ORIGINAL ARTICLE

CONTENTS

Efficacy and safety of apixaban versus warfarin in LVAD patients: A propensity-matched analysis

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ABSTRACT

Aim: The primary endpoint was the incidence of major HRAEs. Secondary endpoints included LVAD thrombosis, stroke, major bleeding, non–central nervous system thromboembolism, and all-cause mortality.

Materials and Methods: We conducted a multicenter retrospective cohort study using the TriNetX database, identifying LVAD patients receiving either warfarin or apixaban. Two cohorts were established based on anticoagulation regimen, and propensity score matching was employed to minimize baseline differences.

Results: After matching, 3,129 patients were included in each group. HRAEs occurred less frequently in the apixaban cohort (19.7%) than in the warfarin cohort (28.4%) (OR: 0.618; 95% CI: 0.513–0.744; $P < 0.001$). Apixaban was also associated with significantly fewer LVAD thrombosis events (OR: 0.088), strokes (OR: 0.721), and major bleeding events (OR: 0.528). Rates of non-CNS thromboembolism and all-cause mortality were similar between groups.

Conclusions: Although warfarin remains the standard anticoagulant for LVAD recipients, apixaban demonstrated lower rates of major adverse events in this large retrospective analysis. Further prospective and randomized studies are warranted to confirm these findings and inform future clinical practice.

KEY WORDS: left ventricular assist device (LVAD), heart failure with reduced ejection fraction (HFrEF), anticoagulation, apixaban, warfarin

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INTRODUCTION

Heart failure with reduced ejection fraction (HFrEF) is a prevalent disease, affecting approximately 1–1.5% of the general population and up to 5% of individuals over 65 years of age [1, 2]. The main focus of heart failure treatment is to support the native heart function through medications and devices. However, some end-stage cases require a heart transplant as the native heart function with all available options can not support the survival of the patient anymore [1, 2].

However, donor hearts are limited, and the waiting time can be too long for patients who have reached the terminal stage of heart failure. This challenge led to the development of left ventricular assist devices (LVADs), which were used as a bridge to transplantation at first. [3, 4] LVAD technology has come a long way since its first introduction in the 1960s [4] with the current use of third-generation devices [5]. LVADs today are not only used as a bridge to transplant but also as destination therapy and, in certain patients, as a bridge to myocardial recovery [3, 4].

At the time of introduction of the initial LVADs, there was only one class of oral anticoagulant, which was vitamin K antagonists (VKAs) with warfarin being the most frequently used agent in the class [6]. Warfarin became the standard of treatment for patients with LVADs, due to the absence of other choices and its well-established efficacy [7]. With the introduction of direct oral anticoagulants (DOACs) in 2010, these medications increasingly replaced warfarin in other indications, such as atrial fibrillation and venous thromboembolism [8, 9].

Encouraged by the success of DOACs for other indications, researchers began investigating DOACs as a potential effective anticoagulant in LVAD patients [10, 11]. Studying the effectiveness of anticoagulant therapies is challenging in this group because of the relatively low number of LVAD patients and the complexity of their medical care. Warfarin is the current standard of care in long-

term LVAD patients, and DOACs in this setting are used off-label or experimental [5]. The objective of the current research is to evaluate the efficacy and safety of apixaban as an alternative to warfarin in patients with LVADs.

AIM

This study compared the outcomes of warfarin versus apixaban in patients with LVADs, aiming to address a gap in the existing literature. The primary endpoint was the occurrence of major hemocompatibility-related adverse events (HRAEs). Secondary endpoints included individual elements of the primary endpoint: LVAD thrombosis, stroke, major bleeding, non-central nervous system thromboembolism, and all-cause mortality.

MATERIALS AND METHODS

DATA SOURCE

This study was conducted using the TriNetX research network, a federated database providing access to electronic health records (EHRs) from 154 healthcare organizations (HCOs). 153 healthcare organizations responded with patients. The TriNetX platform aggregates deidentified patient data, ensuring compliance with HIPAA deidentification standards.

PATIENT POPULATION

We conducted a retrospective observational cohort study of adult patients (≥18 years old) with LVADs, stratified by the anticoagulation agent they were given, either apixaban or warfarin. Cohort 1 (apixaban group) included patients with LVADs who were started on apixaban, and Cohort 2 (warfarin group) included patients with LVADs who were started on warfarin. Patients with LVADs were identified using ICD-10 codes, and anticoagulation drugs were confirmed using RxNorm codes for apixaban and warfarin prescriptions. Additional details regarding cohort definition and study window definitions, including the relevant ICD-10, RxNorm, and Current Procedural Terminology codes, are available in the Supplemental Appendix.

