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Evaluating the Predictive Value of the CHA_2DS_2-VASc Score for Thrombotic Events Following Mechanical Mitral Valve Replacement

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ABSTRACT

Introduction: Mechanical mitral valve replacement is associated with a persistent risk of thrombotic complications despite appropriate anticoagulation. Identifying reliable clinical predictors of thrombosis remains a major challenge in this high-risk population. This study aimed to evaluate the predictive value of the CHA_2DS_2-VASc score for thrombotic events in patients following mechanical mitral valve replacement.

Material and methods: This case-control study was conducted at Shahid Madani Hospital, Tabriz University of Medical Sciences, from 2017 to 2021. It included 100 consecutive patients who underwent mechanical mitral valve replacement. The primary objective was to evaluate the predictive value of the CHA_2DS_2-VASc score for thrombotic events in this cohort.

Results: In this cohort of 100 patients with mechanical mitral valve replacement, no significant differences were observed between patients with and without thrombosis regarding age (p=0.148), sex (p=0.944), comorbidities, valve type, left ventricular ejection fraction (p=0.723), warfarin dose (p=0.447), INR levels (p=0.620), or individual CHA_2DS_2-VASc components (all p>0.05).

Conclusion: This study demonstrates that traditional clinical and demographic risk factors, including those incorporated into the CHA_2DS_2-VASc score, do not independently predict prosthetic valve thrombosis in patients with mechanical mitral valves when anticoagulation intensity is considered.

Introduction

Mechanical mitral valve replacement remains a life-saving intervention for patients with advanced mitral valve disease who are not suitable candidates for valve repair or bio prosthetic replacement. Despite substantial improvements in surgical techniques, prosthesis design, and postoperative management, thrombotic complications continue to represent one of the most serious and potentially fatal long-term adverse outcomes in this patient population. Prosthetic valve thrombosis and systemic thromboembolic events are associated with

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significant morbidity, including stroke, heart failure, valve dysfunction, and mortality, underscoring the critical need for accurate risk stratification and optimized antithrombotic strategies in patients with mechanical mitral valves [1].

The mitral position is inherently associated with a higher thrombotic risk compared with the aortic position due to lower transvalvular flow velocities, larger prosthetic surface area, and greater exposure to blood stasis within the left atrium. Additionally, many patients undergoing mitral valve replacement have concomitant atrial fibrillation, left atrial enlargement, or prior thromboembolic events, all of which further exacerbate the prothrombotic milieu. As a result, lifelong anticoagulation with vitamin K antagonists remains mandatory in patients with mechanical mitral valves; however, thrombotic events may still occur despite apparently adequate anticoagulation, highlighting the multifactorial nature of thrombus formation in this setting [2].

Current guidelines recommend target international normalized ratio (INR) ranges based primarily on prosthesis type and valve position, with limited incorporation of individual patient-level thrombotic risk factors beyond historical thromboembolism or atrial fibrillation. While INR remains the cornerstone of anticoagulation monitoring, it does not fully capture the dynamic interplay between clinical comorbidities, endothelial dysfunction, inflammation, and hemodynamic factors that contribute to thrombus formation. Consequently, there is growing interest in identifying additional clinical risk assessment tools that may improve prediction of thrombotic events and facilitate personalized management in patients with mechanical heart valves [3].

The CHA_2DS_2-VASc score was originally developed as a simple and practical clinical tool for estimating the risk of stroke in patients with non-valvular atrial fibrillation. By incorporating readily available clinical variables—congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, and sex—the score provides a cumulative assessment of systemic thromboembolic risk. Its ease of use and strong prognostic performance have led to widespread adoption in routine clinical practice and inclusion in international guidelines for anticoagulation decision-making in atrial fibrillation [4].

Beyond its original indication, accumulating evidence suggests that the CHA_2DS_2-VASc score may have broader applicability as a marker of global thrombotic risk across diverse cardiovascular populations. Several studies have demonstrated its association with adverse thromboembolic outcomes in patients without atrial fibrillation, including those with heart failure, acute coronary syndromes, and structural heart disease. These findings support the concept that the score captures fundamental pathophysiological determinants of thrombosis, such as endothelial dysfunction, vascular inflammation, and impaired hemodynamics, rather than merely reflecting arrhythmia-related risk [5].

