EDITORIAL COMMENT

Thrombosis of Bioprosthetic Valves
Can We Afford to Ignore It?*

William J. Stewart, MD

Over the 5 decades that bioprosthetic valves (BPVs) have been commonly implanted, the frequency of superimposed thrombosis has been thought to be negligible (1). Thus, early echocardiographic follow-up of patients with BPVs has been sparse, and chronic anticoagulation was mostly avoided. After the baseline post-operative study, current guidelines state that "patients with bioprosthetic valves may be considered for annual echocardiography after the first 5 years in the absence of a change in clinical status," prior to which routine echo is “not indicated” (2). When increased gradients or bioprosthetic leaflet dysfunction is discovered, the treatment recommended is frequently reoperation.

In this issue of the Journal, Egbe et al. (3) add to our understanding of the natural history of BPVs and their all-too-frequent dysfunction. The echocardiographic criteria that their study found valuable were increased cusp thickness, decreased cusp mobility, and increasing gradients. Assuming that the histological classification of the explanted valves differentiates 2 distinct groups, thrombosis and structural failure (leaflet degeneration), their findings have important implications, although they are not completely proven.

Bioprosthetic Valve Thrombosis Frequency

Egbe et al. (3) refute the common misperception that bioprosthetic valve thrombosis (BPVT) is uncommon using an elegant retrospective study. Histologically proven thrombosis occurred in 46 of 397 (11.6%) patients in their series of explanted bioprostheses; this was 46 episodes of BPVT among 3,161 patients with any follow-up echocardiogram after bioprosthesis implantation. Other publications also show a significant incidence of BPVT (4,5).

No other imaging method is as good as echocardiography for diagnosing BPVT or visualizing leaflets, native or bioprosthetic. Unfortunately, echocardiography does not visualize the leaflets perfectly and cannot clearly distinguish the texture of thrombus from that of fibrosis or organized pannus. Echocardiography’s insensitivity to detect thrombus results partly from the acoustic shadow cast by the bioprosthetic stents, obscuring the leaflets.

Computed tomography is sensitive to leaflet calcification and has also been used recently to detect BPVT (5). However, computed tomography cannot measure valve gradients, and its expense and radiation exposure limit its use for serial observations of BPV.

Value of Serial Doppler-Derived Gradients

A change in gradient >50% above baseline within 5 years was 1 of the variables most predictive of BPVT. The authors emphasize the importance of early post-operative “fingerprint” echocardiography to compare subsequent gradient data. Even in their study population, the initial echocardiogram was missing in 12%. Notably, the current prosthetic valve guidelines do call for a baseline echocardiogram 2 to 4 weeks after hospital discharge (2). The peak incidence of BPVT in the first 13 to 24 post-operative months (3,4) makes an early “fingerprint” echocardiogram and subsequent yearly studies an important inclusion.

When surgery is performed at a tertiary center far from the patient’s local echocardiography laboratory, we are reticent to obtain the baseline transthoracic
Echocardiogram (TTE) prior to hospital discharge, when catecholamine levels are typically high. The alternatives include obtaining a “baseline” TTE study later, either locally or back at the surgical center. Skeptics ask: “Will anything be managed differently without the early post-operative TTE?” Egbe et al. (3) answer “yes”; the ability to detect an increase in valve gradients is confounded if baseline data are missing. A patient with long-standing, higher-than-average velocity through a normal prosthesis who is found to have elevated Doppler velocities on follow-up will be falsely assumed to have BPVT if no baseline study is available. Additionally, because most of the thrombosis group have surgery in the first 1 to 4 years, early surveillance echocardiographic studies, performed yearly, seem warranted.

Echocardiography of prosthetic valves should include multiple zoom views designed to visualize the leaflets, careful valve gradients from multiple windows, pulsed Doppler below the valve to calculate valve area, and comparison to that patient’s previous studies and to standard tables stratified by valve type and size (2). To be comparable, transthoracic echocardiography should be done under “street conditions”: euvolemia with a well-controlled heart rate. Fluctuations in Doppler echocardiographic data may result from changes in ultrasound settings, sonographer technique, or reader variability. When equivocal information is obtained, transesophageal echocardiography may better visualize the leaflets of a mitral or tricuspid bioprosthesis. Even with transesophageal echocardiography, stents may obscure the leaflets of an aortic bioprosthesis; thus, there is a need for a special technique, like transgastric zoom views.

