Published in final edited form as:

J Thorac Cardiovasc Surg. 2020 November ; 160(5): 1222–1231. doi:10.1016/j.jtcvs.2019.09.064.

Non-Vitamin K Oral Anticoagulant Use Following Cardiac Surgery is Rapidly Increasing

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Abstract

Objective: The prevalence of non-vitamin K oral anticoagulant (NOAC) use following cardiac surgery is unknown, particularly in patients with bioprosthetic valves. We sought to define the contemporary use and short-term safety of NOACs following cardiac surgery.

Methods: All patients undergoing bioprosthetic AVR, bioprosthetic MVR, or isolated CABG (2011–2018) were evaluated from a multicenter, regional STS database. Patients were stratified by anticoagulant type (NOAC vs. Vitamin K antagonist [VKA]) and era (early [2011–2014] vs. contemporary [2015–2018]).

Results: Of 34,188 patients, 18% (6,063) were discharged on anticoagulation, of whom 23% were prescribed NOACs. Among those receiving anticoagulation, NOAC use has significantly increased from 10.3% to 35.4% in contemporary practice ($p < 0.01$). This trend was observed for each operation type (CABG 0.86%/year, bioprosthetic AVR: 2.15%/year, bioprosthetic MVR: 2.72%/year, all $p < 0.01$). In patients with postoperative atrial fibrillation receiving anticoagulation, NOAC use has increased from 6.3% to 35.4% and 12.3% to 40.3% following bioprosthetic valve replacement and isolated CABG, respectively (both $p < 0.01$). In patients receiving anticoagulation at discharge, adjusted 30-day mortality (OR 1.94, $p = 0.12$) and reoperation (OR 0.79, $p = 0.34$) rates were not associated with anticoagulant choice, while NOAC use was associated with an adjusted 0.9 day decrease ($p < 0.01$) in postoperative length of stay.

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Conflict of Interest: Dr. Ailawadi is a consultant for Abbott, Edwards, Medtronic, Admedus, and Gore. Dr. Speir is a consultant for Medtronic.

Conclusions: NOAC use following cardiac surgery has dramatically increased since 2011. This trend is consistent regardless of indication for anticoagulation including bioprosthetic valves. Short-term outcomes support their safety in the cardiac surgery setting with shorter postoperative hospital stays. Long-term studies on efficacy of NOACs following cardiac surgery are still necessary.

Graphical Abstract

Central Picture Legend: Trends in discharge anticoagulant use for different operations throughout the study period.

Introduction

Non-vitamin K oral anticoagulants (NOACs) have been widely adopted as alternative agents to Vitamin K Antagonists (VKAs) for patients that require therapeutic anticoagulation for many indications.¹ These agents are intended to be given at fixed doses, and lack many of the drug-drug interactions, food-drug interactions, and frequent monitoring required of VKAs. In addition, these agents are now preferred over VKAs for the prevention of stroke and systemic embolism in patients with atrial fibrillation and in the treatment of venous thromboembolism with lower rates of intracranial hemorrhage.^{2, 3}

Despite the robust safety and efficacy profile in the broader population, little is known regarding their use in patients undergoing cardiac surgery, specifically in patients with bioprosthetic valves.⁴ The increased thromboembolic and bleeding complications when dabigatran was given after mechanical valve replacement in the RE-ALIGN trial, coupled with the labeled indication of ‘nonvalvular’ atrial fibrillation, has contributed to some confusion in the role of NOACs and hesitancy to prescribe them, for patients following bioprosthetic valve replacement.⁵ Further, current knowledge about NOACs in the bioprosthetic valve population originates mainly from post-hoc analyses of pivotal NOAC trials for other indications and the current sample size for these analyses remain small.^{6–8}

Given the growing familiarity and preference for NOACs in general cardiovascular practice, one would expect NOACs to have become common in the cardiac surgery setting. Therefore, we hypothesized that the use of NOACs has significantly increased in patients following cardiac surgery, both with and without bioprosthetic valves. The intention of this analysis was to characterize the contemporary use of NOACs after cardiac surgery, evaluate the short-term safety, and to provide a context for the discussion and design of future clinical trials focused on anticoagulation in the post-cardiac surgery setting.

