = 0.419$); however, participants who believed that respecting elders improves emotional well-being were significantly more likely to report favourable perceptions of longevity ($p = 0.013$), although this association was limited by small cell counts and therefore interpreted cautiously. These findings partially align with literature emphasising emotional well-being, respect, and social connectedness as contributors to healthy ageing, while also illustrating the difficulty of quantitatively capturing cultural constructs [15, 16]. In contrast, strong and statistically significant associations were observed between perceptions of longevity and key lifestyle and healthcare-related beliefs, including stress management, access to affordable healthcare, healthy eating, and regular medical check-ups, all demonstrating p-values ≤ 0.001. Participants endorsing these factors showed substantially higher proportions of good perception, reflecting global public-health frameworks that prioritise preventive healthcare and lifestyle modification as core components of healthy ageing [17]. These findings are consistent with regional strategies such as the Gulf Region Longevity Initiative, which emphasise healthcare accessibility, prevention, and system-level planning to extend healthspan alongside lifespan [18].

Contemporary public discourse further reinforces the view of longevity as influenced by behaviour, healthcare engagement, and quality of life rather than genetic determinism alone [19]. Evidence from lifespan neuroscience supports this perspective, demonstrating that brain health and cognitive resilience are strongly influenced by cumulative lifestyle exposures, stress regulation, and healthcare utilisation across adulthood [20]. Moreover, studies examining social determinants of cognitive health consistently report that access to healthcare and health-promoting behaviours are key predictors of favourable ageing outcomes [21, 22]. UAE-specific research has documented evolving public

perceptions of ageing and aged care, highlighting a gradual shift from reliance on traditional caregiving models toward greater acceptance of formal healthcare systems [23, 24], consistent with the present study's finding that caregiver experience alone did not significantly influence longevity perception. Evidence-based cognitive health guidance further emphasises the importance of lifelong engagement in preventive behaviours [25], while psychological research indicates that individuals with positive perceptions of ageing demonstrate better cognitive performance and mental wellbeing [26].

At a regional level, demographic and policy analyses highlight the rapid ageing of GCC populations and the growing importance of healthcare system preparedness [27], reinforcing the public health relevance of participants' strong emphasis on healthcare access. Recent public-health scholarship integrates these dimensions into a comprehensive healthy-ageing framework that situates individual beliefs within broader healthcare and policy environments [28]. Comparative studies across GCC countries further demonstrate that healthcare infrastructure and preventive service utilisation are critical determinants of longevity outcomes [29]. Finally, national strategies implemented by the UAE Ministry of Health and Prevention prioritise preventive care and healthy-ageing promotion [30], and the alignment between these policies and the perceptions identified in the present study suggests convergence between public attitudes and national public health priorities. Overall, by explicitly reporting numerical findings and comparing them with international, regional, and national evidence, this study demonstrates that adult perceptions of longevity in the UAE are more strongly shaped by lifestyle and healthcare beliefs than by exposure or cultural factors alone, while also highlighting the need for cautious interpretation due to statistical limitations.

CONCLUSIONS

In conclusion, this study explored adult perceptions regarding the determinants of longevity among the elderly population. According to the research findings, it highlights that most adults recognize healthy lifestyle behaviors as essential factors in promoting longer life, such as balanced nutrition, regular physical activity, and strong social connections. Participants also emphasized the importance of early prevention, regular medical check-ups, stress management, and maintaining an active and meaningful daily routine. These perceptions reflect an increasing awareness of the role that modifiable risk factors play in healthy aging. The study further suggests that education level, personal experiences with older family members, and exposure to health information may influence how adults understand aging. Although genetics is acknowledged as an important factor, respondents generally believe that lifestyle choices significantly shape health outcomes in later life. Overall, the results underline the need for community-based health promotion programs that encourage preventive behaviors from early adulthood. By strengthening public awareness and providing accessible resources, healthcare systems can better support healthy aging. Promoting informed perceptions today may contribute to improved longevity in future generations.

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REVIEW ARTICLE

CONTENTS

Lifestyle, diet, and physical activity in the prevention and rehabilitation of chronic diseases: A review

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ABSTRACT

Aim: The aim of this review article is to conduct a thorough analysis of scientific publications on the importance of lifestyle, diet, and physical activity in the prevention and rehabilitation of people with chronic diseases.

Materials and Methods: The review article takes into account obesity, type 2 diabetes, and cardiovascular disease due to the high prevalence of these chronic diseases on a global scale. The study is based on a thorough analysis of publications containing up-to-date information on healthy behaviors in people struggling with chronic diseases. The results clearly indicate the positive aspects of leading a healthy lifestyle. It is worth noting that regular exercise, a balanced and nutritious diet, health education, and psychological support have a huge impact on the health of people with chronic diseases. The article also emphasizes the importance of following recommendations, regular check-ups, and appropriate patient motivation under the supervision of medical staff.

Conclusions: The review article clearly indicates that the lifestyle of patients with chronic diseases has a significant impact on their quality of life. Prevention and rehabilitation play a key role in reducing the risk of developing chronic diseases or slowing down their progression.

KEY WORDS: life style, diet, exercise, chronic disease, cardiovascular diseases

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INTRODUCTION

Chronic disease is a global health problem in modern medicine. It is characterized by a long-term treatment process, the need for constant monitoring, and often the inability to achieve a complete cure. Conditions such as type 2 diabetes, obesity and cardiovascular disease significantly affect the quality of life of patients. They usually have a negative impact on patients, affecting their biological, psychological, and social functioning. This is associated with a decline in mood and self-esteem [1]. At the same time, they place a huge burden on healthcare systems and national economies. A factor that reduces the risk of developing or slows the progression of chronic diseases is education focused on behavioral changes in society, such as lifestyle, diet, and physical activity [2]. These are modifiable factors that can be implemented at any stage of a patient's life. It is crucial to provide patients and their families with good guidance and support at every step of the way from medical staff. Appropriately selected prevention and rehabilitation measures can reduce the incidence of chronic diseases and lower the number of premature deaths [3].

AIM

The aim of this study is to analyze and systematize, based on a review of current literature, the role of lifestyle, diet, and physical activity in the prevention and rehabilitation of chronic diseases.

MATERIALS AND METHODS

This review article was conducted in accordance with guidelines and copyright laws. The PubMed and Google Scholar databases were searched to find studies on the importance of lifestyle, diet, and physical activity in the prevention and rehabilitation of chronic diseases such as obesity, diabetes, and cardiovascular disease. The literature search covered the latest publications, which allowed us to present the most up-to-date scientific information. Keywords such as lifestyle, diet, exercise,

chronic diseases, and cardiovascular diseases were used to search the literature.

REVIEW

LIFESTYLE AS A MAJOR RISK FACTOR FOR CHRONIC DISEASES

SCALE OF THE PROBLEM

Chronic illness is much more than just a medical definition of conditions lasting a year or more and requiring ongoing care. It's primarily a complex problem stemming from a combination of genetics, environmental factors, and, to a large extent, our lifestyle and daily behaviors [4]. While communicable diseases are declining, non-communicable ones like diabetes and Alzheimer's are becoming more prevalent. Ischaemic heart disease is the primary global killer (13% of deaths), showing the steepest increase since 2000 - a rise of 2.7 million, totaling 9.0 million deaths in 2021 [5]. Studies show that how we live determines not only our lifespan but, more importantly, how long we will enjoy health free from serious illness [6].

As we celebrate living longer, we face the bittersweet reality. Our aging societies are increasingly burdened by heart disease, type 2 diabetes, and obesity. This means that for many adults, the gift of extra years is often shadowed by the daily challenge of managing complex illnesses rather than enjoying a life free from disease [4, 6, 7].

LIFESTYLE AS A MODIFIABLE FACTOR

Clinically, lifestyle is defined not only as personal preference, but as a composite of specific, habitual behaviors. Physiological stability is influenced by dietary patterns, physical activity, smoking status, sleep hygiene and stress management [8]. Understanding these habits only as individual choices ignores the main role of environmental and behavioral determinants. A patient's physical and socioeconomic surroundings often dictate the availability of healthy options, making behavior inseparable from context [9]. Recognizing this interaction helps for medical intervention, where lifestyle modification serves a dual purpose. It acts as primary prevention to avert the initial onset of chronic disease in healthy populations. At the same time functions as secondary prevention to arrest progression or reduce comorbidities in patients with established diagnoses [10].

PATHOPHYSIOLOGICAL MECHANISMS

The journey from an unhealthy lifestyle to chronic disease is rarely simple because it requires a lot of inattention to the signs given by your own body. Instead it involves a complex, overlapping set of metabolic errors. It usually begins with insulin resistance, a condition heavily driven by physical inactivity and poor diet. This compromises how our muscles and fat tissue process glucose [11]. But this metabolic struggle doesn't happen in isolation. It is closely tied to a state of systemic, chronic inflammation. As adipose tissue grows, it begins to behave like an endocrine organ. It starts releasing inflammatory signals that further block insulin pathways and create a toxic environment for the body's cells [12].

Over time this persistent inflammation disrupts the balance between free radicals and our natural defenses. This is leading to oxidative stress. This excess of reactive oxygen species damages cellular structures and depletes nitric oxide availability [13]. This cascade hits the vascular walls causing endothelial dysfunction. Loss of vascular integrity is often the tipping point where general risk factors turn into actual cardiovascular or renal pathology. The good news is that lifestyle modifications can intercept this process. Exercise helps restore endothelial function through increased shear stress and a nutrient-rich diet can dampen oxidative damage. These actions are effectively breaking the cycle of disease progression [14].

IMPORTANCE OF DIET IN THE PREVENTION AND TREATMENT OF CHRONIC DISEASES

DIET AS A NON-PHARMACOLOGICAL THERAPY IN METABOLIC SYNDROME

Scientific evidence clearly indicates that a proper diet can significantly reduce the risk of developing chronic diseases and serve as a valid therapeutic approach for managing existing illnesses. Metabolic Syndrome (MetS) is especially important because it involves a group of co-occurring cardiovascular and diabetic risk factors, including: abdominal obesity, hypertension, lipid disorders, and elevated blood glucose [15]. Since most individuals with MetS are overweight or obese, body mass reduction through dietary intervention is vital. Weight loss not only improves insulin sensitivity but also has a beneficial impact on other metabolic components of the syndrome. Another key factor is replacing saturated fatty acids with monounsaturated and polyunsaturated fatty acids, which improves the serum lipid profile [16], enhances insulin sensitivity, assists in lowering body mass index (BMI), and reduces blood pressure, ultimately helping to reverse MetS [15]. Therefore, dietary management should focus on adopting comprehensive nutritional models, among

which the Mediterranean and DASH diets have proven to be the most effective.

THE MEDITERRANEAN DIET: COMPOSITION AND CLINICAL BENEFITS

As its name suggests, the Mediterranean diet (Med-diet) originates from the traditional eating habits of people living in Mediterranean countries. It is based on using olive oil as the primary source of fat, along with high amounts of seasonal vegetables and fruits, which are often used instead of sugary desserts. The diet also includes regular consumption of nuts, seeds, legumes, and whole-grain products. Fish and dairy, such as yogurt and cheese, are eaten frequently, while many herbs and spices are used to season meals. On the other hand, sweets are avoided, and red meat is consumed only in small quantities. A fundamental part of the Med-diet is the focus on fresh, unprocessed foods, which is a major difference compared to the high intake of ultra-processed foods commonly seen in developed countries [17]. In one study involving 180 participants with MetS, researchers found that those assigned to a Mediterranean diet achieved greater weight loss and improved endothelial function. These individuals also showed lower levels of inflammatory markers, such as hsCRP, IL-6, IL-7, and IL-18, compared to the control group [18]. In addition, many studies have shown that the Med-diet has a positive effect on metabolic disorders and certain types of cancer. There is also a growing amount of evidence suggesting that the Mediterranean diet can help prevent neurodegenerative diseases and depression [17].

THE DASH DIET AND METABOLIC BENEFITS

Dietary Approaches to Stop Hypertension (DASH) diet is a nutritional model, that was originally created to help prevent and treat high blood pressure. This diet focuses on foods that are high in magnesium, potassium, and calcium. It recommends eating a large amount of fruits and vegetables, lean meat, and low-fat dairy products. It also limits the amount of salt in the daily diet [19]. Reducing sodium intake, which is an element of the DASH diet, helps lower blood pressure in patients who suffer from hypertension and type 2 diabetes [20]. Research has also shown that the DASH diet is effective in lowering the risk of metabolic syndrome and its components, such as high triglycerides, and low serum HDL-C levels. Additionally, individuals following the DASH diet are less likely to suffer from insulin resistance, inflammation, thrombosis, and atherosclerosis [15].

THE ROLE OF PHYSICAL ACTIVITY IN PREVENTION AND REHABILITATION OF CHRONIC DISEASES

WORLD HEALTH ORGANIZATION (WHO) RECOMMENDATIONS ON PHYSICAL ACTIVITY

Physical activity offers a range of benefits for all age groups, regardless of health status. The World Health Organization (WHO) states that even a small amount of physical activity is better than no activity at all.

The WHO states that to achieve significant health benefits, adults should engage in at least 150 to 300 minutes of low-intensity aerobic activity or 75 to 150 minutes of high-intensity aerobic activity, or an equivalent combination.

The main benefits of physical activity in adults include lower mortality from cardiovascular disease, lower incidence of hypertension and type 2 diabetes, and improved obesity rates [21].

THE IMPACT OF ACTIVITY OF VARIOUS INTENSITIES

There are different types of physical activity. Interval training (e.g., HIIT - high-intensity interval training) is characterized by exertion at ≥ 90% of maximal oxygen uptake (VO_2 max) or >75% of maximal power, with periods of rest. Another form of physical activity is moderate-intensity continuous training (MICT), which involves 30-60 minutes of moderate exercise at 40-60% of VO_2 max. Available scientific research clearly indicates that HIIT improves central cardiovascular adaptation and increases metabolic stress, while MICT improves metabolic efficiency and the ability to uptake oxygen from the blood and utilize it in skeletal muscle cells. Interval training, when performed regularly, improves endurance capacity, insulin sensitivity, body composition, and cognitive function. Other benefits include a reduction in cardiovascular events, the risk of breast cancer, metabolic syndrome, osteoarthritis, and rheumatoid arthritis [22]. Both HIIT and MICT improve lipid profiles: they lower total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C), while increasing high-density lipoprotein cholesterol (HDL-C). They also lower alanine aminotransferase (ALT) levels and sensitize cells to insulin. Through these biochemical and cellular changes, both types of physical activity significantly improve prognosis in the treatment of obesity and type 2 diabetes [23].

Comparing moderate and vigorous physical activity, vigorous physical activity is more effective in improving cardiorespiratory fitness [24].

THE IMPACT OF A SEDENTARY LIFESTYLE

A sedentary lifestyle significantly contributes to the increased morbidity and mortality from atherosclerotic cardiovascular disease (ASCVD). Studies show that maintaining a sedentary posture for >6 hours and watching television for >4 hours significantly increase this risk. However, each 30-minute change from sitting, standing or light physical activity to moderate physical activity brings a noticeable improvement in body mass index (BMI), glycated hemoglobin (HbA1c) and lipid profile, which translates into a decrease in cardiovascular incidents [21, 24].

THE IMPACT OF LIFESTYLE INTERVENTIONS ON SELECTED CHRONIC DISEASES

OBESITY

Obesity is a condition characterized by excessive and abnormal accumulation of body fat, which negatively impacts health. It can lead to the development of numerous chronic diseases, a reduced quality of life, and a shortened lifespan. Obesity, and visceral adiposity in particular, plays a key role in the development of insulin resistance, a central component of metabolic syndrome. It is closely linked to dyslipidemia, which manifests as elevated triglyceride levels, increased small, dense LDL particles, and decreased HDL cholesterol. Lipid abnormalities are a characteristic component of metabolic syndrome and significantly increase the risk of cardiovascular disease [25]. A key aspect in the fight against obesity is following a proper diet and a healthy lifestyle. Following a diet that leads to an energy deficit, enabling weight loss and then maintaining the achieved results, regardless of the diet type, is a key element of obesity treatment. Various nutritional strategies, varying in caloric content and macronutrient ratios, can lead to clinically significant weight loss in a short period of time [26]. Maintaining regular physical activity is just as important as a proper diet. Research indicates that both contribute to improving lipid profiles, including lowering total cholesterol, triglycerides, and LDL cholesterol levels, and may also increase the body's sensitivity to insulin [27]. All these activities significantly support the body's health and help prevent the development of many diseases that are caused by obesity.

DIABETES

Lifestyle changes through implementing a proper diet and regular physical activity are also crucial for patients with type 2 diabetes. These actions lead to improved body weight, lower HbA1c levels, and blood pressure regulation, which is associated with a reduction in microvascular complications such as renal dysfunction. Research findings also indicate that intensive lifestyle interventions effectively support the control of cardiovascular risk factors and reduce the need for pharmacological treatment for diabetes [28]. Additionally studies have also shown that a healthy lifestyle primarily reduces the risk of developing and progressing diabetes in previously healthy individuals. A combination of healthy lifestyle habits, including a healthy BMI, a healthy diet, regular physical activity, no smoking, and moderate alcohol consumption, was associated with an approximately 90% lower incidence of type 2 diabetes in individuals compared to those without these factors [29]. A properly balanced diet, rich in all essential nutrients, can not only support the prevention and treatment of diabetes, but also improve metabolic parameters and reduce the risk of other conditions such as depression in these patients [30]. All this data indicate that lifestyle modification could prevent most cases of type 2 diabetes and have a beneficial effect on the course of this disease in the population.

CARDIOVASCULAR DISEASES

Cardiovascular diseases are the leading cause of death and morbidity worldwide. Their development is determined by both genetic predisposition and lifestyle factors. Numerous studies confirm that modifiable health behaviors, such as smoking, physical activity levels, diet, and body mass index (BMI), significantly influence the risk of developing cardiovascular disease [31]. Studies show that people with unhealthy health habits had almost twice the risk of coronary artery disease (CAD) than those with a healthy lifestyle, despite having a similar genetic background [32]. It has also been shown that non-smokers, those with a normal body weight, a healthy diet, at least 30 minutes of physical activity every day and moderate alcohol consumption had an over 80% lower incidence of coronary events compared to the rest of the population [33]. It was also observed that a diet rich in vegetables, fruits, whole grains, fish, and legumes, along with moderate alcohol consumption, was associated with a 57% reduction in the risk of primary heart attack. Combining such a diet with additional beneficial behaviors such as not smoking, regular physical activity, and maintaining a healthy body weight reduced this risk by as much as 92% [34]. Establishing and maintaining good health habits is therefore a fundamental element of the strategy to protect the heart and blood vessels.

DISCUSSION

A review of available research shows that lifestyle plays a key role in both the prevention and treatment of chronic diseases. Many studies demonstrate that changes in diet and physical activity, as well as weight and substance abuse management, can significantly reduce the risk of these conditions and improve treatment outcomes and quality of life. This also demonstrates that non-pharmacological approaches can be a helpful complement to pharmacological treatment and can sometimes even reduce its need.

Both observational and interventional studies indicate that diet plays a key role as a key factor in the prevention and non-pharmacological treatment of chronic diseases. Numerous publications emphasize the beneficial effects of diets based on healthy eating principles. A good example is the Mediterranean diet, which demonstrates significant benefits in the treatment of many common chronic diseases. It has anti-inflammatory and antioxidant effects and helps regulate metabolism and intestinal function. It is a valuable tool for supporting therapy and improving the health of patients with chronic diseases [35]. Another example is the DASH (Dietary Approaches to Stop Hypertension) diet. Its primary goal is to alleviate hypertension and prevent its potential complications. Numerous clinical trials confirm the effectiveness of this diet in controlling blood pressure. In addition to its significant impact on reducing hypertension, the DASH diet has been shown to be beneficial in other conditions, such as heart failure, lipid disorders, dyslipidemia, and uric acid dysregulation. This makes the DASH diet a valuable tool in the treatment of hypertension [36]. Unfortunately, in recent decades, globalization and the rapid growth of fast food chains have contributed to unfavorable changes in people's dietary habits. Traditional diets based on fresh vegetables and fruits, nuts and fish are increasingly being replaced by highly processed, high-energy foods. These products are characterized by a high content of refined carbohydrates, simple sugars, sweetened beverages, and animal fats. Combined with reduced physical activity and a predominant sedentary lifestyle, these changes are among the key factors responsible for the rising incidence of obesity and cardiovascular disease in the population [37].

Regular physical activity is also a crucial element of a healthy lifestyle. Research clearly shows that regular exercise, even at a moderate level, tailored to the patient's age, health status, and functional abilities, contributes to lower blood pressure, better control of cholesterol levels and body weight, and helps prevent some diabetes complications. All of these effects reduce the risk of cardiovascular disease, such as heart attack or stroke. Furthermore, regular physical activity helps reduce the number of medications used to treat diabetes and hypertension [38]. In the rehabilitation of chronic diseases, such as heart failure, physical activity plays a significant role, improving physical fitness, improving patients' quality of life, and reducing the risk of rehospitalization [39]. However, despite the obvious health benefits of physical activity, very few people lead an active lifestyle. This is due to various reasons. These are often personal barriers related to self-efficacy, lack of self-confidence, or lack of time [40].

CONCLUSIONS

Research indicates that the greatest health improvements arise when changes happen in many lifestyle areas together. A mix of a healthy diet and regular exercise and health learning and psychological help works better than concentrating on just one area. But success of these methods hinges on patient adherence to advice which means motivation and understanding and consistent support from the medical staff are vital.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Characteristics of adult patients with juvenile idiopathic arthritis

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ABSTRACT

Aim: Juvenile idiopathic arthritis may remain active into adulthood. This review aims to characterize patients with this condition in terms of quality of life, psychosocial well-being, and various comorbidities, especially those that have recently been described.

Materials and Methods: Methods involved analyzing studies investigating the mentioned features: meta-analyses, reviews, and cohorts.

Conclusions: Results show that quality of life and psychosocial well-being, occupational and social functioning, and, sometimes, cognitive functioning are decreased, while pain and fatigue are increased. In contrast, analyses of emotional health outcomes did not show a higher prevalence of depression or anxiety in adults with JIA. Half of young adults with JIA have active disease, and more than one-third suffer detectable degrees of disability and organ damage. Frequent complaints and conditions are: abdominal pain, TMJ pain, uveitis, and juvenile fibromyalgia syndrome. JIA may also affect BMI, inflammation, and pain of the joints, Growth disorders, overall dysregulation of the immune system, and a negative correlation between disease activity and vitamin D levels. Nevertheless, patients with JIA exhibit lower functional impairment and better quality of life compared to other rheumatic diseases, such as rheumatoid arthritis and spondyloarthropathies. Understanding the lasting impact on health and life satisfaction among adult patients with JIA requires a comprehensive approach that accounts for the multifactorial aspects of the individual's experience with the disease.

KEY WORDS: arthritis, juvenile idiopathic, adult patients, disease progression, quality of life, treatment outcome

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INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a chronic inflammatory disease with variable course and outcome that occurs in children under the age of 16 years, and continues into adulthood in approximately half of the patients [1]. The etiology of JIA remains unknown, and it is associated with prolonged synovial inflammation and structural joint damage influenced by environmental and genetic factors [2]. JIA poses a significant challenge to both patients and health care due to its chronic nature and potential long-term consequences: the course and outcome of JIA may vary considerably, depending on the disease severity The course and outcomes of JIA vary greatly depending on the severity of the disease. It can range from inflammation in one joint of limited duration to unremitting, widespread, disabling arthritis, together with various comorbidities. The processes and problems described above lead to deterioration in health-related quality of life (HRQoL) among patients with this disease [3].

AIM

This article summarizes the characteristics, quality of life, psychosocial well-being, and various comorbidities in adult patients who developed JIA in childhood. Reviews of JIA in adults in recent years have not addressed all the complications recently described. This article aims to fill this gap.

MATERIALS AND METHODS

This systematic review was written based on a search of the PubMed and Google Scholar databases from 1

January 2020 to 31 December 2025. The following keywords were used as search terms: " juvenile idiopathic arthritis", "JIA", "adult patients", "disease progression", "quality of life", "treatment outcome". After excluding incomplete articles and articles in languages other than English, 32 papers corresponding to the research topic were found. This paper was written primarily on the basis of meta-analyses and reviews, as well as cohorts, to provide the broadest possible picture of the researched subject.

REVIEW

HEALTHCARE TRANSITION

Transition is the intentional, planned passage of adolescents and young adults with chronic conditions from child- to adult-focused health care systems [3, 4]. It involves several aspects, including administrative matters, patient and family needs, and multidisciplinary care orientations [4]. Transition can be challenging due to variability in disease progression and outcomes across JIA categories [5]. There are several JIA categories, including systemic-onset arthritis, oligoarthritis, polyarthritis, and enthesitis-related arthritis. Persistent oligoarticular

JIA has the highest rate of remission. Polyarticular and enthesitis-related arthritis have the highest flare rates during follow-up [4, 6]. Transition is best achieved when JIA is stable and/or inactive. However, at the time of transition, up to 50% of the JIA patients have disease activity [3-6], and up to one third will have chronic disability into adulthood [6]. Even those who achieve symptom-free periods in childhood may experience disease flares as adults [3, 5]. JIA categories can change over time, from childhood to adulthood, when these patients are followed closely for features of enthesitis, psoriasis, or spondyloarthritis, often progressing from oligoarticular to polyarticular disease course, especially during the first 5 years of disease [3]. The JIA course remains uncertain, with a variable rate of remissions across cohorts and study designs. The severity and clinical course of JIA are unpredictable, with periods of low disease activity followed by a rebound of signs and symptoms on or off medication. The course of JIA is uncertain due to variable remission rates across cohorts and studies. There may be periods of low disease activity, followed by symptom recurrence during or after treatment discontinuation. Over time, some patients can achieve sustained remission. Even so, despite advances in treatment, active disease has been reported in 37–63% of adult patients with JIA [3]. Predicting disease outcomes in JIA is challenging due to the disease's heterogeneous nature, even within the same JIA category. To enable physicians to answer parents' and children's questions about long-term prognosis, they have had information on prognosis available mostly at the group level, not individually. Moreover, early prediction of the individual child's disease course can facilitate tailored, personalised treatment. Variables suitable for predicting disease outcomes include, among others, patient and disease characteristics, imaging results, and laboratory tests. Disease course is determined by how these variables interact and by the timing of appropriate treatment a child receives, since there is increasing evidence that early treat-to-target treatment modifies prognosis. Drop-out rates from care are used as an outcome measure of successful transition, quantified as a percentage of the entire cohort. However, even with the implementation of transition programs, dropout has been reported to range from 12% to 52% [4]. There is evidence that an inadequate transition from pediatric to adult care is associated with loss of follow-up, higher risk of stopping treatment, more flares, and increased disability [3]. Not necessarily all JIA patients have to be followed by adult rheumatologists [4].

QUALITY OF LIFE AND PSYCHOSOCIAL WELL-BEING

Quality of life (QoL) reflects a patient's subjective assessment of health status and daily functioning. In juvenile idiopathic arthritis (JIA), QoL is commonly evaluated using standardized scales and questionnaires that assess health status and functional ability, and patient-reported symptoms. Together with clinical data, these tools provide a comprehensive assessment of disease burden. An adequately high QoL remains essential for maintaining good mental health and psychological well-being [1, 3, 5]. A multidimensional analysis of functioning across physical, psychological, and social domains allows for the identification of limitations that manifest as disability caused by the disease. This analysis takes into account physical and occupational activity, independence in daily activities, social functioning, and health-related symptoms [1]. The unpredictable course of the disease makes prognostic assessment difficult, thereby reducing the ability to intervene early and modify the disease course, which significantly decreases patients' quality of life [3, 5]. Physical activity is associated with appropriate QoL [7]. JIA leads to joint damage, which presents as movement restrictions, somatic symptoms such as pain or morning stiffness, and reduced physical efficiency, which hinders daily physical activity and decreases quality of life [1, 3]. Clinically, patients frequently

present with reduced handgrip strength and impaired dorsiflexion and plantarflexion of the foot, which contribute to activity avoidance, physical deconditioning, and reduced participation in social and recreational activities [7]._Furthermore, in the second decade of life, a decline in vital capacity measured over two seconds (VC2) has been observed, indicating reduced physical fitness and exercise tolerance. Joint inflammation, as well as the coexistence of chronic conditions, including cardiovascular disorders, contributes to this decline, which in turn increases health risks over time [3, 7]. Serological and immunological markers of rheumatic diseases, such as anti-cyclic citrullinated peptide (anti-CCP) antibodies, rheumatoid factor (RF), antibodies against collagenase II, and the genetic marker of predisposition to their development, human leukocyte antigen B27 (HLA-B27) - are associated with an elevated risk of joint damage and higher disease activity, further contributing to functional limitations and reduced QoL. However, oligoarticular and systemic forms of JIA, compared with polyarticular disease, are generally characterized by less pronounced joint involvement, which results in heterogeneous functional outcomes across different patient subgroups. [3, 5]. Pain is the most common complaint in JIA and has a significant negative impact on health-related quality of life (HRQoL), despite modern treatment and good disease control. The causes of pain are diverse: both biological and psychosocial factors can contribute to the experience of pain [4, 8]. Adults with JIA may have lower pressure pain thresholds (PPTs) and lower temperature thresholds, as measured on the numeric rating scale (NRS). Individuals with inactive JIA had the lowest PPT and cold pain threshold (CPT). There is no association between self-reported pain and pain thresholds [8]. Among the symptoms most strongly affecting QoL, fatigue represents a particularly significant and multifaceted burden in patients with JIA [1,9]. Although its etiology is not fully understood - fatigue likely reflects a complex interaction between chronic inflammation, immune dysregulation, sleep disturbances secondary to pain and stiffness, pharmacological treatment, including diseasemodifying antirheumatic drugs (DMARDs), and female sex [1, 5, 9]. Delayed initiation of disease-modifying antirheumatic drugs (DMARDs) is associated with increased perceived fatigue in the future. Patients with active disease experience greater fatigue than those in remission. Patients who earlier experienced pain experience greater fatigue [3, 5, 9]. It has been demonstrated that combined hydrotherapy and land-based physiotherapy significantly improves physical abilities in patients compared to land-based physiotherapy alone [7]. Early initiation of disease-modifying antirheumatic drugs (DMARDs) also improves joint symptoms, leading to increased physical activity in patients. [3]. The overall dysregulation of the immune system and pharmacotherapy has long-term effects on the health of patients with JIA. An increased prevalence of immune-mediated diseases, malignancies, and recurrent infections further contributes to cumulative disease burden and long-term impairment in QoL [3]. External systemic stressors may exacerbate these effects. For example, fear of infection during the Coronavirus Disease 2019 (COVID-19) pandemic in 2020 was associated with increased disease exacerbations due to missed follow-up visits, treatment interruptions, and reduced access to routine medical care [10]. Functional limitations in JIA substantially affect occupational and social functioning [1, 11]. Although educational attainment is comparable to that of the general population, a decrease in disability has been noted in recent years; many adults with JIA experience difficulties maintaining stable employment [1, 3]. Although educational achievement is comparable to that of the general population, and a decrease in disability has been noted in recent years, many adults with JIA experience difficulties maintaining stable employment. Support from individuals in the patient's close social environment increases the chances of participating in occupational activities, social integration, and self-esteem [3, 11]. Cognitive functioning may also be affected, as lower educational level, longer disease duration, higher disease activity, and the coexistence of other chronic conditions are associated with cognitive impairments, especially in visuospatial functions. Uveitis, a common complication of JIA, can lead to vision loss. This condition occurs more frequently in females with positive antinuclear antibody (ANA) tests. It contributes to functional limitations and significantly reduces QoL [3, 5, 12]. Assessment of emotional health outcomes has not consistently demonstrated a higher prevalence of depression or anxiety in adults with JIA compared with healthy individuals [1, 3, 13]. No association has been identified between symptom frequency and age, sex, disease duration, or disease severity [13].

Nevertheless, somatic symptoms exert a significant influence on body image perception, particularly in patients with polyarticular JIA, affecting social functioning and mental health [1, 3]. Patients with JIA exhibit lower functional impairment and better quality of life compared to other rheumatic diseases, such as rheumatoid arthritis (RA) and spondyloarthropathies (SpA). Compared to RA patients, they have better physical function and lower fatigue levels, with no clear differences in depressive or anxiety symptoms. Clini-

cally, polyarticular JIA with positive rheumatoid factor resembles seropositive adult RA, whereas RF-negative polyarticular and oligoarticular JIA show similarities to seronegative RA [3, 9, 14].

PATIENTS CHARACTERISTICS

A significant association was found between the JIA categories and BMI groups. BMI was associated with disease activity; this association has been relatively little studied in JIA or rheumatic diseases overall.

Obesity has a negative influence on the disease course and on the treatment response in JIA [15]. However, ambivalent results have been revealed [15, 16]. Excess adipose tissue can alter the pharmacokinetics of biological drugs, thereby diminishing treatment response. No relationship between BMI and medication was found. Patients with higher BMI also have higher CRP and ESR. It remains unclear whether elevated inflammatory values were due to rheumatic inflammation or to obesity.

Higher BMI in adults with JIA was associated with fatigue and poor sleep quality; intriguingly, underweight patients had the best sleep quality and reported less fatigue.

JIA patients were found to be less active than their healthy peers. A lower level of physical activity was found to be associated with overweight in patients with JIA [15]. There is a negative correlation between disease activity and 25(OH) vitamin D levels, independent of age, gender, BMI, JIA subtype or duration. Patients with higher disease activity levels may have vitamin D deficiency [16]. Adult patients with JIA are predisposed to inflammation and pain of the joints, as well as joint damage, including irreversible damage to cartilage and bone, and joint deformities. The presence of anti-CCP and RF antibodies in the blood increases the risk of these complications [3]. Studies have observed a correlation between the occurrence of JIA during adolescence and final height. Growth disorders in the form of being below -2SD occur (depending on the extent of JIA) in 10.4% of people with the polyarticular form, to 41% in patients with the systemic form. Limiting disease activity through the use of immunomodulators, cytokine blockers, glucocorticosteroids, and maintaining an appropriate diet adapted to the needs of the growing patient results in slow growth - only 19% of patients will be below -2SD, but only the use of recombinant human growth hormone allows growth close to genetic potential to be achieved [17]. Growth disorders affect not only bone length, but also bone density, which is determined by bone mineral density (BMD). In adults, BMD depends on peak bone mass during puberty and its subsequent decline. People with JIA experience lower mineralisation growth and its faster loss due to genetics, chronic inflammation, delayed puberty (the earlier JIA begins, the more severe the puberty disorders are), low physical activity, nutrient deficiencies, and drug side effects [17, 18]. Due to the chronic nature of JIA and its consequences (joint pain, limited mobility, lean body structure, side effects of treatment, and severe complications, e.g., uveitis potentially leading to vision loss), patients tend to report lower health-related quality of life (HRQoL). Lower HRQoL is related to a higher risk of reduced confidence, anxiety disorder, and depression, although physically active patients have higher HRQoL than patients who lead a sedentary lifestyle [19, 20].

COMORBIDITIES

Half of young adults with JIA have active disease, and more than one-third suffer detectable degrees of disability and organ damage. This leads to multiple comorbidities that impact the patient's biopsychosocial well-being. Their presence can complicate JIA treatment and require specialist care. Abdominal pain is a frequent complaint in young adults with diagnosed JIA. It is associated with female gender, disability, arthritis-related pain, commonly used sDMARDs, and fatigue. Abdominal pain in young adults with diagnosed JIA, even if not related to IBD or other gastrointestinal disorders, should not be underestimated [21]. Uveitis is a condition that can occur for many years after adulthood in patients with JIA. The onset of this disease began in childhood, and women predominated among the study participants. The disease is chronic, characterized by bilateral ocular inflammation and elevated ANA antibody levels. The main complications are: posterior synechiae, glaucoma, cataracts, and increased ocular pressure, which significantly deteriorate vision. Patients require surgical treatment, including cataract and glaucoma removal. Interdisciplinary care is critical to ensuring a good quality of life for patients with this condition [4, 22-25]. In JIA patients, orofacial pain frequency and number of symptoms, including TMJ pain, are the most frequent clinical findings, together with morning stiffness and limitation of chewing, which are observed significantly more frequently than in the normal population. At least 1 orofacial symptom is reported by 1/3 of patients. There is a higher prevalence of TMJ pain on palpation and a reduced maximum interincisal opening among the JIA patients; however, the prevalence of orofacial pain on palpation and asymmetric mouth opening is not different from that seen in the control group. A large number of patients have TMJ symptoms/dysfunctions

despite inactive disease/remission, indicating a need for continued, standardized orofacial monitoring in adulthood [26]. The research has shown that Juvenile Fibromyalgia Syndrome (JFMS) is more likely to develop with age in patients with JIA. It appears more frequently in women, who report significantly more severe pain and other symptoms compared to those with JIA alone. The condition requires appropriate pharmacological treatment to improve daily functioning [27]. Symptoms of anxiety and depression are more common in patients with polyarticular JIA. Suicidal ideation and self-mutilation have been observed among the aged group 18-21. Doctors use psychotherapy more often than pharmacotherapy because they have noticed its greater effectiveness. The occurrence of depression in patients with JIA can significantly worsen the course of the disease due to reduced doctor-patient cooperation and lower compliance with medical recommendations [28]. In the group of young adult patients with JIA, one-quarter had at least one autoimmune disease. The most frequently reported diseases were type 1 diabetes, Hashimoto's thyroiditis, Addison's disease, chronic urticaria, Sjögren's syndrome, Raynaud's syndrome, and vitiligo. The data suggest that regular testing and clinical observation under medical supervision are essential [29, 30].

DISCUSSION

The onset of JIA in childhood and its progression into adulthood pose a challenge for the healthcare system. Research indicates that approximately 50% of adult patients report disease activity, and the main problems they report include multiple comorbidities and chronic disability. JIA has various subtypes and a variable course, complicating clinical prognosis, treatment selection, and care planning. This disease requires a long-term approach to patient care, focusing on preventing complications and monitoring disease severity. The transition of pediatric patients to adult rheumatology care is an important step in the course of JIA. However, data indicate that during these transfers, between 12% and 52% of patients experience discontinuation of specialist care, resulting in treatment discontinuation, functional deficits, and an increased frequency of disease exacerbations. It is important that this optimal transition occurs when the disease is stable or inactive. The study by Laura De Nardi et al., which examined the transfer of pediatric patients with JIA to adult care, emphasizes that a wellorganized transition process enables participation in systematic follow-up visits [31]. Similar conclusions were drawn by Rodrigo Joel de Oliveira et al. and Filipa Oliveira Ramos, who, in their studies, emphasized the consequences of inappropriate transfer of patients with JIA to adult care, namely disease relapses_and treatment discontinuation [3,4]. Modern JIA treatment methods have enabled monitoring of disease activity but have not improved patient functioning. Reduced range of motion, progressive joint destructive changes, and fatigue impact daily life and physical function, while reduced exercise tolerance and muscle strength within certain limits preclude professional and social engagement. Consequences of this disease in patients with early-stage JIA include problems with growth and bone density, which predispose them to osteoporosis in adulthood. Serological markers such as RF and anti-CCP antibodies increase the risk of serious joint deformities and disability. Analysis of the relationship between BMI, physical activity, and the course of the disease suggests that being overweight and obese may exacerbate the disease and increase its symptoms. This emphasizes that treatment outcomes should be additionally assessed based on patients' subjective quality of life. These aspects should be taken into account when individualizing risk assessment and planning long-term therapeutic management. Rodrigo Joel de Oliveira et al. found that more frequent physical activity among JIA patients was associated with better functioning in everyday life and improved well-being [20]. In their works, Armando Di Ludovico et al. and Anita Tollisen et al. also emphasized the great importance of physical activity as a factor in the daily functioning of patients with JIA, and cessation of sports due to pain and motor disorders leads to a reduced social life [1, 7]. The main comorbidities of JIA include abdominal pain, mental disorders, chronic ocular inflammation, and orofacial symptoms associated with TMJ. Research by Bethany Richmond et al. shows that people with JIA are much more likely to experience psychological and social stress compared to healthy people of the same age [32]. Florian Milatz et al. additionally emphasize the negative impact of depression on prognosis due to a lack of communication and cooperation with medical personnel and lack of compliance with therapeutic recommendations [28]. The increased prevalence of autoimmune diseases indicates the need for regular health monitoring and comprehensive medical care. Rapid identification and appropriate treatment of comorbidities help reduce the negative impact on patients' daily activities and improve the course of JIA therapy. In summary, this group of adult patients with JIA requires interdisciplinary care, appropriately tailored treatment, psychological support, and management of complications. This is crucial for improving the patient's biopsychosocial well-being and quality of life, and minimizing the limitations resulting from the disease.

CONCLUSIONS

- The quality of life of patients with JIA is significantly reduced and has a multidimensional character, embracing physical, psychological, and social domains. Its assessment requires the use of standardized scales, questionnaires, and objective clinical indicators.
- A higher quality of life correlates with better mental health, whereas its decline contributes to impaired emotional well-being. Although it isn't consistently demonstrated to have a higher prevalence of clinically significant depression or anxiety in adults with JIA compared with healthy individuals.
- Multidimensional functional limitations, including physical activity, occupational activity, independence, social functioning, and health-related symptoms, lead to a significant reduction in patients' QoL.
- Regardless of disease activity and treatment effectiveness, pain in JIA reduces quality of life, demonstrating the need for an individualized treatment approach. It is necessary to include both biological and psychosocial factors in treatment.
- Fatigue, being one of the most awkward symptoms of JIA, is associated with disease activity, somatic symptoms, sleep disturbances, pharmacotherapy, and female sex. Delayed initiation of disease-modifying treatment is associated with greater fatigue severity later in the disease course.
- Reduced physical activity resulting from joint damage, pain, and decreased physical efficiency hinders daily activities and further diminishes QoL. Furthermore, combined physiotherapy and hydrotherapy, as well as regular, appropriately tailored physical activity, significantly improve patient functioning.
- Early and comprehensive therapeutic management, including pharmacological treatment with particular emphasis on effective pain management, rehabilitation, and psychosocial support, substantially increases the range of physical activity and reduces symptom severity.
- Immunological and laboratory factors are associated with greater disease activity and a higher risk of joint damage. Greater functional impairment is observed in polyarticular forms of JIA than in oligoarticular and systemic forms.
- Physical disability significantly affects patients' occupational and social functioning, reducing QoL. However, support from individuals in the patient's close social environment increases the chances of employment, better emotional well-being, and social integration.
- Despite similarities between JIA and other rheumatic diseases, such as RA and SpA, overall functioning in patients with JIA is better, which emphasizes the importance of individualized therapeutic management.

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REVIEW ARTICLE

CONTENTS

Anatomical variations of hepatic and pancreatic vascularization: A comprehensive review

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ABSTRACT

This review analyzes and deepens our understanding of the anatomical variations of the hepatopancreatic region, a crucial area in many medical fields. Precision and surgical efficiency largely rely on a thorough understanding of anatomical nuances and variations. In recent years, significant emphasis has been placed on exploring anatomical variations, particularly in the context of hepatopancreatic surgery. This review collects key information on the types of lesions within the major vessels of the liver and pancreas and presents their incidence. The cited material is based on a review of studies and observations, textbooks, and other review articles. The collected data highlight the importance of hepatic and pancreatic vascular variability, which should be considered an anatomical feature rather than an exception. Further exploration of the occurrence of such features is crucial. This understanding of anatomy is particularly crucial in hepatobiliary and pancreatic surgery, where anatomical complexity directly impacts procedural planning and surgical strategy.

KEY WORDS: hepatic vessels, pancreatic vessels, anatomical variation, vascular anatomy

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INTRODUCTION

The anatomy of the hepatopancreas region is crucial in many medical fields, encompassing not only basic structures but also complex variations that make each patient unique [1]. As emphasized by the principles of safe surgery, a surgeon's proficiency in hepatopancreatic procedures relies largely on a comprehensive understanding of anatomical nuances and their variations [2]. Navigating the delicate areas of the liver and pancreas requires not only theoretical knowledge but, equally importantly, practical knowledge of the relevant surgical anatomy [3]. In recent years, considerable emphasis has been placed on understanding and appreciating anatomical variations in the context of hepatopancreatic surgery.

AIM

In this publication, we aim to discuss and deepen our understanding of the anatomical variations of the hepatopancreas region, maintaining their importance in the discussion of normal anatomy.

MATERIALS AND METHODS

PubMed and Google Scholar databases were searched in English and Polish. Search keywords: hepatic vascular anatomy variations, pancreatic vascular anatomy variations, hepatic and pancreatic vascularization, anatomical variations of hepatic and pancreatic vessels. Over 40 sources were analyzed.

REVIEW

LIVER

The liver, stituting approximately 2% to 3% of the average body weight, stands as the largest organ. Situated beneath the right hemidiaphragm in the right upper quadrant of the abdominal cavity [4, 5]. The most used anatomical division in surgery and radiology is the one proposed in 1957 by Couinaud, distinguishing eight segments within its parenchyma [6]. These segments are independent in terms of blood supply and biliary drainage, formed by branches of the portal vein and the right, middle, and left hepatic veins. The hepatic veins divide the liver parenchyma into 4 sectors, each receiving its own portal branch. These sectors are the right posterior (postero-lateral), including segments 6 and 7, the right anterior (antero-lateral) including segments 5 and 8, the left medial (anterior), which constitutes segment 4 (a - upper and b - lower according to Bismuth's classification), and the left lateral (posterior), composed of segments 2 and 3. Segments 5, 6, 7, and 8 constitute the right lobe, and 2, 3, and 4 constitute the left lobe. Segment 1, anatomically corresponding to the caudate lobe, has a direct venous outflow to the inferior vena cava, receiving blood supply from the right and left branches of the hepatic artery and the portal vein [7].

VASCULAR LANDSCAPE OF THE LIVER

The liver, a vital organ for sustaining life, boasts a robust circulatory system. Approximately 20%–25% of the cardiac output, equivalent to 1–2 liters per minute, traverses through the liver. Notably, the liver receives a distinctive dual blood supply, comprising oxygen-rich arterial blood from the hepatic artery (HA) and nutrient-laden blood from the portal vein (PV). Within the sinusoids enveloping hepatocytes organized in cord-like structures, arterial and portal venous blood blends seamlessly. Subsequently, this mixed blood flows into the central veins, ultimately draining through the hepatic veins (HV) into the inferior vena cava (IVC). At any given moment, approximately 40% of the liver's blood volume resides in the substantial vessels, while the remaining 60% occupies the sinusoids [8, 9]. Understanding the vascular anatomy of the liver is crucial, as variations in hepatic vascular structure may necessitate adjustments or alternative strategies during medical procedures and surgeries. Proficiency in this knowledge is imperative to navigate potential complexities arising from anatomical differences [8, 10].

PROPER PORTAL VEIN AND ITS ANATOMICAL DIFFERENCES

The portal vein, supplying the liver with about 3/4 of its blood volume, has tributaries in the form of the splenic and superior mesenteric veins. The division into right and left branches occurs in the liver hilum. Branches also arise for segment 1, usually three, but their number can vary from 1 to 6. The right portal branch supplies segments 5 and 8 (anterior branch) and segments 6 and 7 (posterior branch) after division. Both branches supply blood to segment 1. The left portal branch supplies segment 2 with upper posterior branches, segment 3 with left branches, and segment 4 with right branches (ascending 4a and descending 4b) [11].

Anomalies in the anatomy of the portal vein (PV) are infrequent, and among these, the prepancreatic postduodenal portal vein (PPPV) is exceptionally rare. In this anomaly, the portal vein is positioned in front of the pancreas and behind the duodenum, contrary to its typical placement behind both the pancreas and duodenum. While the PPPV is uncommon, the knowledge of this condition plays a pivotal role in preventing catastrophic complications that may arise from unintended PV injury, leading to severe consequences such as massive hemorrhage or ischemic complications affecting the liver or bowel [12].

In the realm of laparoscopic cholecystectomy, surgeons must have a thorough understanding to ensure the safe execution of laparoscopic cholecystectomy. One of the rare but very important anatomical variations of the portal vein is Preduodenal portal vein. PDPV usually presents in the pediatric population as it is the associated congenital anomalies that draw attention to its presence. Out of the identified cases, thirty-four instances (83%) were linked with additional multiple congenital malformations. Among these cases, intestinal malrotation was connected to 80%, situs inversus to 40%, pancreatic malformations to 33%, and biliary atresia, duodenal stenosis, or atresia to 13%. In most of these cases, the primary rationale for operative intervention was the presence of associated malformations rather than the prepancreatic postduodenal portal vein (PDPV) itself [13].

PROPER HEPATIC VEINS AND THEIR ANATOMICAL DIFFERENCES

Unlike portal vessels, hepatic veins do not have a visible wall in imaging studies. The hepatic veins originate in liver lobules, which, by connecting, form increasingly larger trunks, eventually creating the right, middle, and left hepatic veins, emptying into the inferior vena cava. The right hepatic vein receives blood from segments 6, 7, and 8, and partially from segment 5; the middle hepatic vein receives blood from segments 4, 5, and 8, and the left hepatic vein from segments 2, 3, and partially 4 [11].

Traditional anatomical descriptions outline a single superior right hepatic vein (SRHV) that discharges into the inferior vena cava (IVC). Any supplementary vessels originating from the right liver and draining into the IVC are categorized as accessory RHVs. Three recognized variants include an inferior RHV draining segment VI, which directly empties into the IVC just above the liver's inferior border, positioned more than 2 cm away from the hepatocaval junction (HCJ). Additionally, the middle RHV drains segment VII and directly flows into the IVC within a proximity of 1-2 cm from the HCJ. In the population from the eastern Caribbean, only 39% exhibited the typical venous drainage patterns from the right hemi-liver. Various RHV variants were prevalent, including proximal venous confluence (61%), accessory RHVs (49.2%) and nferior RHVs (45%). Interventional radiologists and hepatobiliary surgeons catering to patients from the Caribbean diaspora need to be aware of these distinctions to reduce the risk of complications during invasive procedures and minimize morbidity [14].

