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**STRUCTURAL**
**Clinical Research**

# The Learning Curve in Percutaneous Repair of Paravalvular Prosthetic Regurgitation

## An Analysis of 200 Cases

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**Objectives** This study sought to assess the learning curve for percutaneous repair of paravalvular prosthetic regurgitation.

**Background** Percutaneous repair of prosthetic paravalvular regurgitation is a complex procedure. There is a paucity of data on the professional experience and tools needed to achieve optimal clinical outcomes.

**Methods** We examined the chronological experience of 200 patients (age 66 ± 13 years; 57% men) who underwent percutaneous closure of paravalvular prosthetic regurgitation at our institution. A sequence number of the patient was assigned as a continuous variable for analysis.

**Results** A total of 243 paravalvular defects (74% mitral; 26% aortic) were treated. Device delivery was successful in 92% with an average procedural time of 139 ± 47 min. The 30-day rate of major adverse cardiovascular events was 7%. With increased case experience and adoption of dedicated imaging and catheter techniques, there were decreases in procedural time, fluoroscopy time, contrast volume administered, length of hospital stay, and major adverse cardiovascular events. Procedural success remained unchanged throughout the experience. The predominant reason for procedural failure was prosthetic leaflet impingement, which accounted for 9 of 21 failed cases.

**Conclusions** In this single-center experience, there was evidence of a learning curve that occurred with the adoption of dedicated techniques for catheter delivery and echocardiographic imaging. In experienced operators, the potential for prosthetic leaflet impingement is the predominant limitation of the procedure. These data have implications for physician training and performance in complex structural heart disease interventions. (J Am Coll Cardiol Intv 2014;7:521–9) © 2014 by the American College of Cardiology Foundation

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Paravalvular regurgitation is a common complication of prosthetic valves with an estimated incidence of 3% to 6% among surgical implants (1–3). Patients can have minimal or no symptoms attributable to paravalvular regurgitation or can present with heart failure and/or hemolytic anemia. Percutaneous transcatheter methods for the treatment of paravalvular regurgitation have emerged. Data from a number of clinical registries have demonstrated the clinical efficacy of percutaneous repair, with success rates that approach 80% to 90% in selected patients (4–12). These data have led to an increasing number of patients undergoing the procedure, which can avoid the need for repeat sternotomy and the risks of open cardiac surgery (13–15).

The rapid growth of a variety of transcatheter structural heart disease interventions has spawned considerable interest in the expansion of interventional programs to address the need for physician training in this field of expertise (16). Percutaneous closure of paravalvular prosthetic regurgitation, although an efficacious therapy, is a notably complex procedure that entails a number of traditional and complex catheter techniques. Like other structural heart disease interventions, percutaneous closure requires expertise in techniques that are not commonly used in current physician training programs, leading either to the necessity of performing these cases at highly specialized centers or the need for ongoing on-site proctoring. Thus, for percutaneous closure of paravalvular prosthetic regurgitation and many structural heart disease interventions, the clinical experience required to optimize clinical outcomes remains unknown (16). To test the hypothesis that a substantial learning curve exists for this procedure and to gain insight into the professional experience needed for expertise in structural heart interventions, we examined the learning curve for percutaneous repair of prosthetic paravalvular regurgitation.

**Abbreviations and Acronyms**

**MACE** = major adverse cardiovascular event(s)

**STS** = Society of Thoracic Surgeons

## Methods

**Study population.** The Mayo Clinic Institutional Review Board approved this study. Between February 1, 2004 and April 9, 2013, 203 patients were clinically evaluated and underwent percutaneous repair of paravalvular prosthetic regurgitation at the Mayo Clinic in Rochester, Minnesota. Patients with the following clinical criteria were considered for percutaneous repair: 1) severe symptoms of dyspnea or clinically significant hemolytic anemia; 2) moderately severe or severe paravalvular prosthetic regurgitation; 3) absence of active endocarditis; 4) regurgitation involving one-third or less of the circumference of the prosthetic annulus and absence of an unstable or rocking prosthesis; and 5) informed consent. Although computed tomography has been used for assessing paravalvular prosthetic regurgitation, echocardiography was the primary imaging modality for assessment in these patients. Regurgitation involving one-third of the circumference of the annulus was used as an empirical approximation. Informed consent entailed understanding the need for off-label use of approved devices, expected clinical efficacy, risks associated with the complex catheter techniques (e.g., transseptal access, apical puncture), and a detailed discussion of potential therapeutic options, including open cardiac surgery. Clinically significant hemolytic anemia was defined as anemia (typically hemoglobin $<10$ g/dl, usually transfusion dependent, with or without erythropoietin therapy) with laboratory evidence of intravascular hemolysis (i.e., abnormalities on peripheral smear or in serum levels of antiglobulin antibody, haptoglobin, lactate dehydrogenase, or reticulocyte count) associated with symptoms requiring blood transfusion.

Of the patients who underwent percutaneous repair, 3 declined use of their medical record for research. The remaining 200 patients provided consent to participate in the study in accordance with Minnesota statutes and form the cohort for analysis. The present cohort also includes the patients who were reported in our previous experience with this therapy (11,12).

