ORIGINAL ARTICLE

Intima-media thickness, telomere length and neuropsychological status: is there any connection?

Maria Cherska, Khrystyna Kukharchuk
SI "V.P. KOMISARENKO INSTITUTE OF ENDOCRINOLOGY AND METABOLISM OF THE NAMS OF UKRAINE", KYIV, UKRAINE

ABSTRACT

Aim: To determine the relationship between telomere length and telomerase activity and indicators of oxidative stress in patients with CA and T2DM.

Materials and Methods: to investigate relationship between telomere length and cognitive function and identify predictors of cognitive impairment in patients with cerebral atherosclerosis and type 2 diabetes mellitus. The MMSE and MoCA scales, which are widely used in most modern epidemiological and clinical studies, were used for screening and assessment of cognitive disorders.

Results: Patients were divided into 2 groups: I – with scores on MMSE scale < 26 (moderate cognitive deficit, 26 people), II – with scores on MMSE scale ^{3} 26 (mild cognitive deficit, 135 people). As a result of analysis, it was found that length of telomeres was statistically significantly shorter in patients of group I, the patients studied less, they had more pronounced situational anxiety, more pronounced intima-media thickness in both carotid arteries, and according to MoCA scale, they had pronounced impairment of cognitive functions ($p<0.05$). Group II patients had longer telomeres, studied longer, and had high personal anxiety.

Conclusions: patients with cerebral atherosclerosis and type 2 diabetes mellitus with mild cognitive impairment have longer telomeres, high personal anxiety, and a higher level of education.

KEY WORDS: telomerase activity, cerebral atherosclerosis, MMSE, type 2 diabetes mellitus, cognitive function

Wiad Lek. 2025;78(12):2661-2668. doi: 10.36740/WLek/213488 DOI

INTRODUCTION

Impairment of cognitive functions is one of the most significant characteristics of cerebrovascular pathology, the frequency of which increases with age and with the development of type 2 diabetes mellitus (T2DM). Age is extremely important in determining the functional state of the body and its response to environmental influences. The study of cellular and molecular changes in the blood that coordinate the development of premature cellular aging will make it possible to establish biomarkers associated with this process [1-7]. The study of telomere length, telomerase activity and the genes that regulate these indicators (TERT, TERF1, TERF2) is an important link in the study of biological aging. A number of previous studies have revealed a connection between stress and shortening of telomere regions, a relationship between telomere length and the development of cardiovascular pathology and dementia [5, 6, 9]. On the other hand, shorter telomere length is observed in patients with a combination of prediabetes/diabetes and atherosclerotic diseases compared to cases of isolated diabetes or cardiovascular disease [10, 11]. Olivieri F, et al. showed that patients with diabetes who had a myocardial infarction had shorter telomere lengths compared to those who had diabetes but did not have a history of myocardial infarction [12-17]. Thus, telomere length can be considered as a biomarker of aging or stress. With age, cognitive functions decline and telomere length shortens. Cognitive deficits accompany the aging process and may be related to telomere length. S. E. Harris et al. found an inverse relationship between the verbal test and telomere length [8]. However, no significant correlations were observed with tests of nonverbal reasoning, verbal declarative memory, and dementia screening in patients aged 79 years. Contrasting with this is the study by Valdes et al., where, in a study of 382 female patients with a wide age range (mean age 50 years, range 19 to 78 years), a correlation was found between telomere length and cognitive functions: four out of six cognitive tests, except recognition images and spatial memory tasks [17]. These studies demonstrate that telomere length is associated with cognitive function and may be a biomarker of cognitive aging in patients before the onset of dementia.

There are a large number of various tests for the psychometric diagnosis of disorders of cognitive functions.

The MMSE technique is widely used in most modern epidemiological and clinical studies for screening and assessment of cognitive disorders, which confirms its validity and suitability. At the same time, the question of the role of telomere length in the progression of cognitive functions in elderly people with cerebral atherosclerosis (CA) and T2DM remains relevant.

AIM

The aim of our study is to determine the relationship between telomere length and telomerase activity and indicators of oxidative stress in patients with CA and T2DM.

