Percutaneous Repair of Paravalvular Prosthetic Regurgitation
Acute and 30-Day Outcomes in 115 Patients

Paul Sorajja, MD; Allison K. Cabalka, MD; Donald J. Hagler, MD; Charanjit S. Rihal, MD

Background—Percutaneous repair has emerged as a potential therapy for patients with prosthetic paravalvular regurgitation. However, there is a relative paucity of data on the feasibility and outcome of this procedure.

Methods and Results—All patients in whom percutaneous paravalvular regurgitation closure was attempted at our hospital were identified and included. Under echocardiographic and fluoroscopic guidance, patients underwent implantation of an Amplatzer Septal Occluder, Duct Occluder, Muscular Ventricular Septal Defect Occluder, or Vascular Plug II. Percutaneous repair of 141 paravalvular defects was attempted in 115 patients (age, 67±12 years; men, 53%) with heart failure, hemolytic anemia, or both and who were at high risk of open surgery (mean estimated Society of Thoracic Surgeons mortality, 6.9%). Devices were implanted in 125 defects (89% of total defects), including in 19 patients with multiple defects. Because of the complexity of the procedures, wire exteriorization was required in 29 patients. Overall, successful percutaneous closure (defined as ≤1+ residual regurgitation) was achieved in 88 (77%) patients. Procedural time decreased with increasing case experience for percutaneous repair of both perimital and periaortic defects. Overall, the 30-day complication rate was 8.7% (sudden and unexplained death, 1.7%; stroke, 2.6%; emergency surgery, 0.9%; bleeding, 5.2%). Two devices embolized during the procedure and were retrieved without sequelae. No procedural deaths occurred, but 2 (1.7%) patients died by 30 days.

Conclusions—Percutaneous repair of paravalvular prosthetic regurgitation can be performed with a reasonable rate of procedural success and may be an initial therapeutic option, particularly in patients at significant risk for open surgery. Increased case experience is associated with shorter procedural time. (Circ Cardiovasc Interv. 2011;4:314-321.)

Key Words: angioplasty catheters Amplatzer occluder device regurgitation valves

Surgical placement of a cardiac prosthetic valve improves cardiovascular symptoms and, in many patients, can be a life-saving procedure. Paravalvular prosthetic regurgitation is a recognized complication in patients who otherwise have had successful heart valve surgery. The incidence is estimated at 3% to 6% in follow-up studies but may be underestimated because of a lack of systematic screening and difficulty in making the diagnosis. Although paravalvular prosthetic regurgitation may be associated with minimal or no morbidity, its occurrence can lead to profound symptoms of heart failure, hemolytic anemia, or both. The treatment of paravalvular prosthetic regurgitation traditionally has been repeat open surgery, which may be challenging because of technical factors and can be associated with high operative risk and variable results. Accordingly, we examined the acute and 30-day outcomes of percutaneous repair of paravalvular prosthetic regurgitation in a consecutive cohort of patients.

Methods

Study Population

Between February 1, 2004, and September 30, 2010, 122 patients were clinically evaluated and underwent percutaneous repair of paravalvular prosthetic regurgitation at the Mayo Clinic in Rochester, Minnesota. Patients were considered for percutaneous repair if the following criteria were met: (1) severe symptoms of dyspnea (New York Heart Association class III or class II with significant lifestyle or occupational impairment) or clinically significant hemo-
lytic anemia, (2) moderately severe or severe paravalvular prosthetic regurgitation, (3) absence of active endocarditis, and (4) informed consent. Informed consent entailed understanding the risks associated with complex catheter techniques (eg, transseptal access, apical puncture); the off-label use of approved devices; the limited data on clinical efficacy of the percutaneous procedure; and a detailed discussion of the potential therapeutic options, including open surgical correction. Clinically significant hemolytic anemia was defined as anemia (hemoglobin <13 g/dL in women and <15 g/dL in men) with laboratory evidence of intravascular hemolysis (ie, abnormalities on peripheral smear or in serum levels of lactate dehydrogenase, haptoglobin, antiglobulin antibody, or reticulocyte count) associated with symptoms requiring blood transfusion. Surgical consultation was routinely obtained early in the experience and subsequently on a case-by-case basis (32% of cases overall).

