

Retrospective Analysis of International Normalized Ratio Management in Valve Replacement Patients to Reduce Thromboembolic and Bleeding Complications

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Abstract

Background: Effective management of the International Normalized Ratio (INR) is crucial for patients undergoing valve replacement surgery to minimize the risk of thromboembolic and bleeding complications. Patients with mechanical heart valve replacements are especially vulnerable to thrombus formation and associated risks, necessitating precise anticoagulation management. **Methods:** This retrospective study evaluated the effectiveness of INR monitoring protocols in patients with mechanical heart valve replacements. The primary objectives included assessing the role of routine prothrombin time (PT) testing, optimizing anticoagulant dosage adjustments, and examining the impact of structured patient education on adherence to anticoagulation therapy. INR levels, their correlation with adverse clinical events, and the outcomes of consistent monitoring practices were systematically analyzed. **Results:** Findings highlighted the critical importance of maintaining INR within optimal therapeutic thresholds, which substantially reduced the incidence of thromboembolic and hemorrhagic events. Routine PT/INR testing combined with timely anticoagulant adjustments proved effective in enhancing patient safety. Furthermore, advancements in anticoagulation therapies and emerging point-of-care monitoring technologies contributed to improved clinical outcomes. The implementation of structured patient education and follow-up systems significantly improved therapy adherence and reduced adverse events. **Conclusion:** Standardized postsurgical INR management protocols are essential to enhance the safety and effectiveness of anticoagulation therapy in valve replacement patients. Maintaining INR within target ranges lowers the risk of thromboembolic and bleeding complications, thereby improving overall patient outcomes and reducing mortality rates. Integrating patient education programs and robust follow-up systems further optimizes long-term anticoagulation management and empowers patients in their care.

Keywords: Anticoagulation therapy, international normalized ratio management, mechanical heart valve, patient education, thromboembolic complications

INTRODUCTION

Valvular heart disease (VHD) is a significant cause of morbidity and mortality worldwide, with valve replacement surgery being a common therapeutic intervention for patients with severe valve dysfunction. The need for effective anticoagulation therapy postvalve replacement is critical, as it reduces the risk of thromboembolic events, which can lead to complications such as stroke, systemic embolism, and valve thrombosis.^[1,2] The optimal management of anticoagulation, however, remains complex as the balance between preventing clot formation and minimizing the risk of bleeding complications is crucial for patient safety.^[3] Prothrombin Time (PT) and the International

Normalized Ratio (INR) are widely used to monitor anticoagulation therapy, particularly in patients undergoing

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mechanical valve replacement. These laboratory markers provide a standardized measure of blood clotting tendencies and help guide the dosage of anticoagulants such as warfarin. Maintaining an INR within a therapeutic range (2–3) is essential to prevent adverse outcomes, but variability in anticoagulation response, influenced by genetic, environmental, and clinical factors, often complicates management.^[1]

The patients undergoing valve replacement need careful follow-up in the postoperative period. To avoid early thromboembolic events, the commencement of an efficacious early anticoagulation protocol is important. This is a big challenge to demonstrate a balance between the risks of under-anticoagulation (thromboembolic events) against those of over-anticoagulation (bleeding complications). The optimal approach to early postoperative anticoagulation after mechanical valve implantation remains controversial. These complications occur most commonly within 6 months after implantation and can adversely affect mortality and morbidity.^[4] The need for lifelong anticoagulation in patients with mechanical valves is globally accepted. In general, a recent mechanical valve implantation is a strong risk factor for thromboembolic complications, especially in the first 3–6 months after surgery. In patients not receiving long-term anticoagulation therapy, the average rate of major thromboembolism is estimated to be 4–8 per 100 patients-years. This risk is reduced to 2.2 per 100 patients-years with antiplatelet therapy, and further reduced to 1 per 100 patients-years with oral anticoagulation.^[2,5] Thus, the utilization of postoperative anticoagulation therapy decreases the incidence of major embolism by approximately 75% and has become the standard of care for all patients with valve replacement.

This retrospective study aims to evaluate the efficacy of anticoagulation therapy postvalve replacement in cardiac patients, specifically analyzing the relationship between PT, INR, and clinical outcomes. By reviewing patient data, this study seeks to provide insights into how well current anticoagulation protocols align with desired therapeutic targets and identify potential areas for improving patient care. The findings of this research could contribute to rectifying anticoagulation strategies and enhancing the safety and efficacy of post-surgical management in valve replacement patients.

