Venous and arterial thrombotic complications. Solutions in clinical practice

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Chapter 5

Antithrombotic strategy after bioprosthetic aortic valve replacement in patients in sinus rhythm: evaluation of guideline implementation

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ABSTRACT

Objectives

After elective aortic valve replacement patients are at risk of developing valve thrombosis and systemic arterial thromboembolism. Current guidelines recommend antithrombotic therapy with aspirin or vitamin K antagonists (VKA) during the first three months after the procedure but have level 2 or 3 evidence. As a consequence, the most appropriate antithrombotic therapy is still a matter of debate. This retrospective study analysed all thromboembolic and bleeding complications in patients with either antiplatelet or anticoagulation therapy one year after bioprosthetic aortic valve replacement.

Methods

A total of 402 patients undergoing bioprosthetic aortic valve implantation at the VU University Medical Centre (VUmc) and subsequently treated at three regional hospitals were included. The individual duration of either vitamin K antagonists (acenocoumarol) or aspirin was determined and related to thrombotic and bleeding events. Patients were followed and censored at 1 year postoperatively for survival, cerebral ischemia, myocardial infarction, peripheral arterial embolism and minor and major haemorrhages.

Results

A total of 24 thromboembolic complications and 31 bleeding episodes occurred. Multivariable analyses revealed that acenocoumarol caused more bleedings (relative risk (RR): 8.41, 95%CI: 3,58-19.79) and a similar amount of thromboembolic events (RR: 1.2, 95% CI: 0.47-3.02) compared to aspirin. Prior use of acenocoumarol was found to be a risk factor for thromboembolic events (RR: 3.1, 95% CI: 1.31 to 7.19). Gender, dyslipidemia, prior percutaneous coronary intervention, prior use of acenocoumarol and concomitant coronary artery bypass grafting were found to be predictors for bleeding events.

Conclusions

In patients one year following bioprosthetic aortic valve replacement, acenocoumarol therapy was associated with a significant increased risk in bleeding events and no reduction of thromboembolic events compared to antiplatelet therapy. These findings support the recommendations of aspirin over VKA as post-operative thromboprophylaxis one year postoperatively.

INTRODUCTION

Patients undergoing artificial heart valve replacement are at risk of developing valve thrombosis and systemic thromboembolism. The annual risk of thromboembolic events in patients with a mechanical aortic valve is 1-2% versus 0.7% with a bioprosthetic aortic valve, even with appropriate antithrombotic therapy (1). The need for lifelong anticoagulant therapy is well established in all patients with mechanical heart valves. In patients with bioprosthetic aortic valves anticoagulant therapy is warranted in the presence of thromboembolic risk factors including atrial fibrillation, previous thromboembolism, left ventricular dysfunction and hypercoagulable condition. In patients without one of these risk factors, the appropriate antithrombotic regimen postoperatively is still a matter of debate.

Recommendations of current guidelines are shown in **Table 1** (1-4). Although based on small or retrospective studies without conclusive results, there is a trend towards the recommendation of aspirin after implantation of a bioprosthetic aortic valve (2, 5-10). Therefore, after the 1st of July 2011, the antithrombotic policy in the VU University medical centre (VUmc) was changed and patients with sinus rhythm did no longer receive VKA.

Earlier studies demonstrated that, despite guidelines published by several professional societies, medical practice for the prevention of thrombotic events early after bioprosthetic aortic valve replacement varies widely among cardiac surgical centres (11-14). Thus, despite recommendations, there is still disparity of opinions in clinical practice.

Table 1. Current recommendations for antithrombotic strategy after bioprosthetic aortic valve replacement in patients who are in regular sinus rhythm and have other indications for VKA therapy (1-4).

Organization, year	Recommendation	Grade of evidence
ESC, 2012	Low-dose aspirin should be considered for the first three months after implantation of an aortic bioprosthesis	2C
ACC/AHA,2014	Aspirin 75 mg to 100 mg per day is reasonable in all patients with a bioprosthetic aortic valve. Anticoagulation, with a VKA, to achieve an INR of 2.5 may also be reasonable for the first 3 months after bioprosthetic AVR	2B
ACCP, 2012	In patients with aortic bioprosthetic valves we suggest aspirin (50-100 mg/d) over VKA therapy in the first 3 months	2C
EACTS, 2008	After tissue aortic valve replacement anticoagulation therapy is reasonably safe and may be beneficial. Antiplatelet therapy alone however is an acceptable alternative	2B

Note: ESC = European Society of Cardiology, ACC= American College of Cardiology, AHA= American Heart Association, ACCP= American College of Chest Physicians, EACTS= European Association for Cardio-Thoracic Surgery, VKA= Vitamin K Antagonists.