Of the patients who underwent percutaneous repair, 7 declined use of their medical records for research. The remaining 115 patients provided consent to participate in the study in accordance with Minnesota statutes and, thus, form the present cohort for analysis. This cohort includes the patients who were reported in our initial experience with this therapy and with our previous imaging review.15,18,19 The present investigation was approved by the Mayo Clinic Institutional Review Board.

Percutaneous Repair

Our techniques for percutaneous repair of paravalvular prosthetic regurgitation have been described previously.15 Briefly, for periaortic defects, femoral artery access with a retrograde approach typically is used. The periaortic defect is crossed with steerable diagnostic coronary catheters (eg, 6-F Amplatz Left 1) and an angled-tip, exchange-length glidewire. For patients with perimital prosthetic regurgitation, standard transeptal access is obtained from the femoral vein, and a steerable sheath (eg, 8.5- or 11-F St Jude Agilis catheter) is placed in the left atrium (Figure 1). The deflectable tip of this catheter facilitates antegrade engagement of the perimital defect for crossing with an exchange-length glidewire. For both approaches, either a telescoped coronary guide catheter (eg, 6-F multipurpose) or a long delivery sheath (eg, 8-F Cook shuttle) can be advanced, followed by placement of an appropriately sized occluder device in the defect. The device is released at the site of paraprosthesis defect after demonstration of significant reduction in the regurgitation, absence of prosthesis interference, and confirmation of stability of the occluder. Echocardiographic guidance either through transesophageal (periaortic defects primarily), transthoracic (periaortic defects), intracardiac (periaortic defects) approaches or through a combination of these modalities is essential for completion of the procedure. Three-dimensional transesophageal imaging was used routinely for perimital defects once commercially available. Aortic and mitral paravalvular regurgitation before and immediately after the procedure were graded semiquantitatively using Doppler echocardiography and color-flow imaging (grade I, mild; grade II, moderate; grade III, moderate to severe; grade IV, severe).20

Because of the complex nature of these procedures, special catheter techniques often are necessary for procedural success. The serpiginous, calcific nature of some paravalvular defects frequently necessitates strong support for passage of delivery catheters. In several patients, delivery catheters could not be advanced through the defect using conventional guidewire support (0.035 or 0.038 inches). In these instances, an arteriovenous rail can be created through direct left ventricular puncture (Figure 3). For patients with 2 left-sided mechanical prostheses who require greater support for passage of the delivery sheath, the arteriovenous rail can be created through direct left ventricular puncture (Figure 3).

The Amplatzer Vascular Plug II occluder device, which became commercially available during the experience, was the most commonly used device because of its stability and low profile with minimization of device overlap, which could lead to prosthetic impingement. Nevertheless, in some patients, the currently available devices for percutaneous repair were not fully occlusive because of the crescent-shaped nature of the paravalvular defects. To obtain full coverage of the lesion, relatively large devices sometimes were required. However, placement of large devices in these defects can result in interference with normal function of the prosthesis from overhang of the occluder. In these instances, placement of several smaller devices either simultaneously or sequentially was performed to avoid prosthetic dysfunction (Figure 4).