PROPER HEPATIC ARTERY AND ITS ANATOMICAL DIFFERENCES

The proper hepatic artery is a branch of the common hepatic artery. Its division usually occurs in the liver hilum or the hepatoduodenal ligament. The right hepatic artery supplies the right liver segments (5, 6, 7, and 8), and the left artery supplies the left segments: 4, 2, and 3. Segment 1 receives arterial blood from both the right and left branches.

The most encountered type of blood supply is the common hepatic artery branching off from the celiac trunk and then, after giving off the gastroduodenal artery, running as the proper hepatic artery towards the liver hilum, where it divides into the right and left hepatic arteries. Based on available data, the percentage of patients with vascular variations can range from about 13% [11] to 22.8% [15], and according to some authors, even up to 50% of patients [16]. According to these publications, the most common variations are the right hepatic artery originating from the upper mesenteric artery and the left hepatic artery originating from the left gastric artery, as well as additional hepatic arteries. Preoperative assessment of liver blood supply should be carried out with particular care. It is of great importance, especially for a surgeon planning surgical treatment, as it allows for proper procedure planning and avoids intraoperative complications [10, 11].

PANCREAS

The pancreas constitutes a crucial role in the human body. It is located transversely in the retroperitoneal space, in the upper abdominal cavity in front of the spine at the level of the 1st and 2nd lumbar vertebrae. It produces digestive enzymes and hormones which regulate the blood sugar level. The pancreas is situated near various anatomical structures in the human body. This proximity increases the likelihood of pancreatic cancer spreading to adjacent organs [17]. The pancreas (70-100g, 12-20cm) consists of four parts: the head, neck, body and tail. The pancreas is closely associated with several structures in its upper region. It shares proximity with the starting point of the coeliac trunk, the common hepatic artery and the splenic artery [18].

Anteriorly, you'll find the stomach, lesser sac (omental bursa), and transverse mesocolon. Positioned at the rear are the aorta, inferior vena cava, and portal vein. The head of the pancreas is disc-shaped and is enveloped by the inner curve formed by the initial three segments of the duodenum. It is connected to the duodenum through connective tissue. Positioned to the right of the superior mesenteric artery (SMA) and the superior mesenteric vein (SMV), the head's lower part extends as the uncinate process, resembling a hooked continuation of the inferomedial part of the head. This part is situated within the bend of the fourth part of the duodenum, and the SMV, and occasionally the SMA, run down on its front surface. The common bile duct is situated on the right side of the gastroduodenal artery, along the posterior wall of the initial segment of the duodenum. Often, the gastroduodenal artery passes either in front of or behind the upper part of the common bile duct [17]. The pancreas neck measures 1.5 to 2.0 cm in length. It is partially covered at the front by the pylorus and extends to the right until it reaches the point where the anterosuperior pancreaticoduodenal artery branches off from the gastroduodenal artery.

Behind the neck, the portal vein is formed by the merging of the superior mesenteric and splenic veins. Typically, there are no veins from the pancreas crossing in front of these vessels, but occasionally a few short veins may be present. It might be necessary to carefully lift the neck and tie off such veins if they exist to prevent bleeding, which could complicate the assessment of structures beneath the neck. The pancreatic body is situated on the left side of the superior mesenteric vessels. The front surface of the body is covered by peritoneum, contributing to the formation of the back portion of the lesser sac.

Positioned in front of the aorta, the body extends upwards towards the spleen. The splenic artery traces along the path of the body, forming a groove on its posterior and upper surface. As for the tail, it is closely located near the splenic hilum and is enclosed within the splenorenal ligament [18].

PROPER VASCULARIZATION OF THE PANCREAS

The blood supply to the pancreatic head and uncinate process comes from two sources: the superior pancreaticoduodenal artery (SPDA) and the inferior pancreaticoduodenal artery (IPDA). These arteries contribute to the formation of the anterior and posterior pancreaticoduodenal arcades [18]. The SPDA branches off from the gastroduodenal artery, which originates from the common hepatic artery (CHA), a branch of the coeliac trunk. On the other hand, the IPDA arises from the superior mesenteric artery (SMA). The body and tail of the pancreas are supplied by various branches of the splenic artery [19]. The neck acts as a transitional area between these two vascular systems, and venous drainage occurs through the portal system. The head and neck are predominantly drained by branches of the superior mesenteric vein (SMV) into the portal vein (PV). The rest of the pancreas is drained by delicate branches of the splenic vein. The splenic vein courses behind the body, eventually joining the SMV to form the PV behind the neck [18].

ANATOMICAL VARIANTS

Circumportal pancreas refers to a condition where pancreatic tissue surrounds the portal vein (PV) or superior mesenteric vein (SMV). This occurrence is observed in approximately

1.1–2.5% of individuals and is believed to stem from the abnormal merging of the dorsal and ventral pancreatic buds during development. While patients with this condition typically do not experience noticeable symptoms when planning surgical procedures, as it may elevate the likelihood of specific complications such as postoperative pancreatic fistula [18].

VARIATIONS OF PANCREATIC ARTERIAL VASCULARIZATION

The pancreas has a complex arterial supply, making it essential to pay special attention during arterial interventions for patients with conditions like acute pancreatitis and pancreatic carcinomas. Understanding the anatomy of pancreatic arteries and their territories is crucial for both surgical procedures and interpreting pancreatic angiography and cross-sectional imaging [20].

VARIATION OF THE MAJOR ARTERIES

Out of 162 celiac arteriograms, there were 15 cases where the right hepatic artery was replaced, 3 cases with a replaced common hepatic artery (CHA), and one case with a shared trunk of the celiac artery and superior mesenteric artery (SMA). In one instance, the gastroduodenal artery (GDA) originated from the left hepatic artery, while in another case, the gastroepiploic artery originated from the superior mesenteric artery [20].

VARIATION OF THE SUPERIOR PANCREATICODUODENAL ARTERIES

In all cases examined, the anterior superior pancreaticoduodenal artery (ASPD) consistently arose from the gastroduodenal artery (GDA). Additionally, in 14.2% of cases, a connecting branch was identified, forming an anastomosis between the ASPD and the dorsal pancreatic artery (DPA). Regarding the posterior superior pancreaticoduodenal artery (PSPD), in 96.1% of cases, it originated from the GDA, with some cases showing the presence of two PSPDA branches emerging from the GDA. However, alternative origins of PSPDA were observed, including cases where it arose from the common hepatic artery (CHA), both the GDA and CHA, or the proper hepatic artery. In rare instances, when the PSPDA was not visible in the celiac arteriogram, it was found to arise from the replaced right hepatic artery. An anastomotic branch connecting the PSPDA to the DPA was observed in 11.7% of cases. This study also found that the gastroduodenal artery (GDA), anterior superior pancreaticoduodenal (ASPD), and anterior inferior pancreaticoduodenal (AIPD) artery were present in all cases, while the posterior superior pancreaticoduodenal (PSPD) and posterior inferior pancreaticoduodenal (PIPD) artery were present in 93.34% of cases. Variations in the origin of PSPD, AIPD, and PIPD artery were observed, with anatomical and numerical variations noted in both anterior and posterior arches, with the posterior arch being absent in 20% of cases [20, 21]

VARIATION OF THE INFERIOR PANCREATICODUODENAL ARTERIES

The study of the inferior pancreaticoduodenal artery (IPDA) revealed its presence in 77.5% of cases, with various origins observed. Predominantly, the IPDA originated from the SMA, either independently or in conjunction with the 1st jejunal artery. Alternative sources included a shared trunk with the 1st jejunal artery, a replaced right hepatic artery, or a common trunk with the dorsal pancreatic artery (DP) from the SMA. In IPDA-absent cases, the anterior inferior pancreaticoduodenal artery (AIPDA) typically arose from the SMA or the 1st jejunal artery. Conversely, the posterior inferior pancreaticoduodenal artery (PIPDA) had diverse origins,

including the SMA, 1st jejunal artery, dorsal pancreatic artery, or replaced right hepatic artery. Understanding these variations is crucial for accurate preoperative planning and surgical management [20, 22].

SMALL PANCREATIC BRANCHES SUPPLYING PANCREATIC HEAD

The small branches that provide blood to the pancreatic head were observed in 19.8% of 226 cases. These branches originated from different arteries, including 19 cases from the gastroduodenal artery (GDA), 5 cases from the common hepatic artery (CHA), 2 cases from the right hepatic artery, 2 cases from the splenic artery (SPA), 1 case from both GDA and CHA, 1 case from a replaced right hepatic artery, 1 case from the superior mesenteric artery (SMA), and 1 case from both GDA and a replaced right hepatic artery [20].

VARIATION OF THE DORSAL PANCREATIC ARTERIES

The dorsal pancreatic artery is regarded as the largest vessel branching off from the splenic artery, occasionally reaching a size equivalent to one-third of the splenic artery. Its diameter varies significantly, spanning from 1 millimeter to almost 1 centimeter, with an average measurement typically falling between 1 and 3 millimeters [20, 23]. In set of angiograms, Bertelli E. observed the dorsal pancreatic artery as a relatively sizable vessel in numerous instances, irrespective of its source, occasionally reaching dimensions of up to 1 centimeter [23]. Other research show, that the dorsal pancreatic artery (DPA) was present in 79.6% of cases. Among these cases, 51.2% showed the DPA originating from the splenic artery (SPA). Other sources of the DPA included the common hepatic artery (CHA) in 22.2% of cases, the celiac artery in 5 cases, the gastroduodenal artery (GDA) in 2 cases, and the right inferior phrenic artery in 1 case. There was a unique case where two DPAs were identified, one arising from the SPA and another from the CHA [20]. Regarding numerical variations, identifying double dorsal pancreatic arteries with certainty proved challenging; we encountered this occurrence only once and never observed instances of triple or quadruple dorsal pancreatic arteries [23].

TRANSVERSE PANCREATIC ARTERIES

The transverse pancreatic artery (TPA), also referred to as the horizontal pancreatic artery, described by Popova, could be identified in angiographic studies of the celiac artery, particularly when combined with those of the superior mesenteric artery. However, due to the overlapping of vessels in the gastric and colic areas, the identification of this artery was often uncertain. To estimate its incidence, selective angiographies of the splenic artery, which were less numerous, were relied upon [24]. Under these conditions, the horizontal pancreatic artery could be identified in 25.93% of cases. This artery displayed variability in development and importance, with its diameter ranging from that of a very thin vessel to about one-third the caliber of the splenic artery. While it consistently originated directly from the splenic artery, in rare instances (3% of cases), a vessel resembling the horizontal pancreatic artery appeared as an early branch of the dorsal pancreatic artery [20,24]. This vessel seemed to function more as an anastomotic channel between pancreatic branches descending from the splenic artery than as an independent artery. It shared a longitudinal course close to the superior border of the pancreas with the horizontal pancreatic artery. However, when a regular pancreatica magna artery was identified in these cases, it was considered a second transverse pancreatic artery [24]. The horizontal pancreatic artery supplied variable portions of the distal pancreas, sometimes restricted to the tail of the pancreas or extending to part of the body. In most cases (70.6%), it coexisted with the inferior pancreatic artery and often joined it through several fine descending branches. Occasionally (17.6% of cases), it ended by anastomosing with the caudal pancreatic artery. In rare instances (11.7% of cases), it was the sole artery supplying the distal pancreas with descending branches that did not connect with visible inferior pancreatic arteries. In nearly all cases (88.23%), the horizontal pancreatic artery divided in a comb-like fashion, giving off several descending branches that distributed to the pancreas and/or ended by anastomosing with the inferior pancreatic artery [20, 24].

Anatomy and variations of pancreatic venous vascularization

PANCREATICODUODENAL VEINS

The blood outflow from the duodenum and pancreas can be conceptually split into two regions, ventral and dorsal. Each of these regions has two primary veins responsible for this drainage. For the ventral aspect: the anterior superior pancreaticoduodenal vein (ASPD) and the anterior inferior pancreaticoduodenal vein (AIPD), while the dorsal: posterior superior pancreaticduodenal vein (PSPD) and the posterior inferior pancreaticduodenal vein (PIPD) handle the back region [25].

ANTERIOR SUPERIOR PANCREATICODUODENAL VEIN

Was observed in all of the studied cases. It was single in 51% of cases, represented by two branches in 18%

of cases, and by multiple branches in 31% of cases. In most samples, it drained into the gastro-colic venous trunk (82%) and less frequently into the right gastro-epiploic vein (11%), the superior mesenteric vein (4%), or the portal-mesenteric junction (2%). We can distinguish two types: Type I veins (44%), are responsible for the venous drainage of the upper part of the duodenum, the superior duodenal angle, the proximal two-thirds of the descending part of the duodenum, and the adjacent pancreas. They connect at the middle of an arcade with the AIPD and primarily drain into the gastro-colic venous trunk (70%), but also into the right gastro-epiploic vein (20%), the superior mesenteric vein (5%), or the portal-mesenteric confluence (5%). Type II veins (56%), drain the same area as the Type I veins, but they also cover the entire descending duodenum, the inferior duodenal angle, and the proximal third of the horizontal part of the duodenum [25, 26].

ANTERIOR INFERIOR PANCREATICODUODENAL VEIN

This vein is responsible for the venous drainage of inferior ventral part of the right pancreas. Its unique characteristic is its bipolar ending, meaning it connects to the superior mesenteric vein either directly or through one of the jejunal veins. It was found in only 62% of cases. It anastomoses in some cases with the ASPD vein to form a ventral arch. It terminated in the superior mesenteric vein (35.7%), the gastro-colic venous trunk (35.7%), the first jejunal vein (17.9%), the second jejunal v. (3.6%), the right gastro-epiploic vein (3.6%) or the superior right colic vein (3.6%) [25,27].

POSTERIOR SUPERIOR PANCREATICDUODENAL VEIN

In almost all the cases studied (98%), the PSPD was present. The most consistent observations were related to the posterior superior pancreaticoduodenal vein, which was seen to drain into the portal vein. It is typically formed by the merging of three main tributaries. The anterosuperior tributary is responsible for draining the upper portion of the right pancreas's dorsal surface. In 80% of cases, this tributary was found to receive a vein that originated from the prevenous pancreas and wrapped around the right anterior edge of the portal vein. The posterolateral tributary follows the pars descendens of the duodenum to create the superior crus of the dorsal venous arcade (when present). The posteromedial tributary traverses diagonally across the dorsal surface of the right pancreas. In certain instances, it participated in the drainage of the retrovenous pancreas (draining the uncinate process in 14% of cases, the retromesenteric pancreas in 34% of cases, and the retroportal pancreas in 24% of cases). In some specimens (18% of cases), the PSPD consisted of two distinct veins with different termination points. In these instances, the vein that ended higher on the portal trunk was responsible for draining the prevenous pancreas [27,28].

POSTERIOR INFERIOR PANCREATICDUODENAL VEIN

It was identified in 60% of cases. It originated in the duodenopancreatic sulcus beneath the common bile duct and was responsible for draining blood from the lower portion of the gland's head and the adjacent part of the duodenum. Its path was either within the sulcus or over the surface of the gland. It moved towards the medial edge of the uncinate process, around which it coiled to reach its endpoint. It terminated in the first jejunal tributary, occasionally in conjunction with the anterior inferior pancreatico-duodenal vein. In one instance, the vein terminated in the right limb and connected with a colic vein as it emerged from the mesocolon [29].

DISCUSSION

The vascular anatomy of the liver and pancreas is characterized by considerable variability. This reflects their complex embryological development and topography within the upper abdominal cavity. This review discusses the diversity of the arterial and venous systems supplying these organs.

In the liver, alterations in the portal vein, hepatic veins, and hepatic arteries are common. The branching morphology of the portal vein, such as early segmental division and the presence of additional or replaced hepatic arteries, is associated with the dynamic remodeling of the vitelloabdominal venous network during embryogenesis. Similarly, the hepatic venous system is characterized by a wide spectrum of configurations, ranging from additional inferior hepatic veins to variable vascularization patterns in the posterior segments of the right liver [30, 31].

The pancreas has a more complex vascular architecture, characterized by dense arterial arcades and highly variable venous outflow. The arterial vascularization is dominated by numerous anastomoses connecting the celiac trunk to the superior mesenteric artery, resulting in a greater diversity of pancreaticoduodenal and dorsal pancreatic artery arcades [32]. The venous system reflects this complexity, with numerous drainage patterns to the portal and superior mesenteric veins and frequent connections between the anterior and posterior pancreaticoduodenal veins [33, 34].

The literature reviews analyzed revealed a lack of a universal classification system for variants of pancreatic vascularization, in contrast to well-described patterns of hepatic arterial anatomy. Although the reported prevalence rates vary significantly among available studies, the review considered the most frequently recurring findings. However, this reflects differences in methodology, imaging techniques, population characteristics, and sample size. While cadaveric studies, angiographic series, and modern cross-sectional imaging provide complementary perspectives, each approach carries its own limitations.

CONCLUSIONS

The collected data emphasize that the variability of hepatic and pancreatic vessels should be considered an anatomical feature, not an exception. Further work on standardized nomenclature, large-scale imaging studies, and comprehensive anatomical atlases are essential to deepen our understanding of hepatopancreatic vascular anatomy. A thorough understanding of these vascular anatomy is fundamental in many medical disciplines, particularly in hepatobiliary and pancreatic surgery, where anatomical complexity directly impacts procedural planning and surgical strategy.

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CONFLICT OF INTEREST

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REVIEW ARTICLE

CONTENTS

Biomaterials in cartilage damage

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ABSTRACT

Aim: Cartilage tissue degradation is a common symptom of diseases affecting the musculoskeletal system. Impairment of its function can occur due to numerous factors, both external and internal. Thanks to advances in imaging techniques, identifying pathologies in cartilage tissue is becoming increasingly common, leading to a search for optimal treatment methods. Human cartilage has a limited capacity for self-repair. Treatments such as transplants have many limitations, which is why biocompatible materials are becoming increasingly popular. This article presents selected biomaterials that may be useful in the treatment of cartilage pathologies. Current research on the use of biomaterials in cartilage regeneration was analyzed.

Materials and Methods: The research material consisted of scientific publications describing the use of natural and synthetic scaffolds in animal models and clinical trials. Particular attention was paid to gelatin, silk fibroin, polylactic acid, polycaprolactone, poly(lactic-co-glycolic acid), and commercial biomimetic scaffolds. Methods included analysis of mechanical properties, biocompatibility, and the ability to support chondrogenesis.

Conclusions: The study results indicate that appropriately modified biomaterials can effectively support cartilage regeneration and improve its structure and function. Further research is needed to improve the treatment of cartilage injuries and diseases, and to optimize biomaterials used in cartilage tissue engineering.

KEY WORDS: cartilage injuries, cartilage tissue engineering, tissue scaffolds, biomimetic materials, biocompatible materials

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INTRODUCTION

There are three types of cartilage tissue in the human body: hyaline, fibrous, and elastic. Cartilage tissue provides support and cushioning, enabling smooth movement of bones within joints, shaping human features (e.g., the nose), and providing support, such as reinforcement of the trachea. The proper functioning of cartilage depends on the composition and structure of its extracellular matrix [1]. Deterioration of cartilage tissue and thus impairment of its function can occur due to factors such as aging, repetitive stress during daily activities, degenerative disease, rheumatoid arthritis, and genetic factors [2]. Thanks to advances in imaging techniques and the widespread availability of magnetic resonance imaging, the identification of cartilage tissue pathologies is becoming increasingly common. Unfortunately, human cartilage has limited self-repair capacity [3]. Interventions such as allografts, autografts, and bone marrow stimulation also have numerous limitations. Allografts are at high risk of cell death during storage, and bone marrow stimulation yields cartilage of much lower quality [4]. These limitations have contributed to advances in cartilage tissue engineering. Thanks to this field of science, we can create cartilage-like structures that mimic the biochemical and mechanical properties of natural cartilage [5]. Both natural and synthetic materials have been studied for use in cartilage tissue engineering. Studies have shown that natural polymers (such as gelatin and fibrin) are bioactive and biocompatible. In contrast, synthetic polymers (such as poly(lactic-co-glycolic acid), polycaprolactone, and polylactic acid) are amenable to modification of their mechanical properties and degradation rate [6]. Furthermore, in recent years, commercialized biomimetic scaffolds designed to achieve cartilage regeneration have also appeared on the market. These include MaioRegen, Agili-C, and TruFit [7].

AIM

This article presents selected biomaterials that may be useful for the treatment of cartilage pathologies.

MATERIALS AND METHODS

To create this article, databases such as PubMed and Google Scholar using keyword combinations: "cartilage defects," "natural biomaterials," "synthetic biomaterials," "commercialized biomimetic scaffolds," and "cartilage tissue engineering," as well as "silk fibroin," "gelatin," "polylactic acid," "polycaprolactone," and poly(lactic-co-glycolic acid)" was searched. Ultimately, we included 39 articles, selected based on their high relevance and innovative nature in the context of biomaterials for cartilage repair.

REVIEW

BIOMATERIALS USED IN THE TREATMENT OF CARTILAGE DAMAGE

The basic classification of biomaterials distinguishes between natural and synthetic biomaterials. Plants and animals have become the source of natural biomaterials, while synthetic biomaterials are produced in laboratory conditions [8].

NATURAL BIOMATERIALS

The basic groups of natural biomaterials include glycosaminoglycans (e.g., hyaluronic acid), polysaccharides, proteins, and extracellular matrix materials (e.g., eggshell matrix). Their advantages in the context of tissue engineering include low production costs and good availability, as well as biocompatibility and biodegradability [8]. The basic classification of biomaterials distinguishes between natural and synthetic biomaterials. Plants and animals have become the source of natural biomaterials, while synthetic biomaterials are produced in laboratory conditions [8].

SILK FIBROIN

Silk fibroin is a protein isolated from silk that is rich in glycine, alanine, and serine [9]. Along with other compounds such as collagen and glycosaminoglycans, silk fibroin forms the extracellular matrix of chondrocytes. It plays a crucial role in the maturation and differentiation of these cells and is therefore essential for maintaining the proper structure and function of cartilage tissue [10].

The advantages of silk fibroin in the context of cartilage tissue engineering include high biocompatibility, controlled biodegradability, and a very low risk of immunological reactions. This protein can be processed into a variety of forms, including solutions, powders, fibers, films, sponges, and hydrogels. These forms can be obtained using techniques such as electrospinning, spin coating, and freeze-drying [11]. By combining silk fibroin with other polymers, we can obtain composite scaffolds that can effectively enhance responses such as cell differentiation, proliferation, and adhesion [8]. For example, combining silk fibroin with glycidyl methacrylate gel demonstrates high cellular biocompatibility in vitro and provides a suitable environment for chondrocyte growth and survival. Furthermore, adding growth factors (e.g., insulin-like growth factor) to silk fibroin-based scaffolds improves chondrogenic outcomes and provides an alternative to autologous and allogeneic cartilage implants [12].

GELATIN

Gelatin is a major component of connective tissue, formed by the breakdown of the collagen triple helix [13]. It is a compound that stimulates the formation of the extracellular matrix. The biocompatibility and biodegradability of gelatin, as well as its affordability and ease of production, have made it a widely used compound in tissue engineering [14]. A study led by Maihemuti showed that 3D-printed scaffolds made from gelatin derived from cold-water fish are promising for repairing cartilage defects in the knee joints of mice [15]. Furthermore, the creation of composite scaffolds combining gelatin with other natural or synthetic polymers has also been shown to be effective in cartilage tissue engineering [16]. For example, chemically modifying gelatin by reacting it with methacrylic anhydride increases its thermal stability while maintaining its natural biocompatibility [17]. This fact has been confirmed by a study by Visser et al., which demonstrated that adding methacryloyl gelatin to equine cartilage matrix particles yields a composite with stiffness and elasticity very similar to those of natural cartilage tissue [18].

SYNTHETIC BIOMATERIALS

In orthopedic applications, there are three basic categories of synthetic biomaterials: metals (characterized by high resistance to deformation), ceramics (characterized by chemical inertness and low thermal conductivity), and biodegradable and non-biodegradable polymers (low density and good processability) [8].

POLYLACTIC ACID

Polylactic acid is a biodegradable, non-toxic plastic. This polymer is currently produced primarily from a non-renew-

able raw material, such as crude oil. An alternative route to its production is through the biotechnology industry, using lactic acid derived from renewable resources such as sugarcane. In addition to its biodegradability and non-toxicity, its advantages in tissue engineering include biocompatibility, thermoplasticity, and good moldability [19].

An in vitro study conducted by Liang et al. demonstrated that nanofibers produced by grafting polylactic acid chains onto lignin can positively influence chondrogenic differentiation, thereby facilitating the regeneration of damaged cartilage. They found that lignin-polylactic acid-containing scaffolds had excellent antioxidant properties and promoted favorable expression of cartilage-specific genes. Additionally, they maintained a balance with the expression of late-stage chondrogenesis genes [20].

POLYCAPROLACTONE

Polycaprolactone is a biodegradable aliphatic polyester that is thermally stable at temperatures above 300 degrees Celsius. It is widely used in medicine due to its properties, including good solubility, long degradation time, and low melting point. Polycaprolactone has been approved by the Food and Drug Administration and hailed as an extremely promising compound in tissue engineering due to its thermal stability [21]. In their study, Liu Y. and co-investigators fabricated porous scaffolds from poly(glycerol sebacate)/polycaprolactone using the salting-out technique. This experiments demonstrated that articular chondrocytes successfully adhered and proliferated on these scaffolds during short-term culture. Furthermore, bone marrow-derived stem cells differentiated into chondrocyte-like cells on the same scaffolds. This demonstrated that poly(glycerol sebacate)/polycaprolactone scaffolds are promising for cartilage tissue regeneration; however, further in vivo studies are needed [22].

POLY(LACTIC-CO-GLYCOLIC ACID)

Poly(lactic-co-glycolic acid) is a popular biodegradable polymer. Both the Food and Drug Administration and the European Medicines Agency have approved this compound as safe and effective for various medical applications, including orthopedic stabilization. Its hydrolysis produces lactic and glycolic acid monomers, which are then metabolized via the Krebs cycle. Consequently, it is characterized by extremely low toxicity [23].

Poly(lactic-co-glycolic acid) has many advantages for cartilage tissue engineering. These include controlled biodegradability and a near-complete lack of immunogenicity. This polymer supports cell differentiation and viability, thus offering potential as a scaffold material for the regeneration of cartilage pathologies [24]. A study led by Morille demonstrated that poly(lactic-co-glycolic acid)-based scaffolds can provide an optimal environment for mesenchymal stem cell differentiation into chondrocytes [25]. Furthermore, Toyokawe and co-investigators demonstrated, using a rabbit model, that a cannulated poly(lactic-co-glycolic acid) scaffold can regenerate and repair full-thickness osteochondral defects, thus demonstrating excellent predisposition for regenerating damaged cartilage [26].

COMMERCIALIZED BIOMIMETIC SCAFFOLDS

Commercialized biomimetic scaffolds include MaioRegen, Agili-C, and TruFit. These scaffolds were developed to promote cartilage regeneration and have shown promising results, but are not yet widely used for this purpose. Currently, these biomaterials require further and more extensive research due to discrepancies in radiological findings and the low quality of available studies [7].

MAIOREGEN

MaioRegen (Finceramica, Italy) is the most thoroughly studied biomimetic multilayer scaffold designed for in situ cartilage regeneration. This nanostructured implant consists of varying proportions of collagen and hydroxyapatite arranged in three distinct layers. The first layer, which recreates smooth cartilage, is composed entirely of type 1 collagen, the intermediate layer is composed of 3/5 type 1 collagen and 2/5 hydroxyapatite, and the deepest layer is composed of 30% type 1 collagen and 70% hydroxyapatite [27].

In their study, Kon and co-investigators examined 100 active athletes with symptomatic changes in the cartilage and subchondral layer of the knee joint. Some patients were treated with MaioRegen, while others received microfracture. After a two-year follow-up period, therapy using the biomimetic multilayer MaioRegen scaffold yielded significantly better results in the treatment of osteochondral lesions [28]. Furthermore, the simultaneous use of MaioRegen and bone marrow stimulation results in the scaffolds being filled with cytokines and stem cells from the patient's own bone marrow, stimulating cartilage regeneration directly at the site of injury [29].

AGILI-C

Agili-C (CartiHeal, Israel) is an acellular aragonite scaffold. It was designed to replicate the natural structure

and function of joints. Its action aims to stimulate cartilage and subchondral regeneration and operates through a dual mechanism. The first mechanism involves facilitating the adhesion and differentiation of bone marrow stem cells into chondrocytes. The second mechanism involves stimulating chondrocyte migration and proliferation from surrounding cartilage tissue and their deposition into the extracellular matrix [27].

Chubinskaya conducted a study demonstrating that Agili-C scaffolds supported cartilage regeneration and repair in human knee and ankle joints. The most important finding of the study was that acellular Agili-C scaffolds effectively attracted host chondrocytes and increased their cartilage potential [30].

TRUFIT

The TruFit insert (Smith & Nephew, USA) is an acellular synthetic scaffold composed of polylactide and co-glycolide [27]. Cartilage regeneration using the commercialized biomimetic TruFit scaffold was proposed to involve the infiltration of growth factors and bone marrow-derived cells into the insert, thereby facilitating integration and repair of damaged cartilage [31]. Recent studies recommended discontinuing the use of the TruFit insert due to poor graft integration and lack of significant clinical improvement [27]. TruFit was withdrawn from sale due to its low efficacy compared to other standard treatments for cartilage defects [32].

DISCUSSION

Despite medical advances, treating cartilage damage remains a significant challenge. There is a constant need to develop new methods that can effectively and fully regenerate cartilage. More and more research is being conducted in this direction, and biomaterials and cartilage tissue engineering are proving to be innovative.

Natural biomaterials offer several advantages over synthetic biomaterials in tissue engineering. They include mechanical adaptability, bioactivity that allows them to mimic the naturally occurring extracellular matrix, and numerous active sites [33]. However, their use also presents significant limitations. Challenges that must be considered when using natural biomaterials include their temperature sensitivity, difficult processing, and sometimes very complex chemical structure [34]. Among the most important natural biomaterials are gelatin and silk fibroin [6]. In their study, Maihemuti and colleagues developed gelatin scaffolds from cold-water fish skin, providing a biocompatible, low-immunogenic alternative to porcine gelatin. Using a 3D printer, they fabricated various types of scaffolds, which they used to effectively regenerate cartilage defects in the knee joint in a mouse model [23]. In their study, Li and colleagues developed a hydrogel composed of silk fibroin and carboxymethyl chitosan, which they tested in rabbit and mouse models. They demonstrated that the hydrogel supported chondrogenesis in rabbit joints while not triggering an immune response in mice [35].

The advantage of synthetic biomaterials over natural ones is that they can be modified to achieve a wider range of mechanical and chemical properties. Because they are produced under controlled laboratory conditions, we can predict their mechanical and physical properties and control material contamination. However, their greatest limitation in the context of tissue engineering is their limited biocompatibility [36]. In their study, Liang R. and co-investigators grafted polylactic acid chains of varying lengths onto lignin. They obtained copolymers that differed in the proportions of polylactic acid to lignin and their molecular weight. Using the resulting copolymers, they created nanofibrous scaffolds that served as a platform supporting cell growth and mimicking the environment of the cartilage matrix for cartilage regeneration. Ultimately, it was found that scaffolds containing lignin-polylactic acid 40 have a positive effect on the regeneration of damaged cartilage and may support the maintenance of balanced expression of the Col10al gene, which is responsible for the late phase of chondrogenesis [20]. Liu Y., in turn, conducted studies in which combining poly(glycerol sebacate) with polycaprolactone resulted in scaffolds with longer degradation times and increased stiffness. Furthermore, poly(glycerol sebacate)/polycaprolactone scaffolds demonstrated very good cytocompatibility with both bone marrow-derived stem cells and joint chondrocytes in vitro. In the study, bone marrow-derived stem cells demonstrated chondrogenic potential comparable to joint chondrocytes [22]. Toyokawa and co-investigators conducted a study demonstrating that poly(lactic-co-glycolic acid) scaffolds effectively repaired osteochondral defects measuring 5 mm in diameter in a rabbit model. Their study included a treatment group whose defects were treated with a cylindrical, cannulated poly(lactic-co-glycolic acid) scaffold and a control group (i.e., an untreated group). In the study group, fibrous tissue appeared on the scaffold surface as early as the second week after the procedure. Cartilage gradually formed on the joint surface, and bone was rebuilt in the subchondral layer. The regenerated cartilage remained intact until 24 weeks after surgery. In the control group, the untreated defects filled with hematoma as early as the second week, followed by cartilage and bone formation. However, the regenerated cartilage in the untreated defects failed to prop-

erly organize and exhibited an uneven joint surface. Histological studies showed that the groups treated with poly(lactic-co-glycolic acid) scaffolds achieved significantly better results than the control group at 12 and 24 weeks after surgery [26].

Commercialized biomimetic scaffolds designed for cartilage regeneration include MaioRegen, Agili-C, and TruFit [7]. They are relatively easy to use and offer advantages, such as a single-step procedure. However, to be widely used, these scaffolds require further research and more thorough evaluation of their efficacy [37]. Brix M conducted a study evaluating MaioRegen's ability to regenerate single osteochondral lesions ≥1.5 cm^2 in diameter on the femoral condyle. He enrolled eight patients in his prospective study. He assessed the repair capacity of the MaioRegen scaffold at intervals of 6, 12, 18, and 24 months using magnetic resonance imaging and semi-quantitative morphological analyses. Initially, his study demonstrated that the MaioRegen scaffold effectively filled the osteochondral defect. In seven of eight patients, complete integration of the scaffold at the junction was observed. However, 18 months after surgery, reduced quality of the repaired cartilage tissue was observed [38]. A study by Chubinskaya S et al. confirmed that the Agili-C scaffold supports cartilage regeneration and may provide a single-stage solution for the treatment of full-thickness cartilage defects. The study involved harvesting fresh human cartilage tissue from cadavers of different sexes and ages and then culturing it for 60 days with the Agili-C scaffold. The researchers found that chondrocytes migrated from a post-mortem cartilage explant into the porous scaffold, filling its entire volume with a newly formed extracellular matrix rich in type II collagen and aggrecan [30]. Regarding the effectiveness of the TruFit scaffold for cartilage repair, the available evidence is inconsistent. TruFit scaffolds were examined by MRI by Bedi et al., who analyzed 26 cases over 6 to 39 months. The consistent pattern of integration was observed among them. Initially, MRI results deteriorated between 6 and 12 months, but then improved with longer follow-up. In 90% of cases, TruFit scaffold integration was almost complete after 16 months. Barbar and Dockery, using computed tomography, analyzed 9 cases of TruFit scaffold use and concluded that the scaffold did not integrate successfully in any of the cases. Similarly, Dhollander and colleagues concluded that TruFit scaffold implantation was incomplete after 1 year, suggesting the need for a longer follow-up period [39]. Due to equivocal clinical results and lower efficacy compared to other treatments, TruFit was withdrawn from the market [32].

CONCLUSIONS

Further research is needed to improve the treatment of cartilage injuries and diseases, as well as to optimize the biomaterials used in cartilage tissue engineering. Increasing the number of long-term studies seems particularly important. This will enable the assessment of efficacy, durability, and safety, as well as the identification of the best therapeutic options for patients. Collaboration between clinicians, scientists, and industry representatives is crucial here. By deepening our knowledge of cartilage biology and tissue engineering, we can improve treatment and enhance the quality of life of patients with cartilage disorders.

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REVIEW ARTICLE

CONTENTS

Collagen supplementation and bone health – a narrative review

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ABSTRACT

Osteoporosis is a known skeletal chronic disease which decreases bone mass, damages bone microarchitecture and increases the risk of fragility fractures. Non pharmacological interventions, such as nutritional changes play a significant supportive role in bone health maintenance along with pharmacological treatments. Collagen is a key organic component of the bone matrix, which subjects it to intensive research as a potential dietary supplement, especially in individuals with low bone mass. The review aims to critically evaluate and summarize novel studies between 2020 and 2025 that described the significance of oral collagen supplementation, especially in individuals with poor bone health. A narrative review of human studies published from 2020 to 2025 was conducted. Inclusion criteria included observational studies, randomized controlled trials, systematic reviews, meta-analyses, and clinical guidelines focusing on the evaluation of oral collagen peptide or hydrolyzed collagen supplementation and bone related outcomes. Preclinical and animal studies were excluded. The prevailing evidence suggests that oral collagen has a beneficial supportive effect on bone health, particularly in individuals with early bone loss. Due to the heterogeneous nature of currently available literature and limited studies on fracture outcomes, collagen supplementation can not be considered as a replacement therapy but rather an adjunctive treatment to established osteoporosis regimes.

KEY WORDS: bone density, collagen peptides, dietary supplements, osteopenia, postmenopause

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INTRODUCTION

Osteoporosis is a known skeletal chronic disease which decreases bone mass, damages bone microarchitecture and increases the risk of fragility fractures [1]. Osteoporotic fractures are a leading cause of disability, morbidity and increased mortality rate - especially among the elderly population. This generates immense economic burden on healthcare systems worldwide [2]. With the current aging population, incidences of osteoporosis and osteopenia are expected to increase further which highlights the urgency and importance of effective therapeutic and preventive strategies. Current clinical guidelines emphasize that management of osteoporosis should not be solely based on pharmacological interventions, but healthcare workers should rather have a comprehensive approach inclusive of non pharmacological treatment such as fall prevention, physical activity, and appropriate supplementation [3,4]. Optimal intake of vitamin D, calcium and dietary protein are key determinants of bone health. However, there is a growing interest in the role of other nutritional components that influence bone health including organic compounds that play a key role in maintaining the structure of bone matrix.

Bone integrity is not solely determined by the bone mineral density (BMD) but rather by their overall properties which include microarchitecture, material content of the bone tissue, turnover rate and microdamage accumulation [1]. Approximately 90% of organic bone matrix is composed of Type I collagen which plays a key role in providing elasticity and tensile strength while serving as a scaffold for the hydroxyapatite deposition.

Age-related disorders of collagen synthesis, its post-translational modifications and cross-link forma-

tion adversely affect the mechanical properties of bones which increase the risk of fractures, regardless of bone mineral density [2]. Oral forms of hydrolyzed and specific bioactive collagen peptides are increasingly being recommended as vital supplementation to enhance bone and muscle health. Collagen supplements have been used as known agents to improve skin and hair conditions for a known period of time however the impact of collagen on bone health and the prevention of osteoporosis is a subject of ongoing research [5, 6].

AIM

The narrative review aims to critically evaluate the effects of collagen supplementation on bone mineral density, bone turnover markers and related bone health outcomes in the adult population with marked emphasis on individuals with osteopenia and postmenopausal women based on clinical evidence published between 2020 and 2025.

MATERIALS AND METHODS

This narrative review was conducted based on a structured evaluation of studies involving human participants published between January 2020 and 2025. Publications meeting the inclusion criteria included randomized controlled trials, observational studies, systematic reviews, meta-analyses, and clinical practice guidelines assessing oral supplementation with collagen peptides or hydrolyzed collagen on bone parameters.

Major biomedical databases and key references were searched to identify publications. Studies involving adult participants were included whereas animal and in vitro studies were excluded. As the current review is narrative in nature, emphasis was placed on critical interpretation of key study methodology, population characteristics, and significant clinical evidence.

REVIEW AND DISCUSSION

BIOLOGICAL RATIONALE FOR COLLAGEN SUPPLEMENTATION IN BONE HEALTH

Bone tissue is continuously remodelled by a coordinated process of resorption brought upon by osteoclasts and formation of new bone material arising from osteoblasts. Collagen type I is an essential component of the bone matrix contributing to its strength and resistance to crack propagation. Disturbances in the collagen structure may lead to increased bone fragility, despite the preserved mineral content [2]. Dietary collagen supplementation provides key amino acids such as proline and glycine along with bioactive peptides which influence bone metabolism. Research shows that collagen-derived peptides can influence osteoblast differentiation and extracellular matrix, thereby contributing to the strengthening of bone structure [7-9]. Delving into the mechanisms - collagen supplementation should be treated as a supportive building substrate intervention rather than a direct antiresorptive or anabolic therapy.

RANDOMIZED CONTROLLED TRIALS IN POSTMENOPAUSAL WOMEN WITH OSTEOPENIA

Most clinically relevant conclusions regarding collagen supplementation can be drawn from randomized controlled trials carried out in postmenopausal women with osteopenia. A controlled trial conducted by Argyrou and colleagues examined the effectiveness of vitamin D supplementation in monotherapy and taking vitamin D with 5g/day collagen-derived peptides for a period of 12 months. Women taking vitamin D concomitantly with collagen peptides showed significantly favourable changes in bone turnover parameters, suggesting a modulatory effect on the bone remodelling process [10].

Similarly, Lampropoulou-Adamidou and colleagues expanded the scope of the study by including the assessment of bone mineral density at both sites using dual-energy X-ray absorptiometry, as well as the evaluation of volumetric BMD and bone geometry using peripheral quantitative computed tomography. A minor but statistically significant improvement in BMD and geometric volume parameters was seen in the group supplemented with vitamin D and collagen combined. This suggests an improvement in bone quality that could not be determined by DXA testing alone [11].

These results are clinically significant as bone geometry and volumetric density play a key role in shaping bone strength. However, these studies had their limitations contributed by a small sample size, combined supplementation (collagen plus calcium and vitamin D) and the absence of fracture outcomes.

OBSERVATIONAL AND LONG-TERM EVIDENCE

Long-term observations obtained from clinical studies demonstrate that collagen exerts a sustained effect on bone structure. Zdzieblik et al. found that postmenopausal women who continued supplements containing particular bioactive collagen peptides maintained or gradually improved their BMD over the course of a

long-term follow-up [12]. Although the study lacked a control group and was of observational nature, findings suggest that prolonged collagen supplementation is feasible and might be a contributing factor of sustained skeletal health.

SYSTEMATIC REVIEWS AND META-ANALYSES

Recent systematic reviews and meta-analyses have enabled the synthesis of the growing body of evidence regarding the effects of collagen supplementation on musculoskeletal health. Based on meta-analysis published 2025, collagen peptide supplementation was linked to modest yet statistically significant increases in bone mineral density and markers of bone turnover. This was particularly seen in individuals suffering from osteopenia and in studies evaluating vitamin D and collagen supplementation combined [5].

In a similar manner, a comprehensive systematic review investigated how the effects of collagen type I hydrolysate supplementation affect bone, muscle, and joint health.The strength of the authors' final clinical conclusions was limited by the notable variation in collagen formulation, dosages, duration of intervention, and outcome measures across studies, despite the fact that they found encouraging signals regarding improved bone metabolism [13].

COLLAGEN SUPPLEMENTATION COMBINED WITH PHYSICAL ACTIVITY

Collagen supplementation in combination with structured exercise regimens has been the subject of multiple randomized clinical trials in recent years. Collagen supplementation combined with resistance training or weight-bearing exercise promotes positive musculoskeletal adaptations, such as enhanced tendon properties, muscle strength, and functional performance, according to studies done on athletes and physically active people [14-17]. Given the strong correlation between muscle strength, fall risk, and fracture incidence, the results of these studies are clinically relevant even though they were not specifically designed to evaluate effects on osteoporosis. These findings lend credence to the idea that collagen supplementation bears the potency to depict positive outcomes when combined with appropriate mechanical loading as part of a broader lifestyle intervention.

SAFETY AND CLINICAL CONTEXT

Oral collagen supplementation is generally well tolerated, according to both observational and randomized studies. Serious treatment-related complications are rare, whereas mild gastrointestinal symptoms are the most common side effect of collagen supplementation [12,13]. Collagen dosages in bone health studies usually fall between 5 and 10 g daily. Based on the latest guidelines, it is not recommended to replace pharmacological treatment with oral collagen supplements in patients at high risk of fractures and injuries [3,4]. Rather collagen supplementation should be considered as supportive therapy within a comprehensive approach to osteoporosis treatment which includes calcium and Vitamin D optimization, adequate protein intake and evidence based pharmacotherapy [18, 19].

CONCLUSIONS

Between 2020 and 2025, oral collagen supplementation was repeatedly studied in the context of bone metabolism, with most studies reporting only modest benefits. Some improvements in bone mineral density were observed, particularly in postmenopausal women with osteopenia . The uncertain findings reported in meta-analyses and systematic reviews highlight the need for broader, carefully planned randomized trials that focus specifically on fracture-related outcomes and collagen supplementation. Without further concrete studies based in clinical settings the results rather stay inconclusive. Nevertheless, collagen supplements pose no harm and should be considered as an adjunct therapy for osteoporosis, but they do not hold the potency to replace established medical treatments. It's essential to follow established clinical guidelines with the treatment protocols that have been well-researched and continue to provide effective outcomes in terms of bone health.

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REVIEW ARTICLE

CONTENTS

Role of stem cells in articular cartilage repair – a narrative review

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ABSTRACT

Articular cartilage injuries pose a major clinical obstacle due to their inability to regenerate contributed by cartilages' intrinsic properties and close association with osteoarthritis and progressive joint degeneration. Cartilage damage may be a consequence of acute trauma, repeated mechanical overload or age-related degenerative processes which often leads to chronic pain, joint dysfunction and a deterioration in the quality of life of patients.Established treatments such as; conservative management, intra-articular drug administrations and surgical cartilage repair typically provide relief. However, it's important to note that these treatments rarely lead to complete, permanent regeneration of natural hyaline cartilage. Recently, regenerative medicine has been paying significant attention to stem cell therapies. It aims to support cartilage repair while simultaneously impacting the intra-articular environment. It's safe to say that these approaches are increasingly being considered as potential therapeutic methods. Between the various cell populations, mesenchymal cells have gained particular attention due to their ability to promote chondrogenic differentiation, immunomodulatory properties, and paracrine effects.There is growing evidence suggesting that stem cells effects can be mediated not only by direct source replacement but are also contributed by the secretion of bioactive factors that influence physical processes, cartilage metabolism, and endogenous repair mechanisms. This narrative review aims to concisely summarize and critically evaluate novel evidence and scientific data on the biological repair mechanisms, clinical outcomes and safety assessment of stem cell-based therapies used to treat articular cartilage repair.

KEY WORDS: regenerative medicine, knee osteoarthritis, hyaline cartilage

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INTRODUCTION

Joint cartilage is a highly specialized connective tissue that supports the load-bearing system within synovial joints and enables resistance-free joint movement and efficient transfer [1]. The extracellular matrix of articular cartilage is characterized primarily by a high content of type II collagen and proteoglycans. This combination allows the joint cartilage to withstand significant mechanical loads without losing its ability to move smoothly within the joint. However, the low number of chondrocytes and the lack of blood vessels, nerves, and lymphatics significantly hinder the tissue's natural ability to heal itself after an injury [2]. As a result, cartilage defects, both focal and diffuse, tend to persist and may gradually worsen over time. These changes most often occur as a result of acute joint trauma, repeated mechanical overload or age-related degenerative processes. [1,3]. In the case of inability of effective biological repair, damaged cartilage may lead to deterioration of the joint surfaces, changes in subchondral bone and ultimately contribute to progression of osteoarthritis. This disease process is linked to chronic pain, impaired function, reduced quality of life and pose a major socioeconomic burden[3]. Over the past few decades, various surgical methods for cartilage repair have been developed in an attempt to restore the integrity of the joint surface. These methods include bone marrow stimulation treatments, osteochondral implants, and cell-based therapies such as autologous chondrocyte implantation.

Although these methods may provide better clinical outcomes in short and mid-term in some patients, long-term treatment outcomes are variable and the quality of the resulting regenerative tissue often does not provide optimum outcomes.Following injury, cartilage repair commonly results in the formation of fibrocartilage, which lacks the biomechanical properties and longevity

of native hyaline cartilage [1, 2, 4]. Consequently, conventional therapies frequently fail to achieve complete functional restoration. These limitations underscore the ongoing search for advanced regenerative strategies to improve cartilage repair. As a result, biological therapies are becoming a focus of interest and more spatialized than classical approaches, particularly ones based on modifying the intra-articular environment and promoting endogenous repair mechanisms. A rapidly emerging area of biomedical research, stem cell-based therapies show great promise for treatment. They are a promising approach for the treatment of many conditions because they provide distinct advantages over traditional methods due to their simultaneous trophic, immunomodulatory, and regenerative effects. Better understanding the biological basis and clinical potential of such therapies is key for their application in contemporary cartilage repair regimens.

AIM

This narrative review aims to critically evaluate and summarize the role of stem cells in promoting articular cartilage health post injury with particular emphasis on biological mechanisms of action, sources of stem cells, treatment outcomes and associated safety considerations published in articles between 2020 to 2025 [5].

MATERIALS AND METHODS

The current narrative review is based on analysis of peer-reviewed publications made between January 2020 and December 2025. Publications included in the review were randomized controlled trials, systematic reviews, meta-analyses and selected narrative reviews evaluating stem-cell-based therapies for cartilage repair and knee osteoarthritis[6]. Literature search was performed using major biomedical databases such as PubMed and reference lists of relevant articles were manually screened to confirm eligibility. Publications based on animal findings were excluded from the review. As the review is narrative in nature, no formal risk of bias was assessed.

REVIEW AND DISCUSSION

BIOLOGICAL MECHANISMS OF STEM CELL–MEDIATED CARTILAGE REPAIR

The contribution of mesenchymal stem cells (MSCs) in cartilage repair involves several related and interdependent mechanisms, directly by chondrogenic differentiation and indirectly through paracrine signaling [1,7]. Although in preliminary regenerative strategies, much emphasis was placed on the ability of MSCs to differentiate into a chondrocyte-like cell, novel studies help us understand that the main therapeutic effect of these cells is due to bioactive molecules secretions rather than direct structural replacement of tissue[8,9]. The secreted factors include cytokines, growth factors, and extracellular vesicles which collectively influence inflammatory processes, regulate cartilage metabolism and influence cell activity in the joint. In the osteoarthritic joint environment, paracrine signaling derived from mesenchymal stem cells exerts anti-inflammatory and immunomodulatory effects. This includes downregulating proinflammatory cytokine expression and promoting an anti-inflammatory macrophage phenotype [8].