Patients with mechanical mitral valve replacement represent a particularly compelling population in which to explore the utility of the CHA_2DS_2-VASc score. Many components of the score are highly prevalent in this group, including advanced age, hypertension, diabetes mellitus, heart failure, and vascular disease. Moreover, atrial fibrillation is common both before and after mitral valve surgery, further amplifying thrombotic risk. Despite these overlaps, the CHA_2DS_2-VASc score has not been systematically integrated into risk assessment frameworks for patients with mechanical valves, and its predictive value for prosthetic valve thrombosis and systemic embolic events remains incompletely defined [6].

Prosthetic valve thrombosis is a complex phenomenon influenced by prosthesis-related factors, patient-specific characteristics, and anticoagulation quality. While sub therapeutic INR is a well-recognized precipitating factor, a substantial proportion of thrombotic events occur in patients with therapeutic or near-therapeutic anticoagulation levels. This observation suggests that traditional anticoagulation metrics alone are insufficient to fully explain thrombotic risk and that additional clinical variables may play a decisive role. The CHA_2DS_2-VASc score, by integrating multiple comorbid conditions into a single numerical value, may offer incremental prognostic information beyond INR monitoring alone [7].

From a mechanistic perspective, each component of the CHA_2DS_2-VASc score contributes to a prothrombotic state through distinct but interrelated pathways. Heart failure is associated with low cardiac output and blood stasis, hypertension promotes endothelial injury, diabetes, hypertension, diabetes mellitus, heart failure, and vascular disease. Moreover, atrial fibrillation is common both before and after mitral valve surgery, further amplifying thrombotic risk. Despite these overlaps, the CHA_2DS_2-VASc score has not been systematically integrated into risk assessment frameworks for patients with mechanical valves, and its predictive value for prosthetic valve thrombosis and systemic embolic events remains incompletely defined [6].

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From a mechanistic perspective, each component of the CHA_2DS_2-VASc score contributes to a prothrombotic state through distinct but interrelated pathways. Heart failure is associated with low cardiac output and blood stasis, hypertension promotes endothelial injury, diabetes mellitus induces chronic inflammation and platelet hyperreactivity, and advancing age is linked to impaired fibrinolysis and vascular stiffness. Prior cerebrovascular events reflect an established propensity for thrombosis, while vascular disease signifies systemic atherosclerosis and endothelial dysfunction. These mechanisms are particularly relevant in the context of a mechanical mitral valve, where altered flow dynamics and foreign material further enhance chromogenic potential [8].

Identifying patients at heightened risk for thrombotic complications after mechanical mitral valve replacement has important clinical implications. Enhanced risk stratification may inform closer INR surveillance, more aggressive management of modifiable comorbidities, or consideration of adjunctive antithrombotic strategies in selected individuals. Furthermore, improved prediction of thrombotic events could aid in patient counseling, postoperative follow-up planning, and early detection of prosthetic valve dysfunction. In this regard, a validated, simple, and widely familiar scoring system such as CHA_2DS_2-VASc would be particularly attractive for routine clinical use [9].

Despite the theoretical rationale and emerging evidence from related cardiovascular populations, data specifically addressing the association between CHA_2DS_2-VASc score and thrombotic outcomes in patients with mechanical mitral valves remain limited. Existing studies have often focused on heterogeneous valve positions, mixed prosthesis types, or composite endpoints, making it difficult to draw definitive conclusions for this high-risk subgroup. Moreover, the potential role of the score in predicting both prosthetic valve thrombosis and systemic thromboembolic events has not been comprehensively evaluated in well-defined cohorts of mechanical mitral valve recipients [10].

Against this background, evaluating the predictive value of the CHA_2DS_2-VASc score for thrombotic events following mechanical mitral valve replacement represents an important and clinically relevant research objective. Demonstrating a robust association could support the integration of this score into postoperative risk assessment models and stimulate further studies aimed at refining anticoagulation strategies in this population. Ultimately, such efforts may contribute to reducing the burden of thrombotic complications and improving long-term outcomes in patients living with mechanical mitral valve prostheses.

Material and methods

Study Design: This research was conducted as a case–control study at Shahid Madani Heart Center, affiliated with Tabriz University of Medical Sciences (Tabriz, Iran). The study period extended from early 2017 to late 2021. Patients who had undergone mechanical mitral valve replacement and were regularly followed in the hospital's cardiac surgery and anticoagulation clinics were considered for inclusion. The study was designed to explore the association between the CHA_2DS_2-VASc score and the occurrence of prosthetic valve thrombosis or systemic thromboembolic events during long-term follow-up.