STUDY ENDPOINTS

The index event was defined as the first recorded administration of either apixaban or warfarin for patients with LVAD, identified using medication codes RxNorm 1364430 (apixaban) and RxNorm 11289 (warfarin). LVAD was identified based on ICD-10 codes Z95.811. Patients were assigned to cohorts based on the initial anticoagulation agent; those who received apixaban without warfarin were placed in the apixaban cohort, while those who received warfarin without apixaban were placed in the warfarin cohort. The index date, defined as the time of initial anticoagulation agent administration, marked the beginning of the observation window for evaluating outcomes.

The primary outcome of interest was the incidence of major hemocompatibility-related adverse events (HRAEs) after anticoagulation agent initiation. Secondary outcomes included individual elements of the primary outcome: LVAD thrombosis, stroke, major bleeding, non central nervous system thromboembolism, and all cause mortality. The Supplemental Appendix elaborates on outcome definitions and ICD-10 codes.

STATISTICAL ANALYSIS

Continuous variables are presented as mean ± standard deviation (SD), whereas categorical variables are presented as number (percentage), as appropriate. Baseline characteristics were compared between the apixaban and warfarin groups using independent samples Student's t-tests for continuous variables and chi-square tests for categorical variables. To mitigate baseline differences between cohorts, 1:1 propensity score matching was performed using greedy nearest neighbor matching with a caliper of 0.1 times the pooled SD of the linear propensity scores. Variables included in the matching process were age, sex, race, , comorbidities (hypertension, hyperlipidemia, ischemic heart diseases, cerebrovascular diseases, atrial fibrillation and flutter, cardiomyopathy, diabetes mellitus, overweight and obesity, disorders of the thyroid gland, chronic obstructive pulmonary disease (COPD), asthma, chronic kidney disease (CKD), liver diseases, and nicotine dependence), medication use (aspirin, beta blockers and related agents, diuretics, antilipemic agents, and antiarrhythmics) and laboratory result(cholesterol, hemoglobin A1c, iron, ferritin, blood urea nitrogen, and creatinine). The standardized mean difference represents the difference between the means of two groups in terms of SD units, and is used to assess balance in measured variables in the sample weighted by the inverse probability of treatment. Variables were selected based on their potential effect on overall and HRAEs outcomes.

After propensity score matching (PSM), adjusted outcomes were compared between cohorts using hazard ratios (HRs) and 95% confidence intervals (CIs) derived from Cox proportional hazards regression models. Kaplan–Meier survival analysis was used to assess time-to-event outcomes, with differences between cohorts evaluated using the log-rank test. A P-value < 0.05 was considered statistically significant. All statistical

Table 1. Baseline characteristics of patients in apixaban and warfarin groups before and after propensity score matching (PSM)