Furthermore, MSCs may stimulate anabolic pathways within the cartilage and suppress catabolic processes associated with matrix degradation [9]. These mechanisms offer a commendable biological explanation for the common phenomenon of significant clinical improvement with not consistently structural cartilage regeneration which is demonstrated in imaging studies [10].

SOURCES OF MESENCHYMAL STEM CELLS AND THEIR CHONDROGENIC POTENTIAL

Mesenchymal stem cells can be isolated from various tissue sources, however, bone marrow and adipose tissue are the most common sources of mesenchymal stem cells in clinical practice [11]. Bone marrow derived mesenchymal stem cells demonstrate a high capacity for chondrogenic differentiation not only in vitro but also in vivo; however, the clinical use of these cells is limited due to the invasiveness of sampling procedures and relatively low cell yield [12]. On the contrary, adipose-derived stem cells and the stromal vascular fraction have practical advantages, including cell abundance, low donor-site morbidity and ease of access [13].

Recent clinical trials indicate that populations of adipose-derived cells carry the potential to produce similar efficacy in pain reduction and function as bone marrow derived MSCs for patients with cartilage defects and knee osteoarthritis [14,15]. Nevertheless, methods of administration, heterogeneous cell processing and dosing strategies make direct comparison of results across studies difficult and underscore the need to develop standardized treatment protocols.

CLINICAL OUTCOMES OF STEM CELL THERAPIES IN ARTICULAR CARTILAGE LESIONS AND KNEE OSTEOARTHRITIS

Numerous randomized controlled trials and meta-analyses have investigated the clinical efficacy of stem cell–

based therapies in individuals with knee osteoarthritis. In comparison with placebo, hyaluronic acid, or corticosteroid injections, interventions based on mesenchymal stem cells are consistently associated with clinically significant improvements in pain, functional outcomes, and patient-reported quality of life [16-19]. The positive outcomes were particularly noted in patients with early to moderate disease severity.

The evidence available for long-lasting regenerative capability of cartilage has been inconsistent. Studies have reported negative differences in MRI-derived images of cartilage thickness or composition (and therefore evidence of deterioration) whereas other studies were not able to demonstrate a consistent or definite change in cartilage structure [20,21]. These results highlight how cautious we need to be in interpreting results from imaging studies and that symptomatic improvement may not actually relate back to structural improvement at the cartilage level within the same patient. These results emphasize the importance of cautious and meticulous interpretations of imaging studies and suggest that symptomatic improvement may not correlate with the patient's macroscopic cartilage regeneration.

STEM CELLS COMBINED WITH BIOMATERIALS AND SCAFFOLD-BASED STRATEGIES

The integration of stem cells and biomaterials seeks to improve cell retention viability and incorporation into chondrocyte lesions. Scaffold-based and scaffold-free techniques have exhibited encouraging translational efficacy in preclinical and preliminary clinical investigations [22, 23]. These techniques may offer mechanical stabilization and targeted delivery of regenerative cells although high-level clinical data is scarce.

EMERGING CELL-FREE APPROACHES AND SAFETY CONSIDERATIONS

Novel cell-free methods such as exosomes derived from mesenchymal stem cells are advanced therapeutic options, which seem to preserve the positive paracrine effects of stem cells and evade the potential hazards of live stem cell transplantation [24]. Generally, stem-cell based therapeutic approaches have demonstrated favourable safety profiles in short and mid terms, and the adverse events are often mild and self-limited [25]. However, long-term safety, regulatory aspects and standardization of therapeutic procedures remain the main challenges for possible future clinical application [26].

CONCLUSIONS

Stem cell based therapies present a promising adjunctive treatment approach for the management of damaged articular cartilages as well as early-stage osteoarthritis. Indications of improvement with the therapy, based on published evidence from 2020 to 2025, show consistent positive outcomes for pain reduction as well as functional scores, whereas cartilage regeneration remains inconsistent. Further meticulously designed randomized controlled trials with long term follow up are required to determine and define the actual impact of stem cells on clinical routine practice.

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CONFLICT OF INTEREST
The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Body mass index as a determinant of surgical outcomes in total hip arthroplasty

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ABSTRACT

Body mass index is an important element influencing surgical outcomes after total hip arthroplasty. This review analyses how body mass index influences perioperative complications, infection rates, implant survival and functional results in patients undergoing this procedure. A literature review of the past decade was carried out using PubMed, Scopus and Web of Science, focusing on studies published between 2020 and 2026. Studies involving humans that examined the relationship between body mass index and outcomes of total hip arthroplasty were included if they reported perioperative complications, infections, revision rates, or patient-reported outcome measures. The evidence indicates that a higher body mass index is associated with an increased risk of wound complications, periprosthetic joint infection and the need for revision surgery. It is also associated with a lower possibility of achieving minimal clinically important differences in functional scores. The relationship follows a U-shaped pattern showing that, compared with normal weight, obesity and underweight status are associated with increased risk. Proposed mechanisms include technical surgical challenges, altered immune function, compromised wound healing and greater mechanical stress on implants. Preoperative optimization strategies consist of nonsurgical weight loss and bariatric surgery. They are promising but require more investigation. New pharmacological approaches using glucagon-like peptide-1 receptor agonists are a useful contribution to perioperative care. Future research should focus on finding biomarkers of obesity-related risk and on developing individualized strategies to improve outcomes across the body mass index spectrum.

KEY WORDS: obesity, postoperative complications, prosthesis-related infections, reoperation, treatment outcome

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INTRODUCTION

Obesity has become a major global public health issue and its occurrence is consistently rising in recent decades. This condition is typically assessed using body mass index (BMI), where a BMI of 30 kg/m^2 or higher signifies obesity; further classification includes Class I (30-34.9 kg/m^2), Class II (35-39.9 kg/m^2), and Class III (≥40 kg/m^2), also known as morbid obesity [1]. Consequently, the escalating rates of obesity have significant consequences for orthopedic surgery, especially total hip arthroplasty (THA), given that a growing proportion of patients seeking hip replacement surgeries are obese [2].

The relationship between higher BMI and surgical outcomes of THA has been a subject of research interest and clinical concern. Obesity is known to place additional mechanical stress on the hip joint, accelerating cartilage degeneration as well as necessitating earlier surgical intervention [1]. However, the same excess weight that contributes to joint deterioration can also cause major challenges in the perioperative period and may compromise implant function in the long-term [2].

Numerous systematic reviews and meta-analyses have consistently shown that obese patients undergoing total hip arthroplasty (THA) encounter increased risks across a range of outcomes. A large-scale meta-analysis, encompassing more than 2 million patients, indicated that obese individuals show considerably higher rates of complications, infections and revision surgeries when contrasted with those of normal weight [2]. Furthermore, these observations have been repeat-

edly supported by supplementary systematic reviews that specifically investigate morbidly obese patient populations [3].

Periprosthetic joint infection (PJI) represents one of the most serious complications following THA and its incidence appears to be substantially elevated in patients with obesity. Recent systematic reviews have evaluated this risk and confirmed a linkage between increasing BMI and infection rates [4]. The mechanisms underlying this increased awareness show multiple factors, involving altered immune function, compromised wound healing, and technical complications during surgery [4, 5].

More attention has been directed towards preoperative strategies after considering all of these risks. They aim at reducing BMI before THA and they have taken various forms. Starting with nonsurgical approaches such as diet modification and supervised exercise programs, to more aggressive options like bariatric surgery [6]. Recent developments in this area could involve the use of digital health platforms. These platforms allow patients and dietitians to communicate through mobile applications. This method grants a scalable approach to controlling weight before surgery [6].

Bariatric surgery is the most effective intervention that allows for substantial and sustainable weight loss in morbidly obese patients. Several systematic reviews and meta-analyses have investigated whether prior bariatric surgery improves outcomes of THA [7, 8]. The evidence regarding this approach continues evolving, according to some studies suggesting benefits in terms of fewer complications, while others question whether the timing and extent of weight loss that is achieved through bariatric procedures meaningfully alter the risk profile for arthroplasty surgery [9].

The influence of obesity on the outcomes of total hip arthroplasty (THA) goes beyond the early perioperative period, affecting longer-term factors such as implant survival, functional restoration and patient-reported outcomes. Understanding these complex interconnections is key to effective patient education, making surgical decisions and creating evidence-based perioperative protocols. This review consolidates existing research regarding the impact of body mass index (BMI) on surgical outcomes after total hip arthroplasty. It specifically addresses perioperative complications, infection risks, implant durability, functional outcomes and the effectiveness of different optimization approaches.

AIM

The aim of this review is to assess the impact of BMI on THA surgical outcome. The focus is placed on how varying BMI affects perioperative complications, infections, implant survival and functional outcomes as well as the effectiveness of preoperative optimalization strategy.

MATERIALS AND METHODS

This descriptive literature review was written using structured searches in three electronic databases: PubMed, Scopus and Web of Science. The search strategy prioritized publications from the previous decade, concentrating specifically on studies published between 2020 and 2026. The search used a combination of Medical Subject Headings (MeSH) terms and free-text keywords in English, encompassing: body mass index, BMI, obesity, overweight, underweight, total hip arthroplasty, total hip replacement, THA, surgical outcomes, complications, periprosthetic joint infection, revision, patient-reported outcomes and weight loss interventions. Boolean operators (AND, OR) were utilized to appropriately clarify and expand the search strategy.

Inclusion criteria comprised original human studies such as cohort studies, case-control studies and randomized controlled trials as well as systematic reviews and meta-analyses. These studies examined the relationship between body mass index and outcomes that follow primary total hip arthroplasty in adult patients. Eligible studies were required to report on at least one outcome measure of interest including perioperative complications, infectious complications, implant survival or revision rates, functional outcomes, or the effectiveness of preoperative optimization strategies.

Exclusion criteria included studies focusing exclusively on revision arthroplasty procedures, pediatric populations, non-English language publications, case reports, conference abstracts without full-text availability and editorials or opinion pieces without original data. Studies examining only knee arthroplasty or other joint replacements without specific hip arthroplasty data were also excluded.

The initial database search provided a considerable number of potentially relevant publications. Abstracts were assessed as part of an initial screening to evaluate studies against established inclusion and exclusion criteria; full-text articles were then retrieved from all studies that had been identified as being potentially eligible through this process and each underwent an additional, more detailed assessment to evaluate both the methodological quality of the individual study as well as its relevance to the review's stated objectives. High-quality systematic reviews and meta-analyses were prioritized for establishing background and context regarding the topic under investigation, while relatively recent, primary research studies focusing on

reporting outcomes across BMI categories were given priority for their ability to inform the discussion of specific outcomes.

The focus of data extraction was placed upon evaluating the study design, population characteristics, methods used to classify BMI into different BMI categories, outcome measures evaluated within the study and the main findings of each study. When multiple studies examined the same or similar outcomes, those studies with the largest sample size, longest follow-up period, and/or most rigorous methodological approaches were considered to be of higher value than other studies addressing the same outcomes. The structure of the narrative synthesis was designed to allow for a systematic examination of distinct domains of outcomes while also providing an opportunity to highlight areas where there is agreement among the body of evidence, as well as those areas that remain in debate.

This review does not represent a systematic review conducted according to PRISMA guidelines. However, it does provide a narrative synthesis of the existing evidence and is intended to provide clinicians and researchers with a broad-based understanding of how BMI impacts outcomes throughout the continuum of care associated with total hip arthroplasty.

REVIEW

PERIOPERATIVE AND EARLY POSTOPERATIVE OUTCOMES

The unique characteristics of the immediate perioperative time frame make it challenging for obese patients who undergo total hip arthroplasty. An analysis of outcomes categorized by BMI class found that variables such as operative time, intraoperative blood loss, length of hospitalization and post-discharge readmission rates all demonstrated a relationship with the patient's weight [10].

A study on underweight patients (BMI <18.5 kg/m^2) found that underweight patients were at higher risk for complications of wound healing and perioperative death than normal weight patients [11]. The shape of the risk curve demonstrates an optimal BMI, where there is a correlation between deviation from this BMI and increased morbidity [11].

The pattern of failure modes varies distinctly between high and low BMI populations. Research systematically comparing these groups has identified that obese patients more commonly experience wound-related complications and infectious problems, while underweight individuals demonstrate higher rates of periprosthetic fracture and dislocation events [12]. These disparate failure mechanisms suggest that risk mitigation strategies must be specifically tailored to the weight category of each individual patient [12].

Extreme obesity, defined as BMI > 50 kg/m^2, presents a particularly challenging clinical scenario. Recent investigation of outcomes in this population has raised fundamental questions about whether the magnitude of perioperative risk justifies proceeding with elective surgery [13]. The data revealed significantly elevated rates of major complications, wound problems and venous thromboembolism which led to an ongoing debate about the risk-benefit calculus in patients with such severe obesity [13].

The influence of surgeon experience and case volume appears to substantially influence the relationship between obesity and surgical outcomes. Analysis using propensity score matching methodologies showed that when THA procedures in obese patients are performed by high-volume surgeons, many of the traditionally observed complications are significantly reduced [14]. This finding suggests that technical skills and awareness of the issues posed by excess body fat can partially cancel out obesity related risks [14].

INFECTIOUS AND WOUND-RELATED COMPLICATIONS

It has been confirmed the morbidly obese patients are subjected to 2-3 times higher risk of periprosthetic joint infection when compared to regular individuals [4]. The other factors contributing to the potential infection might be tissue trauma, prolonged operative time, and other factors like decreased patients defenses [4].

Moreover, it has been observed that the complications resulting from postoperative wounds happen more frequently in case of obese patients. These problems might be related to prolonged drainage, superficial infections or dehiscence. However, these facts haven't been confirmed in case of deep infections [10]. Similar conclusions have been presented in [12].

IMPLANT SURVIVAL, REVISION AND REOPERATION

The extensive studies on 83,000 cases recorded in The Swedish Hip Arthroplasty Register (SHAR) documenting total hip replacements reveal the direct correlation between elevated BMI and higher risk of revisions and reoperations [15]. Apart from the later, other complications like prosthesis instability and loosening occur in morbidly obese patients much more frequently [3].

The specific situation concerns super-obese patients (BMI>50). In this group the risk of reoperation is so high, that the potential improvement in patients welfare is a short-term benefit thus questionable in long-term perspective [13].

However, there are studies questioning the above results. For instance the comparative analysis on total hip arthroplasty (THA) operations presented by Kubsad et al [16] do not confirm the direct impact of bariatric surgeries on surgical complications or revisions in the 10-year long time perspective. The reference group were class III obesity patients who did not undergo bariatric surgeries [16].

FUNCTIONAL OUTCOMES

Analysis of post-operative data reported by Mukka S, et al confirms improvement in patients' life quality [17]. But this recovery is not uniform along all studied BMI groups. The highest satisfaction rate has been observed in obese patients, but one should remember, they started from the lower functional level.

The relatively low satisfaction has been reported by morbidly obese patients [18]. The third analyzed group of patients with class III obesity declared slightly contradictory results in one year time frame observations, so the clinically important differences have been classified as minimal [18].

BMI-RELATED OPTIMIZATION STRATEGIES

Interesting results on preoperative treatment have been reported by Seward MW and his research group [6]. In particular the authors analyzed the importance and efficiency of remote dietitian consultations and mobile applications on patients' behavior. The impact was not very strong but still statistically meaningful. The analysis of postoperative data and records of these patients confirmed the reported above correlation between lower BMI and decreased probability of postoperative complications. The similar studies are communicated by Meissner N et al., but authors underline the necessity of further studies on this topic [19]. In particular, the direct relation between the magnitude of weight loss and its timing on operation outcomes should be analyzed.

The economical aspect of BMI, its impact on operations outcomes and potential risk of complications was studied by Akwuole C, et al [20]. The reference dataset in this study was a nationally representative database of 10,366 primary THAs completed from 2016 to 2022. Statistical analysis revealed that increased BMI is associated with higher 90-day costs for THA.

DISCUSSION

The discussed above papers reveal a complex and diverse impact of BMI on THS outcomes, both in short- and long-term perspectives. The unfavorable consequences of being overweight have been confirmed in all the studies. In particular these are infections, higher risk of revisions and reoperations, prosthesis instability and loosening. Underweight patients have also been under examination. Unexpectedly, this group is also at risk of postoperative complications. Therefore, the combined analysis of these results indicates there's an optimal BMI magnitude, when the complications risk is statistically lower.

The effect of preoperative measures related to weight reduction and its timing for better treatment results is still under investigation. Recent studies in this area are relatively extensive and cover for instance the effectiveness of mobile applications and remote consultations on patients' behavior and reaching the optimal BMI.

There's also intensive research on limiting the risk of postoperative complications. For instance, studies reported demonstrated the expected and positive impact of GLP-1 receptor agonists to decrease potential complications occurrence [21-23]. Other reports investigated the impact of preoperative exercises and nutritional recommendations, especially for sarcopenic obesity patients.

An important factor of a successful operation is the doctor's experience [24]. The statistical analysis confirms the experienced surgeons may have very good results and little complications ratio for both normal weight individuals and overweight ones. However, it should be highlighted that most of the reported cases are retrospective ones, BMI records can be burdened with error and sole BMI might not be the perfect reference data.

CONCLUSIONS

Similar to many other health care studies the discussed problem of BMI and its impact on surgical results of hip replacement needs to be considered from multiple perspectives.

The most important one is patients' satisfaction from the operation outcomes and his/her welfare in short and long-term perspective. These are closely related to the risk of potential complications after surgery. Among them infections, revisions and reoperations, prosthesis instability and loosening seem to be the critical hazards for overweight patients.

Therefore, the measures undertaken to reduce these risks are an important topic of ongoing research. In a wider sense these relate also to surgeons' experience, their professional satisfaction and the level of job performance.

The final viewpoint of this study is related to the socio-economical aspects. The potential risk of complications, reoperations and other additional procedures/treatments generate redundant costs. This contributes to increased healthcare expenses, insurance costs etc. It may also limit access to medical services for other patients.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Urinary tract infections in patients undergoing orthopaedic procedures: A contemporary review (2021–2026)

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ABSTRACT

Urinary tract infections are one of the most frequent healthcare-associated infections representing a relevant postoperative complication in orthopedics patients. These infections are associated with increased morbidity, prolonged hospitalizations, and higher rates of readmission. In selected settings, they may coexist with or precede surgical site infections, including periprosthetic joint infections. This review aims to summarize and evaluate recent evidence from the last five years in regards to epidemiology, risk factors, clinical consequences, and preventative strategies for patients undergoing orthopaedic interventions. A narrative literature review was conducted using the PubMed/MEDLINE database utilizing English-language publications from January 2021 to February 2026. Particular emphasis was placed on systematic reviews, meta-analyses, cohort studies, and large database analyses related to hip fracture surgery, total joint arthroplasty, and spine surgery. These studies indicate that urinary tract infections remain particularly common among the geriatric population undergoing hip fracture surgery. Major modifiable risk factors include urinary catheterization and postoperative urinary retention. Symptomatic urinary tract infections briefly prior to surgery are associated with an increased risk of postoperative complications compared to asymptomatic bacteriuria. Avoidance of unnecessary urinary catheterization and routine urine testing in asymptomatic patients reduces the use of unnecessary antibiotics while preserving surgical outcomes. Urinary tract infections continue to represent a significant clinical issue in orthopaedic patients. Evidence supports catheter stewardship, targeted diagnostic strategies, and integrated preventive approaches to reduce infection-related complications.

KEY WORDS: catheter-associated urinary tract infections, hip fractures, postoperative complications, asymptomatic bacteriuria, antimicrobial stewardship

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INTRODUCTION

Urinary tract infection (UTI) is one of the most common healthcare-associated infections. It remains a significant complication in orthopedic care, particularly following hip fracture surgery, total joint arthroplasty (TJA) and spine procedures. In orthopedics, UTI is important not only as a cause of morbidity (delirium, sepsis, prolonged hospitalization, rehospitalization) but also because perioperative bacteriuria may coexist with or precede surgical site infection (SSI). In certain scenarios , it has been analyzed as a potential risk factor for hematogenous periprosthetic joint infection (PJI) [1–4]. Moreover, intensive screening and treatment of asymptomatic bacteriuria (ASB) may lead to inappropriate antibiotic usage, without conclusively reducing the incidence of SSIs or catheter-associated urinary tract infections (CAUTIs) in many contemporary orthopedic cohorts [5,6]. This raises a major concern: how to identify and treat clinically significant infections while maintaining antibiotic stewardship and avoiding catheter-related harm.

Orthopedic patients are exposed to numerous factors that increase the risk of UTI. Such factors include advanced age, frailty, multimorbidity, perioperative bladder catheterization, postoperative urinary retention (POUR), immobilization, blood transfusions and delays in surgical treatment in trauma populations [1,2,7-10]. Recent years have seen a dynamic increase in the number of publications focusing on: (i) the impact of preoperative UTI on the risk of PJI and the importance of timing of its occurrence; (ii) the actual impact of catheter use and catheterization-limiting protocols; (iii) the usefulness of routine urine testing; and (iv) prophylactic packages and rational antibiotic therapy strategies adapted to orthopedic practice.

AIM

- To synthesize the scientific data from the last 5 years (2021–2026) on the incidence, predictors and consequences of urinary tract infections (UTIs) in patients undergoing orthopedic procedures, including joint replacement, hip fracture surgery, and spine surgery.
- Summarize and critically evaluate the current scientific evidence regarding the relationship between perioperative UTI or asymptomatic bacteriuria (ASB) and infectious complications of orthopedic treatment, in particular surgical site infection (SSI) and periprosthetic joint infection (PJI).
- Additionally, the study aims to present evidence-based preventive strategies and clinical management that can be used in perioperative orthopedic care, with particular emphasis on the principles of urinary catheter management and rational antibiotic therapy.

MATERIALS AND METHODS

This narrative review was conducted using a structured literature search strategy. PubMed and MEDLINE base was searched for English-language publications published between January 1, 2021, and February 1, 2026. The search strategy included combinations of keywords and MeSH terms related to the following topics: "urinary tract infection," "catheter-associated urinary tract infection," "asymptomatic bacteriuria," "urinalysis," "urine culture," "postoperative urinary retention," "orthopedics," "proximal femur fracture," "joint replacement," "total hip replacement," "total knee replacement," "periprosthetic joint infection," and "spine surgery." Priority was given to systematic reviews and meta-analyses, randomized or comparative trials, large registry and database analyses, and prospective cohort studies. Studies addressing urinary tract infections (UTIs), asymptomatic bacteriuria (ASB), postoperative urinary retention (POUR), and/or urinary catheterization in the perioperative orthopedic context were included, as well as studies directly assessing the associations with surgical site infection (SSI) or periprosthetic joint infection (PJI). Publications outside the defined time frame, studies addressing non-orthopedic contexts (unless the preventive conclusions were broadly applicable to the care of hospitalized orthopedic patients), and articles retracted from the literature were excluded.

REVIEW

EPIDEMIOLOGY AND CLINICAL BURDEN IN ORTHOPEDIC POPULATIONS

PROXIMAL FEMUR FRACTURES AND ORTHOPEDIC INJURIES

Patients with proximal femur fractures are particularly susceptible to urinary tract infections (UTIs). This is a consequence of their biological fragility, baseline lower urinary tract dysfunction, immobilization and frequent exposure to urinary catheterization. Recent studies indicate a wide range in the incidence of UTIs, depending on the clinical setting and accepted definitions. However, they consistently identify UTIs as a clinically significant postoperative complication associated with an increased risk of sepsis, prolonged hospitalization and rehospitalization [1,2,7]. In a large NSQIP-based analysis of geriatric hip fracture patients without UTI at the time of surgery; postoperative UTI occurred in approximately 3% of patients and was independently associated with sepsis, prolonged hospital stay and readmission [1]. Nursing care studies and adherence analyses in hip fracture care pathways highlight that limiting the use of indwelling catheters and promoting early mobilization are key preventive measures for UTIs. Significant implementation gaps remain in actual clinical practice which are a direct cause of the infections [7,9]. A recent scoping review of postoperative urinary retention (POUR) in older hip fracture patients indicates a strong mechanistic link between urinary retention, the need for catheterization and the subsequent risk of UTI resulting from urinary retention and repeated urinary tract instrumentation [8].

TOTAL JOINT ARTHROPLASTY

The incidence of urinary tract infections (UTIs) in elective joint arthroplasty procedures is generally lower than in populations of patients with hip fractures. However, the very high number of TJA procedures performed means that the grave burden of this complication remains significant. A Polish population-based study based on post-discharge surveillance demonstrated a UTI incidence after hip and knee arthroplasty of less than 1% in administrative data, identifying risk factors related to patient characteristics and the procedure itself, which are important for planning preventive measures [11].

Urinary complications in total joint arthroplasty are closely associated with catheterization practices and postoperative urinary retention (POUR). Meta-analyses indicate that the risk of urinary retention is influenced by factors such as type of anesthesia, pain management strategies, gender, benign prostatic hyperplasia (BPH) and perioperative urological management [12].

SPINE SURGERY

Spine procedures share common risk factors for UTI with joint replacement (older age, opioid use, immobilization). Additional risk may result from longer operative times and greater perioperative fluid balance fluctua-

tions. A 2021 meta-analysis of elective spine surgery found that older age, male gender, benign prostatic hyperplasia (BPH), diabetes, a history of UTI, longer operative times, higher intravenous fluid volumes and multilevel procedures were significantly associated with postoperative urinary retention (POUR). Such causes indirectly increase catheterization and the risk of UTIs [10].

A study published in 2023 assessing the importance of preoperative urine culture and the incidence of postoperative UTIs after spine surgery provides contemporary data indicating that abnormalities in urine tests may be associated with the subsequent development of UTIs. However, the interpretation of these results largely depends on the presence of clinical symptoms and indications for diagnostic tests [13].

RISK FACTORS: REPEATABLE PREDICTORS AND POTENTIALLY MODIFIABLE CAUSATIVE FACTORS

The following predictors have been repeatedly identified in various areas of orthopedics:

- **Patient-related factors:** Advanced age, female gender (in relation to UTI), male gender, and benign prostatic hyperplasia (BPH) in relation to urinary retention, diabetes, high ASA risk class, frailty and/or cognitive impairment and treatment with glucocorticoids [1, 2, 7, 12].
- **Perioperative and systemic factors:** urinary catheterization (both the presence of the catheter and its duration), delayed mobilization, blood transfusions, delayed surgical treatment of proximal femur fractures and prolonged hospitalization [1, 2, 8, 9].
- **Procedure and anesthesia-related factors:** spinal or epidural anesthesia and certain pain management strategies (indirectly by increasing the risk of urinary retention), duration of surgery and the volume of intravenous fluids administered (particularly important in spine surgery) [10, 12].

In a 2024 systematic review and meta-analysis of risk factors for UTI in geriatric patients with hip fracture, urinary catheterization was identified as one of the strongest modifiable risk factors [2]. These findings are consistent with clinical pathways that prioritize early catheter removal and the use of structured protocols for bladder monitoring and support.

THE CATHETERIZATION QUESTION: ROUTINE VERSUS SELECTIVE STRATEGIES

One of the main findings in the literature from 2021 to 2026 is the observation that routine bladder catheterization in modern, fast-track joint replacement surgery is often unnecessary and may increase the risk of urinary tract infections (UTIs). A study published in Arthroplasty Today in 2022, involving primary total hip arthroplasty (THA) under spinal anesthesia concluded that routine catheterization is likely unnecessary and may be associated with an increased number of urological complications, including urinary tract infections (UTIs) [14].

Similarly, a 2025 perspective review published in the Journal of Arthroplasty emphasized that routine catheter use is not required in many patients undergoing primary unilateral TJA, emphasizing the need to assess postoperative urinary retention (POUR) prophylaxis with the risk of UTI [15].

A 2025 retrospective analysis assessing the impact of a protocol change restricting the use of catheters in primary and revision arthroplasty demonstrated that catheter use was associated with a higher rate of UTI and restricting their use reduced infections with only a moderate increase in reversible POUR [16].

PREOPERATIVE URINALYSIS AND ASYMPTOMATIC BACTERIURIA: RECOMMENDATIONS FOR ORTHOPEDICS

ABANDONING ROUTINE URINALYSIS IN ASYMPTOMATIC PATIENTS

A growing body of evidence indicates that routine urinalysis before orthopedic surgery in asymptomatic patients leads to excessive antibiotic use without significantly improving key clinical outcomes. A 2021 study demonstrated that eliminating routine urinalysis before elective orthopedic surgery resulted in a dramatic reduction in antibiotic use, without significantly changing the incidence of surgical site infections (SSIs) or catheter-associated urinary tract infections (CAUTIs) [5].

These findings support antibiotic stewardship strategies, where urine testing should only be performed in patients with clinical symptoms or a clear medical indication.

ASYMPTOMATIC BACTERIURIA (ASB) AND THE RISK OF PERIPROSTHETIC JOINT INFECTION (PJI)

The relationship between ASB and PJI remains a matter of debate, partially due to confounding factors; patients with ASB may be more frail or have a higher comorbidity burden and because microorganisms isolated from urine often differ from those causing PJI. A 2024 systematic review and meta-analysis demonstrated a higher observed incidence of PJI in TJA patients with ASB compared to controls. However, it is important to note that preoperative antibiotic therapy for the eradication of PJI was not found to be significantly beneficial. Furthermore, the studies reviewed noted a lack

of concordance between microorganisms detected in urine and those isolated in periprosthetic joint infections [18].

SYMPTOMATIC PREOPERATIVE UTI AND TIME OF ONSET

Unlike asymptomatic bacteriuria (ASB), symptomatic UTI in the period immediately preceding surgery has consistently been considered clinically significant. A 2022 database study found that UTI diagnosed within 1 week of total knee arthroplasty (TKA) or within 2 weeks of total hip arthroplasty (THA) was associated with an increased risk of periprosthetic joint infection (PJI), whereas previous UTI episodes were not. In this analysis, antibiotic use did not appear to significantly reduce the risk [19].

Not all studies agree on the effect size or causality. At least one recent study found no increase in PJI but reported an increased number of postoperative systemic complications, emphasizing the need to consider UTI as a marker of systemic risk, despite a direct causal relationship with PJI remains uncertain. [20]

A 2024 systematic review and meta-analysis focusing on THA found a statistically significant association between UTI and PJI risk, while the association with ASB was less consistent. [4]

URINARY TRACT INFECTIONS AND SURGICAL SITE INFECTIONS (SSIS) IN ORTHOPEDICS: STRONGEST EVIDENCE IN HIP FRACTURE SURGERY

In orthopedics, the association between perioperative urinary tract infection (UTI) and surgical site infection (SSI) is most consistently documented for hip fracture procedures. A 2023 systematic review and meta-analysis found that perioperative UTI is associated with an approximately 2.4-fold increased risk of SSIs after hip fracture surgery, with the authors emphasizing the heterogeneity of the definitions of UTI used and differences in the timing of its occurrence [3].

From a clinical practice perspective, these results justify careful evaluation of patients for UTI in the perioperative period, immediate treatment of symptomatic infections and rigorous limitation of catheter use to reduce the overall infectious burden.

PREVENTION AND CLINICAL MANAGEMENT STRATEGIES SUPPORTED BY RECENT DATA

PRINCIPLES FOR PREVENTING CATHETER-ASSOCIATED URINARY TRACT INFECTIONS

The 2022 update of the document "Strategies to Prevent Catheter-Associated Urinary Tract Infections in Acute-Care Hospitals" (published in 2023) presents practical recommendations ready for implementation in clinical settings: avoiding unnecessary catheterization, using aseptic catheter insertion technique, maintaining a tight drainage system, ensuring urinary patency and removing the catheter immediately when clinically indicated [21].

These principles have direct application in orthopaedic departments, where excessive catheter use and prolonged catheter retention are common areas requiring improvement in clinical practice.

ADAPTING PRINCIPLES TO ORTHOPEDIC PRACTICE

Recent orthopedic publications indicate that the best preventive outcomes are achieved using protocols that combine the following elements: (i) selective use of catheters based on risk stratification; (ii) standardized bladder monitoring pathways using ultrasound (bladder scan) and intermittent catheterization in cases of urinary retention; (iii) early patient mobilization; (iv) abandoning routine urine testing in asymptomatic patients; (v) supervision of rational antibiotic therapy, limiting prescription of medications based on urine culture results [5, 9, 14, 16].

Interventions aimed at reducing unnecessary catheterization and catheter-associated urinary tract infections (CAUTIs), implemented through structured implementation approaches have also been evaluated in hospital settings. These results support the feasibility of nurse-led protocols that are fully applicable to postoperative orthopedic surgery units [22].

DISCUSSION

This review highlights four practical lessons learned, consistent with the scientific evidence from orthopedic research conducted between 2021 and 2026.

First, urinary tract infection (UTI) remains a clinically significant complication. Particularly in geriatric patients with hip fracture, UTI is associated with an increased risk of sepsis, prolonged hospitalization and frequent readmissions [1, 2]. The hip fracture pathway is particularly susceptible to UTI because patients often require urgent surgery despite having baseline lower urinary tract dysfunction and are frequently catheterized. In this population, UTI also demonstrates the strongest association with an increased risk of surgical site infection (SSI), further justifying the inclusion of urinary tract management in infection prevention in orthopedic trauma [3].

Second, urinary catheterization is the most frequently identified modifiable risk factor across all orthopedic

populations. Data from the field of joint replacement increasingly support the advantage of selective catheterization strategies over routine indwelling catheterization. Supported by cohort analyses of patients undergoing total hip arthroplasty (THA) under spinal anesthesia and studies evaluating the effects of protocol modifications, which have demonstrated a reduction in the incidence of urinary tract infections (UTIs) with a limited increase in postoperative urinary retention (POUR) [14, 16].

In the care plan of patients with hip fractures, guidelines and analyses of actual clinical practice similarly emphasize the need to limit the use of catheters and to provide intermittent catheterization when possible, although the degree of implementation of these recommendations remains variable [7, 9].

Third, routine urinalysis in asymptomatic patients is difficult to justify clinically. Eliminating routine urinalysis before elective orthopedic surgery led to a significant reduction in antibiotic use without an increase in surgical site infections (SSIs) or catheter-associated urinary tract infections (CAUTIs), representing an effective antibiotic stewardship strategy [5].

The problem is particularly acute where a positive urinalysis automatically triggers further cultures and antibiotic prescription despite the absence of urinary symptoms. The literature on asymptomatic bacteriuria (ASB) demonstrates that even when ASB correlates with PJI in observational data, antibiotic treatment does not lead to a convincing reduction in the risk of PJI, and the microorganisms detected in urine rarely overlap with those isolated in periprosthetic infection. These findings suggest that in many cases, ASB may be a marker of increased patient susceptibility rather than a direct cause of PJI [4, 18].

Fourth, both the timing of infection and its phenotype are important. Symptomatic UTI in the period immediately preceding surgery—especially within 1–2 weeks before arthroplasty—has been associated with a higher risk of PJI in large database analyses, justifying postponement of surgery when possible and effective treatment of infection before planned implant placement [19].

Simultaneously, there are conflicting research findings; with some publications suggesting that UTI may primarily predict broader, postoperative systemic complications rather than always directly contributing to PJI [20]. A rational summary suggests that symptomatic infections should be treated and ideally resolved before elective implant surgery, whereas ASB should not automatically lead to the initiation of antibiotic therapy or a delay in surgery unless there are individual patient factors or local protocols to justify such management. From a systems perspective, orthopedic departments can probably achieve the greatest reduction in the UTI burden by focusing on rational catheter management (avoiding unnecessary catheterization, early catheter removal, using structured bladder monitoring protocols) and rational use of diagnostics (investigation and treatment only when clearly clinically indicated).The inclusion of structured guidelines for the prevention of catheter-associated urinary tract infections (CAUTI) in orthopedic care pathways is supported by high-quality implementation recommendations for hospitals [21]. Furthermore, orthopedic studies suggest that the use of these interventions does not significantly worsen clinical outcomes when combined with strategies for managing postoperative urinary retention (POUR) [14, 16].

CONCLUSIONS

1. UTI remains a significant postoperative complication in orthopedics, with the greatest clinical consequences observed in geriatric patients with hip fracture, where UTI is associated with systemic complications and an increased risk of surgical site infection (SSI).
2. Perioperative urinary catheterization, routine use of indwelling catheters and their long-term maintenance are the most frequently identified modifiable risk factors for urinary tract infections (UTIs) in orthopedic care. Current evidence supports a strategy of selective catheter use, early removal and the use of standardized algorithms for bladder monitoring using ultrasound (bladder scan) and intermittent catheterization to manage urinary retention while minimizing the risk of infection.
3. Routine preoperative urinalysis or culture in asymptomatic orthopedic patients is not recommended in many contexts because it leads to overuse of antibiotics without demonstrable benefit in reducing the incidence of surgical site infections (SSIs) or catheter-associated urinary tract infections (CAUTIs). This represents an important area for implementing antimicrobial stewardship strategies.
4. Symptomatic urinary tract infection occurring immediately before planned arthroplasty should be treated and if possible, surgery should be postponed until clinical symptoms resolve. This is justified by data indicating that recent UTI is associated with an increased risk of periprosthetic joint infection (PJI). However, antibiotic treatment of asymptomatic bacteriuria (ASB) does not demonstrate reliable efficacy in PJI prevention and may lead to excessive use of antibacterial drugs.

5. The most practical and implementable preventive measures in orthopedics include: (i) avoidance of catheterization or early removal of catheters; (ii) structured pathways for the prevention and management of postoperative urinary retention; (iii) early patient mobilization; (iv) test-and-treat strategies consistent with guidelines for the prevention of catheter-associated urinary tract infections (CAUTI) and the principles of rational antibiotic stewardship.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Medication nonadherence in osteoarthritis: Review of determinants, consequences and strategies

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ABSTRACT

Osteoarthritis (OA), particularly of the knee, represents a leading cause of chronic pain and functional limitation worldwide. Although pharmacologic therapy remains central to symptom control, real-world treatment effectiveness is frequently compromised by suboptimal medication adherence. To synthesize contemporary evidence on the determinants, clinical consequences, and targeted strategies related to medication nonadherence in osteoarthritis. A narrative review of literature published between January 2021 and February 2026 was conducted using PubMed, Scopus, and supplementary sources. Studies examining determinants of nonadherence, associated outcomes, and adherence-enhancing interventions in OA were thematically integrated. Thirty-nine studies were included. Medication nonadherence in OA is multifactorial, reflecting the interaction of patient-related, therapy-related, and healthcare system determinants. Aging, multimorbidity, cognitive vulnerability, and polypharmacy contribute to unintentional nonadherence, whereas risk perception, safety concerns, and financial barriers frequently drive intentional dose modification or discontinuation. Inconsistent medication use is associated with persistent pain, functional limitation, reduced quality of life, and increased healthcare utilization. Emerging evidence supports patient-centered education, shared decision-making, regimen simplification, pharmacist-led interventions, and digital adherence tools as promising strategies. Medication nonadherence represents a clinically consequential yet underrecognized determinant of treatment effectiveness in osteoarthritis. Addressing adherence through integrated, patient-centered, and system-level strategies is essential to optimizing symptom control, functional outcomes, and healthcare resource utilization in OA populations.

KEY WORDS: medication adherence, polypharmacy, quality of life, health care utilization, patient education

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INTRODUCTION

Osteoarthritis (OA) is a chronic degenerative joint disorder characterized by active pathological processes involving an imbalance between articular tissue degradation and repair, leading to progressive structural damage and functional limitation. The condition primarily affects weight-bearing joints, particularly the knee. OA develops when joint tissues are unable to adequately repair cumulative mechanical and biological insults. Disease progression varies considerably among individuals, and common clinical manifestations include pain, stiffness, reduced range of motion, and muscle weakness [1].

Based on etiology, OA is classified into two main types: primary OA, which develops in the absence of identifiable prior trauma, and secondary OA, which arises from pre-existing joint abnormalities such as mechanical injury or systemic conditions. Established risk factors include obesity, psychological stress, advancing age, genetic predisposition, and physical inactivity [2].

The burden of OA extends beyond structural joint changes. Patients frequently experience progressive physical limitations, chronic pain, and persistent functional impairment, all of which negatively affect health-related quality of life. These consequences may lead to reduced occupational participation, decreased social and recreational engagement, and impaired sleep quality, contributing to broader psychosocial impact [3].

Current guidelines for the diagnosis and management of OA emphasize early implementation of non-pharmacological strategies, including patient education, exercise therapy, and physical therapy. Treatment goals include effective symptom control, improvement in mobility, enhancement of quality of life, reduction of disability, and avoidance of excessive dependence on medications. In early-stage disease, these foundational measures may be sufficient. However, in more advanced stages, pharmacological therapy is often required, with drug selection and administration tailored to the affected joint sites and individual patient risk factors [4].

Given the chronic and progressive nature of OA, pharmacological therapy frequently plays a central role in long-term symptom control and functional maintenance. In this context, medication adherence becomes a critical determinant of therapeutic effectiveness. Medication adherence is defined as the extent to which a patient's behavior aligns with agreed recommendations from a healthcare provider regarding the timing, dosage, and frequency of medication use. Evidence consistently demonstrates that adherence is essential for optimal management of chronic diseases and prevention of long-term complications. Poor adherence is associated with disease progression, increased morbidity, diminished quality of life, higher hospitalization rates, and mortality. Economically, medication non-adherence is estimated to cost the United States healthcare system approximately USD 100 billion annually. Accordingly, higher adherence is linked to improved clinical outcomes and reduced healthcare utilization, whereas non-adherence contributes to worse outcomes and greater overall costs [5].

Despite its recognized importance, medication adherence among patients with arthritis remains suboptimal, consistent with patterns observed across other chronic conditions. In OA, non-adherence may result from multiple factors, including forgetfulness, adverse effects, limited understanding of treatment importance, slow symptomatic improvement, and a perceived lack of therapeutic benefit [6]. Large-scale studies conducted in different countries further demonstrate persistently suboptimal adherence across chronic diseases, underscoring the need to better understand both clinical and patient-related determinants that influence adherence in order to achieve treatment goals [7].

Achieving optimal adherence depends substantially on patients' understanding of their condition, trust in the treatment plan, and ability to manage emotional and financial barriers. Increasing research attention has therefore focused on individual-level determinants, particularly health literacy, defined as the capacity to obtain, process, and understand basic health information needed to make appropriate health decisions. Low health literacy has been consistently associated with poorer adherence and adverse outcomes across chronic diseases [8].

Given the substantial clinical and societal burden of OA and the central role of pharmacotherapy in its management, a comprehensive understanding of medication adherence is essential.

AIM

This review aims to examine the barriers contributing to medication non-adherence in patients with osteoarthritis and to explore strategies to enhance adherence and improve clinical outcomes.

MATERIALS AND METHODS

REVIEW DESIGN

This review employed a narrative design to synthesize current evidence on medication nonadherence in osteoarthritis. The objective was to examine determinants of nonadherence, associated clinical and health system consequences, and potential strategies for improvement. A narrative approach was selected to allow thematic integration of findings across heterogeneous study designs, adherence definitions, pharmacological classes, and outcome measures. Given substantial variability in adherence assessment methods and reporting across studies, quantitative meta-analysis was not undertaken. Instead, a structured thematic synthesis was performed to provide clinically relevant interpretation of the literature. As a narrative review, formal risk of bias assessment tools and PRISMA reporting standards were not applied. Measures to enhance methodological transparency included multi database searching, clearly defined eligibility criteria, and structured thematic categorization. The findings are intended to provide an evidence informed synthesis of current knowledge rather than pooled quantitative effect estimates, particularly given variability in adherence definitions and limited availability of long term osteoarthritis specific longitudinal data.

LITERATURE SEARCH AND DATABASES

A literature search was conducted using PubMed as the primary database, with supplementary searches in Scopus and Google Scholar to ensure comprehensive coverage. The search focused on publications from January 2021 to February 2026. Controlled vocabulary and free text terms were combined to identify relevant studies related to osteoarthritis and medication adherence. Search terms included osteoarthritis, knee osteoarthritis, medication adherence, compliance, persistence, nonadherence, NSAIDs, analgesics, pain management, determinants, barriers, quality of life, healthcare utilization, cost, and adherence enhancing interventions such as education and digital health approaches. Boolean operators were applied to optimize search sensitivity. Reference lists of eligible articles and relevant reviews were also screened to identify additional pertinent studies. Preference was given to recent peer reviewed publications and guideline based recommendations to ensure contemporary clinical relevance.

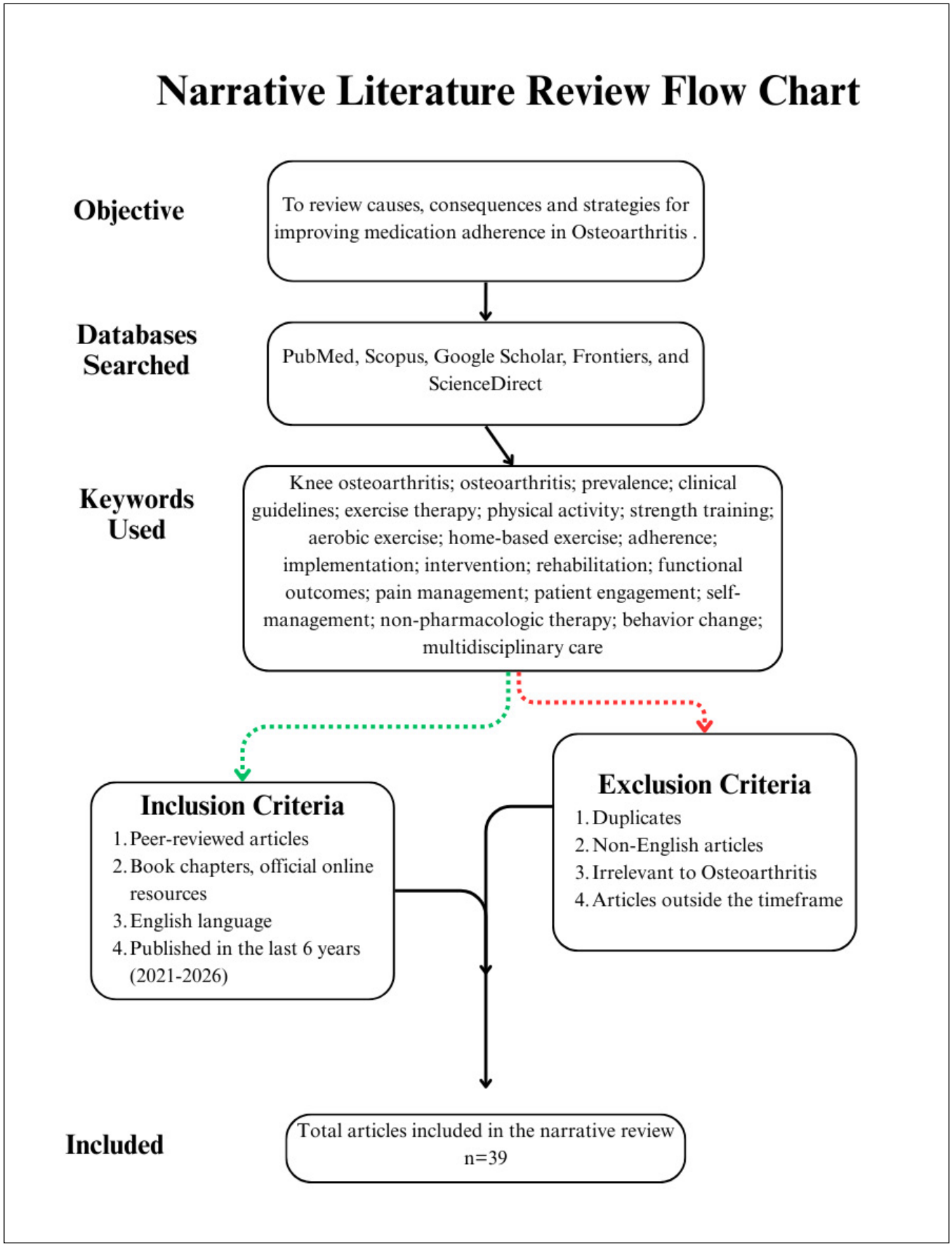

Fig. 1. Methodology flowchart summarizing literature search strategy, inclusion/exclusion criteria, and data synthesis steps used in the review
Source: Own materials

STUDY SELECTION

Given the narrative design, no formal systematic screening protocol was applied. Titles and abstracts were reviewed iteratively to assess relevance to medication adherence in osteoarthritis. Full texts were examined when eligibility was unclear or when studies aligned with the objectives of the review. Selection prioritized methodologically sound and clinically applicable studies. Preclinical research, animal studies, case reports, conference abstracts lacking sufficient methodological detail, non English publications, and studies focusing exclusively on surgical interventions without relevance to pharmacological adherence were excluded. When osteoarthritis specific evidence was limited, findings from broader chronic disease adherence literature were considered when directly applicable and clearly distinguished during synthesis. Study selection decisions were discussed collaboratively to ensure consistency in inclusion.

DATA EXTRACTION AND SYNTHESIS

From each included study, key information was extracted, including study design, population characteristics, pharmacological therapy evaluated, adherence measurement approach, identified determinants of adherence, and reported clinical or economic outcomes. Data extraction and categorization were performed collaboratively, with discussion used to resolve interpretive discrepancies. Studies were organized according to predefined conceptual domains, including patient related factors, therapy related factors, healthcare system influences, clinical consequences, and adherence improvement strategies. Findings were synthesized narratively to identify recurring patterns, areas of consistency, and gaps in the existing evidence. No statistical pooling or quantitative meta-analysis was performed.

SCOPE AND STUDY INCLUSION

A total of 39 studies were included in this review. These comprised observational studies, randomized controlled trials, systematic reviews, guideline syntheses, and interventional studies focused on adherence related outcomes. This sample was considered sufficient to provide a comprehensive and clinically meaningful synthesis of contemporary evidence on medication nonadherence in osteoarthritis. Figure 1 illustrates a flowchart outlining the process used for selecting articles included in this review.

REVIEW AND DISCUSSION

DETERMINANTS OF MEDICATION NONADHERENCE IN OSTEOARTHRITIS

Medication nonadherence in osteoarthritis reflects the interaction of patient-related, therapy-related, and healthcare system determinants. These domains are interdependent and often reinforce one another in older populations with multimorbidity.