Figure 1. Echocardiography of percutaneous repair of paravalvular mitral prosthetic regurgitation. A, Transesophageal echocardiogram showing severe, anterolateral paravalvular prosthetic regurgitation. B, After placement of a 10-mm Amplatzer Vascular Plug II (arrowhead), there is trivial regurgitation. C, Three-dimensional transesophageal echocardiogram showing the Amplatzer Vascular Plug II (arrowhead) in place. LA indicates left atrium; LV, left ventricle.
Figure 2. Creation of an arteriovenous rail using a retroaortic approach. A, After standard transseptal puncture, a steerable sheath is used to place a stiff guidewire across the paravalvular defect into the LV. B and C, A gooseneck snare is advanced retrograde from the femoral artery and across the aortic valve into the LV. D, The gooseneck snare is used to capture the guidewire initially passed across the paravalvular defect. E and F, Fluoroscopic images showing the guidewire passing across a mitral paravalvular defect into the LV and after capture by the snare (arrowheads). Ao indicates aorta; LA, left atrium; LV, left ventricle. Reprinted with permission from the Mayo Foundation for Medical Education and Research.

Clinical Follow-Up

Patients were contacted by mailed questionnaire, telephone, and clinical visit to determine vital status and adverse events. Sudden cardiac death was defined as instantaneous and unexpected death with or without documented ventricular fibrillation within 1 hour after a witnessed collapse in patients who previously were in stable clinical condition or nocturnal death with no antecedent history of worsening symptoms. Appropriate discharge of an implanted internal cardioverter-defibrillator device for therapy of a lethal arrhythmia (ie, sustained ventricular tachycardia or fibrillation) was considered to be sudden cardiac death. Occurrence of stroke was defined according to standard criteria.

Data Analysis

Risk of open surgical repair for each patient was calculated using the Society of Thoracic Surgeons database scoring system. Acute procedural success was defined as successful deployment of an occluder device that resulted in significant reduction in paravalvular regurgitation to mild or less-residual regurgitation in the absence of need for emergency surgery or procedural death. In the presence of multiple defects, the sum of regurgitation from these defects, including those not treated, was used. Patients with perimetal regurgitation were grouped into first, second, third, or fourth quarter of the experience for comparison. Similarly, patients with periaortic regurgitation were grouped into first and second halves of the experience for comparison. For symmetrically distributed data, a Student t test for the 2 periaortic groups and ANOVA for 4 groups of perimetal regurgitation were used for comparison. For comparison of skewed data, Wilcoxon rank sum test for the 2 periaortic groups and Kruskal-Wallis test for the 4 perimetal groups were used. Continuous variables are reported as mean±SD unless otherwise indicated. Statistical significance was inferred at P<0.05.

Results

Patients

Table 1 lists the baseline characteristics of the 115 patients who comprised the study population (mean age, 67±12 years; men, 53%). The clinical indication for the procedure was heart failure in the majority (93%) of the patients. The majority (78%) of the defects were perimetal. Defects involving mechanical mitral prostheses (50%) were the most frequently treated. Significant morbidity in the study population was common, leading to an estimated operative mortality for open surgical repair of 6.9±5.6%. The number of patients with estimated operative mortality of <5%, 5% to 10%, and >10% was 56 (49%), 35 (30%), and 24 (21%), respectively. The majority (60%) of the patients had undergone multiple cardiac surgeries, including 25 (22%) who had had ≥3 prior sternotomies.

Acute Procedural Success

Overall, 141 paravalvular defects were attempted, with permanent device placement in 125 of these defects (Table 2). Twenty-nine (25%) procedures required snaring and wire exteriorization for device delivery. In 7 patients, multiple devices were placed using either simultaneous guides or the anchor-wire technique in single defects to achieve successful reduction in regurgitation. In 13 patients, direct apical puncture was required for passage of the delivery catheter across the paravalvular defect after unsuccessful passage with conventional guidewire support. Overall, acute procedural success occurred in 88 of 115 (77%) patients. Residual regurgitation was grade III in 16 patients and grade IV in 11 patients. The rates of acute procedural success were slightly lower for perimetal prostheses (76%) versus aortic lesions (80%) and for mechanical prostheses (71%) versus bioprostheses (84%). Reasons for procedural failure are listed in Table 3. In 1 patient, percutaneous repair of separate perimetal and periaortic paravalvular defects was performed.