	Before PSM			After PSM		
	Before Matching (Apixiban group, n=7,219)	Before Matching (Warfarin group, n=4,730)	Standardized Difference	After Matching (Apixiban group, n=3,129)	After Matching (Warfarin group, n=3,129)	Standardized Difference
Demographics						
Current Age (Mean ± SD)	70.5± 13.9	62.5± 15.1	0.551	65.4± 15.3	65.5 ± 13.9	0.003
Age at Index (Mean ± SD)	68.5 ± 14.0	59.4± 15.2	0.622	62.8 ±15.3	62.9 ±13.7	0.004
Female (%)	2,539 (35.2%)	1,279 (27.0%)	0.176	949 (30.3%)	921 (29.4%)	0.020
Male (%)	4,310 (59.7%)	3,277 (69.3%)	0.201	2,040 (65.2%)	2,059 (65.8%)	0.013
White (%)	5,012 (69.4%)	2,759 (58.3%)	0.233	1,953 (62.4%)	1,941 (62.0%)	0.008
Black or African American(%)	1,244 (17.2%	1,256 (26.6%)	0.227	731 (23.4%)	729 (23.3%)	0.002
Comorbid conditions						
Hypertension	6,381 (88.4%)	3,756 (79.4%)	0.246	2,589 (82.7%)	2,579 (82.4%)	0.008
Dyslipidemia	5,700 (79.0%)	3,079 (65.1%)	0.313	2,212 (70.7%)	2,214 (70.8%)	0.001
Cardiomyopathy	3,290 (45.6%)	3,234 (68.4%)	0.473	1,871 (59.8%)	1,880 (60.1%)	0.006
Ischemic heart diseases	5,553 (76.9%)	3,311 (70%)	0.157	2,317 (74.0%)	2,317 (74.0%)	<0.001
Atrial fibrillation and flutter	5,627 (77.9%)	2,790 (59.0%)	0.417	2,062 (65.9%)	2,052 (65.6%)	0.007
Diabetes mellitus	3,421 (47.4%)	2,240 (47.4%)	0.001	1,510 (48.3%)	1,513 (48.4%)	0.002
chronic obstructive pulmonary disease	1,774 (24.6%)	977 (20.7%)	0.094	672 (21.5%)	702 (22.4%)	0.023
Asthma	1,167 (16.2%)	614 (13.0%)	0.090	437 (14.0%)	430 (13.7%)	0.006
Cerebrovascular diseases	2,767 (38.3%)	1,823 (38.5%)	0.004	1,199 (38.3%)	1,170 (37.4%)	0.019
Chronic kidney disease	3,415 (47.3%)	2,413 (51.0%)	0.074	1,533 (49.0%)	1,547 (49.4%)	0.009
Diseases of liver	2,145 (29.7%)	1,554 (32.9%)	0.068	1,053 (33.7%)	1,027 (32.8%)	0.018
Nicotine dependence	1,633 (22.6%)	1,080 (22.8%)	0.005	752 (24.0%)	772 (24.7%)	0.015
Overweight and obesity	3,276 (45.4%)	1,980 (41.9%)	0.071	1,349 (43.1%)	1,342 (42.9%)	0.005
Disorders of thyroid gland	2,131 (29.5%)	1,260 (26.6%)	0.064	857 (27.4%)	813 (26.0%)	0.032
Medication use						
Aspirin	5,641 (78.1%)	3,684 (77.9%)	0.006	2,392 (76.4%)	2,399 (76.7%)	0.005
Beta-blockers	6,219 (86.1%)	3,759 (79.5%)	0.178	2,554 (81.6%)	2,555 (81.7%)	0.001
Diuretics	5,980 (82.8%)	4,130 (87.3%)	0.126	2,712 (86.7%)	2,704 (86.4%)	0.007
Antilipemic agents	5,717 (79.2%)	3,254 (68.8%)	0.239	2,273 (72.6%)	2,315 (74.0%)	0.030
Antiarrhythmics	6,463 (89.5%)	4,013 (84.8%)	0.141	2,708 (86.5%)	2,699 (86.3%)	0.008
Laboratory						
Total cholesterol (md/dL)	145.4 ± 44.7	140.7 ± 45.8	0.104	142.7 ± 45.5	140.9 ± 46.4	0.039
Hemoglobin A1c (%)	6.3 ± 1.5	6.3 ± 1.5	0.005	6.4 ± 1.6	6.3 ± 1.5	0.019
Iron (mcg/dL)	58.6 ±43.9	58.2 ± 43.4	0.010	58.2 ± 44.1	58.7 ± 41.6	0.011
Ferritin (ng/mL)	476.9 ± 2084.2	345.1 ± 713.8	0.085	552.0 ± 2535.0	372.1 ±747.2	0.096
Blood urea nitrogen (mg/dL)	25.8 ± 16.1	25.3 ±15.2	0.032	26.8 ± 17.1	25.8 ±15.5	0.063
Creatinine (mg/dL)	1.5 ±3.0	1.4 ± 2.9	0.017	1.6 ±2.7	1.4 ±1.2	0.079

Source: Compiled by the authors of this study

analyses were conducted using integrated R (The R Foundation) within the TriNetX platform.

ETHICS APPROVAL

This study was conducted using de-identified data from the TriNetX research network. In accordance with U.S. federal regulations, studies using only de-identified data are not considered human subjects research and are exempt from institutional review board (IRB) approval. TriNetX, LLC has received a waiver from the Western IRB and complies with the Health Insurance Portability and Accountability Act (HIPAA), with de-identification confirmed through a qualified expert

