Management of Paravalvular Regurgitation

An overview of the current imaging technology, devices, and outcomes associated with closure.

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The management of periprosthetic valvular regurgitation (PVR) is complex and challenging. These challenges include the identification and quantification of periprosthetic regurgitant defects, choosing the most appropriate treatment option (be it medical, surgical, or percutaneous), and the technical aspects involved in percutaneous closure of these defects.

SCOPE OF THE PROBLEM

PVR is a recognized complication of surgical valve replacement and is the most common cause of nonstructural prosthetic valve failure—comprising approximately one-third of prosthetic valve failures.[1] The reported incidence of significant PVR ranges from 1% to 7% in long-term studies, although the exact incidence is difficult to quantify and likely remains unknown for a variety of reasons (including lack of systematic follow-up and technically difficult imaging).[2-6] These defects are difficult to visualize on transthoracic echocardiography and often require transesophageal echocardiographic imaging to provide an accurate diagnosis. Most leaks are small and asymptomatic, but when they are moderate or severe, they can lead to significant morbidity, including heart failure, hemolysis, and endocarditis. Serial echocardiographic studies suggest that these defects are not due to a slowly progressive lesion, but rather, they may occur acutely due to dehiscence of suture material or chronic low-grade inflammation. The median time to diagnosis is 1.5 years postoperatively, although the range is wide and significant leaks can develop years after an operation.[1]

PATHOLOGY AND CLINCIAL PRESENTATION

In general, the pathology underlying these defects involves incomplete apposition of the sewing ring to the native annular tissue. This may be due to tissue friability, as seen in degenerative disease, previous infective endocarditis, chronic low-grade inflammation, or inherent tissue defects as found in Marfan syndrome.[1] Other potential contributing pathologic factors include extensive tissue calcification and suture dehiscence or tension, which is frequent with advanced mitral valve disease. In our experience, defects are more commonly seen with mechanical prostheses (approximately two-thirds), in the mitral position (approximately 80%), and occur most often at the posteromedial or anterolateral annulus.

Patients with significant PVR can present with a wide variety of clinical symptoms and signs ranging from asymptomatic murmurs to decompensated heart failure and hemolysis. Cardiac cachexia is a frequent finding in advanced cases and may be profound. Heart failure is the most common indication for treatment (over 90% of cases in our experience), while some degree of hemolysis can be demonstrated in more than 40% of cases, if screened carefully.

TREATMENT OPTIONS

Once identified, the choice of treatment options for patients with significant PVR can be difficult. Medical therapy is usually of limited success in those with severe symptoms of heart failure and/or hemolysis. Reoperation for surgical repair needs to be considered, and a surgical opinion should be obtained in all cases. Surgical repair is

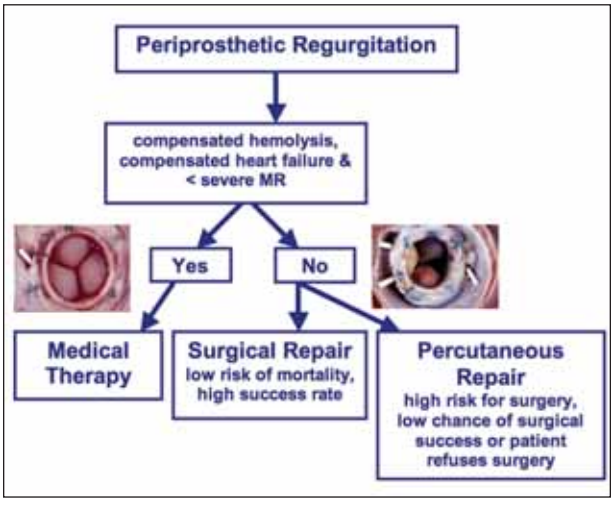

Figure 1. Approach to management of periprosthetic valvular regurgitation.

often difficult and complicated, especially in patients with multiple prior sternotomies. Perioperative mortality is high and in the range of 6% to 15%.[2-4] Increased risks of perioperative complications, residual paravalvular regurgitation, and poor outcomes among hospitalized survivors of operation exist.[2]

Percutaneous device closure of these defects would be ideal if suitable devices existed and procedural techniques were developed to deliver these devices in a safe and effective manner. Percutaneous closure would avoid surgical morbidity and mortality in this complex and high-risk patient subset but is associated with its own issues. Reducing the degree of PVR may provide patients symptomatic relief, even if some residual leak persists. Interest in developing these techniques has grown rapidly, although the procedures are far from being perfected.