**Percutaneous repair.** Our techniques for percutaneous repair of paravalvular prosthetic regurgitation have been described in detail previously (15). In brief, for patients with paramitral prosthetic regurgitation, standard transseptal access was obtained from the femoral vein with placement of a steerable sheath (e.g., 8.5- or 11-French Agilis catheter [St. Jude Medical, St. Paul, Minnesota]) in the left atrium. The deflectable tip of this catheter facilitates antegrade crossing of the defect using an angled-tip, exchange-length glide wire and placement of delivery catheters into the left ventricle, with guidance from fluoroscopy and transesophageal echocardiography. For para-aortic defects, a retrograde approach from the femoral artery typically is used, usually in conjunction with transthoracic or intracardiac echocardiography. The para-aortic defect is crossed with an angled-tip, exchange-length glide wire and steerable diagnostic coronary catheters (e.g., 6-French Amplatz Left 1). For both approaches, either a telescoped coronary guide catheter (e.g., 125-cm 5-French diagnostic inside a 100-cm 6-French Multipurpose) or a long delivery sheath (e.g., 8-French Cook shuttle [Cook Medical, Bloomington, Indiana]) can be advanced followed by placement of appropriately sized occluder device(s) (e.g., Amplatzer Vascular Plug II [St. Jude Medical]). For instances where increased support was needed to pass delivery catheters, a transcatheter rail was created. In this method, an exchange-length guidewire is snared in a chamber distal to the initial approach used for crossing the defect (e.g., snaring in the left ventricle or aorta for a wire passed antegrade from the left atrium) and exteriorized via the femoral

**Table 1. Baseline Characteristics (N = 200)**

| | | Group | | | | |
|---|---|---|---|---|---|---|
| | All Patients | 1 | 2 | 3 | 4 | p Value |
| Age, yrs | 66 ± 13 | 66 ± 12 | 69 ± 12 | 67 ± 14 | 64 ± 14 | 0.30 |
| Male | 115 (58) | 29 (58) | 24 (48) | 29 (58) | 33 (66) | 0.39 |
| Treated prosthesis type | | | | | | |
| Aortic | 51 (26) | 11 (22) | 8 (16) | 15 (30) | 18 (36) | 0.14 |
| Mitral | 149 (74) | 38 (76) | 42 (84) | 35 (70) | 33 (66) | 0.14 |
| Bioprostheses | 86 (43) | 15 (30) | 20 (40) | 28 (56) | 23 (46) | 0.08 |
| Mechanical prostheses | 114 (57) | 34 (68) | 30 (60) | 22 (44) | 28 (56) | 0.08 |
| Time of implantation to percutaneous repair, months | 68 ± 84 | 54 ± 51 | 84 ± 92 | 56 ± 69 | 83 ± 108 | 0.16 |
| Presenting symptoms | | | | | | |
| Heart failure | 187 (94) | 47 (94) | 44 (88) | 49 (98) | 47 (94) | 0.19 |
| Hemolytic anemia | 62 (31) | 20 (40) | 21 (42) | 12 (24) | 9 (18) | 0.02 |
| Right heart failure | 17 (9) | 8 (16) | 5 (10) | 4 (8) | 0 (0) | 0.68 |
| Medical history | | | | | | |
| Coronary artery disease | 62 (32) | 15 (30) | 15 (30) | 14 (28) | 18 (36) | 0.90 |
| Peripheral vascular disease | 14 (7) | 8 (16) | 1 (2) | 2 (4) | 3 (6) | 0.03 |
| Hypertension | 97 (48) | 29 (58) | 20 (40) | 25 (50) | 23 (46) | 0.27 |
| Atrial fibrillation | 105 (52) | 24 (48) | 30 (60) | 27 (54) | 24 (48) | 0.57 |
| Chronic obstructive pulmonary disease | 25 (13) | 9 (18) | 5 (10) | 3 (6) | 8 (16) | 0.24 |
| Previous stroke | 37 (19) | 8 (16) | 14 (28) | 9 (18) | 6 (12) | 0.20 |
| Creatinine clearance, ml/min | 65 ± 38 | 65 ± 41 | 59 ± 30 | 62 ± 37 | 72 ± 44 | 0.42 |
| <60 | 105 (53) | 26 (52) | 27 (54) | 30 (60) | 26 (52) | 0.83 |
| Congenital heart disease | 3 (2) | 0 (0) | 2 (4) | 0 (0) | 1 (2) | 0.30 |
| Radiation heart disease | 7 (4) | 0 (0) | 4 (8) | 2 (4) | 1 (2) | 0.16 |
| Previous procedures | | | | | | |
| ≥2 sternotomies | 106 (53) | 16 (32) | 15 (30) | 7 (14) | 7 (14) | 0.03 |
| Other left-sided valve replacement* | 52 (26) | 17 (34) | 13 (26) | 14 (28) | 9 (18) | 0.28 |
| 2 left-sided mechanical prostheses | 35 (17) | 13 (26) | 7 (14) | 7 (14) | 8 (16) | 0.29 |
| Coronary artery bypass grafting | 55 (28) | 15 (30) | 15 (30) | 16 (32) | 9 (18) | 0.34 |
| Permanent pacemaker | 31 (16) | 7 (14) | 9 (18) | 8 (16) | 7 (14) | 0.94 |
| Implanted defibrillator | 6 (3) | 3 (6) | 1 (2) | 1 (2) | 1 (2) | 0.54 |
| Left ventricular ejection fraction, % | 57 ± 12 | 54 ± 14 | 56 ± 14 | 57 ± 11 | 59 ± 8 | 0.16 |
| Left ventricular end-diastolic diameter, mm | 53 ± 9 | 51 ± 12 | 51 ± 7 | 56 ± 7 | 54 ± 8 | 0.04 |
| Left ventricular end-systolic diameter, mm | 36 ± 9 | 37 ± 11 | 34 ± 8 | 36 ± 7 | 36 ± 7 | 0.60 |
| Right ventricular systolic pressure, mm Hg† | 55 ± 19 | 59 ± 19 | 51 ± 17 | 54 ± 19 | 55 ± 22 | 0.25 |
| Medications | | | | | | |
| Beta-receptor antagonists | 134 (67) | 35 (70) | 31 (62) | 39 (78) | 29 (58) | 0.11 |
| ACE inhibitor or ARB | 84 (42) | 22 (44) | 29 (58) | 20 (40) | 13 (26) | 0.01 |
| Diuretic | 141 (71) | 32 (64) | 40 (80) | 36 (72) | 22 (44) | 0.30 |
| Digoxin | 47 (23) | 12 (24) | 17 (34) | 14 (28) | 4 (8) | 0.01 |
| Warfarin | 120 (60) | 31 (62) | 27 (54) | 25 (50) | 37 (74) | 0.09 |
| STS estimated operative mortality | 6.3 ± 5.0 | 6.6 ± 4.8 | 7.7 ± 6.9 | 9.8 ± 3.1 | 5.5 ± 4.3 | 0.06 |

