

Anticoagulation therapy after bioprosthetic aortic valve replacement in Dutch cardiothoracic centres: acceptance of guidelines does not lead to overall implementation[†]

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Abstract

In 2012, the Netherlands Association of Cardiothoracic Surgery accepted the new guidelines of the European Association for Cardio-Thoracic Surgery on antiplatelet and anticoagulation management in cardiac surgery. The aim of our study was to evaluate knowledge and implementation of these guidelines in Dutch cardiothoracic centres 8 months later, specifically after biological aortic valve replacement. One month prior to and 8 months after acceptance of the new guidelines, a questionnaire was sent to all 16 Dutch cardiothoracic centres about their current anticoagulation management after biological aortic valve replacement, their knowledge and implementation of the guidelines. All centres returned the questionnaire. Fifteen centres declared knowledge of the guidelines of which two adjusted their anticoagulation therapy. Four declared they did not follow the guidelines. However, of the remaining 11 centres, only 7 followed the guidelines. Between the centres, current anticoagulation therapy varied from aspirin to coumarin with different dosages and durations. Despite acceptance of the guidelines, only 7 of 16 centres followed them, and there remains great variability in the postoperative anticoagulation management after biological aortic valve replacement in Netherlands.

Keywords: Aortic valve • Bioprosthesis • Anticoagulation • Antiplatelet

INTRODUCTION

The necessity for postoperative anticoagulation (AC) in patients after bioprosthetic aortic valve replacement (bAVR) has been studied repeatedly over the past years; however, there continues to be a lack of evidence. It is suspected that, in the first 3 months after biological valve replacement, there is a higher risk of thromboembolic events, due to the underlying cause of the valve disease, the design of the valve (stented or stentless) and the time needed for endothelialization of the suture-ring and the sutures of the new valve prosthesis [1, 2].

However, current available investigations do not show the superiority of vitamin K antagonists. They even suggest that treatment with antiplatelet therapy alone in the early postoperative period is adequate, although most of the studies are retrospective, they do not have enough power to show significance and follow-up is inconsistent [2, 3].

Also, recent guidelines are not consistent: All (recently) changed their advice to a regimen of aspirin alone, in the absence of thromboembolic risk factors such as atrial fibrillation, enlarged left atrium or left ventricle or thrombus, although they mention a vitamin K antagonist as a reasonable alternative, and some direct one to other guidelines [1, 4–11].

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In May 2012, during their biannual meeting, the Netherlands Association for Cardiothoracic Surgery (NVT) confirmed the guidelines of the European Association for Cardio-Thoracic Surgery (EACTS) on antiplatelet and anticoagulation management in cardiac surgery (EACTS-AC guidelines), with the intention to implement these guidelines in daily practice and to create uniformity of management [11].

The aim of this study was to evaluate knowledge and implementation of these EACTS-AC guidelines in Dutch cardiothoracic centres after confirmation in May 2012, particularly the recommendation on AC after tissue aortic valve replacement stating: 'After tissue aortic valve replacement and in the absence of other indications for anticoagulation, antiplatelet therapy alone is adequate' [11]. Furthermore, we wondered if these guidelines resulted in more uniform management and therefore checked on dosage, target international normalized ratio (INR) and duration of AC therapy.

METHODS

In April 2012, 1 month prior acceptance of the EACTS-AC guidelines, a survey to evaluate current AC management after bAVR was administered in all 16 cardiothoracic centres in Netherlands to one cardiac surgeon (or the oldest in training) in each centre about general AC management after bAVR in their centre (Table 1, question 1a, 4). The same questionnaire, completed with

Table 1: Questionnaire regarding AC management after bAVR

	Question	Answer (Mark the applicable)
1a	Which type of anticoagulation therapy do you start after biological aortic valve replacement?	
1b	Which type of anticoagulation therapy do you start after biological aortic valve replacement?	<ul style="list-style-type: none"> • None • Aspirin; dosage: duration of therapy: • Vitamin K antagonist; target INR: duration of therapy: • Combination therapy; dosage: target INR: duration of therapy: • NOAC; dosage: duration of therapy: • Other, nl:
2	Are you aware of a guideline about anticoagulation management?	<ul style="list-style-type: none"> • Yes • No
3	Do you follow these guidelines ?	<ul style="list-style-type: none"> • Yes • No
4	Cardiothoracic centre I work in	

bAVR: bioprosthetic aortic valve replacement; NOAC: new anticoagulants; INR: international normalized ratio.

additional questions about dosage, duration of therapy and knowledge and implementation of the guidelines was sent eight months (January 2013) after the acceptance of the EACTS-AC guidelines by the NVT (May 2012) to the same cardiac surgeon (or the oldest in training) in each centre (Table 1, question 1b, 2, 3).

