Published in final edited form as:

J Card Surg. 2020 November ; 35(11): 2887–2894. doi:10.1111/jocs.14902.

Anticoagulation Following Mitral Valve Repair

Tessa M. F. Watt, MD, MSc¹, Shannon L. Murray, MSH¹, Alexander A. Brescia, MD, MSc¹, David A. Burn, PhD², Alexander Wisniewski, MD³, Shazli P. Khan, MD⁴, Matthew A. Romano, MD¹, Steven F. Bolling, MD¹ Michigan Mitral Research Group (MMRG)

¹Department of Cardiac Surgery, University of Michigan, Ann Arbor, MI

²Department of Mathematics, Quinnipiac University, Hamden, CT

³University of Toledo College of Medicine, Toledo, OH

⁴Department of Internal Medicine, University of Pittsburgh Medical Center, Pittsburgh, PA

Abstract

Background and Aim: Anticoagulation after mitral valve repair is controversial and guidelines are not well-established. This study evaluated the association between postoperative warfarin use and complications after mitral valve repair, including bleeding and thromboembolic incidents, readmission, and mortality.

Methods: This retrospective study investigated 1097 patients who underwent elective mitral valve repair between April 2003 and March 2017, and were naïve to atrial fibrillation or prior cardiac surgery. This cohort had no other indication for or against anticoagulation. 775 patients were placed on warfarin with INR goal 2.5, and 322 patients were not anticoagulated. The association between anticoagulation and complications was assessed with univariate comparisons between groups and multiple logistic regression.

Results: Postoperative warfarin use was associated with a reduced composite of bleeding and thromboembolic complications (pulmonary embolism, TIA, stroke, pericardial effusion or cardiac tamponade, GI bleeding, and reoperation for bleeding) with an odds ratio of 0.29 (95% CI 0.13–0.64, $p=0.003$). There was no difference in 30-day or 6-month mortality or readmission rate between groups. Long-term survival estimates were superior in the warfarin group (10-year: 92% vs. 85%; log-rank $p<0.001$).

Conclusions: Our analysis showed that postoperative warfarin use was associated with an overall reduced composite of bleeding and thromboembolic incidents and superior long-term survival. These findings suggest that anticoagulation with warfarin following mitral valve repair may be a safe and effective means for avoiding postoperative complications, and that a large prospective randomized clinical trial is warranted.

Address for correspondence: Tessa M. F. Watt, MD, MSc, 1500 East Medical Center Drive, Ann Arbor, MI 48109, Phone: (734) 936-4981 tmfwatt@med.umich.edu.

This manuscript was presented at the 98th Annual Meeting of the American Association for Thoracic Surgery, San Diego, California, on April 28–May 1, 2018.

Keywords

valve repair/replacement; cardiovascular research

INTRODUCTION

Mitral valve surgery is the treatment of choice for severe mitral regurgitation;^{1–2} however, there is wide variation in the clinical practice of anticoagulation for thromboembolic prophylaxis after mitral valve surgery. Anticoagulation after mitral valve replacement (MVR) is intended to reduce clot formation on new prosthetic material and suture lines, and in turn reduce the risk of thromboembolism until the prosthetic material is fully endothelialized, a process that generally takes three months.^{1,3} Mitral valve surgery has been associated with increased short-term risk of thromboembolic incidents after surgery, with an incidence of ischemic stroke within the first 30 postoperative days reported to be 4.6% $\pm$ 1.5% for MVR with a biological prosthesis, 1.5% $\pm$ 0.4% for mitral valve repair (MVR), and 1.3% $\pm$ 0.8% for a mechanical prosthesis.⁴ In addition, roughly one-third of patients undergoing mitral valve surgery will experience atrial fibrillation postoperatively, which has been associated with increased risk of stroke and early death, and further supports the use of anticoagulation for thromboembolic prophylaxis.^{5–8} In a nonrandomized study, patients who received vitamin K antagonist (VKA) anticoagulation after MVR had a lower rate of thromboembolism than those who did not receive VKA prophylaxis.⁹ However, the potential benefit of anticoagulation therapy must be carefully weighed against the risk of bleeding. The 2017 AHA/ACC Guidelines recommend 3–6 months of anticoagulation with a VKA to achieve INR 2.5 after bioprosthetic MVR.¹ This is a class IIA recommendation based on expert opinion and scant literature as randomized control trials on this topic are lacking.¹ However, there is no consensus on guidelines for anticoagulation following MVR.

