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ORIGINAL RESEARCH

STRUCTURAL

CLASP IID Trial and Registry

2-Year Outcomes of Transcatheter Repair for Degenerative Mitral Regurgitation

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ABSTRACT

BACKGROUND One-year outcomes from the CLASP IID Trial (Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial; NCT03706833) and Registry established the PASCAL transcatheter valve repair system as a safe and effective treatment for prohibitive-risk degenerative mitral regurgitation (DMR). Longer-term follow-up is ongoing.

OBJECTIVES This paper reports the CLASP IID Trial and Registry 2-year outcomes.

METHODS In the CLASP IID Trial, prohibitive-risk patients with 3+/4+ DMR, deemed suitable for both the PASCAL and MitraClip systems, were randomized 2:1 (PASCAL: n = 204; MitraClip: n = 96). Patients with complex anatomy deemed ineligible for randomization were enrolled in the CLASP IID Registry (N = 98) and treated with the PASCAL system.

RESULTS In the randomized cohort, significant and sustained MR reduction was achieved at 2 years. MR ≤2+ rate was 95.0% (96/101) in the PASCAL group vs 91.5% (54/59) in the MitraClip group ($P = 0.500$), and MR ≤1+ rate was 77.2% (78/101) vs 67.8% (40/59) ($P = 0.198$), respectively. Kaplan-Meier estimates for freedom from all-cause mortality, cardiovascular mortality, heart failure hospitalization, and nonelective mitral valve reinterventions were 80.8% vs 86.2% ($P = 0.216$), 88.6% vs 90.4% ($P = 0.666$), 86.4% vs 94.3% ($P = 0.058$), and 97.9% vs 97.9% ($P = 0.962$), respectively. In the registry cohort, 91.9% (34/37) achieved MR ≤2+ and 64.9% (24/37) achieved MR ≤1+. Kaplan-Meier estimates for freedom from all-cause mortality, cardiovascular mortality, heart failure hospitalization, and nonelective mitral valve reinterventions were 77.2%, 84.0%, 85.1%, and 99.0%, respectively. Significant improvements in functional status and quality of life were observed in both cohorts.

CONCLUSIONS Two-year outcomes from the CLASP IID Trial and Registry show favorable survival, and significant and sustained MR reduction with functional and quality-of-life improvements, confirming sustained safety and effectiveness of the PASCAL system in treating a broad population of DMR patients. (JACC Cardiovasc Interv. 2025;18:2392–2404)

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The CLASP IID Trial is the first randomized controlled trial to compare 2 contemporary transcatheter mitral valve edge-to-edge repair (M-TEER) therapies, the PASCAL transcatheter valve repair system (Edwards Lifesciences) and the MitraClip system (Abbott). Primary and secondary endpoints for the trial were met, demonstrating noninferiority of the PASCAL system to the MitraClip system for safety and effectiveness.[1,2] Additionally, results were comparable at 1 year for survival, heart failure hospitalization (HFH), and transmitral gradients, as well as functional and quality-of-life improvements.[3] Patients who were deemed ineligible for randomization due to complex anatomical characteristics (based on the MitraClip Instructions for Use at the time of the study), were treated with the PASCAL system in the CLASP IID Registry.[2] One-year results from the CLASP IID Registry demonstrated significant mitral regurgitation (MR) reduction and improvements in clinical, functional, and quality-of-life measures.[4] We report 2-year outcomes from the randomized CLASP IID Trial and the single-arm CLASP IID Registry.