Methods

Patient Data

Data were obtained from the Virginia Cardiac Services Quality Initiative (VCSQI), which pools voluntarily submitted institutional Society of Thoracic Surgeons (STS) Adult Cardiac Surgery Database patient level data from 19 hospitals and surgical groups in the region. This quality database includes 99% of all adult cardiac surgery in the region and methodologies for clinical data acquisition and cost data methodology have been described previously.^{9, 10} Standard STS definitions were used for all variables.¹¹ This study was exempt from review by the University of Virginia Institutional Review Board due to the de-identified nature of the quality database.

All patients who underwent isolated coronary artery bypass grafting (CABG), bioprosthetic aortic valve replacement (bAVR) or bioprosthetic mitral valve replacement (bMVR) between July 2011 and December 2018 were extracted from the VCSQI database. Patients undergoing concomitant procedures were included except those undergoing ventricular assist device placement, pulmonary thromboembolectomy, surgical ventricular restoration, cardiac tumor removal, left ventricular aneurysm repair or cardiac transplant. Patients with mechanical heart valves and those who died while in the hospital were excluded. The study period was divided into an early (2011–2014) and contemporary (2015–2018) era, to compare changes over time. Patients receiving oral anticoagulants at discharge were then stratified by whether they received a NOAC or VKA at discharge. Baseline characteristics including CHADsVASC and HAS-BLED scores and postoperative complications were compared between groups. Primary outcomes of interest included risk-adjusted 30-day mortality, reoperation for bleeding and postoperative length of stay.

Statistical Analysis

Continuous variables with skewed distributions are presented as median [interquartile range (IQR)], and categorical variables as count (percentage). Wilcoxon rank sum test was used for skewed continuous variables and the Chi-Square test for categorical variables. Cases where discharge NOAC use was missing, these were treated as not having received a NOAC at discharge and this occurred in 2.6% of entries. Hierarchical logistic and linear regression with a generalized linear regression model was used to analyze select outcomes relevant to anticoagulant use with adjustment using appropriate log transformed STS risk score, year of operation, and *a priori* selected clinical characteristics relevant to each outcome. Modeling accounted for center level clustering with hospital treated as a random effect. SAS version 9.4 (SAS Institute, Cary, NC) statistical software was used for analysis with a statistical threshold 0.05 set for significance. Linear regression was also used to determine the trend in NOAC adoption during the study period, specifically the unadjusted annual increase in NOAC utilization. This was determined using Prism 8.1 (GraphPad Software San Diego, CA)

Results

A total of 34,188 patients met the study criteria and were included in the analysis. Overall 6,063 (17.7%) were discharged on anticoagulation, which increased incrementally during the study period from 16.7% to 18.8%, $p<0.001$. While 23% of patients receiving anticoagulation at discharge were prescribed NOACs overall, this increased from 10.3% to 35.4%, $p<0.001$, throughout the study period. An increase in NOAC use over time was seen in all procedures (CABG 0.86%/year, bAVR: 2.15%/year, bMVR: 2.73%/year, all $p<0.01$) (Figure 1) (Central Picture). Of those receiving anticoagulation at discharge, 41.5% had a history of preoperative atrial flutter or fibrillation, 44.3% had postoperative atrial fibrillation, and 5.2% had a postoperative venous thromboembolism.

Between the early and contemporary era, there was an increase in the percentage of patients presenting with a history of atrial fibrillation or flutter from 10.8% to 15.1%, $p<0.001$. In addition, there was a relative increase in the number of bioprosthetic valve replacements performed, from 29.8% to 38.6% of all operations, $p<0.001$. Other baseline characteristics and postoperative events demonstrated statistically significant, but clinically insignificant changes over time (Table 1).

Atrial Fibrillation

Preexisting atrial fibrillation was more common in patients undergoing bioprosthetic valve implantation than those with isolated CABG (23.1% vs. 7.6%, $p<0.001$). In patients with preoperative atrial fibrillation who were treated with anticoagulation at discharge, there was a significant increase in the use of NOACs for both bioprosthetic valve implantation and isolated CABG (bioprosthetic – early: 9.0% vs. contemporary 37.9%, $p<0.001$; CABG – early: 17.5% vs. 48.1%, $p<0.001$). This represents a +321% increase in the bioprosthetic group and +175% increase in the CABG group (Figure 2). In patients with postoperative atrial fibrillation, 2,684 (32.7%) received anticoagulation at discharge with 24.8% of anticoagulated patients receiving NOACs. Between the early and contemporary eras, this

increased from 6.3% to 35.4%, $p<0.001$ and 12.3% to 40.3%, $p<0.01$ for bioprosthetic valves and isolated CABG respectively. By 2018, half of all patients with postoperative atrial fibrillation discharged on anticoagulation were treated with NOACs (Figure 3).