The debate on use of anticoagulation after MVR continues, and current evidence on this topic is discordant.^{10–11} One retrospective study of the Danish National Patient Registry found that VKA anticoagulation after MVR was associated with significantly reduced risk of stroke and death without increased risk of bleeding during the first three months after surgery.¹² However, a retrospective analysis from the University of Toledo found no significant difference in perioperative stroke rate or mortality in patients undergoing MVR or MVR with or without VKA anticoagulation.¹³ These conflicting results have led to wide variation in clinical practice.

To address this issue, this large retrospective study of patients who underwent routine MVR was completed to assess the association between warfarin use and the rate of postoperative bleeding and thromboembolic complications within the first six months after surgery.

MATERIALS AND METHODS

The institutional review board at the University of Michigan deemed this study to be exempt from review.

Patient Population

This study is a retrospective analysis of adults undergoing elective MVr for mitral regurgitation between April 2003 and March 2017 at the University of Michigan. Patients were identified through the University of Michigan's Research Database and the Society of Thoracic Surgery (STS) National Adult Cardiac Surgery Database (ACSD). All patients were in normal sinus rhythm at time of hospital discharge and had a follow-up visit at the University of Michigan, either in cardiology clinic or cardiac surgery clinic, six months after surgery ($\pm$ one month).

Patients who had undergone previous cardiac surgery and those with a history atrial fibrillation, preoperative dialysis, bleeding or clotting disorder, or preoperative anticoagulation for any reason were excluded. Patients undergoing concomitant tricuspid valve repair (TVr) were included, whereas those undergoing concomitant CABG, aortic valve replacement, or left ventricular aneurysm repair were excluded. Patients who developed postoperative atrial fibrillation and remained in atrial fibrillation at the time of hospital discharge were also excluded from our analysis to reduce confounding in assessing anticoagulation among patients in normal sinus rhythm after MVr. The final population of 1097 patients for analysis is depicted in Figure 1.

Treatment Groups

Of the 1097 patients, 775 patients were placed on warfarin prior to hospital discharge and 322 patients were not anticoagulated. The choice of postoperative anticoagulation was based on surgeon preference. Those placed on warfarin had an INR goal of 2.5. Discharge was not delayed to achieve therapeutic INR. The warfarin group was anticoagulated for 30 days from discharge to the 30-day postoperative visit, at which time warfarin was discontinued if they remained in normal sinus rhythm.

All patients were routinely placed on 81mg aspirin regardless of postoperative VKA anticoagulation and were instructed to remain on 81mg aspirin indefinitely. For the extremely small proportion of patients who present with an aspirin intolerance or allergy, aspirin is removed but the medication regimen not otherwise altered. For example, those planning to receive warfarin and an 81mg aspirin would then only receive warfarin, whereas patients intended to receive aspirin alone would not undergo any antiplatelet or anticoagulation therapy.

Data Collection and Outcomes

Data including patient demographics and preoperative risk factors, operative details, and postoperative outcomes at 30 days and 6 months were collected retrospectively from the institutional component of the STS ACSD and supplemented through individual chart review.

The primary outcomes were postoperative bleeding and thromboembolic complications, evaluated both as a composite outcome and separately. Major bleeding complications included postoperative pericardial effusion or cardiac tamponade, gastrointestinal (GI) bleeding, and reoperation for bleeding within six months after MVr. Major thromboembolic

complications included pulmonary embolism, TIA, or stroke within 6 months after MVr. Of note, all of the strokes in this cohort were ischemic. All bleeding and thrombotic events in the warfarin group occurred after warfarin therapy was begun. Secondary outcomes included mortality and readmission within 6 months of MVr.

Statistical Analysis

Preoperative patient characteristics and postoperative outcomes were compared between those anticoagulated with warfarin and those who were not. After appropriate tests for normality were performed, a preliminary analysis was conducted to evaluate heterogeneity of the groups using Student's t-tests for continuous variables and chi-squared tests for categorical variables to determine if the differences were significant. SPSS (IBM, v24.0) and Minitab® 18.1 were used for statistical analysis and significance was determined with 95% confidence at the level $p < 0.05$.