METHODS

STUDY DESIGN AND PATIENT SELECTION. The CLASP IID Trial (Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial; NCT03706833) is a prospective, multicenter, multinational, randomized controlled trial to evaluate the safety and effectiveness of M-TEER procedure with the PASCAL system compared to the MitraClip system in degenerative mitral regurgitation (DMR) patients. The trial enrolled patients deemed to be at prohibitive risk for mitral valve surgery by the local heart team, had grade 3+ or 4+ DMR by transthoracic echocardiography or transesophageal echocardiography as assessed by the echocardiography core laboratory (Cardiovascular Core Lab at Atlantic Health System Morristown Medical Center, Morristown, New Jersey), and were deemed to be candidates for M-TEER with the PASCAL system and the MitraClip system by a multidisciplinary central screening committee (CSC). Patients were randomized in a 2:1 ratio to receive either the PASCAL system or the MitraClip system. Patients deemed ineligible for randomization by the CSC and suitable for the PASCAL system were enrolled in the single-arm CLASP IID Registry.[1,2] The study details and the devices have been described previously[1-6] and are detailed in the Supplemental Methods. Study assessments were performed at baseline, during hospital stay, at discharge or 7 days post procedure (whichever was earlier) with follow-up at 30 days, 6 months, 1 year and annually through 5 years. Echocardiography assessment methods for the trial have been previously reported.[7]

STUDY CONDUCT. The protocol was designed in accordance with the Mitral Valve Academic Research Consortium (MVARC) guidelines[8,9] and approved by the investigational review board/ethics committee at each participating center. All patients provided

ABBREVIATIONS AND ACRONYMS

CSC = central screening committee

DMR = degenerative mitral regurgitation

EQ-5D-5L VAS = EuroQol 5-Dimention 5-Level Visual Analog Score

HFH = heart failure hospitalization

KCCQ = Kansas City Cardiomyopathy Questionnaire

KM = Kaplan-Meier

LV = left ventricular

MR = mitral regurgitation

M-TEER = mitral valve transcatheter edge-to-edge repair

SLDA = single-leaflet device attachment

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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written informed consent, and the study conformed to the Declaration of Helsinki, Good Clinical Practice principles, and ISO 14155:2011. An independent echocardiographic core laboratory evaluated echocardiograms, a multidisciplinary CSC reviewed and approved patient enrollment, and a clinical events committee-adjudicated prespecified adverse events. An independent data safety monitoring board reviewed aggregate safety data and assessed overall safety of the trial. The CLASP IID Trial and Registry were sponsored by Edwards Lifesciences.

STUDY ENDPOINTS AND OUTCOMES. The CLASP IID Trial assessed noninferiority of the PASCAL system compared with the MitraClip system for safety and effectiveness. The primary and secondary endpoints are described in the Supplemental Methods and were previously reported[1,3] along with other key 1-year outcomes.[3] This report presents echocardiographic, clinical, functional, and quality-of-life outcomes from the CLASP IID Trial and Registry through 2-year follow-up.

STATISTICAL ANALYSIS. Statistical analyses were performed with SAS software, version 9.4 or higher (SAS Institute). Continuous variables were summarized with number of observations, mean ± SD or median (Q1-Q3) and 95% CI based on *t* distribution; and compared using Student's *t*-test, Wilcoxon rank sum test, and Kruskal-Wallis test. An analysis of covariance model with baseline values as covariates was used to compare mean changes between groups. The exact McNemar's test was used to assess binary repeated measures. Categorical variables were summarized with patient count, percentage, and 95% CI, and compared using Fisher exact test. Paired analysis for ordinal data was performed using the Wilcoxon signed rank test. Kaplan-Meier (KM) estimates were used to analyze time-to-event variables, and standard error was calculated using Greenwood's formula with log-rank *P* value calculated for intergroup comparisons. Where appropriate, differences between treatment groups were summarized with mean difference and 95% CI, or percentage difference and 95% CI. Estimates of annualized HFH rates are from Poisson regression model, and *P* values for relative reduction rate are based on the Z test. Cox proportional hazards regression analyses were performed post hoc to identify variables significantly associated with increased risk of HFH. Possible variables were initially screened in univariable analysis using the Cox model and those with a significance threshold of $P \leq 0.20$ were included in the final multivariable analysis. The proportional hazards assumption was assessed using the SAS PROC PHREG procedure, and the observed score process component was plotted against the follow-up time along with simulated patterns for treatment variables (TRTP) in the model. Unless noted otherwise, patients with missing data were excluded from the denominator. Baseline characteristics and clinical outcomes are reported for patients with procedure attempted (skin incision) and effectiveness outcomes are reported for patients with device attempted (guide sheath or steerable guide inserted into the femoral vein).