Values are mean ± SD or n (%). *Valve replacement apart from the prosthesis that was treated percutaneously. †Echocardiographic estimation.
ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker.

artery or, in patients with 2 left-sided mechanical prostheses, via a sheath placed in the left ventricular apex (15).

For patients with defects that were either eccentric or difficult to cross, the techniques of anchor wiring or simultaneous deployment of multiple devices may be used. In the anchor wire technique, 2 extra stiff, 0.032-inch exchange-length wires are placed in the left ventricle, followed by placement of a relatively larger sheath (e.g., 8-F Cook shuttle [Cook Medical]) over 1 of the wires. The sheath is used to place a device occluder, with the bare wire left to facilitate rapid recrossing in the event that either a different device or additional devices are required to treat

the regurgitation. In the simultaneous technique, multiple, extra support, exchange-length wires (0.032 inches) are placed across single defect to facilitate placement of multiple occluders through individual telescoping guiding catheters (15).

The device occluder is released at the site of paraprosthetic defect after demonstration of a significant reduction in the regurgitation, confirmation of stability of the occluder, and absence of interference with prosthesis function. The degree of paravalvular regurgitation was graded semiquantitatively using Doppler echocardiography and color-flow imaging (grade I, mild; grade II, moderate; grade III, moderate to severe; and grade IV, severe) before and immediately after the procedure (17,18). When multiple jets were present, the amounts of regurgitation from the separate jets were totaled for semiquantitation.

**Clinical follow-up.** Patients were contacted by telephone, mailed questionnaire, and clinical visit to determine vital status and adverse events within 30 days of the procedure. Major bleeding was defined according to Bleeding Academic Research Consortium criteria (19). Sudden cardiac death was defined as instantaneous and unexpected death with or without documented ventricular fibrillation within 1 h after a witnessed collapse, in patients who previously were in stable clinical condition or nocturnal death with no history of worsening symptoms. Appropriate discharge of an implanted internal cardioverter-defibrillator for therapy of a lethal arrhythmia (i.e., sustained ventricular tachycardia or fibrillation) was considered to be sudden cardiac death (20). Occurrence of stroke was defined according to standard criteria (21).

**Data analysis.** Procedure order of the patient was assigned as a continuous variable for the cohort. Acute procedural success was defined as successful deployment of an occluder device that resulted in significant reduction (≥1 grade) in paravalvular regurgitation to moderate or less residual regurgitation, in the absence of the need for emergency surgery, leaflet impingement, or procedural death. In the presence of multiple defects, the sum of regurgitation from these defects, including those not treated, was used. Device deployment success was defined as any permanent placement of a device occluder in a paravalvular prosthetic defect without embolization or leaflet impingement. Major adverse cardiovascular events (MACE) were defined as occurrence of death, stroke, myocardial infarction, emergency surgery, or major bleeding (Bleeding Academic Research Consortium criteria 3 or 5) (19). Risk of open surgical repair for each patient was calculated using the Society of Thoracic Surgeons (STS) database scoring system (22). Procedure time was defined as time from placement of the patient on the table for cardiac catheterization until the time when the procedure was stopped and the processes were begun to remove the patient from the table (e.g., undraping) as noted in the case log. Patients were stratified into 4 groups by sequence for analysis: group 1, cases 1 to 49; group 2, cases 50 to 99; group 3, cases 100 to 149; and group 4, cases 150 or later. For symmetrically distributed data, analysis of variance was used for comparison. For comparison of skewed data, the Kruskal-Wallis test was used. Continuous variables are reported as mean ± SD unless reported otherwise.

