Thrombosis Research 150 (2017) 104–110

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Antithrombotic therapy after bioprosthetic aortic valve implantation: Warfarin versus aspirin, a randomized controlled trial☆

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ARTICLE INFO

Article history:
Received 7 August 2016
Received in revised form 14 November 2016
Accepted 24 November 2016
Available online 25 November 2016

Keywords:
Anticoagulation
Heart valve prosthesis
Thrombosis
Aspirin
Bioprosthetic valve

ABSTRACT

Background: The optimal medical strategy for prevention of thromboembolic events after surgical bioprosthetic aortic valve replacement (BAVR) is still debated. The objective of this study was to compare warfarin therapy (target INR of 2.0 to 3.0) with aspirin 150 mg daily as antithrombotic therapy for the first three months after BAVR with or without concomitant coronary artery bypass grafting (CABG). The aim was to evaluate thromboembolic complications, major bleeding complications and death.

Materials and methods: Prospective, single-centre, open-label, randomized controlled trial. 370 patients were enrolled, 328 were available for data analysis.

Results: At baseline the warfarin and aspirin groups were comparable. Thromboembolic events were comparable between groups 11 (6.6%) vs. 12 (7.5%), $p = 0.83$. Major bleeding events occurred numerically more often in warfarin patients 9 (5.4%) vs. 3 (1.9%), $p = 0.14$. Warfarin was in multivariate analysis significantly associated with major bleeding OR 5.18 (CI 1.06–25.43), $p = 0.043$. 90-day mortality was comparable between groups 8 (4.7%) vs. 6 (3.7%), $p = 0.79$.

Conclusions: Our results suggest that aspirin might be equally effective as warfarin in preventing thromboembolic events after BAVR, but with less major bleedings. Although this is numerically the largest trial testing this hypothesis in a prospective randomized trial, further adequately powered studies are warranted.

1. Introduction

Aortic valve replacement (AVR) is the most commonly performed valve-procedure in cardiac surgery. Surgical aortic valve replacement can be either with a mechanical or a biological valve prostheses. Bioprosthetic valves have shorter durability than mechanical valves, but a major advantage is that lifelong anticoagulation (with vitamin K antagonists) can be avoided. They are therefore typically preferred in elderly patients [1–3].

Despite low long-term thromboembolic risk with bioprosthetic valves, it has been anticipated that patients are at moderate risk for thromboembolic complications in the first three months after surgery, until the sewing ring has endothelialized [3–5].

For patients at high risk for thromboembolic events (atrial fibrillation, venous thromboembolism, hypercoagulable state or severely impaired left ventricular function) current guidelines recommend oral anticoagulation [1,2].

However, it is still debated, what the optimal antithrombotic therapy should be for the majority of patients after bioprosthetic aortic valve replacement (BAVR). This is reflected in current guidelines from American Heart Association (AHA)/American College of Cardiology (ACC) and European Society of Cardiology (ESC)/European Association of Cardiothoracic Surgery (EACTS) these recommend both low dose aspirin (evidence level IIa), or warfarin therapy (evidence level IIb) for three months after surgery [1,2].

The initial support for postoperative oral anticoagulation came from Heras et al. in 1995; they demonstrated that anticoagulation reduced thromboembolic risk significantly after implantation of a bioprosthetic

Abbreviations: AVR, aortic valve replacement; BAVR, bioprosthetic aortic valve replacement; CABG, coronary artery bypass grafting; CT, computed tomography; DVT, deep vein thrombosis; ECC, extracorporeal circulation; INR, International Normalized Ratio; MI, myocardial infarction; NOAC, newer oral anticoagulants; TCI, transitory cerebral ischemia.

☆ Meeting presentation: Sulman Rafiq presented the findings of this study at the annual meeting of the European society of cardiothoracic surgery in October 2013 in Vienna Austria, and was awarded the "C. Walton Lillehei Young Investigators Award".

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http://dx.doi.org/10.1016/j.thromres.2016.11.021
0049-3848/

valve. However, this observational study examined early generation bioprosthetic valves implanted in the period 1975–1982, and they included both aortic and mitral valve implantations [4].

Two randomized trials (total n = 252) have tested the hypothesis of anticoagulation versus antiplatelet treatment after BAVR [6,7]. Both trials did not demonstrate superiority of anticoagulation over antiplatelet treatment as thrombo-prophylaxis.