Sampling: Sampling was performed through census sampling (complete enumeration) of all eligible patients meeting the inclusion criteria during the defined period. The final sample size comprised 100 patients, including both cases (patients who developed documented thrombotic events after surgery) and controls (patients without any thrombotic complications). Data were collected retrospectively from hospital records and verified through clinical visits and echocardiographic findings.

Inclusion and Exclusion Criteria

Eligible participants were adult patients (≥18 years) who had undergone mechanical mitral valve replacement and had completed regular postoperative follow-up at the study center for at least 12 months. Patients were required to have available clinical, echocardiographic, and laboratory data, as well as a recorded CHA_2DS_2-VASc score derived from their baseline characteristics.

Exclusion criteria included individuals with bio prosthetic or mixed valve replacement, incomplete medical documentation, poor adherence to anticoagulation therapy, coexistent mechanical aortic valve, active malignancy, severe infection or autoimmune disease, and known coagulation disorders unrelated to anticoagulation management. Patients with valve reoperation, endocarditis, pregnancy, or loss to follow-up were also excluded to maintain uniformity and reduce confounding effects.This comprehensive filtering ensured a homogenous sample representative of patients with isolated mechanical mitral valve replacement under standard care conditions.

Procedures

In the first phase, all enrolled patients were identified through the hospital's cardiac surgery registry and anticoagulation clinic database. Demographic variables (age, sex), clinical comorbidities (heart failure, hypertension, diabetes mellitus, prior stroke or transient ischemic attack,

vascular disease), and details of anticoagulation management (INR values, warfarin dosage, and frequency of monitoring) were extracted systematically. The CHA_2DS_2-VASc score was calculated retrospectively for each patient at baseline using these parameters.

In the second phase, postoperative outcomes were reviewed to identify thrombotic events, including confirmed prosthetic valve thrombosis, systemic embolism, or stroke. Diagnosis was based on clinical presentation, transthoracic or trans esophageal echocardiography findings, and radiologic confirmation when available. For valve thrombosis, visualization of restricted leaflet motion, increased transvalvular gradient, or visible thrombus on imaging was required. Cases and controls were matched for age and sex to minimize confounding. In the third phase, data were anonymized and validated independently by two cardiologists to ensure accuracy and consistency. Discrepancies in classification were resolved by consensus. Relevant hematologic parameters, including INR trend, hemoglobin, and platelet counts, were recorded. Duration since valve replacement and overall follow-up time were noted for all subjects.

Statistical Analysis

Data analysis was performed using SPSS software, version 26 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation or median with interquartile range, depending on normality assessed by the Kolmogorov–Smirnov test. Categorical variables were reported as frequencies and percentages.

Comparisons between case and control groups were made using independent t-tests or Mann–Whitney U tests for continuous data and chi-square or Fisher's exact tests for categorical variables. The association between CHA_2DS_2-VASc score and thrombotic events was evaluated using binary logistic regression, both in univariate and multivariate frameworks, adjusting for potential confounders such as sex, age, and time since surgery. A p-value < 0.05 was considered statistically significant. Receiver operating characteristic (ROC) curve analysis was conducted to determine the optimal cutoff value of the CHA_2DS_2-VASc score predicting thrombosis.

Ethical Considerations: The study protocol was reviewed and approved by the Ethics Committee of Tabriz University of Medical Sciences under the code IR. TBZMED.1400.1256. All patient data were kept strictly confidential and analyzed anonymously. The investigation was performed in accordance with the Declaration of Helsinki ethical standards. This research forms part of a postgraduate thesis project (Thesis No. 67370) and represents the first specific objective (Objective No. 1) of that dissertation. Written informed consent was obtained from all participants or their legal guardians prior to inclusion.

Results

In this cohort of 100 patients receiving mechanical mitral valve replacements, the mean age was slightly higher in the non-thrombosis group (56.3 ± 10.31 years) compared to the thrombosis group (51.5 ± 14.68 years), though the difference did not reach statistical significance (p=0.148). Gender distribution was similar between groups, with females comprising 62.82% in the non-thrombosis group and 59.09% in the thrombosis group (p = 0.944), indicating no association between sex and thrombotic events.