MATERIALS AND METHODS

The comprehensive clinical and instrumental study involved 161 patients with the grade of 1–3 CA. The diagnosis "Cerebral Atherosclerosis" (CA) has been formulated in accordance with the classification of atherosclerosis of World Health Organization since 2015 and confirmed by laboratory and instrumental research (Doppler ultrasonography of cerebral arteries, brain magnetic resonance imaging (MRI)).

STUDY DESIGN

Simple, prospective, non-randomized, with sequential inclusion of patients.

The study did not include patients with all forms of atrial fibrillation, uncorrectable blood pressure (BP) >160/90 mm Hg. Art., other rhythm disturbances requiring antiarrhythmic therapy, a decrease in EF <40% assessed by two-dimensional echocardiography (Echocardiography), severe heart failure, renal and hepatic impairment, drug or alcohol dependence, and those who had been suffering from acute inflammatory diseases during previous month. The patients who underwent revascularization as a result of unstable angina or myocardial infarction or rheumatic heart diseases did not participate in the study as well.

All patients underwent generally accepted clinical, laboratory (general blood and urine analysis, determination of lipid profile, creatinine, urea, glucose, aspartate aminotransferase, alanine aminotransferase, bilirubin) and instrumental examination (transthoracic echocardiography, electrocardiography, ECG, transcranial Doppler ultrasound and brain MRI).

ETHICS

The study protocol was approved by the ethics committees of the Institute of Endocrinology and Metabolism and the Institute of Gerontology NAMS of Ukraine. All participants gave the written informed consent. The Declaration of Helsinki (2000) and the applicable national standards regarding their participation in research were taken into account.

COLLECTION AND STORAGE OF BLOOD SAMPLES

Blood samples were taken in the vacutainers containing EDTA. Within 30 minutes after blood sampling, peripheral blood mononuclear cells were isolated on the gradient (1.077 g / cm^3). After isolation, the cells were frozen and stored in liquid nitrogen at -196°C. DNA was isolated from thawed cells with the use of the phenol-chloroform purification method [15]. The purity, concentration, and integrity of DNA were checked with the use of spectrophotometry and agarose gel electrophoresis.

MEASUREMENT OF TELOMERE LENGTH (TL)

Relative telomere length (RTL) was measured with the use of monochrome multiplex quantitative polymerase chain reaction (MMQPCR) [4]. The PCR reaction mixture was prepared by using the commercial Luna® Universal qPCR and RT-qPCR reagent kit (New England Biolabs) supplemented with betaine (Sigma-Aldrich) to the final concentration of 1M. For MMQPCR the pair of *telg* and *telc* telomeric primers (the final concentrations of 450 nmol of each) was combined with the pair of *albu* and *albd* primers (the final concentrations of 250 nmol of each) in a master mix. The list of primers used for the MMQPCR is given below in the Table 1.

The thermal cycling profile was as follows: 95°C for 15 minutes; 2 cycles: 94°C – 15 s and 49°C – 15 s; 32 cycles: 94°C –15 s, 62°C –10 s, 74°C –15 s with signal acquisition, 84°C –10 s, 88°C –15 s with signal acquisition. The calibration curve was built on the points of four concentrations of reference DNA (in duplicate), which span a range of 27-fold serial dilutions.

All DNA samples were analyzed in triplicates. The amplification curves were generated by the Opticon Monitor 3 software. For this, after thermal cycling and initial data collection, by using the Opticon Monitor 3 software the two standard curves were constructed for each formulation: for the telomeric signal and for the signal of the single copy albumin gene. The RTLs were expressed as the T / S ratio, where T is the quantity of telomeric DNA, and S is the quantity of albumin DNA.