Appropriate patient selection for percutaneous device closure can be challenging (Figure 1). Surgical repair of severe, symptomatic paravalvular leaks should be considered and a surgical opinion obtained. Bacterial endocarditis must be excluded as an etiology before consideration of device implantation, although there is concern that standard peripheral blood cultures may not detect localized infections or inflammation. A disturbing finding in a single-surgeon series of 24 cases of periprosthetic regurgitation was macroscopic evidence of infection (broadly defined as bland abscess, vegetation, or friable annulus) at reoperation in 67% of aortic valves and 79% of mitral valves.[7] This was found despite negative blood cultures. Clearly, vigilance and a high index of suspicion is required in excluding infection before considering device implantation.

Technical challenges involved in percutaneous closure of paravalvular defects center around three main issues: (1) adequate visualization of the 3D geometry of these defects, (2) procedural planning and execution of the varying approaches required to deploy closure devices, and (3) the limitations of the currently available devices.

IMAGING

Imaging of periprosthetic defects is crucial not only in diagnosis, but in planning successful device closure. Knowledge of the number of defects and their size and location in 3D, impacts procedural planning and execution. Choice of access route and catheters, transeptal puncture location, and device type are all influenced by periprocedural imaging. A variety of imaging techniques are currently available (Table 1). Transthoracic echocardiography is frequently sufficient for periaortic leaks (as most tend to be anterior). An important issue is flaring of the regurgitant color Doppler jet in the left ventricular outflow tract, which can lead to overestimation of the degree of regurgitation. In some instances, aortography may be necessary to assess the degree of regurgitation. Transthoracic imaging for defects involving the mitral valve is problematic because of extensive acoustic shadowing from valve rings, valve leaflets, and heavily calcified mitral annulae. For perimitral leaks, the most important modality is transesophageal echocardiography (TEE), and we advocate a low threshold for performing TEE in patients with prosthetic mitral valves with any systolic murmur. Real-time (RT) 3D TEE guidance is now available and is our preferred modality for diagnosis, as well as for identifying and successfully crossing defects in the mitral position. RT 3D TEE allows for precise anatomic localization of defect(s) with attention to the following characteristics: shape (crescentic vs round), valve dehiscence, distance from sewing ring, orientation and movement of prosthetic leaflets, and degree of regurgitation. Intracardiac echocardiography is less useful because of acoustic shadowing, but in certain specific instances, it may be useful. Finally, the success of the device closure and identification of complications is greatly aided not only by imaging, but by the development of a common vernacular and understanding of the defects by both the echocardiographer and interventionist. For example, echocardiologists are used to presenting imaging data in the left atrial view, whereas interventional cardiologists will use the left anterior oblique view with caudal angulation, which presents the valve in the mirror image of the standard surgical TEE left atrial view. Lastly, use of anatomically precise language (superior, posterior) rather than colloquialisms (up, down) will aid communication during complex interventional procedures using combined imaging modalities.

Other imaging techniques may be useful, in particular computed tomography, although this cannot be done intraprocedurally. Magnetic resonance imaging is not usual-

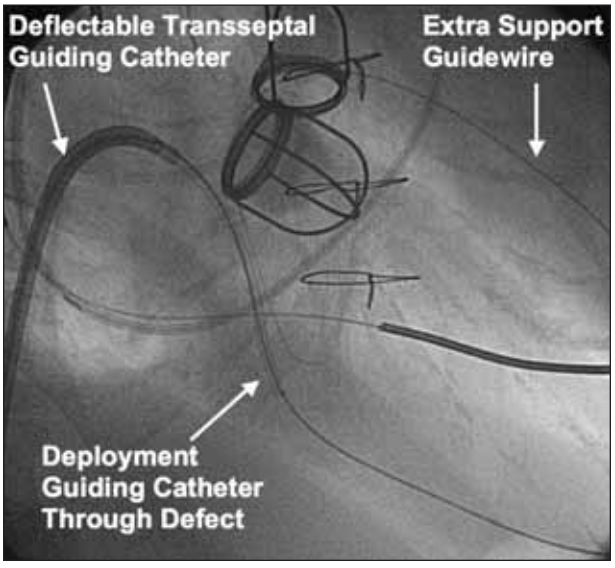

Figure 2. Antegrade approach to periprosthetic mitral defect in patient with Starr-Edwards mechanical valves (Edwards Lifesciences, Irvine, CA).

ly feasible because of the presence of metallic valves. Lastly, use of biplane fluoroscopic imaging is key during procedures to guide crossing of defects and positioning of devices. Before crossing with a delivery system, care must be taken to ensure guidewires are around the valve and not through it. Precise knowledge of the size and shape of the prosthetic valve, its sewing ring, and any struts, as well as where radiographic markers (if any) are located, is essential to these procedures. A rich variety of prosthetic valves exist, and operators must become familiar with them.