**Table 2. Procedural Characteristics**

| | |
|---|---|
| General anesthesia | 165 (82) |
| Echocardiography | |
| Intracardiac | 22 (11) |
| Transthoracic | 25 (13) |
| Transesophageal | 164 (82) |
| Perivalvular defects | |
| No. attempted | 243 |
| Periaortic | 58 |
| Perimitral left ventricle to left atrium | 184 |
| Perimitral left ventricle to right atrium | 2 |
| No. with device implanted | 217 |
| Total devices implanted | 289 |
| Patients with multiple defects closed | 32 |
| Technique used | |
| Periaortic retrograde | 54 (27) |
| Perimitral | |
| Antegrade transeptal | 151 (75) |
| Right internal jugular vein to left ventricle | 2 (1) |
| Apical puncture | 16 (8) |
| Transaortic exteriorization | 61 (31) |
| Multiple devices for single defect | 47 (24) |
| Retrograde aortic approach | 4 (2) |
| Amplatzer occluder* device used | |
| Atrial septal occluder | 14 (7) |
| Vascular Plug II* | 154 (77) |
| Patent ductal occluder | 20 (10) |
| Ventricular septal occluder | 12 (6) |
| Procedure time, min | 139 ± 47 |
| Fluoroscopy time, min | 52 ± 29 |
| Contrast used, ml | 30 ± 46 |
| Procedure success | 178 (89) |
| Residual regurgitation grade ≥2 | 46 (23) |
| Residual regurgitation grade ≥3 | 21 (11) |
| Length of hospital stay after procedure, days | 4.5 ± 5.8 |

Values are n (%) mean ± SD. *St. Jude Medical, St. Paul, Minnesota.

## Results

**Patients.** Overall, 200 patients were treated with percutaneous repair of paravalvular prosthetic regurgitation (mean age 66 ± 13 years; 57% men) (Table 1). Heart failure was the predominant clinical indication for the procedure (94%), with hemolytic anemia also being present in 31%. Significant patient morbidity was common. The majority of the patients had undergone multiple sternotomies for cardiac

**Table 3. Reasons for Procedural Failure**

| | |
|---|---|
| Prosthetic leaflet impingement* | 8 |
| Device deployed with residual severe regurgitation | 6 |
| Device embolization | 5 |
| Inability to cross with guidewire | 3 |
| Inability to cross with delivery sheath | 2 |
| Coronary dissection | 1 |

*1 patient with prosthetic leaflet impingement required emergent cardiac surgery.

surgery (53%). For the entire cohort, the STS estimated operative mortality was 6.3 ± 5% (range 0.9% to 33.7%).

**Procedures.** Procedures in a total of 243 defects were attempted, with the majority being mitral (74%) or involving mechanical prosthetic valves (57%) (Table 2). Devices were successfully deployed in 184 patients (92%) with a mean overall procedure time of 138 ± 48 min. Acute procedural success occurred in 89.5%; the most common reason for failure was prosthetic leaflet impingement (Table 3). A transcatheter heart rail was used in 61 patients (31%). In 47 patients (24%), multiple devices, using either multiple simultaneous guides or the anchor-wire technique, were placed in single defects to achieve successful reduction in regurgitation. In 16 patients (8%), direct apical puncture was required for passage of the delivery catheter across the paravalvular defect. The overall MACE rate at 30 days was 7% (Table 4). There were 5 cases of device embolization.

**Table 4. Procedural and 30-Day Events**

| | | Quartile | | | |
|---|---|---|---|---|---|
| | Total | 1st | 2nd | 3rd | 4th |
| Intraprocedural device embolization | 4 (2.0) | 1 (2.0) | 2 (4.0) | 0 (0.0) | 1 (2.0) |
| Major bleeding | 8 (4.1) | 5 (10.0) | 2 (4.0) | 0 (0.0) | 1 (2.0) |
| Vascular complication | 2 (1.0) | 1 (2.0) | 1 (2.0) | 0 (0.0) | 0 (0.0) |
| Hemothorax | 5 (2.5) | 4 (8.0) | 0 (0.0) | 0 (0.0) | 1 (2.0) |
| Intracranial hemorrhage | 1 (0.5) | 0 (0.0) | 1 (2.0) | 0 (0.0) | 0 (0.0) |
| Embolic stroke | 2 (1.0) | 1 (2.0) | 1 (2.0) | 0 (0.0) | 0 (0.0) |
| Emergency cardiac surgery | 2 (1.0) | 0 (0.0) | 1 (2.0) | 1 (2.0) | 0 (0.0) |
| For prosthetic impingement | 1 (0.5) | 0 (0.0) | 1 (2.0) | 0 (0.0) | 0 (0.0) |
| For device embolization | 1 (0.5) | 0 (0.0) | 0 (0.0) | 1 (2.0) | 0 (0.0) |
| Coronary dissection | 1 (0.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (2.0) |
| Elective cardiac surgery for unsuccessful repair* | 3 (1.6) | 1 (2.0) | 3 (6.0) | 0 (0.0) | 0 (0.0) |
| Death | 4 (2.0) | 2 (4.0) | 1 (2.0) | 1 (2.0) | 0 (0.0) |
| Sudden death | 1 (0.5) | 1 (2.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Cardiac tamponade | 1 (0.5) | 0 (0.0) | 0 (0.0) | 1 (2.0) | 0 (0.0) |
| Sepsis | 2 (1.0) | 1 (2.0) | 1 (2.0) | 0 (0.0) | 0 (0.0) |
| Death, stroke, or emergency surgery | 8 (4.0) | 3 (6.0) | 3 (6.0) | 2 (4.0) | 0 (0.0) |
| Death, stroke, major bleeding, or emergency surgery | 14 (7.3) | 8 (16.0) | 5 (10.0) | 2 (4.0) | 1 (2.0) |