Chi-squared tests were used to evaluate the differences in pre and postoperative categorical variables between the warfarin and non-warfarin groups. Student's t-tests were used to evaluate the differences in pre and postoperative continuous variables between the warfarin and non-warfarin groups. All continuous variables were displayed with mean, standard deviation, and range.

Given that composite outcomes were recorded in two levels, defined by the absence or presence of the event, a multiple logistic regression was implemented to assess the relative impact of preoperative factors on postoperative outcomes. The multiple logistic regression model allowed for the examination of both categorical and continuous predictors on a binary response of composite bleeding outcomes, composite thromboembolic outcomes, and composite bleeding and thromboembolic outcomes.

The first order statistical model provided a p-value to test statistical significance for each factor in the model for the listed composite outcomes. An odds ratio was also included to measure the association between exposure and outcome. Corresponding confidence intervals were computed for each of the odds ratios. A forward selection method with alpha to enter equal to 0.99 was used to fit the logistic regression model to prohibit convergence. In addition, linearity of the relationship between covariates and outcomes were examined prior to entry into the model.

Since there were multiple surgeons involved in this study, cardiopulmonary bypass time and cross-clamp times were further evaluated for differences between surgeons and impact on outcomes. In addition, Bonferroni confidence intervals were used to compare proportions of postoperative warfarin use across surgeons. A chi-square test of association also evaluated the relationship between surgeon and postoperative warfarin use. Separate one-way ANOVAs were performed to assess the correlation between surgeon and postoperative warfarin use, surgeon and cardiopulmonary bypass time, and surgeon and cross clamp time. The collinear relationship between cardiopulmonary bypass time and cross-clamp time was evaluated and the Pearson correlation coefficient was computed.

To compare the postoperative composite complications, we performed a one-sample confidence interval on proportion for the composite bleeding complications, composite thromboembolic complications, and combined bleeding and thromboembolic complications across surgeons. Simultaneous confidence intervals were calculated on a surgeon to surgeon basis using a Bonferroni correction. A Bonferroni adjustment was computed for the individual confidence intervals to ensure a family-wide confidence level of 95%.

A Kaplan-Meier survival analysis was performed to further assess the differences in long-term survival the warfarin and non-warfarin treatment groups. Statistical significance was measured using the log rank test which evaluates survival through entire follow up period. Confidence intervals were then computed for both groups.

RESULTS

This study cohort consisted of 1097 patients with mean age 57 years and range 18–91 years, 44% of whom were women. 775 of these patients were treated with warfarin postoperatively, and 322 patients were not anticoagulated. The mean age of the warfarin group was 57 years with 43.0% women, and mean age of the non-warfarin group was 55 years with 47.8% women.

Table 1 describes patient and case characteristics for the entire cohort and compares them between the warfarin and non-warfarin groups. Overall the only clinically significant differences in preoperative characteristics found between the treatment groups were lower incidence of current tobacco use ($p<0.001$), lower history of infective endocarditis ($p=0.002$), and higher incidence of immunosuppression ($p<0.001$) in the warfarin group compared to the non-warfarin group. The rates of concomitant tricuspid valve repair as well as postoperative atrial fibrillation were comparable between the groups. However, mean cross-clamp time ($p<0.001$) and cardiopulmonary bypass time ($p<0.001$) were both significantly lower in the warfarin group.

Table 2 compares the individual and composite postoperative outcomes between the warfarin and non-warfarin groups. 30-day mortality, six-month mortality, and readmission rates were comparable between the treatment groups. Analysis of bleeding complications revealed no significant difference in GI bleeding or reoperation for bleeding between the groups. However, rate of pericardial effusion or cardiac tamponade was lower in the warfarin group compared to the non-warfarin group ($p=0.045$), and composite bleeding incidents were lower in the warfarin group compared to the non-warfarin group ($p=0.007$). Although there less than half as many incidents of stroke and composite thromboembolic incidents in the warfarin group than the non-warfarin group, statistical analysis of thromboembolic complications revealed no significant difference in rate of pulmonary embolism, TIA, stroke, or composite thromboembolic incidents between the groups. However, overall composite bleeding and thromboembolic incidents were significantly lower in warfarin group compared to the non-warfarin group ($p=0.002$).