MEASUREMENT OF TELOMERASE ACTIVITY

Telomerase activity was determined by using a tandem repeat amplification protocol with real-time detection (TRAP) [1]. The peripheral blood mononuclear cells and the HEK293 cells (positive control) were

Table 1. List of the primers used for quantitative polymerase chain reaction in real time (MMQPCR)

Primer name	Primer nucleotide sequence
TS	5'-AATCCGTCGAGCAGAGTT-3'
ACX	5'-GCGCGGCTTACCCTTACCCTTACCCTAACC-3'
telg	5'-ACACTAAGGTTTGGGTTTGGGTTTG GGTTTGGGTTAGTGT-3'
telc	5'-TGTTAGGTATCC CTATCCCTATCCCTATCCCTATCCCTAACA-3'
albu	5'-CGGCGGCGGGCGGCGCGGGCTGGGCGGAA ATGCTGCACAGAATCCTTG-3'

Source: compiled by the authors of this study

treated with the Invitrogen NP-40 lysis buffer (50 mmol Tris, pH 7.4, 250 mmol NaCl, 5 mmol EDTA, 50 mmol NaF, 1 mmol Na_3VO_4, 1% Nonidet ™ P40 (NP40) 0.02% NaN_3) with 1 mmol PMSF (Sigma-Aldrich) and 10 µl/ml (v / v) solution with a protease inhibitor (Sigma-Aldrich) on ice for 30 minutes. Subsequent centrifugation was carried out at 16400g for 20 min at +4°C. 180 µl of the supernatant was transferred into a fresh tube. Protein concentration was measured using a Pierce™ BCA Protein Analysis Kit (Thermo Scientific) according to the manufacturer's protocol.

The reaction mixture for TRAP was prepared on the basis of Luna Universal qPCR and RT-qPCR (New England Biolabs) with the addition of EGTA to the final concentration of 5 mM. The final concentrations of primers were 400 nM of ACX and 400 nM of TS. The 2 µl of the lysate were added to 23 µl of the TRAP mixture and incubated for 30 min at 30°C. Then, real time qPCR was performed under the following conditions: 95°C for 1 min; 40 cycles: from 95°C – 15 s, 60°C – 1 min and signal acquisition. The PCR products were quantified using Chromo4 (Bio-Rad) and analyzed with the use of the Opticon Monitor v3.1 software. The HEK293 cells were used to generate the standard curve set on the points of the five dilutions.

MEASUREMENT OF THE ACTIVITY OF CATALASE, SUPEROXIDE DISMUTASE, GLUTATHIONE AND OTHER MARKERS OF OXIDATIVE STRESS

To determine the activity of blood catalase, the blood hemolysate that was obtained by osmotic hemolysis of whole blood with distilled water and single freezing cycle followed by centrifugation was used. The diluted blood hemolysate was incubated with a hydrogen peroxide solution and the catalase activity was determined spectrophotometrically for the amount of the reaction product of the residual hydrogen peroxide with ammonium molybdate. To create the calibration graph, the solution of commercially available catalase was used (Sigma, C9322). The results are expressed in the units of enzyme activity per 1 ml of blood.

The activity of superoxide dismutase (SOD, EC 1.1.15.1.) in the plasma of blood was determined by an indirect spectrophotometric method based on the reaction of superoxide-dependent oxidation of quercetin, in an alkaline environment, in the presence of tetramethylethylenediamine. The reaction was accompanied by discoloration of the working solution in the transmission region with the maximum at 406 nm. The enzyme superoxide dismutase intercepts superoxide radicals and inhibits the oxidation of quercetin. At the incubation time of 20 minutes, the degree of inhibition is strictly quantitatively dependent on the concentration of SOD. The enzyme content in the biological material is calculated using a calibration graph obtained on the basis of measuring the activity of commercially available SOD (Sigma, S9697). The SOD activity was expressed in the units of activity based on the 1 ml of plasma.

