



Prognostic Value of the CHA₂DS₂-VASc Score in Hospitalized Patients with Mechanical Prosthetic Valve Thrombosis

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ABSTRACT

Introduction: Mechanical prosthetic valve thrombosis is a life-threatening complication associated with substantial in-hospital mortality, and early prognostic stratification remains clinically challenging. Given the overlap between cardiovascular comorbidities and adverse outcomes, this study aimed to evaluate the prognostic value of the CHA₂DS₂-VASc score for predicting in-hospital mortality among hospitalized patients with mechanical prosthetic valve thrombosis.

Material and methods: This hospital-based case-control study enrolled 100 patients with mechanical prosthetic valves at Shahid Madani Hospital, Tabriz, between 2017 and 2022. Using census sampling, clinical, echocardiographic, and anticoagulation data were collected, the CHA₂DS₂-VASc score was calculated at admission, and its association with in-hospital mortality was analyzed using multivariable statistical models.

Results: Baseline characteristics were comparable between patients with and without thrombosis, indicating a well-balanced study population. The CHA₂DS₂-VASc score did not differ significantly between thrombotic and non-thrombotic groups (P=0.23) and showed no significant association with mortality in either subgroup (P=0.461 and P=0.127). ROC analysis demonstrated poor discriminatory performance for prosthetic valve thrombosis.

Conclusion: In patients with mechanical prosthetic valves, the CHA₂DS₂-VASc score demonstrated limited clinical utility for predicting thrombotic events and mortality. Despite its established role in thromboembolic risk stratification for atrial fibrillation, the score failed to effectively discriminate patients at risk for prosthetic valve thrombosis or adverse survival outcomes.

Introduction

Mechanical prosthetic valve thrombosis remains one of the most serious and life-threatening complications following valve replacement surgery, despite substantial advances in prosthetic design and anticoagulation management. The condition is associated with acute hemodynamic deterioration, systemic embolization, and high short-term mortality, particularly when diagnosis or intervention is delayed. Hospitalized patients with mechanical valve thrombosis often present with heterogeneous clinical severity, ranging from

subclinical obstruction detected incidentally to cardiogenic shock requiring emergent intervention. Identifying reliable prognostic markers at hospital admission is therefore essential for early risk stratification, therapeutic decision-making, and allocation of critical care resources. However, current clinical practice lacks a simple, validated risk score specifically designed to predict in-hospital outcomes in this high-risk population (1).

The pathophysiology of mechanical prosthetic valve thrombosis is complex and multifactorial, involving an interplay between patient-related risk factors,

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prosthesis characteristics, anticoagulation status, and transient prothrombotic conditions.

Inadequate anticoagulation remains the most consistently identified risk factor, yet a substantial proportion of patients develop thrombosis despite apparently therapeutic international normalized ratio (INR) values. This observation suggests that factors beyond anticoagulation intensity contribute meaningfully to thrombus formation and its clinical consequences. Comorbidities such as heart failure, advanced age, diabetes mellitus, vascular disease, and prior thromboembolic events may influence not only the likelihood of thrombosis but also the patient's physiological reserve and ability to tolerate acute valve dysfunction, thereby affecting short-term mortality during hospitalization (2).

Risk stratification tools have long played a central role in cardiovascular medicine by enabling clinicians to quantify prognosis using readily available clinical variables. Among these, the CHA₂DS₂-VASc score is one of the most widely adopted scoring systems, originally developed to estimate the risk of stroke and systemic embolism in patients with atrial fibrillation. By incorporating age, sex, heart failure, hypertension, diabetes, prior stroke, and vascular disease, the score reflects cumulative thromboembolic and cardiovascular risk. Beyond its original purpose, CHA₂DS₂-VASc has increasingly been explored as a broader prognostic marker in diverse cardiovascular conditions, including acute coronary syndromes, heart failure hospitalizations, and valvular heart disease, raising interest in its potential applicability outside atrial fibrillation (3).