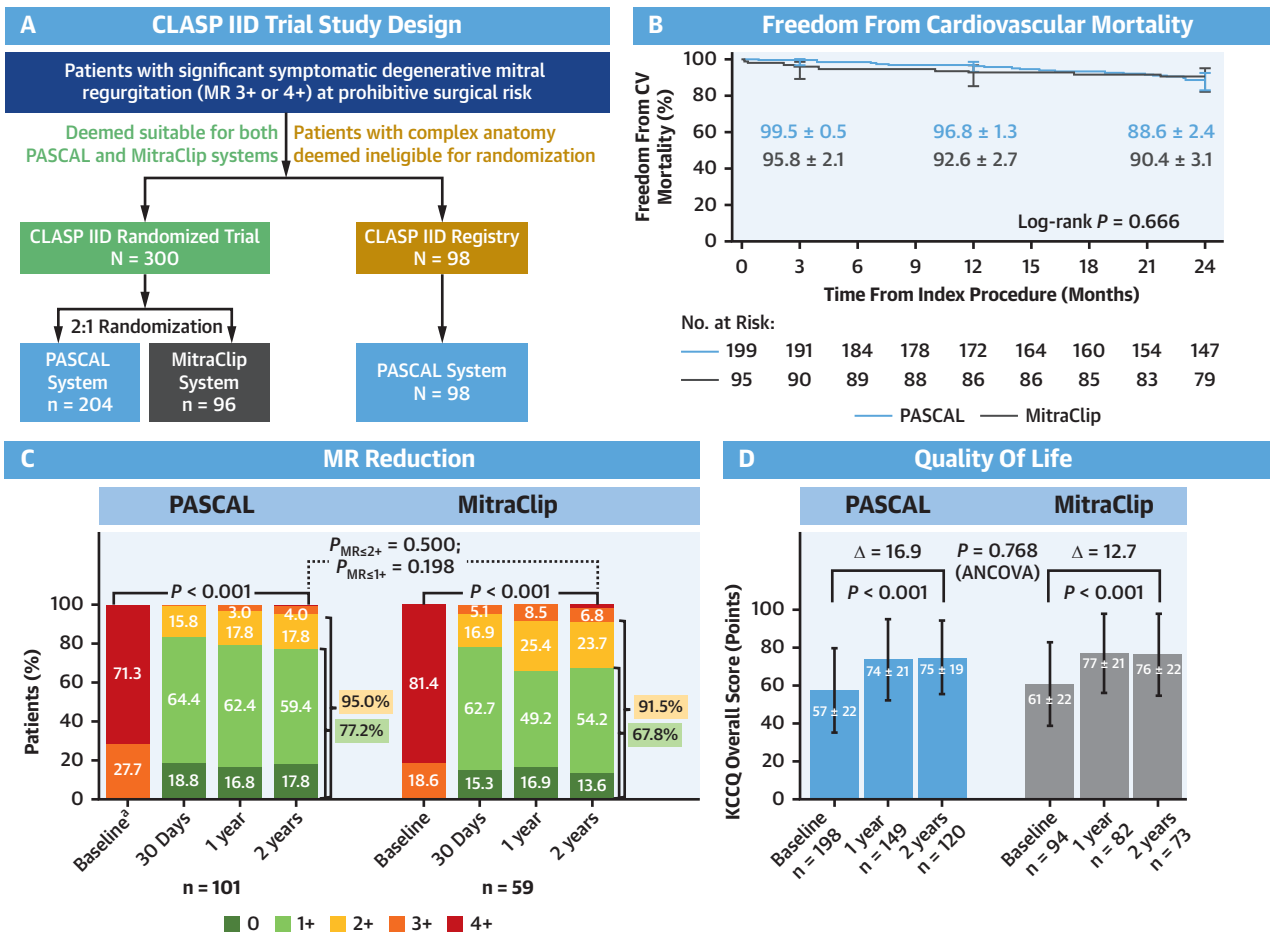
RESULTS

STUDY POPULATION. In the CLASP IID Trial, 300 patients (PASCAL: n = 204, MitraClip: n = 96) were randomized at 54 sites in the United States, Canada, and Europe. At 2 years, follow-up visits were completed for 84.8% (128/151) of eligible patients in the PASCAL group and 95.1% (77/81) in the MitraClip group. The CLASP IID Registry enrolled 98 complex anatomy patients at 35 sites in the United States, Canada, and Europe, and 2-year follow-up visits were completed for 79.4% (54/68) of the eligible patients. The median follow-up duration (Q1-Q3) was 2.7 years (2.1-3.3 years) for the randomized cohort (PASCAL: 2.6 years [1.9-3.2 years]; MitraClip: 2.9 years [2.5-3.5 years]) and 2.7 years (1.7-3.4 years) for the registry cohort. Patient disposition, study flow, and follow-up are shown in Supplemental Figure 1 and Supplemental Table 1.

BASELINE CHARACTERISTICS AND PROCEDURAL OUTCOMES. Baseline characteristics and procedural outcomes for the randomized and registry cohorts were previously reported[1,2] and are summarized in Supplemental Tables 2 and 3.

ECHOCARDIOGRAPHIC OUTCOMES. Two-year TTE data were available for 79.5% (120/151) of eligible patients in the PASCAL group and 91.4% (74/81) in the MitraClip group (Supplemental Figure 1). Patients in both groups experienced significant MR reduction from baseline to 2 years ($P < 0.001$ vs baseline) (**Central Illustration**). In paired analysis, 95.0% (96/101) (95% CI: 88.8%-98.4%) of patients achieved MR ≤2+ in the PASCAL group vs 91.5% (54/59) (95% CI: 81.3%-97.2%) in the MitraClip group ($P = 0.500$). The proportion of patients achieving MR ≤1+ at 2 years was 77.2% (78/101) (95% CI: 67.8%-85.0%) in the PASCAL group compared with 67.8% (40/59) (95% CI: 54.4%-79.4%) in the MitraClip group ($P = 0.198$), which was consistent with the 1-year outcomes (79.2% vs 66.1%, respectively) (**Central Illustration**). Results were similar in the unpaired analysis (Supplemental Figure 2).