The concentration of TBA-active products was measured using the reaction of heating malondialdehyde (MDA) with 2-thiobarbituric acid (TBA) in an acidic medium to form the colored trimethine complex with the maximum of fluorescent radiation at µ = 530 nm under conditions of the light excitation from µ = 484 nm. The blood plasma was incubated in TBA in the presence of trichlorocytic acid with heating. After cooling the samples, TBA-active products were extracted with n-butanol. The fluorescence intensity was measured on a spectrofluorometer. The concentration of TBA-active products (MDA) was calculated according to the calibration curve created using commercial MDA (Sigma, 63287) and expressed as µM per liter. Plasma glutathione (GSH) in was determined by a spectrofluorometric method using orthophthalic aldehyde that results in the formation of highly fluorescent products from GSH, which are excited by the radiation at 350 nm and have the distinct fluorescence peak at 420 nm [16]. The concentration of GSH has been calculated according to the calibration curve created using commercial GSH (Sinbias, Ukraine) and expressed in the units of micromoles per liter. The fluorescence intensity of the glycated proteins in blood plasma was measured by the excitation of 370 nm and emission of 440 nm using

the Varioscan spectrofluorometer, and expressed in the arbitrary units of glycated protein micromoles per liter. Non-enzymatically glycated protein – BSA-glucose was prepared to create the calibration curve. The mixture of BSA and d-glucose in phosphate buffer was incubated at 37°C for 6 weeks.

BASIC MEASUREMENT

Systolic blood pressure (systolic blood pressure) and diastolic blood pressure (diastolic blood pressure) (mmHg) were measured twice using the standard sphygmomanometer in a sitting position after at least 10 minutes of rest. Plasma glucose levels were determined by the standard glucose oxidase method.

NEUROPSYCHOLOGICAL TESTING

Cognitive impairment was assessed using the Mini-mental State Exam (MMSE) scale and the Montreal Cognitive Assessment Scale (MoCA) [17]. Orientation in time and place, concentration of attention and calculation, perception, memory, and language functions were assessed using the 6-item MMSE scale. Absence of cognitive deficit corresponded to 30 points, mild cognitive impairment - 27-26 points, moderate cognitive impairment - 25-24 points, mild dementia - 23-20 points, moderate dementia - 19-11 points, severe dementia - 10 points and less.

Attention and concentration, executive functions, memory, language, visual-constructive skills, abstract thinking, calculation and orientation were evaluated with the help of MoSA. The duration of the MoSA test was 10 minutes, demonstrating cognitive damage was estimated at 26 points or more.

Detection of psychoemotional disorders was carried out using the Spielberger-Khanin anxiety scale. According to the Spielberger-Khanin scale, low anxiety was defined as having 30 points, moderate - 31-45, high - 46 points and more.

HRV was studied on a Schiller AT-10 plus device (Switzerland) using statistical analysis of the time domain and spectral analysis of a short (five-minute) sequence of R-R electrocardiographic intervals at rest. The following parameters of the time analysis were determined: standard deviation (SDNN, ms), standard deviation of the differences in the duration of adjacent R-R intervals (RMSSD, ms). When performing spectral analysis, the following were determined: the total power of the heart rhythm spectrum (tP, ms2), power in the range of 0.00–0.04 Hz (VLF, ms2), 0.04–0.15 Hz (LF, ms2), 0, 15–0.4 Hz (HF, ms2) and lf / hf ratio. The spectral components LF and HF were analyzed both in absolute values and in the normalized units (i.e.) derived from them, which were automatically calculated by the formulas: LFnorm = LF / (tP - VLF) Ч 100% and HFnorm = HF / (tP - VLF) 100%. The spectrum structure was also determined as a percentage of the components: % VLF, % LF, % HF.

STATISTICAL ANALYSIS

In order to provide the results in the case of quantitative variables, the average value of the indicator and its standard deviation (± SD) for the case of the normal distribution law were calculated. Meantime the median value of the indicator (Me) and the values of the first (QI) and third (QIII) quartile for the case of the distribution law different from the normal were calculated. The distribution was checked for normality using the Shapiro-Wilk test. To represent the qualitative features, their frequency (%) was calculated. When comparing the quantitative indicators in the two groups, the t-criterion (in the case of the normal distribution law), the Mann-Whitney criterion (in the case of the distribution law other than the normal) were used. When comparing quality indicators the Fisher's exact test was used.

The method of building and analyzing logistic regression models was used to analyze the relationship between the T/S indicator (dependent variable) and factor characteristics. The odds ratio (OR) and its 95% confidence interval (95% CI) were calculated to assess the degree of association between dependent and independent variables [1]. To analyze the adequacy of regression models, ROC analysis [1] was performed, and the area under the operating characteristics curve (AUC) was calculated. The threshold of significance in all cases was set at $p < 0.05$.