INTERVENTIONAL TECHNIQUES

Operators performing device closures of paravalvular defects must be comfortable with a variety of interventional techniques. The general principles involve positioning a catheter close to the defect (either antegrade or retrograde), crossing the defect with a guidewire and then advancing a delivery catheter, and introducing and deploying the device while maintaining the option of device recovery in the event of inadequate closure or impingement on adjacent structures, particularly the prosthetic leaflets. In particular, tilting disk valves in particular are susceptible to impingement of normal motion by devices or catheters. For periaortic valve defects, our approach is usually in a retrograde fashion via the ascending aorta. Periaortic defects can be localized with standard inferiorly oriented coronary catheters, such as multipurpose or Amplatz curves, and crossed with a hydrophilic 0.035-inch wire. More common mitral defects may be approached antegrade from the left atrium (our preferred technique, Figures 2 and 3) or retrograde through the left ventricular cavity. The antegrade approach requires comfort with transeptal puncture, a procedure no longer commonly performed by interventional cardiologists. It is not uncommon to require additional support to deliver the catheters through calcified defects. This can be accomplished by snaring the wire and exteriorizing it, creating an arteriovenous loop. Snaring can be done in the ascending aorta, if approaching the mitral valve in an antegrade fashion or in the left atrium, if retrograde. In patients with both mechanical aortic and mitral valves, a transapical puncture, another uncommonly performed technique, may be required to snare and exteriorize the wire when additional support is needed. Perimitral leaks may also be crossed directly from the apex in a retrograde fashion. These techniques have a substantial learning curve and carry the risk of serious complications, even in experienced hands, and will likely remain the province of experienced interventional centers and operators.

Potential procedural complications include those relating to the transeptal puncture (perforation, tamponade), air or thromboembolism, device embolization, prosthetic valve disruption, device interference with prosthetic leaflet function, late erosion, and worsening or new-onset hemolysis. Embolic complications can be minimized with adequate anticoagulation and meticulous technique. Integrity of the function of the leaflet occluders must be confirmed by echo- and fluoroscopic assessment. Device embolization is rare with appropriate sizing and ensuring adequate deployment and seating. If it does occur, embolized devices can be recaptured with a variety of percutaneous techniques (snaring, bioptome retrieval) or surgical removal. Partial closure of the defect often reduces regurgitant volume sufficiently to improve heart failure symptoms. The degree of hemolysis may not be affected or could even potentially be worsened with a partial closure due to red blood cell fragmentation with increased shear stress through the residual smaller defect.

DEVICES

There are currently no devices approved by the US Food and Drug Administration that are specifically designed for use in the percutaneous closure of paravalvular leaks. However, commonly used devices include Amplatzer vascular plugs, septal occluders, muscular ventricular septal defect occluders, duct occluders, and vascular coils (AGA Medical Corporation, Plymouth, MN) (Figure 4). Device selection and sizing is empiric. The use of sizing balloons can be fraught with hazard because balloon material may get stuck, tear, or obstruct normal valve motion, and we do not recommend it. Imaging cannot usually identify the true anatomic extent of the defects because the anatomy is complex and irregular in 3D. We empirically recommend

