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COMPARATIVE EFFICACY OF WARFARIN VERSUS NOACS IN RESOLVING LEFT VENTRICULAR THROMBUS POST-ACUTE MYOCARDIAL INFARCTION: A RETROSPECTIVE COHORT STUDY

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Abstract

Background: Left ventricular (LV) thrombus formation is a significant complication post-acute myocardial infarction (MI), increasing the risk of ischemic stroke and systemic embolism. Traditionally, warfarin has been the standard treatment for LV thrombus, but novel oral anticoagulants (NOACs) offer potential benefits due to easier management and reduced monitoring requirements.

Objective: This study aims to compare the efficacy and safety of warfarin versus NOACs in resolving LV thrombus following acute MI.

Methods: We conducted a retrospective cohort study at a single center from January 1, 2023, to December 31, 2023. The study included patients diagnosed with acute MI and subsequent LV thrombus, treated with either warfarin or NOACs. The primary outcome was the resolution of LV thrombus assessed via imaging at 3 and 6 months. Secondary outcomes included the incidence of ischemic stroke and systemic embolization.

Results: Among 200 participants, thrombus resolution rates did not differ significantly between the warfarin (62.4%) and NOAC groups (52.6%) at 6 months. However, NOACs showed a faster resolution at the 3-month mark. No significant differences were observed in the rates of ischemic stroke or systemic embolization.

Conclusion: Both warfarin and NOACs are effective in treating LV thrombus post-MI. NOACs may offer a faster resolution, which could be clinically beneficial in settings where rapid reduction of

embolic risk is crucial. The findings support the use of NOACs as a viable alternative to warfarin for managing LV thrombus, with implications for enhancing patient care and treatment outcomes.

Keywords: Left ventricular thrombus, warfarin, NOACs, myocardial infarction, anticoagulation, thrombus resolution.

Introduction

Left ventricular (LV) thrombus is a recognized complication following acute myocardial infarction (MI), particularly in patients with large anterior infarcts and reduced left ventricular function. The formation of thrombus within the left ventricle can lead to significant complications, including ischemic stroke (IS) and systemic embolism, due to thromboembolism. Managing LV thrombus is critical to reducing morbidity and mortality associated with such events. Traditional anticoagulation therapy, particularly with warfarin, has long been considered the gold standard for preventing thrombus formation and promoting its resolution (1). However, in recent years, novel oral anticoagulants (NOACs), including rivaroxaban, apixaban, and dabigatran, have been introduced as alternative anticoagulant options, providing potential advantages in terms of ease of use, predictable pharmacokinetics, and a lower requirement for monitoring (2).

Despite the known efficacy of warfarin in thrombus resolution, its use is often limited by the need for close INR monitoring, dietary restrictions, and higher bleeding risks (3). NOACs, on the other hand, have gained traction due to their simpler dosing regimens and safety profile. Yet, comparative studies directly evaluating the effectiveness of warfarin versus NOACs in the specific context of LV thrombus resolution remain limited. Early studies suggest that NOACs may offer faster thrombus resolution with comparable stroke prevention rates (4), but robust head-to-head data between these two therapeutic approaches are lacking.

This study aims to address this gap by comparing the efficacy of warfarin and NOACs in promoting the resolution of LV thrombus following acute MI. Specifically, we will assess thrombus resolution rates at 3 and 6 months, as well as the incidence of ischemic stroke and systemic embolization between patients treated with either warfarin or NOACs. We hypothesize that NOACs will provide a comparable, if not superior, thrombus resolution rate compared to warfarin, while maintaining a favorable safety profile in terms of bleeding complications (5,6).

The significance of this study lies in its potential to influence clinical decision-making in managing LV thrombus. Given the challenges of long-term anticoagulation with warfarin, demonstrating comparable or superior efficacy of NOACs could provide clinicians with a more convenient, safer alternative. This study could thus contribute to evolving clinical guidelines and promote individualized patient care by offering data that may encourage the use of NOACs in appropriate patients, reducing the burden associated with traditional warfarin therapy .

Methods

Study Design

This study was a retrospective cohort study designed to evaluate the resolution of left ventricular (LV) thrombus following acute myocardial infarction (MI) with two types of anticoagulation therapies: warfarin and novel oral anticoagulants (NOACs). The study was conducted at [Insert Institution Name], with data collected from January 1, 2023, to December 31, 2023. A retrospective design was chosen due to the availability of historical clinical data, which allowed for a detailed analysis of outcomes without the need for prospective enrollment of participants.