RESULTS

All cardiothoracic centres participated voluntarily and completed the survey in 2012 and 2013. Results are given in Table 2.

In 2012, prior to acceptance of the guidelines, four centres (25%) (Centres 1–4) prescribed only aspirin and four centres (25%) (Centres 10–12, 14) started with coumarin and switched to aspirin after 6 weeks or 3 months of coumarin use. Three centres (18.75%) (Centres 5–7) based their decision on risk factors of the patient, which they identified by using the CHAD2 score or the risk factors described in the EACTS-AC guidelines [11, 12]. Two centres (12.5%) (Centres 8 and 9) prescribed aspirin or coumarin depending on the type of valve implanted-stented or stentless, and two centres (12.5%) (Centres 15 and 16) prescribed a combination of coumarin and aspirin. One centre (6.25%) (Centre 13) did not prescribe any further treatment after 3 months of coumarin.

In 2013, after acceptance of the guidelines, six centres (37.5%) (Centres 1–6) prescribed only aspirin and one (6.25%) (Centre 7) prescribed aspirin or coumarin depending on risk factors. Five centres (31.25%) (Centres 10–14) prescribed coumarin of which one switched therapy after 3 months. Two centres (12.5%) (Centres 15 and 16) prescribed a double therapy with coumarin and aspirin and stopped coumarin after 3 months. Two centres (12.5%) (Centres 8 and 9) prescribed coumarin or aspirin depending on the type of valve implanted-stented or stentless.

This leads to six centres that always prescribe aspirin, four centres that prescribe aspirin or coumarin depending on valve type or risk factors, two centres that always prescribe a combination of aspirin and coumarin and four centres that always prescribe coumarin.

Of the 12 centres prescribing aspirin, the duration of therapy was 3 months in one centre (Centre 7), lifelong in 10 centres (Centres 1–6, 15, 16) and lifelong but starting after 3 months in one centre (Centre 11).

Five centres (Centres 1, 3, 5, 11, and 15) prescribed 80 mg of acetyl salicylic acid (ASA) and five centres (Centres 2, 6, 7, 8, and 16) prescribed 100 mg of carbasalate calcium. The dosage was unknown for two centres (Centres 4 and 9).

Of the 10 centres prescribing coumarin, one (Centre 9) prescribed Fenprocoumon, and the other 9 (Centres 7, 8, 10–16) prescribed Acenocoumarol. The duration of therapy was 6 weeks in two centres (Centres 9 and 12), 3 months in seven centres (Centres 8, 10, 11, 13–16) and lifelong in one centre (Centre 7), but only in the presence of risk factors according to the EACTS-AC guidelines. Target INR ranged between 2 and 2.5 in two centres (Centres 7 and 8), 2–3 in four centres (Centres 10 and 14–16), 2.5–3 in one centre (Centre 12) and 2.5–3.5 in two centres (Centres 11 and 13). The target INR was unknown for one centre (Centre 9).

Thus, the duration of therapy varied from 3 months to lifelong for aspirin, and 6 weeks to 3 months for coumarin, with different dosages, although most centres indicated that the final decision on the duration of treatment is made by the patient's own cardiologist.

On the second question, 15 centres declared knowing the EACTS-AC guidelines. Only one centre (Centre 11) declared not knowing them, and consequently did not know if these guidelines had been followed. Of the other 15 centres, 11 claimed to have followed and 4 not to have followed the guidelines.

DISCUSSION

Despite the acceptance of the EACTS-AC guidelines by the members of the NVT in May 2012, there is one centre that claimed not to know these guidelines and consequently did not follow them nor changed management.

Of the 15 centres that did know the guidelines, 4 centres declared not following them, which is possible by law, although deviation needs explanation, especially when it is structural. We do not know the arguments of these four centres, nor do we know if deviation from the guidelines in other centres is mentioned and explained in institution protocols, because this was not an item in our questionnaire.