One patient required surgery. This patient underwent retrograde transaortic placement of a 16-mm Amplatzer Muscular Ventricular Septal Defect Occluder in a defect involving an ATS Medical mechanical mitral valve that resulted in impingement of the anterior leaflet. The device could not be retrieved percutaneously, and the patient required emergency surgery. In a second patient with a mitral bioprosthesis, device embolization of a 12-mm Amplatzer Vascular Plug II to the left internal iliac artery occurred and was successfully retrieved with a bioptome. A third patient required device retrieval because of malposition in the left
ventricle. This device was retrieved with a snare advanced retrograde from the aorta.

Procedure time was lengthy for treatment of both perimitral (154±52 minutes) and periaortic (122±54 minutes) lesions. However, procedure times improved with case experience (Figure 5). These improvements occurred in the absence of differences in baseline characteristics between the comparison groups. Although procedure time improved, the rates of acute procedure success was not significantly different with case experience. For the periaortic groups, acute procedure success occurred in 10 of 13 (77%) patients in the first half versus 10 of 12 (83%) patients for the second half. Among the patients with perimitral lesions, acute procedure success occurred in 16 of 22 (73%) patients for the first quarter, 18 of 22 (82%) patients for the second quarter, 17 of 23 (74%) patients for the third quarter, and 17 of 23 (74%) patients for the fourth quarter.

Thirty-Day Outcomes
The overall major adverse event rate (death, myocardial infarction, stroke, major bleeding, emergency surgery) at 30 days was 8.7% (Table 4). One patient experienced intracranial hemorrhage while being bridged to warfarin with subcutaneous low-molecular-weight heparin injections. Of the 13 patients who had left ventricular apical puncture, 4 experienced a hemothorax. Two of these patients were managed without drainage, whereas 2 others required placement of a chest tube, including 1 who developed an empyema with sepsis and survived. One patient had sudden death 28 days after successful percutaneous treatment of a defect associated with a 27-mm Starr-Edwards aortic prosthesis. One other patient died of an unknown cause. Three patients underwent elective surgical repair after an unsuccessful percutaneous closure attempt during this time period.

Discussion
The principal findings of this investigation are that (1) percutaneous repair of paravalvular prosthetic regurgitation can be performed with a relatively high rate of procedural success and an acceptable incidence of complications; (2) the procedures are lengthy, requiring expertise in a variety of complex catheter techniques; and (3) a significant learning curve exists, and procedure times can be shortened with increased case experience. The present investigation examined the acute and 30-day outcomes of percutaneous repair of paravalvular prosthetic regurgitation in a cohort of patients. To our knowledge, this study represents the largest published experience with this therapy to date.

We observed a high rate (77%) of acute procedural success. This rate of success is notable for being similar for both mechanical and biological prostheses. Patients with periaortic lesions tended to have lower procedural success, although these patients were a relatively smaller subgroup (n=25) in this study. The incidence of major adverse clinical events (8.7%) was not insignificant. However, these adverse events occurred in a patient population with a high prevalence of significant comorbidity and heightened risk for open surgical repair. The majority of patients were believed to be at high risk for surgery, and percutaneous repair was undertaken as part of a therapeutic strategy rather than as an alternative to surgery. The present study supports the notion of percutaneous repair as initial therapy for patients with severe paravalvular prosthetic regurgitation as part of a
therapeutic strategy, particularly in patients whose operative risk may otherwise be prohibitive.