Regarding comorbidities, hypertension was observed in 33.33% of patients without thrombosis compared to 22.73% in those with thrombosis (p = 0.491). Diabetes mellitus was slightly more frequent among patients with thrombosis (27.27%) than in those without (20.51%), but not statistically significant (p=0.701). Heart failure prevalence was comparable between groups (50.0% vs. 43.59%, p=0.771). Interestingly, prior cerebrovascular accident was less frequent in the thrombosis group (9.09%) compared to the non-thrombosis group (26.92%), yet this difference also failed to reach statistical significance (p=0.142) (figure 1). Overall, no baseline demographic or clinical variable demonstrated a significant association with postoperative thrombotic events in this sample.

Table1. Baseline Characteristics of Patients with Mechanical Mitral Valve Prostheses

Variable	Total Patients	Without Thrombosis	With Thrombosis	P-value
Age* (years)	54.93 (±11.52)	56.3 (±10.31)	51.5 (±14.68)	0.148
	Gender			
Female	62 (62%)	49 (62.82%)	13 (59.09%)	0.944
Male	38 (38%)	29 (37.18%)	9 (40.91%)	

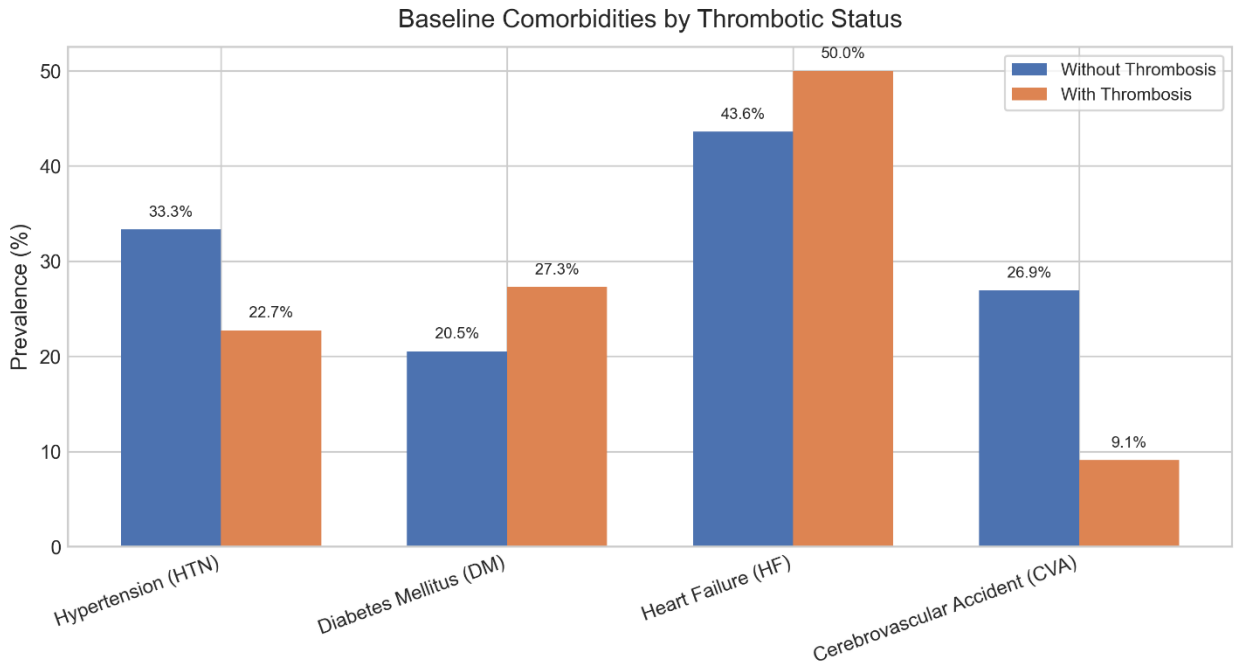

Figure 1. Baseline Comorbidities by Thrombotic Status

Among the study population, 94 patients (94%) had mechanical leaflet valves, while only 6 patients (6%) had mechanical monoleaflet valves. The mean left ventricular ejection fraction (EF) was 44.94% ± 10.39, with no statistically significant difference observed between the thrombosis and non-thrombosis groups (p=0.723) (Table 2-4). The time elapsed since valve replacement surgery was 100 ± 87.64 months in patients without thrombosis and 127 ± 83.38 months in those with thrombosis, showing no significant intergroup difference (p=0.149).