CENTRAL ILLUSTRATION **2-Year Outcomes From the CLASP IID Randomized Trial for Degenerative Mitral Regurgitation**



- In the CLASP IID randomized trial, comparing two contemporary M-TEER therapies in prohibitive risk DMR patients, favorable clinical, echocardiographic, functional and quality-of-life outcomes were maintained to 2 years.
- In the anatomically complex CLASP IID Registry patients, treatment with the PASCAL system resulted in similar outcomes.
- These results confirm the sustained safety and effectiveness of the PASCAL system in treating a broad population of DMR patients.

Makkar R, et al. JACC Cardiovasc Interv. 2025;18(19):2392-2404.

(A) Trial design. (B) Kaplan-Meier estimates for freedom from cardiovascular (CV) mortality (Kaplan-Meier estimate ± SE). Error bars represent 95% CI. (C) Mitral regurgitation (MR) severity by transthoracic echocardiography assessed by echocardiography core laboratory. [a]Transesophageal echocardiography was used for baseline qualification of 1 patient. Graph shows paired analysis. *P* values relative to baseline were calculated using Wilcoxon signed rank test, and *P* values for intergroup comparisons were calculated using Fisher exact test. (D) Graph shows unpaired analysis (mean ± SD). *P* values for intragroup comparisons were calculated from paired analysis using Student's *t*-test, and *P* values for intergroup comparisons were calculated with analysis of covariance model adjusted for baseline values as covariates. CLASP IID = Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial; KCCQ = Kansas City Cardiomyopathy Questionnaire.

