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Review Article—*Special issue: Thrombosis*

Antithrombotic therapy in patients after valve surgery with special attention to the combination of anticoagulant and antiplatelet therapy

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ABSTRACT

Patients after implantation of mechanical valves need life-long anticoagulant therapy. Nearly 30% of these patients have also indication for antiplatelet therapy because of concomitant ischemic heart disease or peripheral arterial disease. Combined anticoagulant and dual antiplatelet therapy (so called triple therapy - aspirin, clopidogrel and vitamin K antagonists) is indicated in patients with acute coronary syndrome and after percutaneous coronary intervention (PCI) for a different time according to the type of stent used during the procedure. Triple therapy is substantially more efficacious in reducing the occurrence of cardiovascular events and mortality in patients undergoing PCI with an indication for long-term anticoagulant therapy, compared with dual antiplatelet therapy. On the other hand it carries 3.5 to 4 times higher risk of bleeding in treated patients. Recently new anticoagulants (dabigatran, rivaroxaban, apixaban) and antiplatelet drugs (prasugrel and ticagrelor) came into clinical practice and new studies using these drugs are underway.

The purpose of this review article is to summarize current approach to patients with indication for anticoagulant and antiplatelet therapy after valve surgery.

Contents

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1. Indication of antithrombotic therapy and its intensity

According to the European Society of Cardiology (ESC) and the Czech Society of Cardiology guidelines [1,2] a lifelong anticoagulant therapy is recommended for all patients with mechanical heart prostheses (class of recommendation I, level of evidence B) and for patients with bioprostheses who have other indications for anticoagulation (atrial fibrillation, venous thromboembolism, hypercoagulable state, severely impaired left ventricular function with ejection fraction <35%)—(class I, level C). Oral anticoagulation should be considered for the first 3 months after implantation of a mitral or tricuspid bioprosthesis and for the first 3 months after mitral or tricuspid valve repair (class IIa, level C).

Warfarin has a narrow therapeutic window and an unpredictable response that requires routine coagulation monitoring and frequent dose adjustment. Despite the disadvantages of warfarin till now there has been no equivalent alternative for this drug. The RE-ALIGN study with dabigatran in patients with mechanical valve prosthesis was stopped because of increased incidence of valve thrombosis and clinical ischemic events (see below).

When anticoagulant therapy is prescribed the prosthesis thrombogenicity, prosthesis position and patient-related factors should be taken into consideration. Generally Carbomedics, Medtronic Hall, St. Jude Medical or ON-X valves belong to the group of prothesis with low thrombogenicity. Lillehei-Kaster, Omniscience, Starr-Edwards, Bjork-Shiley and other tilting-disc valves belong to the group of prosthesis with high thrombogenicity. Other bileaflet valves not mentioned above constitute a group with medium trombogenicity. Unfortunately there are insufficient data on valve thrombosis in newly introduced valves. The thrombogenicity of the prosthesis in the aortic position is generally smaller than in the mitral position; the implantation of the mechanical prosthesis into the tricuspid or pulmonary position is exceptional.

Target international normalized ratio (INR) for prosthesis with low thrombogenicity in patient with no risk factor is 2.5, for patient with more than one risk factor 3.0. Target INR for prosthesis with medium thrombogenicity is 3.0 and 3.5 according to presence/absence of risk factors and for prosthesis with high thrombogenicity 3.5 and 4.0 (Table 1). The following conditions are considered patient-related risk factors: mitral or tricuspid valve replacement, previous thromboembolism, atrial fibrillation, mitral stenosis of any degree and left ventricular ejection fraction <35%.

The most commonly reported anticoagulation regimens had the following rates of early postoperative (30 days) thromboembolism and hemorrhage: oral anticoagulation alone (0.9%, 3.3%); oral anticoagulation with intravenous unfractionated heparin (1.1%, 7.2%); and oral anticoagulation with low molecular weight heparin (0.6%, 4.8%)—[3]. After aortic valve replacement, the risk of thromboembolic events falls from 16 per 100 patient years in the early postoperative period to 1.4 per 100 patient years at 5 years. Similarly, after mitral valve replacement, the risk falls from 21 per 100 patient years to 2.5 per 100 patient years. The rate of thromboembolic events after mechanical valve implantation in patients without anticoagulation therapy is estimated to be 8.6% per year. It could be approximated, that patients with prosthetic valves belong to patients with high risk of embolic event according to CHADS-VASc score, which was developed for patients with atrial fibrillation (Tables 2 and 3). So the utilization of postoperative warfarin therapy reduces the incidence of major embolism by approximately 75%. Neither single nor dual antiplatelet therapy alone are sufficient in reducing the rate of valve thrombosis [4–6]. Only one study (135 patients) supporting the long-term use of dual antiplatelet therapy (aspirin and clopidogrel) in patients with mechanical aortic valves was published [7]. The incidence of strokes in this study dropped from 2.5 %/patient/year to 1.0 %/patient/year after the use of assays to monitor platelet reactivity. No patient developed valve thrombosis. Five patients had bleeding complications (1.2%/patient/year).

Table 1 – Target international normalized ratio (INR) recommended for mechanical prostheses [1].

Prosthesis thrombogenicity	Patient-related risk factors	
	No risk factor	Risk factor ≥1
Low	2.5	3.0
Medium	3.0	3.5
High	3.5	4.0

Patient-related risk factors: mitral or tricuspid valve replacement; previous thromboembolism; atrial fibrillation; mitral stenosis of any degree; left ventricular ejection fraction <35%.

Table 3 – CHADS-VASc score.

		Points
C	Congestive heart failure	1
H	Hypertension	1
A	Age ≥75 years	2
D	Diabetes mellitus	1
S	Stroke/TIA/thromboembolism	2
V	Vascular disease	1
A	Age 65–74 years	1
S	Sex category (female sex)	1
		max. 9

Table 2 – The annual risk (%/year) of stroke and systemic embolism by the CHADS-VASc score in patients with non-valvular atrial fibrillation. *Source:* Danish national patient registry, 10-year follow-up rates (*n*=73,813). Adapted according LaHaye with permission [34].

Score	0	1	2	3	4	5	6	7	8	9
Reported risk	0.6	1.2	2.6	3.9	6.0	9.4	11.6	13.0	13.2	13.9