The statistical analysis was performed with the use of the MedCalc v. 18.10 (MedCalc Software Inc., Broekstraat, Belgium, 1993–2018).

RESULTS

Patients were divided into 2 groups: I – with scores on the MMSE scale < 26 (moderate cognitive deficit, 26 people), II – with scores on the MMSE scale ^{3} 26 (mild cognitive deficit, 135 people) (Table 2).

As a result of the analysis, it was found that the telomere length was statistically significantly shorter in patients of group I, the patients studied less, they had more pronounced situational anxiety, more pronounced thickening of the intima-media complex in both carotid arteries, and according to the MoCA scale, they had a pronounced impairment of cognitive functions ($p<0.05$). Group II patients had longer

Table 2. Clinical-instrumental and laboratory characteristics of patients

Indicator	I group		II group		p
	Me	Q1;Q3	Me	Q1;Q3	
Patients with a stroke, (%)	69.2		42.2		0.04
Patients with a T2DM, %	42.9		44.5		0.16
Fasting blood glucose, mmol/l	4.95±1.86		4.87±1.74		0.76
Glycosylated Hemoglobin (HbA1c), %	6.38±0.76		6.43±0.57		0.82
Duration T2DM, years	4.80±1.78		4.90±2.10		0.80
Catalase	503.92	439.28; 599.68	549.41	446.46;661.93	0.21
Glutathione (GSH), mkM/l	3.45	3.39; 3.63	3.49	3.38;3.60	0.85
SOD	8.51	8.15; 8.87	8.43	7.85; 9.23	0.79
Thiobarbituroreactive Substances (TBARs), mcM/l	17.81	16.91; 21.33	17.54	16.03;19.11	0.35
Glycation End Products (AGE)	27.78	24.54; 33.09	31.66	26.48; 36.45	0.15
TTelomerase activity	2.6	1.96; 3.44	3.2	2.34; 4.29	0.32
Telomere length	2.34	1.91; 2.49	2.74	2.17; 3.58	**0.03**
Stady, years	15.5	12.00; 16.00	16	15.00;18.00	**0.01**
MoCA, points	22	17.00; 22.00	27	25.00;28.00	**0.01**
Situational anxiety, points	45	37.00; 45.00	36	32.00;42.00	**0.03**
Personal anxiety, points	45	36.50; 46.50	47	42.00; 51.00	**0.03**
Age, years	65.5	61.00; 79.00	63	59.00; 70.75	0.14
LDL, mmol/l	2.73	2.17; 4.02	2.98	2.73; 4.32	0.14
CIMT right, cm	1	1.00; 1.10	1	0.96; 1.10	**0.03**
CIMT left, cm	1	1.00; 1.20	1	1.00; 1.10	**0.03**
Distance per day, км	2	1.00; 3.00	2	1.00;3.00	0.09
Time watching TV, hour	3	2.00; 5.50	3	2.00; 5.00	0.78
Index HRV	6.50	5.00; 10.00	8	6.00; 9.00	0.17

To present the results in the case of quantitative variables, the mean value of the indicator and its standard deviation (± SD) were calculated in the case of a normal distribution law, or the median value of the indicator (Me) and the value of the first (QI) and third (QIII) quartiles in the case of a distribution law that was different from normal p< 0.05 - statistically significant differences; CIMT – carotid intima-media thickness, HRV index - heart rate variability index, EDV - end-diastolic volume, EF - ejection fraction, LVMM - left ventricular myocardial mass, E/A and E/E' - indicators of left ventricular diastolic function

Source: compiled by the authors of this study

Table 3. Multivariate analysis of indicators

Independent variables	Regression coefficient, b±m	The level of significance of the difference of the coefficient from 0, p*	OR (95% CI)
Years of study	0.31±0.15	0.03	1.37 (1.02–1.84)
IMT	–8.77±3.41	0.01	0.0002 (0.001–0.12)
Telomere length	1.33±0.62	0.03	1.78 (1.13–12.65)

*p< 0.05 - statistically significant differences

Source: compiled by the authors of this study

telomeres, studied longer, and had high personal anxiety. Both groups were comparable in terms of age, sex, and telomerase activity (p<0.05).