Bioprosthetic Valve Replacement

A total of 11,632 patients underwent bioprosthetic valve replacement with 9,868 undergoing bAVR and 2,163 undergoing bMVR. Within this cohort of valve replacement, 3,693 (31.8%) were discharged on anticoagulation with 25.7% of bAVR and 59.8% of bMVR receiving anticoagulation. Overall, anticoagulation use did not change between eras from 31.9% to 31.6%, $p=0.749$. Of those receiving anticoagulation, the relative prevalence of NOACs compared to VKAs has significantly changed over time from 6.6% to 32.1%, $p<0.001$ during the study period. This trend was seen for both bAVR (8.0% to 37.8%, $p<0.001$) and bMVR (2.4% to 19.5%, $p<0.001$). Of the patients discharged on anticoagulation, 745 (20.2%) did not have a history of preoperative atrial fibrillation, postoperative atrial fibrillation or postoperative venous thromboembolism, suggesting that the bioprosthetic valve was the primary indication for anticoagulation. Traditional VKAs remained more prevalent in this population without other indication for anticoagulation, but the use of NOACs in this population is growing (early: 4.9% vs. contemporary: 13.1%, $p<0.001$), most notably in those with bAVR (6.6% to 18.3%, $p<0.001$; bMVR: 1.7% to 7.0%, $p=0.040$; double valve 0% to 7.4%, $p=0.296$).

NOAC compared to VKAs

A total of 1,395 (22.9%) patients received NOACs and 4,668 (76.9%) received VKAs. Compared to patients who received VKAs, patients who received NOACs were equivalent in age (71 [64–77] vs. 71 [64–77], $p=0.274$), ischemic risk (CHADS-VASc: 4 [3–5] vs. 4 [3–5], $p=0.592$), and bleeding risk (HAS-BLED: 3 [2–3] vs. 3 [2–3], $p=0.493$), but had a lower operative risk (STS Predicted Risk of Mortality: 2.1% [1.1–4.0%] vs. 2.5 [1.3%–4.8%]; Table 2). However, those patients who were discharged on NOACs, were more likely to have a history of atrial fibrillation (50.9% vs. 38.7%, $p<0.001$) or to have developed postoperative atrial fibrillation (47.7% vs. 43.3%, $p=0.004$).

There was no difference in 30-day mortality (0.9% vs. 0.6%, $p=0.390$) between groups. For both NOACs and VKAs, significant pericardial bleeding was uncommon (reoperation for bleeding: 2.7% vs. 3.3%, $p=0.282$; pericardial effusions requiring pericardiocentesis: 0.3% vs. 0.3%, $p=1.000$). Patients receiving NOACs had other notable differences in unadjusted outcomes, including shorter postoperative length of stay (7 [5–10] vs. 8 [6–12] days, $p<0.001$), lower rates of pleural effusion requiring drainage (6.3% vs. 10.4%, $p<0.001$), but incrementally higher readmission rates (15.8% vs. 13.6%, $p=0.036$). However, after risk-adjustment, the only significant difference associated with anticoagulant choice was an adjusted 0.88 day ($p=0.002$) decrease in postoperative length of stay with NOACs versus titration of VKAs (Table 3) (Figure 4).

Discussion

In this regional analysis of over 34,000 cardiac surgery patients over the last 8 years, we demonstrate a dramatic rise in the use of NOACs for discharge anticoagulation in patients undergoing cardiac surgery. Since first receiving approval by the Food and Drug Administration in 2010, NOACs are now the anticoagulant used after cardiac surgery in approximately half of all patients. Moreover, this trend is consistent across different types of surgical procedures and indications for anticoagulation. These observations reflect the current practice environment, and future studies of anticoagulant use in cardiac surgical patients should include NOACs in their study design. Finally, we demonstrate the short-term safety of these agents in the cardiac surgery setting, along with a reduction in the postoperative length of stay.