In summary, antithrombotic management after bioprosthetic aortic valve replacement is still a matter of debate. Therefore, the purpose of this study was to analyse thromboembolic events and bleeding complications in patients with either antiplatelet or anticoagulation therapy one year following bioprosthetic aortic valve surgery. For this purpose, different antithrombotic regimens before and after 2011 were compared. In addition, individual duration of either vitamin K antagonists or aspirin was related to thrombotic and bleeding events.

MATERIALS AND METHODS

The local Human Subjects Committee of the VU University Medical Centre approved this retrospective evaluation and waived the requirement to obtain informed consent.

This was an observational retrospective study of consecutive patients who underwent an isolated bioprosthetic aortic valve replacement to measure postoperative outcomes. Data were collected from the prospective database of the department of cardiothoracic surgery of the VUmc. Patients had undergone isolated aortic valve replacement between 2008 and 2014 and had been subsequently seen in three regional hospitals. In all three hospitals postoperative medical files were obtained and evaluated. Additionally, the thrombosis service was consulted about the duration of the treatment, the international normalized ratios (INRs), and target values of patients who received the vitamin K antagonist drug acenocoumarol. Except for patients undergoing concomitant bypass surgery, all other patients with concomitant procedures were excluded. Thromboembolic events and bleeding complications that occurred at the first postoperative day were not taken into consideration because antithrombotic treatment was started only at this day.

All patients were operated at the department of cardiac surgery at the VUmc and received an aortic bovine pericardial bioprosthesis (type, Carpentier-Edwards PERIMOUNT, Edwards Lifesciences, USA). Low-molecular-weight heparin (LMWH) nadroparin 2850 IU/day, or 2850 IU twice a day if a patient's weight was above 100 kg, was started on the first postoperative day followed by acenocoumarol or aspirin. Nadroparin was continued until acenocoumarol reached therapeutic levels, as shown by a prothrombin time (PT) according to the international normalized ratio (INR) (range, 2.5 to 3.5 according to the Dutch Thrombosis Service guidelines) or as soon as the patient was ambulant when patients received aspirin. Anticoagulation with acenocoumarol was maintained for three postoperative months, then discontinued at the discretion of the referring cardiologist and most often replaced by aspirin. Those with concomitant coronary artery bypass grafting did not receive double antithrombotic therapy (warfarin plus aspirin) but received aspirin only. After 1st of July 2011, a new treatment regimen was installed in the VUmc and patients no longer received standard VKA treatment bridged by LMWH.

The policy was changed because of lack of scientific evidence for indication of VKA and also anecdotal reporting of post-operative complications due to VKA therapy, especially early tamponade (2). From then on, aspirin (100mg per day) was started on the first postoperative day and continued lifelong in patients with sinus rhythm (see **table 2** regimes). Aspirin therapy could be changed to VKA therapy if thrombotic risk factors such as atrial fibrillation and thromboembolism were present.

Table 2. Post-operative antithrombotic strategies of different regional hospitals after bioprosthetic aortic valve replacement, in the absence of risk factors. *Change of policy was at the 1st of July 2011*

	Antithrombotic Strategy	
Regional hospital	**Before change of policy**	**After change of policy**
MCA	three months acenocoumarol substituted with life-long aspirin	life-long aspirin
ZMC	three months acenocoumarol substituted with life-long aspirin if concomitant coronary artery disease	life-long aspirin
KG	three months acenocoumarol substituted with life-long aspirin	life-long aspirin

Note: MCA = Medical Centre of Alkmaar, ZMC = Zaans Medical Centre, KG = Kennemer Gasthuis