Although percutaneous repair of paravalvular regurgitation was first performed in 1992, there has been increasing interest only in the past decade with the advent of suitable catheter-based technology.8–19 Percutaneous repair of paravalvular prosthetic regurgitation is a complex transcatheter interventional procedure. Specific challenges to the procedure include the absence of dedicated device delivery systems and occluders as well as the frequently difficult anatomy of the culprit lesions.24 As a result, special catheter techniques often are necessary to facilitate the delivery of closure devices. Use of the arteriovenous rail helps to overcome technical challenges in many patients. Not uncommonly, periprosthetic defects are calcified and tortuous, posing difficulties in placement of delivery sheaths and catheters across the lesions. In 13 patients, passage of a delivery sheath with conventional guidewire support could not be performed, and direct left ventricular puncture was performed for creation of an arteriovenous rail. Notably, there was a high frequency of bleeding complications (4 patients with hemothorax) among these patients. Of note, closure devices were not used for sheath withdrawal. Although these patients survived, the need for left ventricular puncture and the potential for its complications highlight the complex nature of this therapy.25 Careful consideration of the risks and alternatives to such approaches should be undertaken in these patients.

Prosthetic impingement is a major potential complication of percutaneous repair. Paravalvular lesions frequently are oval or crescent shaped, leading to difficulties with successful closure using a single device unless a relatively large occluder is used. Mechanical valves may be more susceptible to prosthetic impingement from device overhang because they typically do not have buttressing struts. In the present study, the overall incidence of prosthetic impingement that could not be avoided with device placement was 4.3% and was slightly higher for mechanical valves (4/72, 5.6%) than for bioprostheses (1/43, 2.3%). One patient required emergency cardiac surgery for impingement, in which the device could not be retrieved percutaneously. In our recent experience, we have addressed the potential for prosthetic impingement by placing multiple, relatively smaller devices either simultaneously or sequentially. The use of multiple smaller devices in large defects reduces overhang across the prosthetic annulus and may help to avoid leaflet impingement from the procedure.

Given the complexity of the patients in the present study, a multidisciplinary approach to evaluation and treatment was used, including surgical consultation in many patients. Expertise in all echocardiographic modalities is a prerequisite for procedural success, with proper coordination of imaging

Figure 4. Techniques for multiple device delivery. A, Transesophageal echocardiogram showing severe paravalvular prosthetic mitral regurgitation (arrowhead). B, After engagement of the paravalvular defect, 2 6-F multipurpose guide catheters are passed over 2 separate exchange-length stiff guidewires (arrowhead). C, Transesophageal echocardiogram showing the 2 guide catheters that have been passed from the LA into the LV across the paravalvular defect. D, Two separate 8-mm Amplatzer Vascular Plug II devices are placed through the delivery sheaths into the LV. E, Transesophageal echocardiogram showing elimination of the regurgitation with the devices in place. F, Final fluoroscopic image of the devices in place (arrowhead) after their release. LA indicates left atrium; LV, left ventricle.
planes between the invasive specialist and the echocardiographer needed. With increased case experience, we observed significant reductions in procedure time. This observation reflects a significant learning curve, which also has been observed in other catheter-based therapies. Although
too few events were available for analysis of the impact of case experience on procedure success or adverse events, this learning curve has implications for professional training. The present investigation examined only acute and 30-day clinical outcomes. Thus, further study of the durability of the procedure with regard to residual regurgitation, clinical efficacy (eg, symptom improvement, reduction in need for intravascular hemolysis), and safety beyond the subacute time period is required. These studies also are needed to understand the outcomes of percutaneous repair in a broader group of patients and potentially help to establish standards of care for the therapy.

Study Limitations
The present investigation is a retrospective study with the inherent limitations of this study design. In particular, all patients were referred for this procedure, and referral bias likely is significant. Data were collected prospectively and entered into a dedicated database for analysis. With exclusion of patients who did not provide informed consent for research use of their medical records, the present investigation consists of a consecutive cohort of patients. The relatively small number of procedural failures and adverse events, although not inconsequential, did not allow comparisons across subgroups of patients or determination of predictors of favorable clinical outcome. Operative mortality was estimated using the Society of Thoracic Surgeons database, which does not consider several notable risk factors, such as porcelain aorta or radiation heart disease. Finally, data on defect size and shape could have helped to determine technical success but were not available. Because technical success in the treatment of relatively small defects may not translate into significant changes in symptoms, further study on the long-term clinical efficacy of the procedure is required.