PATIENT-RELATED DETERMINANTS

AGING, FUNCTIONAL DECLINE, AND MULTIMORBIDITY

Osteoarthritis predominantly affects older adults. In the United States, approximately 80 percent of individuals over 65 years demonstrate radiographic evidence of osteoarthritis, although only around 60 percent are symptomatic [9]. Advancing age is associated with accumulation of biological damage, declining physical and cognitive capacity, multimorbidity, and geriatric syndromes including frailty and falls, all of which may hinder consistent medication use [10].

Visual impairment, reduced manual dexterity, polypharmacy, and complex dosing regimens further complicate self-management. Evidence indicates that visually impaired older adults frequently struggle to distinguish tablets or packaging, may take incorrect doses, and often require assistance for safe medication administration [11]. These factors increase the risk of unintentional nonadherence.

COGNITIVE VULNERABILITY

Emerging research suggests that osteoarthritis is associated with increased risk of dementia and structural brain changes [12]. Cognitive decline affecting memory, executive function, and organizational skills may therefore be more prevalent in this population. Such impairment reduces capacity to maintain long-term adherence, particularly when regimens are complex or involve multiple agents.

RISK PERCEPTION, BELIEFS, AND INTENTIONAL NONADHERENCE

Intentional nonadherence is frequently driven by safety concerns. Patients with osteoarthritis often weigh potential gastrointestinal, cardiovascular, and renal risks of nonsteroidal anti-inflammatory drugs more heavily than anticipated symptom relief [13,14]. Preference studies demonstrate that avoidance of adverse effects

Table 1. Integrated framework of determinants, mechanistic pathways, clinical consequences, and targeted interventions for medication nonadherence in osteoarthritis

Domain	Determinant	Type of Nonadherence	Mechanistic Pathway	Clinical / System Consequence	Targeted Intervention Strategy
Patient-related	Advanced age, frailty	Unintentional	Reduced physical capacity and self-management ability	Missed doses, inconsistent use, symptom fluctuation	Regimen simplification, caregiver involvement
	Cognitive impairment	Unintentional	Memory and executive dysfunction impair medication organization	Irregular dosing, treatment gaps	Pill organizers, digital reminders, caregiver supervision
	Fear of NSAID adverse effects	Intentional	Risk perception outweighs anticipated analgesic benefit	Dose reduction, early discontinuation	Shared decision-making, risk–benefit counseling
	Use of complementary and alternative medicine	Intentional	Perceived safety of non-pharmacologic alternatives	Reduced persistence with prescribed therapy	Education addressing comparative effectiveness and safety
Therapy-related	Adverse effect profile (GI, CV, renal risks)	Intentional	Tolerability concerns lead to discontinuation	Switching, intermittent use	Individualized therapy selection, topical NSAIDs
	Polypharmacy	Both	Cognitive and logistical burden from multiple medications	Regimen confusion, missed doses	Medication reconciliation, deprescribing where appropriate
	Complex dosing schedules	Both	Increased treatment burden and reduced convenience	Non-persistence	Once-daily or simplified regimens
Healthcare/system	Inadequate patient education	Both	Limited understanding of duration and purpose of therapy	Incorrect PRN vs continuous use	Structured counseling and reinforcement
	Financial constraints	Intentional	Cost burden leads to dose stretching or delayed refills	Reduced persistence	Cost transparency, insurance navigation
	Fragmented care pathways	Both	Lack of coordinated monitoring and follow-up	Poor long-term adherence tracking	Multidisciplinary care models
Downstream consequence	Persistent pain	NA	Inadequate analgesic exposure	Functional limitation	Reassessment including adherence evaluation
	Reduced mobility	NA	Ongoing symptom burden	Loss of independence	Integrated pharmacologic and exercise therapy
	Reduced quality of life	NA	Chronic uncontrolled symptoms	Psychosocial impact	Comprehensive pain management strategy
	Increased healthcare utilization	NA	Treatment instability and therapeutic cycling	Escalation of care, switching	Proactive adherence monitoring

Source: Developed by the authors based on literature synthesis

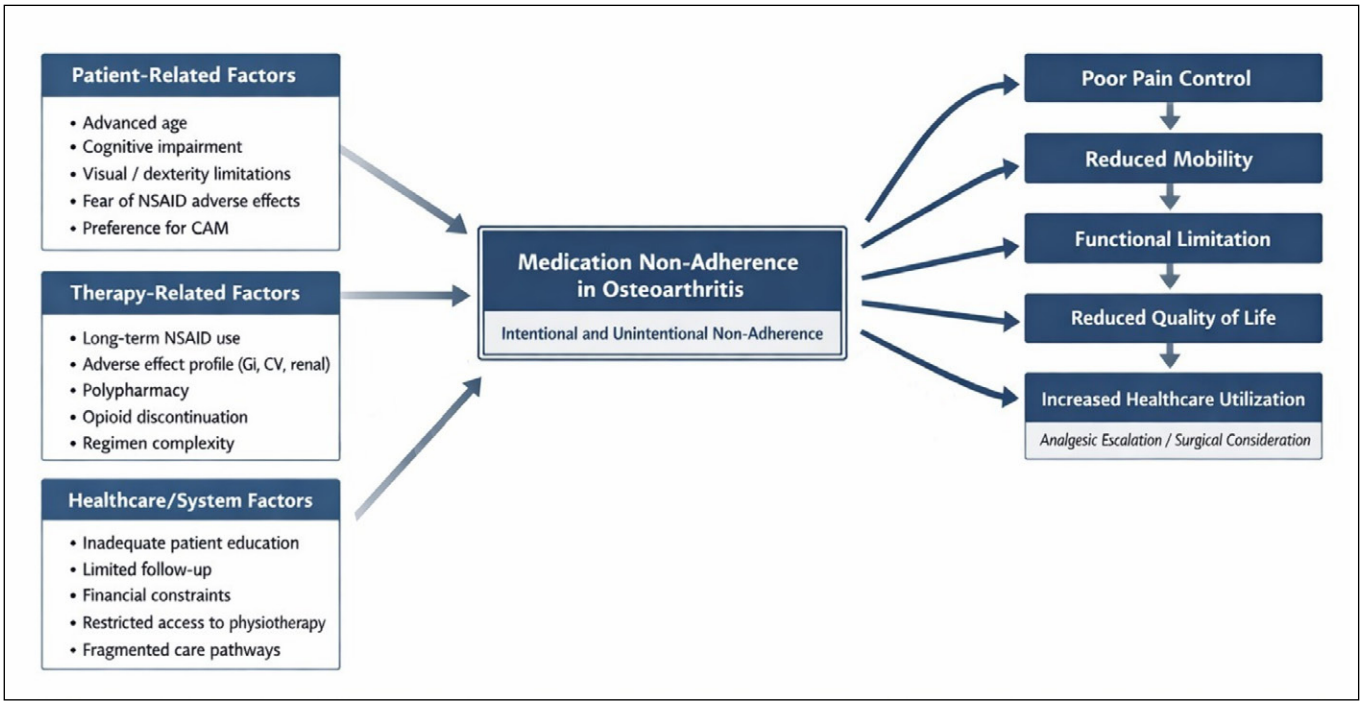

Fig. 2. Conceptual framework illustrating the multidimensional determinants and downstream clinical and healthcare consequences of medication nonadherence in osteoarthritis
Source: Own materials

is a dominant determinant of treatment decisions, sometimes outweighing expected improvements in pain or function [14]. Consequently, some patients independently reduce doses, intermittently use medications, or discontinue therapy without consulting healthcare providers [13, 14].

USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE

High utilization of complementary and alternative medicine further reflects concerns regarding conventional pharmacotherapy. Cross-sectional data indicate that more than 60 percent of individuals with osteoarthritis report using herbal remedies, dietary supplements, or other alternative approaches for symptom management [15]. Preference for perceived natural or safer therapies, particularly among rural populations and those not consistently taking conventional medications, may reduce adherence to prescribed pharmacologic regimens [15].

THERAPY-RELATED DETERMINANTS

ANALGESIC CLASS AND TOLERABILITY

Medication characteristics influence persistence. Observational evidence from hip and knee osteoarthritis populations demonstrates higher adherence among patients initiated on better tolerated agents such as paracetamol alone or combined with nonsteroidal anti-inflammatory drugs, compared with those prescribed opioids, which are associated with earlier discontinuation. Differences in adverse effect profiles and perceived tolerability directly influence continuation patterns.

REGIMEN COMPLEXITY AND POLYPHARMACY

In older adults with multimorbidity, medication regimens are often complex. Multiple prescriptions and dosing schedules increase cognitive and logistical burden. Such complexity contributes to both intentional simplification by patients and unintentional missed doses, particularly in the presence of cognitive or functional limitations [10, 11].

HEALTHCARE SYSTEM AND SOCIOECONOMIC DETERMINANTS

EDUCATION AND COMMUNICATION

Nonadherence is more common among individuals who do not fully understand the benefits, potential side effects, and expected duration of therapy. Limited counselling may leave uncertainty regarding whether medication should be taken continuously or only during symptom exacerbations.

FINANCIAL BARRIERS

Financial factors, including medication cost, are consistently associated with reduced adherence. Economic burden may lead patients to reduce doses or delay refills. Interventions that reduce cost barriers improve adherence outcomes.

LIMITED INTEGRATION OF NONPHARMACOLOGIC CARE

Restricted access to physiotherapy and nonpharmacologic support may weaken treatment engagement. When pharmacologic therapy is not integrated within comprehensive management, patients may question its role or discontinue treatment during fluctuating symptoms.

Taken together, medication nonadherence in osteoarthritis reflects convergence of aging-related vulnerability, cognitive decline, safety concerns, medication tolerability, regimen complexity, financial constraints, and system-level gaps.

The determinants described above rarely operate in isolation. Rather, they interact dynamically within aging populations with multimorbidity, influencing both intentional and unintentional medication-taking behaviors. To conceptualize these interrelationships and their downstream implications, a framework integrating patient-related, therapy-related, and healthcare system determinants with clinical consequences is presented in Figure 2.

Patient-related, therapy-related, and healthcare system factors interact to produce intentional and unintentional nonadherence behaviors. These behaviors contribute to persistent pain, functional decline, reduced quality of life, and increased healthcare utilization, including therapeutic escalation.

CONSEQUENCES OF MEDICATION NONADHERENCE IN OSTEOARTHRITIS

Medication adherence is fundamental to effective osteoarthritis management because pharmacologic therapy is primarily used to reduce pain and preserve function. Although direct longitudinal evidence linking adherence to structural progression remains limited, osteoarthritis-focused observational studies, patient-reported outcomes research, real-world prescribing analyses, and adherence-related interventional studies provide consistent indications of clinical and health service consequences when treatment is inconsistent [19, 23–28, 30].

CLINICAL CONSEQUENCES

Pain is the dominant symptom driving pharmacologic therapy in osteoarthritis. In thumb base osteoarthritis, baseline pain has been associated with adherence patterns, supporting a relationship between symptom burden and treatment behavior [23]. Dissatisfaction with medication effectiveness or tolerability is common and is linked to perceived benefit and safety concerns, reinforcing discontinuation or inconsistent use [25]. In digital self-management programs, baseline pain medication use has been associated with longer duration of high adherence within the program, suggesting clustering of treatment engagement behaviors [19].

Functional limitation in osteoarthritis, including impairment in walking, stair climbing, and daily activities, is closely related to symptom severity. Studies in knee osteoarthritis populations demonstrate strong associations between clinical factors and impaired function and health-related quality of life [28]. Digital self-management research identifies predictors of adherence and engagement and suggests that sustained participation is associated with improved self-reported outcomes, although causal direction may not always be definitively established [24].

Health-related quality of life reflects cumulative effects of pain, mobility restriction, and psychosocial burden. In knee osteoarthritis populations, worse symptoms are consistently associated with poorer quality-of-life scores [28]. Systematic review evidence for exercise and nonpharmacologic interventions indicates that sustained participation improves pain and quality-of-life outcomes [29], reinforcing the broader importance of consistent therapeutic engagement.

Osteoarthritis is characterized by fluctuating symptoms. Real-world prescribing studies demonstrate variable and intermittent nonsteroidal anti-inflammatory drug use patterns among osteoarthritis patients [27]. Although direct longitudinal quantification of adherence-related flare risk remains limited, inconsistent medication-taking plausibly contributes to unstable symptom control in clinical practice.

HEALTHCARE AND ECONOMIC CONSEQUENCES

When symptoms remain uncontrolled, patients frequently seek reassessment. Real-world analyses of nonsteroidal anti-inflammatory drug prescribing and utilization reflect substantial ongoing medication management needs in osteoarthritis populations [27], consistent with frequent healthcare contact.

Variable utilization patterns suggest cycling between agents or adjustment of therapy over time [27]. Persistent pain and disability may lead to escalation of management intensity. Although surgical referral decisions are multifactorial, uncontrolled symptoms remain a central driver of care progression.

Broader osteoarthritis reviews describe the substantial public health and healthcare burden of the disease, including ongoing treatment needs and associated resource consumption [30]. Although adherence-specific cost analyses remain limited, interventions that improve engagement and adherence demonstrate improvements in adherence-related measures and selected clinical outcomes [26], suggesting potential to reduce avoidable healthcare utilization.

Overall, converging evidence indicates that medication nonadherence in osteoarthritis is associated with persistent pain, functional impairment, reduced quality of life, and increased healthcare engagement.

STRATEGIES TO IMPROVE MEDICATION ADHERENCE IN OSTEOARTHRITIS

Medication adherence in osteoarthritis refers to the extent to which medication-taking behavior corresponds with the agreed therapeutic plan. In a single-centre study of patients with knee osteoarthritis, nonadherence reached 55.08 percent [6]. Common contributors include limited understanding, safety concerns, discouragement when improvement is gradual, regimen complexity, multimorbidity, and polypharmacy [6, 33, 36].

PATIENT-CENTERED STRATEGIES

Guideline syntheses emphasize patient-centered care integrating pharmacologic and nonpharmacologic strategies [31,3 2]. Educational discussions should clarify realistic goals, expected time-to-benefit, and risk-benefit considerations. Because avoidance of adverse effects strongly influences treatment preferences [36], addressing safety concerns directly may improve persistence. Shared decision-making aligns therapy selection with patient priorities [31, 32, 36].

Systematic review and meta-analytic evidence across chronic conditions demonstrates overall improvements in medication adherence with mobile application interventions [39]. A randomized controlled trial in older adults with polypharmacy also reported improved adherence following use of a medication management application [37]. In arthritis populations, digital interventions frequently demonstrate positive adherence-related effects, although results vary by intervention design and engagement level [34]. Such tools are best integrated as adjuncts supporting reminders, monitoring, and follow-up [34, 39].

PROVIDER-FOCUSED STRATEGIES

Apparent treatment failure may reflect inconsistent medication use. Expert guidance on nonsteroidal anti-inflammatory drug use in osteoarthritis emphasizes periodic reassessment of treatment response and adherence [33]. Brief standardized tools, including Morisky-type scales used in adherence research, may support structured evaluation when validated for the relevant context [39].

INDIVIDUALIZED TREATMENT PLANNING

Individualized management that accounts for cardiovascular, gastrointestinal, and renal risk enhances safety and acceptability [33]. Topical nonsteroidal anti-inflammatory drugs may reduce systemic exposure when appropriate [35]. Patient-centered framing of pharmacologic options supports confidence and sustained engagement [31, 32, 36].

SYSTEM-LEVEL STRATEGIES

Guideline syntheses recommend integrated care models combining education, pharmacotherapy, physiotherapy referral, and lifestyle interventions [31, 32]. Coordinated follow-up and medication review may reduce fragmentation and support long-term adherence [33].

A cluster-randomized community pharmacy trial reported improved osteoarthritis and pain-management knowledge following pharmacist-led education and medication review, with modest improvements in pain scores [38]. This supports pharmacist integration within multidisciplinary osteoarthritis management [38].

Digital interventions in arthritis populations frequently demonstrate adherence-related benefits, though outcomes vary according to engagement and integration into care [34]. Broader chronic disease meta-analytic evidence supports overall adherence benefits from app-based interventions [39]. Digital approaches are therefore best framed as complements to clinician follow-up rather than replacements [34, 39].

The determinants, mechanisms, downstream consequences, and adherence-enhancing strategies discussed throughout this review are closely interconnected rather than occurring in isolation. Patient vulnerability, medication characteristics, and healthcare system factors converge to shape intentional and unintentional medication-taking behaviors, which subsequently influence symptom stability, functional outcomes, and healthcare utilization. To provide an integrated synthesis of these multidimensional relationships and their corresponding intervention targets, Table 1 summarizes key determinants, mechanistic pathways, clinical consequences, targeted strategies, and representative supporting evidence.

This table provides an integrated synthesis of patient-related, therapy-related, and healthcare system determinants of medication nonadherence in osteoarthritis. For each determinant, corresponding mechanistic pathways, downstream clinical and healthcare consequences, and targeted intervention strategies are outlined. The framework reflects thematic integration of the evidence discussed throughout this review.

CONCLUSIONS

Medication nonadherence in osteoarthritis represents a multifactorial and clinically consequential challenge that directly influences symptom control, functional outcomes, and healthcare utilization. As synthesized in this review, nonadherence arises from interacting patient-related, therapy-related, and healthcare system determinants, often reflecting both intentional and unintentional behaviors. Its consequences extend beyond persistent pain to include functional decline, reduced quality of life, therapeutic escalation, and increased economic burden. Importantly, nonadherence remains insufficiently addressed in routine clinical practice, despite its central role in determining real-world treatment effectiveness.

FUTURE DIRECTIONS

Future research should focus on standardizing adherence assessment methods specific to osteoarthritis populations and conducting high-quality prospective studies evaluating multimodal, patient-centered adherence interventions. Greater integration of digital health tools, pharmacist-led models, and structured behavioral strategies may offer scalable solutions. Additionally, incorporating adherence outcomes into clinical trials would provide a more accurate representation of therapeutic effectiveness in real-world settings. Recognizing medication adherence as a therapeutic target rather than a peripheral issue is essential to improving long-term outcomes in osteoarthritis care.

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REVIEW ARTICLE

CONTENTS

Iliotibial band and lumbar spine pain – a hidden connection

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ABSTRACT

The iliotibial band (Latin: *tractus iliotibialis*; ITB) is most commonly associated with patellofemoral pain syndrome, also referred to as runner's knee. However, the impact of its imbalance on the lumbar spine is substantial and frequently overlooked. As a significant thickening of the fascia lata, the iliotibial band serves as a crucial component for the lateral stabilization of the entire kinematic chain of the lower extremity and the pelvis. Restricted tissue gliding, gluteus medius insufficiency and weakness of the core musculature may present as primary contributors to pain syndromes manifesting in the lumbar region of the spine. This article highlights the relationship between the dysfunction of the iliotibial band and chronic lumbar spine pain to propose a comprehensive rehabilitation approach. This approach should include soft tissue relaxation techniques, loading of muscle structures, and correction of movement patterns. The attention given to the flexibility of the iliotibial band allows for a substantial reduction in the pain of the sacroiliac region.

KEY WORDS: rehabilitation, treatment, kinesio tape

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INTRODUCTION

Pain in the lumbar spine is affecting more and more people. The problem affects not only athletes due to repetitive movements and overexertion [1]. Most people with sedentary lifestyles, including disabled people who spend a lot of time in wheelchairs, complain of discomfort in the lumbar spine. The increasing number of women reporting chronic back pain during pregnancy, postpartum, and in the period following delivery is expanding the group of patients with lumbosacral pain. These complaints become chronic.

The causes vary greatly, ranging from insufficient physical activity to an ill-chosen training plan. The result is poor biomechanics of the entire body.

Patients are characterized by muscle imbalance. The symptom is hypotonia of the abdominal muscles with simultaneous resting hypertonia of the muscles: iliopsoas, quadratus lumborum, gluteus maximus, tensor fascia lata, and vastus lateralis.

AIM

The aim of the current article is to highlight the often-overlooked relationship between iliotibial band (ITB) dysfunction and chronic lumbar spine pain, and to propose a comprehensive rehabilitation approach that integrates assessment of the ITB, targeted manualtherapy techniques, and progressive core stabilization exercises to alleviate lowback discomfort and improve overall pelviclumbar biomechanics.

MATERIALS AND METHODS

In order to develop a comprehensive therapeutic model, the following research and clinical methods were utilized:

1. Literature Review: A systematic search of electronic databases (PubMed, Google Scholar, Scopus) was conducted to identify biomechanical correlations between the iliotibial band (ITB) and the lumbopelvic complex;
2. Clinical Diagnostic Tests: The model incorporates the use of the Ober test for the clinical assessment of ITB tension and flexibility;
3. Physiotherapeutic Procedures: The efficacy of the following manual therapy techniques was analyzed:
   - o Deep Tissue Massage and "Pin & Stretch": Aimed at improving myofascial gliding and reducing tissue adhesions;

- Post-Isometric Relaxation (PIR): Utilized to normalize the muscle tone of the lumbopelvic structures;
- Trigger Point Therapy: Targeted at eliminating referred pain patterns within the kinetic chain.

4. Supplementary Methods: The analysis included the application of kinesiotaping for structural support and biofeedback training to enhance motor control and postural self-correction.

REVIEW AND DISCUSSION

The iliotibial band is located on the lateral side of the thigh. It consists of longitudinally arranged fascial connective tissue. It is formed by the connection of tendinous tissue fibers with the tensor fascia lata muscle at the front, centrally in the extension of the thick, tendinous fascia of the gluteus medius, and with the fibers of the gluteus maximus muscle at the back [2].

The proximal part is divided into three layers:

–superficial – from the anterior superior iliac spine to the fascia lata;

–intermediate – from the ilium to the tensor fascia lata muscle;

–deep – the supracondylar fossa.

All layers connect at the distal end (tensor fascia lata tendon) and pass through the greater trochanter without attachment. The distal course is firmly attached to the linea aspera of the femur via the lateral intermuscular septum.

The iliotibial band ends by attaching to the lateral condyle of the femur, the lateral retinaculum of the patella, and the anterolateral side of the tibial condyle (Gerdy's tubercle) [2, 3].

The ITB is composed of fibrous connective tissue. It exhibits significant mechanical integrity and plays a key role in the transmission of tension in the musculoskeletal system. It is characterized by a high potential for structural adaptation in response to progressive mechanical and functional loads.

The fascia does not have its own motor innervation but is closely connected to the nerves supplying the muscles:

–tensor fascia lata – superior gluteal nerve (L4 – S1);

–gluteus maximus muscle – inferior gluteal nerve (L5 – S2) [4].

The most common dysfunction is iliotibial band syndrome (ITBS). It causes pain on the outside of the knee. It mainly affects athletes and people with mobility issues.

Those most at risk of strain injuries are people who lead a sedentary lifestyle, women who have been pregnant, and people who perform physical work involving repetitive movements (lifting and passing weights to one side).

The most common symptoms are:

–dull pain in the lower back, worsening in the evening;

–feeling of stiffness in the hip, radiating to the lumbar spine;

–pain in the lumbar spine radiating to the side of the thigh, confused with sciatica, without neurological symptoms;

–stiffness in the lateral part of the thigh;

–increased tension in the quadratus lumborum, gluteus maximus, and hip flexors;

–weakness of the gluteus medius muscle (responsible for stabilizing the pelvis during walking);

–pain in the lumbosacral region (mistakenly diagnosed as a disc problem).

Reduced gluteus medius muscle function causes a deficit in dynamic pelvic stabilization. The compensatory mechanism is excessive activity of the tensor fascia lata (TFL) and gluteus maximus (GLUT MAX) muscles. This causes a chronic increase in ITB tone, especially in the central and posterior parts [5].

The mechanism most commonly found in women who were in advanced pregnancy involves a decrease in the muscle tone of the abdominal press. The result is a lack of control over pelvic mobility. Anterior pelvic tilt, increased lumbar lordosis, excessive activation of the hip flexor muscles, and hyperactivity of the tensor fascia lata muscle (which transfers tension to the iliotibial band) [6]. When unilateral tension occurs, the pelvis becomes tilted, resulting in functional shortening of the lower limb and lateral curvature of the spine.

REHABILITATION

Patients presenting with lumbar spine pain often undergo local rehabilitation in the area where the pain occurs. It is worth paying attention to the iliotibial band even if the Ober test is negative. The tissue of the band is very susceptible to mechanical overload. Myofascial stiffness tends to compress deep structures. The priority in the initial stage of improvement is to separate the iliotibial band from the hamstrings and quadriceps, which often pull the band backward or forward.

When the patient is lying on their healthy side, the hip and knee joints remain bent at approximately 40 degrees. The therapist places their hands on the side of the thigh, palpating the ITB.

PIN & STRETCH TECHNIQUE

Hook the band and gently stretch it, looking for the direction of tension: up and down and sideways until we achieve smooth tissue gliding.

Fig. 1. Skin rolling technique of the ITB
Source: Own materials

In order to increase tissue flexibility, soft tissue mobilization is performed using the skin fold rolling method. The technique is performed by grasping the fold, starting from the distal segments (lateral femoral epicondyle area), maintaining constant tissue traction, in the proximal direction (up to the level of the anterior iliac spine). The therapist works on all parts of the anterior, central, and posterior ITB. The goal is to achieve smooth tissue gliding and reduce interfascial adhesions (Fig. 1) [7].

After initial superficial treatment, we move on to targeted neuromuscular therapy of deeper structures. We use deep transverse massage along the entire length of the iliotibial band, perpendicular to the direction of the fibers (Fig. 2).

Continuing therapy in the proximal direction, we focus on the gluteus maximus muscle and the tensor fascia lata muscle. The goal is to normalize the muscle tone of the structures that tighten the ITB (Fig. 3, 4) [7,8].

In the chronic phase, an important treatment is Trigger Point Therapy, which often targets the vastus lateralis, tensor fascia lata, and gluteus maximus muscles. The presence of active trigger points in these areas often induces referred pain that mimics or exacerbates ITB symptoms.

Fig. 2. Deep transverse massage of the ITB
Source: Own materials

Ischemic compression – involves applying strong pressure to a point, e.g., with a thumb or elbow. Positional relaxation – positioning the patient's body in a position where the pain disappears.

Self-treatment – using balls, e.g., tennis balls, and rollers.

This therapy is often painful for the patient, but it brings immediate relief [9]. A key element of the therapy is the normalization of tension in the sciatic-shin group and gluteal muscles using the Post-Isometric Relaxation (PIR) method. The technique utilizes the phenomenon of autogenic inhibition, which allows for the safe elongation of muscle-fascial structures (Fig. 5, 6).

In women who have given birth by caesarean section, the scar should be examined to check its tenderness and mobility. Most women avoid pain by walking in a bent position. Scar therapy is a key element in returning to full fitness. We begin mobilization with stroking and gentle planar sliding, then use gentle movements to traction the scar from the fascia. When working with scars, rehabilitation may be longer and more laborious

Fig, 3. Manual rolling of the TFL
Source: Own materials

Fig. 4. Deep manual therapy of the TFL
Source: Own materials

Fig, 5. PIR of the gluteal muscles
Source: Own materials

Fig. 6. PIR of the sciatic-shin group
Source: Own materials

Fig. 7. Kinesiotaping of the ITB
Source: Own materials

in the later stages. Many physical therapists also perform Dry Needling therapy. Kinesiotaping is used as a supportive therapy method (Fig. 7)

After completing manual therapy and myofascial release, core stabilization training is essential. Its purpose is to strengthen the lumbar-pelvic-hip complex (LPHC). Particular emphasis is placed on activating the rectus abdominis, oblique muscles, transverse abdominis, and gluteus medius muscles in order to improve the efficiency of the deep stabilizers of the torso [9].

Due to advanced structural and muscular imbalance, we begin the rehabilitation process with static muscle activation.

EXAMPLE EXERCISE FOR THE RECTUS ABDOMINIS MUSCLE

Starting position – lying on your back, lower limbs bent at the hip and knee joints, feet stabilized.

The patient performs an isometric contraction of the rectus abdominis muscle, which involves applying axial pressure with the hands to the surface of the thighs while reducing the lordosis of the lumbar spine.

Next, we activate the remaining muscle groups involved in core stabilization.

The next phase of rehabilitation involves introducing exercises of increased intensity and fewer points of support, while maintaining stabilization of the lumbar spine through even tension of the abdominal and gluteal muscles.

An important form of improvement is working with biofeedback, which allows the patient to continuously self-correct their pelvic alignment [10].

The recommendation for the patient for subsequent home rehabilitation is to perform the following exercises after learning them with a therapist:

–rolling the iliotibial band and the front of the thigh,
–stretching the gluteus maximus and hamstrings,
–strengthening the lumbar-pelvic-hip complex.

The patient should pay attention to the quality of movement and stabilization of the muscle corset.

CONCLUSIONS

It is worth checking the iliotibial band not only in known cases such as ITBS (causing pain in the outer part of the knee joint), but also in chronic lumbar spine pain.

Effective rehabilitation should be comprehensive. It should include soft tissue relaxation techniques (an important component), progressive loading of muscle structures (a key element of therapy), and correction of movement patterns.

Attention to the flexibility and proper function of the iliotibial band leads to a significant reduction in pain in the sacroiliac region.

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REVIEW ARTICLE

CONTENTS

Effects of psychological stress on skin aging: A literature review

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ABSTRACT

Skin aging is a multifactorial biological process driven by the interplay of intrinsic and extrinsic influences. Progressive deterioration of the dermal collagen fiber network represents a central structural hallmark of this process. Both the quantity and functional quality of cutaneous collagen are modified by numerous factors, including autoimmune disease, chronological aging and psychological stress. This narrative review synthesizes current evidence on the neuroendocrine, molecular and cellular pathways through which psychological stress may influence dermal collagen and elastin remodeling, thereby contributing to premature skin aging. Available evidence suggests that chronic activation of the hypothalamic–pituitary–adrenal axis and sympathetic nervous system leads to increased glucocorticoid and catecholamine signaling, oxidative stress, extracellular matrix degradation and impaired epidermal barrier function. Understanding these mechanisms may support the development of integrated therapeutic strategies targeting stress-responsive pathways to preserve skin structure and function. Future studies that track patients over time and examine molecular changes are needed to turn these findings into ways to prevent or treat stress-related skin aging.

KEY WORDS: collagen, epidermal barrier, oxidative stress, hypothalamo-hypophyseal system

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INTRODUCTION

Genetic programming, hormonal changes and cellular senescence are the main causes of intrinsic aging, whereas environmental stressors such UV radiation, pollution, smoking and nutrition are the main causes of extrinsic aging. [1] Psoriasis, atopic dermatitis, pathological impairment of barrier function and wound healing are among the cutaneous dermatoses that may be triggered by psychological stress. [2] Chronic stress is frequently associated with poor sleep, dietary imbalance and decreased self-care, all of which worsen oxidative and inflammatory damage. [1] There is currently only one publication that discusses obvious aging symptoms brought on by psychological stressors. This study was carried out on participants who were subjected to occupational stress brought on by a particular kind of professional job under very particular circumstances. [3] The effects of psychological stress on the autonomic nervous system, renin-angiotensin system (RAS) and hypothalamus-pituitary-adrenal (HPA) system are widely known, despite the fact that direct evidence connecting psychological stress to aging is still developing. These systems are recognized to play a role in DNA damage, oxidative stress and inflammation all of which are recognized aging processes in all tissues, including the skin. [4] Chronic psychological stress is an additional potential element in aging that accelerates telomere shortening. It manifests as indications of skin aging in both people and rats. [5,6] According to recent studies, psychological stress may also affect skin aging by interfering with the integrity of the dermal extracellular matrix and the homeostasis of the epidermal barrier. Stress hormone signaling has been shown in both experimental and clinical studies to decrease the production of structural proteins and lipids in the epidermis. It also hinders stratum corneum hydration and increases transepidermal water loss. These changes not only compromise cutaneous defense but may also make the skin more susceptible to premature aging. [7]. In the dermis, stress-responsive molecular pathways have been shown to alter collagen and elastin networks through modulation of fibroblast activity, enzymatic

remodeling and oxidative injury. This weakens the biomechanical resilience and contributes to wrinkle formation and loss of elasticity [8-10]

AIM

The aim of this narrative review is to evaluate the current evidence on the relationship between psychological stress and skin aging. It seeks to summarize the underlying neuroendocrine and molecular mechanisms involved, examine clinical and epidemiologic findings.

MATERIALS AND METHODS

A literature search was conducted in PubMed and Google Scholar for articles published between 2016 and 2026. The following search terms were used in various combinations: "psychological stress," "mental stress", "perceived stress","skin aging,""dermal aging","wrinkles". Searches were limited to studies published in English and involving adult human subjects.

REVIEW

The database search yielded 44 records on PubMed and 17,800 on Google Scholar. After removal of duplicates and screening of titles and abstracts, 18 full-text articles and 6 abstracts were assessed for eligibility, of which 13 met the inclusion criteria. Included studies were published between 2016 and 2026.

Several studies reported that exposure to psychological stress activates the hypothalamic–pituitary–adrenal axis, resulting in increased production of stress hormones both systemically and within the skin. This neuroendocrine response was associated with impaired epidermal barrier function, including reduced synthesis of lipids and structural proteins, lower stratum corneum hydration and elevated transepidermal water loss. [7] Integrative studies highlight that persistent neuroendocrine activation enhances inflammatory signaling, induces oxidative damage and disrupts matrix metalloproteinase control, hence expediting the destruction of collagen and elastin. [11, 12]

Studies commonly assessed skin aging through clinician-based visual inspection, focusing on wrinkles, pigmentation changes and reduced elasticity. According to the literature, psychological stress contributes to skin aging through multiple interconnected mechanisms. It promotes cellular senescence and alters extracellular matrix remodeling. Stress also activates neuroendocrine pathways and increases oxidative damage within skin tissues. In addition, it influences subjective perceptions of aging, further linking psychological burden to visible cutaneous changes.

General reviews of skin aging describe the combined effects of intrinsic and extrinsic influences. Intrinsic factors include genetic predisposition, telomere shortening, immunological decline, hormonal changes, and cumulative oxidative stress. These internal processes interact with environmental exposures such as ultraviolet radiation, pollution, smoking, diet, and sleep disturbances. Together, they contribute to the development of wrinkles, skin laxity, pigmentary alterations, and surface irregularities.[9, 10, 13]

Clinical investigations provide human evidence supporting these observations.In a clinical study involving 36 participants, 18 were exposed to mild psychological stress and 18 to moderate psychological stress. Adults in the moderate stress group showed reduced antioxidant capacity. They also exhibited impaired epidermal integrity. In addition, this group demonstrated more pronounced microrelief changes, including increased fine lines and surface irregularities, compared with individuals experiencing lower levels of stress.

[11]. Cellular analyses from the same cohort indicated that elevated cortisol and epinephrine levels were associated with reduced extracellular matrix synthesis, DNA damage, delayed wound closure and altered expression of genes regulating collagen production and barrier maintenance [11]. Additionally, experimental research demonstrated that stress mediators directly affect cutaneous fibroblasts. A molecular role for sympathetic signaling in speeding up dermal aging is supported by the findings that epinephrine exposure caused premature cellular senescence, elevated pro-inflammatory pathways and reduced wound-healing capacity. [5] Complementary molecular reviews have explained that stress-responsive signaling pathways disrupt collagen and elastin networks. These pathways alter fibroblast activity and promote enzymatic remodeling of the extracellular matrix. As a result, the biomechanical integrity of the skin is weakened. This structural decline contributes to wrinkle formation and tissue laxity. [8]. Population-based surveys and observational studies reinforce these biological findings. Among young Asian women, higher levels of perceived psychological stress were linked to increased self-reported signs of early skin aging. These included a dull complexion, rough skin texture, and a perception of slower skin metabolism. In parallel, dermatologists and psychologists frequently identified dryness, acne, and irritation as common cutaneous features associated with psychological stress [14].

DISCUSSION

Chronic activation of stress-responsive systems, particularly the sympathetic nervous system and the

hypothalamic–pituitary–adrenal axis, appears to play a central role in stress related skin aging. Persistent stimulation of these pathways is associated with reduced extracellular matrix integrity and impaired epidermal barrier function. Across narrative, clinical, and epidemiologic studies, this neuroendocrine activation has been linked to the development of visible cutaneous aging features.[2,7,15]. These findings extend the current understanding of intrinsic and extrinsic skin aging by situating psychological stress as a physiologically reasonable and clinically significant modification of the aging trajectory [11,13].

A substantial amount of research links stress to changes in skin collagen. Stress's duration is a key distinguishing factor. Dysregulation of the circadian cortisol/corticosterone rhythm is a key sign of chronic stress's negative consequences. [16] The disturbance of epidermal homeostasis by catecholamines and glucocorticoids is one of the most often documented mechanisms. Stress-related decreases in structural protein expression, lipid synthesis and stratum corneum hydration, along with elevated transepidermal water loss, may weaken the barrier's integrity and increase susceptibility to environmental aggressors such contaminants and UV light [7,15]. This breakdown of the barrier may accelerate age-related decrease in the dermal and epidermal compartments by sustaining low-grade inflammation and oxidative damage. [1,10] These findings lend credence to the idea that stress not only causes aging-related alterations but may also intensify other external factors that cause skin damage [13]. Chronic psychological stress raises the level of reactive oxygen species (ROS) and causes lipid peroxidation in keratinocytes and fibroblasts. Elevated ROS levels damage cellular membranes and DNA, causing mitochondrial malfunction and decreasing dermis flexibility [1].

Another important way that psychological stress seems to affect skin aging is through changes in dermal extracellular matrix remodeling. Long-term exposure to stress mediators may affect the skin's structural support and mechanical resilience, according to experimental evidence showing stress-induced fibroblast senescence and poor wound healing as well as molecular analyses of collagen and elastin network disruption. [2,10]. These changes are consistent with biomechanical modeling studies showing that collagen degradation lowers the threshold for wrinkle formation and contributes to laxity and textural changes [9]. Together, these results give the clinical relationships between stress and outward signs of aging a mechanical foundation [5, 7].

These molecular findings are supplemented by human observational and survey-based studies that show correlations between self-reported or clinician-assessed indicators of aging and perceived stress, even in very young populations [8, 5]. The case for a clinically significant connection between psychological stress and cutaneous aging processes is strengthened by the convergence of subjective sensations with objective biophysical and cellular measurements [7]. However, a large portion of the human evidence is still cross-sectional, which restricts the ability to draw conclusions about causality and increases the likelihood that observed links could be influenced by reverse relationships, such as distress brought on by skin problems [5, 8].

Future research should emphasize longitudinal cohort studies to clarify temporal links between stress exposure and progressive skin aging, as well as interventional trials assessing whether stress reduction can meaningfully modify biological age indicators in the skin [5, 7]. Standardizing stress measurements, including objective biomarkers like hair cortisol and integrating high-resolution imaging and genetic profiling would increase causal inference [7, 15]. Additionally, expanding research across diverse populations and age groups will be essential to ensure generalizability and to identify vulnerable subgroups [8].

CONCLUSIONS

Psychological stress should be acknowledged as a biologically significant modulator of skin aging, functioning via interrelated neuroendocrine, cellular and extracellular systems rather than as a peripheral or solely subjective effect. Its effects extend beyond obvious skin changes, influencing barrier function, extracellular matrix integrity and cellular resilience, as well as interacting with other inherent and extrinsic aging factors. This viewpoint reframes skin aging as a multifaceted phenomena in which psychological and physiological systems interact, emphasizing the significance of incorporating mental health into dermatological research and clinical procedures.

Furthermore, current research suggests that unexplored intervention opportunities exist: addressing stress-responsive pathways pharmacologically, nutritionally or behaviorally may supplement established treatments targeted at protecting collagen, elastin and barrier function. Conceptually, these findings show that skin aging is not only the result of chronological or environmental variables, but also a dynamic reflection of systemic stress exposure, stressing the need of viewing the skin as both a biological endpoint and a visible indication of holistic health.

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REVIEW ARTICLE

CONTENTS

The role of regional government in the development of international academic cooperation in health care: Experiences from the Lublin region

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ABSTRACT
Health care systems increasingly require cooperation between public administration, medical universities, and international partners. Regional governments can act as integrators and coordinators in this process. The aim of this paper is to present a model of cooperation between the Marshal's Office of the Lublin Voivodeship, the Medical University of Lublin, and Gulf Medical University. The article presents the perspective of regional administration and focuses on the practical aspects of initiating and supporting international academic collaboration. The role of regional government in creating organizational and institutional frameworks for joint activities in medical education and health workforce development is described. Attention is also given to the importance of such partnerships for improving the quality of health care services and for the internationalization of the academic environment. The presented model of cooperation may serve as a useful reference for other regions seeking effective forms of collaboration between science, public administration, and clinical practice.

KEY WORDS: public health, international cooperation, medical education, healthcare systems

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INTRODUCTION
International cooperation in the field of health care is of great importance today. In a globalized world, health problems often extend beyond the borders of a single country. Cooperation between institutions and universities from different countries can form the basis for better education, research, and the development of new clinical solutions [1]. Academic and research partnerships support the exchange of knowledge and resources. Such cooperation can foster the development of competencies of universities and organizations on both sides of the partnership [1,2]. Lau et al. emphasized that joint research projects create opportunities for mutual exchange of experience and research activities in response to local and global health challenges [2]. Regional governments, as entities responsible for health policy, can act as coordinators of such partnerships. They can support not only the initiation of contacts but also the creation of conditions for sustainable institutional relationships. This role may be particularly effective in the context of medical education and health workforce training, with tangible benefits for the health care system.

AIM
This article presents a model of cooperation between three institutions: the Marshal's Office of the Lublin Voivodeship, the Medical University of Lublin, and Gulf Medical University. The model illustrates how regional government can support international academic cooperation and the benefits it brings to the medical and educational communities.

MATERIALS AND METHODS
The presented analysis is based on a qualitative case study approach focusing on institutional cooperation between the Marshal's Office of the Lublin Voivodeship, the Medical University of Lublin, and Gulf Medical University. Data were gathered from official strategic

documents, regional development plans, institutional reports, and interview summaries from key stakeholders involved in the tripartite cooperation model. Document analysis was used to trace how the cooperation developed over time, to identify the main governance structures supporting it, and to examine the role of regional authorities in promoting international academic collaboration. In addition, semi-structured interviews with administrative representatives and academic staff were carried out to better understand the motivations, challenges, and perceived outcomes of the partnership. The interview material was analyzed thematically and compared with the document findings in order to strengthen the credibility of the results. This approach made it possible to explore in detail the institutional relationships and governance mechanisms shaping the Lublin region's model of international academic cooperation.

REVIEW

THE ROLE OF REGIONAL GOVERNMENT IN THE HEALTH CARE SYSTEM

With the ongoing decentralization of health care systems, the role of regional government has become stronger. Increasingly, the regional level is responsible for strategic planning and coordination of health-related activities. This includes both the organization of services and the support of medical education and workforce development [3]. Research indicates that effective governance at the regional level helps align health policy with local needs. It also allows for more flexible responses to changing demographic and epidemiological challenges [4]. In this setting, regional government acts as an intermediary between central administration, academia, and clinical practice. An important area of activity for regional authorities is cooperation with medical universities. Such partnerships enable educational goals to be linked with the real needs of the health care system. The literature emphasizes that integrating health planning with workforce training contributes to improving the quality of patient care [5]. Regional government may also support the internationalization of universities and health institutions. These activities include creating formal frameworks, providing organizational support, and stabilizing long-term partnerships. Analyses of public health governance suggest that engagement of regional administration increases the sustainability of international cooperation and its practical relevance [6]. In this context, regional government moves beyond a purely administrative function. It becomes an active participant in health system development. Its role involves aligning the interests of different stakeholders and creating conditions for cooperation based on trust and shared goals.

ACADEMIC AND CLINICAL POTENTIAL OF THE MEDICAL UNIVERSITY OF LUBLIN

Medical universities play a key role in the functioning of health care systems. They are responsible for training the workforce, advancing research, and transferring knowledge into clinical practice. Their importance goes beyond education alone and includes a real impact on the quality of patient care [7]. The Medical University of Lublin serves as a leading academic and clinical center in the region. The institution combines teaching activities with hospital-based practice and scientific research. This model supports the training of physicians and other health professionals in conditions that reflect the actual needs of the health care system. The literature emphasizes that strong academic capacity is essential for the development of modern medicine. Medical schools that actively participate in research and international collaboration better prepare graduates to work in a rapidly changing clinical environment [8]. An important aspect of medical university activity is social responsibility. The concept of social accountability of medical schools assumes a close alignment between education, research, and the health needs of the population [9]. In this context, cooperation with public administration and international institutions becomes a tool for fulfilling this mission. The development of academic potential requires stable institutional conditions. Support from regional government can strengthen a university's capacity to undertake international initiatives. This applies to both educational projects and scientific research. Such activities increase the visibility of the academic center and contribute to the long-term development of the region.

THE INTERNATIONAL DIMENSION OF ACADEMIC COOPERATION

The internationalization of medical universities is now one of the key directions of their development. Cooperation with foreign partners contributes to improving the quality of education and research. It also helps prepare health professionals to work in culturally and organizationally diverse health care environments [10]. International partnerships enable the exchange of educational and clinical experience. The literature emphasizes that such relationships strengthen the capacity of institutions on both sides of the collaboration. This

applies to educational programs as well as joint research initiatives [11]. In this context, cooperation with Gulf Medical University plays an important role. The institution operates within a dynamically developing health care system. Experience gained in an international environment may complement the European perspective. The exchange of knowledge and best practices supports a better understanding of different models of education and health care organization. Research indicates that effective international collaboration requires clearly defined objectives and stable institutional frameworks [12]. Engagement of public entities is also crucial, as they can ensure continuity and coordination of activities. Without such support, cooperation often remains limited to isolated and short-term initiatives. Collaboration between medical universities from different regions of the world may generate systemic benefits. These include the development of teaching staff competencies, increased academic mobility, and improved preparation of graduates for the challenges of modern medicine. In this perspective, international cooperation becomes an important element of regional health system development strategies.

THE TRIPARTITE COOPERATION MODEL AS AN EXAMPLE OF GOOD PRACTICE

Effective cooperation in health care requires a clear division of roles. This is particularly important in projects carried out by entities with different competencies and responsibilities. A tripartite model that includes public administration as well as domestic and international academic partners allows for better coordination of activities [13]. In the case analyzed here, regional government acts as the initiator and stabilizing force of cooperation. It provides organizational frameworks and ensures continuity. As a result, collaboration is not limited to single events or short-term projects. It can develop in a structured and long-term manner. The medical university contributes scientific and educational capacity. It provides access to expert staff and educational and clinical infrastructure. The international partner broadens perspective and enables exchange of experience within a different health care system. This combination of competencies supports the creation of projects with practical relevance. The literature on public health governance indicates that multisector partnerships increase the effectiveness of systemic actions. Their success depends on strong leadership and clearly defined objectives [14]. In this view, the role of public administration extends beyond formal responsibilities and includes active management of collaborative processes. The presented tripartite cooperation model aligns with the concept of an integrated approach to health system development. It combines education, clinical practice, and health policy. It may serve as a reference for other regions seeking effective forms of institutional collaboration.

DISCUSSION

The presented cooperation model shows that effective partnerships in health care require the involvement of multiple stakeholders. Collaboration between universities alone, even at the international level, may be insufficient. The lack of stable institutional frameworks often limits sustainability and real system impact [18]. Without administrative anchoring, many initiatives remain dependent on individual engagement and may lose continuity over time. Engagement of regional government may reduce this risk. Public administration has tools that allow coordination of activities and ensure continuity. The literature emphasizes that strong leadership and clear governance structures are essential for the success of complex health initiatives [19]. In practical terms, this includes setting strategic priorities, supporting resource allocation, and facilitating long-term institutional dialogue. These functions help maintain operational stability and reinforce shared accountability among partners. Another important dimension relates to policy coherence. Academic collaboration may generate valuable outcomes, but their system-level relevance depends on alignment with regional health priorities. Government involvement supports integration of educational and research initiatives with broader health system objectives. This integration strengthens the translation of academic outputs into practical benefits for patient care and workforce planning. The model also highlights the importance of trust-building between institutions. Long-term cooperation requires predictability, transparency, and mutual recognition of institutional autonomy. Administrative engagement may serve as a stabilizing factor that mitigates uncertainty and reinforces confidence among participants. Such conditions foster open exchange of expertise and facilitate sustainable collaboration beyond single projects. It should also be noted that international cooperation is not without challenges. Cultural, organizational, and systemic differences may complicate the achievement of shared goals. These may include variations in regulatory frameworks, educational structures, or clinical governance models. However, research indicates that clearly defined roles and a shared vision of development can mitigate these difficulties [20]. Structured communication and regular evaluation of progress further support adaptive problem solving. Exposure

to diverse operational contexts may itself be beneficial. Interaction with alternative approaches to education and health system organization broadens institutional awareness and stimulates innovation. This process encourages reflective evaluation of existing practices and may support modernization of training and service delivery models. Such outcomes illustrate the indirect but meaningful impact of international collaboration. The collaborative framework also enhances circulation of knowledge between academia and administration. Bidirectional communication enables scientific insight to inform policy development, while policy priorities shape academic focus. This dynamic contributes to a more responsive and context-sensitive health system environment. Over time, such interaction may strengthen institutional learning capacity. An important aspect of the discussed model is its potential reproducibility. Although cooperation between the Medical University of Lublin and Gulf Medical University is shaped by local conditions, the mechanisms presented here may be adapted in other regions. This applies particularly to the role of regional government as an entity supporting and integrating academic and clinical activities [18,19]. Successful transferability depends on governance capacity, institutional maturity, and commitment of stakeholders. It is equally important to acknowledge potential limitations. The present discussion is based on an institutional perspective and does not include quantitative outcome evaluation. Future research could examine measurable indicators such as educational outcomes, mobility patterns, or clinical impact. Such analyses would strengthen the evidence base for the effectiveness of similar cooperation models. Discussion of this model fits within the broader debate on health system governance. Increasing attention is given to integrated approaches that connect education, research, and clinical practice. In this context, tripartite partnerships may represent an important element of modern health policy. Their continued development may contribute to more resilient health systems capable of responding to demographic change, workforce shortages, and technological transformation.