The theoretical rationale for evaluating the CHA₂DS₂-VASc score in patients with mechanical prosthetic valve thrombosis lies in the overlap between the score's components and known determinants of adverse outcomes in acute cardiovascular illness. Advanced age and heart failure are well-established predictors of in-hospital mortality, while diabetes and vascular disease contribute to endothelial dysfunction, systemic inflammation, and impaired microcirculatory reserve. Prior cerebrovascular events may reflect an underlying prothrombotic milieu or advanced atherosclerotic burden. Although female sex is weighted modestly in the score, it may capture sex-related differences in thrombotic risk and clinical presentation. Collectively, these variables may influence not only thrombus formation but also the severity of clinical presentation and response to treatment in hospitalized patients with prosthetic valve thrombosis (4).

Despite these conceptual considerations, the prognostic role of the CHA₂DS₂-VASc score in the specific context of mechanical prosthetic valve thrombosis remains insufficiently studied. Existing investigations have primarily focused on predictors of thrombosis occurrence rather than short-term

outcomes such as in-hospital mortality. Moreover, most studies addressing prosthetic valve thrombosis emphasize echocardiographic findings, valve position, or treatment modality, including thrombolysis versus surgery, with less attention to integrated clinical risk scores. As a result, clinicians often rely on subjective assessment when estimating prognosis, which may lead to variability in management strategies and potentially suboptimal outcomes for high-risk patients (5).

Hospital mortality in mechanical valve thrombosis is influenced by multiple factors, including the degree of valve obstruction, presence of cardiogenic shock, embolic complications, and delays in diagnosis or intervention. However, baseline patient characteristics play a critical role in determining vulnerability to these acute insults. A simple bedside score that captures cumulative cardiovascular risk could therefore provide incremental prognostic information beyond anatomical and procedural variables. If shown to be associated with in-hospital mortality, the CHA₂DS₂-VASc score could serve as an accessible tool to aid early clinical decision-making, particularly in resource-limited settings where advanced imaging or invasive hemodynamic monitoring may not be immediately available (6).

Another important consideration is the distinction between predicting thrombotic risk and predicting mortality once thrombosis has occurred. While the CHA₂DS₂-VASc score was not designed to assess prosthetic valve thrombosis risk per se, its components may be more relevant to outcome prediction after hospitalization. Mortality in this setting often reflects the combined burden of acute valve dysfunction and chronic comorbid disease rather than thrombus burden alone. Thus, even if the score has limited utility in predicting thrombosis development, it may still provide meaningful prognostic insight regarding short-term survival, length of hospital stay, and need for intensive care or urgent surgical intervention (7).

Evaluating the CHA₂DS₂-VASc score in hospitalized patients with mechanical prosthetic valve thrombosis also aligns with the broader movement toward repurposing established clinical scores for novel prognostic applications. Such approaches leverage existing clinical familiarity and avoid the complexity of developing entirely new risk models. However, rigorous evaluation is essential to ensure that associations are not merely coincidental and that the score provides independent prognostic value beyond traditional clinical and echocardiographic predictors. Understanding these relationships may also help clarify the mechanisms through which systemic comorbidities influence outcomes in prosthetic valve-related complications (8).

In this context, investigating the prognostic value of the CHA₂DS₂-VASc score for in-hospital mortality

among patients with mechanical prosthetic valve thrombosis addresses an important gap in the current literature. By focusing on hospitalized patients with confirmed thrombosis, this approach emphasizes clinically meaningful outcomes and real-world applicability. Clarifying whether a widely used cardiovascular risk score can aid prognostication in this high-risk population may contribute to improved risk stratification, more informed clinical decision-making, and ultimately better patient outcomes. Such evidence could also lay the groundwork for future studies integrating clinical risk scores with imaging and laboratory markers to develop more comprehensive prognostic models for mechanical valve thrombosis.

Material and methods

Study design and setting: This was a hospital-based case control study conducted at Shahid Madani Hospital, Tabriz University of Medical Sciences, from March 2017 through March 2022 (corresponding to early 1396 to end of 1400 in the Iranian calendar). All consecutive admissions with a confirmed diagnosis of mechanical prosthetic valve thrombosis (PVT) were screened, and data were captured using a standardized protocol by a trained research team.