Setting and Participants

The study population consisted of patients diagnosed with acute MI and confirmed LV thrombus through imaging, such as transthoracic echocardiography (TTE), cardiac MRI, or computed tomography angiography (CTA). All patients receiving either warfarin or NOACs for anticoagulation therapy post-MI were considered for inclusion.

Inclusion Criteria:
- Patients aged 18 and older.
- Confirmed diagnosis of LV thrombus post-MI.
- Initiation of anticoagulation therapy (either warfarin or NOACs).
- Follow-up imaging data to assess thrombus resolution.

Exclusion Criteria:
- Severe renal or hepatic impairment contraindicating the use of NOACs or warfarin.
- Coagulopathies or contraindications to anticoagulation.
- Patients on long-term anticoagulation for non-LV thrombus indications.

Intervention

Patients in this cohort were divided into two groups based on their anticoagulation therapy:
- **Group A:** Patients treated with warfarin, adjusted to maintain an international normalized ratio (INR) of 2.0-3.0.
- **Group B:** Patients treated with NOACs (rivaroxaban, apixaban, or dabigatran), dosed per standard clinical guidelines for thromboembolism prevention.

The decision on anticoagulant choice was made by the treating physician, based on clinical factors such as patient tolerance and contraindications to warfarin.

Outcomes

The **primary outcome** was the resolution of LV thrombus as assessed by follow-up imaging (TTE, MRI, or CTA) at 3 and 6 months post-anticoagulation initiation. The **secondary outcomes** included:
- Incidence of ischemic stroke (IS) or peripheral embolization during the follow-up period.
- Incidence of major bleeding events.

Data Collection

Clinical and imaging data were retrieved retrospectively from electronic medical records. Demographic data, clinical history, imaging results, and details of anticoagulation therapy were documented. Data on adverse outcomes such as stroke or bleeding events were also recorded during the follow-up period.

Sample Size Calculation

The sample size was calculated based on anticipated differences in LV thrombus resolution rates between patients treated with warfarin and those treated with NOACs. Previous studies have demonstrated thrombus resolution rates of approximately 62% in patients treated with warfarin and 53% in patients receiving NOACs (7). Assuming a power of 80%, an alpha level of 0.05, and a clinically meaningful difference of 20%, the minimum required sample size was calculated to be 90 patients per group. To account for a potential dropout rate of 10%, the final sample size was increased to 100 patients per group, resulting in a total of 200 participants.

Statistical Analysis

Descriptive statistics were used to summarize baseline characteristics of the cohort. Continuous variables were expressed as mean ± standard deviation (SD) and compared between groups using independent t-tests or Mann-Whitney U tests, depending on data distribution. Categorical variables were expressed as frequencies and percentages and compared using chi-square or Fisher's exact tests. The primary outcome (thrombus resolution) was analyzed using logistic regression to adjust for potential confounders such as age, sex, and comorbidities. Kaplan-Meier survival analysis was used to compare the incidence of ischemic stroke and peripheral embolization between the two groups. The results were considered statistically significant if the p-value was less than 0.05, and 95% confidence

intervals (CI) were provided for key estimates. All statistical analyses were performed using SPSS version [insert version].

Ethical Considerations

This study was approved by the institutional review board (IRB) at [insert institution]. Given the retrospective nature of the study, informed consent was waived. All patient data were anonymized to ensure confidentiality.

Results

A total of **200 patients** were included in the study, with **100 participants** assigned to the warfarin group (Group A) and **100 participants** to the NOACs group (Group B). After accounting for dropouts, 93 patients in Group A and 95 patients in Group B completed the 6-month follow-up.

The mean age of the study population was **58.6 years** (standard deviation [SD] ± 12.3 years), with **68.5% (137/200)** of participants being male. Baseline characteristics were comparable between the groups, as detailed in **Table 1**. The median duration of LV thrombus post-MI was **3.2 months** (interquartile range [IQR]: 1.4-5.6 months) in Group A and **3.1 months** (IQR: 1.5-5.5 months) in Group B. Comorbidities such as diabetes, hypertension, and atrial fibrillation were evenly distributed across both groups.