To establish the exact period of the administration of acenocoumarol within a year, the thrombosis service was consulted. The exact period of aspirin use was assumed to be according to the prescription of the treating physician without interruption. Patients were followed and censored at one-year for administrative reasons and were observed on occurence of death, cerebral ischemia, including cerebrovascular accidents (CVAs) and transient ischemic attacks (TIAs), peripheral embolisms, myocardial infarction and minor and major bleeding. All thromboembolic events were defined according to the guideline reported by Edmunds *et al.* (15). Bleeding was defined as major if overt and associated with a decrease in hemoglobin level of 2 g per decilitre or more, required the transfusion of 2 or more units of blood, occurred into a critical site – i.e. intracerebral, intra-ocular, intraspinal, or intra-articular, or contributed to death. Clinically relevant non-major bleeding was defined as overt bleeding not meeting the criteria for major bleeding but associated with medical intervention, contact with a physician, interruption of antithrombotic treatment, or discomfort or impairment in carrying out activities of daily life. These events were examined in relation to the antithrombotic therapy and in relation to potential predictive risk factors such as gender, age, diabetes, hypertension, dyslipidemia, a history of smoking, prior embolism, prior cardiac surgery and prior use of antithrombotic therapy. Risk factors were defined according to the documentation provided by the treating physician.

Statistics

Baseline characteristics were stratified according to patients who underwent surgery before and after policy change of the VUmc in 2011. The Pearson's Chi-square test was used to compare the distribution of categorical variables, whereas the Mann-Whitney and independent *t*-tests were used for non-normal and normal distributed continuous variables respectively. Purely for descriptive purposes for thromboembolic and bleeding events we calculated Kaplan-Meier curves over a year. Patients were censored at date of last medical chart documentation or after loss to follow-up.

Risk (Rate) Ratios (RRs) for the occurrence of thromboembolic and bleeding events on the cumulative number of days of antithrombotic therapy of one antithrombotic therapy versus the other were estimated with Poisson regression using generalized estimating equations (GEE). To assess the influence of independent predictive risk factors on thromboembolic and bleeding events a multivariable Poisson regression was performed using all potential risk factors simultaneously which in univariable Poisson regressions had a p-value lower than 0.15 and those of clinical importance. All analyses were performed using SPSS version 21.

RESULTS

In total 402 patients were included (mean age 75 years, 56.2% men). **Table 3** shows an overview of baseline characteristics. The individual duration of either acenocoumarol or aspirin use could be assessed in 384 patients and related to the number of thromboembolic and bleeding events. In 22 patients data on the exact number of days of medication use were not complete, because detailed information of potential therapy changes could not be retrieved from medical files. As expected, the cumulative number of days of aspirin use was less before than after the adjustment of treatment policy. A total of 51 patients experienced an event; 20 patients had a thromboembolic event and 26 patients had a bleeding episode. In four patients both a thromboembolic and a bleeding event occurred. One patient had two minor bleeding events. The number of events before and after 2011 did not differ significantly (bleeding events: p= 0.35, thromboembolic events: p=0.59).

Table 4 lists the sites of bleeding and thromboembolic events and the treatment regimen. Of 31 bleeding events, 14 were major bleedings. Most bleedings were gastrointestinal (42%) of which one was fatal. In total, 81% of the bleeding events occurred during treatment with acenocoumarol. Most of the thromboembolic events were transient ischemic attacks (41%). The patient who experienced a myocardial infarction received both aspirin and acenocoumarol. The occurrence of thromboembolic events was similar for both acenocoumarol and aspirin.