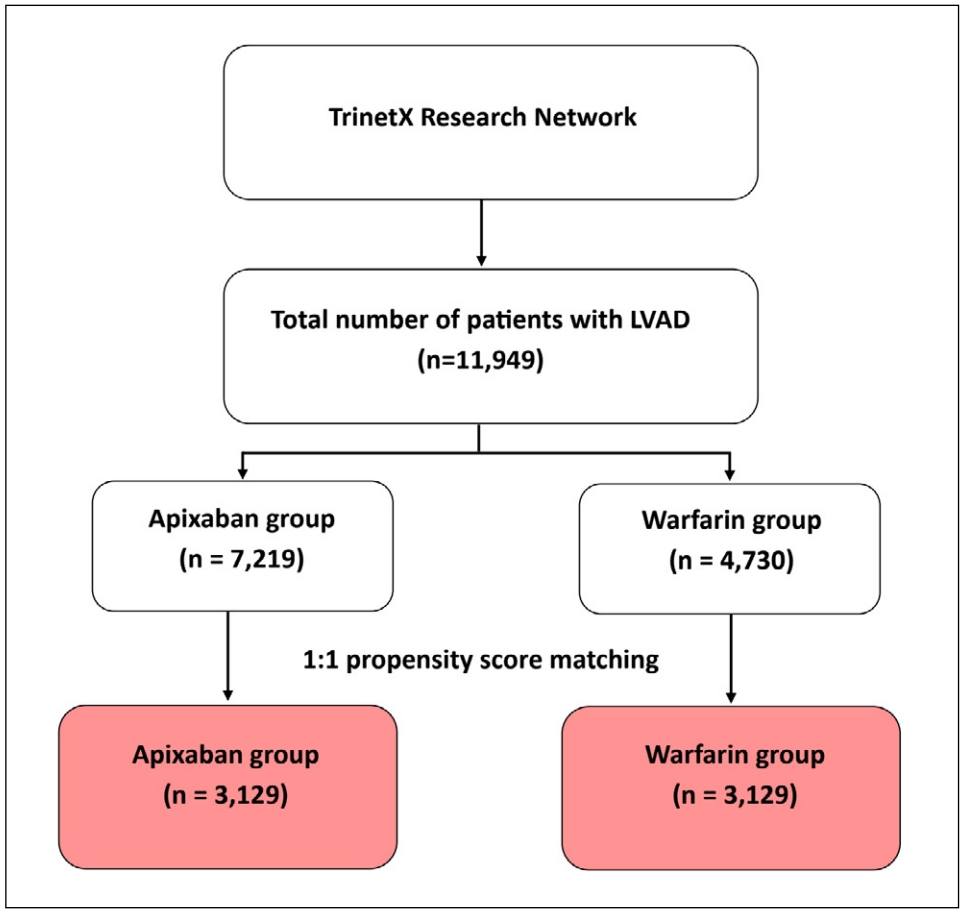

Fig. 1. Flow diagram of patient selection and cohort derivation following propensity score matching.
Source: Own materials

determination as defined in Section §164.514(b)(1) of the HIPAA Privacy Rule.

RESULTS

STUDY POPULATION

This retrospective cohort study identified a total of 11,949 patients with LVAD who were receiving apixaban or warfarin. Among them, 7,219 patients received apixaban , and 4,730 patients received warfarin. After applying 1:1 propensity score matching (PSM) to balance baseline characteristics, 3,129 patients were included in each cohort (apixaban and warfarin groups) for the final analysis (Fig. 1).

PATIENT CHARACTERISTICS

The baseline characteristics of the study cohorts, before and after propensity score matching (PSM), are shown in Table 1. In the unmatched cohort, patients receiving apixaban were slightly older at index (mean age:68.5 ± 14.0 years *vs.* 59.4 ± 15.2 years, $P < 0.001$) compared to those receiving warfarin. The proportion of male patients was slightly lower in the apixaban group (59.7%% vs. 69.3%, $P < 0.001$), while the apixaban group had a higher proportion of female patients (35.2% *vs.* 27.0%, $P < 0.001$). Regarding racial distribution, the apixaban group was more likely to be white (69.4% *vs.* 58.3%) compared to the warfarin group, while black or affrican american more in warfarin group comparing to apixaban group (26.6% *vs.* 17.2%, $P < 0.001$).

Before matching, the apixaban group exhibited a higher prevalence of hypertension (88.4% *vs.* 79.4%, $P < 0.001$), ischemic heart disease (76.9% *vs.* 70.0%, $P < 0.001$), atrial fibrillation and flutter (77.9% *vs.*59.0%, $P < 0.001$), overweight and obesity (45.4% *vs.* 41.9%, $P < 0.001$), thyroid gland disease (29.5% *vs.* 26.6%, $P < 0.001$), chronic obstructive pulmonary disease (24.6% *vs.* 20.7%, $P < 0.001$), asthma (16.2% *vs.* 13.0%, $P < 0.001$), hyperlipidemia (79.0% *vs.* 65.1%, $P < 0.001$), and conversely, cardiomyopathy (68.4% *vs.* 45.6%, $P < 0.001$), chronic kidney disease (51.0% *vs.* 47.3%, $P < 0.001$), diseases of liver (32.9% *vs.* 29.7%, $P < 0.001$) were more frequently observed in the warfarin group while cerebrovascular diseases, diabetes mellitus and nicotine dependence were almost the same in the two groups.