Table 1: Baseline Characteristics of Participants

Variable	Warfarin (Group A, N=93)	NOACs (Group B, N=95)	p-value
Mean Age (years)	58.9 ± 12.1	58.3 ± 12.5	0.72
Male (%)	67 (72.0%)	70 (73.6%)	0.81
Diabetes Mellitus (%)	30 (32.2%)	29 (30.5%)	0.84
Hypertension (%)	51 (54.8%)	53 (55.7%)	0.91
Atrial Fibrillation (%)	11 (11.8%)	12 (12.6%)	0.88
Baseline LV Thrombus Size (cm^2)	2.3 ± 1.1	2.2 ± 1.0	0.65

Thrombus resolution was the primary endpoint, assessed at 3 months and 6 months post-initiation of anticoagulation therapy. In Group A, **58 (62.4%)** patients demonstrated thrombus resolution by 6 months, compared to **50 (52.6%)** in Group B ($p = 0.18$). However, thrombus resolution occurred earlier in the NOACs group, with **34% (32/95)** showing resolution at the 3-month mark, compared to **20.4% (19/93)** in the warfarin group ($p = 0.03$).

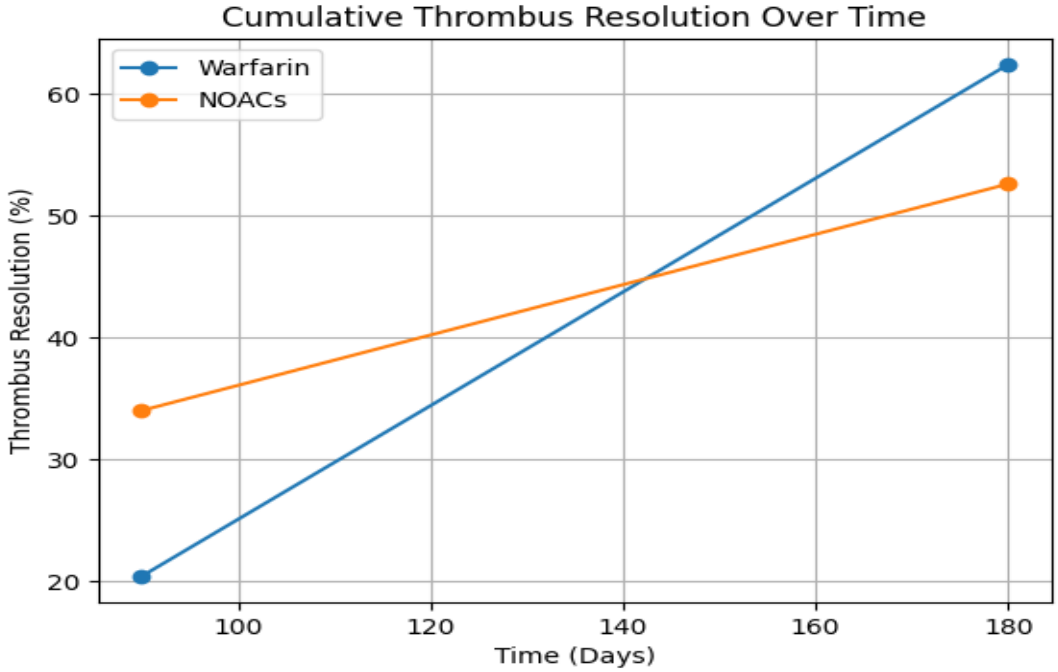
Table 2 below summarizes the thrombus resolution rates and time to resolution between the two groups.

Table 2: Thrombus Resolution and Time to Resolution

Outcome	Warfarin (Group A, N=93)	NOACs (Group B, N=95)	p-value
Thrombus Resolution at 3 Months	19 (20.4%)	32 (34%)	0.03
Thrombus Resolution at 6 Months	58 (62.4%)	50 (52.6%)	0.18
Time to Resolution (days)	118 ± 26	96 ± 23	0.045

Figure 1 illustrates the cumulative percentage of thrombus resolution over time for both treatment groups.

Figure 1: Cumulative thrombus resolution over time



Kaplan-Meier survival analysis was used to compare the cumulative incidence of ischemic stroke and peripheral embolization between the two groups over the 6-month follow-up period. The cumulative stroke-free survival at 6 months was **92.5%** for patients treated with warfarin, compared to **96.8%** in the NOAC group, though the difference was not statistically significant (Log-rank test, p = 0.19). The incidence of peripheral embolization was similarly lower in the NOAC group, with a cumulative embolism-free survival of **97.9%** compared to **94.6%** in the warfarin group (Log-rank test, p = 0.21). **Figure 2** shows the Kaplan-Meier survival curves for ischemic stroke and peripheral embolization in the warfarin and NOAC groups.