Table 3. Baseline characteristics

Characteristic		total (n=402)	before change of policy (n=163)	after change of policy (n=239)
Age (y), mean ± st. dev		74,9 ± 6,9	76,0 ± 6,6	74,2 ± 7,1
Gender	male	226 (56,2)	86 (52,8)	140 (58,6)
	female	176 (43,7)	77 (47,2)	99 (41,4)
logEuroscore, mean ± st. dev		7,3 ± 5,1	8,3 ± 5,7	6,5 ± 4,5*
	missing, no.	19		19
Prior CVA, , no (%)		29 (7,2)	11 (6,7)	18 (7,5)
Prior MI, no (%)		37 (9,2)	9 (5,5)	28 (11,7)*
Prior embolism, no (%)		42 (10,4)	19 (11,7)	23 (9,6)
LV function, no (%)	>40%	355 (88,3)	146 (89,6)	209 (87,4)
	20-40%	32 (8,0)	12 (7,4)	20 (8,4)
	<20%	14 (3,5)	5 (3,1)	9 (3,8)
	missing	1 (0,2)	0	1 (0,4)
Preoperative AF, no. (%)		51 (12,7)	22 (13,5)	29 (12,1)
	missing	31 (7,7)	7 (4,3)	24 (10)
Dyslipidemia, no. (%)		130 (32,3)	48 (29,4)	82 (34,3)
	missing	1 (0,2)	1 (0,6)	
Previous CABG, no. (%)		14 (3,5)	5 (3,1)	9 (3,8)
Previous PCI, no. (%)		44 (10,9)	13 (8,0)	31 (13,0)
Smoking, no. (%)		75 (18,7)	30 (18,4)	45 (18,8)
Preoperative aspirin, no. (%)		178 (44,3)	81 (49,7)	96 (40,2)
Previous acenocoumarol, no. (%)		59 (14,7)	17 (10,4)	43 (18,0)*
Aortic disease, no. (%)	stenosis	353 (87,7)	143 (87,7)	210 (87,9)
	regurgitation	21 (5,2)	8 (4,9)	13 (5,4)
	mixed	27 (7,6)	11 (6,7)	16 (6,7)
	missing	1 (0,2)	1 (0,6)	0
Concomitant CABG, no. (%)		169 (42)	73 (44,8)	96 (40,2)
	missing, no.	2	2	0
Repeat thoracotomy, no (%)		25 (6,2)	17 (10,4)	8 (3,3)*
	missing	31 (7,7)	0	31 (13,0)
Sum of days of therapy use, days (median)	Aspirin	67725 (202)	22028 (162)	46062 (242)*
	Acenocoumarol	56469 (112,5)	30482 (154)	25987 (0)*
	missing, no.	18	12	6
Number of bleeding events, no. (%)		32 (8,0)	16 (9,8)	16 (6,7)
Number of thromboembolic events, no. (%)		24 (6,0)	11 (6,7)	13 (5,4)

Note: y=years, st. dev.=Standard Deviation, CVA=Cerebrovascular Accident, MI=Myocardial Infarction, LV=Left-ventricular, AF=Atrial Fibrillation, CABG=Coronary Artery Bypass Graft, PCI=Percutaneous Coronary Intervention

Table 4. Bleeding and thromboembolic events

			Antithrombotic therapy		
		No. Events	Acenocoumarol	Aspirin	Neither
Bleeding events		32	26 (81%)	6 (19%)	0
Site of events, no. (%)					
	Cerebral	2 (6%)	2 (100%)	0	0
	Gastrointestinal	14 (44%)	11 (79%)	3 (21%)	0
	Urinary	7 (22%)	5 (83%)	1 (17%)	0
	Epistaxis	4 (13%)	3 (75%)	1 (25%)	0
	Other	5 (16%)	4 (80%)	1 (20%)	0
TE events		24*	12 (52%)	11 (45%)	2 (8%)
Site of events, no. (%)					
	CVA	7 (32%)	3 (43%)	4 (57%)	0
	TIA	9 (41%)	6 (67%)	2 (22%)	1 (11%)
	Myocardial infarction	1 (4,5%)	1 (50%)	1 (50%)	0
	Pulmonary embolism	1 (4,5%)	0	1 (100%)	0
	Deep vein thrombosis	2 (9%)	0	1 (50%)	1 (50%)
	other	4 (18%)	2 (50%)	2 (50%)	0

Note: CVA = Cerebrovascular Accident, TIA = Transient Ischemic Attack

Univariable analysis of risk factors on events is shown in **Table 5**. There was a highly increased risk in the incidence of bleeding events when using acenocoumarol after one year of follow-up compared to aspirin (RR: 18.32, 95% CI: 5,41 to 62,07). In addition, seven other risk factors were predictive for bleedings: gender (p=0.001), age (p<0.001), prior percutaneous coronary intervention (p<0.001), hypertension (p=0.004), dyslipidemia (p<0.001) and concomitant coronary artery bypass grafting (p<0.001). In multivariable analysis the incidence of bleeding events remained significantly higher in patients using acenocoumarol compared to patients with aspirin use (RR: 8.41, 95%CI: 3.58 to 19.79). Gender, prior percutaneous coronary intervention, dyslipidemia, prior use of acenocoumarol and concomitant coronary artery bypass grafting remained all independent predictors for bleeding events (**Table 6**). Also for *major* bleedings acenocoumarol remained a predictor in univariable and multivariable analyses (multivariable: RR: 14.60, 95%CI: 1.95 to 109.37). For thromboembolic events, both in uni- and multivariable analysis, there was no significant difference one year postoperatively when using acenocoumarol or aspirin (multivariable RR: 1.2, 95% CI: 0.47-3.02). Only prior use of acenocoumarol appeared to be an independent predictor of thromboembolic events both in uni- and multivariable analysis (p=0.007).