Warfarin dosage did not differ significantly between the two groups (p=0.447) (figure 2). Similarly, the mean of the three most recent international normalized ratio (INR) measurements was comparable between patients with and without thrombosis, with no statistically significant difference detected (p=0.620).

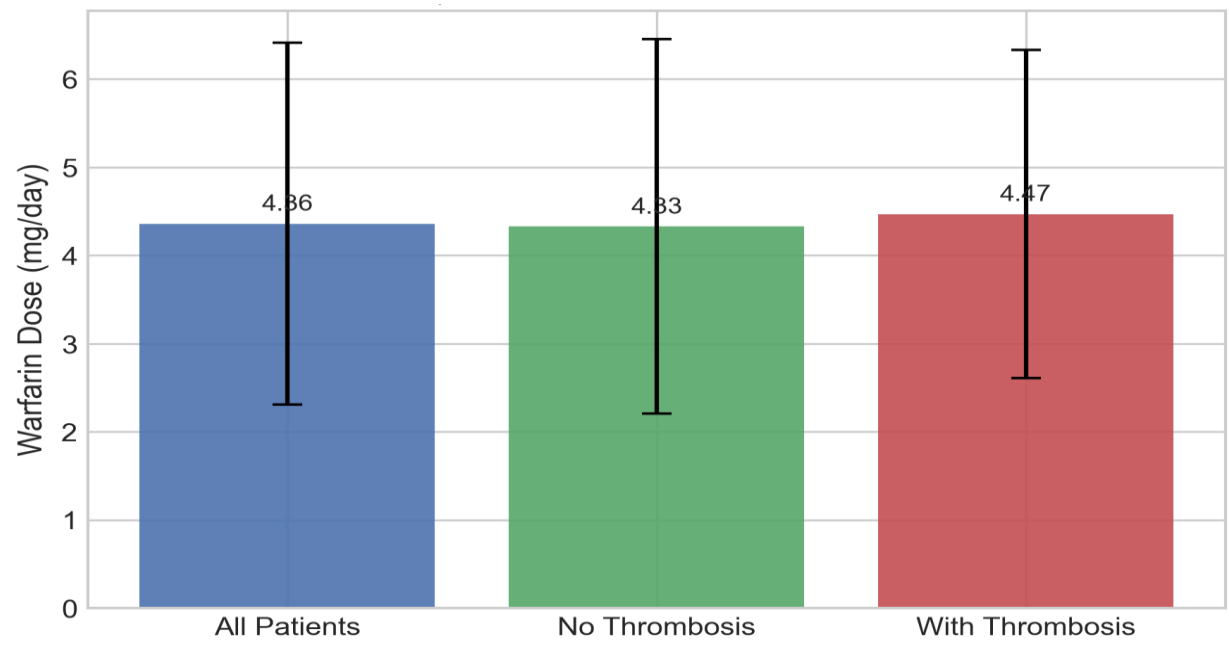

Figure 2. Mean Daily Warfarin Dose by Thrombotic Status

Comparison of CHA_2DS_2-VASc individual components revealed no statistically significant differences between patients with and without thrombotic events following mechanical mitral valve replacement. Advanced age demonstrated similar distribution across groups: only two patients were aged ≥75 years, both without thrombosis, and age ≥65 years occurred in 20.5% of the non-thrombosis group and 22.7% of those with thrombosis (P=1.000 for both age criteria). A history of cerebrovascular accident or transient ischemic attack was more frequent in patients without thrombosis (26.9% vs. 9.1%), but this difference did not reach statistical significance (P=0.142) (table 2). Other comorbid contributors to the CHA_2DS_2-VASc score also showed comparable patterns between groups. Hypertension (33.3% vs. 22.7%, P=0.491) and diabetes mellitus (20.5% vs. 27.3%, P=0.701) were similarly distributed, indicating no differential burden of these risk factors in patients with thrombosis. Heart failure, the most prevalent item, was present in half of the thrombosis group and 43.6% of the non-thrombosis group (P=0.771). Likewise, female sex and vascular disease showed no meaningful group differences (P=0.814 and P=0.502, respectively). Overall, none of the CHA_2DS_2-VASc components individually demonstrated a significant association with postoperative thrombotic events in this population (table 2).