The method of constructing logistic regression models was used to identify factors affecting cognitive functions. The following categories were used when building the models: MMSE < 26 (moderate cognitive deficit, 26 patients) – case (Y=1), MMSE ^{3} 26 (mild cognitive deficit, 161 patients) – non-case (Y=0)

It is important to take into account the fact that it is the combination of risk factors, and not each individual risk factor separately, that can lead to telomere shortening

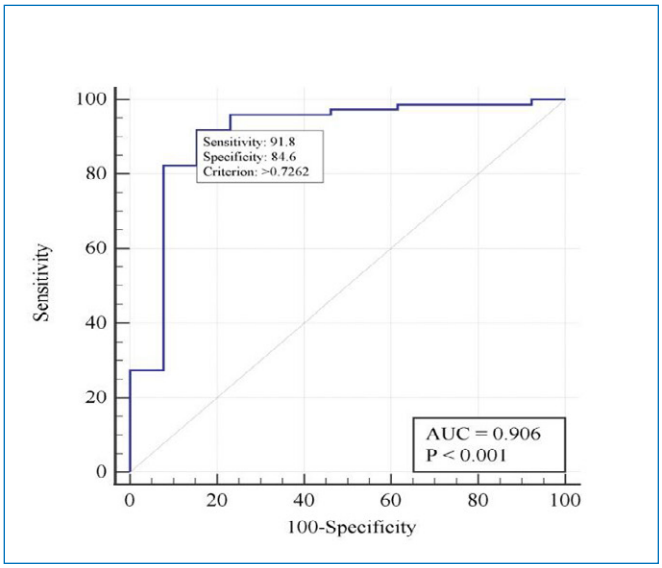

Fig. 1. ROC curve of the 3-factor model for predicting the risk of cognitive decline AUC = 0.91 (95% CI 0.82-0.96)
Picture taken by the authors

[14]. The method of stepwise inclusion/exclusion of features was used to select a set of significant risk factors (Stepwise at the exclusion threshold p>0.15 and the inclusion threshold p<0.03). A multivariate logistic regression model was built on the selected significant risk factors, which included the indicators presented in Table 3.

A good agreement of the selected factor characteristics with the risk of deterioration of cognitive functions was revealed - AUC = 0.91 (CI 0.82 - 0.96) (Fig. 1), which may indicate the completeness of the model and predictors of deterioration of cognitive functions considered in this study. All indicators presented in table 3 are significant in the general multifactor model.

DISCUSSION

The question of the relationship between the carotid intima-media thickness (CIMT) and the biology of telomeres is currently not fully resolved. Some researchers believe that there is no connection between the manifestations of subclinical atherosclerosis and the length of telomeres, emphasizing that shorter telomeres are not associated with atherosclerosis [3, 5]. On the other hand, there are a number of works in which the opposite results were obtained [14, 15]. It can be assumed that the relationship between the length of telomeres and the development of cardiovascular diseases (CVD) can be mediated by the influence of so-called modulating factors that determine the severity of oxidative stress and chronic inflammation. Accelerated shortening of telomeres can lead to aging of the endothelium and the occurrence of atherosclerosis with subsequent development of CVD.