METHODS

Ethical considerations

This study was conducted in strict accordance with the ethical principles outlined in the Declaration of Helsinki and adhered to all relevant institutional and national guidelines for research involving human subjects. The study protocol received formal approval from the Institutional Ethics Committee (IEC) of Madras Medical Mission Hospital, Chennai (ECR/140/Inst/TN/2013/RR-20), with the committee reviewing and approving the protocol on July 5, 2021. The study team took all necessary precautions to protect patient privacy and maintain data security throughout the research process. Access to patient information was restricted to authorized personnel only,

and all findings are presented in aggregate form to prevent identification of individual patients. These measures were implemented to uphold the highest ethical standards and to safeguard the rights and welfare of all participants included in the study.

Type of sampling and reasons for selection

A purposive sampling technique was used for this retrospective study. Patient medical records were selected based on predefined inclusion criteria: individuals who had undergone valve replacement surgery and were on oral anticoagulation therapy during the study period. The sampling was limited to patients with documented follow-up data on PT and INR values. The purposive approach ensured that only relevant cases with complete and reliable clinical data were included for analysis. This method was appropriate given the study's retrospective nature and the need to evaluate the quality of anticoagulation management post-surgery.

Study design and patient selection

This retrospective cohort study was conducted to evaluate the anticoagulation therapy following valve replacement in cardiac patients, specifically focusing on the PT and INR. The study was carried out at The Madras Medical Mission Hospital, Chennai, involving 50 patients who underwent valve replacement procedures between 2016 and 2020. The study protocol received approval from the IEC, and patient confidentiality was strictly maintained in accordance with ethical guidelines. Patients were included if they met the following criteria: adults aged 18 years and above at the time of surgery; those who underwent mechanical valve replacement procedures, including mitral, aortic, or double valve replacement; and those who received anticoagulation therapy, specifically warfarin, following surgery. In addition, eligible patients had to have at least two documented PT and INR values recorded during their follow-up period, along with complete medical records containing clinical, surgical, follow-up visit details, and anticoagulation monitoring data.

Patient consent statement

This study was conducted as a retrospective analysis utilizing anonymized data extracted from existing medical records. In accordance with the guidelines set forth by the IEC and the Declaration of Helsinki, individual patient consent was not required, as no identifiable personal information was collected or reported. A waiver of informed consent was formally obtained from the IEC prior to commencing the study. All data were handled with strict confidentiality, and patient privacy was rigorously protected throughout the research process.

Inclusion criteria

Patients who were above 18 years of age, with single and double mechanical valve replacement done from the year 2016 to 2020 are included.

Exclusion criteria

Patients were excluded if they had severe heart failure, renal impairment, malignancy, active or latent Hepatitis B or active

Hepatitis C infection, or other serious comorbidities such as HIV, tuberculosis, or psychiatric illness. Data were collected from electronic medical records (EMRs) and analyzed to assess anticoagulation management practices, clinical outcomes, and associated complications in this population.

Data availability statement

The data used in this study were obtained from institutional medical records and contain patient information. Due to ethical and privacy restrictions, the datasets are not publicly available. However, de-identified data may be made available from the corresponding author on reasonable request and with prior approval from the IEC.

Data collection and outcome measures

Data were analyzed from EMR, which includes demographic data such as age, gender, comorbidities (e.g., hypertension and diabetes), and risk factors. The surgical data, such as type of valve replacement (mitral/aortic/double valve), date of surgery, and any intraoperative complications, anticoagulation therapy as type of anticoagulant prescribed (warfarin or other), dosing regimen, and any adjustments made during the follow-up period, were reviewed. The laboratory parameters as PT and INR levels, were recorded at multiple time points during the post-operative period, typically at monthly intervals, during follow-up visits. The clinical outcomes were based with regards to thromboembolic events (e.g., stroke, systemic embolism), bleeding complications (e.g., major or minor bleeds), and mortality, as well as any hospital readmissions related to anticoagulation management.