Anticoagulation for postoperative atrial fibrillation

Almost half of the patients receiving anticoagulation in this study had postoperative atrial fibrillation, likely the primary indication for their anticoagulation. In patients with new onset postoperative atrial fibrillation there exists a significant thromboembolic risk though this may be diminished when compared to those with non-valvular atrial fibrillation in the general population.^{12, 13} However, neither the minimum atrial fibrillation burden to warrant anticoagulation, the ideal agent, nor the duration of treatment has been rigorously tested in this population, leading to calls for prospective clinical trials on the anticoagulation management of postoperative atrial fibrillation.¹⁴ While our study does not address differences in treatment duration, we do demonstrate inconsistency in choice of anticoagulant agent, with one third of patients receiving anticoagulation for postoperative atrial fibrillation being treated with NOACs in the contemporary cohort of this study.

The variability in medication choice for this indication in the current analysis is consistent with a survey of the European Heart Rhythm Society, in which survey respondents demonstrated a wide range of attitudes regarding use of NOACs in patients with postoperative atrial fibrillation.⁴ In the same study, concern was raised regarding a potential for increased risk of major pericardial bleeding with NOACs compared to warfarin. While we could not determine the relative timing of anticoagulation initiation, in our study, the rate of reoperation for bleeding, percutaneous pericardial drainage and pleural effusion requiring drainage was similar in those treated with VKAs and those treated with NOACs. A recently opened clinical trial ([NCT03702582](#)) comparing the use of Warfarin to Rivaroxaban for new onset atrial fibrillation following cardiac surgery will help to answer some of these questions.

Initial antithrombotic regimen following bioprosthetic valve replacement

Another area of controversy is the ideal initial antithrombotic regimen in patients with bioprosthetic valves. For bioprosthetic valves in either the aortic or mitral position, the incidence of thromboembolism is thought to be highest postoperatively and decreases over time as the prosthetic valve endothelializes.¹⁵ Given this early increased thrombotic risk, for patients undergoing bAVR or bMVR, the 2017 update of the ACC/AHA guidelines include a IIa (Level of Evidence B-NR) recommendation for anticoagulation with a VKA for 3–6

months in patients at low risk for bleeding.¹⁶ While the 2012 CHEST guidelines take a more liberal stance following bAVR with aspirin recommended over VKAs (Grade 2C) for the first 3 months and provide a similar recommendation for bMVR with VKA recommended over no therapy for the first 3 months.¹⁷ For both valve positions, there is significant reported variability in the utilization of a VKA or an aspirin based regimen in current practice. Brennan et. al., in a national STS cohort of patients that underwent bAVR, showed that in those without an absolute indication or absolute contraindication for anticoagulation, at discharge 49% received aspirin alone and 35% received a VKA with or without aspirin.¹⁸ In a 2016 national study utilizing the STS database only 58% of patients receiving bMVR were prescribed VKAs on hospital discharge.¹⁹ Neither of these studies focused on the use of NOACs following bioprosthetic valve implantation, which was the main focus of the present analysis. The preference of anticoagulant choice seen throughout the current study changed significantly over time. Although the majority of patients receiving anticoagulation following bioprosthetic valves without another specific indication continue to receive VKAs, the percentage receiving NOACs has more than doubled in contemporary practice compared to the earlier time period.

Anticoagulation for existing atrial fibrillation in patients with bioprosthetic valves

For the patient who has a bioprosthetic valve in place and anticoagulation is indicated for atrial fibrillation, should the choice of anticoagulant be influenced by the presence of the bioprosthetic valve? There is limited data on this subject and what is known is largely drawn from post-hoc analyses of pivotal trials of NOACs as well as data drawn from smaller retrospective and cohort studies.^{6–8, 20–22} Overall, the published experience with NOACs in patients with bioprosthetic valves includes only a few hundred patients.²¹ Due to the present study's limitation of capturing only short-term data it does not specifically answer this question, but does reflect surgeons' perceptions of this management decision. In order to address this we looked at the relative growth in NOAC use for patients with a history of preoperative atrial fibrillation in the isolated CABG population and in the bioprosthetic valve population. We observed dramatic growth in both populations, suggesting that there is little hesitancy to continue NOACs in patients with pre-existing atrial fibrillation that undergo bioprosthetic valve replacement.

Summary

This study highlights the growing use of NOACs following cardiac surgery for a broad range of indications and that their use has outpaced high quality randomized evidence on these topics. In addition, we report the use of NOACs in three areas of clinical uncertainty in postoperative cardiac surgery patients. The wide variability in practice patterns exhibited across this regional cohort speaks to the clinical equipoise regarding the use of NOACs for postoperative atrial fibrillation, thromboembolic risk reduction for bioprosthetic valve replacement and for atrial fibrillation in those with a bioprosthetic valve.