Eight surgeons had cases that were included in this study. To evaluate for potential confounding factors at the surgeon level, the number of cases for each surgeon, along with

the tendency of each surgeon to prescribe postoperative warfarin, are depicted by Figure 2. There was a wide variation in number of cases performed by each surgeon. Surgeon A performed 855 cases, Surgeon B performed 153 cases, and six of the surgeons performed 50 or fewer cases and as a result were grouped together in the “Others” category with 89 total cases. The relative proportion of postoperative warfarin use for these surgeons was 82.7% for Surgeon A, 28.8% for Surgeon B, and 27% for Others. One-way ANOVA revealed significant differences across surgeons in the tendency to prescribe postoperative warfarin ($p<0.001$).

Figure 3 depicts mean cardiopulmonary bypass time by surgeon with standard deviation (SD) and 95% confidence intervals. Surgeon A had mean bypass time of 74 ± 18 minutes, Surgeon B had mean bypass time of 120 ± 37 minutes, and Others had mean bypass time of 141 ± 55 minutes. One-way ANOVA revealed significant differences in bypass time across surgeons ($p<0.001$). The variation in cross-clamp time by surgeon was similarly evaluated. Surgeon A had mean cross-clamp time of 53 ± 14 minutes, Surgeon B had mean cross-clamp time of 97 ± 32 minutes, and Others had mean cross-clamp time of 108 ± 42 minutes. One-way ANOVA revealed significant differences in cross-clamp time across surgeons ($p<0.001$).

Since the measurement of cardiopulmonary bypass time encompasses the time spanned by cross-clamp time, the potential for multicollinearity between these variables was investigated. The resulting Pearson correlation coefficient was 0.95 ($p<0.001$), which was sufficiently large to warrant inclusion of only one of these variables in the logistic regression model. Cardiopulmonary bypass time was chosen for inclusion because it had a more significant relationship with the composite bleeding and thromboembolic outcomes.

Table 3 depicts the results of a multiple logistic regression model designed to evaluate the association between patient characteristics, comorbidities, and operative details and the composite outcome of bleeding and thromboembolic complications. The only independent negative predictor of the composite outcome was postoperative warfarin use, which was associated with a reduction in composite bleeding and thromboembolic complications (OR 0.29 [95% CI 0.13–0.64, $p=0.003$]). This multiple logistic regression model was also used to assess the impact of the predictor variables on composite bleeding incidents alone and composite thromboembolic incidents alone. Again, the only independent negative predictor of composite bleeding complications was postoperative warfarin use (OR 0.30 [95% CI 0.09–0.93, $p=0.036$]). There were no independent predictors of postoperative thromboembolic complications.

Long-term survival was superior in the warfarin group compared to the non-warfarin group (10-year: 92.3% vs. 84.8%, log-rank $p<0.001$; Figure 4).

DISCUSSION

This retrospective study showed that for otherwise healthy patients, who had no indication for or against anticoagulation, postoperative warfarin use after routine MVR was not associated with an increased 30-day or six-month mortality or readmission rate. Although the difference in thromboembolic complications between the groups did not reach statistical

significance, this study revealed less than half the incidence of both stroke and composite thromboembolic incidents in the warfarin group. This suggests that warfarin may confer protection from thromboembolism after MVr; however, with such a low event rate it is likely that a larger study is needed to fully assess this question. Most importantly, overall composite bleeding and thromboembolic incidents were significantly lower in the warfarin group, which was confirmed through multiple logistic regression analysis. Finally, long-term survival estimates were superior in the warfarin group compared to the non-warfarin group.

Surprisingly, the warfarin group had significantly fewer composite bleeding incidents than the non-warfarin group in both univariate and multivariable analyses. While it may seem counterintuitive that there were more bleeding complications in the non-warfarin group, one possible explanation for this could be that patients who seemed more likely to have bleeding incidents after surgery were less likely to receive anticoagulation based on surgeon preference. In addition, this discrepancy could also be explained by surgeon-dependent factors, such as experience level or threshold for taking patients back to the operating room for bleeding.