Mean transmitral valve gradients and measures of left ventricular remodeling are summarized in Table 1. Mean transmitral valve gradients remained stable and below 5 mm Hg from discharge (PASCAL: 3.8 mm Hg and MitraClip: 3.6 mm Hg) to 2 years (PASCAL: 3.9 mm Hg and MitraClip: 3.5 mm Hg). Significant reductions in key echocardiographic MR indices were observed at discharge and sustained to 2 years in both groups ($P < 0.05$ vs baseline for all). Left ventricular (LV) end-diastolic volume decreased

TABLE 1 Echocardiographic Outcomes at 2 Years for the CLASP IID Randomized Trial as Assessed by Echocardiographic Core Laboratory

	LVEDV, mL	LVESV, mL	LVEDD, mm	LVESD, mm	Transmitral Mean Gradient, mm Hg
PASCAL					
Baseline	144.3 ± 50.55 (192)	60.4 ± 30.09 (192)	56.9 ± 6.41 (198)	38.0 ± 7.47 (196)	2.5 ± 1.06 (187)
Discharge	131.3 ± 47.16 (171)	58.7 ± 28.76 (171)	54.0 ± 6.54 (186)	37.6 ± 7.24 (180)	3.8 ± 1.52 (191)
Δ From baseline to discharge	−13.9 ± 21.19 (167)	−3.1 ± 12.85 (167)	−2.8 ± 3.20 (186)	−0.20 ± 4.118 (179)	1.3 ± 1.43 (179)
	−9.3 (−97.3, 36.8)	−1.1 (−67.8, 40.2)	−2.0 (−12.0, 6.0)	0.0 (−12.0, 16.0)	1.3 (−3.0, 6.4)
P value	<0.001	0.002	<0.001	0.526	<0.001
2 y	109.9 ± 48.27 (115)	49.9 ± 34.81 (115)	50.7 ± 6.50 (112)	34.9 ± 6.85 (111)	3.9 ± 1.81 (117)
Δ From baseline to 2 years	−27.1 ± 30.34 (112)	−7.5 ± 21.78 (112)	−5.8 ± 4.12 (112)	−2.2 ± 4.54 (109)	1.4 ± 1.64 (114)
	−22.7 (−106.8, 87.3)	−6.3 (−82.9, 122.8)	−6.0 (−18.0, 4.0)	−1.0 (−13.0, 8.0)	1.1 (−2.7, 6.2)
P value	<0.001	<0.001	<0.001	<0.001	<0.001
MitraClip					
Baseline	150.1 ± 48.17 (94)	63.5 ± 30.71 (94)	57.4 ± 6.80 (93)	39.3 ± 8.39 (92)	2.3 ± 0.97 (87)
Discharge	130.3 ± 38.53 (84)	59.1 ± 26.71 (84)	55.2 ± 6.01 (89)	39.2 ± 7.71 (87)	3.6 ± 1.33 (93)
Δ From baseline to discharge	−17.8 ± 22.63 (84)	−3.0 ± 14.85 (84)	−2.3 ± 3.04 (88)	−0.35 ± 3.703 (86)	1.3 ± 1.62 (86)
	−14.7 (−99.5, 55.4)	−2.3 (−50.9, 55.3)	−2.0 (−13.0, 5.0)	0.00 (−11.0, 11.0)	1.4 (−2.4, 5.4)
P value	<0.001	0.066	<0.001	0.385	<0.001
2 y	118.6 ± 41.50 (72)	56.2 ± 34.63 (72)	51.9 ± 5.66 (72)	35.8 ± 7.30 (72)	3.5 ± 1.18 (74)
Δ From baseline to 2 years	−32.2 ± 25.18 (72)	−7.3 ± 16.11 (72)	−5.2 ± 3.86 (71)	−2.9 ± 5.50 (70)	1.2 ± 1.40 (68)
	−29.7 (−105.2, 18.1)	−8.3 (−47.7, 49.4)	−5.0 (−16.0, 5.0)	−3.0 (−24.0, 10.0)	1.1 (−1.7, 4.3)
P value	<0.001	<0.001	<0.001	<0.001	<0.001
PASCAL vs MitraClip					
P value, ANCOVA	0.588	0.869	0.161	0.794	0.257