Limitations

This study is limited in that it is retrospective which exposes the analysis to selection bias. In addition, only information on discharge anticoagulation, not target INR, medication dose, or intended duration was captured. Further, all outcomes captured by the STS database are

short-term (30-day) outcomes thus limiting the ability to draw conclusions about long-term efficacy. Importantly, with the current data, it is impossible to know what medications the patients were taking prior to surgery. The discharge anticoagulant choice may reflect a decision to continue the preoperative anticoagulant, which in part speaks to the general use of NOACs and VKAs in the community. Finally, the specific indication for anticoagulation was not specified, but rather inferred from other clinical data.

Conclusions

There is a growing use of NOACs in contemporary clinical practice following cardiac surgery. Regardless of whether anticoagulation is initiated for the treatment of postoperative atrial fibrillation, thromboembolic risk reduction with bioprosthetic valve, or for the treatment of existing atrial fibrillation, NOACs are increasingly commonplace. Utilization of NOACs in cardiac surgery may be a means to safely reduce the postoperative length of stay for patients requiring anticoagulation. This is particularly relevant in the setting of an increased interest in enhanced recovery protocols, which among other targets, aim to reduce the length of stay. While risk adjusted, short-term outcomes appear to be similar, there is a paucity of long-term data in this setting. Prospective clinical trials comparing anticoagulation and antiplatelet regimens are needed in patients with postoperative atrial fibrillation and/or bioprosthetic valve replacement to determine long-term effectiveness.

Funding:

This work was supported by the National Heart, Lung, and Blood Institute (grant T32 HL007849 UM1HL088925)

Glossary

bAVR	Bioprosthetic Aortic Valve Replacement
bMVR	Bioprosthetic Mitral Valve Replacement
CABG	Coronary Artery Bypass Grafting
IQR	Interquartile range
NOAC	Non-Vitamin K Oral Anticoagulant
STS	Society of Thoracic Surgeons
VCSQI	Virginia Cardiac Services Quality Initiative

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Central Message:

Non-vitamin K oral anticoagulant use is rapidly increasing for an array of indications in the postoperative cardiac surgery setting.

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Perspective Statement:

The availability of high quality data on non-vitamin k oral anticoagulants in the post-cardiac surgery setting is lacking. Yet, despite this gap in the literature, these medications have been broadly incorporated into clinical practice. This study demonstrates the short-term safety of these agents, but evaluation of the long-term efficacy warrants prospective study.

Invited Discussant: Dr. Thomas A. Schwann, MD

320. Novel Oral Anticoagulant Use for Atrial Fibrillation and Bioprosthetic Valves Following Cardiac Surgery. Paper presented by Robert B. Hawkins, MD, Charlottesville, VA. E-mail: rbh6x@virginia.edu

Discussion by Thomas Schwann, MD, Massachusetts E-mail: thomas.schwannmd@baystatehealth.org Dr. T. Schwann (Springfield, MA):

Thank you very much for the wonderful presentation and the opportunity to review your manuscript, which is clearly written and very interesting. I really appreciate the opportunity to discuss your presentation here, and this is yet another thought-provoking presentation from our colleagues at the Virginia Cardiac Surgical Quality Initiative. As with any good project, it provides interesting information and forces us to pause and re-evaluate the basis of what perhaps has become dogma as to how we take care of patients after cardiac surgery who need anticoagulation in the perioperative period.

NOACs have been approved for the prevention of venous thromboembolism in orthopedic procedures and in preventing systemic thromboembolic phenomenon in patients with nonvalvular atrial fibrillation. I think as you already pointed and I need to re-emphasize, as of 2019, despite a documented rise in the use of NOACs, there is no data to support their safety or efficacy in observational or prospective studies in cardiac surgery as an alternative to warfarin.

So aside from demonstrating a shift in practice of Virginia surgeons away from warfarin in favor of NOACs, what are the take-home messages from your study? I believe that the first take-home message is that we as cardiac surgeons don't incorporate practice guidelines into our clinical activities as evidenced here by the low rates of anticoagulation, especially of bioprosthetic aortic valves, an approach that contradicts the 2017 ACC/AHA focused update of the 2014 management of patients with valvular disease. The skepticism about warfarin efficacy in patients receiving bioprostheses noted here has been corroborated by Brennan, et al., where he found only 35% of patients who received bioprosthetic AVRs were discharged on warfarin. Similarly, Vinod Thourani in a single institutional study and our group from an analysis of the National STS Database found that only 55 to 58% of patients undergoing bioprosthetic mitral valve replacements received warfarin at discharge. Compared to those patients discharged on warfarin, none of these patients showed any increased evidence of perioperative risk of thromboembolic phenomenon or bleeding.