Table 2. Distribution of CHA_2DS_2-VASc Score Components in Patients with Mechanical Mitral Valve Prostheses, Stratified by Thrombotic Status

CHA_2DS_2-VASc Component	Total Patients (n=100)	No Thrombosis (n=79)	Thrombosis (n=22)	P-value
Age >75 years	2 (2%)	2 (2.56%)	0 (0%)	1.000
CVA/TIA	23 (23%)	21 (26.92%)	2 (9.09%)	0.142
Hypertension (HTN)	31 (31%)	26 (33.33%)	5 (22.73%)	0.491
Age >65 years	21 (21%)	16 (20.51%)	5 (22.73%)	1.000
Diabetes Mellitus (DM)	22 (22%)	16 (20.51%)	6 (27.27%)	0.701
Heart Failure (HF)	45 (45%)	34 (43.59%)	11 (50.00%)	0.771
Female Sex	59 (59%)	47 (60.26%)	12 (54.55%)	0.814
Vascular Disease	26 (26%)	22 (28.21%)	4 (18.18%)	0.502

Multivariable analysis adjusting for the potential confounding effect of patients' INR levels demonstrated no statistically significant association between the CHA_2DS_2-VASc score and prosthetic valve thrombosis (p=0.248). After controlling for anticoagulation intensity, the distribution of CHA_2DS_2-VASc scores remained comparable between patients with thrombotic events and those without, indicating that differences in baseline clinical risk captured by this score did not independently contribute to thrombus formation. These findings suggest that, in contrast to its established role in atrial fibrillation, the CHA_2DS_2-VASc score does not effectively discriminate thrombotic risk between the two groups in patients with mechanical mitral valve replacement when INR is taken into account.

Discussion

Overall, the findings of this study indicate that among patients undergoing mechanical mitral valve replacement, neither baseline demographic and clinical characteristics, nor individual components of the CHA_2DS_2-VASc score, nor the total score itself were able to meaningfully discriminate between patients with and without prosthetic valve thrombosis. In addition, the intensity and quality of anticoagulation assessed by warfarin dose and INR values did not differ significantly between the two groups. Multivariable analysis further demonstrated that after adjustment for INR, no independent association was observed between the CHA_2DS_2-VASc score and prosthetic valve thrombosis. Collectively, these findings suggest that the mechanisms underlying thrombosis of mechanical heart valves may differ fundamentally from the traditional thromboembolic risk factors incorporated into the CHA_2DS_2-VASc score [11,12].

Regarding baseline characteristics, the absence of significant differences in age and sex between the two groups suggests that, in patients with mechanical mitral valves, the risk of thrombosis may be driven more by prosthesis-related factors, valve hemodynamics, and interactions with the coagulation system than by demographic variables. Unlike many cardiovascular conditions in which advanced age and female sex are associated with higher thrombotic risk, patients with mechanical valves are inherently exposed to a uniformly high-risk state. The presence of a metallic foreign body in the mitral position may therefore exert a dominant effect on coagulation activation, overshadowing the influence of age and sex [13,14]. Similarly, the lack of a significant association between comorbidities such as hypertension, diabetes mellitus, and heart failure and prosthetic valve thrombosis is noteworthy. Although these conditions are well-established thromboembolic risk factors within the CHA_2DS_2-VASc framework, their

relevance is largely derived from populations with atrial fibrillation, where thrombus formation typically occurs in the left atrium. In contrast, thrombosis of mechanical valves is primarily related to disturbed flow patterns, non-endothelial zed artificial surfaces, and direct activation of platelets and coagulation factors. Consequently, classical metabolic and hemodynamic risk factors may play a secondary role in the presence of a mechanical valve and may be insufficient to generate meaningful differences in thrombosis risk on their own [15,16].