Prothrombin time and international normalized ratio evaluation methodology

The evaluation of PT is typically analysed by a laboratory technologist on an automated instrument at 37°C. Blood is drawn into a test tube containing liquid sodium citrate, which acts as an anticoagulant by binding the calcium in a sample. The blood is mixed, and then centrifuged to separate blood cells from plasma (as PT is most commonly measured using blood plasma). A sample of the plasma is extracted from the test tube and placed into a measuring test tube (Note: for an accurate measurement, the ratio of blood to citrate needs to be fixed and should be labeled on the side of the measuring test tube by the manufacturing company; many laboratories will not perform the assay if the tube is under filled and contains a relatively high concentration of citrate-the standardized dilution of one part anticoagulant to nine parts whole blood is no longer valid). Next, an excess of calcium (in a phospholipid suspension) is added to the test tube, thereby reversing the effects of citrate and enabling the blood to clot again. Finally, in order to activate the extrinsic/tissue factor clotting cascade pathway, tissue factor (also known as factor III) is added, and the time the sample takes to clot is measured optically. Some laboratories use a mechanical measurement, which eliminates interferences from lipemic and icteric samples. PT and INR were measured using standard laboratory procedures, and INR values were obtained using the International Sensitivity Index

corresponding to the local testing methods. The therapeutic INR range was defined according to the type of valve replacement, as mechanical valves INR goal of 2.0–3.0. Variability in PT/INR values was assessed over time to determine the adequacy of anticoagulation therapy.

Statistical analysis

Descriptive statistics were used to summarize patient demographics, clinical characteristics, anticoagulation regimens, and outcomes. Continuous variables were reported as mean $\pm$ standard deviation or median with interquartile range, depending on data distribution, while categorical variables were presented as frequencies and percentages. The association between PT/INR levels and clinical outcomes including thromboembolic events, bleeding complications, and mortality was assessed using chi-square tests for categorical variables and either independent t-tests or Mann-Whitney U tests for continuous variables, as appropriate. Logistic regression analysis was performed to identify independent predictors of poor anticoagulation control (defined as time in therapeutic range $< 70\%$) and adverse outcomes. All statistical tests were two-tailed, and a $P < 0.05$ was considered statistically significant. Analyses were conducted using standard statistical software. This approach ensured a robust evaluation of the relationship between anticoagulation management and clinical outcomes in patients following valve replacement surgery.

RESULTS

A total of 50 patient records were reviewed during the study period to evaluate clinical profiles, adherence to anticoagulation therapy, and associated outcomes in individuals who underwent valve replacement surgery. Among these patients, 28 (56%) were male and 22 (44%) were female [Figure 1], indicating a slight male predominance in the surgical cohort. This distribution aligns with previous literature suggesting higher prevalence and earlier onset of VHD among males. Regarding the type of valve replacement procedure, mitral valve replacement was the most frequently performed (48%), followed by aortic valve replacement (32%) and double valve replacement (20%) [Figure 2]. The prevalence of mitral valve replacement is consistent with the dominant etiology in the cohort, rheumatic heart disease, reported in 50% of patients.

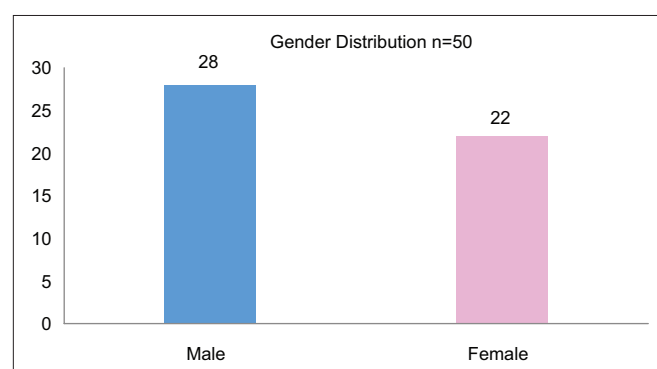


Figure 1: Gender distribution of valve replacement in patients

Longitudinal follow-up of INR monitoring over 5 years showed a steady decline in adherence [Figure 3]. In the 1st year, nearly 100% of patients underwent INR testing regularly. However, this adherence dropped to 80% in the 2nd year, 70% in the third year, 55% in the fourth year, and 40% by the 5th year. Although no statistical subgroup analysis was performed, this downward trend strongly suggests declining patient engagement over time. The contributing factors include a lack of health education reinforcement, limited follow-up infrastructure, and asymptomatic status leading to decreased perceived need for monitoring. This decline was clinically significant, as patients with irregular INR follow-up were disproportionately represented among those experiencing adverse events, underscoring the critical link between consistent monitoring and patient safety.