Two centres changed their management according to these guidelines. Together with the four centres that had already prescribed aspirin only, and the one centre prescribing aspirin

Table 2: AC therapy in the Netherlands 2012 and 2013

Centre	2012 Prior to the acceptance of the EACTS guidelines Type of AC therapy	2013 After the acceptance of the EACTS guidelines			
		K	Type of AC therapy	S	FG
1	Aspirin	X	Aspirin	X	X
2	Aspirin	X	Aspirin	X	X
3	Aspirin	X	Aspirin	X	X
4	Aspirin	X	Aspirin	X	X
5	Aspirin, Coumarin in high-risk patients (CHAD)	X	Aspirin	X	X
6	Aspirin <70 years, LMWH>70 years, Coumarin in high-risk patients (EACTS guideline)	X	Aspirin	X	X
7	Aspirin, Coumarin in high-risk patients (EACTS guideline)	X	Aspirin or Coumarin depending on risk	X	X
8	Aspirin if stentless valve, Coumarin if stented valve	X	Aspirin if stentless valve, Coumarin if stented valve	X	
9	Aspirin if stentless valve, Coumarin if stented valve	X	Aspirin if stentless valve, Coumarin if stented valve		
10	Coumarin for 3 months, then switch to Aspirin	X	Coumarin		
11	Coumarin for 3 months, then switch to Aspirin		Coumarin		
12	Coumarin for 6 weeks, then switch to Aspirin	X	Coumarin		
13	Coumarin	X	Coumarin	X	
14	Coumarin for 3 months, then switch to Aspirin	X	Coumarin	X	
15	Coumarin and Aspirin for 3 months	X	Coumarin and Aspirin, stop Coumarin after 3 months		
16	Coumarin for 3 months and Aspirin lifelong	X	Coumarin and Aspirin, stop Coumarin after 3 months	X	

K: knowledge of the guidelines; S: supposition to follow the guidelines, FG: follow the guidelines; LMWH: low-molecular-weight heparin; AC: anticoagulation.

depending on risk factors, this leads to seven centres following and eight centres deviating from the guidelines in 2013. These eight centres did not prescribe aspirin according to the guidelines, but they prescribed coumarin as an acceptable alternative, as mentioned in the same guidelines, mainly because of the absence of clear evidence in favour of aspirin only. In view of these findings, we can conclude that, with an audit, it is not enough to just ask if a centre follows the guidelines, but that this should be reflected in daily practice as well.

Dosage, target INR and duration of therapy differ between centres, and since no specific dosage or duration is recommended in the guidelines, it will be difficult to reach uniformity. This means that despite implementation of guidelines, a uniform management has not been reached.

Remarkably, five centres prescribe 80 mg of ASA, whereas five other centres prescribe 100 mg of carbasalate calcium, which is equivalent in action but double in price [13]. Interestingly, new anticoagulants (NOACs) such as Apixaban (Eliquis, Bristol-Myers Squibb, Anagni, Italy), Rivaroxaban (Bayer, Leverkusen, Germany) and Dabigatran (Boehringer Ingelheim, Ingelheim am Rhein, Germany) were currently not prescribed by any centre, although only Dabigatran has a registered contraindication to its use with valve prostheses [13].

These findings may seem unexpected and confusing, but they are in line with earlier, comparable studies, mainly in the UK [4, 14–16]. In the Action Registry in 2008, Colli showed that 33% of centres prescribed aspirin according to the guidelines, 43% of centres prescribed a vitamin K antagonist, 20% prescribed both and 4% did not prescribe anything from discharge until Month 3 [4]. In 2010, 194 cardiac surgeons in the UK were surveyed by Nowell. Eighty-eight percent responded, of which 58% followed the guidelines by prescribing aspirin for 3 months (10%) or more (48%), 15% prescribed warfarin for 3 months, 10% prescribed no medication at all and 17% followed other regimens [15]. In 2011, a national audit in the UK among 37 hospitals showed that 62.2% of them were aware of the current EACTS-AC guidelines; 11.6% followed these guidelines, 73.1% did not and 15.3% did not know of them [15].

The variability in prescription in our study of the centres in Netherlands is not different from that in these surveys with 44% prescribing aspirin, 31% prescribing coumarin, 13% prescribing both and 12% following other regimens, although awareness of the guidelines is higher (94%).

LIMITATIONS

Although all centres participated in this survey, there is the possibility of variation in AC management between surgeons in the same centre. Another important limitation of this study is that cardiac surgeons start AC management directly postoperatively, but when patients return to their attending cardiologists, they will take a decision about the final type and duration of therapy. These cardiologists did not participate in this survey, so we have no documented data of AC therapy after discharge.