**THERAPEUTIC WARFARIN TREATMENT**

Once thrombosis is diagnosed by higher-than-expected gradients with thick, restricted leaflets, the current paper recommends treatment with warfarin, with close echocardiographic follow-up. With echocardiography-derived suspicion of BPVT without symptoms, warfarin seems less formidable than thrombolysis or surgery.

Patients with a BPV, but without atrial fibrillation or other indications for anticoagulation, are not currently considered to have high enough risk to merit prophylactic anticoagulation. When prophylactic warfarin is utilized, it is usually stopped empirically after a few months. In the Egbe et al. (3) study, only 10% of patients with BPV dysfunction were on anticoagulation therapy at the time of diagnosis, and much of it was subtherapeutic.

**IS BPVT A PREAMBLE TO BPV DEGENERATION?**

These 2 entities may represent the same disease process at different points in time. When a dysfunctional bioprosthesis is explanted for early failure, the histology looks like thrombus. When explantation is done later, perhaps fibrotic organization of the thrombus has produced what we see as structural failure. Many patients requiring later reoperation for “degenerated leaflets” may have gone through an earlier thrombotic phase, when “rescue” from valve reoperation with early anticoagulant therapy might have been feasible. Hence, early detection and treatment of thrombosis is important.

Clots do readily stick to bioprosthetic leaflets and their stents. Quite possibly, thrombosis of

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**FIGURE 1 Bioprosthetic Valve Thrombosis**

<table>
<thead>
<tr>
<th>TTE baseline 1–12 weeks after BPV implantation</th>
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</thead>
<tbody>
<tr>
<td>Yearly TTE starting with year 1</td>
</tr>
<tr>
<td>Gradient up &gt;50%, thickened cusps, AND restricted cusp mobility?</td>
</tr>
<tr>
<td>no</td>
</tr>
<tr>
<td>Continue yearly TTE</td>
</tr>
<tr>
<td>Thickened cusps AND restricted cusp mobility?</td>
</tr>
<tr>
<td>yes</td>
</tr>
<tr>
<td>Trial of anticoagulation</td>
</tr>
<tr>
<td>Improved gradient</td>
</tr>
<tr>
<td>Continue anticoagulation, repeat TTE in 6 months</td>
</tr>
</tbody>
</table>

Echocardiography helps guide management of bioprosthetic valve (BPV) thrombosis. Adapted with permission from Pislaru et al. (8). TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

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bioprostheses is merely less well recognized than thrombosis of mechanical valves because it is less likely to slip off and embolize; yet, premature explantation due to thrombus is equally problematic. Several of these issues could best be answered by a prospective clinical trial. The strength of the data by Egbe et al. (3) is their basis on pathology in an established database at a single, high-quality institution. Still, different pathologists may have different thresholds for naming the histology as thrombus, particularly in a BPV explanted early after surgery.

Research is also needed on the effectiveness and risk of anticoagulation using current valve models and designs or with new anticoagulant regimens. The benefit and cost effectiveness of screening all bioprosthetic valve patients with annual echocardiographic studies needs testing.

When BPVT is diagnosed and anticoagulation is unsuccessful in reducing progressive stenosis, the remaining options are thrombolysis or surgery. A prospective trial might help weigh the likelihood of success with the risk of bleeding, stroke, and death from these strategies (6,7).

Concerned that our inattention to the potential for thrombi to develop on BPV may “blind” our echocardiographic diagnosis of the thrombotic process, Pislaru et al. (8) proposed an algorithm for managing BPVT that has been adapted in Figure 1 to include the active surveillance strategies and management options mentioned in this editorial.

Assuming that the patient groups manifest the important differences between thrombosis and degenerative changes of BPV, this paper by Egbe et al. (3) has important implications. It incites us to search more diligently for BPVT, obtain baseline “fingerprint” echocardiographic studies, perform yearly echocardiographic studies even in the early post-operative period, and lower the threshold for prophylactic and therapeutic anticoagulation in patients with BPVs.

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REFERENCES


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