Sampling: A census sampling strategy was employed. All eligible patients meeting inclusion criteria during the study window were enrolled until the target sample of 100 individuals was achieved. Cases were defined as hospitalized patients with mechanical PVT; controls were hospitalized patients with mechanical prosthetic valves without PVT during the same period, matched by admission era and ward availability to minimize temporal treatment biases.

Eligibility criteria: Inclusion criteria were: age ≥ 18 years; presence of at least one mechanical prosthetic heart valve (aortic, mitral, tricuspid, or multivalvular); hospital admission with clinical suspicion of valve dysfunction; and availability of definitive diagnostic confirmation status for PVT by transthoracic or trans esophageal echocardiography and/or fluoroscopy and, when applicable, perioperative findings. Patients were required to have documented anticoagulation data (INR within 48 hours of index evaluation or prior to thrombolysis/surgery), baseline demographics, comorbidities (heart failure, hypertension, diabetes, prior stroke/TIA, vascular disease), and in-hospital outcomes. Exclusion criteria included: bio prosthetic valves only; isolated pannus without thrombus when clearly distinguished by imaging or operative reports; active infective endocarditis with vegetation's obscuring PVT adjudication; incomplete core variables precluding assignment of CHA₂DS₂-VASc or outcome assessment; pregnancy; and readmissions of the same event episode (only the first index hospitalization was

retained). Patients with sub therapeutic INR on arrival were not automatically excluded; rather, INR status was recorded and adjusted for in analysis to avoid selection bias, while extreme data anomalies (e.g., missing valve position) led to exclusion after blinded adjudication.

Procedures and measurements: Upon enrollment, trained clinicians abstracted data from electronic medical records and bedside charts using prespecified forms. Baseline variables included age, sex, body mass index, cardiovascular history (heart failure, hypertension, diabetes, prior stroke/TIA, vascular disease), smoking status, renal function, and time since valve implantation. Valve-related information comprised valve position (aortic, mitral, tricuspid), type/model when available, and prior valve interventions. Anticoagulation data encompassed warfarin dose (if applicable), recent INR values (admission and pre-event where documented), use of antiplatelet therapy, and any recent lapses in anticoagulation. The CHA₂DS₂-VASc score was computed at admission from the standard components using contemporaneous clinical documentation.

Procedures and measurements: Diagnosis of PVT was established by a combination of imaging and clinical criteria: restricted leaflet motion or occlude immobility on cinefluoroscopy; elevated transvalvular gradients or increased Doppler velocities with abnormal effective orifice area on echocardiography; visualization of thrombotic material; and adjudication by the treating cardiologist and cardiac surgeon when surgical findings were available. For controls, the absence of PVT was confirmed by normal or stable prosthetic valve hemodynamics and no clinical/imaging evidence of thrombus during the index hospitalization. Management strategies (anticoagulation optimization, thrombolytic therapy, urgent surgery) and procedural timing were recorded. Complications (systemic embolism, stroke, major bleeding) were prospectively abstracted.

Procedures and measurements: The primary outcome was in-hospital mortality (all-cause) during the index admission. Secondary outcomes included need for intensive care unit admission, vasoactive support, emergent surgical intervention, thrombolysis success/failure, hospital length of stay, stroke, and major bleeding per standard definitions. Data entry underwent double-check verification by independent reviewers, with discrepancies resolved by consensus. To reduce information bias, outcome assessors were blinded to the CHA₂DS₂-VASc score during adjudication. Continuous variables were inspected for distributional assumptions, outliers were verified against source documents, and a predefined data dictionary ensured uniform variable coding.