CONCLUSIONS

The presented cooperation model shows that regional government can play a meaningful role in the development of health care. This role is not limited to administrative functions. It also includes initiating and supporting sustainable academic partnerships. Such an approach promotes stability and continuity of activities. Cooperation between medical universities and international partners brings educational and organizational benefits. Exchange of experience and exposure to different models of training and clinical practice strengthen the competencies of health professionals. These effects are long term and may influence the quality of patient care. An important component of the model is a clear division of roles among partners. Regional government provides institutional frameworks and coordination. Universities are responsible for educational and scientific activities. This structure supports effectiveness and reduces the risk of fragmented initiatives. The experience presented indicates that tripartite cooperation can serve as an effective tool of regional health policy. The model may be adapted in other regions when local organizational and systemic conditions are considered. This requires deliberate engagement of public administration and a long-term vision for health system development.

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REVIEW ARTICLE

CONTENTS

The gut-brain axis and its role in obesity-induced homeostatic dysregulation

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ABSTRACT

Aim: The gut–brain axis (GBA) plays a crucial role in maintaining systemic homeostasis through bidirectional communication between the central nervous system and the gastrointestinal tract. This review aims to summarize current evidence regarding the impact of obesity on GBA function and to discuss potential therapeutic strategies targeting this pathway.

Materials and Methods: A narrative literature review was conducted using scientific publications indexed in databases including PubMed, ScienceDirect, and the European Journal of Endocrinology. Studies addressing obesity-related alterations in neural signaling, gut microbiota composition, and peptide hormone regulation (e.g., cholecystokinin, peptide YY, ghrelin) were analyzed. Particular attention was given to mechanisms involving dopaminergic reward circuits and emerging therapeutic targets such as ghrelin antagonists, gamma-aminobutyric acid modulators, and melanocortin-4 receptor agonists.

Evidence indicates that obesity is associated with significant alterations in gut microbiota composition, vagal signaling, and neuroendocrine regulation of appetite and reward pathways. These changes contribute to dysregulation of nutrient absorption, inflammatory responses, and metabolic homeostasis. Both invasive and non-invasive interventions - including dietary modification, microbiome-targeted therapies, pharmacological agents, and neurostimulation techniques - show potential to modulate GBA signaling and restore physiological balance.

Conclusions: Understanding the complex relationship between obesity and the gut–brain axis may provide novel therapeutic targets for improving metabolic regulation and reducing obesity-related complications. Further clinical and translational studies are required to confirm the long-term effectiveness of GBA-oriented interventions.

KEY WORDS: obesity, vagus nerve, cholecystokinin, ghrelin

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INTRODUCTION

Over the last few years, numerous studies have been conducted on the gut-brain axis (GBA) due to its relevance in multifactorial diseases, including obesity [1]. The GBA is a bidirectional communication between the central and the enteric nervous system. The gut microbiota is a complex bidirectional communication system that can directly and/or indirectly interact with the following systems: the enteric nervous system, immune system, and enteroendocrine systems [1, 2]. Signal transmission via spinal nerves, the vagus nerve (VN), and the circulatory system to the central nervous system (CNS) is also facilitated by gut microbiota. In addition, neurotransmitters such as dopamine, serotonin, norepinephrine, gamma-aminobutyric acid (GABA), etc., are involved in bidirectional communication [1]. Modifications in the GBA have been shown to influence neurological disorders along with obesity.

With obesity turning into a global pandemic in this research review, we analyze and discuss the effect of obesity on the GBA, focusing our discussion on the pathophysiology of the neurological system and its influence on the gastrointestinal microbiota, along with future technologies and treatments that affect the GBA.

AIM

This article presents obesogenic diets and neuroplasticity in the mesolimbic pathway, vagal nerve stimulation, impact of diets on gut-brain communication, along with future technologies affecting obesity.

MATERIALS AND METHODS

The following article includes various original papers and research reviews from PubMed, Science Direct to the European Journal of Endocrinology using keyword combinations such as: "obesity", "gut-brain axis", "vagus nerve", "cholecystokinin" (CCK), "peptide YY" (PYY), "Glucagon-like peptide-1" (GLP-1). Ultimately, we included

40 resources selected on their high relevance describing the relationship between the gut-brain axis.

REVIEW AND DISCUSSION

VASAL PATHWAYS AND NEURAL FEEDBACK IN OBESITY

The VN is a key component of the nervous system responsible for relaying messages between the gut and the brain. It plays a central role in regulating metabolic homeostasis, appetite, and the stress response. Interestingly, the VN does not have direct receptors within the intestinal lumen [3]. Instead, it receives signals from enteroendocrine cells, which convey information about nutrient intake and gut distention to the afferent nerve. This signal is then transmitted to the brain, indicating satiety. Subsequently, the brain triggers changes in blood glucose levels, enzyme secretion, metabolic hormones, gallbladder contraction, gut motility, gastric acidification, and gastric emptying[4]. These responses collectively help regulate appetite, digestion, absorption, and overall energy homeostasis.

Signals that stimulate the VN and induce hunger include ghrelin and galanin. Conversely, leptin, CCK, GLP-1, insulin, short-chain fatty acids, the melanocortin-4 receptor (MC4R) gene, and PYY suppress vagal activity. Under stressful conditions, the VN is also suppressed, as it is a key regulator of parasympathetic nervous system activity. Stress compromises the optimal environment for *Lactobacillus* populations—beneficial bacteria in the human gut microbiota—leading to increased gut permeability, sympathetic overactivity, and lymphoid tissue abnormalities [5, 6]. Stress disrupts immune function, metabolic patterns, and gut microbiome composition. Under chronic stress, however, the VN may become overstimulated, resulting in aging-like changes in intestinal stem cells, including growth arrest and mitochondrial fragmentation [7].

Aside from normal physiological responses, damage to vagal afferent and efferent nerves may influence the development of obesity. Individuals with low vagal tone typically exhibit delayed gastric emptying, causing food to remain in the stomach for a longer period, particularly within the proximal–distal region of the small intestine[8]. However, hypersensitivity of vagal afferent nerves may also contribute to functional dyspepsia [9]. High-fat diet consumption has been shown to reduce vagal afferent sensitivity to stretch and mucosal stroking, resulting in hyperphagic behavior [9, 10]. Specifically, chronic high-fat intake dampens vagal afferent responses to GLP-1 signaling, leading to a delayed sensation of satiety [11].

The circadian system has also been shown to modulate vagal afferent sensitivity, leading to alterations in meal size and feeding behavior [12]. Obesity impairs leptin-mediated vagal afferent signaling through the actions of protein tyrosine phosphatase 1B and suppressor of cytokine signaling 3, resulting in hyperleptinemia and an impaired satiety response [13]. Although impaired vagal afferent signaling contributes to physiological imbalance, Lyu et al. demonstrated that inactivation of the dorsal motor nucleus of the VN reduces the length of intestinal microvilli, suggesting a potential mechanism for decreasing fat absorption [14].

FOOD REWARD, CRAVING, AND BRAIN CIRCUIT MODULATION

Food-seeking behavior arises from both a survival instinct and the brain's reward system, which reinforces this behavior. However, the reward system can also promote increased appetite and food cravings, regardless of the calories required to fuel the body. Ghrelin and liver-expressed antimicrobial peptide 2 stimulate the growth hormone secretagogue receptor (GHSR), regulating the mesocorticolimbic pathway and modulating complex reward-related behaviors toward various stimuli [15]. Animal studies have shown that GHSR stimulation causes rodents to gravitate toward palatable stimuli due to ghrelin signaling, independently of caloric needs.

Cholecystokinin (CCK), released by enteroendocrine cells (ECs) in the intestine, stimulates the VN to promote sugar preference, though it does not specifically influence fat preference [16]. The sodium glucose-linked transporter 1 (SGLT1) receptor, located on intestinal ECs, has been identified as the primary sugar-preference receptor. Concurrent signaling from fat-only and combined sugar, fat, and amino acid vagal pathways in the intestinal tract is required to establish fat-preference behavior. Both circuits utilize G protein-coupled receptors, GPR40 and GPR120, which serve as gut–brain receptors for fat preference. Notably, fat, sugar, and amino acid signals converge at a unique class of vagal neurons (VIP-UTS2b) before behavioral preference is triggered. McDougle et al. confirmed that the gut vagal system contains two distinct sensory populations that regulate physiological responses to fat or sugar ingestion [17]. When these populations are activated simultaneously by combined fat and sugar consumption, nigrostriatal dopamine release increases exponentially compared to their separate activation, resulting in motivated feeding behavior and overeating. Specifically, ventral tegmental area (VTA) dopamine neurons increase activity following sugar ingestion [18]. However, impairment

of the hepatic branch of the VN disrupts post-ingestive activation of VTA dopamine neurons.

These findings support the development of an obesogenic diet characterized by excess calories, high saturated fat, and high sugar intake, including ultra-processed foods, fast food, and sugary beverages, coupled with low consumption of fruits, vegetables, and whole grains [19]. Natural sugars can activate the preference circuit, whereas artificial sweeteners fail to fully replicate this effect [20]. High-fat consumption reduces the responsiveness of nodose ganglion neurons to CCK and serotonin in obese mice, delaying satiety and promoting hyperphagia [10]. Moreover, insulin receptor signaling is dampened, dopamine transmission is impaired, and striatal dopaminergic network responsiveness is blunted [21]. Although this remains to be fully confirmed, these changes may create a cycle of increased intake of obesogenic foods, further exacerbating hyperphagic behavior.

It is widely accepted that changes in dietary intake can affect the composition of the gut microbiota. Conversely, alterations in microbiota composition may also influence host food preferences. Various animal models have demonstrated that shifts in microbiota can significantly impact host food preference behaviors [22, 23]. Peterson et al. observed that bacterial families such as *Ruminococcaceae* and *Lachnospiraceae* influence behavioral measures of impulsivity, attention, reward learning, and locomotor responses to novelty in both male and female rats [23]. Additionally, the genus *Barnesiella* specifically affects impulsivity in female rats.

In a randomized controlled human trial, fecal microbiota transfer was associated with increased brain dopamine transporter (DAT) levels, with *Bacteroides* correlating with increased DAT and *Prevotella* spp. correlating with decreased DAT [24]. Lower food-addictive behavior was observed in participants whose microbiota contained the genus *Blautia* and members of the phylum Actinobacteria, and intake of non-digestible carbohydrates such as lactulose and rhamnose is known to promote *Blautia* growth [25].

Overall, bacterial taxa including *Prevotella*, *Bacteroides*, *Lactobacillus*, *Bifidobacterium*, *Clostridium*, *Enterococcus*, and *Ruminococcus* have been shown to affect dopamine signaling, thereby influencing food preference behaviors in animals and contributing to pathological conditions related to dopaminergic dysfunction [26].

THERAPEUTIC INTERVENTIONS TARGETING THE GUT–BRAIN AXIS IN OBESITY

MICROBIOME-MODULATING THERAPIES

Microbiome-modulating therapies are treatments for obesity primarily targeted on the gut's microbial ecosystem. Research shows that the human gut contains around 100 trillions microbes with more than 5,000 species. Since the gut microbiome plays a crucial role in nutrient absorption, metabolism, energy regulation and appetite regulation, making it a potential target for obesity treatment. Common approaches include dietary modification, taking prebiotics and probiotics (combining both called synbiotics) and using fecal microbiota transplantation (FMT).

Obesity and gut microbial ecology are closely linked, with normal-weight individuals having higher Bacteroidetes and lower Firmicutes than obese individuals. The gut microbiota comprises Firmicutes and Bacteroidetes, comprising 70-90% of the population. Recent research has shown a positive association between obesity and the Firmicutes: Bacteroidetes (F/B) ratio in humans. However, this relationship may not be universally applicable across different populations. Obese individuals often have a higher F/B ratio compared to lean individuals, with studies showing an increase in body mass index (BMI) and a positive correlation with metabolic markers. Dysbiosis, an imbalance in gut microbiota, is linked to obesity [27].

Probiotics are live microorganisms and prebiotics are indigestible fibers that feed those good bacterias, combining them together is called synbiotics. In a randomized, double-blind, placebo-controlled trial, eighty individuals with obesity were given daily synbiotics supplement for a 12-weeks period to observe its effect. The participants were assigned either to placebo group or synbiotic group, with body composition, blood lipids, gut hormones, bile acids, and gut microbiota measured before and after the intervention. The synbiotic group result showed significantly reduced body fat percentage, waist circumference, and LDL-C, alongside increases in satiety-related hormones. Additionally, synbiotic supplementation improved gut microbial balance and enhanced beneficial bile acids, including chenodeoxycholic acid. These changes were more significant in people who had high cholesterol, suggesting that synbiotics may help with weight loss by improving gut health, bile acid levels, and appetite-related hormones [28].

FMT is a medical procedure that involves transferring processed fecal matter from a healthy donor into the gastrointestinal tract of the recipient. It works by restoring gut microbial diversity and improving immune regulation, which can help with metabolic health and weight control. The effectiveness of FMT, however, depends on several factors including donor microbiota, recipient characteristics, and diet or medication. Major challenges include the absence of standardized methods, donor screening, and limited knowledge of

gut microbiota dynamics. Further research should focus on identifying the key microbes and advanced personalised FMT strategies for better results [29].

PHARMACOLOGICAL INTERVENTIONS

Pharmacological interventions for weight loss and obesity have become more widely adopted in recent years due to their efficacy in clinical studies and positive outcomes, complementing lifestyle modification strategies. GLP-1 receptor agonists (GLP-1RA)—such as semaglutide, liraglutide, and tirzepatide—are among the widely used agents in class. They enhanced satiety which then reduced calories intake. In addition, emerging pharmacotherapies including dual and triple incretin analogs, ghrelin antagonists, GABA modulators, and MC4R agonists, offer novel mechanisms to modulate homeostasis and promote weight loss.

GLP-1RA are primarily used as a type 2 diabetes treatment to lower blood glucose levels and contribute to weight loss. Its mechanism is to mimic the hormone GLP-1, which leads to glucagon-dependent insulin secretion, inhibition of glucagon release, delayed gastric emptying and increased satiety. Available agents include both short-acting and long-acting GLP-1RA such as exenatide and semaglutide, respectively, as well as dual and triple receptor agonists such as tirzepatide, and retatrutide. These agents show significant efficacy in sustainable weight loss for obesity and type 2 diabetes as a monotherapy or in combination with lifestyle modification. Furthermore, they improve glycemic control, regulate appetite, and enhance cardiovascular health. The most common side effects are gastrointestinal symptoms, which are typically transient and manageable. Potential risks such as pancreatitis, thyroid disorder and depression, remain under investigation and require careful monitoring of use. Overall, GLP-1RAs represent promising therapeutic benefits, though ongoing research is needed to elucidate their long-term safety and optimize clinical use [30].

Novel therapeutic targets for obesity include ghrelin antagonists - blocking action of ghrelin at its receptor primarily in the hypothalamus, thereby, reduce appetite, GABA modulators - altering neural circuits to reduce food intake and increase satiety, and MC4R agonists - decreases food consumption and promotes energy utilization.

Ghrelin is a peptide hormone secreted mainly in the stomach and often called hunger hormone. It stimulates appetite and growth hormone secretion through activation of GHS-R1 receptors. Ghrelin levels are typically suppressed in obese individuals, resulting in decreased growth hormone release. Blocking ghrelin signaling reduces appetite, thereby representing a potential therapeutic approach for obesity management.

GABA is the primary inhibition neurotransmitter in the human brain and is commonly used for stress reduction and improved sleep. Although it has limited ability to cross the brain-blood barrier, GABA may regulate appetite and body weight through vagal nerve signaling when administered with food.

In conclusion, there are several pharmaceutical interventions in obesity management that targets the GBA. Each with its own unique advantages and clinical benefits, treatments should be individualized to optimize the best outcomes for each patient.

NEUROSTIMULATION AND BIOELECTRONIC MEDICINE

Neurostimulation and Bioelectronic Medicine are the use of electrical stimulators to modulate and restore neuronal activity. Various neurostimulation approaches have been one of the key alternative interventions for obesity management, including vagal nerve stimulation (invasive and non-invasive), transcranial magnetic stimulation (TMS) and deep brain stimulation.

The parasympathetic VN, a key component of the autonomic nervous system, regulates satiety, gastric motility and gastric emptying. Dysfunction of theVN is commonly observed in obese patients, hence reducing its efficacy. Vagus nerve stimulation(VNS) can be either non-invasive(n-VNS)—using external stimulators or invasive(iVNS)—surgical implantation of the device. nVNS devices are either placed on the outer ear to activate the auricular branch of VN or on the neck to activate the cervical branch of VN. Studies have shown that transcutaneous auricular VNS (taVNS) promotes the efficacy of gastric emptying since it activates the VN to regulate motility and secretion [31]. The invasive VNS device is placed subcutaneously in the chest wall, an electrode cuff positioned around the left cervical VN, and connected through the flexible wire. Research supporting the therapeutic potential of using VN stimulators has continued to grow for various treatments such as epilepsy, headache, pain-related disorders, cardiovascular disease and obesity [32].

TMS targets the dorsolateral prefrontal cortex of the brain. This area is crucial for cognitive control over food consumption and cravings. TMS is a non-invasive technique using an electromagnetic coil placed on a patient's scalp to deliver magnetic resonance to the targeted nerve cells.Studies demonstrated encouraging results, though further research is necessary to validate this outcome.

Electrical stimulators are directly targeted by GBA, modulating gut signals via the nervous system through

both invasive and non-invasive approaches. These interventions represent promising therapeutic alternatives for obesity management.

DIET AND BEHAVIORAL INTERVENTIONS

Overconsumption is what causes obesity. Dietary and behavioral modification are the most effective, accessible and sustainable methods for weight loss. Dietary choices such as mediterranean diets and ketogenic diets have gained more attention in the past years since it influences gut microbiota composition and improves communication between GBA, thereby supporting weight management. In addition, mind-gut therapies, including mindfulness and cognitive-behavioral therapy, help regulate eating behaviors, stress-related metabolic effects and appetite.

Ketogenic diets , focus on consumption of high-fat food, adequate amount of protein and minimal carbohydrate intake. Patients with ketogenic diets show an improvement of weight management as well as glycemic control, lower HbA1C level and increased high-density lipoprotein level [33]. Mediterranean diets promote beneficial gut microbiota, and ketogenic diets shift metabolism toward ketone bodies; therefore both diets influence GBA and support appetite regulation.

Mind-gut therapies are a key factor for sustained weight loss by improving self-awareness and eating behaviors. Mindfulness promotes awareness of food choices and portion control, while cognitive-behavioral therapy helps patients develop healthier coping strategies. Together, these approaches support long-term health management, self-esteem, overall body functioning and patients quality of life.

Despite pharmaceutical and dietary advancements obesity remains a global pandemic. With emerging technologies such as metabolomics and neuroimaging we have a greater understanding of the relationship between the GBA.

Advancements in technology have opened new avenues for studying the GBA in obesity. Multimodal approaches have enabled researchers to examine this topic from various perspectives. Metagenomic studies focus on the entire microbial community within the human gut using sequencing technologies. This approach provides insight into the composition, function, and diversity of the gut microbiota.

In metagenomics, genetic material is obtained and sequenced, with short DNA fragments assembled to analyze the types of species present. Previously, many of these microorganisms were difficult or nearly impossible to culture in the laboratory and were therefore largely unstudied. In addition to identifying microbial species, metagenomic studies allow researchers to assess the functions these organisms perform.

With respect to the GBA and obesity, metagenomic analyses have been instrumental in revealing that microbial imbalances can alter the production of metabolites such as short-chain fatty acids and lipopolysaccharide. These changes can disrupt gut barrier function, indirectly contributing to obesity development. Applying this knowledge may inform therapeutic strategies, such as probiotics or prebiotics, offering potential preventative measures against obesity [34].

Metabolomics is the study of metabolic processes in the body through the analysis of metabolites. Therapeutic diets, including prebiotics, probiotics, and fiber-rich nutrition, have been shown to influence metabolism. By detecting molecules involved in biochemical activities, researchers can gain insight into metabolic pathways and alterations. In the context of obesity, investigations have revealed varying levels of free fatty acids, which can alter lipid metabolism [35]. Other studies have examined changes in metabolism following dietary or exercise interventions, focusing on amino acid levels. These studies demonstrate that amino acid profiles can shift in response to different dietary patterns [36]. Notably, linear increases in cysteine levels have been associated with the progression of metabolic dysfunction [37].

Neuroimaging involves the use of computational and imaging techniques to study the structure and function of the CNS in disease. In obesity research, neuroimaging has been instrumental in understanding structural and functional changes in the human brain. Structural abnormalities have been observed through imaging, and importantly, longitudinal studies allow researchers to track changes over time. Magnetic resonance imaging techniques, for example, have been used to monitor alterations in the frontal cortex related to insulin sensitivity [38]. Other studies have examined sex-specific differences in obesity treatment, comparing outcomes and treatment responses between male and female participants, as well different types of brain imaging performed [39]. Applying similar neuroimaging technology can allow for the study of brain connectivity in relation to GBA. Thus, neuroimaging has proven important in showing how imbalances in microbiota can affect structures and connectivity within the brain, showing links between differences in GBA and obesity [40].

CONCLUSIONS

This study aimed to analyze the correlation between the gut–microbiota–brain axis and obesity. In recent years, the prevalence of obesity has increased dra-

matically. Obesity itself has been linked to numerous conditions and diseases, including, but not limited to, type 2 diabetes, cardiovascular disease, and sleep apnea. Recent studies have explored the role of the GBA - a communication network between the CNS and the microbiota of the enteric nervous system - in obesity. Examining the influence of the intestinal microbiome on obesity and its associated pathways may inform the development of individualized treatments targeting the microbiome. While neuroimaging studies and research involving diverse populations can help guide therapy design, further investigation is required to confirm the effectiveness and efficiency of GBA-targeted interventions in obesity.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Artificial Intelligence for predicting adverse surgical outcomes: Challenges, limitations and implications for clinical translation – a narrative review

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ABSTRACT

The rise in the number of surgeries per year has led to the development of many artificial intelligence models for predicting surgical complications. Despite their ever-growing use in healthcare, artificial intelligence is not up to the mark yet. We need to search and critically overcome the hurdles preventing their safe and reliable use in surgical care. This narrative review aims to find and analyze the main limitations and challenges of artificial intelligence in predicting surgical outcomes. Across the reviewed literature, key limitations were identified in four domains: data-related, methodological limitations, performance and generalizability, and barriers to clinical implementation. Common issues included missing and imbalanced datasets, small sample sizes, retrospective single-center designs, high risk of bias, and inadequate external validation. Although several studies reported high predictive performance, these findings were often derived from non-representative datasets and lacked prospective validation. Additional concerns included limited interpretability, ethical and privacy risks, workflow integration difficulties, and potential amplification of healthcare disparities. Despite their potential, AI models for surgical outcome prediction remain constrained by multiple challenges. Substantial improvements in data quality, transparency, fairness, and robust multicenter prospective validation are required before AI can be safely and reliably integrated into routine surgical decision-making.

KEY WORDS: bias, transparency, postoperative complications, risk assessment

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INTRODUCTION

According to the World Health Organization (WHO) more than 234 million major surgical procedures are performed worldwide each year, highlighting the vast scale of surgical care [1]. Despite advances in perioperative management, 10 to 25 percent of surgical patients experience major postoperative complications leading to higher mortality, prolonged hospitalization, increased need for intensive care, and greater healthcare costs [2, 3]. Importantly, nearly half of these adverse events are related to surgical care itself and are considered preventable. These complications typically arise from the the combination of multiple variables, and it is humanly impossible to understand and predict all their linked effects on the surgical outcome [3].

In this context, artificial intelligence (AI) has gained increasing attention in surgery. AI in general can be understood as computer systems that perform tasks such as prediction, classification, and decision-making. Machine learning (ML), a key branch of AI, uses algorithms to pick up patterns from a set of data, while deep learning can use multilayered neural networks to find complex associations within the data [4-6]. Predicting surgical complications using AI models can now be achieved because of the large amount of digital data available from health care centers [5]. Hence, ML has an upper hand over traditional prediction methods that use statistics [6].

Despite considerable enthusiasm surrounding AI in healthcare, it has several drawbacks that have prevented it from being utilized on a larger scale [7, 8]. There is a pressing need not only to develop validated predictive models but also to ensure that AI outputs are reliable, interpretable, transparent, ethical and clinically meaningful to support safe surgical decision-making.

AIM

This narrative review aims to find and analyze the main limitations and challenges of artificial intelligence in predicting surgical outcomes.

MATERIALS AND METHODS

SEARCH STRATEGY

A literature search was conducted using PubMed for articles published within the last ten years. The following Medical Subject Headings (MeSH) terms were applied: "Artificial Intelligence", "Deep Learning", "Surgical Procedures, Operative", "Risk Assessment", "Treatment Outcome". The following keywords were additionally searched in titles and abstracts: limitations, challenges, drawbacks, barriers, bias, transparency, "black box".

Inclusion criteria:

Studies were included if they:

1. Discussed the use of AI in surgery, and
2. Focused on predicting surgical outcomes, and
3. Addressed limitations of AI in surgical practice.

Exclusion criteria:

1. Non-English articles
2. Conference abstracts without full text

No ethical approval was required as this study is based on published literature.

REVIEW

DATA-RELATED LIMITATIONS

Across the included studies, substantial limitations related to data quality, representativeness, and structure were consistently reported. Several authors highlighted the problem of missing data [2, 7, 9, 10]. Moglia et al.(2021) reported that most studies did not describe how missing data were handled, representing a major potential source of bias. Likewise, two studies emphasized that substantial missing data and exclusion of patients with incomplete records distorted training datasets[9,10]. One article noted that in their study outcomes were often derived from administrative codes rather than manual chart review, raising concerns that automated data may not fully reflect clinical reality [2].

Population imbalance and lack of representativeness were also recurring issues. Sargiotis et al. (2024) described how reliance on datasets like United Network for Organ Sharing (UNOS) registries led to overrepresentation of White and male patients introducing demographic bias into predictive models [10]. Zander et al.(2025) similarly argued that inadequate numbers of patients within certain demographic groups limited the ability to build fair prediction models [11]. In pediatric cardiac surgery, Florquin et al.(2024) highlighted severe class imbalance as a major stumbling-block to predicting complications, moreover rare but critical complications were difficult for algorithms to learn [12].

Finally, beyond issues of missingness and representativeness, several studies highlighted structural limitations in how surgical data are generated, organized, and shared. The inherently heterogeneous nature of surgical datasets was described as a barrier for the AI models to interpret and process it [13]. Moglia et al. (2021) emphasized that characteristically different data require costly and labor-intensive anonymization, curation, and standardization further restricting dataset availability [7]. Interoperability barriers between institutions further impede data pooling, as differences in electronic health record systems, privacy regulations, and security concerns limit multicenter collaboration [14].

METHODOLOGICAL LIMITATIONS

Many authors emphasized that single-centre and retrospective designs limited clinical applicability because the data were prone to selection bias and the models were developed without prospective validation in real clinical workflows [15-18].

Small sample size further constrained model reliability in several surgical contexts. Göktürk et al.(2025) acknowledged that limited sample size weakened statistical power despite the use of synthetic minority oversampling technique (SMOTE), while Golubovic et al.(2025) and Takkavatakarn et al.(2023) noted that models were built on small, procedure-specific cohorts. Moglia et al.(2021) also attributed limited robustness of models to consistently small datasets across studies [8, 14, 16].

Risk of bias in model development was widespread. A review found that 29 of 31 models were at high risk of bias as per Prediction model Risk Of Bias Assessment Tool (PROBAST), largely due to inadequate sample size, overfitting, excessive predictors relative to events, and lack of external validation [9]. Nayebirad et al.(2025) also reported very high PROBAST bias across percutaneous coronary intervention (PCI) prediction studies, with overfitting being a central concern [19]. Sargiotis et al. (2024) further documented bias arising from exclusion of certain patient groups, use of non-standardized registries, and poor calibration reporting [10].

External validation practices were generally weak. Groot et al.(2021) found that only 10 of 59 orthopedic ML models had any external validation and none were prospective [20]. Moglia et al.(2021) similarly noted that no robot-assisted surgery model had been tested on external datasets, preventing conclusions about robustness or required training sample size [7]. Göktürk et al.(2025), Bektaş et al.(2022), and Golubovic et al.(2025) all stressed the need for large, multicenter, prospective validation before clinical deployment

[8,16,17]. Yu et al.(2025) reported that only 2 of 10 PCI studies conducted external validation despite high reported accuracy [18].

Finally, methodological inconsistency was evident. Moglia et al.(2021) noted that studies failed to define appropriate performance thresholds or agree on which metrics should be prioritized to deem AI models safe to use clinically, while Takkavatakarn et al.(2023) highlighted the lack of head-to-head comparison between models across populations [7, 14].

PERFORMANCE AND GENERALISABILITY

Xue et al (2021). achieved high Area Under the Receiver Operating Characteristic Curve (AUROC) for multiple complications, indicating great model performance, but acknowledged that single-center data and incomplete variable sets limited transferability to other hospitals [2]. Göktürk et al. (2025) described their model only as proof-of-concept lacking external validation [8].

A few reviews questioned whether superior performance translated into meaningful clinical benefit. Nayebirad et al.(2025) found that although ML models had numerically higher c-statistics than traditional logistic regression, differences were not statistically significant [19]. Sargiotis et al. (2024) highlighted that outcomes beyond one year post-transplant were undermined by loss to follow-up and missing data, weakening reliability for chronic risk prediction [10].

Florquin et al.(2024), Göktürk et al.(2025), Salah et al.(2025) all stated that the generalizability was significantly reduced by their single-center and retrospective designs [8,12,15]. Xue et al (2021) goes on to mention that absence of certain clinical values can potentially hinder predictive accuracy as well as generalizability [2]. Ethnic and geographic specificity further constrained generalizability. Dong et al. (2025) demonstrated strong performance for post surgical gastrointestinal bleeding in predominantly Chinese cohorts but explicitly stated that global applicability required prospective, multicenter validation [6]. Similarly, Yu et al.(2025) reported that most PCI studies were conducted in Asian registries [18].

CLINICAL IMPLEMENTATION CHALLENGES

Interpretability ("black box") was a dominant barrier across studies for clinical implementation. Although Dong et al. (2025), Göktürk et al.(2025)zha, and Salah et al.(2025) employed explainable Ai tools, all acknowledged that they do not fully resolve transparency problems or provide clear, actionable guidance when models conflict with clinical judgment [6,8,15]. Nayebirad et al.(2025) further added that this opacity may make ML unpopular despite their better performance [19]. Harris & Matthews (2024) emphasized that narrow, task-specific algorithms lack holistic clinical reasoning and will possibly struggle with atypical cases [5].

Workflow integration posed additional challenges. Balch et al. (2021) described persistent difficulties embedding AI tools into electronic health records, citing usability issues, cost, and clinician mistrust [4]. Moglia et al.(2021) likewise warned that the abundant use of technical explanations discouraged adoption by surgeons and other healthcare professionals [7]. Bedford et al.(2024) noted the absence of clear guidelines for perioperative AI [21].

Ethical, legal, and privacy risks were repeatedly raised across the literature. Dong et al. (2025) identified the difficulty of securing consent for massive datasets and the persistent danger of re-identifying people from supposedly anonymous data [6]. Moglia et al.(2021) expanded on these concerns, noting broader risks involving cybersecurity, liability for AI-related harm, and the need for updated professional credentialing and certification [7]. D'Oria et al.(2024) emphasized that these technologies could threaten patient autonomy while potentially making existing healthcare inequalities even worse [13].

Fairness and equity concerns were noted. Lucas et al.(2024) demonstrated clear racial disparities in colorectal cancer readmission models, including higher false negatives for "Other" race and higher false positives for Black patients [22]. Bedford et al.(2024) and Sargiotis et al. (2024) both warned that biased data could propagate inequities in risk assessment and treatment allocation [10, 21].

DISCUSSION

Many studies demonstrate promising predictive performance; unfortunately, reality reveals persistent and interconnected problems related to data quality, methodology, generalisability, and clinical implementation that currently restrict the safe and reliable integration of AI into perioperative care. These shortcomings appear to be systemic spanning the entire lifecycle of AI development.

The most fundamental building block of a prediction model is high quality and quantity data [7]. A common phrase used is "Garbage in, Garbage out", highlighting that AI is only as robust as the data they ingest. Consistent findings of missing data, class imbalance, small sample size and demographic skew

give way to bias and noise. Missing data emerged as a pervasive problem, with several reviews showing that incomplete records and inconsistent reporting distort model training [7, 9, 10]. As highlighted by Xue et al (2021)., many models are trained on proxies of clinical reality rather than true clinical events due to the use of administrative codes [2]. This raises concerns that some AI tools may fail to learn patterns in meaningful physiological or surgical risk factors. Demographic and class imbalance further threaten fairness and validity. The algorithms often reflect the biases of available datasets rather than the diversity of real world patients. Additionally, structural barriers to data sharing including heterogeneity of formats, privacy concerns, and interoperability limitations prevent the creation of truly representative and multicenter datasets.

A striking finding of this review is the dominance of retrospective, single-center study designs. This suggests that much of the current evidence base for surgical AI reflects model performance in historical datasets rather than showcasing clinical effectiveness. The widespread risk of bias identified is particularly concerning. Models with too many complexities, combined with minimal to no external validation, create a high likelihood of overfitting which means models capture noise rather than true associations. Therefore, they perform well with training data-sets but fail in new clinical environments. The scarcity of robust prospective external validation represents a major gap between research and practice. Without testing models across different hospitals, populations, and workflows, it remains unclear whether AI tools are truly generalizable.

These factors taken along with the lack of transparency in understanding these tools demotivates professionals in using them in their practice. This 'black-box' nature breeds mistrust and confusion as to how reliable the decision making of the model is, especially in comparison to the years of experience and critical thinking of a physician. Even if the prediction tools were transparent and accurate, the legal and ethical implications can not be overlooked. The concerns raised by Dong et al. (2025) regarding potential re-identification of anonymized patient data highlights a deeper tension between the drive for large-scale data sharing and the duty to protect patient privacy [6]. As predictive models become increasingly dependent on massive, multi-institutional datasets, the traditional frameworks of informed consent and confidentiality may no longer be sufficient, necessitating new regulatory and ethical standards for data in surgical research and practice. Moglia et al. (2021)'s emphasis on cybersecurity risks and medico-legal liability further illustrates that integrating AI into operative environments introduces vulnerabilities [7]. If an AI system contributes to a harmful clinical decision, it remains unclear whether responsibility lies with the surgeon, the institution, or the technology developers. This ambiguity could discourage clinical adoption and requires clearer legal frameworks before AI can be safely embedded into surgical workflows.

CONCLUSIONS

Artificial intelligence for predicting adverse surgical outcomes shows clear potential but remains premature for routine clinical use. At present, AI functions more as a research tool than a dependable clinical decision aid. Moving forward, meaningful progress will depend less on developing ever more complex algorithms and more on improving data quality, conducting large prospective multicenter validations, and ensuring transparency, fairness, and accountability. If these challenges are addressed, AI could evolve into a valuable adjunct that reliably supports clinical judgment in surgical care.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Regional versus general anesthesia for hip fracture surgery in older adults: A focused research review

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ABSTRACT

Hip fractures in the elderly population are associated with considerable complications such as morbidity, mortality, and enduring functional deterioration. Thus, they render perioperative management an essential element of strategies aimed at fostering healthy aging. Regional anesthesia (RA) and general anesthesia (GA) constitute the two predominant methods for the surgical intervention of hip fractures; however, the most effective technique remains a subject of ongoing scholarly debate.

This research review seeks to systematically assess and compare regional anesthesia to general anesthesia in elderly patients undergoing surgical treatment for hip fractures, focusing on perioperative safety, mortality rates, functional recovery, cardiopulmonary issues, and cognitive outcomes to understand their implications for encouraging healthy aging.

A concentrated narrative review of pertinent literature published from the year 2020 onwards was executed, utilizing databases such as PubMed and Google Scholar. Studies were included for consideration if they provided a comparative analysis of regional anesthesia and general anesthesia in adults aged 65 years and above undergoing surgical procedures for hip fractures. Recent extensive randomized trials indicate that spinal anesthesia does not show an advantage over general anesthesia concerning survival rates, functional recovery, or significant postoperative results, including the return to ambulation at a 60-day follow-up. Meta-analyses indicate that both anesthetic methods demonstrate similar safety profiles; however, regional anesthesia might lead to reduced intraoperative blood loss, shorter operative times, and slight decreases in hospital stay for certain patient groups.

KEY WORDS: pain, delirium, recovery pathways, perioperative care

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INTRODUCTION

The incidence of hip fractures among the elderly is on the rise worldwide. It is estimated that by 2050, there will be an incidence of 4.5 to 6.25 million fractures [1, 2]. Physiologically, it is a great challenge to deal with such patients since they usually have decreased cardiovascular and pulmonary reserves [3]. In the past, the medical community has always opted to use Regional Anesthesia (RA), speculating that it lowers the incidence of Postoperative Delirium (POD) and pulmonary complications. It is believed to provide better analgesia and decrease the systemic inflammatory response [4].

However, with the results of the last few studies, the trend seems to be changing. Some studies have suggested that RA decreases 30-day mortality. But with the publication of the last few studies, it seems that it does not [5, 6]. It has been found that time to surgery and multidisciplinary treatment are more considerable outcomes than the type of anesthesia [7,8]. This review aims to summarize the literature to determine if one is better than the other in the present clinical scenario.

AIM

The aim of this systematic research review is to evaluate and compare the use of regional anesthesia with that of general anesthesia for the surgical management of hip fractures in the elderly population. The key areas of interest are the safety, mortality rates, functional recovery, cardiopulmonary outcomes, and cognition to highlight their role in promoting healthy aging.

MATERIALS AND METHODS

A focused narrative review was conducted using recent literature (2020 onward). Searches were performed in PubMed, Google Scholar, and major clinical databases using combinations of the following terms:

"hip fracture anesthesia elderly"
"regional vs general anesthesia delirium"
"spinal anesthesia hip fracture randomized trial"
"postoperative delirium elderly anesthesia"
Inclusion criteria:
Studies published 2020–2025
Patients ≥65 years
Comparative studies or reviews of RA vs GA
Outcomes including delirium, mortality, or recovery
Priority was given to randomized trials, systematic reviews, and meta-analyses.

REVIEW

POSTOPERATIVE DELIRIUM: CENTRAL OUTCOME

Postoperative delirium remains a significant determinant of recovery in elderly patients who undergo hip fracture surgeries. A recent large randomized study published in the Journal of the American Medical Association exhibited that regional anesthesia has little effect in reducing the occurrence and severity of delirium compared with general anesthesia, which challenges the conventional belief [9].

Recent systematic reviews and meta-analyses have failed to show any significant variation in the occurrence of delirium between regional anesthesia and general anesthesia, despite the theoretical neuroprotective effects of regional anesthesia [10, 11].

It is evident from the continued occurrence of delirium in various anesthetic modalities that the cause of delirium is likely related to cognitive status, inflammatory response, sedation, and the general condition of the patient, and not the anesthetic technique used. Some studies have reported decreased rates of delirium following spinal anesthesia, but this has not been consistent and may be biased due to other factors [12].

Therefore, the current trend of research suggests moving beyond the debate of regional and general anesthetics and their role in the development of delirium and rather look for individual approaches to neuroprotection.

NEUROPHYSIOLOGICAL MECHANISMS AND BRAIN VULNERABILITY

Both anesthetic methods have the potential to affect cerebral physiology. General anesthetic methods have the risk of exposing the patient to deeper levels of sedation and systemically administered anesthetics. Regional anesthesia requires the administration of sedation that is known to vary widely among institutions.

It is thought that neuroinflammation and neurotransmitter imbalance are key factors in the pathogenesis of delirium. Meta-analysis studies have emphasized the importance of perioperative factors such as hypotension, sleep deprivation, and the use of multiple medications on cognitive outcomes irrespective of the anesthetic technique used.

Current studies on the effects of various methods of sedation used in neuraxial anesthetic procedures have emphasized the importance of the degree and type of sedation on the risk of delirium [13].

MORTALITY AND FUNCTIONAL RECOVERY

In addition to delirium, survival and functional outcomes have been commonly assessed as an endpoint in the comparison of regional anesthesia (RA) with general anesthesia (GA). Large trials have demonstrated that spinal anesthesia does not have any advantage over general anesthesia in terms of survival or the ability to ambulate at 60 days postoperatively.

The results of the meta-analyses also support the conclusion that there is little difference in mortality among the anesthetic techniques, which may reflect the impact of improved perioperative care in reducing outcome differences among the anesthetic approaches.

CARDIOPULMONARY AND HEMODYNAMIC EFFECTS

Regional anesthesia is often associated with reduced blood loss, reduced duration of operation, and reduced pulmonary problems in some studies.

Spinal anesthesia may reduce the severity and need for vasopressors to treat hypotension compared with the use of general anesthesia, although the evidence is inconsistent [14].

Despite these physiological differences, advances in modern anesthetic monitoring appear to minimize the historical disadvantages of general anesthesia.

PAIN CONTROL AND RECOVERY PATHWAYS

Pain management has a significant effect on delirium risk. Some umbrella review articles show that regional analgesia (RA) may lead to reduced pain and opioid requirements after surgery, which could be beneficial for early mobilization [15].

However, randomized studies show that pain management may be related to adjunctive analgesia techniques rather than types of anesthesia.

These studies highlight the increasing importance of multimodal analgesia and enhanced recovery programs to promote positive outcomes for older people.

DISCUSSION

Recent findings have also challenged the long-held belief that regional anesthesia (RA) has a positive impact on the occurrence of delirium in the elderly population who undergo hip fracture surgery. Recent high-quality randomized trials have confirmed that the rate of delirium is similar with both regional anesthesia (RA) and general anesthesia (GA). This suggests that the modality of anesthesia does not play an important role in the occurrence of delirium.

The perioperative care process seems to play a more important role in the occurrence of delirium. This is a change in the way anesthesiology works; the focus is no longer on the modality of anesthesia but rather on the care process.

Regional anesthesia may still have an advantage over other forms of anesthesia in certain patient groups; for example, it results in less blood loss or a shorter length of stay in the hospital.

In the context of initiatives for healthy aging, the preservation of cognitive function with the maintenance of functional independence may be achieved with the help of an integrated perioperative care process rather than the modality of anesthesia.

CONCLUSIONS

The existing literature does not suggest that regional anesthesia offers any advantage over general anesthesia in preventing delirium in the older patient with hip fractures. Physiological differences exist, but it seems that the patient's characteristics are more important in determining the cognitive outcome. A personalized approach could be more beneficial to health aging than the method of anesthesia.

LIMITATIONS OF CURRENT EVIDENCE

- Significant heterogeneity in study design and delirium assessment tools
- Variable sedation practices during regional anesthesia
- Selection bias in observational cohorts
- Lack of standardized frailty measures across trials

These factors contribute to conflicting conclusions and limit definitive recommendations.

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REVIEW ARTICLE

CONTENTS

Current perspectives on 3D-printed casts

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ABSTRACT

Aim: Fractures of the distal radius and ulna are among the most common skeletal injuries and are traditionally treated with cast immobilization. However, conventional casting techniques have significant limitations. In recent years, three-dimensional (3D) printing technology has emerged as a promising alternative in the production of personalized post-traumatic stabilization devices. The aim of this review was to present current information and perspectives on the development of 3D-printed casts, with particular emphasis on the diversity of designs, material properties, and clinical applications.

Materials and Methods: A literature review was conducted using the PubMed and Google Scholar databases. The results of the analyzed studies indicate that additive technologies enable the production of lightweight, ventilated, individually tailored orthoses with high mechanical strength and improved moisture resistance compared to traditional casts and glass fiber casts.

Conclusions: Materials such as polylactide (PLA) and PLA composites produced by Fused Filament Fabrication (FFF) demonstrate superior properties in static and dynamic tests. Furthermore, 3D-printed casts offer improved hygiene, greater comfort, a reduced risk of skin complications, such as wound healing, and high aesthetic acceptability. Clinical applications also include planning corrective osteotomies and the production of personalized surgical instruments. Although further research is needed on long-term durability and broad clinical outcomes, current reports indicate that 3D printing is a promising and increasingly viable alternative to traditional cast immobilization.

KEY WORDS: 3D printing, distal radius fracture, durability

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INTRODUCTION

Closed fractures of the distal radius and ulna are among the most common skeletal injuries and can occur in all age groups. Routine treatment involves temporary immobilization of the limb with a plaster cast. However, traditional plaster application techniques can be labor-intensive, largely dependent on the experience of the operator, and do not always provide optimal results [1]. Commonly used plaster materials have limitations, such as low mechanical strength and moisture resistance, difficulties in maintaining hygiene, and unpleasant odors [2]. From a clinical perspective, plaster casts are often perceived as uncomfortable; they can cause skin irritation and sometimes temporary numbness of the superficial branch of the radial nerve [1,3]. A significant problem with conservative treatment with plaster remains the high rate of secondary displacement of bone fragments [3]. Individually designed orthoses manufactured using 3D printing are increasingly becoming an alternative to traditional casts [3]. 3D printing is a rapidly developing technology that may, in the future, provide an alternative to traditional plaster casts [2]. It is gaining increasing importance in orthopedics, primarily due to the ability to individually tailor products to the patient and their efficient manufacturing process. Conservative fracture treatment has begun to utilize the concept of creating personalized 3D-printed immobilization devices, which are characterized by

precise fit to the patient's anatomy and an openwork, ventilated structure [4]. Three-dimensional (3D) printing, classified as additive manufacturing (AM) and rapid prototyping, involves building a three-dimensional object by applying successive layers of material. Unlike classical subtractive machining methods, where material is gradually removed from a solid block to achieve the desired shape, 3D printing creates a component by gradually adding it. This method is characterized by high versatility, enabling the production of complex structures from a variety of materials, such as polymers, ceramics, metals, and composites. This technology allows the design and production of structures with various geometries, both high density and macro- or microporous structures [5].

AIM

The review aimed at briefly presenting up-dated information on advances in 3D printed casts for perspective focusing on its diversity and need for complex approach.

MATERIALS AND METHODS

The research material was a review of the current literature advances in 3D printed casts for rehabilitation. For this purpose, the available data base was searched using Pub Med website, Google Scholar.

REVIEW

CAST AND 3D-PRINTING

Thanks to advances in medical imaging technologies and computer software, it is now possible to convert two-dimensional axial images into other planes (sagittal and coronal) as well as into three-dimensional (3D) virtual models that accurately replicate the individual anatomy of a patient. These digital data can then be thoroughly analyzed by orthopedic specialists to plan procedures tailored to the specific patient. The use of 3D printing in medicine is growing and becoming increasingly popular, as surgeons and researchers more frequently take advantage of the flexibility of this technology in producing a variety of objects. 3D printing is a manufacturing process in which materials such as plastics or metals are deposited layer by layer to create a three-dimensional object based on a digital model [6]. Advances in computer-aided design (CAD) software and 3D printing technology for personalized orthoses have opened new possibilities for improving conservative treatment. While these modern solutions allow for individualized design and production of orthoses, they also present challenges for researchers regarding the selection of appropriate designs, materials, and additive manufacturing methods. Different materials have specific properties that can influence the quality of the final print, and the chosen printing techniques determine the production time. Ideally, a 3D-printed orthosis should be precisely tailored to the patient's anatomy, providing optimal stabilization and immobilization of the fracture while offering greater comfort compared to a traditional plaster cast [3]. 3D digital models can be generated from CT scans using freely available software. These models can then be used to create physical models, plan procedures, or design surgical guides that assist the orthopedic surgeon during complex operations [7]. The development of 3D printing technology has enabled the introduction of new, standardized procedures for immobilization: additive manufacturing (AM) involves creating highly personalized cast models based on 3D anatomical data using digitally controlled material deposition tools. Compared to traditional plaster casts, AM-produced casts can potentially reduce the risk of skin complications while meeting mechanical and clinical requirements for functionality, comfort, and aesthetics [1].

Additive manufacturing represents a promising technology that can be used to produce personalized, more comfortable, and lightweight forearm orthoses and casts, although it requires careful selection of materials and process parameters [2]. The end result is a personalized 3D-printed cast with a highly ventilated structure, low weight while maintaining high strength, and hygienic benefits, reducing the risk of skin complications, potentially improving treatment efficacy, and increasing patient satisfaction [1].A malunion of the distal radius is a common complication following conservatively treated fractures in this region. When the malunion is clinically significant, treatment involves performing a corrective osteotomy (CO). The aim of corrective osteotomy is to restore the original bone alignment as accurately as possible by cutting the bone at the site of the previous fracture (osteotomy), followed by repositioning and stabilizing the bone fragments in a near-anatomical alignment.

Modern CO techniques combine three-dimensional (3D) preoperative virtual planning with the use of 3D-printed, patient-specific surgical instruments (PSI). In virtual planning, 3D models of both the affected and contralateral healthy radius are created based on bilateral computed tomography (CT) scans of the patient's forearm [8,9]. Additive manufacturing provides an advantage in producing objects with complex, freeform geometries, which is difficult or impossible to achieve using traditional subtractive methods [6].

