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ABSTRACT

OBJECTIVES The authors report the CLASP (Edwards PASCAL Transcatheter Mitral Valve Repair System Study) expanded experience, 1-year outcomes, and analysis by functional mitral regurgitation (FMR) and degenerative mitral regurgitation (DMR).

BACKGROUND The 30-day results from the CLASP study of the PASCAL transcatheter valve repair system for clinically significant mitral regurgitation (MR) have been previously reported.

METHODS Eligible patients had symptomatic MR ≥3+, were receiving optimal medical therapy, and were deemed candidates for transcatheter mitral repair by the local heart team. Primary endpoints included procedural success, clinical success, and major adverse event rate at 30 days. Follow-up was continued to 1 year.

RESULTS One hundred nine patients were treated (67% FMR, 33% DMR); the mean age was 75.5 years, and 57% were in New York Heart Association functional class III or IV. At 30 days, there was 1 cardiovascular death (0.9%), MR ≥1+ was achieved in 80% of patients (77% FMR, 86% DMR) and MR ≥2+ in 96% (96% FMR, 97% DMR), 88% of patients were in New York Heart Association functional class I or II, 6-min walk distance had improved by 28 m, and Kansas City Cardiomyopathy Questionnaire score had improved by 16 points (p < 0.001 for all). At 1 year, Kaplan-Meier survival was 92% (89% FMR, 96% DMR) with 88% freedom from heart failure hospitalization (80% FMR, 100% DMR), MR ≥1+ in 82% of patients (79% FMR, 86% DMR) and ≥2+ in 100% of patients, 88% of patients were in New York Heart Association functional class I or II, and Kansas City Cardiomyopathy Questionnaire score had improved by 14 points (p < 0.001 for all).

CONCLUSIONS The PASCAL transcatheter valve repair system demonstrated a low complication rate and high survival, with robust sustained MR reduction accompanied by significant improvements in functional status and quality of life at 1 year. (The CLASP Study Edwards PASCAL Transcatheter Mitral Valve Repair System Study [CLASP]; NCT03170349) (J Am Coll Cardiol Intv 2020;13:2344–57) © 2020 by the American College of Cardiology Foundation.
Mitral regurgitation (MR) is the most prevalent valvular disease in the United States and the second most common in Europe\(^{(1,2)}\). MR is associated with increased mortality and heart failure hospitalizations. Despite this, only 15% of patients with MR undergo mitral surgery\(^{(3,7)}\).

Percutaneous technologies, including transcatheter mitral valve repair and replacement devices, are under investigation for treating patients with functional MR (FMR)\(^{(8,9)}\). The COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) trial demonstrated a significant reduction in hospitalizations for heart failure and all-cause mortality in patients treated with the MitraClip (Abbott Vascular, Santa Clara, California) compared with medical therapy alone\(^{(10)}\).

The PASCAL transcatheter valve repair system (Edwards Lifesciences, Irvine, California) is a leaflet repair therapy for the treatment of MR\(^{(11,12)}\). The PASCAL repair system uses 2 clasps and paddles to achieve plication of the mitral valve leaflets, while placing an anatomic spacer to fill the regurgitant orifice between the native valve leaflets. The clasps are adjustable for optimal leaflet positioning, and the contoured paddles are designed to reduce leaflet stress.

**METHODS**

**PATIENT SELECTION AND STUDY CONDUCT.**

Eligible patients were ≥18 years of age with symptomatic grade 3+ or 4+ MR as confirmed by echocardiograms reviewed by the core laboratory prior to enrollment. All patients were in New York Heart Association (NYHA) functional class II, III, or ambulatory IV despite optimal medical therapy and deemed appropriate candidates for transcatheter mitral valve repair by the local multidisciplinary heart team, including specialists in heart failure, interventional cardiology, cardiac surgery, and imaging. Echocardiographic eligibility criteria included presence of a noncommissural primary regurgitant jet with absence of a clinically significant secondary jet and left ventricular (LV) ejection fraction ≥20%. Patients with FMR etiology were subjected to additional eligibility criteria requirements of 6-min walk distance (6MWD) ≥150 m and ≥400 m within 2 months prior to intervention, brain natriuretic peptide >150 pg/ml or corrected N-terminal pro-brain natriuretic peptide >600 pg/ml measured within 3 months prior to enrollment, or heart failure hospitalization within 1 year prior to enrollment.

