Bioprosthetic valve thrombosis: What we know and what we need to know

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ABSTRACT

Bioprosthetic valve thrombosis account for 11% of all reoperations for bioprosthetic valve dysfunction, and preoperative diagnosis can be made based on echocardiographic features. Early reoperation can be prevented if BPVT is identified and treated preoperatively. (J Thorac Cardiovasc Surg 2016;152:975-8)

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Central Message

Bioprosthetic valve thrombosis is not an uncommmon cause of bioprosthetic dysfunction. It should be considered during evaluation for prosthetic dysfunction.

Perspective

Preoperative diagnosis of bioprosthetic valve thrombosis can be made based on echocardiography. Further research is required to delineate its pathophysiology, and the optimal strategy for the treatment and prevention of this disease.

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The predominant mechanism of bioprosthetic valve dysfunction is structural deterioration.[1,2] The risk of bioprosthetic valve thrombosis (BPVT) is unknown but generally considered very low. A recent study reported in the December 2015 issue of the *Journal of American College of Cardiology*[3] has challenged this paradigm by demonstrating that BPVT is not an uncommon cause of prosthetic valve dysfunction. Here we review important findings from this recent study, and highlight unresolved questions and areas of future research in BPVT.

HOW COMMON IS BPVT?

Egbe and colleagues[3] identified bioprosthetic valve thrombosis in 46 out of 397 (11%) bioprosthetic valves explanted at Mayo Clinic. In contrast to the misconception that BPVT is a perioperative phenomenon, this study revealed that 65% of all reoperations for BPVT occurred more than 1 year after implantation, and up to 15% of these reoperations occurred more than 5 years after the initial implantation. The authors estimated the incidence of BPVT as 1% based on 3161 patients with an implanted bioprosthetic valve who underwent follow-up echocardiography at their institution.

Although this study highlights the role of BPVT as an important cause of prosthetic valve dysfunction requiring reoperation, the incidence of BPVT in the community is unknown. The 1% incidence reported in this study was

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Abbreviation and Acronym
BPVT = bioprosthetic valve thrombosis

based solely on a subset of the cohort of patients who had follow-up echocardiography. Unfortunately, almost one-half of the patients who underwent bioprosthetic valve implantation within the study period were excluded from the analysis because of a lack of follow-up echocardiograms available for review, and thus the true incidence of BPVT cannot be ascertained. Furthermore, the report of Egbe and colleagues was based on a single tertiary center experience, and the demographics of that patient population might not be representative of the general population with valvular heart disease owing to referral bias.

The second unresolved epidemiologic question is the timing of BPVT occurrence. This study used the ''time to explantation'' as surrogate for ''time to thrombosis.'' Because the interval from the occurrence of BPVT thrombosis to reoperation is unknown, it is logical to assume that substituting the time to explantation for time to thrombosis will result in overestimation. A different study design is needed to determine BPVT incidence and the timing of BPVT occurrence.

The occurrence of BPVT is not restricted to surgically implanted bioprosthetic valves, but has also been observed after transcatheter aortic valve replacement (TAVR). A recent study in reported reduced leaflet motion in 22 of 55 patients (40%) after TAVR.[4] Restoration of leaflet motion was noted in all patients who received anticoagulation, suggesting that the bioprosthetic dysfunction observed in 40% of that cohort was due to BPVT. Furthermore, Del Trigo and associates[5] observed deterioration in the hemodynamic function of transcatheter valves (>10 mmHg increase in gradient) in 4.5% of their patients over a mean follow-up of 20 months.[5] In a multivariate analysis, failure to anticoagulate patients at hospital discharge was associated with an increased risk of valve dysfunction (hazard ratio, 3.35), lending additional support to thrombosis as a cause of valve dysfunction in some patients.

HOW DO WE DIAGNOSE BPVT?

In this study, the diagnosis of BPVT was considered in only 6 of 45 patients (13%) who underwent transesophageal echocardiography. A significant proportion of the patients with BPVT were misdiagnosed as having structural failure and referred for reoperation. This attests to the low level of awareness of the existence of BPVT and the lack of well-defined diagnostic criteria.

The authors have proposed a BPVT diagnostic model based on echocardiography characteristics, including a 50% increase in prosthetic gradient within 5 years of implantation, increased cusp thickness, and abnormal cusp mobility. The presence of all 3 echocardiographic features reliably diagnosed BPVT with a sensitivity of 72% and a specificity of 90% when applied to the 138 patients included in the study. It is important to note that the performance of this diagnostic model was tested in highly selected cohort that underwent reoperation for severe bioprosthetic valve dysfunction. Perhaps this diagnostic model may be less predictive in other populations.

Routine annual echocardiography is not recommended within the first 5 years of bioprosthetic valve implantation.[6] This recommendation is based on the assumption that the risk of structural failure (ie, cusp calcification or tear), which was thought to be the sole mechanism of bioprosthetic valve dysfunction, was very low within the first 5 years after valve implantation. This study shows that 85% of cases of BPVT occurred within the first 5 years, the period during which routine echocardiography is not recommended.

The occurrence of BPVT resulting in significant prosthetic dysfunction may be signaled by abnormal physical examination findings that should prompt echocardiographic examination, but clinical evaluation of progressive valve dysfunction is not completely reliable. If the objective is prompt identification of BPVT and early initiation of anticoagulation therapy, then reliance on abnormal physical examination findings as a prerequisite for echocardiography might not be the most effective surveillance strategy. In addition to transthoracic and transesophageal echocardiography, the use of other complementary imaging modalities, such as computed tomography, could be very effective in identifying subtle BPVT, as has been demonstrated in a study of bioprosthetic dysfunction after transcatheter aortic valve replacement.[4]

HOW DO WE TREAT BPVT?

In an initial study from the Mayo Clinic group,[7] 14 of 15 patients (93%) with a presumed diagnosis of BPVT responded to anticoagulation therapy with warfarin and subsequently avoided reoperation. Several other case series, including studies of BPVT in transcatheter valves, have reported similar findings.[8-11]

A response to anticoagulation therapy for BPVT is usually observed within 4 to 12 weeks after the initiation of therapy.[7-9] The optimal duration for trial of anticoagulation therapy, and the most effective anticoagulant (vitamin K antagonist vs novel oral anticoagulant) remain unknown, however.

HOW DO WE PREVENT BPVT?

The American College of Cardiology/American Heart Association and European Society of Cardiology guidelines do not recommend anticoagulation for bioprosthetic valves beyond the first 3 months after implantation.[12,13] In the study by Egbe and colleagues,[3] perioperative anticoagulation data were available for 63 patients (46%),