Values are n (%). *The 3 patients who had elective cardiac surgery each had an uncomplicated, unsuccessful attempt at percutaneous repair before surgery.

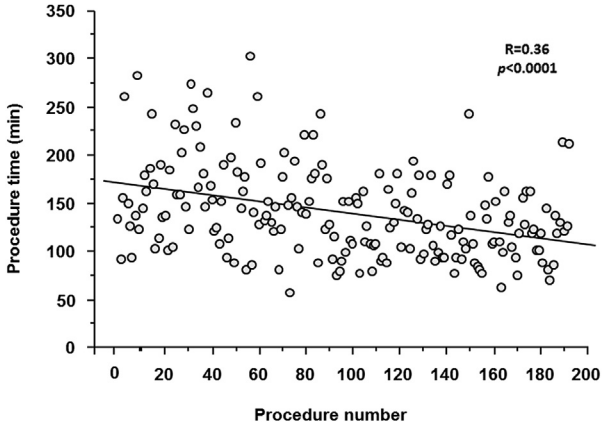


**Figure 1. Procedure Time (Y-Axis) According to Procedure Sequence (X-Axis)**

With increased case experience, there was a significant reduction in time required to complete percutaneous repair of paravalvular prosthetic regurgitation.

Successful percutaneous retrieval using either a snare or a bioptome was possible in 4 patients; emergent cardiac surgery was required in 1 patient due to device embolization into the left ventricle in the setting of aortic and mitral mechanical prostheses. Separately, another patient underwent emergent cardiac surgery for prosthetic leaflet impingement that became evident only after decoupling of the device from its delivery cable.

**Learning curve.** Among the 4 groups, there was a nonsignificant trend for higher surgical risk in earlier patients ($p = 0.06$ for STS risk score), but there was no change in patient selection according to location of prosthesis, size, or location of the defect (Table 1). Compared with the other groups, patients in group 1 underwent the procedure with greater use of left ventricular apical puncture for creation of an arteriovenous rail (22% vs. 0 to 6% in other groups; chi-square = 18.7; $p = 0.0003$). Sequential device and anchor wire techniques were also used almost exclusively for those in the latter 2 groups (group 3, 48%; group 4, 43%) compared with earlier patients (group 1, 0%; group 2, 4%; chi-square = 49.4; $p < 0.0001$). Procedure order was inversely related to procedure time ($p < 0.0001$), contrast volume administered ($p = 0.01$), fluoroscopy time ($p = 0.08$), and length-of-hospital stay ($p = 0.007$) (Figs. 1 and 2). These changes plateaued soon after increased use of 3-dimensional echocardiography and more operator experience with special catheter techniques (e.g., the transcatheter heart rail, simultaneous device deployment, and anchor wire), with no significant improvements being present in groups 3 and 4 (Fig. 3). Of note, although the effects of 3-dimensional echocardiography may be difficult to separate from those of other techniques, there was no significant association of