Patients were excluded because of mitral valve area <4.0 cm\(^2\) as measured by planimetry; LV end-diastolic diameter >8.0 cm; previous mitral valve surgery or transcatheter procedure; severe aortic stenosis (aortic valve area <1.0 cm\(^2\)) or regurgitation; severe tricuspid valve regurgitation; untreated significant coronary artery disease, unstable angina, myocardial infarction (MI), transient ischemic attack, or stroke within 30 days prior to intervention; and percutaneous cardiovascular intervention, carotid surgery, cardiovascular surgery, rhythm management device implantation, or atrial fibrillation ablation within 90 days prior to intervention. Other exclusion criteria have been previously detailed\(^{(12)}\).

Patient eligibility was evaluated by a multidisciplinary central eligibility committee. All echocardiograms were analyzed by an independent core laboratory (Cardiovascular Core Lab at Morristown Medical Center, Morristown, New Jersey), and all major adverse events (MAEs) were adjudicated by an independent clinical events committee. The study was approved by local ethics committees and respective health authorities of the participating centers, multinational, single-arm, prospective study. The COAPT (Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation) trial demonstrated a significant reduction in hospitalizations for heart failure and all-cause mortality in patients treated with the MitraClip (Abbott Vascular, Santa Clara, California) compared with medical therapy alone\(^{(10)}\).
CENTRAL ILLUSTRATION  PASCAL Transcatheter Mitral Valve Repair System With 1-Year Survival and Echocardiographic Outcomes From the Edwards PASCAL Transcatheter Mitral Valve Repair System Study

A  PASCAL Transcatheter Mitral Valve Repair System
(1) Optimized leaflet capture  
(2) Broad paddles and spacer for effective mitral regurgitation reduction  
(3) Elongation for safe subvalvular maneuvering

B  Kaplan-Meier Survival Analysis

![Kaplan-Meier Survival Graph]

No. at Risk:
- Overall: 62 58 57 54
- FMR: 38 35 34 32
- DMR: 24 23 23 22

Time from Implant:
- 0 30 Days
- 6 Months
- 1 Year

Survival (%):
- 100 ± 0%
- 98 ± 2%
- 97 ± 3%
- 100 ± 0%
- 97 ± 2%
- 95 ± 4%
- 96 ± 4%
- 92 ± 4%
- 89 ± 5%

C  Mitral Regurgitation

![Mitral Regurgitation Graph]

- Severe (4+): 44% 57%
- Moderate-Severe (3+): 18% 64%
- Mild-Moderate (2+): 82% 100%
- Mild (1+): 66% 66%
- None/Trace (0-1+): 100% 100%


(A) PASCAL transcatheter mitral valve repair system. (B) Kaplan-Meier survival analysis. (C) Reduction in mitral regurgitation. Graphs show unpaired data. The p values were calculated using the Wilcoxon signed rank test for paired patients (n).
During instances of implant repositioning, the PASCAL repair system also allows elongation of the implant for low-profile and atraumatic maneuvering within the subvalvular anatomy (Central Illustration).

**THE PASCAL IMPLANTATION PROCEDURE.**

Transvenous, transseptal access to the left atrium is obtained using standard percutaneous techniques. The guide sheath with introducer is inserted over the central illustration, especially in complex anatomy. The broad contoured paddles are designed to maximize leaflet coaptation and minimize stress concentration on native leaflets. The low-profile delivery system consists of a 22-F guide sheath, with 3 independent catheters that facilitate simplified maneuvering in 3 different planes and stabilizers that lock catheter handles in place for procedural ease. During instances of implant repositioning, the PASCAL repair system also allows elongation of the implant for low-profile and atraumatic maneuvering within the subvalvular anatomy (Central Illustration).