Furthermore, adherence to the guidelines is not obligatory; they serve as a guide in best practice for professionals and as a standard of care for patients and their lawyers, although deviation from them needs argumentation, especially when this is structural [17]. We did not ask centres for their motivation in deviating from the guidelines, nor if this deviation is mentioned and explained in institution protocols.

CONCLUSION

Eight months after acceptance of the EACTS guidelines on antiplatelet and AC therapy, little has changed in AC management after bAVR in the direct postoperative care in cardiothoracic centres in Netherlands. Despite the fact that 15 of 16 centres declared knowing the guidelines, only 7 centres did follow them. Furthermore, the implementation of this guideline did not result in a uniform AC management. Research and publication may lead to more centres following these guidelines.

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REFERENCES

- [1] Hermans H, Vanassche T, Herijgers P, Meruis B, Herregods MC, van de Werf F *et al.* Antithrombotic therapy in patients with heart valve prostheses. *Cardiol Rev* 2013;21:27–36.
- [2] Efthymiou CA, Mills RJ, O'Regan DJ. Early postoperative thrombosis of an aortic bioprosthetic valve: should anticoagulation be patient specific? *J Card Surg* 2013;28:723–9.
- [3] Mydin MI, Dimitrakakis G, Younis J, Nowell J, Athanasiou T, Kourliouros A. Optimal thromboprophylaxis following bioprosthetic aortic valve replacement: still a matter of debate? *Interact CardioVasc Thorac Surg* 2012;15:109–14.
- [4] Colli A, Verhoye JP, Heijmen R, Strauch JT, Hyde JAJ, Pagano D *et al.* Antithrombotic therapy after bioprosthetic aortic valve replacement: ACTION Registry survey results. *Eur J Cardiothorac Surg* 2008;33:531–36.
- [5] Jamieson WR, Cartier PC, Allerd M, Boutin C, Burwash IG, Butany J *et al.* Canadian Cardiovascular Society Consensus Conference: surgical management of valvular heart disease 2004. *Can J Cardiol* 2004;20(Suppl E):E7–E120.
- [6] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, Guyton RA *et al.* 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 practice guidelines. *J Am Coll Cardiol* 2014;63:e57–e185.
- [7] Whitlock RP, Sun JC, Fremes SE, Rubens FD, Teoh KH. American College of Chest Physicians. 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:e576S–600S.
- [8] Keeling D, Baglin T, Tait C, Watson H, Perry D, Baglin C *et al.* Guidelines on oral anticoagulation with Warfarin—4th edition. *Br J Haematol* 2011;154:311–24.
- [9] Svensson LG, Adams DH, Bonow RO, Kouchoukos NT, Miller DC, O'Gara PT *et al.* Aortic valve and ascending aorta guidelines for management and quality measures. *Ann Thorac Surg* 2013;95:S1–S66.
- [10] Vahanian A, Alfieri O, Andreotti F, Antunes MJ, Barón-Esquivias G *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:S1–44.
- [11] Dunning J, Versteegh M, Fabbri A, Pavie A, Kolh P, Lockowandt U *et al.* Guideline on antiplatelet and anticoagulation management in cardiac surgery. *Eur J Cardiothorac Surg* 2008;34:73–92.
- [12] Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial fibrillation. *JAMA* 2001;285:2864–70.
- [13] De Boer JE, Boomkamp MD, Broekhuijsen F, Cheung PK, Danz M, Douma T *et al.* Independent drug information for healthcare professionals. <http://www.fk.cvz.nl> (April 2014, date last accessed).
- [14] Nowell J, Jahangiri M. Anticoagulation after bioprosthetic aortic valve replacement. *J Thorac Cardiovasc Surg* 2010;140:1201–2.
- [15] Hosmane S, Birla R, Marchbank A. Current practice of antiplatelet and anticoagulation management in post-cardiac surgery patients: a national audit. *Interact CardioVasc Thorac Surg* 2012;14:474–5.
- [16] Colli A, Verhoye JP, Heijmen R, Atunes M. Action Investigators. Low-dose acetyl salicylic acid versus oral anticoagulation after bioprosthetic aortic valve replacement. Final report of the ACTION registry. *Int J Cardiol* 2013;168:1229–36.
- [17] Koerselman GF, Korzec A. A proposed checklist when deviating from guidelines (Dutch). *Ned Tijdschr Geneesk* 2008;152:1757–9.