Conclusions
The present study demonstrates a high rate of favorable clinical outcomes with percutaneous repair of paravalvular prosthetic regurgitation. Because of the complexity of the procedure, there is a significant learning curve. These data support percutaneous repair as part of a comprehensive therapeutic strategy for this challenging subset of patients.

Disclosures
None.

References

Table 4. Thirty-Day Events

<table>
<thead>
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<th>n</th>
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<tr>
<td>Sudden death</td>
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<tr>
<td>Unexplained death</td>
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<tr>
<td>Emergency cardiac surgery for prosthetic impingement</td>
<td>1</td>
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<tr>
<td>Sepsis</td>
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<tr>
<td>Hemothorax</td>
<td>4</td>
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<tr>
<td>Intracranial hemorrhage</td>
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<tr>
<td>Embolic stroke</td>
<td>2</td>
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<tr>
<td>Vascular complication</td>
<td>1</td>
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<tr>
<td>Elective surgery for unsuccessful repair*</td>
<td>3</td>
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</table>

*The 3 patients who had elective cardiac surgery each had an uncomplicated, unsuccessful attempt at percutaneous repair before surgery.

Figure 5. Changes in procedure time with case experience for percutaneous repair of perimital (A) and periaortic (B) prosthetic valvular regurgitation.
Paravalvular prosthetic regurgitation is a recognized complication in patients who otherwise have had successful heart valve surgery. Although many patients have minimal or no morbidity, paravalvular regurgitation can lead to profound symptoms of heart failure, hemolytic anemia, or both. The treatment of paravalvular prosthetic regurgitation traditionally has been open surgical repair, which may lead to increased risk because of the need for reoperation, patient morbidity, and technical challenges that could have initially contributed to the regurgitation. As a less-invasive alternative, percutaneous approaches to treatment of paravalvular prosthetic regurgitation have emerged. The present study examined the early outcomes of percutaneous repair of symptomatic paravalvular prosthetic regurgitation in a cohort of 115 patients (age, 67 years; men, 53%) who were at high risk of open surgery (estimated surgical mortality, 6.9%). Successful percutaneous closure, defined as ≤1+ residual regurgitation, was achieved in 77% of patients, with a 30-day complication rate of 8.7%. The majority of complications were related to bleeding. No procedural deaths occurred, but 2 (1.7%) patients died within 30 days. Procedural time decreased with increasing case experience. The present investigation demonstrates a high rate of favorable clinical outcome, but there is a significant learning curve due to complexity of the procedure. These data support percutaneous repair as an initial therapeutic option, particularly in patients at significant risk for open surgery.

**CLINICAL PERSPECTIVE**

Paravalvular prosthetic regurgitation is a recognized complication in patients who otherwise have had successful heart valve surgery. Although many patients have minimal or no morbidity, paravalvular regurgitation can lead to profound symptoms of heart failure, hemolytic anemia, or both. The treatment of paravalvular prosthetic regurgitation traditionally has been open surgical repair, which may lead to increased risk because of the need for reoperation, patient morbidity, and technical challenges that could have initially contributed to the regurgitation. As a less-invasive alternative, percutaneous approaches to treatment of paravalvular prosthetic regurgitation have emerged. The present study examined the early outcomes of percutaneous repair of symptomatic paravalvular prosthetic regurgitation in a cohort of 115 patients (age, 67 years; men, 53%) who were at high risk of open surgery (estimated surgical mortality, 6.9%). Successful percutaneous closure, defined as ≤1+ residual regurgitation, was achieved in 77% of patients, with a 30-day complication rate of 8.7%. The majority of complications were related to bleeding. No procedural deaths occurred, but 2 (1.7%) patients died within 30 days. Procedural time decreased with increasing case experience. The present investigation demonstrates a high rate of favorable clinical outcome, but there is a significant learning curve due to complexity of the procedure. These data support percutaneous repair as an initial therapeutic option, particularly in patients at significant risk for open surgery.
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