After propensity score matching (PSM), the two cohorts were well balanced across key baseline characteristics, including age, sex, race, medications, laboratory results, and comorbidities, with standardized mean differences (SMDs) < 0.1 for most variables, indicating

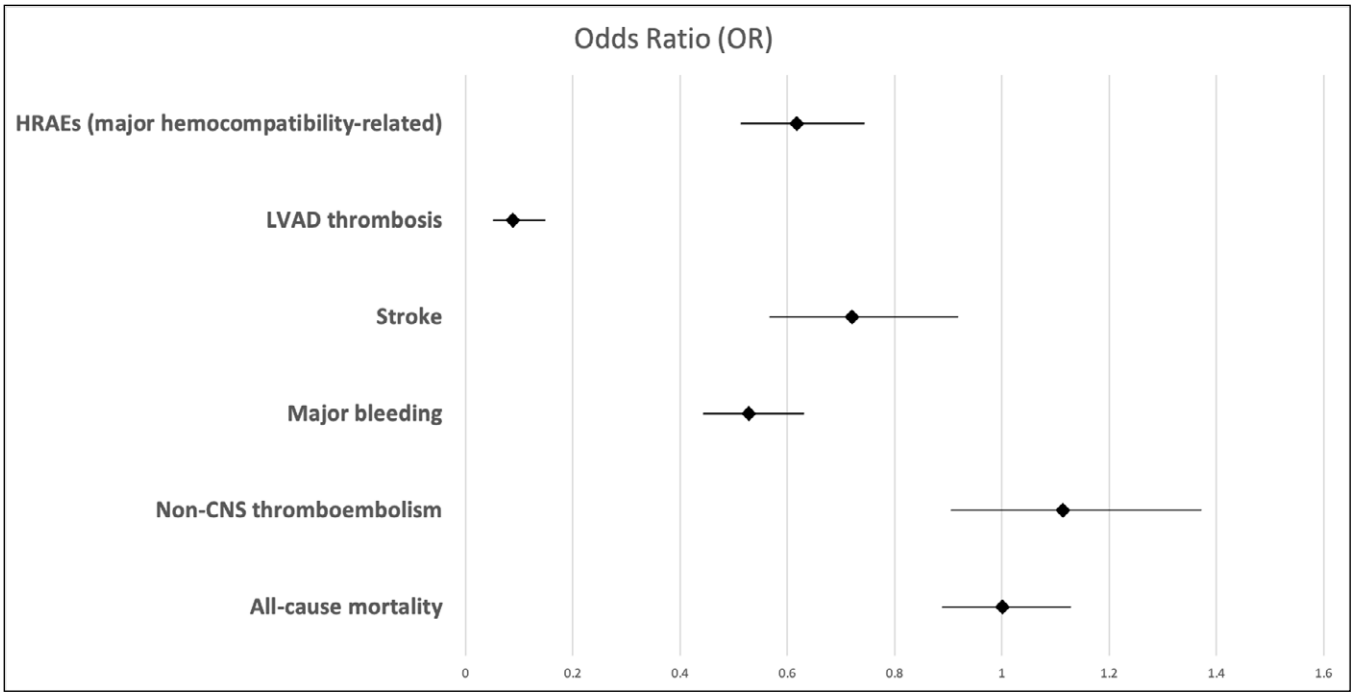

Fig. 2. Forest plot of primary and secondary clinical outcomes: apixaban *vs.* warfarin in lvad patients
Source: Own materials

a well-matched cohort. The final matched cohort consisted of 3,129 patients in the apixaban group and 3,129 patients in the warfarin group.

PRIMARY ENDPOINT: MAJOR HEMOCOMPATIBILITY-RELATED ADVERSE EVENTS (HRAES)

After matching, during the follow-up period, a total of 374 patients (28.4%) in the warfarin cohort experienced major hemocompatibility-related adverse events, compared to 234 patients (19.7%) in the apixaban cohort. Receiving apixaban was associated with a significantly lower risk of HRAEs (OR: 0.618; 95% CI: 0.513 - 0.744; P < 0.001). Kaplan–Meier survival analysis revealed a significantly lower incidence of new-onset atrial fibrillation in the apixaban group compared to the warfarin group (log-rank P < 0.001). The hazard ratio for having HRAEs was 0.649 (95% CI: 0.551-0.765), indicating that patients receiving warfarin had more risk of developing HRAEs relative to those receiving apixaban. The proportional hazards assumption was not violated ($P = 0.001$) (Table 2, Fig. 2).

Secondary endpoints: LVAD thrombosis, stroke, major bleeding events, non-central nervous system thromboembolism, and all-cause mortality

After matching, the secondary outcomes demonstrated significant differences between the apixaban group and the warfarin group. LVAD thrombosis events were less frequently reported in the apixaban group, with an odds ratio (OR) of 0.088 (95% CI: 0.051–0.149, $P < 0.001$), and a hazard ratio of 0.094 (95% CI: 0.055–0.159). Stroke was also less frequently reported in the apixaban group, with an OR of 0.721 (95% CI: 0.567–0.918, $P = 0.008$), and a hazard ratio of 0.775 (95% CI: 0.613–0.980). Major bleeding events were less commonly reported in the apixaban group, with an OR of 0.528 (95% CI: 0.443–0.631, $P < 0.001$), and a hazard ratio of 0.557 (95% CI: 0.473–0.657). non-central nervous system thromboembolism events showed no difference between the two groups, with an OR of 1.114 (95% CI: 0.905–1.372, $P = 0.308$), and a hazard ratio of 1.153 (95% CI: 0.946–1.406). All cause mortality showed no difference between the two group OR of 1.001 (95% CI: 0.888–1.129, $P = 0.987$), and the hazard ratio was 1.072 (95% CI:0.964–1.192) (Table 2, Fig. 2).