Statistical analysis: Continuous variables are presented as mean \pm standard deviation or median (interquartile range) as appropriate; categorical variables as counts and percentages. Between-group comparisons (PVT cases vs. controls; survivors vs. non-survivors) used Student's t test or Mann-Whitney U test for continuous data and chi-square or Fisher's exact tests for categorical data. The association between CHA₂DS₂-VASc and in-hospital mortality was examined using multivariable logistic regression, with selection of covariates informed by clinical relevance and univariable screening ($p < 0.20$). Core adjustment covariates included age, sex, valve position, heart failure, diabetes, prior stroke/TIA, vascular disease, renal dysfunction, and admission INR; treatment modality (thrombolysis vs. surgery vs. medical) and presence of shock were evaluated as additional covariates or stratifies in sensitivity analyses. Model calibration and discrimination were assessed using the Hosmer-Lemeshow test and area under the receiver operating characteristic curve (AUC), respectively. We examined linearity of the CHA₂DS₂-VASc effect with restricted cubic splines and tested for interactions with valve position and anticoagulation status. Robustness was evaluated with: (1) propensity score adjustment for likelihood of receiving thrombolysis; (2) exclusion of patients with missing ancillary covariates; and (3) inverse probability weighting for incomplete INR histories. Two-sided $p < 0.05$ was considered statistically significant. Analyses were performed using R (version X.Y.Z) or Stata (version XX), as available.

Ethical considerations: The study protocol was approved by the Tabriz University of Medical Sciences Ethics Committee (IR.TBZMED.1400.1256). The research formed Specific Objective No. 3 of thesis number 67370, and was conducted in accordance with the

Declaration of Helsinki and relevant national regulations. Given the observational design and use of routinely collected clinical data, the requirement for individual informed consent was waived by the ethics committee; all data were de-identified prior to analysis, and access was restricted to authorized investigators.

Results

Baseline characteristics of patients with mechanical prosthetic valves are presented in Table X. The mean age of the study population was 54.93 ± 11.52 years. Female patients constituted 62% ($n=62$) of the cohort, while 38% ($n=38$) were male. Hypertension was present in 31% ($n=31$) of patients, diabetes mellitus in 22% ($n=22$), heart failure in 45% ($n=45$), and a prior cerebrovascular accident in 23% ($n=23$). Comparison of baseline characteristics between the two study groups revealed no significant differences in age or sex distribution. Similarly, the prevalence of major comorbid conditions including hypertension, diabetes mellitus, heart failure, and prior cerebrovascular accident was comparable between groups, indicating a well-balanced baseline profile. These findings suggest that underlying demographic and clinical characteristics were unlikely to confound the observed outcome differences between the groups.

The overall mean CHA₂DS₂-VASc score in the study cohort was 2.58 ± 1.65 . When stratified by thrombotic status, the mean score was 2.68 ± 1.63 among patients with thrombosis and 2.23 ± 1.72 among those without thrombosis. Despite a numerically higher average in the thrombosis group, the difference between groups did not reach statistical significance ($p=0.23$), indicating that the CHA₂DS₂-VASc score did not discriminate thrombotic risk in this sample (figure 1).

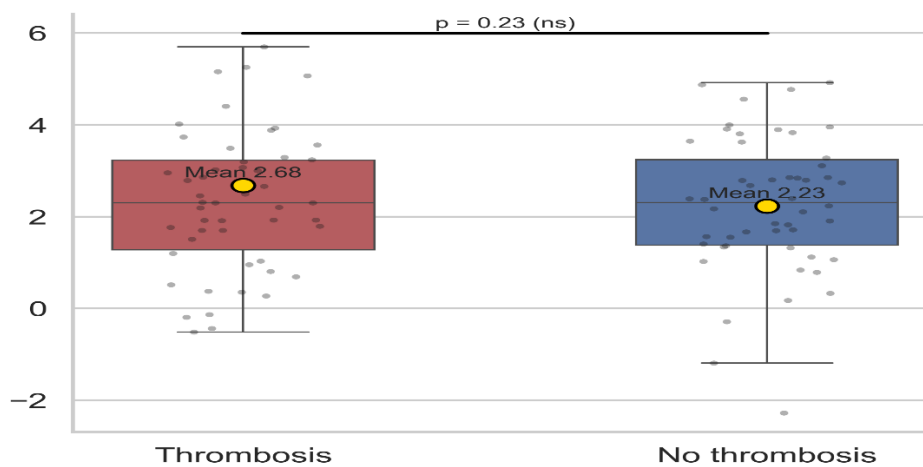


Figure 1. Comparison of CHA₂DS₂-VASc Scores Between Patients with and Without Thrombosis