Given the well-known shortcomings of warfarin which have been articulated, including the need for close monitoring, its extensive interaction with multiple foods and medications, and the difficulty of maintaining therapeutic anticoagulation with out-of-range INR being reported as high as 70%, it is no wonder that surgeons look for circumstantial data to support alternative clinical practices, such as avoiding anticoagulation entirely or resorting to NOACs. Despite the guidelines, the current knowledge gap does not permit us to definitively state whether bioprosthetic patients should be discharged on no anticoagulation, warfarin or NOACs.

The second take-home message I believe is that surgeon dissatisfaction with the current standard of care incorporated into clinical guidelines is a driving force for innovation in clinical medicine. Clearly warfarin-based anticoagulation is neither patient nor provider friendly. There is a precedent for clinician dissatisfaction with the standard of care leading to innovative alternatives, such as the development of PCI, multi-arterial coronary artery bypass grafting, and, more recently, TAVR. I suspect that given the shortcomings of warfarin therapy, it is only a matter of time before NOACs supplement warfarin therapy for patients who present in atrial fibrillation following cardiac surgery, given their increased superiority in efficacy, their improved safety profile and provider and patient user friendliness, which has been documented in the general A-fib population in the RE-LY study, the ROCKET AF study, and particularly in the ARISTOTLE trials, in which NOACs have actually had an improved impact on mortality in patients with atrial fibrillation.

But surgical innovators have the responsibility to ensure each individual patient's safety and interests. We need to be thoughtful and circumspect in how we approach innovation. We all need to be innovators, but we cannot be cowboys. Center-to-center variability in practice based on reasonable and logical extension of available data to similar but not identical circumstances should serve as a basis for such innovation. But if we choose to be involved in innovation in off-label applications of medications and procedures, we must be meticulous in our follow-up and our data analysis to ensure that we comply with the most basic mantra of health care, which is *primum non nocere*.

So given these controversies, I would ask you the following two questions. What is your recommendation for anticoagulation management in patients undergoing bioprosthetic AVR and bioprosthetic MVR? And then secondly, what is your recommendation for anticoagulation management in patients who develop new onset postoperative A-fib?

Thanks for the opportunity to discuss this wonderful study.

320. Novel Oral Anticoagulant Use for Atrial Fibrillation and Bioprosthetic Valves Following Cardiac Surgery. Response by Robert B. Hawkins, MD, Charlottesville, VA.

DR. HAWKINS: You picked the two controversial aspects of anticoagulation in cardiac surgery. I do think that the main point of this study and some of the others that we have looked at within VCSQI is that cardiac surgeons and guidelines don't necessarily agree. In this case, we see that that dissatisfaction with guidelines is leading to off-label use of NOACs. The point of this study was to see if that's safe, at least with the data that we have available, and all the data that we have available, which is limited, seems to show that that's the case.

In terms of recommendations for bioprosthetic AVR use, I think that multiple studies have demonstrated a small but consistent risk for thromboembolic complications. I don't think that we have the data yet to make strong and clear recommendations, and so the point of this study was to try to demonstrate some level of equipoise to where we can get to that point.

I firmly believe, particularly with the data coming out of ARISTOTLE, that certain agents are going to have clear benefits in terms of reducing that risk after bioprosthetic

implantation with better safety profiles. I really think with a better safety profile, they will lead to a more rigorous recommendation after implantation.

In terms of postoperative atrial fibrillation, it is a process we don't fully understand, we can't really consistently provide prophylaxis for, and we really don't have a firm understanding of who should get anticoagulation. We don't understand what duration of postop A-fib is needed to trigger the risk/benefit ratio. And again, the same points here, where a better safety profile would lower that threshold for anticoagulation.

So with some degree of short-term equipoise, a trial looking at NOAC use with detailed information about duration and type of arrhythmia postoperatively, other bleeding risks for risk adjustment, and comparison among all three arms, for VKA, NOAC and non-anticoagulation use, would be beneficial to really derive a true recommendation.

So those aren't really answers but they are recommendations.