Age distribution analysis revealed that the majority of patients (42%) were aged 51–60 years [Figure 4], with this group likely representing the peak incidence for surgical intervention due to cumulative valve degeneration or long-standing rheumatic disease. Only 2% were in the 20–30 age group, and 4% were over 70, indicating relatively lower surgical intervention at age extremes. Adverse events were observed in 23 patients (46%) during the follow-up period [Figure 5]. Drug-induced coagulopathy was the most frequent complication (24%), followed by valve-related events (18%). Hematoma formation was rare (2%), and mortality was recorded in two patients

(4%) due to medication noncompliance. These findings show direct clinical consequences of inadequate INR control. The descriptive data show reduced INR adherence to a higher incidence of adverse outcomes.

Baseline clinical characteristics [Figure 4 and Table 1] show the complexity of patient profiles. Atrial fibrillation was present in nearly one-quarter of patients, and 18% had a reduced left ventricular ejection fraction (LVEF) (<40%), suggesting compromised cardiac function in a notable proportion. The predominance of rheumatic pathology underscores the continued burden of preventable heart disease in this population. Sociodemographic profiling [Figure 5 and Table 2] showed that 76% of patients were from urban areas, which may reflect both better access to surgical services and regular follow-up care. The high survival rate (96%) suggests that surgical valve replacement, when paired with adequate monitoring and management, is associated with favorable long-term outcomes. However, the small but significant mortality due to nonadherence signals the need for intensified follow-up, especially as monitoring adherence declines over time.

CONCLUSION

The results of this study support the hypothesis that consistent INR monitoring and adherence to anticoagulation protocols are vital for improving outcomes in valve replacement patients.

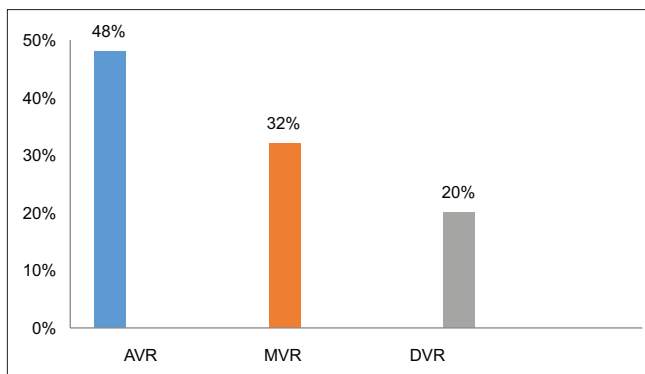


Figure 2: Procedure type distribution

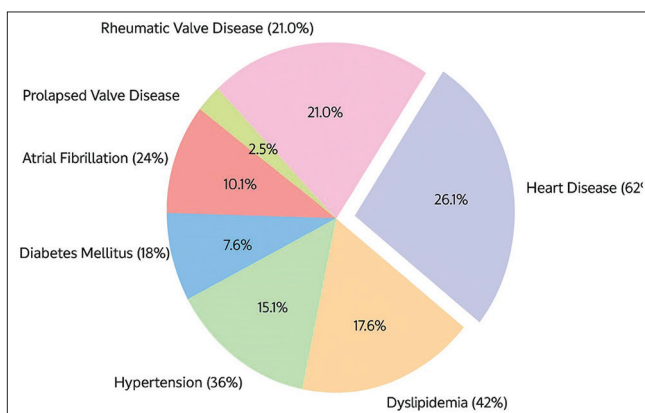


Figure 4: Demographic and clinical profile of valve replacement patients

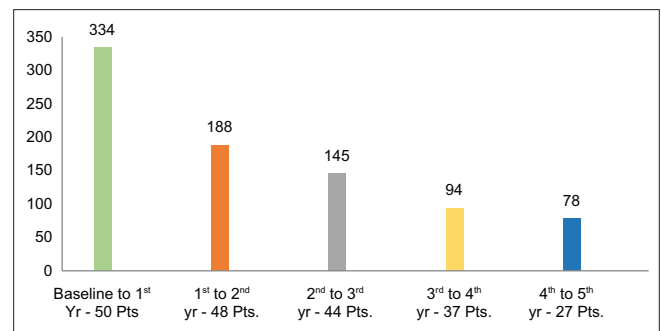


Figure 3: Number of international normalized ratio assays per year during the periodic review