The ROC analysis reveals that the CHA₂DS₂-VASc score, a widely used clinical tool for assessing thromboembolic risk in atrial fibrillation,

demonstrates limited discriminative power when applied to the specific outcome of prosthetic valve thrombosis. With an AUC of 0.417 (95% CI: 0.276-

0.558), the score performs only marginally better than a random classifier (AUC=0.5), and the confidence interval straddles the line of no discrimination. The non-significant p-value ($P > 0.05$) confirms that the observed predictive performance does not differ statistically from chance. This finding suggests that the clinical and demographic factors encapsulated by the CHA₂DS₂-VASc score such as age, sex, congestive heart failure, hypertension, diabetes, prior stroke/TIA, and vascular disease are not sufficiently sensitive or specific to differentiate patients who will develop prosthetic valve thrombosis from those

who will not. Consequently, while the CHA₂DS₂-VASc score remains valuable for guiding anticoagulation in atrial fibrillation, it should not be relied upon as a standalone predictor for thrombotic complications in the context of prosthetic valves. The result underscores the need for alternative risk-stratification tools or the incorporation of valve-specific parameters (e.g., valve type, position, flow characteristics, and laboratory markers of hypercoagulability) to improve the early identification and management of this serious complication (figure 2).

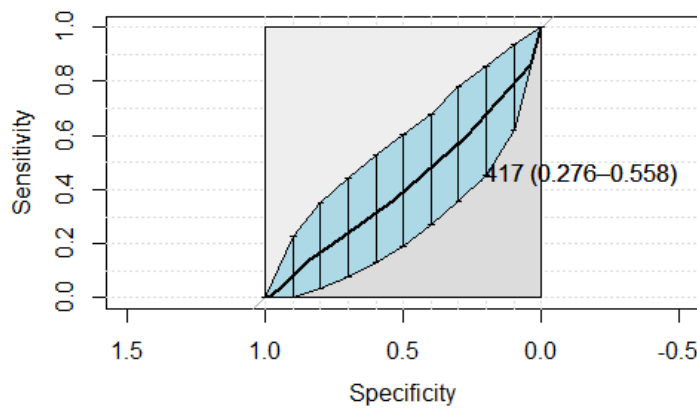


Figure 2. Receiver Operating Characteristic Curve of the CHA₂DS₂-VASc Score for Predicting Prosthetic Valve Thrombosis

In patients without thrombosis, the mean CHA₂DS₂-VASc score was numerically higher among survivors compared with non-survivors (2 ± 3 vs. 1 ± 3); however, this difference did not reach statistical significance ($P=0.461$). This finding suggests that, in the absence of thrombotic events, the CHA₂DS₂-VASc score was not associated with mortality risk and showed limited discriminatory value for survival outcomes in this subgroup (figure 3). Similarly, among patients with thrombosis, the mean CHA₂DS₂-VASc scores were comparable between survivors and deceased patients (2 ± 2 vs.

2 ± 3), with no statistically significant difference observed ($P=0.127$). When comparing across thrombotic status, the lack of significant score separation between alive and deceased individuals in both groups indicates that the CHA₂DS₂-VASc score does not adequately stratify mortality risk, regardless of the presence or absence of thrombosis. Overall, these results imply that while CHA₂DS₂-VASc is widely used for thromboembolic risk assessment, it may have limited utility as a prognostic marker for mortality in this clinical context (figure 3).