In the literature, there is a rather limited number of works devoted to the study of the connections between cognitive and emotional mental processes with DNA sections that do not encode the amino acid sequence of peptide and protein molecules, but actively participate in the adaptation of the organism to external environmental conditions, aging and determining life expectancy. Telomeres are non-coding regions of DNA. Telomeres are the terminal structures of eukaryotic chromosomes that protect linear chromosomes from degradation and fusion, are involved in the process of cell division and in maintaining the stability of the genome. The telomere consists of repeated double-stranded sections of DNA (5'TTAGGGn-3') and a single-stranded 3' protruding section - the G chain, which, intertwined with the double-stranded section, forms a t loop. The length of a human telomere is 250-1500 repeats of the TTAGGG sequence [11]. As a result of each cell division, telomeres are shortened, which is associated with incomplete replication of chromosome ends [16]. The process of telomere shortening is limited by the so-called Hayflick limit, the limit of the number of divisions of human somatic cells, which die after approximately 50 divisions and show signs of aging when approaching this limit. The shortening of telomere length with age underlies the mechanism of replicative senescence. Maintenance of a certain length of telomeres occurs due to the activity of the enzyme - telomerase, which forms a single functional telomere-telomerase system with telomeres. It is assumed that the mechanism of functioning of the telomere-telomerase system and the gene expression of physiologically active substances associated with this system are at the basis of mental activity processes.

A study of the age-related deterioration of cognitive functions associated with a short leukocyte telomere length in healthy men aged 65-91 showed that it is combined with a change in a number of peripheral blood parameters: a decrease in the concentration of albumin, the level of beta-amyloid, an increase in the content of glucose, CRP and pro-inflammatory IL-6, cystatin C, which is a predictor of chronic renal failure and CVD. The authors suggested that the common cause of shortening of telomeres and deterioration of cognitive functions is oxidative stress associated with mitochondrial dysfunction [9].

Increased inflammatory activity accelerates the shortening of telomeres both due to the activation of cell reproduction and the release of reactive oxygen species [9, 11]. The relationship between telomerase activity and chronic inflammation is ambiguous. Early chronic inflammation through different signaling

pathways (involving NF-κB, protein kinase C, or Akt kinase) via phosphorylation or transcription of hTERT is able to activate telomerase, which likely compensates for accelerated telomere shortening. However, in the late stages of delayed inflammation, telomerase activity decreases, which leads to telomere shortening [15]. In our study, T2DM was not associated with telomere length and telomerase activity. This is consistent with the results of M. Sampson et al. no connection was found between shortening the length of lymphocyte telomeres and indicators of carbohydrate metabolism. Perhaps this can be explained by the short duration of diabetes and the absence of long-term severe hyperglycemia, since it is long-term hyperglycemia that is associated with the development of severe and persistent oxidative stress. It is important to emphasize that, according to our data, the level of oxidative stress, chronic inflammation and telomerase activity in patients with T2DM did not differ significantly. It can be assumed that with a short duration of T2DM, the genetically determined long telomere length protects patients from the harmful effects of oxidative stress and chronic inflammation, ensuring better and faster recovery of damaged tissues. In our study, we established: a negative relationship of cognitive decline with the size of the IMT of carotid arteries and positive relationships with the length of telomeres and the duration of education regardless of the presence of T2DM.

CONCLUSIONS

1. Patients with cerebral atherosclerosis and T2DM with moderate cognitive impairment are characterized by short telomeres, more pronounced situational anxiety and thickening of the IMT of the carotid arteries.
2. Patients with cerebral atherosclerosis and T2DM with mild cognitive impairment have longer telomeres, high personal anxiety and a higher level of education.
3. For patients with CA of various stages with T2DM, predictors of cognitive impairment are the length of telomeres, the thickness of the IMT of the common carotid arteries and the duration of training AUC = 0.91 (95% CI 0.82 - 0.96).