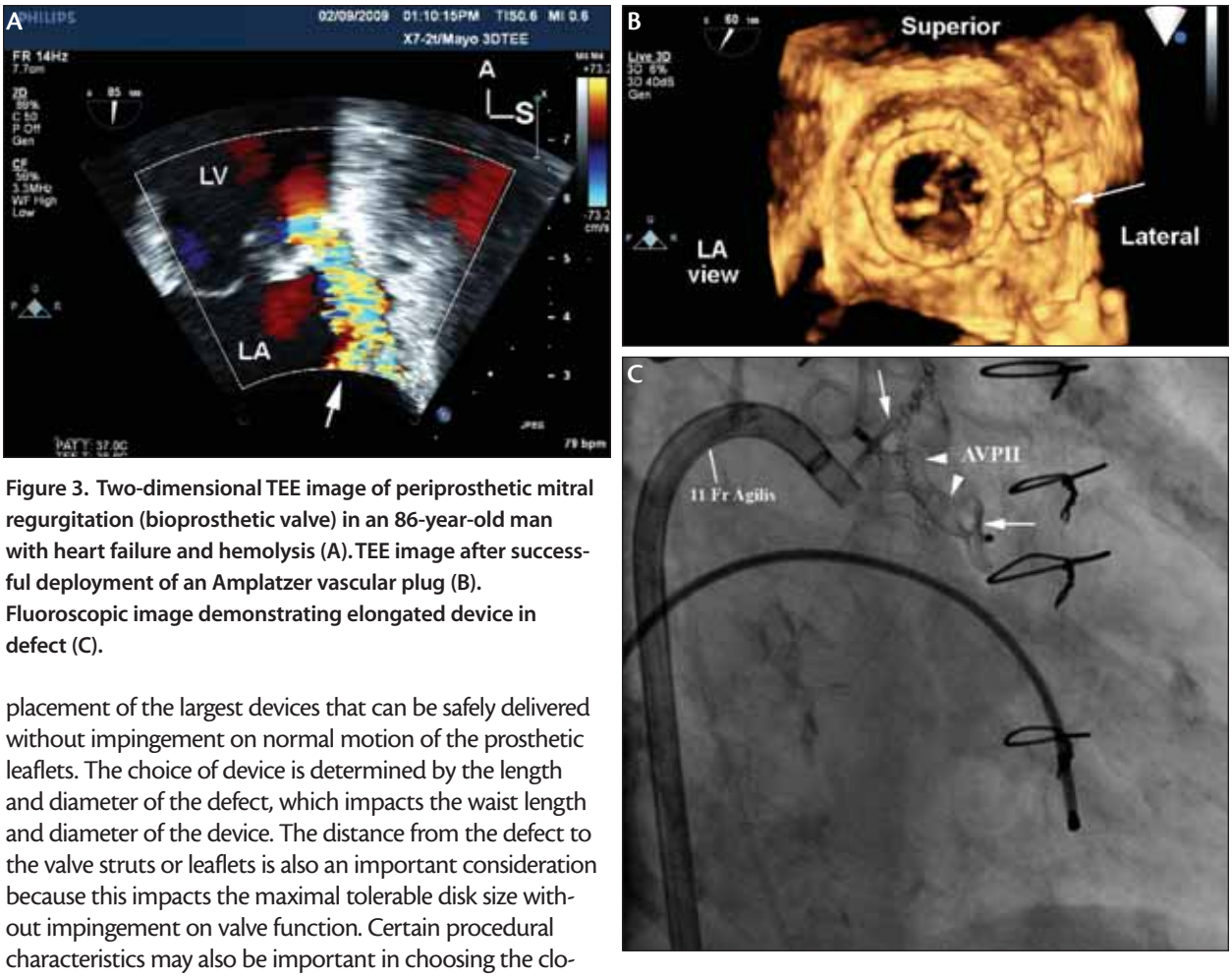

Figure 3. Two-dimensional TEE image of periprosthetic mitral regurgitation (bioprosthetic valve) in an 86-year-old man with heart failure and hemolysis (A). TEE image after successful deployment of an Amplatzer vascular plug (B). Fluoroscopic image demonstrating elongated device in defect (C).

placement of the largest devices that can be safely delivered without impingement on normal motion of the prosthetic leaflets. The choice of device is determined by the length and diameter of the defect, which impacts the waist length and diameter of the device. The distance from the defect to the valve struts or leaflets is also an important consideration because this impacts the maximal tolerable disk size without impingement on valve function. Certain procedural characteristics may also be important in choosing the closure device. For example, the duct occluder cannot be used with a retrograde approach to a mitral defect due to its single retention disk. This would be seated on the left atrial side of the defect and would place it at substantial risk of embolization. Importantly, defects are rarely round, flat, or regularly shaped; more often, defects are crescentic and represent partial dehiscences of the sewing ring. They are also often calcified and rigid and may not allow the device to adequately mold to the required shape. This may lead to oversizing the devices to maximize the degree of defect closure and enhance device stability, reducing the risk of embolization. This comes at a tradeoff because the larger

TABLE 1. ECHOCARDIOGRAPHIC IMAGING MODALITIES FOR DEVICE CLOSURE OF PVR

Echocardiographic Modality	Advantages	Disadvantages
Transthoracic (TTE)	Ease of use, patient comfort, no general anesthesia, low cost.	Limited windows and poor image quality in some patients, acoustic shadowing limits mitral visualization, inadequate visualization of transeptal puncture.
Transesophageal (TEE)	Excellent mitral visualization, real-time 3D, widely available, low cost, transeptal guidance.	Patient discomfort/risk, conscious sedation or general anesthesia, acoustic shadowing may limit aortic visualization.
Intracardiac (ICE)	Detailed intracardiac images, transeptal guidance, alternate modality if limited view TTE/TEE.	Limited operator experience, expensive, invasive, often substantial mitral shadowing compared to TEE.