The majority of studies addressing this issue are observational; they have generally demonstrated that warfarin and aspirin are equally effective in preventing thromboembolic episodes, but notably with less bleeding complications with aspirin [8–13]. This is summarized in a recent review [14]. However a recent retrospective database study has suggested benefit of oral anticoagulation in the first six months after BAVR [15].

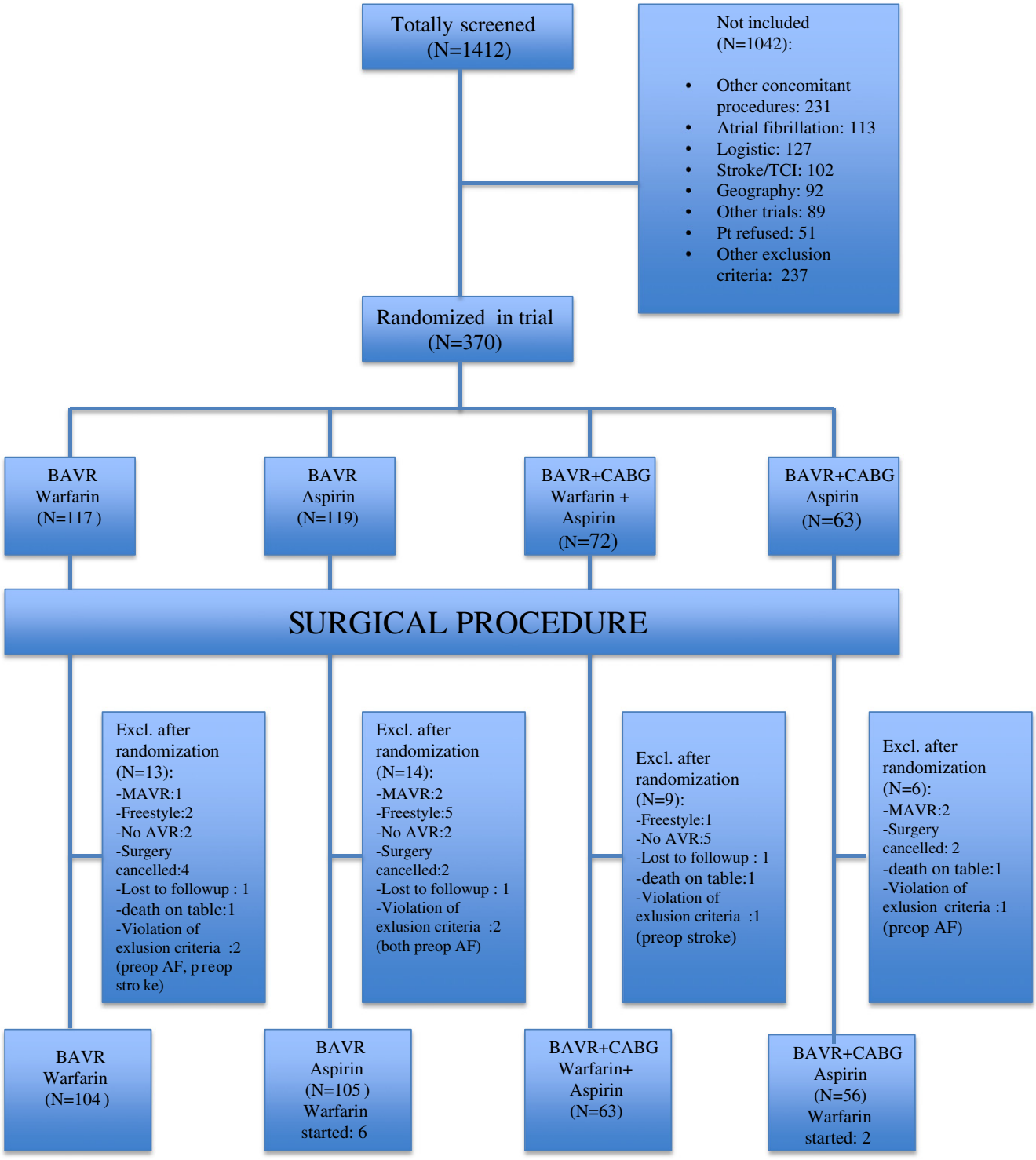

Fig. 1. CONSORT flow diagram. AF: atrial fibrillation, AVR: aortic valve replacement, BAVR: bioprosthetic aortic valve replacement, MAVR: mechanical aorta valve replacement, Excl: excluded.