TECHNOLOGIES

The cast model is first created based on patient images to achieve an individualized fit. A specialized method for creating geometric references has been developed to allow precise modeling of the cast. Its funnel-shaped design helps smooth edges and reduces the risk of bruising caused by minor limb movements. Ventilation patterns and holes are incorporated into the surface to improve hygiene and wearing comfort. Additionally, the cast can be adjusted to accommodate limb swelling during treatment [10]. To produce a 3D-printed cast, technicians use imaging data containing three-dimensional spatial information of the limb, obtained via a 3D scanner or medical imaging devices. Computer-aided design is then used to generate a stereolithography (STL) file ready for 3D printing [4]. A comparison was conducted between traditional materials standard plaster and fiberglass plaster and Polylactic Acid (PLA) materials as well as PLA–$CaCO_3$ composites produced using Fused Filament Fabrication (FFF), and functional casts were made from each of these materials. The materials were tested for tensile and bending strength. The results showed that tensile and bending strength decreased as the $CaCO_3$ content in the composite increased. In fatigue tests, traditional plaster and fiberglass plaster did not exhibit typical fatigue curves, whereas 3D-printed materials did. Cyclic loading tests further revealed that traditional casts cannot maintain the same load at the same deflection after previously being subjected to higher loads. These results clearly indicate that 3D-printed materials demonstrate superior properties in both static and dynamic mechanical tests. Therefore, 3D printing technology could soon provide an attractive alternative for personalized splints and casts. Materials produced using the FFF method, such as PLA and PLA–$CaCO_3$, exhibit better mechanical properties and higher water resistance compared to traditional plaster or fiberglass casts. Cyclic loading tests showed that 3D-printed casts do not require replacement after impact or loading, as PLA and $CaCO_3$ materials recover their original shape. These characteristics are beneficial for both patients and the healthcare system, improving treatment efficiency, enhancing patient compliance, and reducing the risk of complications such as infections or re-injury [2].

DISCUSSION

CAD software enables the development of designs tailored to the individual patient's anatomy, providing an alternative to conventional plaster casts. An orthosis designed in this manner can subsequently be manufactured using 3D printing technology and further refined through additive manufacturing techniques. The materials used in the analyzed designs are lighter than traditional plaster, water-resistant, and characterized by high mechanical strength. However, further studies are still required to evaluate their resistance to typical functional loads and accidental impacts. Some of the materials employed, such as polycarbonate, additionally exhibit flexibility, impermeability, UV resistance, and do not interfere with radiological imaging quality. The most commonly applied manufacturing method is FDM, valued for its low cost and its ability to produce complex, precise, and durable structures. The openwork design of 3D-printed orthoses enhances ventilation, facilitates skin inspection, improves hygiene, and increases aesthetic acceptance [3]. Prototypes produced using 3D printing technology are exceptionally lightweight, with a mass of approximately 10% of that of traditional solutions. Importantly, even a technician with limited experience can design such a cast within a short time, approximately 20 minutes using the proposed method [10]. A personalized 3D-printed cast ensures accurate adaptation to the limb, effectively immobilizing the injury site and maintaining proper alignment of bone fragments [11]. Studies have shown that this type of orthosis can generate appropriately directed corrective forces, supporting the maintenance of proper forearm alignment and resulting in satisfactory clinical outcomes and high patient comfort [4]. An individualized design reduces the risk of complications associated with localized excessive pressure, while the lightweight and ventilated structure minimizes skin-related issues and facilitates daily functioning. Improvements in the visual appearance of the cast, enhanced anatomical fit, and a beneficial effect on hand function during immobilization have also been reported. In numerous publications, patients express a clear preference for 3D-printed casts compared to traditional plaster casts [11-15]. The ability to precisely control the internal scaffold structure and to incorporate various materials, including bioactive components, enables the creation of an environment conducive to the healing process [1,10,16-19]. No serious complications have been reported with 3D-printed casts, whereas moderate adverse events have been observed more frequently with traditional plaster casts [17]. Personalized casts produced using dedicated software have been shown to be safe in the treatment of distal radius buckle fractures in children, which encourages the extension of this technology to more complex injuries [20]. Furthermore, screw fixation supported by a 3D-printed cast demonstrated superiority over minimally invasive plate osteosynthe-

sis in terms of operative time, fluoroscopic radiation exposure, restoration of calcaneal morphology, and functional outcomes in the treatment of displaced intra-articular calcaneal fractures (DIACFs) [21]. The rapid advancement of 3D printing technology highlights its growing importance in the production of personalized orthopedic and rehabilitation devices [10].

CONCLUSIONS

3D printing presents a promising future for casts development, offering personalized, cost-effective, and efficient solutions for patients. While challenges persist, ongoing research and technological advancements are likely to address existing limitations, paving the way for broader clinical adoption and improved patient care.

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REVIEW ARTICLE

CONTENTS

Atrial fibrillation as a driver of cognitive decline

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ABSTRACT

Traditionally, Atrial Fibrillation (AF) has been managed to reduce the risk of stroke, but there is an increasing amount of evidence to suggest that atrial fibrillation is also related to a decline in cognitive function (dementia) and not necessarily related to blood clots or interruptions to blood flow. The aim of this review is to evaluate different mechanisms contributing to the relationship between atrial fibrillation and dementia through hemodynamic and inflammatory pathways. In order to achieve this, a systematic review of longitudinal studies, randomized trials from the past five years, and neuroimaging studies (2013–2026) was conducted to examine the neurocognitive variables relative to atrial fibrillation through the PubMed and Cochrane database. The results of this study suggest that patients with atrial fibrillation are at increased risk of developing dementia independent of thromboembolic events (1.4–2.2 times). Primary risk factors affecting this relationship include silent cerebral infarcts (40% of patients will have these) and chronic cerebral hypoperfusion associated with beat-to-beat variability. Of particular note, patients with atrial fibrillation who achieve early rhythm control using catheter ablation demonstrate a 27%–30% lower risk of cognitive dysfunction as compared to those with rate control. There are numerous and complex physiological changes that can occur from atrial fibrillation that can lead to cognitive decline.

KEY WORDS: cognitive dysfunction, dementia, neuroprotection, catheter ablation

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INTRODUCTION

According to the World Health Organization, it is estimated that the global prevalence of atrial fibrillation (AFib) will reach 12 million in the United States by 2030 [1]. Previously, cognitive dysfunction related to AFib was thought to be exclusively related to thromboembolic strokes, but recent longitudinal studies have uncovered a cognitive gap, referring to AFib patients with no history of stroke and an increased probability of experiencing dementia compared with those in sinus rhythm [2]. This indicates that AFib is likely a chronic and silent source of erosion of the brain's cognitive reserve; therefore, there needs to be a shift from macro-vascular disease as the primary pathological process affecting patients with AFib to micro-vascular integrity.

AIM

The main aim of this literature review is to classify the various non-embolic modes of contribution that atrial fibrillation has to neurodegenerative disease. Additionally, this study will investigate the measurable neuroprotective effect of the modern treatment modalities utilized on elderly patients, namely catheter ablation and direct oral anticoagulants (DOACs).

MATERIALS AND METHODS

A systematic literature search of PubMed, Google Scholar and the Cochrane Library was performed between 2013 and 2026. The data extraction for the review was based on randomised controlled trials (RCTs), systematic reviews and neuroimaging studies using 3T/7T MRI as preferred data sources. The inclusion criteria for the studies were limited to a minimum sample size of n = 1,000, or longitudinal follow-up (> 5 years) of sufficiently high-fidelity. The evidence was synthesised according to the pathophysiological drivers, and the relative effectiveness of rhythm-control compared to rate-control strategies of cognitive preservation scores were compared.

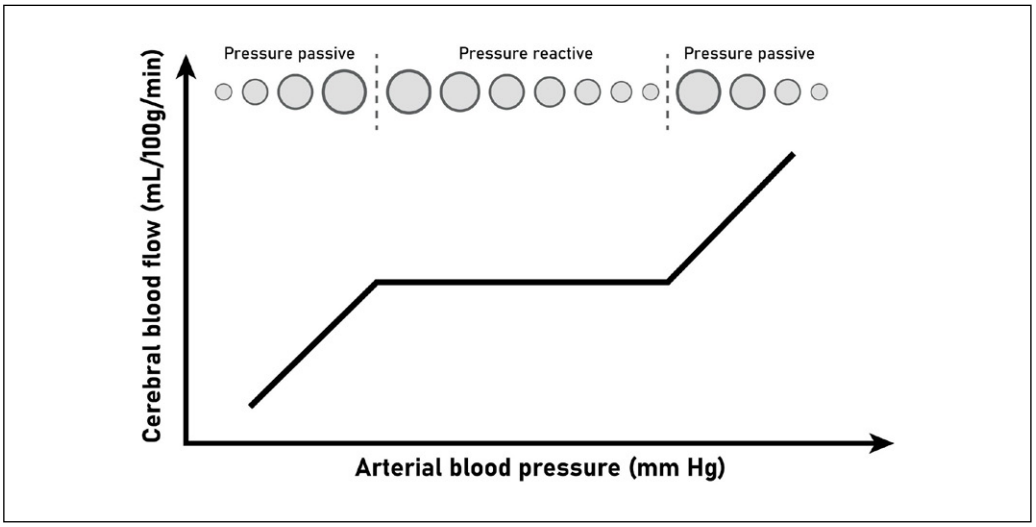

Fig. 1. Two critical physiological „barriers" and „flows" that connect heart health to brain function [4]

REVIEW AND DISCUSSION

HEMODYNAMIC DISTURBANCE AND INSUFFICIENT BLOOD PERFUSION

The altered variance within the R-R interval of atrial fibrillation is responsible for beat-to-beat variation in stroke volume. Compared with normal sinus rhythm, which has stable pulsatile flow through the arteries into the brain, the chaotic nature of hemodynamics caused by atrial fibrillation overwhelms the ability of the brain to autoregulate blood flow [3]. The rapid ventricular responses associated with atrial fibrillation shorten the duration of diastole, resulting in a significant reduction in stroke volume. Figure 1 represents the two critical physiological "barriers" and "flows" that connect heart health to brain function [4].

When the brain experiences this type of long-term instability (cerebral hypoperfusion), it receives 10-20% less adequately profused (oxygenated) blood than it needs to adequately perform its functions [5]. The current study indicates that chronic cerebral hypoperfusion is especially deleterious to watershed areas of the brain (the areas, throughout the brain, where blood supply comes from at least two different arteries), the white matter of the brain, and the hippocampus, which all have particularly high susceptibilities to oxygen debt [6].

SILENT CEREBRAL INFARCTS (SCIS) AND MICROBLEEDS

High-resolution MRI studies involving the Swiss-AF cohort have demonstrated that silent brain lesions are found in as many as 40% of patients with atrial fibrillation, or AF [7]. Silent cerebral infarcts (SCIs) are small clusters of tissue death (infarction) that occur in the brain in an asymptomatic fashion and are essentially a cumulative process that decreases the structural integrity of the brain [8]. While anticoagulant therapy may prevent strokes, the results of this study suggest that they do not completely eliminate the risk of suffering microembolic showers—microscopic clots that do not cause any motor deficits, but negatively impact cognitive processing speed [9].

NEUROINFLAMMATION AND DYSFUNCTION OF THE BLOOD-BRAIN BARRIER (BBB)

AFib is considered a pro-inflammatory state with high levels of C-reactive protein and interleukin-6 present in patients with this condition [10]. This systemic inflammatory process begins to disrupt the tight junctions of the BBB, allowing both neurotoxins and peripheral immune cells to gain access to the brain parenchyma .

It has been suggested through developing theoretical models in 2026 that the loss of the rhythmic pulsating motion of the heart has disrupted the function of the glymphatic system (the mechanism that removes waste from the brain). The rhythmic pumping action created by the arteries allows for the efficient clearance of amyloid-beta/Tau proteins, two of the biological characteristics of Alzheimer's Disease [11, 12].

NEUROPROTECTION AND THERAPEUTIC INTERVENTIONS

The current debate in the field revolves around the question of whether a restoration of normal cardiac rhythm via catheter ablation can be considered to slow down the rate of dementia progression. In light of data obtained through early rhythm control trials

(EAST-AFNET 4) suggesting a 27-30% decrease in the likelihood of developing dementia following successful intervention [13]. Additionally, when compared to Warfarin, DOACs appear to provide greater neuroprotective properties based upon their ability to reduce the incidence of subclinical microbleeds [14, 15]. However, they are less effective than ablation at rectifying issues related to mechanical hypoperfusion resulting from irregular heart rhythms due to hypoperfusion [16-18].

CONCLUSIONS

Atrial Fibrillation is an independent and powerful contributor to cognitive erosion. Primary treatment goals should expand beyond preventing stroke to encompass total brain preservation. It is suggested by the present study to achieve this through early and aggressive rhythm control, consistent cognitive assessments via accepted instruments such as the MoCA, and an overall holistic approach to cardiovascular wellness.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Exercise interventions for knee osteoarthritis: A narrative review of mechanisms, modalities, and clinical implementation

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ABSTRACT

Knee osteoarthritis (OA) is a chronic, multifactorial joint disorder involving cartilage degeneration, subchondral bone changes, synovial inflammation, and neuromuscular dysfunction. Exercise is first-line therapy, yet heterogeneity in modalities, dosing, and delivery limits practical guidance. A narrative review was conducted using PubMed, Scopus, Google Scholar, Frontiers, and ScienceDirect (2021–2026), focusing on aerobic, resistance, aquatic, and mind–body exercise studies. Data were extracted on type, intensity, frequency, duration, delivery, and outcomes, and synthesized narratively to provide clinically relevant insights. Exercise improves pain, function, and quality of life through enhanced muscle strength, joint stability, optimized loading, anti-inflammatory effects, and central pain modulation. Aerobic and resistance training enhance cardiovascular fitness, quadriceps and hip strength, and functional performance. Aquatic therapy reduces joint stress and improves adherence, while mind–body interventions support flexibility, balance, and stress reduction. Long-term, thrice-weekly protocols offer maximal benefit, and hybrid models combining supervised and home-based exercise optimize adherence and outcomes. Exercise is a cornerstone of knee osteoarthritis management. Individualized programs considering patient characteristics, modality-specific benefits, and delivery method are essential. Future research should refine exercise dosage, intensity, progression, and hybrid delivery strategies to maximize long-term clinical effectiveness.

KEY WORDS: exercise therapy, resistance training, aerobic exercise, aquatic therapy, mind-body interventions

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INTRODUCTION

Knee osteoarthritis (OA) is a chronic, progressive joint disorder characterized by structural and functional alterations involving articular cartilage, subchondral bone, synovium, and periarticular soft tissues. Rather than representing isolated cartilage "wear and tear," knee OA reflects a whole-joint pathology driven by the interaction of mechanical stress, low-grade inflammation, metabolic dysregulation, and neuromuscular dysfunction [1]. Pathological features include synovial activation, osteophyte formation, ligamentous remodeling, and progressive impairment of joint integrity, ultimately manifesting as pain, stiffness, and reduced mobility. Importantly, alterations in muscle strength and motor control contribute not only to symptom expression but also to abnormal joint loading patterns, providing a mechanistic basis for exercise-based interventions.

The development and clinical presentation of knee OA are influenced by multiple interacting factors, including aging, prior joint injury, repetitive mechanical loading, metabolic syndrome, and genetic predisposition [2]. These determinants shape both structural progression and symptom burden, which often do not correlate directly with radiographic severity. This discordance highlights the complex and multifactorial nature of pain generation in OA and underscores the need for comprehensive management strategies that extend beyond structural modification alone.

The global burden of knee OA continues to rise. In 2020, an estimated 595 million individuals worldwide were affected by osteoarthritis, with the knee representing the most frequently involved joint [3]. Knee OA ranks among the leading causes of years lived with disability and has demonstrated a marked increase in disability burden over recent decades. The condition commonly coexists with obesity, diabetes mellitus, and cardiovascular disease, establishing a bidirectional relationship in which reduced mobility exacerbates metabolic dysfunction, further amplifying functional

decline [4]. This convergence of musculoskeletal and systemic consequences underscores knee OA as both a clinical and public health priority.

Current pharmacological therapies primarily provide symptomatic relief and do not modify underlying disease progression. Topical nonsteroidal anti-inflammatory drugs (NSAIDs), such as diclofenac, are recommended as first-line pharmacologic treatment because of their lower systemic risk compared with oral agents. However, oral NSAIDs are associated with increased cardiovascular, gastrointestinal, and renal adverse effects, particularly in older adults with comorbidities [2, 5]. Consequently, long-term reliance on pharmacotherapy alone is insufficient for sustainable disease management.

Major international guidelines, including those from NICE and OARSI, consistently recommend exercise as first-line therapy for knee OA across age groups and disease severities. Exercise interventions encompass aerobic conditioning, resistance training, and mind–body modalities such as Tai Chi, aiming to enhance muscle strength, improve neuromuscular control, optimize joint loading, and reduce pain [5]. Despite the expanding body of literature, heterogeneity in study design, intervention protocols, and outcome measures limits clear clinical guidance.

AIM

The current review aims to synthesize and critically evaluate current evidence on exercise-based interventions in knee osteoarthritis, integrating mechanistic rationale, comparative effectiveness across modalities, and practical considerations related to implementation and long-term sustainability in clinical practice and clinical implementation.

MATERIALS AND METHODS

REVIEW DESIGN

This review employed a narrative design to synthesize current evidence on exercise-based interventions in knee osteoarthritis (OA). A narrative approach was chosen to integrate findings from randomized controlled trials, meta-analyses, and clinical guidelines, allowing a clinically oriented synthesis across various exercise modalities, including aerobic, resistance, aquatic, and mind–body interventions. This design was preferred due to heterogeneity in study designs, outcomes, and exercise protocols, which precluded quantitative meta-analysis, while still enabling thematic integration of evidence relevant to clinical practice. As a purely narrative review, formal risk-of-bias assessment was not performed, consistent with the narrative design. Measures to minimize bias included multi-database searching, clear eligibility criteria, and iterative selection based on relevance. The findings are intended to summarize and interpret trends in evidence rather than provide pooled effect sizes.

LITERATURE SEARCH AND DATABASES

A literature search was conducted in PubMed as the primary database, with supplementary searches in Scopus, Google Scholar, Frontiers, and ScienceDirect to ensure comprehensive coverage. The search focused on publications from January 2021 to February 2026, covering studies that evaluated exercise interventions for knee OA. Each author independently conducted searches within their assigned exercise domain, followed by collaborative discussion to resolve overlap and finalize inclusion.

STUDY SELECTION

Given the narrative design, no formal title or abstract screening process was employed. Instead, studies were iteratively reviewed for relevance, clinical applicability, and alignment with the aims of the review. Selection prioritized high-quality and representative studies while excluding preclinical research, non-English publications, case reports, and studies unrelated to exercise-based interventions.

DATA EXTRACTION AND SYNTHESIS

From each included study, key information was extracted, including study design, population characteristics, exercise type, duration, frequency, intensity, and primary outcomes. Data were synthesized narratively, integrating findings across exercise modalities and clinical contexts to highlight clinically relevant evidence, practical applications, and gaps in current knowledge. No statistical pooling or meta-analysis was performed.

SCOPE AND STUDY INCLUSION

A total of 33 studies were included in the review, encompassing randomized controlled trials, meta-analyses, and clinical guidelines. This sample was considered sufficient to provide a balanced synthesis of current evidence while maintaining focus on clinically meaningful interventions. Figure 1 illustrates a flowchart outlining the process used for selecting articles included in this review.

REVIEW AND DISCUSSION

MECHANISTIC RATIONALE FOR EXERCISE IN KNEE OSTEOARTHRITIS

Exercise is recommended as a first-line therapy in knee osteoarthritis (OA) because it targets key biomechanical, physiological, and neuromodulatory factors that contribute to pain and functional limitation. Rather than acting through a single mechanism, exercise produces integrated benefits that improve joint stability, optimize loading, reduce low-grade inflammation, and modulate pain perception.

MUSCLE STRENGTHENING AND JOINT STABILITY

Quadriceps weakness is a hallmark characteristic in people with knee OA and is strongly associated with impaired physical function and altered joint mechanics. Strength deficits reduce dynamic support during weight-bearing activities such as walking, stair climbing, and standing from sitting, contributing to uneven joint loading and increased symptomatic burden. Structured resistance training enhances muscle force production and neuromuscular control, thereby improving joint stability and lowering mechanical stress at the knee.

A recent narrative review reported that strengthening exercises improve quadriceps and hip muscle performance and are consistently associated with reduced pain and improved physical function in knee OA patients. Improvements in muscle strength translate into better shock absorption and more balanced load distribution across articular surfaces [6].

REDUCTION IN JOINT LOADING AND BIOMECHANICAL OPTIMIZATION

Mechanical loading contributes significantly to symptom expression in knee OA. Excessive joint contact forces, particularly in the medial compartment, are linked to pain and functional decline. Exercise improves load management through enhanced muscular support and improved movement patterns.

Low-impact aerobic activities such as cycling and controlled walking reduce joint compressive forces while enhancing cardiovascular fitness and lower-limb endurance. A scoping review confirmed that aerobic and strengthening exercises improve pain and functional performance without adverse structural outcomes [7].

Weight reduction achieved through exercise also contributes to reduced joint load per step. Clinical studies integrating exercise with behavioral lifestyle modification demonstrate meaningful reductions in pain and mechanical stress, highlighting the combined mechanical benefit of weight loss and physical activity [8].

ANTI-INFLAMMATORY EFFECTS OF PHYSICAL ACTIVITY

Osteoarthritis is increasingly recognized as having an inflammatory component in addition to mechanical degeneration. Sedentary behavior is associated with elevated systemic inflammatory markers, which may exacerbate pain sensitization and chronicity.

Moderate-intensity exercise reduces circulating pro-inflammatory mediators and improves metabolic health. Structured physical activity programs in knee OA populations have demonstrated improvements in pain and stiffness alongside reductions in inflammatory indicators, supporting a systemic anti-inflammatory effect of regular exercise [7].

PAIN MODULATION AND CENTRAL ADAPTATION

Pain in knee OA often does not correlate directly with radiographic severity, suggesting involvement of central pain processing mechanisms. Physical activity influences pain perception through both peripheral and central pathways. Peripherally, improved muscular support reduces nociceptive input from joint stress. Centrally, exercise stimulates endogenous pain inhibitory systems and reduces sensitivity to painful stimuli.

Evidence consistently supports exercise as an analgesic intervention in knee OA, producing meaningful reductions in pain intensity and improving function across diverse patient subgroups [8, 9].

These interconnected mechanisms collectively contribute to clinically meaningful improvements in pain, stiffness, and functional capacity in individuals with knee osteoarthritis. The multidimensional pathways through which exercise exerts its effects are summarized in Figure 2.

TYPES OF EXERCISE AND EVIDENCE

AEROBIC EXERCISE

Aerobic exercise elevates heart rate and oxygen consumption, forming a cornerstone of physical activity recommendations. For people with knee OA, exercises must be tailored to individual age and fitness levels. High-intensity exercise engages large muscle groups and likely enhances VO2 max. Non-

Table 1. Comparative overview of exercise modalities, dosage parameters, mechanistic effects, and clinical considerations in knee osteoarthritis

Exercise Modality	Typical Dosage / Frequency	Delivery Format	Mechanistic Benefits	Population / Clinical Considerations
Aerobic (walking, cycling, aquatic)	30 min, ≥3 days/ week, moderate intensity	Home-based / supervised	Cardiovascular fitness, lower-limb endurance, modest pain relief, reduced joint load	Suitable for most; caution in severe joint degeneration; may have minimal biomechanical improvements alone
Resistance / Strengthening	2–3 times/week; high-speed RT: 47% 1RM, 35 weeks, 640 reps/ week	Supervised / hybrid	Increased quadriceps and hip strength, improved joint stability, reduced mechanical load, functional improvements	Target quadriceps and gluteus maximus; can reverse pain-induced atrophy; may combine with hip abductor & stretching
Aquatic Therapy	30–45 min, 2–3 times/week	Supervised / aquatic facility	Reduced joint load, improved circulation, pain relief, higher adherence	Ideal for patients with pain, stiffness, or mobility limitations; accessibility & cost considerations
Mind–Body (Yoga, Tai Chi)	30–60 min, 2–3 times/week, ≥16 weeks	Home-based / supervised	Flexibility, balance, neuromuscular control, modest pain relief, stress reduction, reduced inflammation	Complementary to strengthening; less effective than high-speed RT for pain reduction; adherence depends on motivation
Exercise Dosage / Guidelines	Long-term: >16 weeks, 3x/week; Short-term: ≤16 weeks, 2–3x/ week depending on goal	N/A	Improves pain, function, and general health; supports guideline adherence	Programs should be individualized; follow international guideline recommendations
Home-Based vs Supervised	Structured sessions per above modalities	Home-based, supervised, or hybrid	Adherence, comfort, practicality, and safety	Supervised programs generally outperform home-based alone; hybrid models optimize long-term adherence

Source: Developed by the authors based on literature synthesis

weight-bearing exercises, such as cycling and aquatic aerobics, reduce joint load and are preferred for low injury risk, but may provide less cardiovascular stimulus [10].

Guidelines suggest a frequency of 30-minute walks ≥3 days per week at moderate intensity, emphasizing perceived health benefits. However, these recommendations may overlook joint-specific effects; prolonged walking can increase knee joint loading and contact forces, potentially contributing to structural degeneration. Evidence shows walking alone or combined with other activities produces minimal changes in discrete biomechanical moments or impulses in mild-to-moderate knee OA. Small improvements in gait speed, spatiotemporal, and kinematic metrics are observed, but biomechanical outcomes remain largely unchanged [11].

RESISTANCE TRAINING

Resistance training is a widely prescribed rehabilitative modality in OA, improving muscle strength, joint stability, and function, while reducing joint load to slow cartilage degeneration and relieve pain. Isokinetic muscle strengthening (IKMS) is considered safe and effective for OA rehabilitation [12].

A systematic review and network meta-analysis from China found high-speed resistance training (RT) provided the greatest improvements in pain, stiffness, and function. This modality involves performing concentric contractions at maximum speed and requires symptom-specific dosing. Optimal pain reduction was achieved with 47% of 1RM over 35 weeks, with 640 repetitions per week. High-speed RT maximizes muscle activation, neuromuscular efficiency, and proprioception, enhancing joint stability and reducing mechanical load [13].

Substantial muscle mass loss and functional decline are common in OA. The painful limb shows selective reductions in knee extensors (quadriceps) and hip extensors (gluteus maximus), leading to patellofemoral pain, giving-way episodes, heaviness, focal myalgia, and fall risk. Targeted strengthening can reverse or compensate for pain-induced atrophy and fatty degeneration [14]. Studies also demonstrate additional functional benefits when stretching and hip abductor strengthening are combined with quadriceps exercises [15].

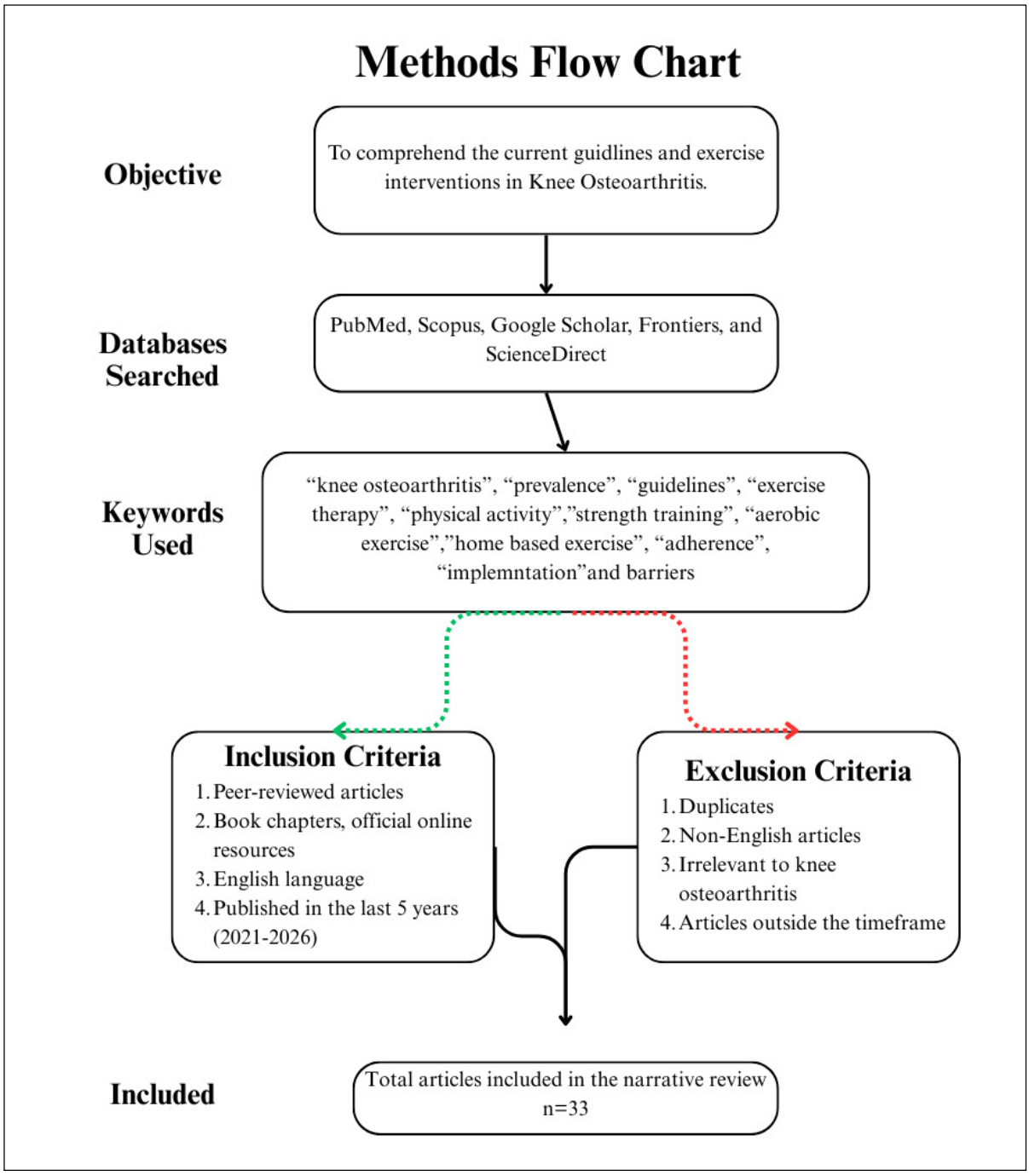

Fig. 1. Methodology flowchart summarizing literature search strategy, inclusion/exclusion criteria, and data synthesis steps used in the review
Source: Developed by the authors

AQUATIC PHYSICAL THERAPY

Aquatic therapy is ideal for patients with pain, stiffness, or weakness during land-based exercises. Buoyancy reduces joint load, while warmth and water pressure improve circulation and reduce discomfort. Compliance is higher than with other modalities [16]. Recommendations are conditional on accessibility and cost. Optimal water parameters (temperature, depth, composition) remain unclear, affecting exercise outcomes [17].

MIND–BODY EXERCISES:

Strengthening exercises focus on knee joint muscle power, stability, and mechanical pain reduction. Yoga combines postures, mindfulness, and breathing techniques, offering modest pain relief through flexibility and stress reduction. A randomized trial (2025) showed yoga outcomes were modest compared to strength training [18].

Tai Chi, an aerobic mind–body practice, incorporates mindful movement and abdominal breathing. It im-

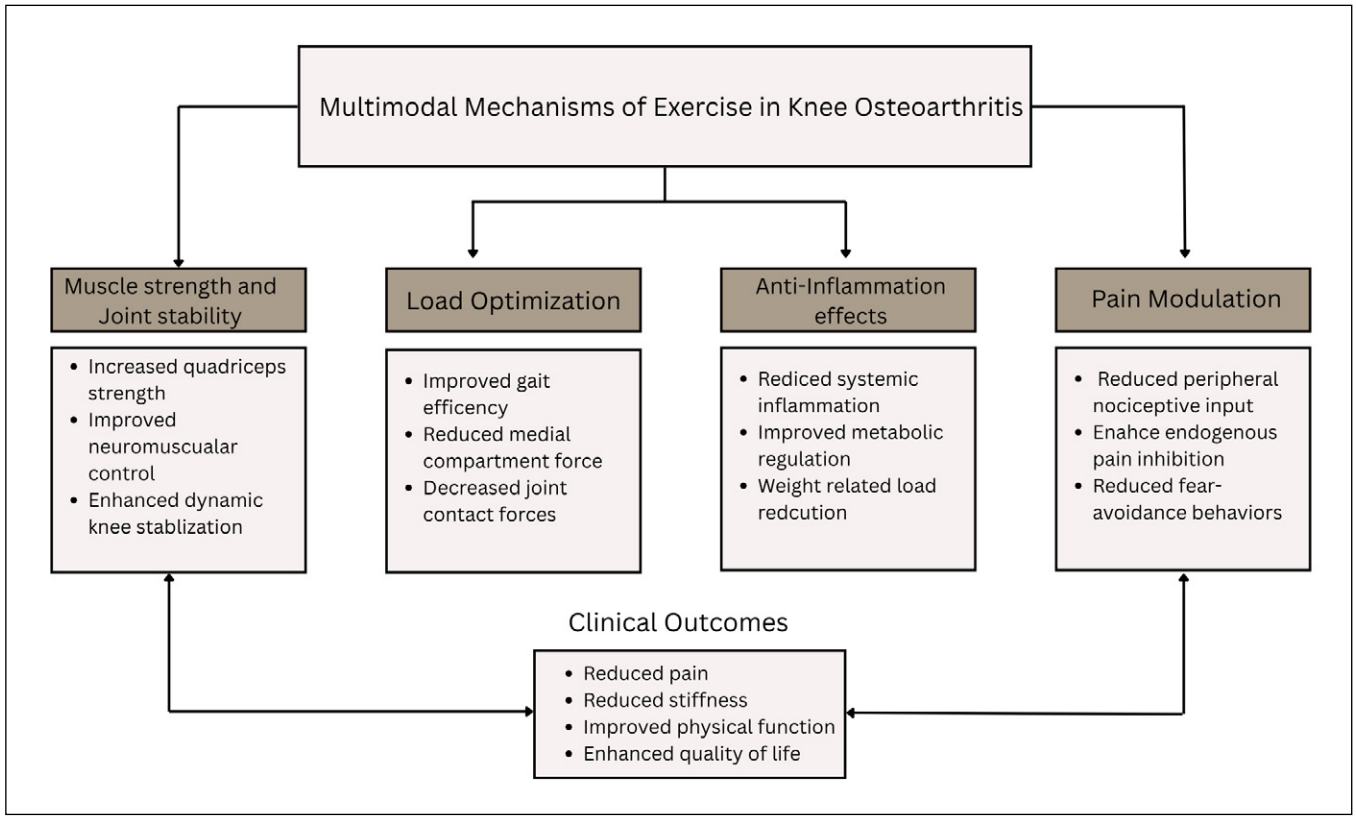

Fig. 2. Multidimensional mechanisms underlying the effects of exercise in knee osteoarthritis
Source: Developed by the authors based on literature synthesis

proves alignment, strengthens lower limbs, stabilizes the knee, and reduces local and systemic inflammation, facilitating healing [19].

EXERCISE DOSAGE AND GUIDELINES

Preliminary evidence (2025) suggests long-term (>16 weeks)/three-times-weekly protocols improve pain and function; short-term (≤16 weeks)/three-times-weekly protocols alleviate stiffness; short-term (≤16 weeks)/twice-weekly protocols enhance general health [20].

Multiple international guidelines recommend therapeutic exercise as first-line for knee OA, highlighting benefits and cost-effectiveness. However, delivery is often sub-optimal, with insufficient guidance for healthcare professionals on best practice [21].

HOME-BASED VS SUPERVISED EXERCISE

Hospital-based programs do not provide long-term advantages over home-based exercise (HBE), which is cost-effective, practical, highly compliant, comfortable, and low-risk [22]. Supervised exercises outperform HBE in achieving patient goals due to structured guidance, real-time feedback, and tailored progression. HBE may lack supervision, leading to inconsistent adherence and limited progression. Hybrid models combining supervised and home-based exercise may optimize outcomes and engagement [23].

Table 1 provides a consolidated summary of exercise modalities for knee osteoarthritis, including typical dosage, delivery methods, mechanistic benefits, and clinical considerations, offering a practical reference for evidence-based implementation.

CLINICAL IMPLEMENTATION AND ADHERENCE CHALLENGES

PATIENT-LEVEL FACTORS

Long-term adherence often declines after supervised care ends. Secondary analysis of an RCT found higher adherence with physiotherapist-supervised exercises than app-based instruction. Higher education and self-efficacy promoted adherence, while fatigue reduced it [24].

Sustaining engagement requires more than simple prescriptions. Exercise adherence frequently declines after therapist contact ceases, emphasizing the need for behavioral strategies [25].

Cognitive, social, and environmental factors strongly influence participation. Fear of pain or self-doubt may cause avoidance, whereas encouragement and favorable conditions support continued engagement.

PROVIDER AND SYSTEM-LEVEL FACTORS

Healthcare provider and system barriers include limited awareness of physiotherapy services, difficulty accessing affordable care, and perceptions of patient non-adherence [25]. Even when exercise is recognized as first-line, structural issues such as accessibility, funding, and referral processes may hinder effective implementation.

STRATEGIES TO IMPROVE ADHERENCE

Patient expectations, such as believing surgery is inevitable or fearing exercise-induced pain, impact adherence [26]. Clear education about benefits and reassurance regarding manageable discomfort are critical.

Exercise adherence reporting remains inconsistent across trials, complicating interpretation and tailoring strategies [27]. Effective programs should integrate behavioral support, accessible delivery methods (supervised, hybrid, app-based), and motivational strategies. Programs must be tailored to individual beliefs, social contexts, and lifestyle factors for long-term engagement.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

Exercise remains the cornerstone of knee osteoarthritis management. Current guidelines recommend individualized programs incorporating strengthening, aerobic, and neuromuscular training for all patients, irrespective of disease severity [28]. Meta-analytic evidence indicates that exercise provides pain relief comparable to oral NSAIDs and paracetamol, while avoiding the long-term systemic risks associated with pharmacotherapy [29]. Programs combining aerobic and resistance training confer broader functional benefits, though variability in dosage, intensity, and progression may influence clinical outcomes [30].

Despite strong evidence, exercise is underutilized in routine practice. Inconsistent prescription, limited monitoring, and lack of structured progression or follow-up are commonly reported [31]. Long-term adherence often declines once clinician supervision ceases, highlighting the need for behavioral support, patient education, and structured follow-up to maintain engagement [32]. Home-based exercise programs are accessible, practical, and cost-effective, whereas supervised interventions generally achieve superior improvements in pain, function, and adherence. Hybrid models combining supervised initiation with ongoing home-based programs may offer a pragmatic approach to optimize patient outcomes [33].

CONCLUSIONS

Exercise is a foundational, evidence-based intervention for managing knee osteoarthritis, yielding substantial improvements in pain, physical function, and overall quality of life. Despite robust guideline support, implementation in routine practice remains suboptimal, underscoring the need for innovative delivery strategies and sustained patient engagement.

FUTURE DIRECTIONS

Future research should define optimal exercise dosage, intensity, and progression across diverse patient populations and identify subgroups most likely to benefit from tailored interventions. Evaluating hybrid models that integrate supervised initiation with ongoing home-based programs, alongside behavioral support strategies, will be critical to enhance long-term adherence and clinical effectiveness. Strengthening implementation frameworks within primary care and community settings is essential to ensure that these evidence-based interventions translate into meaningful, real-world benefits for the growing population affected by knee osteoarthritis.

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REVIEW ARTICLE

CONTENTS

From longevity to healthy ageing: A conceptual review of the 6W public health preparedness framework

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ABSTRACT
Population ageing is one of the most profound demographic transformations of the 21st century and represents a major public health success driven by advances in medicine, public health, and socio-economic development. By 2050, the global population aged 60 years and above is projected to exceed 2.1 billion, with the most rapid increases occurring in low- and middle-income countries. However, gains in life expectancy have not been matched by equivalent improvements in healthy life expectancy, resulting in longer survival with chronic disease, disability, and functional decline. This manuscript examines the concept of healthy ageing through a public health lens, emphasizing the importance of functional ability, quality of life, and equity across the life course. Using the 6W framework, the paper explores why population ageing matters, what demographic and epidemiological transitions are occurring, who is affected, where interventions are most effective, when action is required, and how public health systems must respond. Key challenges, including multimorbidity, polypharmacy, disability, loneliness, and health system strain, are discussed alongside opportunities offered by primary health care, community-based interventions, digital health, and policy reform. The manuscript highlights the critical role of preparedness in transforming longevity into healthy ageing and underscores the need for integrated, life-course-oriented, and equity-focused public health strategies.

KEY WORDS: life expectancy, HALE, multimorbidity, disability, life-course approach

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INTRODUCTION
Population ageing is reshaping societies worldwide and represents one of the most profound demographic shifts of the 21st century. Extended survival has not been accompanied by equivalent gains in healthy life expectancy, resulting in longer years lived with chronic disease, disability, and functional decline. As populations age, health systems face rising demands related to multimorbidity, long-term care, and social support. These changes necessitate a reconceptualization of ageing within a public health preparedness framework that prioritizes functional ability, equity, and life-course strategies.

WHY LONGEVITY MATTERS
Longevity refers to the length of time an individual or a population lives and is most commonly measured using life expectancy, which represents the average number of years a person is expected to live under prevailing mortality conditions [1]. From a public health perspective, longevity is widely regarded as a major societal achievement, reflecting sustained advances in medicine, sanitation, nutrition, education, and socioeconomic development [2]. The dramatic increase in global life expectancy since the mid-20th century has largely resulted from reductions in infant and maternal mortality, effective control of infectious diseases through vaccination and antibiotics, and improvements in living conditions[3, 4]. Improvements in sanitation, vaccination, nutrition, maternal and child health, disease control, and socio-economic conditions have collectively contributed to unprecedented survival gains worldwide[3, 5]. Global life expectancy increased from approximately 46 years in 1950 to over 73 years by 2023, reflecting sustained progress across most regions [1]. By 2050, one in five people globally will be aged 60 years or older, fundamentally reshaping demographic structures, dependency ratios, and health system demands [1]. Living longer does not necessarily equate to living healthier. Many populations are experiencing extended years lived with disability, multimorbidity, and reduced

functional capacity, shifting the public health focus from mortality reduction to morbidity management and wellbeing promotion [6]. A reconceptualization of ageing is needed that moves away from disease-centred models toward approaches prioritizing functional ability, independence, dignity, and quality of life.

GLOBAL POPULATION AGEING AND LIFE EXPECTANCY TRENDS

Addressing this paradox requires a reconceptualization of ageing that moves away from disease-centred models toward approaches that prioritize functional ability, independence, dignity, and quality of life across the life course. Contemporary public health frameworks emphasize that increases in life expectancy alone are insufficient indicators of population health, as many societies experience widening gaps between life expectancy and healthy life expectancy (HALE). This gap reflects the growing burden of years lived with disability (YLDs), driven by chronic diseases, multimorbidity, and functional decline among ageing populations. As a result, healthy ageing is increasingly defined by the ability to maintain intrinsic capacity and functional ability rather than survival alone. This shift underscores the need for health systems and policies that focus on reducing disability, delaying functional decline, and improving quality of life, thereby ensuring that longevity gains translate into healthier years lived rather than prolonged morbidity[5, 8, 9].

DEMOGRAPHIC AND EPIDEMIOLOGICAL TRANSITIONS

The demographic transition, characterized by sustained declines in fertility and mortality, has profoundly reshaped population age structures across the world, leading to a rapidly growing proportion of older adults. Recent evidence highlights that reductions in infant and child mortality driven by expanded immunization coverage, improved maternal and neonatal care, and strengthened infectious disease control have been central to these shifts, particularly in low- and middle-income countries [10, 11]

In parallel, the epidemiological transition has resulted in a marked shift in disease burden from communicable diseases to non-communicable diseases (NCDs), including cardiovascular diseases, diabetes, cancers, and chronic respiratory conditions. This transition has been accelerated by population ageing, urbanization, changing lifestyles, and environmental exposures, leading to an increasing prevalence of multiple chronic conditions among older adults[6, 9]. Consequently, ageing populations now require long-term, integrated, and person-centred care models that move beyond episodic and disease-specific approaches to address multimorbidity and functional decline effectively.

AIM

This conceptual review reframes population ageing through a public health preparedness lens. It distinguishes longevity from healthy ageing by emphasizing functional ability and life-course equity. Using the 6W framework, it organizes ageing challenges and identifies priority strategies, including primary health care strengthening, integrated care models, surveillance, and multisectoral policy action.

REVIEW AND DISCUSSION

CONCEPTUAL APPROACH

This manuscript adopts a conceptual synthesis approach to examine healthy ageing through a public health preparedness lens. It integrates the World Health Organization's definition of healthy ageing with life-course and health systems perspectives. This paper synthesizes existing evidence and organizes it using the 6W framework. This approach facilitates a comprehensive analysis that connects theory, demographic and epidemiological trends, and policy action within a coherent public health framework.

CONCEPTUALIZING HEALTHY AGEING

The World Health Organization (WHO) defines healthy ageing as "the process of developing and maintaining the functional ability that enables wellbeing in older age"[4]. This definition moves beyond chronological age and disease absence, emphasizing what individuals can do and value throughout later life. Functional ability is shaped by intrinsic capacity (physical and mental capacities), environmental factors, and the interaction between the two. Healthy ageing is inherently a life-course process. Health trajectories in older age are strongly influenced by exposures, behaviours, and social determinants accumulated from early childhood through adulthood [7]. Consequently, policies that promote physical activity, healthy diets, tobacco cessation, and reduced harmful alcohol use benefit not only older adults but the entire population. The WHO Decade of Healthy Ageing (2021–2030) underscores global commitment to creating age-friendly environments, aligning health systems to older populations, providing integrated long-term care, and fostering research and

innovation[5]. These principles form the foundation of a comprehensive public health response to ageing.

PUBLIC HEALTH PREPAREDNESS AND MEASURING SUCCESS

Public health preparedness is central to transforming increased longevity into healthy ageing. Effective preparedness requires robust surveillance systems to monitor key ageing indicators such as life expectancy, healthy life expectancy (HALE), disability prevalence, and functional ability[4]. These indicators help clarify what is changing in ageing populations and who is most affected, thereby guiding evidence-based public health planning[4]. Surveillance data also inform when and where interventions are required across the life course and within specific demographic and geographic contexts[16]. Preparedness further depends on policy frameworks that integrate ageing into national development strategies, promote age-friendly environments, and ensure financial protection and social security[5, 17]. These measures address why population ageing must be prioritised within public health systems and how multisectoral action can prevent avoidable disability and dependency[4, 5]. Importantly, success in public health preparedness should not be assessed solely by survival gains, but by improvements in functional ability, independence, and quality of life[4]. Standardised instruments assessing activities of daily living, instrumental activities of daily living, and perceived wellbeing provide critical insights into whether ageing populations are living healthier and more autonomous lives [18].

Within this preparedness context, the 6W framework for healthy ageing offers a structured public health lens to translate data and policy into action. By systematically addressing who is ageing, what changes occur, when vulnerabilities emerge, where inequalities persist, why ageing trajectories diverge, and how health systems and societies should respond, the framework operationalises preparedness across surveillance, policy, and service delivery[4, 17]. The 6W approach ensures that public health preparedness moves beyond extending life expectancy to sustaining functional ability, equity, and wellbeing throughout the ageing process[5].

KEY INSIGHTS

This section synthesizes the principal insights emerging from the conceptual analysis of population ageing. It highlights the growing burden of multimorbidity, disability, and social isolation, and underscores the implications of demographic and epidemiological transitions for health systems. Using the 6W framework, the analysis identifies critical leverage points for intervention across the life course, emphasizing functional ability, integrated care, and equity.

LONELINESS AS AN EMERGING PUBLIC HEALTH CHALLENGE

Loneliness and social isolation have increasingly been recognized as major global public health challenges, affecting a substantial proportion of older adults across all regions of the world. Recent estimates indicate that approximately one in four older adults experiences social isolation, with comparable prevalence observed in high, middle and low-income countries [12]. A growing body of post-2020 evidence demonstrates that loneliness is associated with elevated risks of cognitive decline and dementia, cardiovascular disease, stroke, depression, anxiety, and premature mortality, independent of traditional risk factors [6, 13]. From a biological perspective, chronic loneliness is linked to sustained activation of stress pathways, including increased cortisol secretion, systemic inflammation, and immune dysregulation, which contribute to the onset and progression of chronic non-communicable diseases[14]. Recognizing the scale and health impact of loneliness, the World Health Organization has recently established an international commission on social connection, underscoring that the health risks associated with loneliness are comparable to those of well-established behavioural risk factors such as smoking and physical inactivity [12].

SOCIAL ISOLATION AND LONELINESS AS EMERGING PUBLIC HEALTH CHALLENGES

Social isolation and loneliness, while closely related, represent distinct but overlapping public health concerns that have gained increasing attention in ageing research and policy. Social isolation refers to the objective lack of social contacts, relationships, or participation in social activities, whereas loneliness is a subjective experience reflecting the perceived gap between desired and actual social connections. Both conditions are increasingly prevalent among older adults due to factors such as retirement, bereavement, declining mobility, sensory impairments, chronic illness, and reduced community engagement [12, 14]. Recent global evidence indicates that social isolation and loneliness are widespread across all regions, affecting approximately one in four older adults, with similar prevalence observed in high, middle and low-income countries [12]. Both conditions are strongly associated with adverse health outcomes, including increased risks

of depression, anxiety, cognitive decline, dementia, cardiovascular disease, stroke, frailty, and premature mortality [9, 13]. Emerging evidence also links social isolation to poorer health behaviours, reduced adherence to medical treatment, delayed healthcare seeking, and accelerated functional decline, thereby contributing to increased years lived with disability and reduced healthy life expectancy.

From a biological perspective, prolonged social isolation and loneliness activate chronic stress pathways, including dysregulation of the hypothalamic–pituitary–adrenal axis, elevated cortisol levels, systemic inflammation, and impaired immune function, which collectively increase vulnerability to non-communicable diseases [14]. The COVID-19 pandemic further highlighted the health consequences of social disconnection among older adults, reinforcing the need to address social relationships as fundamental determinants of healthy ageing [12]. Recognizing their substantial health impact, the World Health Organization has framed social isolation and loneliness as critical public health priorities and has established an international commission on social connection. This initiative emphasizes that the health risks associated with social disconnection are comparable to those of established behavioural risk factors such as smoking, physical inactivity, and obesity, and calls for integrated, community-based, and health system–led interventions to strengthen social participation and connectedness in later life [12].