Kaplan Meier survival curves for the first episode of any event, including mortality, are shown in **figure 1**. 50% of the bleeding and 63% of the thromboembolic complications occurred within 3 months. Comparing the events before and after policy change in

Table 5. Univariable analysis of risk factors on bleeding and thromboembolic events in 384 patients (unless specified otherwise) one year after bioprosthetic aortic valve replacement.

	Bleeding events			TE events		
Variable	RR	95%CL	P-value	RR	95%CL	P-value
Acenocoumarol	18,32	5,41-62,07	<0,001	1,11	0,44-2,77	0,83
Male	0,15	0,05-0,46	0,001	0,815	0,36-1,85	0,62
Age	1,07	1,04-1,11	<0,001	1,01	0,95-1,07	0,8
LogEuroscore (n=365)	1,04	0,98-1,12	0,21	0,99	0,93-1,07	0,97
Prior CVA	2,01	0,64-6,36	0,23	1,2	0,30-4,92	0,79
Prior CABG	0,24	0,03-2,17	0,2	1,37	0,20-9,39	1,75
Prior PCI	32,09	17,26-59,66	<0,001	0,8	0,20-3,31	0,76
Prior embolism	0,31	0,06-1,58	0,16	0,87	0,21-3,56	0,84
Diabetes	1,5	0,74-3,04	0,26	1,43	0,58-3,54	0,44
Smoking	0,34	0,08-1,36	0,13	1,34	0,51-3,52	0,55
Hypertension	6,2	1,82-21,3	0,004	1,47	0,60-3,59	0,4
Dyslipidemia (n=383)	4,74	3,00-7,48	<0,001	1,27	0,54-2,96	0,58
Repeat thoracotomy (n=354)	0,54	0,08-3,75	0,53	0,85	0,12-5,60	0,87
Prior ASA (n=381)	1,47	0,77-2,78	0,24	0,72	0,30-1,70	0,45
Prior Acenocoumarol (n=381)	0,27	0,5-1,35	0,11	3,06	1,31-7,19	0,01
History of AF (n=351)	0,65	0,20-2,07	0,46	1,55	0,52-4,57	0,43
Concomitant CABG	2,83	2,13-3,76	<0,001	1,55	0,68-3,52	0,3
Before policy change	0,54	0,21-1,39	0,21	0,79	0,26-2,39	0,67

Note: TE = thromboembolic, RR=Relative Risk, CI=Confidence Interval, MI= Myocardial infarction, CVA = Cerebrovascular Accident, CABG= Coronary Artery Bypass Grafting, PCI=Percutaneous Coronary Intervention, AF= Atrial Fibrillation

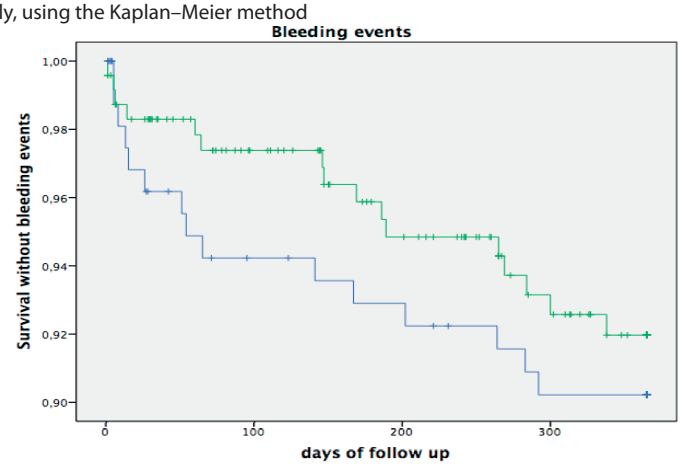
Table 6. Multivariable Poisson regression with selected independent predictors that had p-values below 0.15 and were of clinical importance in 384 patients (unless specified otherwise) after bioprosthetic aortic valve replacement.