Values are mean ± SD (n). Δ represents the change from baseline from paired analysis and is provided as mean ± SD and median (min, max). Intragroup *P* values were calculated using Student's *t*-test. Intergroup *P* values are calculated from analysis-of-covariance (ANCOVA) model. Discharge was within 7 days postprocedure.

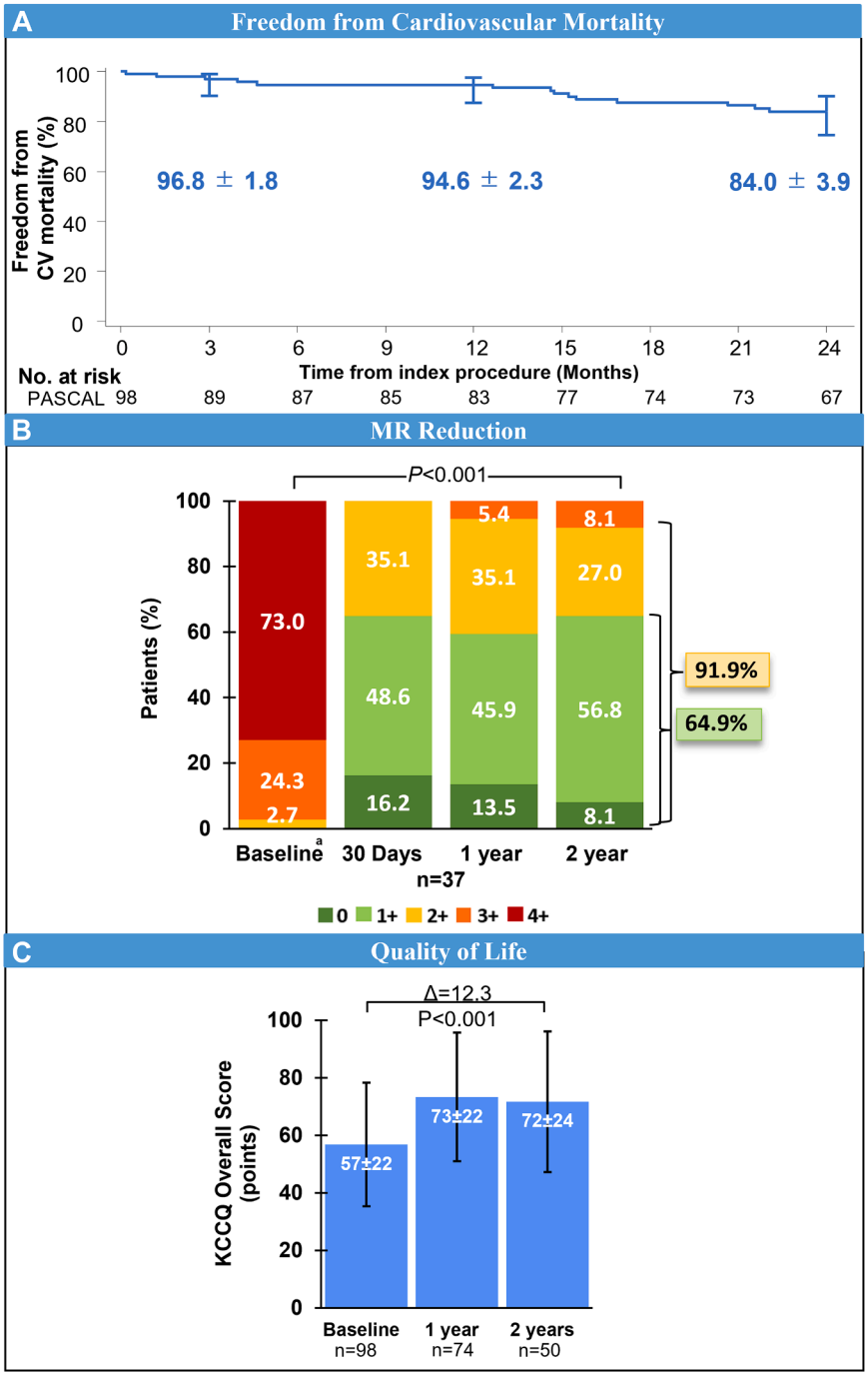
LVEDD = left ventricular end-diastolic dimension; LVEDV = left ventricular end-diastolic volume; LVESD = left ventricular end-systolic dimension; LVESV = left ventricular end-systolic volume.

