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Outcomes of Warfarin Therapy for Bioprosthetic Valve Thrombosis of Surgically Implanted Valves

A Prospective Study

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ABSTRACT

OBJECTIVES The aim of this study was to assess the efficacy of warfarin in the treatment of bioprosthetic valve thrombosis (BPVT) of surgically implanted valves.

BACKGROUND There are limited data about treatment outcomes for BPVT.

METHODS This was a prospective study of patients with suspected BPVT of surgically implanted valves who received warfarin therapy at the Mayo Clinic from January 2013 to January 2016. BPVT score was calculated using previously described echocardiographic criteria. One point was assigned for each criterion: a 50% increase in prosthetic gradient within 5 years of implantation, increased cusp thickness, and abnormal cusp motion.

RESULTS Fifty-two patients were enrolled in the study (mean age 61 ± 18 years, 34 men [66%]). The mean follow-up duration from presumed BPVT was 86 ± 24 weeks. Prosthesis positions were aortic in 31 patients (60%), mitral in 17 (32%), pulmonary in 2 (4%), and tricuspid in 2 (4%). Positive responses (defined as a 50% reduction in prosthesis gradient) occurred in 43 patients (83%) within 11 weeks (interquartile range [IQR]: 6 to 22 weeks) of anticoagulation with warfarin. Nine patients (17%) did not respond to warfarin, and these patients underwent surgical valve replacement (n = 5), transcatheter valve replacement (n = 1), and intervention (n = 3). BPVT scores were calculated for 48 patients (92%) with good-quality echocardiographic images; 9 had BPVT scores of 2, and 39 had BPVTs score of 3. A BPVT score of 3 predicted a positive response to anticoagulation therapy with sensitivity of 88% and specificity of 93%.

CONCLUSIONS A trial of anticoagulation was effective in 83% of patients with suspected BPVT, and most patients responded within 3 months. BPVT score was predictive of response to therapy and should be considered during patient selection.
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The predominant mechanism of bioprosthetic valve dysfunction is structural failure (1,2), but bioprosthetic valve thrombosis (BPVT) is increasingly being recognized as an important and potentially reversible cause (3,4). BPVT is present in 11% of bioprosthetic valves explanted because of prosthesis dysfunction (4). The treatment strategies for suspected BPVT are reoperation,

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ABBREVIATIONS AND ACRONYMS

BPVT = bioprosthetic valve thrombosis

INR = international normalized ratio

IQR = interquartile range

TAVR = transcatheter aortic valve replacement

thrombolytic therapy, and anticoagulation. Data from several small case series, including 1 from our group, suggest that warfarin may be beneficial as a first-line therapy for suspected BPVT (3,5,6).

A recent study from the Mayo Clinic described the echocardiographic characteristics of BPVT, which are a 50% increase in prosthesis gradient within 5 years after implantation, increased cusp thickness, and presence of abnormal cusp motion (4). A BPVT risk score calculated using these 3 criteria was shown to increase the diagnostic sensitivity and specificity of BPVT.

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There are no prospective studies evaluating the role of anticoagulation therapy in the treatment of BPVT. The purpose of this study was to describe the outcomes of warfarin therapy for the management of BPVT of surgically implanted valves on the basis of a prospective case registry.

METHODS

PATIENT SELECTION AND STUDY DESIGN. After our initial report (3), a strategy of warfarin anticoagulation for suspected BPVT was recommended to the cardiologists and cardiac surgeons at the Mayo Clinic. We maintained prospectively a registry of patients who had tentative diagnoses of BPVT of surgically implanted valves between January 2013 and January 2016. Clinical, echocardiographic, and surgical data were reviewed, and pathology data for explanted prostheses were examined. Risk factors for thromboembolic complications were reviewed, and the CHA_2DS_2-VASc score was calculated for each patient.

The criteria for inclusion in this study were suspected diagnosis of BPVT, trial of anticoagulation therapy with warfarin, and follow-up transthoracic or transesophageal echocardiography performed at least 4 weeks after the initiation of anticoagulation therapy. A suspected BPVT diagnosis was on the basis of the impression of the attending cardiologist using echocardiographic features such as cusp thickness, abnormal cusp mobility, increased transvalvular gradient, and presence of intracardiac thrombus. The decision to initiate anticoagulation was left at the discretion of the primary cardiologist and the patient. The Mayo Clinic Institutional Review Board approved the study protocol.

The primary endpoint was a positive response to anticoagulation therapy, defined as a 50% reduction in prosthesis gradient after the initiation of warfarin. This is the same endpoint used in our prior retrospective series of outcome of anticoagulation for suspected BPVT (3). The secondary endpoint was to assess the performance of previously described echocardiographic criteria for BPVT diagnosis (4) in predicting response to anticoagulation therapy.

ANTICOAGULATION. All patients received warfarin with or without heparin bridging at the time of suspected BPVT diagnosis. Warfarin dose was adjusted to maintain an international normalized ratio (INR) of 2.0 to 3.0, and patients were monitored for bleeding complications. All patients were followed until the endpoint of response to anticoagulation therapy, valve replacement, or the end of study period.

Major bleeding events were defined as intracranial bleeding, pericardial or pleural hematoma requiring drainage, or any bleeding requiring transfusion. Minor bleeding events were defined as cutaneous bleeding, epistaxis, gastrointestinal bleeding, or any bleeding event that did not meet the criteria for major bleeding events. These definitions are derived from previous studies (7,8).

ECHOCARDIOGRAPHY. Digitally stored images of transthoracic echocardiograms (n = 52) and transesophageal echocardiograms (n = 38) were systematically analyzed by one author (A.C.E.) for the presence of echocardiographic characteristics of BPVT (4): a 50% increase in prosthesis gradient within 5 years after implantation, increased cusp thickness (defined as thickness >2 mm or significantly increased thickness compared with the initial post-operative echocardiogram), and presence of abnormal cusp motion. BPVT risk score was calculated on the basis of the presence of these 3 criteria, and 1 point was assigned for each criterion. Thus, a prosthesis with all 3 echocardiographic criteria had a BPVT score of 3.

Two echocardiographers (P.A.P. and H.M.C.) with experience in valvular disease and BPVT reviewed randomly selected studies in one-half of the cohort. All reviewers were blinded to the interpretations of others and the outcomes of anticoagulation therapy.

PATHOLOGY. Surgically resected specimens were reviewed by a cardiovascular pathologist (J.J.M.), and the gross and histological features were documented. Thrombus formation was documented if fibrin-rich material was identified either grossly or microscopically present on the valve cusps. Pannus formation was noted when obstructive fibrous ingrowth was present on either the inflow or outflow surface of the valve and was noted as mild if it did not affect the