As a retrospective study, we were not able to control for all possible confounding factors; however, we did identify strong associations between surgeon and postoperative warfarin use, and surgeon and cardiopulmonary bypass time. However, when cardiopulmonary bypass time was factored into the regression analysis, postoperative warfarin use emerged as the only independent predictor associated with reduced composite bleeding and thromboembolic complications. This analysis supports the claim that postoperative anticoagulation with warfarin does not increase the rate of major bleeding complications, and may, in fact, reduce overall bleeding and thromboembolic complication rate. These findings may also mitigate the fear of anticoagulation causing late cardiac tamponade.

To date, current guidelines on anticoagulation after MVr remain highly discordant and clinical practice varies widely.^{14–15} A recent study of 13,082 patients in the STS database who underwent MVr in North America from 2008 to 2010 aimed to determine the incidence and predictors of VKA use after isolated MVr. This study revealed extreme variability in postoperative VKA use, which was largely driven by surgeon or institution preference rather than patient clinical characteristics. While this study associated longer hospital stay with VKA use after surgery, there was no data on bleeding or thromboembolic complications associated with anticoagulation status.¹⁴ Similar to our findings, another retrospective study from a single academic United States institution found that use of postoperative warfarin following MVr or replacement did not significantly reduce the incidence of stroke at early follow up; however, there was a trend for improved long-term outcomes in patients receiving postoperative warfarin therapy.¹⁶

In broad terms, routine MVr has one of the lower risk adverse event profiles in open-heart surgery. As a result, there is little tolerance for postoperative complications, particularly in asymptomatic and otherwise healthy patients. In light of continued debate about postoperative anticoagulation and highly variable clinical practices, the findings of this study emphasize the importance of further investigating this issue with a randomized clinical trial. Future studies may consider evaluating novel oral anticoagulants (NOACs) such as apixaban

and rivaroxaban. However, the lack of reversibility of these anticoagulants should be weighed into this clinical decision.

Limitations

Our study has several key limitations. The retrospective nature of data collection and absence of randomized criteria for the treatment groups limits the conclusions that can be drawn from this study. In addition, this study reflects 14 years of clinical practice involving several surgeons at an academic, high-volume mitral center. We are unable to account for all elements of selection bias, changes in clinical practices over time, and the findings may not be generalizable to other populations. In addition, this study did not track patient's INR values after discharge, and as a result we are unable to correlate bleeding and thromboembolic complications with subtherapeutic or supratherapeutic anticoagulation levels. The effect of individual surgeon may have driven outcomes, which cannot be fully accounted for in a retrospective study. However, to help mitigate this bias, individual surgeon was included in our logistic regression model and not found to be a significant predictor of bleeding or thromboembolic events. This study also did not monitor aspirin dosing. Finally, this study did not match the patient cohort according to distribution of preoperative patient characteristics. However, we utilized multiple logistic regression analysis to mitigate baseline differences, and none of the preoperative patient characteristics were found to impact the composite outcomes.

Conclusions

This study showed that postoperative warfarin use was associated with less overall bleeding and thromboembolic incidents compared to patients who were not anticoagulated. In addition, postoperative warfarin may be associated with improved long-term survival. While this retrospective study has several key limitations, this study did not reveal increased bleeding complications in the warfarin group, suggesting that anticoagulation with warfarin following MVR may be a safe and effective means for reducing postoperative complications. Although this is a negative study, this large experience of anticoagulation after MVR is an important addition to the currently sparse existing literature on this topic. Importantly, a large prospective randomized clinical trial is warranted for further investigation and to establish evidence-based guidelines on this topic.

Disclosure:

AAB is supported by the National Research Service Award postdoctoral fellowship (No. 5T32HL076123).

REFERENCES

1. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2017;70(2):252–289. [PubMed: 28315732]
2. Bonow RO, Carabello BA, Chatterjee K, et al. 2008 focused update incorporated into the ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to revise the 1998 guidelines for the management of patients with valvular

heart disease). Endorsed by the Society of Cardiovascular Anesthesiologists, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2008;52(13):e1–142. [PubMed: 18848134]