**THE PASCAL IMPLANTATION PROCEDURE.**

Transvenous, transseptal access to the left atrium is obtained using standard percutaneous techniques. The guide sheath with introducer is inserted over the subannular anatomy. The broad contoured paddles are designed to maximize leaflet coaptation and minimize stress concentration on native leaflets. The low-profile delivery system consists of a 22-F guide sheath, with 3 independent catheters that facilitate simplified maneuvering in 3 different planes and stabilizers that lock catheter handles in place for procedural ease.

**TABLE 1 Baseline Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N = 109)</th>
<th>FMR (n = 73)</th>
<th>DMR (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>75.5 ± 11.0</td>
<td>73.1 ± 11.6</td>
<td>80.5 ± 7.7</td>
</tr>
<tr>
<td>Male</td>
<td>54.1 (59)</td>
<td>54.8 (40)</td>
<td>52.8 (19)</td>
</tr>
<tr>
<td>NYHA functional class III or IV</td>
<td>57.4 (62)</td>
<td>60.3 (44)</td>
<td>51.4 (18)</td>
</tr>
<tr>
<td>NT-proBNP (μg/ml)</td>
<td>4148.7 ± 6430.8</td>
<td>5122.3 ± 7271.9</td>
<td>1617.2 ± 2018.9</td>
</tr>
<tr>
<td>eGFR (mL/min/1.73 m²)</td>
<td>59.0 ± 20.5</td>
<td>59.1 ± 20.8</td>
<td>58.8 ± 20.2</td>
</tr>
<tr>
<td>Mitral annular calcification mild or less</td>
<td>96.3 (105)</td>
<td>97.3 (71)</td>
<td>94.4 (34)</td>
</tr>
<tr>
<td>Vena contracta width, A-P (mm)</td>
<td>6.3 ± 1.4</td>
<td>6.2 ± 1.4</td>
<td>6.7 ± 1.5</td>
</tr>
<tr>
<td>Jet width, commissural (mm)</td>
<td>13.3 ± 3.8</td>
<td>13.7 ± 3.6</td>
<td>12.5 ± 4.1</td>
</tr>
</tbody>
</table>

**TABLE 2 Procedural Measures**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N = 109)</th>
<th>FMR (n = 73)</th>
<th>DMR (n = 36)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful implantation</td>
<td>95 (104)</td>
<td>96 (70)</td>
<td>94 (34)</td>
</tr>
<tr>
<td>Time from skin incision to femoral vein access closure (min)</td>
<td>128.2 ± 59.9</td>
<td>134.1 ± 65.2</td>
<td>116.3 ± 44.9</td>
</tr>
<tr>
<td>Fluoroscopy duration (min)</td>
<td>34.8 ± 25.1</td>
<td>36.2 ± 26.9</td>
<td>31.9 ± 20.9</td>
</tr>
<tr>
<td>Contrast volume, if used (ml)</td>
<td>20.6 ± 21.7</td>
<td>24.6 ± 24.2</td>
<td>11.2 ± 11.5</td>
</tr>
<tr>
<td>Number of devices implanted, mean</td>
<td>1.4</td>
<td>1.5</td>
<td>1.3</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>2.4 ± 3.3</td>
<td>2.5 ± 3.8</td>
<td>2.2 ± 2.1</td>
</tr>
<tr>
<td>Patients discharged home</td>
<td>93.5 (101)</td>
<td>91.7 (66)</td>
<td>97.2 (35)</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n) or % (n). *Aortic valve disease includes regurgitation and stenosis. †Pulmonic valve disease includes rheumatic, synecope, and thromboembolic. Tricuspid valve disease includes regurgitation and stenosis. ACE = angiotensin-converting enzyme; A-P = anteroposterior; AV = atrioventricular; DMR = degenerative mitral regurgitation; eGFR = estimated glomerular filtration rate; FMR = functional mitral regurgitation; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association; TIA = transient ischemic attack.
guidewire and positioned securely across the septum using the flex mechanism. The implant system is inserted into the guide sheath using a loader and advanced until the PASCAL implant exits the distal end of the guide sheath. Using transesophageal echocardiographic guidance, the steerable catheter and guide sheath are maneuvered until the implant is appropriately centered in the target leaflet coaptation zone and aligned with the mitral annular plane. The implant catheter within the steerable catheter is advanced across the mitral valve, and the implant is opened in the capture-ready position. Implant position and leaflet capture are confirmed by systematically assessing the residual MR and transvalvular gradient. The implant can be adjusted as necessary to achieve optimal desired outcome before final deployment.