The findings related to prior stroke or transient ischemic attack can also be explained from a pathophysiological perspective. Although this variable represents one of the strongest components of the CHA_2DS_2-VASc score, a history of cerebrovascular events does not necessarily imply a greater propensity for mechanical valve thrombosis. Such events may arise from alternative mechanisms unrelated to the prosthesis, including atherosclerotic disease or transient cardiac emboli. Furthermore, patients with a prior history of stroke are often subjected to closer clinical surveillance and more stringent anticoagulation management, which may mitigate the risk of prosthetic valve thrombosis and attenuate any direct association between prior cerebrovascular events and valve thrombosis [17,18]. With respect to valve-related and cardiac functional parameters, the absence of significant differences in mechanical valve type and left ventricular ejection fraction between groups suggests that, within a certain range of systolic function, the risk of thrombosis does not vary in a linear manner with ejection fraction. Although severe left ventricular dysfunction may promote blood stasis and increase thrombotic risk, compensatory mechanisms and optimized anticoagulation in patients with moderate impairment may counterbalance this effect. In addition, the predominance of leaflet mechanical valves in the study population may have limited structural variability, reducing the ability to detect differences related to valve design [19,20].

The lack of a significant difference in the interval between surgery and study enrollment is another important observation. This finding implies that the risk of mechanical valve thrombosis is not confined to a specific postoperative period but may persist chronically over time. Alternatively, it may reflect progressive therapeutic adjustments and anticoagulation optimization during follow-up, leading to a more homogeneous risk profile across different postoperative intervals [21,22].

In terms of anticoagulation therapy, the similarity between the two groups with respect to warfarin dose and recent mean INR values carries important clinical implications. This observation suggests that achieving standard INR targets alone may not be sufficient to fully prevent prosthetic valve thrombosis and that factors beyond numerical INR control contribute to this complication. Moreover, INR represents a snapshot of coagulation status and does not capture temporal variability, treatment adherence, or brief periods of sub therapeutic anticoagulation. Therefore, the lack of observed differences may partly reflect the intrinsic limitations of INR as the sole marker of anticoagulation quality [23,24].

Analysis of individual CHA_2DS_2-VASc components revealed that none were independently predictive of mechanical valve thrombosis. This is conceptually unsurprising, as the CHA_2DS_2-VASc score was specifically developed to estimate the risk of systemic embolism in patients with atrial fibrillation, with a primary focus on clinical factors associated with left atrial thrombus formation. Mechanical valve thrombosis, however, predominantly occurs at the prosthetic surface and is driven by blood–material interactions, representing a pathophysiological process distinct from atrial thrombogenesis. Consequently, direct application of a predictive tool from one clinical context to another without appropriate modification or validation may substantially reduce predictive accuracy [25,26].

The central finding of this study the absence of an independent association between the overall CHA_2DS_2-VASc score and prosthetic valve thrombosis after adjustment for INR further supports the notion that this score provides limited incremental predictive value in this specific population. Accounting for INR as a confounding variable demonstrated that even after controlling for anticoagulation intensity, no meaningful difference remained between patients with and without thrombosis. This indicates that the cumulative risk factors incorporated in the CHA_2DS_2-VASc score fail to adequately capture the complex mechanisms underlying thrombosis in mechanical heart valves [27,28].

In conclusion, the results of this study suggest that the use of the CHA_2DS_2-VASc score as a predictive tool for mechanical mitral valve thrombosis should be approached with caution. Patients with mechanical valves likely require more tailored risk-stratification models that extend beyond traditional clinical variables to include valve-specific hemodynamic characteristics, flow patterns, longitudinal INR variability, individual responsiveness to warfarin, and potentially novel inflammatory or coagulation biomarkers. Development of such dedicated predictive models may ultimately enable more accurate identification of high-risk patients and lead to improved strategies for thrombosis prevention in this complex patient population.

Conclusion

This study demonstrates that traditional clinical and demographic risk factors, including those incorporated into the CHA_2DS_2-VASc score, do not

independently predict prosthetic valve thrombosis in patients with mechanical mitral valves when anticoagulation intensity is considered. Despite its validated role in estimating thromboembolic risk in atrial fibrillation, CHA_2DS_2-VASc failed to discriminate thrombotic risk in this distinct clinical context. The absence of significant associations after adjustment for INR highlights the dominant influence of valve-related and hemodynamic factors over conventional systemic risk markers. These findings underscore the need for valve-specific risk stratification models that integrate prosthesis characteristics, flow dynamics, longitudinal anticoagulation control, and potentially novel coagulation or inflammatory biomarkers to improve prediction and prevention of mechanical valve thrombosis.

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Conflicts of interest
The authors declare that they have no competing interests.

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Authors' Contributions
All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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