3. Paparella D, Di Mauro M, Bitton Worms K, et al. Antiplatelet versus oral anticoagulant therapy as antithrombotic prophylaxis after mitral valve repair. *J Thorac Cardiovasc Surg*. 2016;151(5):1302–1308.e1301. [PubMed: 26832208]
4. Russo A, Grigioni F, Avierinos JF, et al. Thromboembolic complications after surgical correction of mitral regurgitation incidence, predictors, and clinical implications. *J Am Coll Cardiol*. 2008;51(12):1203–1211. [PubMed: 18355659]
5. Asopa S, Patel A, Dunning J. Is short-term anticoagulation necessary after mitral valve repair? *Interact Cardiovasc Thorac Surg*. 2006;5(6):761–765. [PubMed: 17670707]
6. Santos HN, Magedanz EH, Guaragna JC, et al. Predictors of stroke in patients undergoing cardiac surgery. *Rev Bras Cir Cardiovasc*. 2014;29(2):140–147. [PubMed: 25140462]
7. Echahidi N, Pibarot P, O'Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. *J Am Coll Cardiol*. 2008;51(8):793–801. [PubMed: 18294562]
8. Horwich P, Buth KJ, Légaré JF. New onset postoperative atrial fibrillation is associated with a long-term risk for stroke and death following cardiac surgery. *J Card Surg*. 2013;28(1):8–13. [PubMed: 23186205]
9. Heras M, Chesebro JH, Fuster V, et al. High risk of thromboemboli early after bioprosthetic cardiac valve replacement. *J Am Coll Cardiol*. 1995;25(5):1111–1119. [PubMed: 7897124]
10. Vahanian A, Alfieri O, Andreotti F, et al. Guidelines on the management of valvular heart disease (version 2012): the Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur J Cardiothorac Surg*. 2012;42(4):S1–44. [PubMed: 22922698]
11. Whitlock RP, Sun JC, Fries SE, Rubens FD, Teoh KH. Antithrombotic and thrombolytic therapy for valvular disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest*. 2012;141(2 Suppl):e576S–e600S. [PubMed: 22315272]
12. Valeur N, Mérie C, Hansen ML, Torp-Pedersen C, Gislason GH, Kober L. Risk of death and stroke associated with anticoagulation therapy after mitral valve repair. *Heart*. 2016;102(9):687–693. [PubMed: 26729693]
13. Schwann TA, Engoren M, Bonnell M, et al. Mitral valve repair and bioprosthetic replacement without postoperative anticoagulation does not increase the risk of stroke or mortality. *Eur J Cardiothorac Surg*. 2013;44(1):24–31. [PubMed: 23293318]
14. Suri RM, Thourani VH, He X, et al. Variation in warfarin thromboprophylaxis after mitral valve repair: does equipoise exist and is a randomized trial warranted? *Ann Thorac Surg*. 2013;95(6):1991–1998; discussion 1998–1999. [PubMed: 23706423]
15. Vaughan P, Waterworth PD. An audit of anticoagulation practice among UK cardiothoracic consultant surgeons following valve replacement/repair. *J Heart Valve Dis*. 2005;14(5):576–582. [PubMed: 16245494]
16. Thourani VH, Gunter RL, Hurst S, et al. Postoperative warfarin following mitral valve repair or bioprosthetic valve replacement. *J Heart Valve Dis*. 2013;22(5):716–723. [PubMed: 24383387]

Figure 1.
Patient population CONSORT diagram.

Figure 2.

Case volume and postoperative warfarin use by surgeon. Six of the eight surgeons included in this study had 50 or fewer cases and were grouped together in the “Other” category. Within each bar, the relative proportion of postoperative warfarin use by surgeon is depicted.

Figure 3.

Mean cardiopulmonary bypass time by surgeon box-and-whiskers plot. Six of the eight surgeons included in this study had 50 or fewer cases and were grouped together in the “Other” category. The upper and lower borders of the box represent the upper and lower quartiles. The middle horizontal line represents the median. The upper and lower whiskers represent the maximum and minimum values.

Figure 4.

Kaplan-Meier survival analysis of warfarin versus non-warfarin groups. The shaded areas represent 95% confidence intervals and the number of patients at risk for each year after surgery are provided in the embedded table.

Table 1.