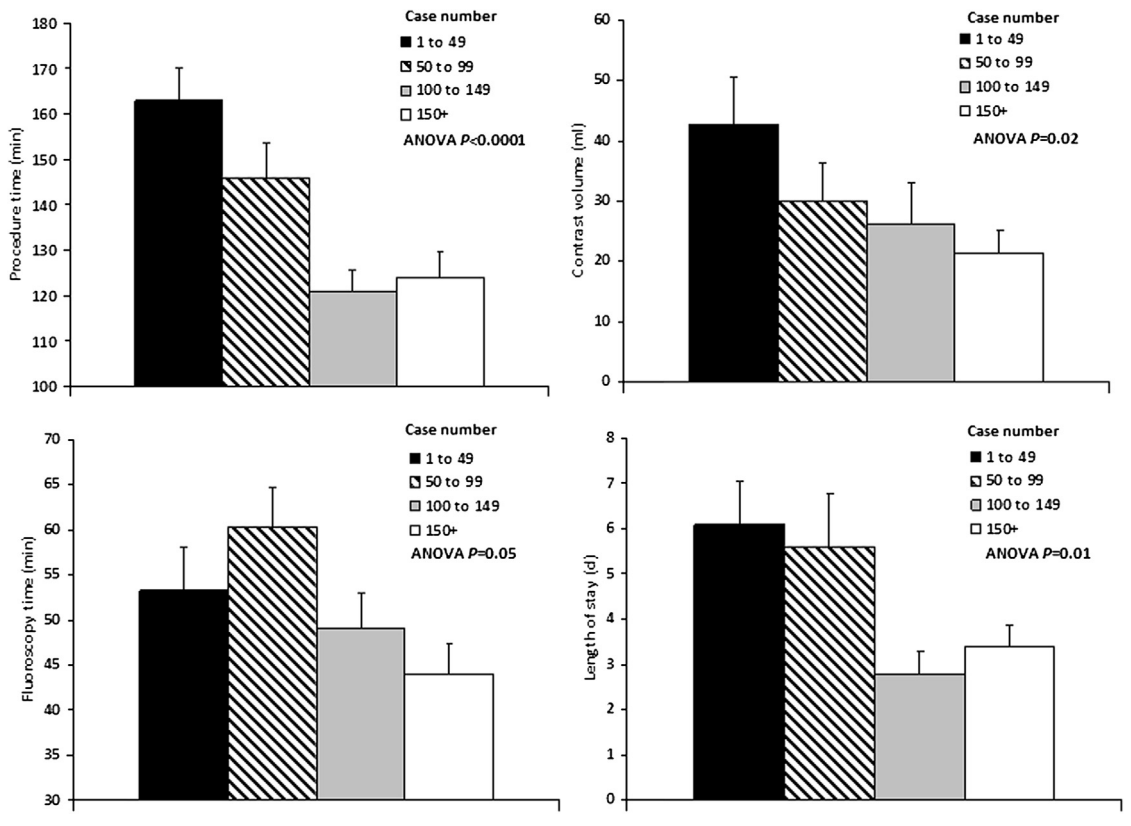


**Figure 2. Case Experience and Procedural Changes**

Procedure time **(top left)**, fluoroscopy time **(bottom left)**, contrast volume administered **(top right)**, and length of hospital stay **(bottom right)** improved with increased case experience. ANOVA - analysis of variance.

procedure number with procedure duration, contrast volume, or length of stay among patients who had 3-dimensional echocardiography.

Notably, the relationship of procedure order to procedure duration ($p < 0.0001$), contrast volume administered ($p = 0.003$), and length of hospital stay ($p = 0.04$) was evident in patients with defects involving mitral prostheses as well as aortic prostheses ($p = 0.05$, $p = 0.04$, and $p = 0.09$, respectively).

There were no differences in the achievement of device deployment (range for 4 groups, 86% to 94%) or acute procedure success over the course of the clinical experience. The predominant reason for failure was prosthetic leaflet impingement, which accounted for 9 of 21 failed cases (Table 3). The incidence of prosthetic impingement that could not be avoided during device placement was 4% and was slightly higher for mechanical valves (7 of 114 or 6.1%) than for bioprostheses (1 of 86 patients or 1.2%; chi-square = 3.2; $p = 0.08$). Prosthetic leaflet impingement, inability to cross with either the guidewire or delivery sheath, persistent severe regurgitation despite deployment of an occluder, and device embolization occurred in both early and later patient groups.

There was a lower rate of 30-day MACE with increased clinical experience (Fig. 4). The higher rate of MACE in the earliest experience (group 1) was due to bleeding from apical puncture in 4 patients, unexplained sudden death in 1 patient, and stroke related to transition of anticoagulation in 1 patient (Table 4). Among the patients in the remaining groups, MACE rates ranged from 2% to 4% (Fig. 3).

## Discussion

The principal findings of this investigation are the following: 1) percutaneous repair of paravalvular prosthetic regurgitation is a complex procedure with a learning curve that improves with experience in dedicated techniques for catheter delivery and imaging; 2) this learning curve shows reductions in procedure duration, fluoroscopy time, length of hospital stay, and MACE; and 3) achievement of procedure success is largely unaffected by clinical experience, primarily