**STUDY ENDPOINTS.** The primary safety endpoint was a composite of MAEs, defined as cardiovascular mortality, stroke, MI, new need for renal replacement therapy, severe bleeding (major, extensive, life-threatening, or fatal bleeding defined by the Mitral Valve Academic Research Consortium) (13), and reintervention for study device-related complications at 30 days.

The primary performance endpoints included procedural success and clinical success. Procedural success was defined as at least 1 device deployed and delivery system successfully retrieved as intended at the time of the patient’s exit from the cardiac catheterization laboratory and evidence of MR reduction ≤2+ without the need for a surgical or percutaneous intervention prior to hospital discharge. Clinical success was defined as procedural success with absence of MAEs at 30 days.

Secondary endpoints included MR reduction, MAEs, all-cause mortality, recurrent heart failure hospitalization, and reintervention rates for MR at 1 year. Clinical outcomes included change in NYHA functional class, 6MWD, and quality-of-life score as measured using the Kansas City Cardiomyopathy Questionnaire and EuroQol–5 Dimension at 30 days and 1 year.

**ECHOCARDIOGRAPHIC ASSESSMENT.** Transthoracic echocardiography and transesophageal echocardiography were performed and their results assessed by an independent core laboratory (Cardiovascular Core Lab at Morristown Medical Center) for patient screening, baseline, and follow-up evaluations according to core laboratory protocols and American Society of Echocardiography guidelines (13–16), previously described (12). Patients with mixed etiology were further assessed by the core laboratory for determination of predominant FMR or degenerative MR (DMR) and included in the respective etiology for analysis.

**STATISTICAL ANALYSIS.** Continuous variables are presented as mean ± SD and categorical variables as percentages. Comparison between a specific time point and baseline was statistically analyzed using paired Student’s t-tests for continuous variables and Wilcoxon signed rank tests for categorical variables. Analysis of variance was used for analyses of transvalvular gradient. Significance tests were 2 tailed at a confidence level of 95%. Delta values were calculated using paired analyses. Event-free rate was estimated using Kaplan-Meier survival method, and the standard error was calculated using the exponential Greenwood method (17). The duration of follow-up is summarized as median (interquartile range). All analyses were performed using SAS version 9.4 (SAS Institute, Cary, North Carolina).

**RESULTS**

Between June 2017 and September 2019, 109 patients were treated at 14 sites worldwide, inclusive of roll-in patients. We previously reported 30-day results from 62 patients, which supported Conformité Européenne mark approval of the PASCAL repair system for mitral valve reconstruction (12). We currently report the expanded 30-day experience with 109 patients from the ongoing CLASP study, 1-year follow-up of the 62 patients, and analysis by FMR and DMR etiologies. For the 62 patients, the median duration of follow-up is 596 days (interquartile range: 544 to 642 days).
Baseline characteristics are provided in Table 1. In the overall patient population, the mean age was 75.5 years, 54% were men, and the mean Society of Thoracic Surgeons score was 4.7%. All patients had MR grade 3+ or 4+, with 57% of patients in NYHA functional class III or IV. Etiologic classification resulted in 67 patients (61.5%) with FMR, 34 (31.2%) with DMR, and 8 (7.3%) with mixed disease. The cases of mixed disease were further assessed by the core laboratory and categorized as either predominantly FMR (n = 6) or DMR (n = 2), resulting in a total of 73 patients (67%) with FMR and 36 patients (33%) with DMR for analysis.