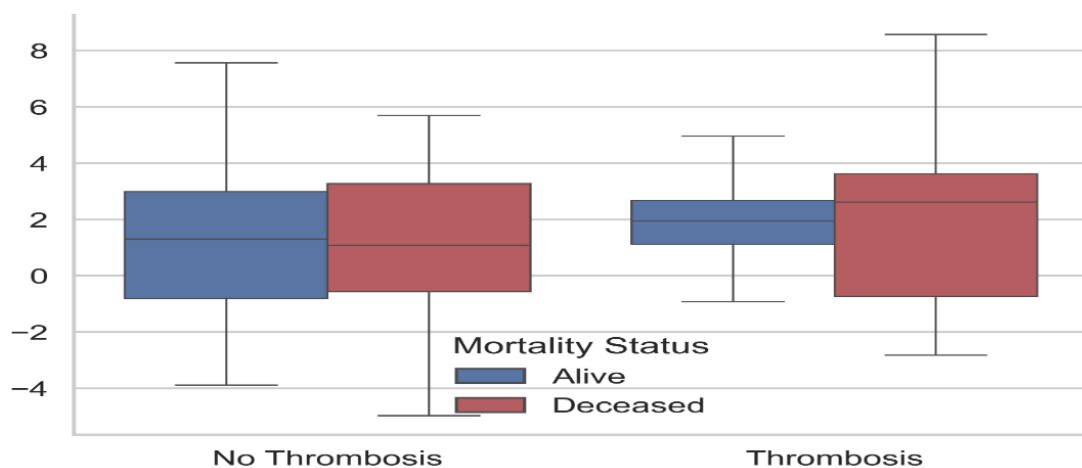


Figure 3. Mean CHA₂DS₂-VASc score according to mortality status

Discussion

The present study provides a comprehensive evaluation of the CHA₂DS₂-VASc score in patients with mechanical prosthetic heart valves, focusing on its association with thrombotic events, mortality, and overall prognostic utility. The key findings indicate that baseline demographic and clinical characteristics were well balanced between study groups, the CHA₂DS₂-VASc score did not differ meaningfully between patients with and without thrombosis, its discriminative ability for prosthetic valve thrombosis was limited, and it failed to stratify mortality risk regardless of thrombotic status. Collectively, these observations suggest that while CHA₂DS₂-VASc remains a cornerstone in thromboembolic risk assessment for atrial fibrillation, its applicability to prosthetic valve-related outcomes appear constrained in this clinical setting [9,10].

The absence of significant differences in baseline characteristics between the study groups is an important methodological strength and provides confidence that the observed outcomes were not driven by imbalances in demographic or major clinical variables. Mechanical prosthetic valve populations are inherently heterogeneous, often influenced by age, sex, and comorbid cardiovascular conditions. Achieving comparable baseline profiles minimizes confounding and allows for a more focused assessment of the predictive performance of risk scores. This balance suggests that subsequent differences or lack thereof in thrombotic and mortality outcomes are more likely attributable to disease-specific or valve-related factors rather than underlying patient characteristics. Similar observations have been reported in prior valve-focused cohorts, where baseline equivalence enhanced the interpretability of prognostic analyses [11,12].

The finding that CHA₂DS₂-VASc scores were comparable between patients with and without prosthetic valve thrombosis highlights a fundamental limitation of applying this score beyond its original clinical context. CHA₂DS₂-VASc was developed to estimate thromboembolic risk in non-valvular atrial fibrillation, incorporating systemic risk factors such as age, hypertension, diabetes, and prior cerebrovascular events. Prosthetic valve thrombosis, however, is a pathophysiologic ally distinct entity, often driven by mechanical factors, altered hemodynamics, prosthesis design, anticoagulation quality, and local flow disturbances. As a result, systemic vascular risk factors may play a secondary role, which could explain why the score failed to differentiate thrombotic risk in this population. This discrepancy underscores the challenge of extrapolating established clinical tools to specialized cardiovascular conditions without validation [13,14].

The limited discriminative performance observed in the ROC analysis further reinforces the notion that CHA₂DS₂-VASc is not well suited for predicting prosthetic valve thrombosis. A risk model's predictive accuracy depends on its alignment with the underlying mechanisms of the outcome of interest. In the case of prosthetic valve thrombosis, factors such as sub therapeutic anticoagulation, pannus formation, prosthesis position, and patient prosthesis mismatch are known to exert a stronger influence than traditional vascular risk markers. The inability of CHA₂DS₂-VASc to capture these determinants likely contributes to its poor classification performance. This finding aligns with previous research suggesting that valve-specific variables outperform generalized cardiovascular risk scores in predicting prosthesis-related complications [15,16].