Figure 1:

Trends in anticoagulant use following cardiac surgery in (A) Isolated Coronary Artery Bypass Grafting (B) Bioprosthetic Aortic Valve Replacement (bAVR) (C) Bioprosthetic Mitral Valve Replacement (bMVR). CABG, coronary artery bypass grafting; VKA, Vitamin K Antagonist; NOAC, Non-Vitamin K Oral Anticoagulant.

Figure 2:

Growth in non-vitamin k oral anticoagulant in patients who have history of atrial fibrillation or flutter. CABG, Coronary Artery Bypass Grafting; NOAC, Non-Vitamin K Oral Anticoagulant.

Figure 3:

Growth in non-vitamin k oral anticoagulant in patients with postoperative atrial fibrillation. CABG, Coronary Artery Bypass Grafting; NOAC, Non-Vitamin K Oral Anticoagulant.

Non-Vitamin K Oral Anticoagulant Use Following Cardiac Surgery is Rapidly Increasing

Figure 4:

Graphical Abstract: The study population included over 34,000 patients in the Virginia Cardiac Services Quality Initiative. Over time, the use of non-vitamin k oral anticoagulants has increased significantly for all included subgroups. Risk adjusted outcomes after cardiac surgery are similar to patients being prescribed vitamin k antagonists with an associated reduction in length of stay. (NOAC: non-vitamin k oral anticoagulant)

Table 1:

Comparison of baseline characteristics, unadjusted postoperative events and discharge antithrombotic medications between eras.

N	Early 17,839	Contemporary 16,349	p-value
Baseline Characteristics			
Age	66 [59–74]	67 [59–74]	0.042
Female	5,214 (29.2%)	4,825 (29.5%)	0.566
Procedure			
Isolated CABG	12,516 (70.2%)	10,040 (61.4%)	<0.001
bAVR	4,398 (24.7%)	5,071 (31.0%)	
bMVR	757 (4.2%)	1,008 (6.2%)	
bAVR+MVR	168 (0.9%)	230 (1.4%)	
Concomitant Procedures			
Atrial Appendage Ligation	848 (4.8%)	1,156 (7.1%)	<0.001
Atrial Fibrillation Ablation	893 (5.0%)	883 (5.4%)	0.100
History Atrial Fibrillation/Flutter	1,920 (10.8%)	2,461 (15.1%)	<0.001
CHADS-VASc Score	3 [2–4]	3 [2–4]	<0.001
HAS-BLED Score	3 [2–3]	3 [2–3]	<0.001
STS Predicted Risk of Mortality	1.3 % [0.7–2.8]	1.4% [0.7–2.8]	<0.001
STS Predicted Risk of Morbidity or Mortality	13.1% [8.5–21.4]	12.7% [8.3–20.8]	<0.001
Unadjusted Postoperative Events			
Postoperative Atrial Fibrillation	4,182 (23.4%)	4,028 (24.6%)	0.010
Postoperative Permanent Stroke	225 (1.3%)	205 (1.3%)	0.957
Postoperative Venous Thromboembolism	275 (1.5%)	196 (1.2%)	0.007
Reoperation for Bleeding	376 (2.1%)	372 (2.3%)	0.290
Major Morbidity	2,297 (12.9%)	1,833 (11.2%)	<0.001
30-Day Mortality	77 (0.4%)	74 (0.5%)	0.770
Readmission	1,693 (9.7%)	1,755 (11.2%)	<0.001
Discharge Medications			
Aspirin at Discharge	17,148 (96.1%)	15,707 (96.1%)	0.799
ADP Inhibitor at Discharge	4,273 (24.0%)	4,397 (26.9%)	<0.001
Anticoagulation at Discharge	2,987 (16.7%)	3,076 (18.8%)	<0.001
NOAC	307 (10.3%)	1,088 (35.4%)	<0.001
Vitamin K Antagonist	2,680 (89.7%)	1,988 (64.6%)	<0.001
Anticoagulant + Aspirin	2,703 (15.2%)	2,791 (17.1%)	<0.001
NOAC	279 (10.3%)	982 (35.2%)	<0.001
Vitamin K Antagonist	2,424 (89.7%)	1,809 (64.8%)	<0.001
Triple Therapy *	185 (1.0%)	146 (0.9%)	0.174

* Triple therapy reflects those receiving aspirin, an ADP inhibitor and an anticoagulant at discharge. (ADP: Adenosine Diphosphate; bAVR: bioprosthetic aortic valve replacement; bMVR: bioprosthetic mitral valve replacement; CABG: Coronary Artery Bypass Grafting; NOAC: Non-Vitamin K Oral Anticoagulant Anticoagulant STS: Society of Thoracic Surgeons).