PROCEDURAL OUTCOMES. Successful implantation was achieved in 104 patients (95%). Of the 5 unsuccessful implantations, there were 3 cases of inability to adequately grasp leaflets to allow desirable MR reduction, 1 case of unsuitable venous anatomy, and 1 case of single-leaflet device attachment that was successfully converted to surgical mitral valve replacement. Among patients who underwent successful implantation, the mean number of implants was 1.4 per patient, with 49% of patients receiving 1 implant, 45% receiving 2 implants, and 2% receiving 3 implants. The mean time from skin incision to femoral vein access closure was 128 min. Only 16% of procedures required contrast media, with a mean volume of 20.6 ml. The mean length of hospital stay was 2.4 days, and 94% of patients were discharged home. The overall procedural success rate was 94% (100 of 107 patients). Additional procedural measures are provided in Table 2.
Clinical success was achieved in 86.0% (92 of 107 patients). The primary safety endpoint, defined as a composite MAE rate at 30 days in 109 patients, was 8.3% (Table 3). At 30 days, there was 1 cardiovascular death (0.9%) due to sequelae from contralateral arterial access-site bleeding further complicated by disseminated intravascular coagulation, as previously described (12). One patient experienced a stroke (0.9%) presenting with cognitive deficits 15 days post-procedure, confirmed by computed tomography as an ischemic stroke with a modified Rankin Scale score of 1 and adjudicated as...
possibly procedure related. There was no MI or new need for renal replacement therapy. One patient had a surgical reintervention (0.9%) because of single-leaflet device attachment as previously described. Severe bleeding occurred in 8 patients (7.3%). Analysis by etiology revealed that all events at 30 days and 1 year occurred in the FMR population except for 1 bleeding event in the DMR population. The all-cause mortality rate at 1 year was 8.1%. Kaplan-Meier 1-year survival estimates for the overall, FMR, and DMR populations were 92%, 89%, and 96%, respectively.

The heart failure hospitalization rate at 1 year was 12%. Freedom from heart failure hospitalizations at 1 year for the overall, FMR, and DMR populations was 88%, 80%, and 100%, respectively (Figure 1).

**ECHOCARDIOGRAPHIC RESULTS.** At 30 days, 80% of patients had MR ≤1+ and 96% of patients had MR ≤2+ (p < 0.001 vs. baseline). In the 62 patients at 1 year, 82% of patients had MR ≤1+ and 100% had MR ≤2+ (p < 0.001) (Figure 2). In the FMR population at 30 days, 77% of patients achieved MR ≤1+ and 96% MR ≤2+. At 1 year, 79% achieved MR ≤1+ and 100% MR ≤2+. In the patients with DMR at 30 days, 86% of patients achieved MR ≤1+ and 97% MR ≤2+. At 1

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**Table 4 Echocardiographic Outcomes at 30 Days and 1 Year: Overall**