Patient and Operative Characteristics

	All Patients n=1097	Warfarin n=775(68.8%)	Non-Warfarin n=322(29.4%)	p-value
Age	57±14	57±13	55±15	0.003 [*]
Male	610(56.6%)	442(57.0%)	168(52.2%)	0.1
Female	487(44.4%)	333(43.0%)	154(47.8%)	0.1
Ejection Fraction	58±14%	57±12%	57±15%	0.8
Hypertension	500(45.6%)	347(44.8%)	153(47.5%)	0.7
Diabetes	112(10.2%)	74(9.6%)	38(11.8%)	0.3
Current Tobacco Use	154(14.0%)	82(10.6%)	72(22.4%)	<0.001 [*]
Infective Endocarditis	62(5.7%)	33(4.3%)	29(9.0%)	0.002 [*]
Liver Disease	9(0.8%)	6(0.8%)	3(0.9%)	0.8
Immunosuppression	24(2.2%)	131(16.9%)	11(3.4%)	<0.001 [*]
Cancer	35(3.2%)	26(3.4%)	9(2.8%)	0.6
Peripheral Vascular Disease	27(2.5%)	16(2.1%)	11(3.4%)	0.2
Concomitant TVr	161(14.7%)	120(15.5%)	41(12.7%)	0.1
Postoperative Atrial Fibrillation	313(28.5%)	230(29.7%)	83(25.8%)	0.2
Cross-Clamp Time	64±29	58±22	78±37	<0.001 [*]
Cardiopulmonary Bypass Time	86±35	79±27	103±45	<0.001 [*]

^{*} Denotes statistical significance with p-value <0.05

Age – mean age in years ±SD

Ejection Fraction (EF) – mean EF % ±SD

Cardiopulmonary Bypass Time – mean time in minutes ±SD

Cross-Clamp Time – mean time in minutes ±SD

Table 2.

Postoperative Outcomes in Warfarin and Non-Warfarin Groups

	Warfarin n=775(68.8%)	Non-Warfarin n=322(29.4%)	p-value
30-Day Mortality	4(0.5%)	0(0.0%)	0.2
6-Month Mortality	8(1.0%)	6(1.9%)	0.3
Readmission	71(9.2%)	32(9.3%)	0.7
Composite Bleeding Incidents	7(0.9%)	10(3.1%)	0.007 [*]
Reoperation for Bleeding	1(0.1%)	1(0.3%)	0.5
Gastrointestinal Bleeding	5(0.7%)	6(1.8%)	0.1
Pericardial Effusion / Cardiac Tamponade	1(0.1%)	3(0.9%)	0.045 [*]
Composite Thromboembolic Incidents	12(1.5%)	10(3.1%)	0.1
Pulmonary Embolism	0(0.0%)	1(0.3%)	0.1
Transient Ischemic Attack	3(0.4%)	1(0.3%)	0.1
Stroke	9(1.2%)	8(2.5%)	0.1
Composite Bleeding and Thromboembolic Incidents	19(2.5%)	20(6.2%)	0.002 [*]

^{*} Denotes statistical significance with p-value <0.05

Table 3.

Impact of Predictors on Composite Bleeding and Thromboembolic Events

	Odds Ratio	95% CI	p-value
Age	1.01	0.98–1.03	0.60
Male Sex	0.90	0.45–1.78	0.75
Ejection Fraction	1.01	0.98–1.04	0.60
Hypertension	1.63	0.80–3.30	0.17
Diabetes	1.41	0.53–3.71	0.50
Current Tobacco Use	0.44	0.13–1.45	0.15
Infective Endocarditis	1.75	0.53–5.75	0.38
Liver Disease	2.63	0.27–25.50	0.45
Immunosuppression	4.10	1.06–15.88	0.07
Cancer	1.44	0.31–6.65	0.66
Peripheral Vascular Disease	0.70	0.09–5.60	0.72
Concomitant TVr	0.70	0.25–1.92	0.47
Postoperative Atrial Fibrillation	1.68	0.82–3.44	0.16
Surgeon			
B vs. A	0.34	0.11–1.13	0.15
Others vs. A	0.33	0.07–1.45	0.15
Others vs. B	0.95	0.24–3.73	0.15
Surgical Approach			
Thoracotomy vs. Sternotomy	0.48	0.10–2.35	0.33
Cardiopulmonary Bypass Time	1.01	1.00–1.02	0.05
Postoperative Warfarin Use	0.29	0.13–0.64	0.003 *

* Denotes statistical significance with p-value <0.05

95% Confidence Interval (CI) – lower bound - upper bound

New York Heart Association (NYHA), Tricuspid valve repair (TVr)