	Bleeding			TE events		
Predictor	RR	95%CI	P-value	RR	95%CI	P-value
Acenocoumarol	8,41	0,36-19,79	<0,001	1,2	0,47-3,02	0,7
Male	0,14	0,36-1,62	<0,001	0,82	0,36-1,89	0,65
Age	1,02	0,96-1,08	0,49	1,01	0,95-1,07	0,77
Prior MI	0,35	0,07-1,69	0,19	-	-	-
Prior PCI	10,75	5,54-20,88	<0,001			
Smoking	1,6	0,65-3,95	0,31	-	-	-
Hypertension	1,82	0,80-4,16	0,16	-	-	-
Dyslipidemia (n=383)	2,29	1,26-4,19	0,007	-	-	-
Prior Acenocoumarol (n=381)	2,46	1,32-4,56	0,004	3,1	1,37-7,4	0,007
Concomitant CABG	3,32	1,70-6,48	<0,001	-	-	-

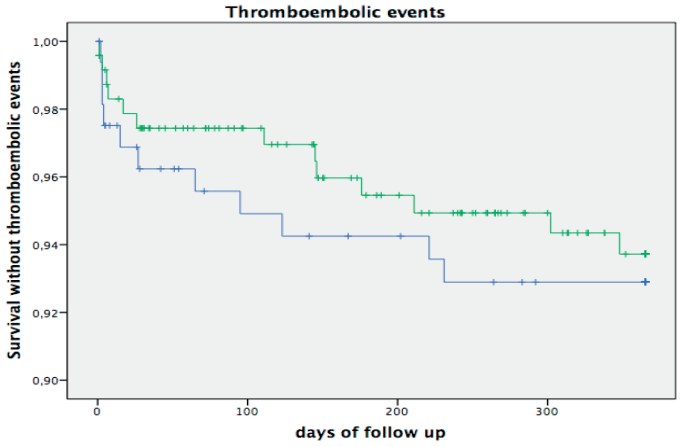
Note: TE = thromboembolic, RR=Relative Risk, CI=Confidence Interval, MI = myocardial infarction, PCI = percutaneous coronary intervention, CABG = coronary artery bypass surgery.

Figure 1. Survival to bleeding (A), thromboembolic events (B) and overall survival (C) in 402 patients 1 year postoperatively, using the Kaplan–Meier method

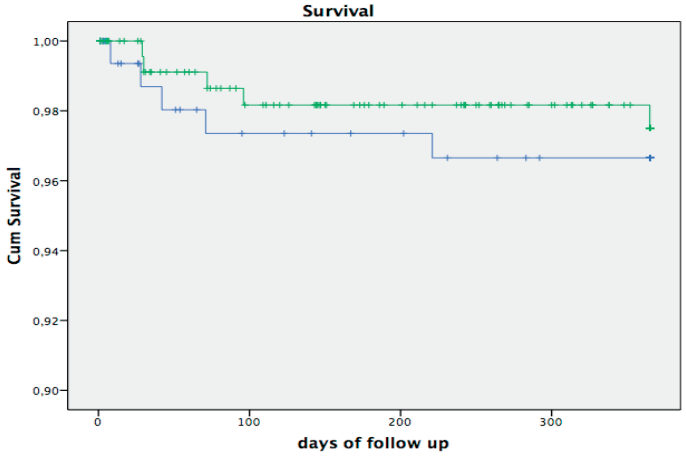
A.



B.



C.



Blue = before policy change 2011, green = after policy change 2011.

2011, no significant difference in event-free survival could be demonstrated (bleeding: p=0.48, thromboembolism: p=0.83, mortality: p=0.58), possibly due to the larger number of patients using acenocoumarol preoperatively, which is a predictor for bleeding, after policy change in 2011. During one year follow-up 10 patients (2%) died, of who four died before the antithrombotic policy change at the VUmc. Approximately 50% of all events occurred within 100 days after aortic valve implantation. Causes of death were sepsis (three patients), cardiac arrest, gastrointestinal bleeding, aortic dissection, respiratory failure and post-anoxic encephalopathy. In one patient, the cause of death was unknown.

DISCUSSION

The main finding of this study was a significantly increased incidence of minor and major bleeding events without a reduction of thromboembolic events during acenocoumarol therapy compared to aspirin use one year after bioprosthetic aortic valve replacement.