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 109)</th>
<th>30 Days (n = 109)</th>
<th>p Value</th>
<th>Baseline (n = 62)</th>
<th>1 Year (n = 62)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV end-diastolic mm</td>
<td>61.2 ± 7.9 (108)</td>
<td>58.5 ± 8.6 (104)</td>
<td>&lt;0.001</td>
<td>59.4 ± 6.9 (61)</td>
<td>56.1 ± 7.8 (49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV end-diastolic ml</td>
<td>176.9 ± 59.5 (94)</td>
<td>164.5 ± 62.0 (88)</td>
<td>0.001</td>
<td>168.8 ± 47.3 (54)</td>
<td>147.2 ± 45.6 (43)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>44.9 ± 14.4 (109)</td>
<td>44.0 ± 13.6 (105)</td>
<td>0.009</td>
<td>46.7 ± 13.8 (62)</td>
<td>46.4 ± 12.8 (50)</td>
<td>0.044</td>
</tr>
<tr>
<td>PISA EROA (cm²)</td>
<td>0.38 ± 0.16 (88)</td>
<td>0.17 ± 0.21 (24)</td>
<td>&lt;0.001</td>
<td>0.39 ± 0.17 (46)</td>
<td>0.16 ± 0.06 (6)</td>
<td>NA</td>
</tr>
<tr>
<td>Mean gradient (mm Hg)</td>
<td>2.3 ± 1.0 (93)</td>
<td>3.9 ± 1.7 (103)</td>
<td>&lt;0.001</td>
<td>2.3 ± 0.9 (52)</td>
<td>4.0 ± 1.9 (50)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regurgitant volume (ml)</td>
<td>57.2 ± 20.6 (86)</td>
<td>24.9 ± 19.1 (24)</td>
<td>&lt;0.001</td>
<td>59.7 ± 24.3 (45)</td>
<td>24.8 ± 8.8 (6)</td>
<td>NA</td>
</tr>
<tr>
<td>Vena contracta width, A-P (mm)</td>
<td>6.3 ± 1.4 (97)</td>
<td>4.4 ± 1.2 (43)</td>
<td>&lt;0.001</td>
<td>6.0 ± 1.1 (52)</td>
<td>4.1 ± 1.4 (22)</td>
<td>0.001</td>
</tr>
<tr>
<td>PASP (mm Hg)</td>
<td>45.8 ± 12.9 (99)</td>
<td>42.0 ± 11.2 (87)</td>
<td>0.004</td>
<td>45.5 ± 13.3 (56)</td>
<td>40.9 ± 11.5 (42)</td>
<td>0.169</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n). The p values were calculated using Student’s t-test or the Wilcoxon signed rank test compared with baseline. *Number of measurements was limited because of the difficulty of measuring small regurgitant volumes. Bold values indicate statistical significance.

**Table 5 Echocardiographic Outcomes at 30 Days and 1 Year: Functional Mitral Regurgitation**

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n = 73)</th>
<th>30 Days (n = 73)</th>
<th>p Value</th>
<th>Baseline (n = 38)</th>
<th>1 Year (n = 38)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV end-diastolic mm</td>
<td>64.4 ± 6.7 (72)</td>
<td>61.7 ± 7.7 (69)</td>
<td>&lt;0.001</td>
<td>62.7 ± 6.2 (37)</td>
<td>59.1 ± 7.9 (29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV end-diastolic ml</td>
<td>194.3 ± 58.6 (64)</td>
<td>186.4 ± 62.4 (57)</td>
<td>0.045</td>
<td>186.1 ± 47.3 (33)</td>
<td>166.1 ± 47.1 (25)</td>
<td>0.007</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>37.7 ± 10.5 (73)</td>
<td>37.1 ± 9.6 (70)</td>
<td>0.113</td>
<td>38.6 ± 10.2 (38)</td>
<td>39.5 ± 10.4 (29)</td>
<td>0.847</td>
</tr>
<tr>
<td>PISA EROA (cm²)</td>
<td>0.33 ± 0.11 (61)</td>
<td>0.19 ± 0.25 (16)</td>
<td>0.004</td>
<td>0.32 ± 0.10 (29)</td>
<td>0.17 ± 0.07 (4)</td>
<td>NA</td>
</tr>
<tr>
<td>Mean gradient (mm Hg)</td>
<td>2.2 ± 1.0 (59)</td>
<td>4.1 ± 1.8 (68)</td>
<td>&lt;0.001</td>
<td>2.1 ± 0.8 (30)</td>
<td>4.4 ± 2.3 (29)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regurgitant volume (ml)</td>
<td>49.9 ± 13.1 (61)</td>
<td>24.7 ± 22.3 (16)</td>
<td>&lt;0.001</td>
<td>47.2 ± 11.3 (29)</td>
<td>25.6 ± 10.5 (4)</td>
<td>NA</td>
</tr>
<tr>
<td>Vena contracta width, A-P (mm)</td>
<td>6.2 ± 1.4 (67)</td>
<td>4.5 ± 1.2 (25)</td>
<td>&lt;0.001</td>
<td>5.7 ± 0.9 (32)</td>
<td>4.0 ± 1.3 (13)</td>
<td>0.021</td>
</tr>
<tr>
<td>PASP (mm Hg)</td>
<td>46.0 ± 12.1 (66)</td>
<td>42.9 ± 11.9 (57)</td>
<td>0.049</td>
<td>45.7 ± 11.3 (34)</td>
<td>41.7 ± 11.2 (26)</td>
<td>0.454</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n). The p values were calculated using Student’s t-test or the Wilcoxon signed rank test compared with baseline. *Number of measurements was limited because of the difficulty of measuring small regurgitant volumes. Bold values indicate statistical significance.