DISCUSSION

Warfarin has been the standard anticoagulant since the introduction of LVADs. At the time of LVAD development in the 1960s, warfarin was the only oral anticoagulant available. [12] With the emergence of DOACs in 2010s as an alternative to warfarin in nonvalvular atrial fibrillation, their use for anticoagulation in other indications has been extensively investigated. [13] This interest was driven by the simpler clinical use of these medications, without the need for INR monitoring, and the possibility of a lower incidence of bleeding and/or a better protective effect against thrombosis.

Although apixaban lacks the extensive evidence supporting its use in LVAD patients, it has been used on a case-by-case basis. In this large multicenter retrospec-

Table 2. Primary and secondary clinical outcomes: Apixaban *vs.* warfarin in LVADs patients

Outcome	Risk of Event, % (Apixaban group)	Risk of Event, % (Warfarin group)	Odds Ratio (95% CI)	P Value
Primary Outcome				
Major Hemocompatibility-Related Adverse Events (HRAEs)	234 (19.7%)	374 (28.4%)	0.618 (0.513 – 0.744)	P < 0.001
Secondary Outcome				
LVAD thrombosis	15 (0.5%)	152 (5.3%)	0.088 (0.051 – 0.149)	P < 0.001
Stroke	120 (4.8%)	168 (6.5%)	0.721 (0.567 – 0.918)	P = 0.008
Major bleeding	231 (10.5%)	368 (18.2%)	0.528 (0.443 – 0.631)	P < 0.001
Non-central nervous system thromboembolism	192 (10.0%)	200 (9.1%)	1.114 (0.905 – 1.372)	P = 0.308
All cause mortality	679 (21.9%)	680 (21.9%)	1.001 (0.888 – 1.129)	P = 0.987
Values are n (%)				

Source: Compiled by the authors of this study

tive cohort study, we aimed to investigate apixaban as a potential oral anticoagulant for patients with LVADs.

In the DOT-HM3 study, Netuka et al. (2024) demonstrated the feasibility of using a direct oral anticoagulant, with or without aspirin, in patients chronically supported with an HM3 LVAD for six months [10]. In the DOAC LVAD study, Mehta et al. (2025) found no statistically significant differences between warfarin and apixaban in the incidence of death, stroke, device thrombosis, major gastrointestinal bleeding, aortic root thrombus, or arterial non-CNS thromboembolism [11].

The results of our study suggest that apixaban is more effective in preventing major hemocompatibility-related adverse events, defined as a composite of LVAD thrombosis, stroke, major bleeding, non-central nervous system thromboembolism, and all-cause mortality. These findings do not suggest that apixaban is an equivalent alternative to warfarin, but they suggest that it may be a superior anticoagulation option for LVAD patients.

A major limitation across all previous studies investigating anticoagulation in LVAD patients is the small sample size. In our large multicenter retrospective cohort, we included 6,258 patients after propensity score matching. The statistical power of the analysis was substantially increased, enabling the detection of differences that smaller previous studies were unable to identify.

The results were further analyzed according to secondary endpoints. LVAD thrombosis was notably less frequent in the Apixaban cohort compared to the Warfarin cohort. Previous randomized controlled trials (DOT-HM3 study and DOAC LVAD study) [10, 11] were underpowered to detect this rare complication; both arms in these trials reported zero cases of pump thrombosis. While these results suggest that both anticoagulants are generally safe regarding pump thrombosis, they do not provide definitive evidence as to which agent is superior in this regard. In our study, there was a large difference between two groups with an odds ratio (OR) of 0.088, indicating a potentially better safety profile for apixaban compared to warfarin.

The incidence of stroke was lower in the apixaban group compared to the warfarin group, with an odds ratio of 0.721. Similarly, major bleeding events were less frequently reported in the apixaban group, with an OR of 0.528. These findings are not only statistically significant, but also clinically significant as they could represent a breakthrough in the management of LVAD patients. The previous RCTs and retrospective studies did not show a similar effect on LVAD patients, which can be attributed to the small size of the sample.