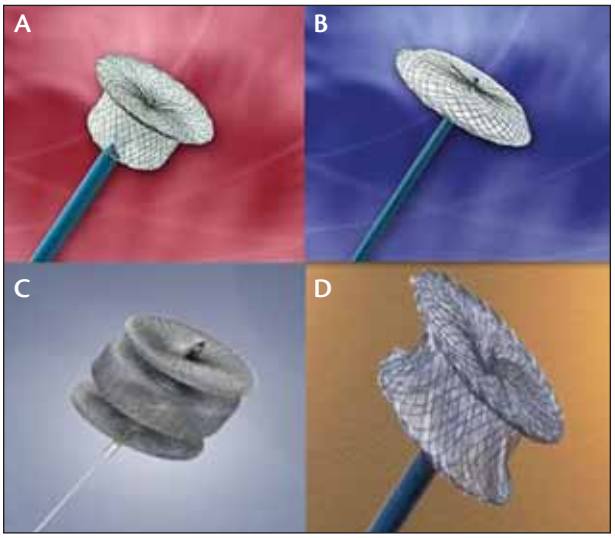

Figure 4. Amplazter devices (AGA Medical Corporation, Plymouth, MN) commonly used in closure of PVR. Duct occluder device: low-profile, stability concerns, limited to antegrade mitral approach (A); septal occluder device: greater stability, higher profile, extensive clinical experience (B); vascular plug: low-profile, moderate stability, antegrade or retrograde approach (C); muscular ventricular septal defect occluder: moderate profile and stability, antegrade or retrograde approach (D).

the device, the more likely it is to impinge on adjacent structures. The compromise between stability and profile occasionally results in patients with defects for which there is no suitable device for percutaneous closure. We tend to favor the Amplatzer vascular plug but have used a variety of devices dependent on the circumstances of the case.

Currently, there is a need for devices designed specifically for closure of these paravalvular defects. An ideal device would be resistant to embolization, conform to various sizes and shapes of defects, and carry a low profile to reduce leaflet impingement and to facilitate delivery. The possibility exists for material composition or local drug delivery to be designed to modify the tissue response or promote healing.[1]

OUTCOMES

Technical successes haven been reported in modestly sized series ranging from 63% to 89%.[2-5] Clinical success with improvement in heart failure symptoms and/or a reduction in the degree of hemolysis was seen in 37% to 63% of patients.[2-5]

Our experience at the Mayo Clinic has continued to grow, with almost 80 procedures completed. Approximately 80% are mitral leaks and 65% are mechanical prostheses. Nearly all patients present with heart failure symptoms (97%) and 44% have transfusion-dependent hemolysis. Nearly two-thirds of patients have had at least two sternotomies. The successful closure rate is approximately 80%. To date, there has been no procedural death, myocardial infarction, stroke, valve dehiscence, or urgent surgeries. There have been two late hemothoraces after left ventriclular puncture. Two devices were removed due to malposition (one perimitral and one trapped in the left ventricular outflow tract strut). One embolized device was removed percutaneously from the left iliac artery. In ongoing follow-up, two patients had continued hemolysis and were referred to surgery. There is an improvement (mean from III to II) in New York Heart Association functional class. There has been one sudden death, three heart failure deaths, and one noncardiac death.

CONCLUSION

The management of paravalvular regurgitation is challenging. Both surgical and percutaneous options should be considered. With growing experience with techniques for percutaneous device closure of paravalvular leaks and advancements in imaging technology, closure devices and delivery systems hold the promise of safe and effective percutaneous closure for patients with severe PVR. The development of devices specific to this problem will represent an important step forward for these patients. Structural interventionists should be familiar with treatment options and a wide variety of procedural techniques before attempting percutaneous closures. Close collaboration with imaging colleagues is essential for diagnosis and successful procedural execution. ■

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