Abbreviations as in Table 4.
year, 86% of patients with DMR had MR ≤1+ and 100% MR ≤2+.

Echocardiographic measurements for overall patients are shown in Tables 4 to 6. There were significant reductions in all echocardiographic MR indexes at 30 days. Proximal isovelocity surface area effective regurgitant orifice area decreased from 0.38 to 0.17 cm² (p < 0.001), regurgitant volume decreased from 57.5 to 24.9 ml (p < 0.001), and LV end-diastolic diameter decreased from 61.2 to 58.5 mm (p < 0.001). At 1 year, LV end-diastolic diameter showed a sustained reduction from 59.4 to 56.1 mm (p < 0.001). Significant improvements were observed at 30 days and 1 year in both the FMR and DMR populations (Tables 5 and 6).

At 30 days, patients with ≥2 implants showed higher mean transvalvular gradients (4.4 mm Hg; p = 0.03) compared with patients with 1 implant (3.6 mm Hg).

### FUNCTIONAL AND QUALITY-OF-LIFE OUTCOMES

At 30 days, 88% of patients were in NYHA functional class I or II (p < 0.001 vs. baseline) (Figure 3). Functional improvements were sustained at 1 year, with 88% of patients in NYHA functional class I or II (p < 0.001 vs. baseline). Mean 6MWD (Figure 4) increased by 28 m at 30 days (p < 0.001). In patients with 1-year follow-up, 6MWD showed sustained improvement of 21 m (p = 0.124). Average Kansas City Cardiomyopathy Questionnaire score (Figure 5A) improved by 16 points at 30 days (p < 0.001) and showed sustained improvement of 14 points at 1 year (p < 0.001). Mean EuroQol-5 Dimension score (Figure 5B) improved by 11 points at 30 days (p < 0.001), with sustained improvement of 6 points at 1 year (p = 0.0788). Similar functional and quality-of-life improvements were observed in the FMR and DMR populations.

### DISCUSSION

The results with the PASCAL repair system in the CLASP study demonstrate favorable clinical and echocardiographic results in a heterogeneous population of patients with FMR and DMR. MAE rates were low at 30 days and 1 year, and MR was reduced to ≤2+ in 96% and 100% of patients, and ≤1+ in 80% and 82%, respectively. There was a significant reduction in all echocardiographic MR indexes and resultant LV reverse remodeling with a significant reduction in both LV end-diastolic diameter and volume. One-year mortality was 8%, and heart failure hospitalizations at 1 year were only 12%. Functional status and quality-of-life indexes were also significantly improved. These results compare favorably with experience with other transcatheter mitral valve repair devices (10,18–20).

The COAPT trial examined the use of the MitraClip system in patients with severe FMR (10). Although the 2 studies cannot be compared directly because of different trial designs and populations, two-thirds of CLASP patients were treated for FMR. At 1 year, the reduction in MR grade to ≤2+ and ≤1+ was seen in 100% and 79% of CLASP patients with FMR (n = 73) versus 95% and 69% reported in COAPT (n = 273). The reduction in NYHA functional class to I or II at 1 year was seen in 83% of CLASP patients with FMR versus 72% in COAPT patients.