REFERENCES

1. Banerjee P, Jagadeesh S. Non-Radioactive Assay Methods for the Assessment of Telomerase Activity and Telomere Length. Methods in Molecular Biology. 2009, pp.383-394. doi:10.1007/978-1-59745-190-1_25. DOI
2. Benetos A, Toupance S, Gautier S et al. Short Leukocyte Telomere Length Precedes Clinical Expression of Atherosclerosis. Circul Res. 2018;122(4):616-623. doi:10.31612/2616-4868.4(10).2019.06. DOI
3. Cawthon R. Telomere length measurement by a novel monochrome multiplex quantitative PCR method. Nucleic Acids Res. 2009;37(3):e21-e21. doi:10.1093/nar/gkn1027. DOI
4. Collerton J, Barrass K, Bond J et al. The Newcastle 85+ study: biological, clinical and psychosocial factors associated with healthy ageing: study protocol. BMC Geriatrics. 2007;7(1). doi:10.1186/1471-2318-7-14. DOI
5. Denil S, Rietzschel E, De Buyzere M et al. On Cross-Sectional Associations of Leukocyte Telomere Length with Cardiac Systolic, Diastolic and Vascular Function: The Asklepios Study. PLoS ONE. 2014;9(12):e115071. doi:10.1371/journal.pone.0115071. DOI
6. Medical Statistics 3rd Edition Direct Textbook. 2019. https://www.directtextbook.com/isbn/9781405180511 [Accessed 11 Jule 2019]
7. Ellehoj H, Bendix L, Osler M. Leucocyte Telomere Length and Risk of Cardiovascular Disease in a Cohort of 1,397 Danish Men and Women. Cardiology. 2015;133(3):173-177. doi:10.1159/000441819. DOI
8. Harris SE, Deary IJ, MacIntyre A et al. The association between telomere length, physical health, cognitive ageing, and mortality in non-demented older people. Neurosci Lett. 2006;406(3):260-4. doi:10.1016/j.neulet.2006.07.055. DOI
9. Jin X, Pan B, Dang X et al. Relationship between short telomere length and stroke. Medicine. 2018;97(39):e12489. doi:10.1097/MD.0000000000012489. DOI
10. Khalangot M, Krasnienkov D, Vaiserman A et al. Leukocyte telomere length is inversely associated with post-load but not with fasting plasma glucose levels. Exp Biol Med (Maywood).. 2017;242(7):700-708. doi:10.1177/1535370217694096. DOI
11. Koriath M, Müller C, Pfeiffer N et al. Relative Telomere Length and Cardiovascular Risk Factors. Biomolecules. 2019;9(5):192. doi:10.3390/biom9050192. DOI
12. Olivieri F, Lorenzi M, Antonicelli R et al. Leukocyte telomere shortening in elderly Type2DM patients with previous myocardial infarction. Atherosclerosis. 2009;206(2):588-93. doi: 10.1016/j.atherosclerosis.2009.03.034. DOI
13. Sambrook J, Russell D. Purification of Nucleic Acids by Extraction with Phenol: Chloroform. CSH Protoc. 2006;(1). doi:10.1101/pdb.prot4455. DOI
14. Staerk L, Wang B, Lunetta K et al. Association Between Leukocyte Telomere Length and the Risk of Incident Atrial Fibrillation: The Framingham Heart Study. J Am Heart Assoc. 2017;6(11). doi:10.1161/JAHA.117.006541. DOI

15. Streltsova L, Tkacheva O, Plokhova E et al. Vozrastnyye izmeneniya variabel'nosti serdechnogo ritma i ikh svyaz' s dlinoy telomer leykotsitov. [Age-related changes in heart rate variability and their relation with leucocyte telomere length]. Kardiovaskulyarnaya terapiya i profilaktika. 2017;16(1):54-60. doi:10.15829/1728-8800-2017-1-54-60. (Russian) DOI
16. Toupance S, Labat C, Temmar M et al. Short Telomeres, but Not Telomere Attrition Rates, Are Associated With Carotid Atherosclerosis. Hypertension. 2017;70(2):420-425. doi:10.1161/HYPERTENSIONAHA.117.09354. DOI
17. Valdes AM, Deary IJ, Gardner J et al. Leukocyte telomere length is associated with cognitive performance in healthy women. Neurobiol Aging. 2010;31(6):986-92. doi: 10.1016/j.neurobiolaging.2008.07.012. DOI

CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Maria Cherska
V.P. Komisarenko Institute of Endocrinology and
Metabolism of the NAMS of Ukraine
69 Vyshgorodska st, 04114, Kyiv, Ukraine
e-mail: emariya83@gmail.com

ORCID AND CONTRIBUTIONSHIP

Maria Cherska: 0000-0002-3689-2683 A B C D E F
Khrystyna Kukharchuk: 0000-0002-2495-2693 B D

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

RECEIVED: 08.10.2024
ACCEPTED: 22.10.2025