ROLE OF TECHNOLOGY AND INNOVATION

Digital health innovations offer significant opportunities to support healthy ageing. Telemedicine improves access to care, particularly for older adults with mobility limitations or those living in underserved areas [15]. Remote monitoring, mobile health applications, and wearable devices enable early detection of deterioration, support self-management, and enhance patient engagement. However, digital solutions must address barriers such as digital literacy, accessibility, and equity to avoid widening health disparities.

THE 6W FRAMEWORK FOR HEALTHY AGEING

WHY

Multimorbidity, polypharmacy, and disability have emerged as central challenges of population ageing, largely driven by increasing life expectancy and the cumulative burden of chronic conditions[5]. Multimorbidity, commonly defined as the coexistence of two or more chronic conditions, is now highly prevalent among older adults and is strongly associated with reduced functional ability, poorer quality of life, and increased healthcare utilization, particularly in ageing societies[9]. The growing prevalence of multimorbidity has contributed to widespread polypharmacy, which increases the risk of adverse drug reactions, drug–drug interactions, and treatment burden, especially in older populations with altered physiological reserves[6]. In parallel, gains in longevity have resulted in a substantial rise in years lived with disability, predominantly due to non-fatal but disabling conditions such as musculoskeletal disorders, stroke, dementia, and sensory impairments, shifting the public health focus from premature mortality to prolonged morbidity[9]. This transition underscores the need for person-centred, coordinated, and function-focused models of care that address complexity rather than single diseases.

WHAT

Functional decline represents a key consequence of population ageing and is characterized by age-related reductions in mobility, balance, muscle strength, vision, and hearing, which substantially increase the risk of falls, injuries, social isolation, and loss of independence among older adults [5]. As functional ability declines, the demand for long-term care, rehabilitation services, and assistive technologies rises, placing growing pressure on health systems and increasing healthcare expenditure as well as the physical, emotional, and financial burden on families and caregivers [9]. These trends necessitate a shift in health system responses from acute, episodic, disease-focused care toward integrated, person-centred, and continuous care models that prioritize the maintenance of intrinsic capacity and support independent living in older age [8].

WHO

While older adults are the primary beneficiaries of healthy ageing initiatives, responsibility for promoting and sustaining healthy ageing is shared across multiple stakeholders, including families and informal caregivers, primary and specialist healthcare providers, public health professionals, policymakers, community and civil society organizations, and international agencies. Contemporary frameworks emphasize that coordinated, multisectoral engagement is essential to address the complex health, social, and environmental determinants of ageing and to ensure that health systems, social protection mechanisms, and community environments are responsive to the needs of ageing populations [5, 19].

WHERE

Effective healthy ageing interventions operate across multiple settings, including primary health care, community and neighbourhood environments, homes, workplaces, educational institutions, hospitals, long-term care facilities, and increasingly, digital and virtual platforms. Primary health care serves as the cornerstone of these interventions by enabling prevention, early detection of health risks, continuity of care, and coordination across services, particularly for older adults with complex health needs [5]. Community-based and home-centred settings further support functional ability, social participation, and independent living, while digital health platforms enhance access to care, monitoring, and self-management, especially for populations with mobility or geographical barriers [9, 11].

WHEN

Timely intervention across the entire life course is essential for promoting healthy ageing, as exposures and behaviours accumulated from early life through older age significantly influence health outcomes in later life. Evidence from recent life-course frameworks highlights that early-life nutrition, education, and preventive health measures shape intrinsic capacity and resilience in adulthood, while effective management of behavioural and metabolic risk factors during midlife can substantially reduce the risk of chronic disease, functional decline, disability, and dependency in older age [5, 11].

WAY FORWARD- TRANSLATING LONGEVITY INTO HEALTHY AGEING

The sixth "W" of the healthy ageing framework focuses on what must be done to ensure that gains in longevity are translated into healthier, more autonomous, and dignified lives for ageing populations. Public health responses must move beyond disease-centred and episodic care towards integrated, life-course-oriented, and equity-focused strategies that address the complex biological, social, and environmental determinants of ageing. Strengthening primary health care (PHC) is central to this response. PHC provides the most effective platform for prevention, early detection of risk factors, continuity of care, and coordination of services for older adults experiencing multimorbidity and functional decline. Evidence consistently shows that health systems with a strong PHC orientation are better equipped to manage chronic conditions, reduce avoidable hospitalisations, and support functional ability in older age [4, 17].

A second priority is the development of integrated and person-centred care models that respond to the growing burden of multimorbidity, polypharmacy, and disability. Traditional disease-specific models are increasingly inadequate for ageing populations with complex health needs. Integrated care models that link health services, long-term care, rehabilitation, and social support have been shown to improve functional outcomes, patient experience, and health system efficiency[8,9]. Such models should prioritise maintenance of intrinsic capacity, shared decision-making, and continuity of care across settings. Addressing the social determinants of healthy ageing is equally critical. Socioeconomic conditions, housing, transportation, education, and opportunities for social participation strongly influence ageing trajectories and contribute to inequalities in health and functional ability. Public health strategies must therefore adopt multisectoral approaches that promote age-friendly environments, reduce social isolation, and strengthen community engagement [19]. The increasing recognition of loneliness as a major public health risk factor further highlights the importance of community-based interventions and social prescribing to enhance social connectedness in later life [12, 13].

Public health preparedness also requires robust surveillance and monitoring systems to track key ageing indicators, including life expectancy, healthy life expectancy (HALE), disability prevalence, and functional ability. Standardised instruments assessing activities of daily living, instrumental activities of daily living, and participation provide essential evidence for evaluating whether ageing populations are living healthier and more autonomous lives [18]. Such data are critical for guiding policy, planning services, and monitoring progress towards healthy ageing goals.

Digital health and technological innovation offer important opportunities to support healthy ageing when implemented in an inclusive and equitable manner. Telemedicine, remote monitoring, and assistive technologies can improve access to care, enhance self-management, and support independent living, particularly among older adults with mobility limitations or those living in underserved areas [15]. However, these approaches must address barriers related to digital literacy, affordability, and accessibility to prevent the widening of existing health inequalities. In summary, the sixth W emphasises that preparedness for population ageing requires coordinated and sustained public health action. By strengthening primary health care, integrating services, addressing social determinants, improving surveillance, and leveraging technology, public health systems can ensure that longer lives are

accompanied by improved functional ability, independence, and wellbeing [4, 20].

CONCLUSIONS

Healthy ageing within a public health preparedness perspective, using the 6W framework to structure system-level responses. Strengthening primary health care, integrating services, addressing social determinants, improving surveillance, and leveraging equitable digital innovation are essential. Ultimately, success should be measured not only by survival, but by sustained functional ability, independence, and dignity.

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CONFLICT OF INTEREST
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REVIEW ARTICLE

CONTENTS

Current perspectives on the etiology and pathogenesis of tendinopathy - a literature review

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ABSTRACT

Aim: Tendinopathy is a pain-dysfunction syndrome of tendons resulting from an imbalance between the processes operating within the tissue and the external factors to which it is exposed. Contemporary concepts of pathogenesis indicate the overlap of many mechanisms: from mechanical overload leading to abnormal matrix remodeling, through inflammatory processes, to intratendinous compression causing hypoxia and pathological vascularization. The aim of this study was to review information regarding the current state of knowledge about the pathogenesis and mechanisms driving tendinopathies, based on available scientific research.

Materials and Methods: A comprehensive literature review was conducted, including clinical trials, systematic reviews, and meta-analyses that investigated the mechanisms influencing the pathogenesis of tendinopathy.

Conclusions: The heterogeneity of the clinical and histological presentation confirms the multifactorial nature of tendinopathy and explains the therapeutic challenges and frequent treatment failures. The authors suggest that integrating knowledge regarding mechanotransduction, inflammation, metabolism, and the role of intratendinous pressure may provide a basis for developing more precise and effective treatment strategies for tendinopathy.

KEY WORDS: inflammation, intratissue pressure, mechanical loading, mechanotransduction

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INTRODUCTION

Tendinopathy, defined as a clinical syndrome of pain and tendon dysfunction, is one of the most common musculoskeletal disorders, exerting a significant socio-economic impact on modern society [1]. This problem is particularly acute in sports, where tendinopathies are responsible for up to one in three overload injuries [2]. However, tendinopathy also affects a wide range of the general population. Epidemiological data indicate that although the condition occurs in children and youth [3], its incidence increases with age. Studies predict that approximately 1–2% of adults will experience this lower limb problem during their lifetime [4]. The growing scale of the problem is confirmed by the EU report on the development of occupational diseases in selected musculoskeletal disorders, which shows that the number of cases of tenosynovitis and enthesopathy increased by approximately 10% between 2013 and 2019. In addition to the painful and debilitating impact on patients' daily lives, tendon disorders still constitute an underestimated financial burden [1]. The scale of costs is illustrated by data from individual countries – for example in the Netherlands the annual costs associated with lower limb tendinopathies are counted in millions of euros, making them a significant problem for the healthcare system [5].

Despite significant advances in tendon tissue research in recent decades, our understanding of the mechanisms underlying the development of these pathologies remains limited. Consequently, effective treatment of this

debilitating condition remains a significant challenge for clinicians. This problem likely stems from the fact that current therapeutic approaches do not directly address all aspects of the complex course of the disease. Clinical practice guidelines recommend load management, patient education, manual therapy, and shockwave therapy as the most effective treatments for tendinopathy [6]. Unfortunately, the criteria for selecting exercises, their types, intensity, and volume, have not yet been thoroughly researched. Similarly, manual therapy is known for its nonspecific effects. Furthermore, these methods exhibit antagonistic effects in certain areas. This may explain why treatment fails to produce the intended results in many patients, suggesting the need for further research. A more detailed understanding of the mechanisms and factors moderating the development of tendinopathy seems crucial. The continuum model, developed by Professor Jil Cook, was a milestone in this regard [7]. This model notes that depending on the patient's tendinopathy phenotype, a different treatment approach may be required, targeting the actual source of pain and dysfunction. However, 10 years have passed since the publication of this model. Therefore, the authors conducted a literature review of the current state of scientific knowledge on this topic.

AIM

The aim of the study was to review information regarding the current state of knowledge about the pathogenesis and mechanisms driving tendinopathies, with particular attention paid to the role of inflammation, mechanical loading and intratendinous compression based on available scientific research.

MATERIALS AND METHODS

This work was based on a review of scientific studies from PubMed, Google Scholar, Web of Science and MEDLINE, using combinations of the following keywords: tendinopathy, inflammation, interstitial pressure, mechanical loading and mechanotransduction. The materials were collected from 2004 to 2025, beginning with Scott et al.'s significant knowledge of inflammation and continuing with the most recent available research on the etiology and pathogenesis of tendinopathy, which formed the basis of the work. Studies were selected based on the following inclusion criteria: meta-analyses, systematic reviews, clinical practice guidelines, and narrative review articles. The following were excluded from the search: conference abstracts, case reports, and articles written in languages other than English.

REVIEW AND DISCUSSION

INFLAMMATION

Contemporary literature revises the view that tendinopathy is exclusively degenerative in nature. Researchers point to inflammation as the primary etiological factor, rather than merely a secondary consequence [8], and furthermore, it is recognized that it is not a transient process, but rather reflects a dysregulated, self-perpetuating network that destabilizes tendon homeostasis [8]. The pathogenesis is coordinated by the dynamic interaction of three interrelated cellular compartments: the stroma compartment (including tenocytes and tendon stem and progenitor cells), the immune compartment (resident macrophages and mast cells), and the infiltrating compartment, which consists of recruited immune cells [8]. Recent advances in immunology and pathology research have enabled the identification of macrophages, T cells, and B cells in structures affected by chronic changes, proving that the defensive response is not suppressed at any stage of the disease [9]. Importantly, recent analyses have revealed the presence of a unique subpopulation of immunocompetent cells referred to as "tenophages," which are characterized by the expression of markers specific to tendons and macrophages [8]. Interleukin-1β (IL-1β - a pro-inflammatory cytokine) acts as a "pathological switch", meaning that it reprograms stromal cells and induces a pro-inflammatory activation state in tenocytes [8]. The cytokine IL-1β promotes overexpression of collagenases (MMP-1, MMP-13 - extracellular matrix metalloproteinases) and stromelysins (MMP-3 - extracellular matrix metalloproteinase 3) while simultaneously suppressing the response of TIMP inhibitors - tissue inhibitors of metalloproteinases, leading to the degradation of the extracellular matrix (ECM) and thus driving the progression of tendinopathy [9,10]. In addition, IL-1β alters the fate of tendon stem/progenitor cells (TSPCs) by promoting their degeneration. It inhibits the expression of tenogenic markers (tenomodulin, scleraxis) and type I collagen, promoting cell differentiation towards non-tenogenic lines [8]. At the intracellular level, these processes are driven by the NF-κB signaling pathway - nuclear factor kappa-B, which stimulates the production of further pro-inflammatory cytokines (IL-6 - interleukin 6, TNF-α - tumor necrosis factor alpha), creating a feedback loop that perpetuates inflammation [9]. Neurogenic inflammation is an important element of pathophysiology. Studies confirm the presence of nerve ingrowth markers (PGP 9.5 - protein gene product 9.5) and the involvement of the glutamatergic system (glutamate, NMDAR receptors - N-methyl-D-aspartate receptors, mGLUT

- metabotropic glutamate receptors) and sympathetic systems (NPY - neuropeptide Y, adrenoreceptors) in diseased tendons [11]. Substance P and CGRP (calcitonin gene-related peptide), released from nerve endings, can indirectly stimulate mast cell degranulation and histamine release, which intensifies vasodilation, edema, and angiogenesis [11,12]. Excessive stimulation of nociceptors by these mediators is directly related to the sensation of pain [11]. Other causes that may contribute to the development of tendinopathy include diabetes and hypercholesterolemia [13]. Chronic hyperglycemia induces the accumulation of advanced glycation end-products (AGEs), which destabilize the collagen architecture, reducing tendon elasticity [13]. Obesity also correlates with the development of tendinopathy, due to systemic inflammation and increased mechanical stress [13]. Metabolic danger patterns (DAMPs - signaling molecules released as a result of cell damage), such as LDL cholesterol - low-density lipoprotein, fatty acids, or hyperglycemia, induce the phenomenon of trained immunity - they permanently regulate the activity of the innate immune system [10]. Chronic low-grade inflammation is a risk factor for healing failure [12]. Tenocytes can retain "inflammatory memory" through epigenetic changes, showing hyperresponsiveness to cytokine stimuli even years after the initial injury has resolved [8]. A key therapeutic challenge is restoring the balance in macrophage polarization. In normal healing, proinflammatory (M1) macrophages should give way to a repair phenotype (M2). Disruption of this switch leads to fibrosis and chronic degeneration [12]. The understanding that inflammation, mechanical stress, and vascularization form a self-perpetuating "tendinopathic loop" suggests the need for targeted therapies that precisely modulate, rather than completely suppress, the inflammatory response [10].

MECHANICAL LOAD

The etiopathogenesis of tendinopathy is closely correlated with disruption of mechanical homeostasis within the extracellular matrix (ECM). Contemporary biomechanical models point to the "Goldilocks zone" as the optimal loading window, which is essential for maintaining tissue anabolic properties [14, 15]. Inappropriate mechanical loading – including both chronic overload and mechanical underload – induces tenocytes to enter a catabolic state. This leads to progressive dysregulation of the molecular composition of the matrix and loss of its structural integrity [14, 16]. Mechanosensitivity and mechanotransduction are key processes that integrate external mechanical stimuli with intracellular signaling pathways, determining cellular phenotype and tissue architecture [17]. This is a dynamic interface that allows tenocytes to adaptively remodel the matrix in response to a variable load profile, determining tenogenic differentiation and proliferation [1, 17]. This process depends on the integrity of the actin cytoskeleton and integrin complexes, and PIEZO1 ion channels play a key role in detecting shear stress [18]. Their activation determines a transient influx of calcium ions (Ca2+), modulating the expression of enzymes responsible for collagen structure stabilization [17, 18]. Under pathological conditions, excessive mechanical stimulation induces nonphysiological expression of proinflammatory cytokines (IL-1β), which, through autocrine pathways, increases the activity of matrix metalloproteinases (MMPs) discussed in the previous paragraph. This results in accelerated proteolysis of structural proteins and initiation of the inflammatory cascade [14, 16, 19]. At the ultrastructural level, pathological loading leads to disorganization of the parallel arrangement of type I collagen fibers and their substitution by thinner fibrils with lower mechanical strength [16, 20]. These changes lead to the pathological accumulation of glycosaminoglycans (GAGs), which drastically alters the biomechanical properties of the tissue: fibrosis processes correlate with increased stiffness, while the degenerative phase is characterized by the loss of the ability to effectively transfer loads [16, 21]. ECM stiffening observed in the course of fibrosis (scarring) may disturb the response of cells to physical stimuli, leading to changes in their motility, proliferation, adhesion, and differentiation [17, 18]. An important phenomenon in this context is the stress shielding mechanism, resulting from the uneven distribution of stresses within the damaged structure [21]. As a result of local fiber disorganization, healthy fibrils absorb excessive loads, while adjacent pathological areas are paradoxically excluded from force transmission. This lack of physiological stress in the shielded areas induces tenocyte apoptosis and further matrix degradation, completing a vicious cycle of tissue degeneration [16, 18]. The degradation process is driven by cumulative microtrauma that exceeds the metabolic repair capacity of tenocytes [14]. This process drastically increases with age and metabolic disorders, which lead to loss of matrix elasticity and pathological stiffening. In this context, a critical etiological factor is compressive forces, occurring at specific anatomical points where the tendon changes direction, wrapping around bony structures [1, 14]. It is in these zones that ischemic and mechanical stresses accumulate, which, combined with the limited biomechanics of the stiffened matrix, becomes a trigger for degenerative processes.

INTRATENDINOUS COMPRESSION

Scientific analyses emphasize the role of disturbances in intratissue pressure homeostasis in the pathogenesis of tendinopathy. Classical mechanical models ignored

this factor, focusing primarily on tensile forces. Current evidence is changing the perspective on the mechanisms of pathological changes [2]. Each structure in the body has a specific total tissue pressure (TTP), which is the sum of interstitial fluid pressure (IFP) and the solid stress (SSR) exerted by matrix components such as collagen, cells, and proteoglycans [2]. Under physiological conditions, TTP remains low (below 10 mm Hg); its increase is observed in many pathologies, such as pressure-induced neuropathies, osteoarthritis, and cancer [2]. Pressure imbalance within the tendon is currently considered a significant factor influencing the cellular response of tenocytes and the progression of degenerative processes [2, 22]. Increased intratendinous resting pressure (IRP) in tendinopathy is referred to in the literature as "miniature compartment syndrome." This term describes a phenomenon in which the volumetric expansion of the extracellular matrix encounters mechanical resistance from surrounding low-compliance structures. In the case of a tendon, the limiting "walls" of the compartment are the perimysium (epitenon), which surrounds the entire tendon, and the intratendonium (endotenon/IFM), which surrounds individual fascicles. The resistance offered by these sheaths to the swelling tissue induces internal pressure, analogous to the mechanism observed in compression neuropathies, where fluid accumulates under the impermeable epineurium [2, 22]. The main factor in swelling is the pathological accumulation of hydrophilic glycosaminoglycans (GAGs) and proteoglycans, which increase the so-called solid stress [22]. This was confirmed by ex vivo experimental studies on human Achilles tendons, providing quantitative evidence of this relationship. It was shown that infusion of 2 ml of physiological fluid into the native tendon caused an approximately 2.2-fold increase in resting pressure – from a mean value of 18.87 mmHg to 41.02 mmHg ($p<0.001$) [22]. A similar effect was observed in the case of changes in biochemical composition: injection of 80 mg of glycosaminoglycans (GAGs) resulted in an increase in resting pressure to 40.74 mmHg [22]. The final pressure value is determined by the location [2]. The internal compartment, i.e. the tendon fascicle, is characterized by a much smaller diffusion space than the surrounding interfascicular matrix (IFM) [2]. By analogy with studies on nerves, it has been suggested that even a small increase in the volume of fluid enclosed within the fascicle is associated with a drastic increase in pressure (reaching up to 750 mmHg in nerves), while the same volume in the looser IFM tissue generates a much lower pressure (up to 60 mmHg) [2]. This means that the measured mean pressure across the entire tendon may mask critically high pressure peaks occurring locally within individual fascicles [2]. These disturbances in resting homeostasis become critical under dynamic loading conditions. One of the protective mechanisms of a healthy tendon is its ability to reduce its volume under stretching. As demonstrated by Ahmadzadeh et al. [23], the Poisson's ratio for human tendons often exceeds 0.5, which forces radial fluid exudation from the matrix outward. This phenomenon manifests clinically as an immediate reduction in the tendon's cross-sectional area after exercise [24]. However, in tendinopathy, this mechanism is drastically impaired. The pathological accumulation of water-binding GAGs and PGs reduces the hydraulic permeability of the matrix [2, 25]. As a result, instead of being safely squeezed out, fluid becomes trapped within the intractable tendon bundles. Cyclic loading then leads to rapid increases in intratendinous dynamic pressure (IDP) [2]. It is speculated that increased IDP induces a state of functional ischemia by compressing the intratendinous microcirculation. Consequently, pathological tendons—unlike healthy tendons—do not exhibit physiological thickness reduction after exercise, indicating the perpetuation of an intramatrix "compartment syndrome" [2, 25]. This creates a destructive vicious cycle: any attempt to load the tendon exacerbates the pathology by generating pressures exceeding the physiological adaptive threshold of tenocytes. It should be emphasized that the presented mechanism constitutes a novel research paradigm. The authors emphasize the conceptual nature of these considerations [2], pointing out that the role of fluid dynamics and intratendinous pressure is still in the process of being discovered, which may open new avenues for therapeutic strategies to improve tendon healing.

CONCLUSIONS

A review of the scientific literature indicates the direction of modern tendinopathy treatment. Research by renowned medical experts demonstrates that the inflammatory process is not merely a consequence of injury but serves as the primary etiological factor in a self-perpetuating cascade. A key element of this dynamic is ECM degeneration and the inhibition of tendon repair processes. However, inflammation remains closely correlated with impaired mechanotransduction. Therefore, optimal mechanical loading is essential for maintaining anabolic tissue homeostasis. Both excessive and insufficient loading trigger a vicious cycle of degeneration, leading to pathological stiffening of the ECM. Such a tendon is characterized by an impaired physiological response to physical stimuli. Systemic factors such as obesity and diabetes can further fuel these

processes. This highlights the importance of patient education regarding changes in habits, lifestyle, and diet. The concept of the role of intratendinous pressure and compression, while very interesting, seems insufficiently researched to be currently used in treating tendinopathies. However, the authors do not rule out a change in this stance in the future, as this model helps explain many unknowns in the pathogenesis of tendinopathies. Clinicians aware of the mentioned mechanisms should focus their treatment on interrupting the "tendinopathic loop" through precise load management and, when necessary, suppressing active inflammation. The review authors suggest that rehabilitation teams should focus on kinesiotherapy, which utilizes mechanotransduction processes to stimulate matrix remodeling. This is crucial for a very large group of patients, such as athletes. For them, the treatment outcome should be not only improved pain but, above all, rapid return of highly specialized function, which determines success in their field. Therefore, further research on tendinopathies is needed to precisely manage treatment methods and effectively prevent them.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Periodontitis as a systemic inflammatory disorder – implications for cardiovascular and neurodegenerative diseases

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ABSTRACT

Aim: Periodontitis is a chronic inflammatory condition associated with oral microbiome dysbiosis and the dominance of Gram-negative bacteria such as Porphyromonas gingivalis. It is characterized by progressive destruction of the supporting tissues of the tooth, leading to loss of connective tissue attachment, resorption of the alveolar bone, and, consequently to tooth loosening and loss. If left untreated, it leads to recurrent bacteremia and persistent systemic inflammation. The aim of this study is to discuss the mechanisms linking periodontitis to cardiovascular and neurodegenerative diseases.

Materials and Methods: A comprehensive literature review was conducted examining clinical studies, systematic reviews, and meta-analyses assessing the impact of periodontal disease on the development of cardiovascular and neurodegenerative diseases.

Conclusions: Chronic activation of the immune response, oxidative stress, and lipid metabolism disorders promote endothelial dysfunction and the progression of atherosclerosis, increasing the risk of cardiovascular events. At the same time, systemic inflammation can affect the permeability of the blood-brain barrier and exacerbate neuroinflammatory processes, promoting β-amyloid accumulation and the progression of Alzheimer's disease. Analysis of the literature indicates the significant, albeit complex, nature of these relationships, emphasizing the importance of prevention and treatment of periodontal disease as part of comprehensive patient care. The key in the approach to periodontal patients is an interdisciplinary perspective, integrating dentistry, cardiology, neurology, and geriatrics.

KEY WORDS: prophyromonas gingivalis, cardiovascular disease, Alzheimer's disease

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INTRODUCTION

The human oral microbiome consists of hundreds of microorganisms, the composition of which changes dynamically depending on the host environment. When healthy, it remains in balance, and Gram-positive bacteria dominate the composition of dental plaque. However, certain factors such as the presence of carbohydrates, a decrease in pH, or poor oral hygiene can disrupt homeostasis and increase the proportion of Gram-negative anaerobic bacteria. This leads to oral dysbiosis, which in turn leads to pathologies such as periodontitis [1]. This is a progressive disease in which bacteria trigger a cascade of inflammatory reactions, leading to the destruction of the tissues supporting the teeth, i.e., the periodontium. Periodontitis is the sixth most common disease in the world, with an overall prevalence of 45-50% [2, 3].

Periodontal disease is mainly associated with infection with *Porphyromonas gingivalis* as well as *Prevotella intermedia*, *Treponema denticola, Tannerella forsythia, Campylobacter rectus, Aggregatibacter actinomycetemcomitans*, and *Fusobacterium nucleatum*. These microorganisms penetrate the subgingival tissues, cause bacteremia, and release inflammatory mediators and toxins which, once in the bloodstream, disrupt the body's homeostasis and contribute to the development of systemic inflammation [1, 4]. Chronic, persistent inflammation predisposes the body to many systemic diseases, including cardiovascular and neurodegenerative diseases.

Cardiovascular diseases are one of the leading causes of death worldwide [5, 6]. In Europe, they account for 3.9 million deaths, which is about 45% of all deaths. More specifically, the main causes of death are ischemic heart disease, stroke, and heart failure caused by hyper-

tension [2]. At the core of most cardiovascular diseases lies atherosclerotic disease. It is characterized by progressive narrowing of the vascular lumen caused by the accumulation of atherosclerotic plaques, accompanied by endothelial dysfunction and a persistent low-grade chronic inflammatory state [6, 7].

Despite the multifactorial pathogenesis of periodontitis and cardiovascular diseases, current scientific reports indicate a significant relationship between these conditions [8]. One of the proposed mechanisms linking these diseases is the systemic inflammatory response of the body to periodontopathogenic bacteria and their products, which, once they enter the bloodstream, may promote the formation, maturation, and destabilization of atherosclerotic plaques [7].

Alzheimer's disease (AD) is the most common neurodegenerative disease, accounting for approximately 50–60% of all cases of dementia. It is characterized by memory loss, impaired language function, impaired visual-spatial abilities, impaired judgment, and personality changes. A growing number of studies indicate that periodontal pathogens are associated with this form of dementia. Many publications have shown that periodontal disease, led by the pathogenic bacterium - Porphyromonas gingivalis, may indirectly contribute to the development of Alzheimer's disease [4, 9]. Chronic inflammation and recurrent bacteremia associated with periodontal disease can induce neuroinflammatory and neurodegenerative processes, promoting the deposition of β-amyloid plaques, the formation of neurofibrillary tangles, and neuronal damage characteristic of Alzheimer's disease [10].

AIM

The aim of this study is to understand the potential mechanisms linking periodontal inflammation to the development of cardiovascular disease and Alzheimer's disease.

MATERIALS AND METHODS

A comprehensive literature search was conducted across PubMed from 2020 to 2025 to identify studies investigating the association between periodontitis and systemic diseases, specifically cardiovascular disease and Alzheimer's disease. Search terms included "periodontitis", "cardiovascular disease", "Alzheimer's disease", "inflammation", "Porphyromonas gingivalis", and "neurodegenerative disorders" as well as related variations. We included systematic reviews and meta-analyses, randomized controlled trials, prospective and retrospective original research, narrative reviews, protocol papers, and case series.

REVIEW AND DISCUSSION

PATHOGENESIS OF PERIODONTAL DISEASE

Periodontal disease is the result of chronic dysbiosis of the oral microbiome, characterized by an increased presence of pathogens such as *Porphyromonas gingivalis*, *Aggregatibacter actinomycetemcomitans, Fusobacterium nucleatum,* and *Treponema denticola* [11,12]. Disruption of the microbiological homeostasis of the oral cavity promotes the formation of dental plaque, deepening of periodontal pockets, and the development of chronic inflammation. Inflamed periodontal tissues are more susceptible to mechanical microtrauma caused by daily hygiene activities such as brushing and flossing. The accompanying bleeding allows periodontopathogenic bacteria and their products to enter the bloodstream, leading to transient bacteremia [11]. Gram-negative bacteria associated with dysbiotic biofilm, such as

P. gingivalis and *Tannerella forsythia*, initiate the influx of neutrophils and the production of lipid mediators (including prostaglandin E2), which promotes local inflammation and bone resorption [3]. These pathogens further disrupt the host's immune and lipid homeostasis [12]. Microorganisms use specialized mechanisms to deliver virulence factors, including outer membrane vesicles (OMVs), which enable interaction with pattern recognition receptors (PRRs) in distant tissues, initiating a systemic inflammatory response [12]. Periodontal disease generates chronic inflammation that can affect distant organs. Patients with periodontitis show elevated levels of inflammatory markers such as CRP (C-reactive protein), proinflammatory cytokines (IL-1, IL-6, IL-8, TNF), and leptin, while simultaneously showing decreased concentrations of anti-inflammatory markers such as interleukin 10 (IL-10) and adiponectin [11, 13].

PERIODONTAL DISEASE AND CARDIOVASCULAR DISEASE

Chronic periodontal dysbiosis leads to persistent systemic inflammation, which disrupts endothelial function and promotes the development of cardiovascular disease. Gram-negative pathogens, such as *Porphyromonas gingivalis*, activate molecular pattern recognition receptors (TLR2/MyD88), increasing the expression of NADPH oxidase (NOX4) and the production of superoxide anion ($O_2^{\bullet-}$). As a result, oxidative stress increases, limiting the availability of nitric oxide (NO), intensifying lipid peroxidation, and causing endothelial dysfunction - a key stage in the development of atherosclerosis. In addition, P. gingivalis lipopolysaccharide causes post-translational modifications of LDL

molecules, increasing their atherogenic properties and facilitating their uptake by macrophages, which promotes the formation of foam cells and the progression of atherosclerotic changes. At the same time, HDL dysfunction is observed, manifested by a reduction in their anti-inflammatory properties and a limitation of their ability to remove cholesterol from macrophages, which further enhances the process of atherogenesis [12]. Chronic inflammation caused by periodontal dysbiosis, oxidative stress, endothelial dysfunction, and lipid metabolism disorders constitute the molecular basis for the observed links between periodontal disease and cardiovascular pathologies [14]. These mechanisms translate into real changes in vascular function: patients with periodontitis show increased carotid intima-media thickness (CIMT), reduced flow-mediated dilation (FMD) and greater arterial stiffness measured by pulse wave velocity (PWV) [11].

At the same time, periodontal disease is associated with an increased risk of coronary artery disease, heart attack, stroke, and peripheral artery disease (PAD) [11]. In addition, a higher risk of heart failure and atrial fibrillation in people with periodontitis [11].

Chronic inflammation, activation of pattern recognition receptors (TLR2/MyD88), increased oxidative stress via NOX4, LDL modifications, and HDL dysfunction observed in people with periodontal disease are clinical parameters that directly affect vascular function and the development of cardiovascular diseases [14].

PERIODONTAL DISEASE AND NEURODEGENERATION

Inflammation is a common risk factor for both periodontal disease and the most common neurodegenerative disease, Alzheimer's disease (AD), affecting the development and progression of both conditions. Periodontal disease leads to local degradation of tooth supporting tissues, neutrophil and macrophage infiltration, and increased activity of metalloproteinases and serine proteases. Chronic periodontitis causes systemic inflammation, manifested by elevated concentrations of IL-1β, IL-6, IL-8, TNF-α, and CRP, which may modulate the course of neurodegenerative diseases [15]. Preclinical studies have shown that periodontal pathogens can increase the permeability of the blood-brain barrier, including by reducing claudin-5 expression and degrading collagen and fibronectin in the brain endothelium, which facilitates the penetration of inflammatory mediators and bacteria into the brain [15].

In AD, the accumulation of β-amyloid peptide activates microglia and astrocytes via Toll-like receptors (TLR2/TLR4) and the NF-κB pathway, enhancing the secretion of proinflammatory cytokines, reactive oxygen species, and other neuroinflammatory mediators, which promotes amyloidogenesis, hyperphosphorylation of tau protein, Aβ accumulation, and the formation of neurofibrillary tangles, ultimately leading to neuronal degeneration [15]. Recent clinical studies conducted by Gil-Montoya et al. indicate that severe or moderate periodontitis in older adults with mild cognitive impairment (MCI) is associated with a higher risk of abnormal β-amyloid accumulation in the brain, as demonstrated in amyloid-PET studies, while individuals with mild periodontitis or healthy periodontium did not show such an association.

These findings support the hypothesis that chronic inflammation associated with periodontal disease may contribute to the initiation or acceleration of amyloid protein accumulation in the brain, regardless of the patient's cognitive status [16]. A study by Ide et al. showed that active periodontitis in patients with AD is associated with faster cognitive decline, regardless of the number of teeth lost. An increase in pro-inflammatory status and a decrease in anti-inflammatory status were observed, supporting the hypothesis that systemic inflammation links periodontal disease to neurodegeneration. These data suggest that the treatment and prevention of periodontal disease may help preserve cognitive function in patients with AD [13].

THE ROLE OF THE DENTIST

The dentist is responsible for the prevention and treatment of periodontal disease. Prevention includes patient education, daily oral hygiene, and regular checkups, which slow the progression of periodontal disease and thus reduce the risk of cardiovascular complications. The treatment of periodontal disease includes standard non-surgical methods such as scaling and root planing, often supplemented with antibiotic therapy, and in more severe cases, surgical procedures aimed at reducing inflammation and regenerate periodontal tissues [11, 14].

In patients with Alzheimer's disease, the presence of active periodontitis is associated with a faster decline in cognitive function, regardless of the initial condition, which emphasizes the importance of periodontal prevention and treatment in potentially slowing down the progression of the disease [13].

INTERDISCIPLINARY PATIENT CARE – DENTISTRY AND GENERAL MEDICINE:

Considering the latest research, periodontal disease is not only a local condition, but a chronic inflammatory

disease that is a risk factor for the development of systemic diseases, including cardiovascular and neurodegenerative diseases such as Alzheimer's disease [11, 15]. Numerous studies have shown that patients with AD have poorer oral health than older people without dementia and increasing difficulties in daily hygiene with more severe dementia can exacerbate this problem [13]. Chronic inflammation in periodontal disease can lead to neuroinflammatory processes and blood-brain barrier dysfunction, potentially accelerating neuronal degeneration [16]. In addition, chronic periodontitis, associated bacteremia, and increased concentrations of circulating inflammatory factors may contribute to the progression of atherosclerosis and coronary artery disease [11].

Effective care for patients with periodontal disease, therefore requires an interdisciplinary approach, integrating dentistry, cardiology, neurology, and geriatrics. A joint diagnostic and therapeutic strategy enables early detection of risk factors, treatment of periodontitis, and monitoring of cardiovascular health and cognitive function, which can greatly contribute to slowing the progression of both systemic and neurodegenerative diseases.

CONCLUSIONS

A review of the literature on the links between periodontal disease and cardiovascular and neurodegenerative diseases points to a complex but significant relationship. Periodontal disease is not only a local oral health problem but also a potential factor influencing the development of systemic diseases. Complex mechanisms involving chronic inflammation, bacteremia, and systemic immune response indicate the multidirectional nature of this relationship. However, it should be emphasized that periodontal disease, cardiovascular disease, and Alzheimer's disease all have multifactorial etiologies, and the observed associations require further clinical research to clearly define cause-and-effect relationships. Taking into account current data, the role of the dentist goes beyond the treatment of local lesions - effective care of periodontal patients requires an interdisciplinary approach.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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REVIEW ARTICLE

CONTENTS

Obesity as an interdisciplinary medical and social problem: Therapeutic opportunities

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ABSTRACT

Aim: This review aimed to summarize current knowledge regarding overweight and obesity as chronic diseases. The health, social, and economic consequences were assessed. Diagnostic and therapeutic possibilities available in primary care practice were presented.

Materials and Methods: This work is a narrative review. Literature on the epidemiology, pathophysiology, and treatment of overweight and obesity was analyzed. Current guidelines from scientific societies were considered. Randomized trials, systematic reviews, and meta-analyses were included. Publications with significant clinical relevance were selected.

Results: Obesity is a multifactorial disease that leads to metabolic and cardiovascular complications. It increases the risk of type 2 diabetes and malignancies and impairs quality of life. The cornerstone of treatment is lifestyle modification, including caloric reduction and increased physical activity. In selected cases, pharmacotherapy or surgical intervention may be indicated. Acupuncture may serve as an adjunctive therapy.

Conclusions: Obesity management requires a comprehensive and individualized approach. Long-term monitoring of treatment outcomes is essential. Primary care physicians play a pivotal role in the diagnosis and management of this condition.

KEY WORDS: body mass Index, weight loss, primary health care, lifestyle, acupuncture therapy

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INTRODUCTION

Obesity, previously considered merely a risk factor for health, has recently been recognized as a disease [1]. Individuals affected by obesity typically present with a range of metabolic disturbances that warrant clinical attention. Excess body weight also negatively impacts social functioning, employment, and overall quality of life, ultimately extending beyond direct health care costs [2].

Both direct and indirect consequences of overweight and obesity require attention at individual and population levels [3]. The economic burden associated with these conditions has increased substantially over recent years, potentially threatening the sustainability of health care systems worldwide [3, 20]. Social intolerance toward individuals with overweight or obesity further exacerbates negative psychological outcomes [4].

Overweight and obesity can significantly limit functional capacity and reduce quality of life [2]. Cardiovascular health generally inversely correlates with body mass, particularly regarding the development of hypertension [3]. Pulmonary function is also impaired in individuals with excess weight [5]. Type 2 diabetes development, often reversible with normalization of body mass index (BMI), is directly associated with obesity [4,3]. Consequences also extend to the gastrointestinal system, including non-alcoholic fatty liver disease (NAFLD) [6].

Obesity is linked to malignancies [3], as well as degenerative joint disease, particularly in the knees and lumbar spine [7]. Weight normalization improves clinical status, reduces symptoms, and may partially reverse degenerative changes in knee menisci [7].

AIM

The purpose of this review is to summarize current knowledge on overweight and obesity as chronic diseases and discuss their health, social, and economic consequences. Additionally, diagnostic and therapeutic strategies available in primary care are presented, emphasizing nonpharmacologic, pharmacologic,

surgical, and adjunctive interventions, including effective co-treatment with acupuncture.

MATERIALS AND METHODS

This is a narrative review. Scientific literature on the epidemiology, pathophysiology, health consequences, and treatment strategies for overweight and obesity was analyzed. Current international society guidelines, randomized trials, systematic reviews, and meta-analyses were considered. Literature selection prioritized clinical relevance and applicability to daily primary care practice.

REVIEW AND DISCUSSION

OVERWEIGHT AND OBESITY IN PRIMARY CARE: OPPORTUNITIES FOR INTERVENTION

Obesity is a multifactorial disease involving genetic, environmental, hormonal, and behavioural determinants [1, 8]. Diagnostic evaluation should exclude secondary causes, such as endocrine disorders, including hypothyroidism or Cushing syndrome [8]. Given the high prevalence of overweight and obesity in family practice [9, 18], primary care physicians represent a critical point of intervention in both Poland and other developed countries [3],

As a chronic disease with multiple, often uncontrollable determinants, obesity presents a challenge, particularly in environments unfavourable to weight reduction [7]. It is frequently stigmatized, inducing feelings of guilt in affected individuals [4]. Clinically overlooked, treatable causes of obesity warrant attention [8]. Waist circumference assessment as an indicator of visceral obesity and cardiovascular risk is helpful in primary care [3]. Diagnostic evaluation should identify metabolic complications, such as insulin resistance or prediabetes [3]. Individualized diagnostic approaches enhance the effectiveness of subsequent therapeutic interventions [8]. Repeated weight-loss attempts, initially successful but ultimately failing, may erode patient trust and hinder communication with the physician [8].

DETERMINING THE CAUSE OF OBESITY

BMI-based diagnosis is a fundamental step in obesity management [1]. Individualized assessment allows for more targeted therapy. Comorbid conditions, particularly cardiovascular disease and type 2 diabetes, must be considered when planning treatment. Medication review is essential, as certain drugs may promote weight gain [8]. Assessment of lifestyle, including diet, physical activity, and psychosocial factors, is crucial [7].

THERAPEUTIC STRATEGIES

Obesity management should be comprehensive and long-term, incorporating lifestyle modification, pharmacotherapy, and, in selected cases, surgical intervention [1,8]. Lifestyle change remains the cornerstone, emphasizing lasting dietary modification and increased physical activity [8,10]. Behavioural support aimed at maintaining patient motivation is critical [8]. Therapy should be tailored to obesity severity and comorbidities [3].

Lifestyle interventions are key to successful treatment, focusing on caloric restriction and structured physical activity [10]. Long-term collaboration with a multidisciplinary team is essential. Effective interventions can achieve approximately 9% weight reduction within the first year.[8] Recurrence is common [1], and insufficient response at the primary care level should prompt referral to specialized obesity treatment centres [8]. Escalation of therapy according to current guidelines should be considered when conservative measures fail [8]. Because obesity is relapsing, monitoring and early response to weight gain are necessary [1]. Successful management requires an interdisciplinary team approach [8].

DIETARY RECOMMENDATIONS

Weight reduction requires a negative energy balance achieved through caloric restriction [10]. Diet should be individualized according to age, sex, physical activity, and clinical status [10]. Various dietary models can be effective, provided a caloric deficit is maintained [10]. Food quality is important, including limiting highly processed foods and simple sugars [7]. Increased intake of vegetables, dietary fibre, and low-glycaemic-index foods is recommended [10]. Long-term adherence is critical for sustained effectiveness [2]. Nutritional education in primary care can significantly improve therapy outcomes [8].

PHYSICAL ACTIVITY

Regular physical activity is a cornerstone of obesity prevention and treatment [10]. It positively affects metabolic parameters, even with moderate weight reduction [3]. Aerobic exercise promotes fat loss, while resistance training preserves lean mass [10]. Regular activity reduces the risk of type 2 diabetes and hypertension [3]. Gradual progression is advised to minimize injury risk in obese individuals [10]. Physical activity alone rarely results in significant weight loss without caloric restriction, but it is essential for metabolic health and maintaining treatment effects [10]. International

guidelines recommend moderate-intensity exercise at least 5 days per week, with muscle-strengthening exercises twice weekly [10]. Physical activity is particularly important in preventing weight regain after initial loss [1]. Primary care physicians should support patients in choosing safe and realistic activity forms [8].

PHARMACOLOGIC SUPPORT FOR OBESITY

Pharmacotherapy is indicated for patients meeting BMI criteria and should follow current guidelines [8]. It complements lifestyle interventions for patients with BMI ≥30 kg/m^2 or ≥27 kg/m^2 with comorbidities [8]. Anti-obesity medications act by reducing appetite, increasing satiety, or affecting nutrient absorption.[8] Drug selection should consider patient clinical profile and potential adverse effects [8]. Pharmacotherapy is more effective when combined with lifestyle modification [8]. Regular monitoring allows treatment adjustment or discontinuation [8]. Evidence indicates effective pharmacotherapy can significantly reduce metabolic complications [3]. Long-term monitoring of safety and efficacy is required [8].

SURGICAL MANAGEMENT OF OBESITY

Bariatric surgery is indicated for patients with morbid obesity or significant metabolic complications [3, 8]. Common procedures include restrictive and malabsorptive operations, leading to sustained weight loss [8]. Surgery improves glycaemic control and can induce remission of type 2 diabetes [3]. Reduced cardiovascular risk and all-cause mortality have been observed following bariatric procedures [3]. Patients require long-term specialist follow-up and selected nutrient supplementation [8]. Candidate selection should assess psychological readiness and willingness to adopt lifestyle changes [8]. Numerous studies demonstrate efficacy in reducing the risk of type 2 diabetes, malignancy, and all-cause mortality [3].

ACUPUNCTURE IN OBESITY MANAGEMENT

Acupuncture is a complementary medicine method used adjunctively in obesity treatment [11]. Proposed mechanisms include appetite modulation and neurohormonal regulation [12, 17]. Interest in acupuncture as an adjunctive obesity therapy has increased in recent decades [11]. Meta-analyses of randomized trials suggest potential efficacy in weight reduction compared with placebo or lifestyle modification alone [12-16, 19]. Authors caution that results should be interpreted carefully due to study heterogeneity [11]. Acupuncture may be considered as part of a combined approach with diet and exercise [12, 16]. Reports also suggest beneficial effects on metabolic parameters, including glucose and lipid levels [12]. Further high-quality randomized trials are needed to definitively assess efficacy [11].

CONCLUSIONS

Obesity is a chronic disease with substantial health and social consequences. It is relapsing and progressive. It leads to numerous metabolic and cardiovascular complications, increases the risk of type 2 diabetes and malignancy, and impairs quality of life and social functioning. Effective management requires early diagnosis, comprehensive evaluation, and individualized therapeutic strategies. Diagnosis should be based on BMI assessment and identification of complications, including environmental and behavioural factors. Treatment must be comprehensive and long-term, with lifestyle modification as the foundation. Pharmacotherapy may be indicated in selected cases, and surgery remains the most effective intervention for morbid obesity. Primary care physicians play a central role throughout management, and adjunctive methods, including acupuncture, can safely support standard therapy. Success depends on collaboration between the patient and the care team, and early intervention can limit complications and improve prognosis.

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REVIEW ARTICLE

CONTENTS

Periarticular artery embolization as a minimally invasive treatment for pain in osteoarthritis

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ABSTRACT

Osteoarthritis (OA) is a leading cause of chronic pain and disability worldwide, affecting approximately 607 million people in 2021, with projections exceeding 1.1 billion by 2050. The knee is the most commonly affected joint and many patients experience inadequate symptom relief with conservative management or are not candidates for total knee arthroplasty. Periarticular arterial embolization, particularly genicular artery embolization (GAE), has emerged as a minimally invasive treatment targeting pathological neovascularization and synovial inflammation in OA pathogenesis. This review aims to synthesize current evidence on the use of periarticular embolization in the treatment of OA across multiple joints including the knee, hip, shoulder, hand and temporomandibular joint (TMJ). A comprehensive literature review was conducted examining clinical studies, systematic reviews and meta-analyses evaluating periarticular artery embolization for OA treatment. Periarticular artery embolization represents a promising minimally invasive treatment option for patients with mild-to-moderate OA who have failed conservative therapy. It demonstrates high technical success rates (approaching 100%) with favourable safety profiles for knee OA, with emerging applications in other joints. However, standardized procedural protocols, long-term outcome data and multicenter randomized control trials are needed to definitively establish its role in OA treatment and optimize patient selection criteria.

KEY WORDS: genicular artery embolization, transarterial embolization, periarticular embolization

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INTRODUCTION

OA is the most prevalent form of arthritis globally, affecting approximately 607 million people worldwide in 2021. The knee is the most commonly affected joint, with more than 37% of Americans over age 60 experiencing chronic pain from knee OA [1]. It has been projected that by 2050 over 1.1 billion individuals will be affected by OA, driven by population aging and increasing obesity rates [2]. OA represents a leading cause of chronic pain and disability, particularly in older adults, creating substantial limitations in mobility and quality of life (QOL) and imposing a significant economic burden on healthcare systems [2]. Progressive synovial inflammation and neoangiogenesis play a critical role in OA pain through synovial lining hyperplasia, macrophage and lymphocyte infiltration, neoangiogenesis and fibrosis. These changes correlate with more severe pain and joint dysfunction and may predict faster rates of cartilage loss [2].

Current treatment paradigms for symptomatic OA primarily rely on conservative management, including patient education, exercise, weight loss and pharmacological interventions [2]. However, many patients experience inadequate symptom relief with these measures alone [2]. Gold standard alternative therapy for OA of the knee is a total knee arthroplasty (TKA), although many patients are not ready for surgery or have comorbidities that preclude surgical candidacy [3]. This treatment gap has driven the search for minimally invasive alternatives.

Periarticular arterial embolization is a minimally invasive, image-guided procedure targeting abnormal neovascularization and synovial inflammation implicated in OA pathogenesis. The most extensively studied proce-

Fig. 1. Angiography of the popliteal artery prior to embolization, showing embolus causing significant impairment of blood flow, classic for knee OA. *Source: Own materials*

Fig. 2. Angiography of the popliteal artery after embolization demonstrating successful occlusion of the vessel lumen with absence of distal flow *Source: Own materials*

dure is genicular artery embolization (GAE) for knee OA. The procedure selectively occludes pathologic periarticular vessels, aiming to disrupt the cycle of inflammation and nociceptive signaling, thereby reducing pain and improving function [4]. Periarticular arterial embolization represents a potentially valuable treatment option for patients with mild-to-moderate OA who have exhausted conservative treatment options, warranting further investigation to define its role in OA treatment [4].

AIM

The aim of this study is to provide a review of current data on the use of periarticular embolization in the treatment of osteoarthritis of different joints.

MATERIALS AND METHODS

A comprehensive literature search was conducted across multiple electronic databases including PubMed, Embase and Cochrane library from 2021 through January 2025, to identify studies on periarticular embolization for OA treatment. Search terms included "osteoarthritis", "genicular artery embolization", "transarterial embolization", "periarterial embolization", "TAPE", "knee osteoarthritis", "hip osteoarthritis" and related variations. We included systematic reviews and meta-analyses, randomized controlled trials, prospective and retrospective original research, narrative review, protocol papers and case series.