The EXPAND (n = 422) and EVEREST (n = 82) studies reported the use of the MitraClip system in patients with DMR at 30 days and 1 year, respectively (18,21). At 30 days, the reduction in MR grade to ≤2+ was seen in 97% and NYHA functional class I or II in 88% of CLASP patients with DMR (n = 36), similar to EXPAND, which reported 97% of patients with MR grade ≤2+ and 84% in NYHA functional class I or II. One-year outcomes in the CLASP
FIGURE 3 Functional Outcomes at 30 Days and 1 Year

Graphs show unpaired data. The p values were calculated using the Wilcoxon signed rank test for paired patients (n).

(A) Overall population; (B) FMR cohort; (C) DMR cohort. Abbreviations as in Figure 1.
**FIGURE 4** 6-Minute Walk Distance at 30 Days and 1 Year

(A) Overall

- **p<0.001**
  - (n=99; Δ=28)
- **p=0.124**
  - (n=44; Δ=21)

(B) FMR

- **p=0.009**
  - (n=65; Δ=23)
- **p=0.261**
  - (n=24; Δ=24)

(C) DMR

- **p=0.004**
  - (n=34; Δ=38)
- **p=0.303**
  - (n=20; Δ=19)

(A) Overall population; (B) FMR cohort; (C) DMR cohort. Mean ± 95% confidence interval. Graphs show unpaired data. The p values were calculated using Student’s t-test for paired patients (n). Delta values are for paired patients corresponding to p values.
patients with DMR (n = 24) continued to be favorable, with 100% of patients achieving MR grade ≤2+ and 95% in NYHA functional class I or II compared with EVEREST, which reported 83% patients with MR grade ≤2+ and 87% in NYHA functional class I or II.

Achieving a suboptimal reduction in MR post-implantation has been shown to result in poor clinical outcomes in both surgical and transcatheter treatment of severe MR, emphasizing the need to achieve MR ≤1+ (22–24). There are now increasing transcatheter options for severe MR, including transcatheter mitral valve replacement, which have shown very low rates of significant residual MR (8,25,26). As such, there are theoretical design advantages to the PASCAL repair system. The maneuverability of the PASCAL repair system simplifies navigation into the left atrium, while the broad paddles, spacer, and ability to independently capture leaflets help achieve reduction of MR with no detrimental impact on post-procedural mitral valve gradient. Previous results suggest that these unique features of the PASCAL repair system allow treatment of patients with challenging mitral anatomies, such as short posterior leaflets and flail and prolapse gaps >10 mm, for which other transcatheter therapies were judged inappropriate (11). Hence, the PASCAL repair system may potentially increase the number of patients eligible for transcatheter mitral valve repair.

Characteristics of the PASCAL repair system also may allow a reduction in the number of implants required, thereby reducing procedural time and complexity. The mean number of devices implanted in the COAPT trial was 1.7 per patient, with 62% of patients requiring more than 1 device. In the CLASP study, the mean number of devices implanted overall and in patients with FMR was 1.4 and 1.5 per patient, with 47% and 54% requiring more than 1 device, respectively. Patients with ≥2 implants still maintained mean gradients <5 mm Hg.

**STUDY LIMITATIONS.** This study was limited by the sample size of the overall population and commensurately by that of each etiology. The sample sizes for some quantitative echocardiographic measurements were limited in part because of technological difficulty in measuring small regurgitant volumes, but this is also likely reflective of general limitations in obtaining consistent and high-quality imaging in this study. The study protocol did not stipulate data collection regarding medications at discharge and during the follow-up period. Therefore, these data were not collected during the course of the trial. One-year follow-up was achieved by a subset of patients, and continued follow-up will be important.

![Image of Figure 5: KCCQ and EQ5D Scores at 30 Days and 1 Year](Image)
CONCLUSIONS

At 1 year, the PASCAL transcatheter repair system resulted in high survival and low complication rates with robust and sustained MR reduction, accompanied by significant improvements in functional status and quality of life. Analysis by etiology showed similar favorable results in patients with FMR or DMR. The CLASP IID/IIF randomized clinical trial is under way.

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