significantly ($P < 0.001$ vs baseline) by 27.1 mL in the PASCAL group and 32.2 mL in the MitraClip group, a reduction of 18.8% and 21.5%, respectively. A significant decrease ($P < 0.001$ vs baseline) was also observed in LV end-diastolic diameter (PASCAL: 5.8 mm and MitraClip: 5.2 mm). Analysis of covariance analysis showed no difference between treatment groups in echocardiographic outcomes ($P > 0.05$ for all) at 2 years (Table 1). Single-leaflet device attachment (SLDA) occurred in 2.0% (4/199) of patients in the PASCAL group and 1.1% (1/95) of patients in the MitraClip group at 2 years. Of the 4 SLDA in the PASCAL group, 1 patient underwent a transcatheter mitral valve reintervention with an additional device, resulting in mild-to-moderate residual MR. The remaining 3 patients underwent surgical mitral valve replacement. In the MitraClip group, 1 new SLDA was detected 686 days postprocedure, for which no reintervention was performed.

In the registry cohort, 2-year TTE data were available for 70.6% (48/68) of eligible patients (Supplemental Figure 1). Significant MR reduction was sustained at 2 years ($P < 0.001$ vs baseline) with 91.9% (34/37) (95% CI: 78.1%-98.3%) at MR ≤2+ and 64.9% (24/37) (95% CI: 47.5%-79.8%) at MR≤1+ in paired analysis (Figure 1). Analysis of unpaired data showed similar results (Supplemental Figure 3). The mean transmitral valve gradient increased from 2.5 mm Hg at baseline to 4.1 mm Hg at discharge and remained stable at 4.2 mm Hg at 2 years. LV end-diastolic volume and LV end-diastolic diameter decreased significantly by 28.2 mL and 5.7 mm (both $P < 0.001$ vs baseline), respectively (Supplemental Table 4). There were no SLDA in the registry cohort after 6 months.