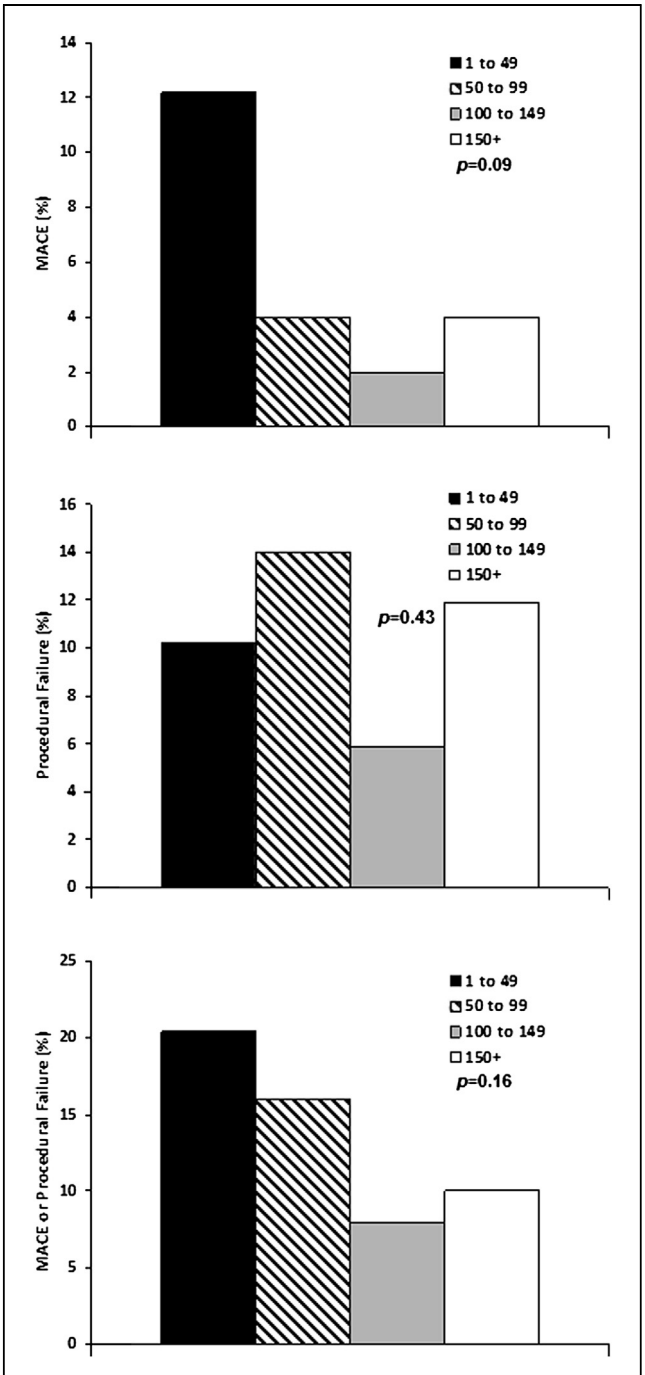


**Figure 3. MACE and Procedural Failure According to Case Experience**

Changes in major adverse cardiovascular events (MACE) **(top)**, procedural failure **(middle)**, and the combination of MACE or procedural failure **(bottom)**, with increased case experience. MACE = major adverse cardiovascular event(s).

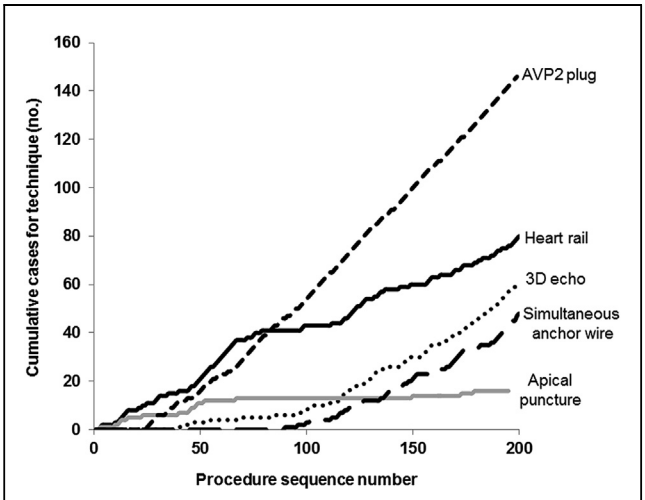


**Figure 4. Use of Dedicated Techniques According to Procedure Sequence Number**

Cumulative experience with dedicated techniques for imaging and device delivery according to procedure sequence number. 3D = 3-dimensional.

due to the potential for leaflet impingement by device occluders.

Percutaneous transcatheter repair has emerged as an effective and relatively safe procedure for the treatment of symptomatic patients with paravalvular prosthetic regurgitation. The present investigation, which is the largest examination of this therapy to date, extends previous studies by demonstrating effective reduction of paravalvular prosthetic regurgitation in 89% of patients treated. Notably, these results were achieved with relatively low rates of procedural mortality (1%) and MACE (7%), which were observed in a population at high risk of open surgery (STS estimated operative mortality = 6.3%). These data support the notion that percutaneous repair is a viable therapeutic alternative to open surgical repair, particularly in those patients who are at increased surgical risk due to the need for repeat sternotomy and concomitant morbidity (4–14).

Nonetheless, it is well recognized that percutaneous repair of paravalvular prosthetic regurgitation is a challenging procedure. The therapy requires expertise in traditional as well as complex catheter techniques, such as transseptal access, manipulation within the left atrium, wire snaring, left ventricular apical puncture, and creation of wire rails (15). Percutaneous repair is also associated with unique and complex complications. Percutaneous device retrieval was required in 5 patients (4 for embolizations, 1 with leaflet impingement after deployment), whereas 2 others required emergent cardiac surgery (1 for embolization, 1 for leaflet impingement). Hemothorax, related to left ventricular apical puncture, also occurred in 5 other patients. Of note, the technique of apical puncture used was strictly percutaneous, in contrast to open surgical exposure currently used for transcatheter valve implantation. Open exposure and use of closure devices may reduce bleeding related to direct apical access, which has its own learning curve and should be used

only when absolutely necessary for completion of the procedure (23,24).