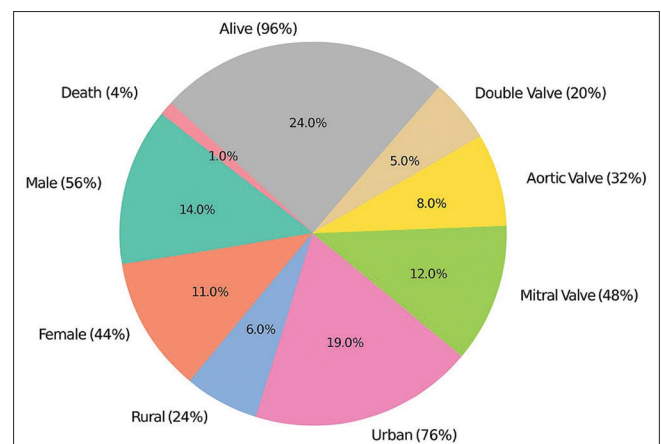


Figure 5: Clinical characteristics and health profile distribution

Table 1: Baseline characteristic of the valve replacement patients

Characteristics	n=50, n (%)
Age (years), mean±SD (range)	52.2±11.2 (27–76)
Atrial fibrillation	12 (24)
Comorbidity	
Diabetes mellitus	9 (18)
Hypertension	18 (36)
Dyslipidaemia	21 (42)
Heart disease	31 (62)
Echocardiographic findings	
LVEF (96%) mean±SD	51.3±11.62
LVEF < 40%	9 (18)
Pathology of valve disease	
Rheumatic	25 (50)
Prolapsed	3 (6)

SD: Standard deviation, LVEF: Left ventricular ejection fraction

Table 2: Sociodemographic and clinical profile of patients

Parameters	n (%)
Gender	
Male	28 (56)
Female	22 (44)
Residence	
Rural	12 (24)
Urban	38 (76)
Replaced valve	
Mitral only	24 (48)
Aortic only	16 (32)
Mitral and aortic	10 (20)
Outcome	
Alive	48 (96)
Dead	2 (4)

The findings also highlight key areas such as rural access, patient education, and procedure-specific follow-up needs where targeted interventions can enhance long-term patient care.

Key findings

Among the 50 patients studied, 56% were male, with the majority (42%) aged between 51 and 60 years. Mitral valve replacement was the most common procedure, accounting for 48% of cases, followed by aortic valve replacement (32%) and double valve replacement (20%). Adherence to INR monitoring declined significantly over time, from nearly 100% in the 1st year to just 40% by the 5th year. Adverse events were reported in 46% of the patients, with drug-induced coagulopathy being the most frequent (24%). There were two deaths (4%), both attributed to medication noncompliance. Rheumatic heart disease emerged as the leading underlying cause, affecting 50% of the cohort, while 18% had a reduced LVEF of < 40%. The majority of patients (76%) were from urban areas, and the overall survival rate during the study period was 96%.

DISCUSSION

Patients with valve replacement face a higher risk of complications due to altered coagulation status, as they require long-term oral anticoagulant therapy following surgery. Studies done in Asian population have reported a marked decrease in bleeding and effective prevention of thromboembolism with appropriate anticoagulation (INR 2–3) in patients with valve replacement.^[6] The discussion of this study highlights the critical role of effective anticoagulation management in improving outcomes for patients undergoing valve replacement. Despite advancements in surgical techniques and anticoagulation therapies, adverse events such as thromboembolic complications, bleeding, and mortality remain significant concerns.^[7] One of the primary challenges identified is the variability in INR levels, which can result from poor adherence to medication, inadequate patient education, or irregular follow-up. Drug-induced coagulopathy and thromboembolic events, observed in a substantial proportion of patients, underscore the need for stringent monitoring and timely intervention.^[8] The Importance of health education plays a pivotal role in empowering patients to actively participate in their care. Providing patients with clear, concise information about the importance of maintaining therapeutic INR levels, recognizing symptoms of complications, and adhering to prescribed medications can improve compliance and reduce the risk of adverse events. Health education, including audio tutorial aids as one-on-one counseling, can address gaps in understanding and foster better health practices.^[9] With regards to regular INR monitoring and follow-up, consistent INR monitoring is a cornerstone of anticoagulation therapy. Regular checks enable early detection of deviations from the therapeutic range, allowing for prompt dose adjustments to prevent complications. Appropriate follow-up care, including reminders for INR testing and consultations, ensures ongoing engagement with healthcare providers and reduces the likelihood of medication non-compliance.^[10] With discussion on potential outcomes of improved practices, it is studied that reduced thromboembolic events will be maintaining INR within the target range, minimizing the risk of clot formation and associated complications. The decreased bleeding incidents and early identification of elevated INR levels can prevent excessive anticoagulation and subsequent bleeding episodes. The lower mortality rates and comprehensive management, including health education and regular follow-up, can mitigate life-threatening complications and improve survival rates.