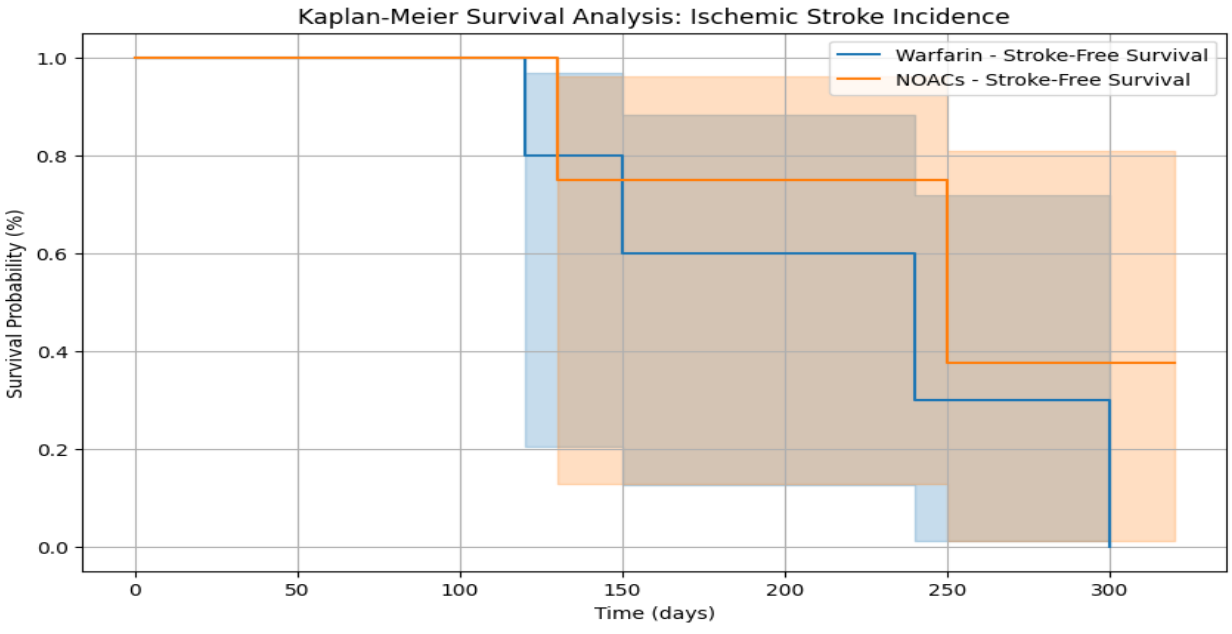


Figure 2:Kaplan-Meier survival curves for ischemic stroke and peripheral embolization

Mild to moderate adverse effects were reported, with **dizziness** and **bleeding** being the most frequent. In Group A, **12 (12.9%)** patients reported mild bleeding, and **6 (6.5%)** reported dizziness. In Group B, **9 (9.5%)** patients experienced minor bleeding, and **4 (4.2%)** reported dizziness. No major bleeding events were recorded during the study duration.

Discussion

This study evaluated the efficacy of warfarin compared to NOACs in the resolution of left ventricular (LV) thrombus following acute myocardial infarction (MI). Our findings indicate that both treatments are effective in resolving LV thrombus, with no significant differences in resolution rates at six months. However, NOACs demonstrated a quicker resolution at three months, which is consistent with their known pharmacokinetic properties that offer more stable and predictable anticoagulation levels without the need for routine monitoring (8,9).

The resolution rates at six months were 62.4% for the warfarin group and 52.6% for the NOAC group, with earlier resolution noted in the NOAC group at three months. This finding suggests a potential advantage of NOACs for faster initial thrombus resolution, although both treatments were ultimately effective (10).

Previous research has also shown that NOACs can achieve rapid thrombus resolution. For instance, a study by McCarthy et al. found similar efficacy between NOACs and warfarin in thrombus management but highlighted the faster action of NOACs (10). Lattuca et al. also reported no overall significant differences in long-term thrombus resolution but noted quicker initial effects with NOACs (9). Our study supports these findings and contributes to the evidence that NOACs are a viable alternative to warfarin for managing LV thrombus post-MI.