The present investigation demonstrates that there is a significant learning curve for percutaneous treatment of paravalvular prosthetic regurgitation. There were significant decreases in time to complete the procedure, fluoroscopy exposure, complications (i.e., 30-day MACE), and hospital length of stay with increased clinical experience, with these changes reaching a plateau after adoption of dedicated techniques for imaging and catheter delivery. It is critically important to note that this learning curve was observed in the setting of a multidisciplinary team of dedicated operators (2 adult structural and 2 congenital) and an interventional imaging service committed to the performance of this procedure. The interventional operators have collaborated closely and frequently, performing the procedures together to attempt, to evaluate, and to develop techniques that expedite the care of these challenging patients. The multidisciplinary team collaborates on these procedures, which have been increasing in frequency during the experience (Fig. 5).

This collaborative effort has resulted in significant improvements in the procedure. The communication between the interventional operators and echocardiographers has evolved to rely on language using imaging landmarks for the co-location of paravalvular leaks, with an emphasis on the relationships of the left atrial appendage, atrial septum, and aortic valve using anatomically correct terminology (i.e., anterior vs. posterior, inferior vs. superior, lateral vs. medial) (15). This language emphasizes anatomic orientation for the entire multidisciplinary team, a key element for expediting procedure completion. Moreover, there has been increased technical practice in the snaring and creation of wire rails, which were necessary for delivery catheter placement in 31% of the patients. Single defects in the latter cohort of patients were more frequently treated with multiple device occluders. Improvement in procedural expediency was made possible with experience in simultaneous and sequential device deployment using the anchor wire technique, which reduces the need for de novo rewiring of the defects.

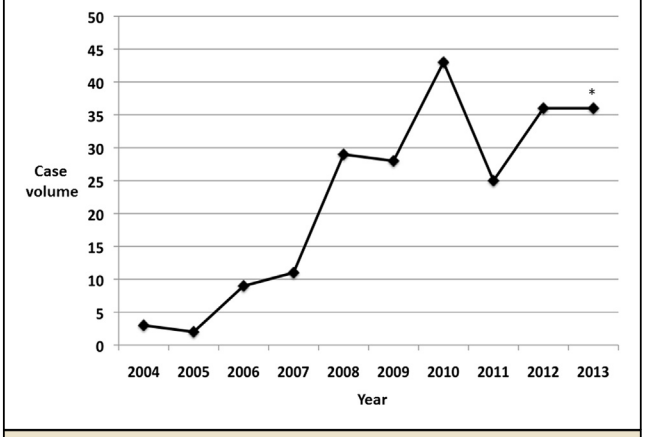


**Figure 5. Institutional Case Volume per Year**

The number of cases for 2013 is an annualized estimate, using procedural total through April 14, 2013.

The improvements in operational efficiency have important implications given the significant resources in personnel needed to perform this therapy. Procedure duration frequently exceeds 2 or 3 h (average time in this study was 139 ± 47 min). Importantly, these improvements also are noteworthy as percutaneous repair of paravalvular prosthetic regurgitation can serve as a learning model because it shares catheter techniques and imaging requirements with other structural interventional therapies (e.g., Mitraclip placement, balloon mitral valvuloplasty, left atrial appendage closure, device closure of infarct-related ventricular septal defect). Similar to these other interventions, the techniques of percutaneous repair of paravalvular prosthetic regurgitation are not taught routinely in current physician training programs. Recent expert consensus documents have highlighted the need for professional training in structural heart disease interventions due to the rapid growth in this field, yet there are virtually no data on the professional experience required to optimize clinical outcomes (16,25,26). Therefore, the learning curve demonstrated in this investigation has implications for the professional training in this rapidly emerging field of expertise.

Prosthetic leaflet impingement was the predominant cause of procedural failure (9 patients or 43% of failed cases), which occurred with similar frequency throughout the experience. This complication arises due to device overhang, which may occur when defects are either close to the sewing ring or when the lesions are irregular and require relatively large occluders for closure. Mechanical valves may be more susceptible to leaflet impingement due to the absence of buttressing struts. To help overcome the potential for leaflet impingement, multiple smaller devices, rather than relatively large single occluders, were used more commonly in the latter experience for eccentric defects. Among the patients who had multiple smaller devices placed in single defects (n = 46), however, the acute procedural success rate was 90.2% and not different from other patients. Given these data, the small number of procedural failures overall (n = 21), and the nonrandomized nature of our study, the ability to determine the impact of the multiple device approach on acute procedural success was limited. Nonetheless, the present data do support the need for the development of technology dedicated to the procedure to reduce the potential for prosthetic leaflet impingement and other complications.

**Study limitations.** The present investigation is a retrospective analysis with known inherent limitations, particularly the potential for referral bias. Data were collected prospectively and entered into a dedicated database for analysis. The

cohort consisted of consecutive patients treated at our institution with the exception of patients who did not provide informed consent for research use of their medical record. The echocardiographic evaluation of prosthetic regurgitation is challenging. The present study used semi-quantitative methods to determine the degree of regurgitation, which lack the precision of techniques for evaluation of native valvular regurgitation (17,18).

## Conclusions

Percutaneous repair of paravalvular prosthetic regurgitation is an efficacious procedure with a significant learning curve. As a state-of-the-art therapy that encompasses multiple complex catheter techniques, these data on percutaneous repair of paravalvular prosthetic regurgitation have implications for professional training that are specific to not only this procedure, but also for other similar structural heart disease interventions.

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**Key Words:** paravalvular ■ prosthesis ■ regurgitation ■ training ■ transcatheter.