Although prior RCTs were unable to establish this relationship in LVAD patients, the use of warfarin was compared against apixaban for the prevention of thromboembolic events in atrial fibrillation In the ARISTOTLE study, Granger et al. (2011) demonstrated that apixaban was superior to warfarin in reducing the risk of stroke or systemic embolism in patients with atrial fibrillation, while also showing a lower risk of major bleeding [9]. These results align with our findings, supporting the notion that apixaban may offer a more favorable safety profile without compromising efficacy. Taken together, both the reduced incidence of stroke and major bleeding suggest that apixaban could be a preferable anticoagulant option, particularly in LVAD patients who are at higher risk for bleeding complications and thromboembolic events.

Our study found no significant differences between the two groups in non–central nervous system thromboembolic events or all-cause mortality, consistent with previous RCTs [11, 10] and the most recently published systematic review [14].

STUDY LIMITATION

Our study involved a large number of patients and used propensity score matching to balance baseline characteristics between the two cohorts and reduce confounding. But, Our study was conducted using the TriNetX database, which identifies diagnoses according to ICD codes. This system is susceptible to coding errors by its nature and unable to determine medication dose and adherence. Although this study was unable to quantify the potential effect of previously mentioned limitations on the study findings, the two cohorts would likely be affected similarly, minimizing the effects on outcomes.

Furthermore, since it is a retrospective cohort study, our analysis is constrained by the nature of observational data, as they are unable to establish causal relationships due to potential residual confounding and selection bias in addition to unmeasured variables. While they can identify associations and generate hypotheses, retrospective designs do not provide the same level of evidence provided by prospective, randomized trials and are therefore limited in their ability to generate fully informative or definitive conclusions.

CONCLUSIONS

In conclusion, this large retrospective study found that using apixaban in LVAD patients was associated with a lower incidence of major hemocompatibility-related adverse events, including LVAD thrombosis, stroke, and major bleeding. These findings suggest that apixaban could potentially be a safer option than warfarin. A safer anticoagulant can improve overall LVAD safety and could shift clinical practice toward using apixaban as a preferred anticoagulant in LVAD patients. However, due to the limitations of retrospective studies, it is important to interpret these results carefully. Large randomized clinical trials are necessary to confirm these findings.

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AVAILABILITY OF DATA AND MATERIALS

The data supporting the findings of this study are available through the TriNetX research network but are subject to licensing restrictions. Access to TriNetX data can be obtained upon reasonable request and with permission from TriNetX, LLC.

CONFLICT OF INTEREST

The Authors declare no conflict of interest

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APPENDIX A – TEXT REPRESENTATION OF THE COHORTS DEFINITION

This section lists all terms used in the definitions of the two cohorts.

Query Criteria for Cohort 1 (Apixaban)

Patients must have:
Age (Age) (at least 18 years (most recent occurrence).
Patients cannot have:
- Warfarin (NLM:RXNORM:11289).
All the following must be satisfied:
- Apixaban: The terms in this group occurred between Sep 10, 2020 and Sep 10, 2025
- Patients must have all of the following:
- Presence of heart assist device (UMLS:ICD10CM:Z95.811); and
- Apixaban (NLM:RXNORM:1364430).

Query Criteria for Cohort 2 (warfarin)

Patients must have:
- Age (Age) (at least 18 years (most recent occurrence).
Patients cannot have:
- Apixaban (NLM:RXNORM:1364430).
All the following must be satisfied:
- Warfarin: The terms in this group occurred between Sep 10, 2020 and Sep 10, 2025
Patients must have all of the following:
- Presence of heart assist device (UMLS:ICD10CM:Z95.811); and
- Warfarin (NLM:RXNORM:11289).

APPENDIX B – TEXT REPRESENTATION OF THE ANALYSIS SETUP

This section contains the Index Event definition for each cohort.
The index event for Cohort 1 (Apixaban) is defined as the following:
All the following must be satisfied:
- Apixaban: The terms in this group occurred between Sep 10, 2020 and Sep 10, 2025
Patients must have all of the following:
- Presence of heart assist device (UMLS:ICD10CM:Z95.811); and
- Apixaban (NLM:RXNORM:1364430).
The index event for Cohort 2 (warfarin) is defined as the following:
All the following must be satisfied:
- Warfarin: The terms in this group occurred between Sep 10, 2020 and Sep 10, 2025
Patients must have all of the following:

- Presence of heart assist device (UMLS:ICD10CM:Z95.811); and
- Warfarin (NLM:RXNORM:11289).