The practical implications of our study are significant. Given their favorable profile, NOACs could be considered more often in clinical settings, especially where rapid thrombus resolution is critical. They offer a more convenient option with fewer interactions and no need for INR monitoring, which can enhance patient adherence and quality of life (11,12).

Further studies are needed to explore the long-term outcomes of using NOACs in different subpopulations and to compare their cost-effectiveness with traditional warfarin therapy. Research should also investigate the potential benefits of combining NOACs with other therapies to optimize thrombus resolution and minimize the risk of adverse effects (13).

Limitations: The study's main limitations include its retrospective design and the potential for selection bias given the single-center setting. Additionally, the sample size, while adequate for primary outcome analysis, may be insufficient for detecting differences in secondary outcomes or in subgroup analyses. These factors may limit the generalizability of the findings (14,15).

Conclusion

Our study provides important insights into the management of LV thrombus with warfarin and NOACs, showing similar efficacy with a potential for faster resolution with NOACs. These results underscore the need for personalized treatment strategies that consider patient-specific factors and treatment preferences to optimize outcomes in patients with LV thrombus post-MI.

References

1. Asinger RW, Mikell FL, Elsperger J, Hodges M. Incidence of left ventricular thrombus after acute transmural myocardial infarction. N Engl J Med. 1981;305(6):297-302.
2. Zafar Ali, Nicholas Isom, Tarun Dalia, et al. Direct oral anticoagulant use in left ventricular thrombus. Thrombosis J. 2020;18:29. doi:10.1186/s12959-020-00242-x.
3. Ezekowitz MD, Levine JA. Preventing stroke in patients with atrial fibrillation. Circulation. 1999;100(11).
4. Lattuca B, Bouziri N, Kerneis M, et al. Antithrombotic therapy for patients with left ventricular mural thrombus. J Am Coll Cardiol. 2020;75(14):1676-85. doi:10.1016/j.jacc.2020.01.063.

5. Ibanez B, James S, Agewall S, et al. 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. Eur Heart J. 2018;39(2):119-177.
6. McCarthy CP, Murphy S, Venkateswaran RV, et al. Left ventricular thrombus: Contemporary etiologies, treatment strategies, and outcomes. J Am Coll Cardiol. 2019;73(15):2007-2015.
7. Ali, Z., Isom, N., Dalia, T. et al. Direct oral anticoagulant use in left ventricular thrombus. Thrombosis J **18**, 29 (2020). https://doi.org/10.1186/s12959-020-00242-x
8. Chiarito M, Silbiger JJ, Ferlini M, et al. Direct oral anticoagulants in patients with left ventricular thrombus: A systematic review and meta-analysis. Thromb Haemost. 2021;121(9):1177-1186. doi:10.1055/a-1362-0460.
9. Lattuca B, Bouziri N, Kerneis M, et al. Antithrombotic therapy for patients with left ventricular mural thrombus. J Am Coll Cardiol. 2020;75(14):1676-85. doi:10.1016/j.jacc.2020.01.063.
10. McCarthy CP, Vaduganathan M, McCarthy KJ, et al. Left ventricular thrombus after acute myocardial infarction: Screening, prevention, and treatment. JAMA Cardiol. 2018;3(7):642-649. doi:10.1001/jamacardio.2018.1086.
11. Renda G, Ricci F, Giugliano RP, et al. Edoxaban versus warfarin in patients with left ventricular thrombus: A systematic review and meta-analysis. J Am Heart Assoc. 2020;9(6). doi:10.1161/JAHA.119.015363.
12. Zafar Ali, Nicholas Isom, Tarun Dalia, et al. Direct oral anticoagulant use in left ventricular thrombus. Thrombosis J. 2020;18:29. doi:10.1186/s12959-020-00242-x.
13. Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41(4):543-603. doi:10.1093/eurheartj/ehz405.
14. Ferlini M, Wiefels C, Seropian IM, et al. Thrombus resolution and clinical outcomes with DOACs versus warfarin in patients with LV thrombus. J Am Coll Cardiol. 2021;77(18_Suppl_1):2344.
15. Lip GYH, Pan X, Kamble S, et al. Real-world comparison of major bleeding risk among nonvalvular atrial fibrillation patients initiated on apixaban, dabigatran, rivaroxaban, or warfarin: A cohort study. Thromb Haemost. 2021;121(7):1023-1033. doi:10.1055/a-1326-8995.