Our study reinforces the recommendations of the ACC/AHA, ACCP, ESC and the EACTS guidelines suggesting antiplatelet therapy as adequate or acceptable thromboprophylaxis. These recommendations have been revisited in the last decade after more recent publications about the absence of a beneficial effect of warfarin (1-4). Five studies have compared antiplatelet with anticoagulation therapy in patients with bioprosthetic aortic valves (**Table 7**) (5-7, 16, 17). Four of them found no advantages in performing early anticoagulation therapy compared with a low-antiplatelet regimen. Colli *et al.* (2013) demonstrated higher morbidity in patients using VKA after bioprosthetic aortic valve replacement. Other recent studies comparing early to no anticoagulation have reported no significant difference in bleeding episodes and no reduction in thromboembolism (9, 18). Elbardassi *et al.* and Jamieson *et al.* even suggested that early antithrombotic therapy had no beneficial effect in patients without risk factors (19, 20). As a result, since most studies have been either retrospective or underpowered, the thrombotic prophylaxis after bioprosthetic aortic valve replacement remains controversial. The treatment policy of the VUmc, based on current guidelines, was changed in 2011 and now advises the use of aspirin instead of VKA in patients without risk factors (2).

In contrast to the findings by Goldsmith *et al*., age, hypertension, diabetes, dyslipidemia, a history of smoking and left ventricular function were no predictors of postoperative thromboembolic events (21). In our study only prior use of acenocoumarol was found to be a predictive risk factor for thromboembolic events. Those who received acenocoumarol before operation may have been more sensitive to thromboembolism by other risk factors, mostly atrial fibrillation.

Table 7. Summary of findings: Antiplatelet versus anticoagulation therapy after bioprosthetic aortic valve replacement (5-7, 16, 17)

Author, year	Study design, follow up	Conclusion
Blair *et al.* 1994	Retrospective, 3 months	No significant differences
Gherli *et al.* 2004	Prospective observational, 3 months	No significant differences
Aramendi *et al.* 2005	Prospective, 6 months	No significant differences
Colli *et al.* 2007	Prospective, 3 months	No significant differences
Colli *et al.* 2013	Prospective, 6 months	Higher morbidity within 6 months using VKA

Note: VKA= vitamin K antagonists

Most studies have found no significant differences in thromboembolic events or bleeding complications between patients treated with anticoagulation therapy and patients treated with an antiplatelet regimen, whereas our study demonstrated that antiplatelet therapy has an apparent safety benefit in the first year after bioprosthetic aortic valve replacement and that this does not come with an increased thromboembolic risk. Still, in this uncontrolled setting, there could have been unknown risk factors that may have influenced these results. Nevertheless, our results indicate that aspirin should be considered the preferred antithrombotic regimen compared to acenocoumarol. This is in line with the recommendations of aspirin use after bioprosthetic aortic valve replacement by the AHA/ACC, ACCP, ESC and EACTS guidelines. Moreover, we think that our findings suggest that AHA/ACC and EACTS should revisit the recommendation of vitamin K antagonists as an acceptable alternative. This recommendation of the ACC/AHA guidelines is based on a recent retrospective study that demonstrated a clear benefit associated with warfarin versus no warfarin during the initial three months after surgery (8). These findings, however, are based on different study populations. In our study two more homogenous groups could be compared. The beneficial effect of aspirin compared to no treatment at all cannot be answered from the results of our study.

Strength of our study is the fact that we included a cohort of consecutive patients with a fixed regime of antithrombotic prophylaxis prior to and after the change in the local antithrombotic policy in July 2011. In our study all surgeons and cardiologists strictly adhered to both guidelines before and after July 2011. We think this adds to the external validation of our findings. Surprisingly, the number of bleeding events before and after policy change did not differ significantly. This might be due to the larger number of patients using acenocoumarol preoperatively, which is a predictor for bleeding, after policy change in 2011. However, when comparing the number of days on aspirin versus acenocoumarol bleeding events were significantly lower in the aspirin group. The number of thromboembolic events was similar in both analyses. Our study had the inherent limitations of being retrospective. Treatment was not randomly allocated. Second, medical files were mostly but not entirely complete. Ideally, future randomized clini-

cal trials comparing aspirin with VKA therapy are necessary to provide evidence-based recommendations for the implementation of optimal antithrombotic strategy.

In conclusion, our study shows a beneficial effect of aspirin compared to acenocoumarol one year after bioprosthetic aortic valve replacement, which reinforces the recommendation of aspirin by current guidelines.

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