CONCLUSION

This study is highly significant for the management of patients with mechanical heart valve replacements. The study demonstrates that rigorous and routine monitoring of INR, coupled with timely adjustments to anticoagulant therapy, substantially reduces the incidence of both thromboembolic and bleeding complications. This finding reinforces the

necessity of maintaining INR within the recommended therapeutic range (typically 2.0–3.0), as deviations can lead to serious adverse outcomes such as stroke, valve thrombosis, or major hemorrhage. In addition, it highlights the positive impact of structured patient education and robust follow-up systems, which were shown to improve adherence to therapy and further decrease the risk of complications. These results align with previous reports, which have consistently shown that effective anticoagulation management can reduce the rate of major thromboembolic events from 4 to 8 per 100 patient-years (without therapy) to approximately 1 per 100 patient-years with oral anticoagulation. However, this study adds further value by emphasizing the role of patient engagement and systematic follow-up, areas that have often been under-addressed in earlier research. By providing real-world data from a retrospective cohort, the manuscript supports current guidelines while also advocating for enhanced patient education and monitoring strategies to optimize long-term outcomes in this high-risk population.

Outcome of the study

This retrospective study evaluated anticoagulation control among patients who underwent valve replacement surgery and who were on long-term oral anticoagulation therapy. A significant proportion of patients exhibited suboptimal INR control, with frequent deviations from the therapeutic range. Patients with poor INR regulation were found to have a higher incidence of complications such as minor bleeding and thromboembolic events. The findings prove the importance of regular INR monitoring and adherence to anticoagulation protocols to ensure therapeutic effectiveness and mainly reduce adverse events. In addition, the results highlight the need for improved patient education and follow-up strategies to enhance anticoagulation management and minimize the risks associated with both over- and under-anticoagulation.

Rationale of the study

Patients undergoing valve replacement surgery require lifelong oral anticoagulation therapy to prevent thromboembolic complications. Warfarin remains the most commonly used anticoagulant in these patients, and its effectiveness is closely monitored through PT and INR values. Maintaining INR within the therapeutic range is critical, as both under- and over-anticoagulation can lead to serious complications, including stroke, valve thrombosis, or bleeding events. In spite of the established protocols, anticoagulation management remains a challenge in clinical practice, particularly due to factors such as poor patient adherence, irregular monitoring, and variable response to therapy. In low-resource settings, these issues are often amplified by limited access to routine INR testing and inadequate patient counseling.

This retrospective study was conducted to evaluate real-world patterns of anticoagulation control in patients after valve replacement, assess the frequency of INR deviations, and identify associated clinical outcomes. The findings aim to highlight gaps in current management practices and provide

insights for improving follow-up care, patient education, and adherence to anticoagulation guidelines.

Limitations of this study

The retrospective nature of this study may have introduced selection bias, as it depended on the accuracy and completeness of existing patient records. In addition, variations in anticoagulation management protocols across different healthcare providers limit the generalizability of the findings. The study also relied on INR values, which can be influenced by confounding factors such as dietary habits, drug interactions, and patient adherence variables that were not fully accounted for. Furthermore, since the study was conducted in a single institute, the results may not be representative of broader or international patient populations. Despite these limitations, the study offers valuable real-world insights into anticoagulation management practices and highlights critical areas for improving patient education, therapy adherence, and prevention of mortality and hospital admissions due to bleeding events and thromboembolism.

Author contribution statement

Juno Angel Jebasingh designed the study, collected, analyzed the data, and drafted the manuscript. Ramkumar Soli Rajaram was involved in clinical data acquisition and interpretation of clinical outcomes and provided critical revisions to the manuscript. Marutha Priya Sriskanda Rajah assisted in data collection, literature review, and statistical analysis. Abirami Gopalakrishnan and Jayanthi Malayandi contributed to data analysis and manuscript editing. Ashok Kumar Krishna Kumar provided contributed to the interpretation of cardiovascular findings and reviewed the manuscript. Suganthi Muthusamy provided overall project supervision and critically revised the manuscript.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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