APPENDIX C – TEXT REPRESENTATION OF THE OUTCOMES DEFINITION

This analysis includes the following outcomes: major hemocompatibility-related adverse events (HRAEs)

Patients must have any of the following:

- Thrombosis due to cardiac prosthetic devices, implants and grafts (UMLS:ICD10CM:T82.867); or
- Thrombosis due to cardiac prosthetic devices, implants and grafts, initial encounter (UMLS:ICD10CM:T82.867A); or
- Thrombosis due to cardiac prosthetic devices, implants and grafts, subsequent encounter (UMLS:ICD10CM:T82.867D); or
- Thrombosis due to cardiac prosthetic devices, implants and grafts, sequela (UMLS:ICD10CM:T82.867S); or
- Cerebral infarction (UMLS:ICD10CM:I63); or
- Hemorrhage, not elsewhere classified (UMLS:ICD10CM:R58); or
- Gastrointestinal hemorrhage, unspecified (UMLS:ICD10CM:K92.2); or
- Hemorrhage from respiratory passages (UMLS:ICD10CM:R04); or
- Nontraumatic intracranial hemorrhage, unspecified (UMLS:ICD10CM:I62.9); or
- Gross hematuria (UMLS:ICD10CM:R31.0); or
- Other abnormal uterine and vaginal bleeding (UMLS:ICD10CM:N93); or
- Embolism and thrombosis of thoracic aorta (UMLS:ICD10CM:I74.11); or
- Pulmonary embolism with acute cor pulmonale (UMLS:ICD10CM:I26.0); or
- Pulmonary embolism without acute cor pulmonale (UMLS:ICD10CM:I26.9); or
- Embolism and thrombosis of abdominal aorta (UMLS:ICD10CM:I74.0); or
- Embolism and thrombosis of other and unspecified parts of aorta (UMLS:ICD10CM:I74.1); or
- Embolism and thrombosis of arteries of the upper extremities (UMLS:ICD10CM:I74.2); or
- Embolism and thrombosis of arteries of the lower extremities (UMLS:ICD10CM:I74.3); or
- Embolism and thrombosis of arteries of extremities, unspecified (UMLS:ICD10CM:I74.4); or
- Embolism and thrombosis of iliac artery (UMLS:ICD10CM:I74.5); or
- Embolism and thrombosis of other arteries (UMLS:ICD10CM:I74.8); or
- Embolism and thrombosis of unspecified artery (UMLS:ICD10CM:I74.9); or
- Other venous embolism and thrombosis (UMLS:ICD10CM:I82).

LVAD thrombosis

Patients must have any of the following:

- Thrombosis due to cardiac prosthetic devices, implants and grafts (UMLS:ICD10CM:T82.867); or

- Thrombosis due to cardiac prosthetic devices, implants and grafts, initial encounter (UMLS:ICD10CM:T82.867A); or
- Thrombosis due to cardiac prosthetic devices, implants and grafts, subsequent encounter (UMLS:ICD10CM:T82.867D); or
- Thrombosis due to cardiac prosthetic devices, implants and grafts, sequela (UMLS:ICD10CM:T82.867S).

Stroke

Patients must have:

- Cerebral infarction (UMLS:ICD10CM:I63).

Major bleeding

Patients must have any of the following:

- Gastrointestinal hemorrhage, unspecified (UMLS:ICD10CM:K92.2); or
- Hemorrhage, not elsewhere classified (UMLS:ICD10CM:R58); or
- Hemorrhage from respiratory passages (UMLS:ICD10CM:R04); or
- Nontraumatic intracranial hemorrhage, unspecified (UMLS:ICD10CM:I62.9); or
- Gross hematuria (UMLS:ICD10CM:R31.0); or
- Other abnormal uterine and vaginal bleeding (UMLS:ICD10CM:N93).

Non-central nervous system thromboembolism

Patients must have any of the following:

- Pulmonary embolism with acute cor pulmonale (UMLS:ICD10CM:I26.0); or
- Pulmonary embolism without acute cor pulmonale (UMLS:ICD10CM:I26.9); or
- Embolism and thrombosis of abdominal aorta (UMLS:ICD10CM:I74.0); or
- Embolism and thrombosis of other and unspecified parts of aorta (UMLS:ICD10CM:I74.1); or
- Embolism and thrombosis of arteries of the upper extremities (UMLS:ICD10CM:I74.2); or
- Embolism and thrombosis of arteries of the lower extremities (UMLS:ICD10CM:I74.3); or
- Embolism and thrombosis of arteries of extremities, unspecified (UMLS:ICD10CM:I74.4); or
- Embolism and thrombosis of iliac artery (UMLS:ICD10CM:I74.5); or
- Embolism and thrombosis of other arteries (UMLS:ICD10CM:I74.8); or
- Embolism and thrombosis of unspecified artery (UMLS:ICD10CM:I74.9); or
- Other venous embolism and thrombosis (UMLS:ICD10CM:I82); or
- Embolism and thrombosis of thoracic aorta (UMLS:ICD10CM:I74.11).

All cause mortality

Patients must have:

- Deceased (Deceased).