Table 2:

Comparison of baseline characteristics, unadjusted postoperative events and discharge antithrombotic medications for patients discharge on different classes of anticoagulants.

	Coumadin	NOAC	p-value
N	4,668	1,395	
Baseline Characteristics			
Age	71 [64–77]	71 [64–77]	0.274
Female	1561 (33.4%)	411 (29.5%)	0.005
Procedure			
Isolated CABG	1728 (37%)	642 (46%)	<.001
bAVR	1834 (39.3%)	599 (42.9%)	
bMVR	929 (19.9%)	127 (9.1%)	
bAVR+MVR	177 (3.8%)	27 (1.9%)	
Concomitant Procedures			
Atrial Appendage Ligation	894 (19.2%)	328 (23.5%)	<0.001
Atrial Fibrillation Ablation	882 (18.9%)	279 (20%)	0.357
History Atrial Fibrillation/Flutter	1803 (38.7%)	710 (50.9%)	<.001
CHADS-VASc Score	4[3–5]	4 [3–5]	0.592
HAS-BLED Score	3 [2–3]	3 [2–3]	0.493
STS Predicted Risk of Mortality	2.5% [1.3–4.8]	2.1% [1.1–4]	<.001
STS Predicted Risk of Morbidity or Mortality	19.2% [12.4–29.2]	16.4% [10.3–25.2]	<.001
Unadjusted Postoperative Events			
Postoperative Atrial Fibrillation	2019 (43.3%)	665 (47.7%)	0.004
Postoperative Permanent Stroke	97 (2.1%)	23 (1.7%)	0.314
Postoperative Venous Thromboembolism	273 (5.9%)	44 (3.2%)	<.001
Reoperation for Bleeding	154 (3.3%)	38 (2.7%)	0.282
Major Morbidity	975 (20.9%)	186 (13.3%)	<.001
30-Day Mortality	30 (0.6%)	12 (0.9%)	0.390
Discharge Medications			
Aspirin at Discharge	4233 (90.7%)	1261 (90.4%)	0.747
ADP Inhibitor at Discharge	312 (6.7%)	120 (8.6%)	0.015
Triple Therapy *	251 (5.4%)	80 (5.7%)	0.606

* Triple therapy reflects those receiving aspirin, an ADP inhibitor and an anticoagulant at discharge. (ADP: Adenosine Diphosphate; bAVR: bioprosthetic aortic valve replacement; bMVR: bioprosthetic mitral valve replacement; CABG: Coronary Artery Bypass Grafting; NOAC: Non-Vitamin K Oral Anticoagulant STS: Society of Thoracic Surgeons).

Table 3:

Logistic and Linear Regression for Relative Risk of Non-Vitamin K Oral Anticoagulant Oral Anticoagulants vs. Vitamin K Antagonist in Patients Requiring Anticoagulation following Cardiac Surgery.

	Risk-Adjusted Odds Ratio^a	95% Confidence Interval	p-value	C statistic
30-Day Mortality ^b	1.942	0.840 – 4.489	0.121	0.722
Reoperation for Bleeding ^c	0.792	0.493 – 1.275	0.337	0.659
Readmission ^d	1.025	0.812 – 1.294	0.838	0.610
Pleural Effusion Requiring Drainage ^e	0.788	0.576 – 1.078	0.136	0.748
	Parameter Estimate^a	95% Confidence Interval	p-value	
Postoperative Length of stay ^f	–0.881	–1.448 – –0.314	0.002	

^a Adjusted-Odds Ratio and Parameter Estimate Referenced to Vitamin K Antagonist

^b Adjusted for Hospital, log(Predicted Risk of Morality), CHADS-VASc, HAS-BLED, Ejection Fraction, Major Morbidity, year of surgery

^c Adjusted for Hospital, log(Predicted Risk of Reoperation), HAS-BLED, year of surgery

^d Adjusted for Hospital, log(Predicted Risk of Morbidity or Morality), CHADS-VASc, HAS-BLED, Postoperative length of stay, Major Morbidity, year of surgery

^e Adjusted for Hospital, log(Predicted Risk of Morbidity or Mortality), Ejection Fraction, HAS-BLED, Major Morbidity, year of surgery

^f Hospital, log(Predicted Long Length of Stay, Atrial Fibrillation, Major Morbidity, year of surgery)