REVIEW

Periarticular artery embolization is performed via femoral or radial arterial access using fluoroscopic guidance, with selective catheterization of periarticular arteries using microcatherters [4, 5]. Prior to the procedure, digital subtraction angiography is performed to identify abnormal hyperemia and neovascularization, as seen in Figure 1 [4, 5]. These pathologic vessels are then occluded using embolic agents while preserving normal arterial inflow, as seen in Figure 2 [4, 5]. Arresting the pathological neoangiogenesis to the inflamed synovium and nociceptive subchondral bone disrupts the inflammatory cascade and prevents pathological neoinnervation that drives OA pain [4, 5]. Biomarker studies demonstrate that GAE reduces serum levels of vascular endothelial growth factor (VEGF), nerve growth factor (NGF) and interleukin receptor antagonist (IL-1Ra), suggesting both anti-inflammatory and anti-nociceptive effects that contribute to sustained pain relief [6].

GAE is the best documented application of periarticular artery embolization for OA, with robust evidence from prospective studies, systematic reviews and guidelines supporting its use for knee OA pain refractory to conservative therapy [7]. Safety profiles are favorable for GAE, with high technical success rates and mostly mild, self-limited adverse events [7]. Most studies report improvements in pain scores (VAS, WOMAC, KOOS) sustained up to 12 months [5, 7].

EMBOLIZATION IN KNEE OSTEOARTHRITIS

GAE demonstrates high technical success rates, a favourable safety profile and significant reduction in knee OA pain [7]. A systematic review and meta-analysis evaluating 10 studies encompassing 351 treated knees demonstrated that GAE provides durable reduction in pain scores across all OA severity grades [7]. Patients who underwent GAE showed significant declines in VAS pain scores at 1 month (-34 points), 3 months (-30 points), 6 months (-41 points) and 12 months (-37 points) [7]. The effect sizes (Hedges' g) ranged from -1.2 to -1.4 across follow-up intervals, indicating large and clinically meaningful treatment effects [7]. A more recent meta-analysis of 14 studies (510 patients, 567 knees) confirmed these findings, reporting pooled pre-post pain reductions of approximately 30 points on a 0-100 scale at 6-12 months, with 78-92% of patients achieving clinically meaningful improvement (>50% pain reduction or ≥ 10-15 point change) by 1 year post-procedure [8].

Comprehensive reviews confirm that GAE consistently achieves high technical success rates with improved VAS, WOMAC and KOOS metrics at short- to mid-term follow-ups [5]. Beyond pain relief, GAE significantly improves joint function and physical capacity. A systematic review of 17 studies (533 patients, 620 knees) reported mean improvements at 12 months for VAS ranging from 10 to 59 points and WOMAC scores, which encompasses pain, stiffness and physical function, ranging from 35.3 to 47 points, with additional improvements in KOOS subscales including Pain, Quality of life, sport and symptoms [9]. Prospective data demonstrate that WOMAC scores decreased significantly from 49.4 at baseline to 27.4 at 12 months in patients with mild to moderate OA ($p<0.001$) representing a 45% improvement in overall joint function [10].Notably patients with mild-to-moderate OA demonstrated better outcomes than those with severe disease, and decreasing minimal clinically important difference (MCID) achievement was observed between 3 and 6 months, suggesting that patient selection may influence durability of response [9,10].

Prospective trial data further support these findings. In an interim analysis of a single-arm prospective trial using 250-um microspheres, technical success was achieved in 100% of procedures, with 83% of patients (5 of 6) achieving the MCID for WOMAC pain score at 12 months [6]. Notably, biomarker analysis revealed a statistically significant decrease in nerve growth factor (NGF) levels at 12 months, suggesting that GAE may contribute to pain reduction through anti-nociceptive mechanisms and potentially slowing cartilage degeneration [6]. Both temporary and permanent embolic agents have demonstrated comparable clinical results, though variability in vessel targets, embolic particle size and periprocedural protocols across studies limits direct comparisons and pooled analyses [5].

GAE safety profile is favourable and reported complications are uncommon and typically resolve without interventions [4, 5]. The most common adverse events include: Transient skin discoloration or erythema at the embolication site, which typically resolves spontaneously within days to weeks, self-limited paresthesias in the distribution of cutaneous nerves, minor access site complications such as hematoma or bruising at the femoral or radial puncture site, and transient post-procedural pain or swelling of the treated knee [5, 8, 9]. In prospective trials, no major adverse events have been reported [6]. Serious complications such as non-target embolization causing skin necrosis, muscle infarction or nerve injury are rare when proper technique is employed, including careful angiographic assessment prior to embolization and use of appropriately sized embolic particles [4, 5]. Current evidence supports GAE as a safe and efficacious treatment for symptomatic knee OA refractory to conservative management [4-7]. However, standardized procedural methods, uniform outcome reporting and robust multicenter randomized controlled trials are needed to confirm long-term safety and efficacy, optimize patient selection and criteria and definitively establish GAE's role within the knee OA treatment algorithm [5].

EMBOLIZATION IN SHOULDER OSTEOARTHRITIS

Documented cases of therapeutic embolization of the shoulder joint for relief of osteoarthritic symptoms are rare. One case report describes a patient suffering from shoulder OA who was treated with transarterial periarticular embolization (TAPE) [16]. VAS preprocedure was 7 during the day and 8 at night, and the American Shoulder and Elbow Surgeons (ASES) score was 34.3. Severe restrictions in anteversion (90 degrees), and abduction (passive - 80 degrees, active - 40 degrees) were present [16]. Access was gained through the radial artery and a catheter was guided to the target anterior and posterior circumflex humeral branches, coracoid branch, and circumflex scapular artery. Upon discharge, significant pain relief was present (VAS score - 4 daytime and 0 night; ASES score - 63.3), and significant mobility improvements were seen (anteversion - 180 degrees; passive abduction - 160 degrees, active abduction - 120 degrees) [16]. However, due to the nature and size of this study, its use is limited, and can only be interpreted as a prognostic factor for the future use of therapeutic embolization in joint pain relief and mobility improvements in patients with OA.

EMBOLIZATION IN HIP OSTEOARTHRITIS

In a prospective, single-arm trial, 18 patients with a mean age of 67.2 ± 5.7 years underwent transarterial embolization (TAE) due to contraindications for total hip arthroplasty [14]. Currently, patients who don't qualify for total hip arthroplasty (THA) (up to 30% of patients), are confined to conservative treatment such as intra-articular injections, platelet-rich plasma, and nerve blocks. Therefore, the possibility of TAE for osteoarthritic pain and dysfunctionality of the hip to become mainstream would benefit a large population [14]. Brachial access was obtained and the catheter was guided to the lateral circumflex femoral artery (LCFA) targeted for hip TAE. VAS and Harris-Hip Score (HHS) were assessed at 0 weeks, 4 weeks, 8 weeks, and 12 weeks. HHS improved by 14.4 points post-op (45.5 ± 4.7 to 59.9 ± 7.1, p<0.01), and the increase concluded at week 8 (62.6 ± 6.0). The scores remained stable at week 12, showing early benefit and stable outcomes. The VAS score shared a similar improvement, decreasing post-op (7.8 ± 1.3 to 4.2 ± 2.0, p<0.01), improved by week 8 (3.7 ± 2.7), and concluded at week 12 at 4.3 ± 2.2, showing significant and sustained reduction in pain. [14]. Due to the small cohort (n=18) and no control group, it is impossible to determine long term effectiveness and predictability in the general population without larger scale studies.

A single-center prospective cohort analysed the long term effects of TAE of the hip in 13 patients spanning over 6 months using VAS and WOMAC [15]. Preprocedure VAS score on average was 10, and after 6 months 3 points, p=0.002. WOMAC score had a statistically significant decrease from a mean 77 preprocedure to 27 points after 6 months, p=0.001. There were no long term side effects noted, with one patient presenting a small groin hematoma which spontaneously resolved after 15 days and two patients had posterior thigh numbness resolving in 21 and 30 days [15].

Due to lack of published data, there are a few notable limitations to TAE of the hip. The tumor-like blush signifying abnormal neovasculature, especially in knee osteoarthritis, is not commonly present, making identification of abnormal angiogenesis difficult. Instead, corkscrew-like arteries are more common [15]. There is also an unknown risk of aseptic hip necrosis (AHN). In TAE of the LCFA, imipenem/cilastatin embolic agent is preferred due to the lowest risk of ischemia, however, there is no documented long term proof of efficacy or risk of AHN occurrence in LCFA [15].

EMBOLIZATION IN OTHER LOCATIONS

More unconventional locations in therapeutic embolization to treat osteoarthritic symptoms include the hands and temporomandibular joint (TMJ). In a retrospective cohort pilot study conducted on 9 patients with osteoarthritic hand pain, overall VAS scores significantly decreased at 1-week, 1-month, 3-months, and 6-months after TAE (34 ± 18mm, P<0.001; 32 ± 11mm, p<0.001; 21 ± 15mm, P<0.001; 18 ± 19mm, P = 0.002) [11]. Cannula insertion was performed into the distal radial artery and advanced anterograde, with two sessions scheduled for each patient, the second at 1-month after the first TAE [11]. Responders to treatment were defined as patients with a ≥50% pain reduction, and measured at the above-mentioned timeframes they were 66.7%, 77.8%, 88.9% respectively [11,12]. 100% of the patients reported significant decrease in joint restriction, with 75% of these patients unsuccessfully undergoing steroid injection therapy prior to TAE [12] The only adverse effect reported was early recurrence of joint pain in 44% of patients, potentially due to partial recanalization of abnormal vessels or revascularization. However, this was milder than before TAE treatment [11]. Some limitations to these studies include no restriction on the use of conservative therapy after treatment and the lack of a control group [11]. The small sample sizes (9 patients and 4 patients) are unlikely to accurately represent the broader population [12].

In a retrospective case series involving 3 patients with TMJ osteoarthritic pain and dysfunctionality, TAE was performed after referral from oral maxillofacial surgeons [13]. Arterial access was obtained through the femoral artery and a microcatheter was guided into the proximal part of the superficial temporal artery [13]. Postprocedure the patients were assessed using the NRS as well as the Oral Health Impact Profile - Temporomandibular Joint (OHIP-TMJ) questionnaire, and outcomes were measured at baseline, 6 weeks, and 3 months. OHIP-TMJ score decreased from 38, 45 and 45 to 31, 39, and 28, respectively. NRS scores improved from 9, 10, and 9 to 7, 7, and 5, respectively. Joint function improved in all 3 patients, however, patient 2 only showed temporary improvement in joint function [13].

DISCUSSION

The pathophysiology of osteoarthritis centers around degradation of the cartilage, synovium, and subchondral bone due to mechanical stress and inflammation. However, imaging evidence also points to vascular contribution to disease progression [14]. Increased interosseous pressure contributes to amplified degradation of subchondral bone, and upregulated vascular endothelial growth factor leads to increased neovasculature accompanied by sensory nerve branches [4, 14]. These pierce normally avascular joint regions in areas

of increased mechanical stress, leading to nociceptive signalling and chronic pain. Superselective embolization of this neovasculature allows us to individually choose abnormal vessels causing pain and block them, inhibiting nociceptive signals and further vascular proliferation.

TAPE provides an excellent therapeutic choice for OA patients who have not had symptomatic improvement with conventional therapies. Its minimally invasive approach allows for faster patient recovery and better prognostic outcomes, and the procedure is much quicker (15-30 minutes) than the next therapeutic option (THA or TKA). More than 80% of patients have an observable improvement in function and QOL [3, 6, 15]. It also shows promise of an effective middle ground between conventional therapies with steroids, NSAIDs, physiotherapy and arthroplastic procedures. Since up to 30% of patients do not qualify for THA in hip OA, it would provide a much-needed therapeutic option for those. Currently, its main setback is the lack of published evidence confirming long-term benefits and efficacy. The most widely studied area of TAPE is genicular artery embolization, however, the longest period of patient monitoring we see is 12 months [8]. While no severe side effects were observed, there are concerns over slowly developing pathologies such as avascular necrosis (AVN). Other joints have even less data, with sample sizes not exceeding a few patients. So, while preliminary results are promising, our current data makes it impossible for us to predict outcomes on the general population and implement TAPE as a standard in the therapeutic ladder for OA.

As of now, there is no set criteria for qualifying patients with OA for periarticular artery embolization. It is purely based on individual circumstances and on physician's assessment. Some reports suggest that severity of OA may influence effectiveness of TAPE. Patients with mild to moderate OA may respond better than with severe OA [9, 10]. Inclusion criteria also vary within different studies, but commonly include older age (>60), prior ineffective management with 2+ conservative therapies, duration of symptoms >1 year, and 1+ contraindication for surgical management [14].

CONCLUSIONS

Transarterial periarticular embolization, especially involving the genicular arteries, has proven to be a safe and effective method for alleviating pain in osteoarthritis resistant to conservative treatment. Due to its relatively recent emergence, no standardized indications have been formulated for its use, currently being based only upon a physician's opinion. Minimal published data for other locations, indicates the need for more research prior to TAE becoming a mainstream therapy for OA. However, described cases show promise and therapeutic potential to expand to many other pain pathologies.

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COFLICT OF INTEREST

The Authors declare no conflict of interest

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CASE STUDY

CONTENTS

Postoperative rehabilitation of a patient with resected aggressive parasagittal meningioma infiltrating the superior sagittal sinus and presenting with paraplegia

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ABSTRACT

The aim of this case report is to describes the postoperative neurological complications and importance of early rehabilitation course of a patient with an aggressive parasagittal meningioma. The particular emphasis on the role of intensive, multidisciplinary rehabilitation in the setting of postoperative spastic paraplegia. The program included physiotherapy, assisted verticalization, gait and locomotion training, proprioceptive neuromuscular facilitation techniques, and psychological support. Clinical status, imaging findings, and functional recovery were evaluated during rehabilitation. A 47-year-old woman with fronto-parietal parasagittal tumor infiltrating the superior sagittal sinus underwent preoperative embolization followed by microsurgical resection. Postoperatively, patient developed bilateral spastic paralysis of the lower limbs, complicated by cerebrospinal fluid leakage and surgical-site infection. After neurosurgical treatment of parasagittal meningiomas involving the superior sagittal sinus severe neurological deficits may occur. This case shows the importance of early, structured and multidisciplinary rehabilitation as an essential component of postoperative care. Early rehabilitation may contribute to functional improvement and preservation of quality of life even in patients with severe motor deficits.

KEY WORDS: neurological deficits, multidisciplinary rehabilitation , physiotherapy, paresthesia

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INTRODUCTION

Parasagittal meningiomas involving the superior sagittal sinus (SSS) (Figure1) a significant clinical and surgical challenge. This is due to their close proximity to the primary motor cortex and the brain's critical venous drainage system [1,2]. Invasion of the SSS increases the risk of perioperative complications. These include cerebral venous infarction, peritumoral brain edema, and postoperative neurological deficits such as motor weakness or paraplegia [2–5]. Although most meningiomas are histologically benign, tumors extending into major dural sinuses tend to behave more aggressively. The presence of bone erosion is also associated with higher morbidity [1,5]. Rehabilitation in this patient group is equally challenging. Neurological deficits after resection of SSS-involving meningiomas often require comprehensive and multidisciplinary care. Such an approach is essential to optimize functional recovery [6–9]. This case report describes a patient with an aggressive parasagittal meningioma complicated by postoperative spastic paraplegia. It also outlines the rehabilitation strategies used to support neurological and functional improvement. Figure 1 shows the parasagittal meningioma involving the superior sagittal sinus

AIM

The aim of this case report is to describes the postoperative neurological complications and importance of early rehabilitation course of a patient with an aggressive parasagittal meningioma. The particular emphasis on the role of intensive, multidisciplinary rehabilitation in the setting of postoperative spastic paraplegia.

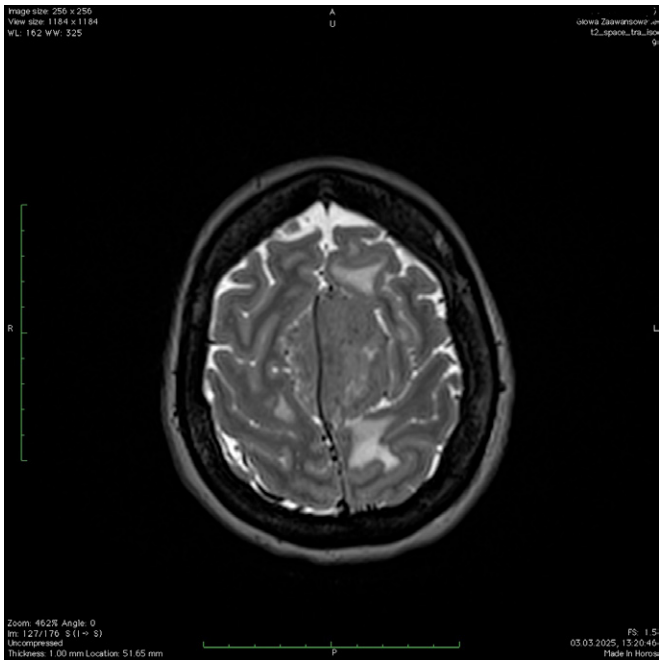

Fig. 1. Parasagittal meningioma involving the superior sagittal sinus
Source :Own materials

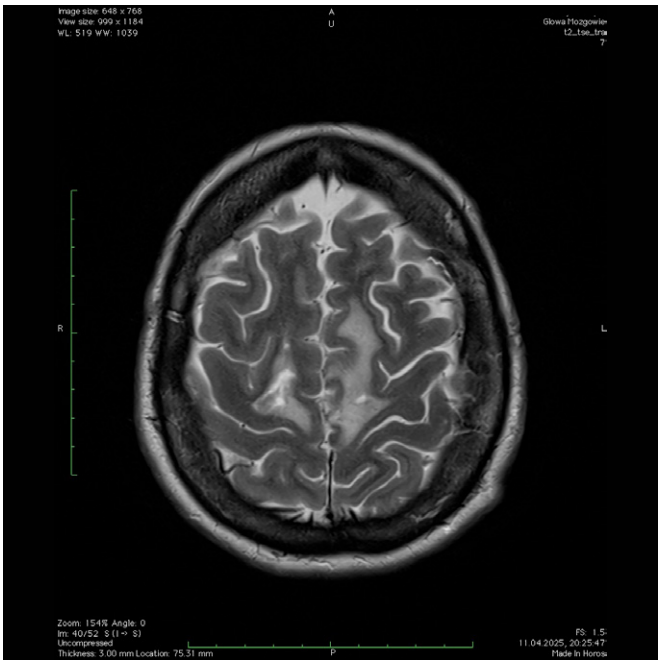

Fig. 2. Postoperative imaging after SSS-involving meningioma resection showing no residual tumour and regression of edema
Source :Own materials

CASE REPORT

A 47-year-old woman with arterial hypertension and type 2 diabetes mellitus presented with new-onset left-sided paresthesia. The symptoms involved the face, upper limb, and lower limb. She also reported chronic lumbar pain. The initial neurological examination revealed a positive Lasègue's sign on the left side.

The first imaging study was a non-contrast CT scan. It revealed a 54 × 50 × 42 mm lesion in the left frontoparietal convexity. A finger-like pattern of peritumoral edema and skull involvement were observed. Subsequent MRI confirmed an aggressively enhancing mass measuring 59 × 58 × 42 mm. The lesion involved the superior sagittal sinus and caused adjacent bone destruction and midline shift. Imaging findings suggested an aggressive meningioma [1, 2].

Preoperative embolization was performed, followed by surgical resection. After surgery, the patient developed spastic paralysis of both lower limbs. She also experienced a cerebrospinal fluid (CSF) leak and a surgical-site infection caused by *Staphylococcus epidermidis* (methicillin-resistant coagulase-negative staphylococci). These complications were treated with targeted intravenous antibiotic therapy, including levofloxacin and vancomycin, followed by linezolid and ceftriaxone. CSF leakage is a known risk factor for postoperative infection after craniotomy [14, 15].

During the rehabilitation phase, the patient underwent an individualized program aimed at improving physical function and psychological well-being. Care was provided by a multidisciplinary team that included physiotherapists, occupational therapists, and mental health professionals. The goal was to support functional recovery and adaptation [6–9].

Psychological intervention included autogenic training to reduce stress and promote mental balance. Supportive psychotherapy was also provided to strengthen coping strategies and maintain motivation during recovery.

The physiotherapy program consisted of targeted interventions. Active exercises were used to improve joint mobility, muscle strength, and overall physical conditioning. Passive verticalization was introduced to safely restore upright positioning. This approach helped adapt the cardiovascular system and prevent orthostatic hypotension [9,11]. Proprioceptive neuromuscular facilitation techniques were applied to enhance motor control and coordination [12]. Passive manual exercises were performed regularly to maintain joint integrity and prevent contractures. Structured gait and locomotion training focused on restoring safe walking patterns, balance, and movement control [6–9, 12].

Follow-up imaging showed no residual tumor and marked regression of edema (Fig. 2). The surgical wound healed well under conservative management. The patient was discharged with a diagnosis of paraplegia, unspecified (ICD-10: G82.2).

DISCUSSION

Tumors of the parasagittal region that invade the superior sagittal sinus (SSS) represent a major neurosurgical and rehabilitative challenge. This is mainly due to their close anatomical relationship with the primary motor cortex and the brain's main venous drainage pathways [1, 2]. The preferred surgical approach is maximum safe resection. Complete tumor removal should be avoided when it carries a high risk of neurological or venous injury [1, 4, 5]. Current consensus guidelines emphasize that preservation of neurological function and venous integrity must take precedence over radical resection in high-risk cases [1].

Invasion of the SSS independently increases perioperative morbidity. Patients have higher rates of cerebral venous infarction, worsening peritumoral brain edema, and new postoperative motor deficits compared with tumors that do not involve the sinus [2–5]. In a retrospective series of 212 patients, the overall perioperative complication rate was 23.6%. Peritumoral edema greater than 1 cm and higher Sindou sinus invasion grades (V–VI) were independent risk factors. Tumor recurrence was more strongly associated with the degree of sinus invasion than with the extent of resection alone [3].

In the present case, several factors likely contributed to the development of postoperative spastic paraplegia. These included large tumor volume, calvarial involvement, and confirmed invasion of the SSS. Preoperative embolization and subsequent microsurgical resection further increased the risk. The most plausible mechanisms were cerebral venous infarction due to impaired sinus or bridging vein flow, worsening peritumoral edema, or direct injury to adjacent motor pathways during surgery [4,5]. Reported rates of symptomatic venous infarction in parasagittal meningioma surgery range from approximately 5% to 10% [4, 5]. Given the severity of the resulting motor deficit, early venous imaging and prompt initiation of rehabilitation were essential to optimize recovery [6–9].

The role of preoperative embolization in hyper vascular meningiomas remains controversial. Its primary goals are to reduce intraoperative blood loss, shorten operative time, and facilitate resection. However, recent studies report mixed outcomes. Some show improved surgical conditions without consistent benefits in functional recovery or recurrence-free survival [10–12]. In this case, embolization was used selectively to support surgery. It should not be considered a predictor of neurological outcome.

Postoperative cerebrospinal fluid (CSF) leakage and surgical-site infection further complicated recovery. CSF leakage is a well-established independent risk factor for infection after craniotomy. The risk is particularly high in cases involving dural reconstruction, devitalized tissue, or sinus manipulation [14, 15]. Optimal management requires early recognition, culture-guided antimicrobial therapy, and careful wound and dural care. These measures help reduce reoperation rates and long-term complications [14, 15].

Rehabilitation played a central role in this patient's recovery. Early, structured mobilization after brain tumor surgery reduces secondary complications such as joint contractures, muscle atrophy, orthostatic intolerance, and pressure injuries. It also promotes faster functional improvement [6–9, 13]. In patients with severe motor deficits and spasticity, assisted verticalization allows safe early upright positioning. This approach limits cardiovascular deconditioning and supports early lower-limb activation and gait training [9, 11, 13]. Available evidence supports the safety and feasibility of such protocols in neuro-oncology and neurocritical care settings [9–11, 13].

Advances in neurorehabilitation highlight the brain's capacity for neuroplastic reorganization, even after major neurosurgical procedures. Patients undergoing brain tumor surgery may achieve meaningful motor recovery despite severe initial deficits. Early and intensive rehabilitation can promote cortical and subcortical reorganization by engaging alternative neural pathways. Reports of functional improvement in patients with benign tumors support this concept [16]. In the present case, task-specific gait training, PNF techniques, and verticalization likely contributed to recovery by enhancing neuroplastic adaptation.

Rehabilitation timing and intensity are also important prognostic factors. Studies show that earlier mobilization, often within two to three weeks after surgery, and higher daily therapy intensity are associated with better functional outcomes and shorter hospital stays [17, 18]. Functional recovery is further influenced by preoperative neurological status, postoperative complications, and comorbidities such as diabetes and hypertension. All of these factors were relevant in this patient. These findings reinforce the need for structured and individualized rehabilitation programs in neurosurgical patients with motor deficits. Rehabilitation should be viewed as an integral component of treatment rather than a supportive adjunct.

Motor relearning approaches such as proprioceptive neuromuscular facilitation (PNF) are well supported in neurorehabilitation literature, particularly in stroke populations. A recent systematic review and meta-analysis demonstrated improvements in

balance and gait speed following PNF-based therapy [12]. Although data specific to post-meningioma deficits are limited, the underlying neurophysiological principles remain applicable. In this case, combining PNF with task-oriented gait and balance training was consistent with established practice and likely contributed to improved mobility.

This case illustrates a modern, integrated approach to the management of meningiomas involving the SSS. Key elements include balanced surgical decision-making, selective use of adjunctive techniques, careful management of postoperative complications, and early multidisciplinary rehabilitation. Together, these strategies increase the likelihood of meaningful functional recovery and improved quality of life, even in the presence of severe neurological deficits.

CONCLUSIONS

This case highlights the complexity of the postoperative course in patients with parasagittal meningiomas involving the superior sagittal sinus. The challenge is particularly evident when severe neurological deficits, such as spastic paraplegia, develop. Despite these complications, early and well-coordinated rehabilitation played a crucial role in preserving functional abilities and supporting gradual recovery.

A comprehensive rehabilitation program combining verticalization, targeted physiotherapy, gait training, and psychological support helped prevent secondary complications and promote motor improvement. This case underscores the importance of timely and individualized rehabilitation as an essential component of care following complex neurosurgical procedures

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CASE STUDY

CONTENTS

From hip pain to MAS: A case of gonococcal arthritis in a child

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ABSTRACT

Joint pain in children presents a diagnostic challenge due to its multifaceted etiology, ranging from musculoskeletal injuries to systemic infections. This case report details a 3-year-and-5-month-old girl with bilateral hearing impairment and congenital cytomegalovirus infection, who was admitted with thigh pain, high fever, and difficulty walking. Despite being hemodynamically stable and without apparent infection signs, extensive diagnostic evaluations revealed gonococcal hip arthritis. This condition, caused by Neisseria gonorrhoeae, is unusual in young children and typically associated with perinatal transmission or sexual abuse. The diagnosis was confirmed through molecular testing, highlighting the importance of considering rare etiologies in pediatric joint pain cases. The patient's management included multidisciplinary consultations, various imaging and laboratory tests, and specific antimicrobial therapies. The case underscores the necessity of a comprehensive diagnostic approach in pediatric patients with joint pain, especially when associated with other health conditions, to ensure accurate diagnosis and appropriate treatment.

KEY WORDS: gonorrhea, neisseria gonorrhoeae, septic arthritis, child, macrophage activation syndrome

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INTRODUCTION

Joint pain in children is a common issue frequently encountered by primary care doctors, particularly in pediatric clinics or emergency rooms. This condition can have various causes, which makes diagnosis difficult. Causes of joint pain in children include direct injuries like sprains or fractures, as well as inflammatory conditions such as reactive or purulent arthritis, juvenile idiopathic arthritis (JIA) [1], Legg-Calve-Perthes disease, or Slipped Capital Femoral Epiphysis. Juvenile Idiopathic Arthritis has several subtypes, some of which may be complicated by macrophage activation syndrome (MAS) – a serious hyperinflammatory condition that requires prompt diagnosis and treatment [2].

Other rare causes include infections like septic arthritis and systemic diseases such as systemic lupus erythematosus (SLE) or Kawasaki disease, which can also present with joint pain [3, 4]. Additionally, benign conditions like growing pains can cause significant discomfort, especially in the lower limbs, usually at night [5]. The diagnostic challenge is increased by the variety of symptoms, which may include pain, swelling, redness, and limited movement [6]. Accurate diagnosis is essential for guiding appropriate treatment, which can range from simple pain relief to more intensive therapies for severe or chronic conditions.

Gonorrhea is an inflammatory disease caused by the gram-negative bacterium Neisseria gonorrhoeae, transmitted through sexual contact (STI). At-risk groups include men who have sex with men, those who do not use physical contraception during intercourse, individuals with a history of STIs, and people with low socioeconomic status [7, 8]. Newborn infections occur due to transmission of gonococci during childbirth through natural pathways. In older children, it may also result from sexual abuse [9]. Colonization most commonly occurs in the mucous membranes of the genital organs; however, this bacterium has also been confirmed to affect other organs such as the eyeball, nasopharynx, anus, and joints like the hip, knee, and elbow [10-12]. As a result of infection, patients may experience symptoms such as fever, discharge, intermenstrual bleeding, pain during intercourse, purulent discharge from the penis, painful or swollen testicles, rectal bleeding, rectal itching, rectal pain, and pain or

burning during urination. In cases of joint inflammation, local symptoms include redness, pain during movement or at rest in the affected limb, tenderness on palpation, and swelling over the joint. Due to the most common site of inflammation, there is a risk of spreading to the pelvic organs, leading to pelvic inflammatory disease (PID) [8].

An illustrative case is described by Kumar et al., in which a child presented with arthritis of the knee as the initial sign of disseminated gonococcal infection, despite the lack factors [13]. This emphasizes the importance of maintaining a broad differential diagnosis in pediatric patients with joint complaints, including rare infectious etiologies such as gonorrhea.

According to the epidemiological report from the European Centre for Disease Prevention and Control, in 2022, 70,881 cases of gonorrhea were reported across 28 European Union/Economic Area countries. This amounts to 17.9 cases per 100,000 people and represents a 48% increase compared to 2021 and a 59% rise from 2018. Age-dependent rates were highest in the 20-24 age group for both men and women, with over half of the reported cases (60%) involving men with homosexual contact [14].

AIM

The objective of this case report is to highlight the problematic diagnosis of arthritis in children with existing other diseases and/or syndromes, emphasize the most important diagnostic tests when suspecting arthritis in children and resent a rare case of gonococcal arthritis in this age group.

CASE REPORT

A 3-year and 5-month-old girl was admitted to the Emergency Department of the University Children's Hospital in Lublin on June 27, 2021 late in the evening. She exhibited symptoms persisting for three days before admission, including groin pain, elevated body temperature up to 39°C, limping, and difficulty walking. The patient has a history of congenital cytomegalovirus (CMV) infection and bilateral hearing impairment, as well as cerebral palsy classified as level I according to the Gross Motor Function Classification System (GMFCS). Upon examination, she was hemodynamically stable with no meningeal irritation. The abdominal exam was unremarkable, vesicular breath sounds were present, and the abdomen was soft and pulsatile. The throat exam showed no abnormalities. Laboratory tests were ordered, including serum C-reactive protein (CRP) level and a complete blood count with an automatic differential. Elevated levels of CRP at 11,9 mg/dL (normal range 0-0,5 mg/dL), leukocytes at 17,14 x10^^{3}/mm^3, and neutrophils at 11,38 x10^^{3}/mm^3 indicate an ongoing inflammatory process. An ultrasound examination revealed an increased exudation in the hip joints. Combined with the symptoms presented by the patient, this led the medical team to suspect septic hip arthritis, and the patient was admitted to the Pediatric Orthopedics Department for further treatment.

The patient was hospitalized from June 27, 2021, to July 14, 2021, in the Pediatric Orthopedics Department of University Clinical Hospital in Lublin, and from July 14, 2021, to July 22, 2021, in the Pediatric Pulmonology and Rheumatology Clinic of the same hospital.

Soft tissue and full hip joint ultrasounds were performed the next day morning. The ultrasound of the left hip showed a moderately increased amount of fluid, signs of increased vascularization on Power Doppler, and an anterior recess measuring 11 mm in height. Similarly, there was an increased amount of fluid in the right hip joint, with the fluid thickness in the anterior recess measuring 6 mm, along with signs of increased vascularization of the joint capsule and surrounding tissues. Arthrotomy is the preferred treatment for septic arthritis. In this case, the decision was made to perform a left hip joint arthrotomy and right hip joint aspiration in the afternoon, immediately after an ultrasound examination revealed joint effusion and signs of inflammation. The empirically administered antibiotic prior to the procedure was cloxacillin. The pus obtained from the left hip joint and inflammatory joint fluid was submitted for bacterial culture. No bacterial growth was detected.

During hospitalization in the Orthopedics Department, a series of laboratory and imaging tests were conducted. These included a chest X-ray (which showed no pathology), an abdominal X-ray in the left lateral decubitus position (which showed no pathology), an echocardiogram (revealing normal heart anatomy and function), and an abdominal ultrasound.

Biochemical blood tests showed elevated ESR (120 mm/hr, normal range 2-15), decreased albumin level (2.45 g/dl, normal range 3.8-5.4), elevated ALT (106.6 U/l, normal range 0-39), decreased amylase level (18.97 U/l, normal range 28-100), elevated CRP (27.64 mg/dl, normal range 0-0.5), increased alpha-1 globulin (5.8%, normal range 2-3.4), increased alpha-2 globulin (19.1%, normal range 8.7-14.6), elevated LDH (1778 U/l, normal range 0-615), high ferritin level (17240 ng/ml, normal range 6-67), and elevated glucose level (113 mg/dl, normal range 70-99). Specialized tests revealed elevated CK-MB (30.3 U/l), normal RF and ASO levels, and elevated pro-BNP (389.3 pg/ml). Coagulation tests revealed elevated D-dimer levels (5760 ng/ml; normal range <500) and a prolonged prothrombin time (14.7 seconds; normal range 10.6-14.2). Inflammatory markers were also tested, showing a high procalcitonin level (21.1 ng/ml; values above 10 indicate severe bacterial shock or sepsis) and an elevated IL-6 level (50.6 pg/ml, normal range 0-7).

Virological and serological tests showed an indeterminate result for the *Mycobacterium tuberculosis* Quantiferon test, a

Table 1. Pharmacological treatment

Antibiotic therapy	**Cloxacillin 4 × 500 mg**	**Day 1 to Day 5**
	Cefotaxime 3 × 500 mg	Day 5 to Day 8
	Vancomycin 4 × 100 mg, then increased to 4 × 250 mg	Day 8 to Day 18
	Meropenem 3 × 320 mg, then 3 × 600 mg	Day 8 to Day 18
	Clindamycin 1 × 150 mg	Day 9 to Day 13
	Trimethoprim–sulfamethoxazole 2 × 3 ml, then 2 × 5 ml	Day 14 to Day 18
	Fluconazole 1 × 100 mg	Day 12 to Day 18
Parenteral nutrition	Numeta G16E, 300 ml	Day 12 to Day 18
Supplementation	Soluvit N (formerly: Sluvit N) 5 ml; Peditrace 10 ml; Vitolipid N 5 ml	
Additional medications	Paracetamol (acetaminophen); Ibuprofen; Morphine; Metamizole (dipyrone); Lactobacillus rhamnosus GG (formerly: LactoDR); Probiotic multistrain preparation (formerly: Synbiox Baby); Ondansetron; Fluid therapy	

Source: Own materials

non-reactive Wassermann test, and a non-reactive HIV test. Additionally, a positive SARS-CoV-2 IgM result was found, with negative IgG, PCR nasal swab, and antigen test results.

Despite joint arthrotomy, no improvement in the child's general condition was observed. The arthrotomy of the hip joint was repeated 7 days after the primary procedure. A sample of joint fluid was sent to a molecular testing laboratory for a PCR test. *Neisseria gonorrhoeae* genetic material was detected. In the given situation, additional tests for sexually transmitted diseases were performed. Antibodies to *Chlamydia pneumoniae*, *Chlamydia trachomatis*, *Yersinia*, and *Toxoplasma* were negative. A gynecological examination revealed an intact hymen and an anovaginal area.

A positive *Neisseria gonorrhoeae* result from molecular testing of joint content prompted a consultation with the National Consultant for Microbiology. Continuation of meropenem (3×600 mg, 2-hour infusions) and an increased dose of vancomycin (4×250 mg) with therapeutic drug monitoring was recommended. Antibiotic therapy was continued under consultant supervision and further management, including subsequent treatment modifications and concomitant medications, is summarized in Table 1.

The case was reported to the prosecutor's office.

Noted maculopapular rash on the limbs and trunk, eyelid swelling, and significantly elevated inflammatory markers: ESR, CRP, PCT, and ferritin. Blood tests revealed anemia, lymphopenia, hyponatremia, and increased levels of pro-BNP, LDH, transaminases (AST > ALT), triglycerides, and low albumin. Previously, fibrinogen and D-dimer levels had also been elevated. Additionally, SARS-CoV-2 IgM was positive, CMV PCR was positive, and the Quantiferon test was indeterminate. Given a persistent fever lasting over two weeks, markedly elevated inflammatory parameters, hematological abnormalities, a rash, signs of coagulopathy, and positive SARS-CoV-2 IgM, the differential diagnosis included PIMS-TS and systemic-onset juvenile idiopathic arthritis (soJIA), with a possible complication of macrophage activation syndrome (MAS). Further diagnostics and treatment were planned after central venous line placement, with a bone marrow biopsy scheduled for July 14, 2021, which did not reveal any leukemia or other hematological disorders.

As a consequence of this consultation, the patient was transferred to the Rheumatology Clinic, where she continued to receive treatment in accordance with current guidelines for systemic-onset JIA.

DISCUSSION

In this case, a 3-year-old girl with a complex medical history, including congenital cytomegalovirus infection and cerebral palsy, was admitted with symptoms of fever, thigh pain, and difficulty walking. Initially, common pediatric causes like transient synovitis were considered, but the fever and elevated inflammatory parameters suggested septic arthritis. However, despite arthrotomy and an antibiotic course, the lack of clinical response to typical treatment and rising inflammatory markers prompted further investigation. The diagnosis was revised when *Neisseria gonorrhoeae* was detected in joint fluid samples and later confirmed through molecular testing, which identified the pathogen's genetic material. Due to the sexually transmitted nature of the infection, the attending physician notified law enforcement and child protection authorities, as well as the child's caregivers, in accordance with legal requirements.

A gynecological exam was also conducted. Vaginal swabs were taken, and no trauma or abnormalities were observed; the hymen was intact and there were no visible signs of injury. Although these findings did not confirm sexual abuse, the presence of gonorrhea in a child this age required formal reporting and further evaluation [15, 16].

The patient was transferred to the Pediatric Pulmonology and Rheumatology Clinic of USD in Lublin with a diagnosis of M00.8 – "Other Bacterial Joint Infections." Persistent fever, cytopenias, coagulopathy, transaminasemia, high ferritin levels, and systemic inflammation complicated her hospital course. These findings led to the diagnosis of systemic-onset

juvenile idiopathic arthritis (SoJIA), complicated by macrophage activation syndrome (MAS) [17, 18]. The patient's history of cerebral palsy and congenital CMV infection, in combination with bacterial arthritis and recent SARS-CoV-2 IgM seropositivity, may have contributed to immune dysregulation and the development of MAS.

MAS is a life-threatening, hyperinflammatory syndrome resulting from excessive activation of macrophages and T lymphocytes. It is a known complication of SoJIA and often triggered by infections or immune stressors [19]. The patient required prolonged immunosuppressive therapy and close monitoring due to symptom recurrence and persistent inflammation, especially involving the hip joints.

This case highlights the diagnostic complexity of joint pain in children, which may include infections, inflammatory diseases such as JIA, and benign conditions such as growing pains [20, 21]. It underscores the necessity of a comprehensive, multidisciplinary approach in pediatric care, particularly in the context of increasing rates of sexually transmitted infections and expanding recognition of pediatric autoimmune conditions [22,23]. It is also important to note that gonococcal infections—though typically sexually transmitted—can rarely be seen in young individuals without a history of sexual activity. For example, an 18-year-old female with polyarticular arthritis tested positive for N. gonorrhoeae despite denying sexual contact, highlighting the importance of thorough and unbiased diagnostic workups in atypical presentations [24]. The recent rise in gonorrhea cases across Europe, including among vulnerable populations such as young children, emphasizes the need for vigilance and strict diagnostic standards in pediatric settings [25].

The course of her treatment underscores the challenges in managing patients with multifaceted conditions and the importance of coordinated care across specialties to address the evolving clinical picture. This case illustrates the intricate interplay between orthopedic and rheumatologic conditions and the critical need for ongoing, specialized care to manage both the primary disease and its complications effectively.

CONCLUSIONS

This case highlights the vital need for a vigilant, multidisciplinary approach to pediatric care, especially when dealing with complex presentations that challenge initial diagnostic assumptions. The unexpected diagnosis of gonococcal arthritis in a young child stresses the importance of considering a broad differential diagnosis, even for rare and atypical conditions. Additionally, the legal and protective measures implemented in response to potential abuse emphasize the intersection of medical and social responsibilities in pediatric practice. The subsequent management of systemic-onset juvenile idiopathic arthritis (SoJIA) with related complications further underscores the need for coordinated, continuous care across multiple specialties. This case not only demonstrates the complexity of diagnosing joint pain in children but also calls for greater awareness and improved diagnostic protocols to better address the rising incidence of sexually transmitted infections and autoimmune diseases in this vulnerable population.

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VARIA

CONTENTS

Local cryotherapy and thermovision assessment of cooling effects during cryostimualtion procedure

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ABSTRACT
In physical medicine, cryotherapy refers to the brief exposure of a selected body region (local cryotherapy) or the whole body to extremely low temperatures. In practice, this involves local cryotherapy devices and various types of cryogenic chambers. Local cryotherapy remains an important adjunct in treatment and rehabilitation, while integration of the blower nozzle with a thermovision camera expands procedural monitoring capabilities. Thermovision enables assessment of temperature distribution before, during, and after cooling, supporting both patient safety and improved adaptation of procedural parameters to the treated area.

KEY WORDS: cryotherapy, cryostimulation, thermovision

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INTRODUCTION

In physical medicine, cryotherapy refers to the brief exposure of a selected body region (local cryotherapy) or the whole body to extremely low temperatures. In practice, this involves local cryotherapy devices and various types of cryogenic chambers. The primary aim is to elicit reflexive physiological responses to cold and to influence metabolic processes, thereby supporting core treatment and rehabilitation [1].

EVOLUTION OF LOCAL CRYOTHERAPY DEVICES

Devices dedicated to local cryotherapy, originally developed several decades ago, have fundamentally retained their capacity to achieve low temperatures. Over the years, nomenclature, branding, and design have evolved. Manufacturers have focused on efficiency, such as reducing gas consumption during procedures (e.g., by introducing air pumps to gas tanks instead of standard heaters). Improvements have also been made in the insulation of cryogenic tubing to minimise energy losses, while larger screens and touch controllers have enhanced device operation.

REVIEW AND DISCUSSION

BLOWER NOZZLE WITH INTEGRATED THERMOVISION CAMERA

Recently, a solution has been developed enabling the use of a blower nozzle with an integrated infrared thermovision camera for assessing the effectiveness of local cryotherapy procedures. This system is designed for cryotherapy devices powered by nitrogen vapour and equipped with such a nozzle. The concept is based on principles that both enhance procedural safety and facilitate highly effective cooling.

The most crucial parameter is body temperature, which reflects the energetic state of the organism. Elevated temperature is associated with increased metabolism, such as inflammation and processes leading to increased blood flow in skin vessels. Conversely, decreased temperature is observed with impaired blood flow and in degenerative or necrotic tissue conditions. Therefore, thermograms obtained prior to cryotherapy show hyperthermic zones in areas of inflammation and hypothermic zones in areas of degeneration [2-8].

Thermographic examination allows the detection of a skin temperature difference of 0.25±0.2°C over the examined region compared to the corresponding area on the opposite side of the body or surrounding healthy tissue, which may indicate pathological changes. As skin temperature varies according to anatomical structure, gender, and age, accurate thermogram interpretation requires the use of thermal maps of the human body. Cooling during local cryotherapy highlights differences in surface skin temperature distribution. Post-cooling thermal imaging may reveal details not visible on pre-procedure thermograms, offering more precise information regarding cooling heterogeneity and the localization of pathological changes. Consequently, a thermogram taken

immediately after the procedure enables assessment of the cooling effect and verification of proper procedural execution. The nozzle with an integrated camera allows for more uniform cooling of the treated area; if post-procedure thermograms reveal inadequately cooled spots, this guides the therapist to increase airflow intensity in subsequent sessions to optimize therapeutic outcomes [9-14].During procedures using nitrogen vapor, current guidelines recommend: a nozzle outlet distance from the skin of no less than 15 cm; procedure duration for a single body region ranging from 30 seconds to 3 minutes; and therapeutic mechanisms and safety principles are taken into account. The expected outcome is a reduction in mean temperature of the treated region by between 5°C and 15°C, which can be confirmed by comparing thermograms taken before and immediately after the procedure [7,13-18,24]. Due to the substantial number of factors influencing surface body temperature and the course of temperature measurement, reliable interpretation of thermograms before and after treatment is only possible with proper patient preparation and strict adherence to thermographic examination protocols, in accordance with current standards [15-22].

RESEARCH AND DEVELOPMENT PROJECT (POIR.01.01.01-00-1192/17)

The blower nozzle with thermovision camera indicating tissue surface temperature (measured before, during, and after the procedure) was constructed and evaluated according to the objectives of project POIR.01.01.01-00-1192/17: "Innovative nozzle for local cryotherapy with integrated infrared imaging and efficacy assessment support system". The following outcomes were achieved.

Industrial research was conducted, developing a procedural methodology for cryotherapy with IR camera (8-12 µm), taking environmental conditions and medical standards into account. The FLIR Lepton 3.5 sensor (160×120 px) was selected as optimal for nozzle integration. Dedicated control electronics were designed for indicators, RGB diode, and interface. Comparative tests with the FLIR T1020 camera and system calibration were performed, examining environmental impacts on measurements. Methodology followed standards including ISO/TR 80601-2-56:2013, ASTM, IACT, and the Glamorgan protocol.

Development work included creation of an algorithm for thermogram analysis using a measurement grid and colour-coded therapeutic decision signals. The algorithm underwent clinical validation by Prof. Agata Stanek, MD, PhD. Software integrating the IR camera with user interface was developed, and ergonomic nozzles (Solid Edge) were designed and evaluated by physiotherapists. Prototypes were produced using injection moulding, and functional tests were conducted. A total of 100 test procedures were performed (average ergonomic score 9.8/10, software score 4.9/5). Expert validation by Prof. Grzegorz Cieślar, MD, PhD, confirmed the solution's efficacy and safety. Intellectual property protection was sought: patent application in Poland (P.451922) and community design in the EU (MTC-3/2021).

CONCLUSIONS

Local cryotherapy remains an important adjunct in treatment and rehabilitation, while integration of the blower nozzle with a thermovision camera expands procedural monitoring capabilities. Thermovision enables assessment of temperature distribution before, during, and after cooling, supporting both patient safety and improved adaptation of procedural parameters to the treated area.

Thermal imaging increases the objectivity of cooling efficacy assessment and facilitates detection of cooling heterogeneity within the treated region. A thermogram taken immediately after the procedure supports procedural correctness and planning of subsequent sessions by indicating areas requiring adjustment of airflow intensity.

Integration of the IR camera with the nozzle allows real-time insight into the procedure and enhances safety (enabling rapid response to excessively low local temperatures).

Standardisation of measurement and interpretation methodology (environmental conditions, thermal maps, decision thresholds) is crucial for comparability of results and accurate interpretation of thermographic data.

Design work and prototype validation indicate practical feasibility of implementation and highlight the potential for personalised therapy according to local pathological changes.

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CONFLICT OF INTEREST

The Author declare no conflict of interest

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A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

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METRUM CRYOFLEX

Discover the future of physiotherapy and rehabilitation!

Metrum Cryoflex presents a revolutionary local cryotherapy device that combines the latest technological advancements with practical clinical needs. The innovative blower nozzle is equipped with a FLIR Lepton 3.5 thermal imaging camera and a thermogram analysis algorithm, which allows for precise monitoring of skin temperature and maximizing the effectiveness of the treatment.

CRYO-T | Vital

Industrial Research

· A treatment methodology for cryotherapy with an IR camera (8–12 µm) was developed, taking into account environmental conditions and medical standards.
· The FLIR Lepton 3.5 sensor (160×120 px) was chosen as the optimal sensor for nozzle integration.
· Dedicated electronics have been designed to control the indicators, RGB diode and interface.
· Benchmarks with the FLIR T1020 camera and system calibration were performed.
· The influence of environmental conditions on the measurements was investigated – human skin is an ideal thermal imaging object.
· Methodology compliant with ISO/TR 80601-2-56:2013, ASTM, IACT and Glamorgan protocol.

Development

· An algorithm for the analysis of thermograms with a measuring grid and color signaling was developed:
Blue: continue cooling.
White: optimal temperature.
Red: Stop cooling.
Black: Critical Temperature.
· The algorithm was clinically validated by Prof. Agata Stanek, MD, PhD.
· Software was created that integrates the IR camera into the user interface.
· Ergonomic nozzles in Solid Edge have been designed, evaluated by physiotherapists.
· Prototypes were made using injection molding technology and functional tests were carried out.
· 100 test procedures were carried out – average ergonomics rating: 9.8/10, software: 4.9/5.
· Expert validation by Prof. Grzegorz Cieślar, MD, PhD, confirmed its effectiveness and safety.
· Patent application in Poland (P.451922) and Community design in the EU (MTC-3/2021).

POIR.01.01.01-00-1192/17
"Innovative nozzle for local cryotherapy with integrated infrared imaging system and support for the evaluation of the effectiveness of the treatment"

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