Another important observation from this study is the lack of association between CHA₂DS₂-VASc score and mortality, irrespective of thrombotic status. Mortality in patients with mechanical valves is multifactorial, influenced by procedural factors, long-term anticoagulation management, bleeding risk, infection, and progression of underlying cardiac disease. While components of the CHA₂DS₂-VASc score reflect general cardiovascular risk, they do not adequately encompass the complexities that govern survival in this patient population. Consequently, the score's failure to stratify mortality risk is not unexpected and highlights the limitations of using a single, simplified scoring system to predict a multifaceted outcome such as death in valve recipients [17,18].

The comparable CHA₂DS₂-VASc scores observed between survivors and non-survivors within both thrombotic and non-thrombotic subgroups further emphasize the score's limited prognostic scope. This finding suggests that once patients enter the clinical trajectory of mechanical valve implantation, outcomes are driven less by baseline vascular risk factors and more by dynamic clinical variables encountered during follow-up. These may include anticoagulation stability, adherence to therapy, valve-related complications, and undercurrent illnesses. Such factors evolve over time and are not captured by static baseline scores, thereby reducing the relevance of CHA₂DS₂-VASc for long-term prognostication in this setting [19,20].

From a clinical perspective, these results have important implications. Reliance on CHA₂DS₂-VASc for risk stratification in patients with mechanical prosthetic valves may lead to a false sense of reassurance or, conversely, unnecessary concern, neither of which is desirable in clinical decision-making. Instead, clinicians should prioritize valve-specific risk assessment strategies that incorporate echocardiographic findings, prosthesis characteristics, anticoagulation parameters, and markers of systemic or local

thrombogenicity. Integrating these elements into composite risk models may offer superior predictive accuracy and improve patient outcomes through earlier identification of high-risk individuals [21,22].

The findings of this study also highlight the broader issue of score generalizability in cardiovascular medicine. Risk models developed for one population or outcome are often applied to others due to convenience or familiarity, despite differing pathophysiological contexts. This practice underscores the need for rigorous external validation and, when necessary, the development of novel tools tailored to specific disease states. In the era of precision medicine, moving beyond one-size-fits-all risk scores toward more nuanced, condition-specific models is increasingly recognized as a priority in improving prognostic accuracy and therapeutic targeting [23,24].

Several considerations may help explain why CHA₂DS₂-VASc underperformed in this cohort. Mechanical prosthetic valve thrombosis is a relatively rare but severe complication, often precipitated by abrupt changes in anticoagulation status or localized mechanical issues. These triggers may overshadow chronic vascular risk factors included in the score. Furthermore, the binary weighting system of CHA₂DS₂-VASc may inadequately reflect the relative contribution of individual components in the context of prosthetic valves. Such structural limitations reduce the score's flexibility and adaptability to outcomes outside its original scope [25,26].

In summary, the present findings demonstrate that the CHA₂DS₂-VASc score has limited utility for predicting prosthetic valve thrombosis and does not effectively stratify mortality risk in patients with mechanical heart valves. While the score remains indispensable in atrial fibrillation management, its role should not be extended uncritically to valve-related complications. Future research should focus on developing and validating dedicated risk stratification models that integrate clinical, echocardiographic, and laboratory parameters specific to prosthetic valve pathology. Such efforts are essential to enhance risk prediction, optimize patient monitoring, and ultimately improve clinical outcomes in this high-risk population.

Conclusion

In patients with mechanical prosthetic valves, the CHA₂DS₂-VASc score demonstrated limited clinical utility for predicting thrombotic events and mortality. Despite its established role in thromboembolic risk stratification for atrial fibrillation, the score failed to effectively discriminate patients at risk for prosthetic valve thrombosis or adverse survival outcomes. These findings suggest that thrombotic complications and mortality in this population are likely driven by

valve-specific, hemodynamic, and anticoagulation-related factors not captured by the CHA₂DS₂-VASc framework. Therefore, reliance on this score alone may be insufficient for risk assessment in patients with mechanical valves. Future research should focus on developing and validating dedicated prognostic models incorporating prosthesis characteristics, anticoagulation quality, and markers of hypercoagulability to improve risk stratification and clinical decision-making in this high-risk population.

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Conflicts of interest

The authors declare that they have no competing interests.

Disclosure Statement

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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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