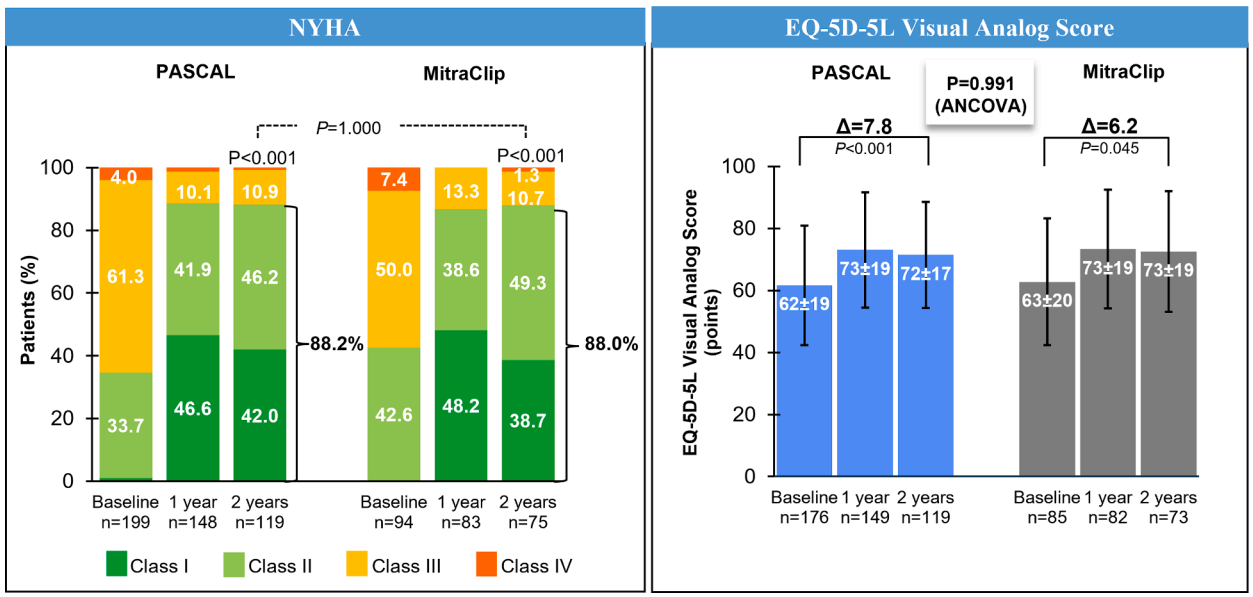
FUNCTIONAL AND QUALITY-OF-LIFE OUTCOMES. In both treatment groups of the randomized cohort, significant improvements were sustained in NYHA functional class, overall Kansas City Cardiomyopathy Questionnaire (KCCQ) score and EuroQol 5-Dimention 5-Level Visual Analog Score (EQ-5D-5L VAS) ($P < 0.05$ vs baseline for all) at 2 years (Central Illustration, Figure 2). NYHA functional class I/II was achieved in 88.2% (105/119) ($P < 0.001$ vs baseline) of patients in the PASCAL group and 88.0% (66/75) ($P < 0.001$ vs baseline) in the MitraClip group. The overall KCCQ score improved by 16.9 points (95% CI: 13.2-20.7 points) ($P < 0.001$ vs baseline) and 12.7 points (95% CI: 7.2-18.2 points) ($P < 0.001$ vs baseline), respectively. The EQ-5D-5L VAS increased by 7.8 points (95% CI: 4.3-11.2 points) ($P < 0.001$) and 6.2 points (95% CI: 0.1-12.3) ($P = 0.045$), respectively. There was no significant difference between the 2 groups in functional and quality-of-life outcomes at 2 years ($P > 0.05$ for all) (Central Illustration, Figure 2).

FIGURE 1 Key Outcomes at 2 Years for the CLASP IID Registry



(A) Kaplan-Meier estimate for freedom from cardiovascular (CV) mortality (Kaplan-Meier estimate ± SE). Error bars represent 95% CI. (B) Mitral regurgitation (MR) severity by transthoracic echocardiography assessed by echocardiography core laboratory. [a]Transesophageal echocardiography was used for baseline qualification of 1 patient. Graph shows paired analysis, and the *P* value relative to baseline was calculated using the Wilcoxon signed rank test. (C) Graph shows unpaired analysis (mean ± SD). *P* value was calculated from paired analysis using Student's *t*-test. CLASP IID = Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial; KCCQ = Kansas City Cardiomyopathy Questionnaire.

FIGURE 2 Functional and Quality-of-Life Outcomes at 2 Years for the CLASP IID Randomized Trial

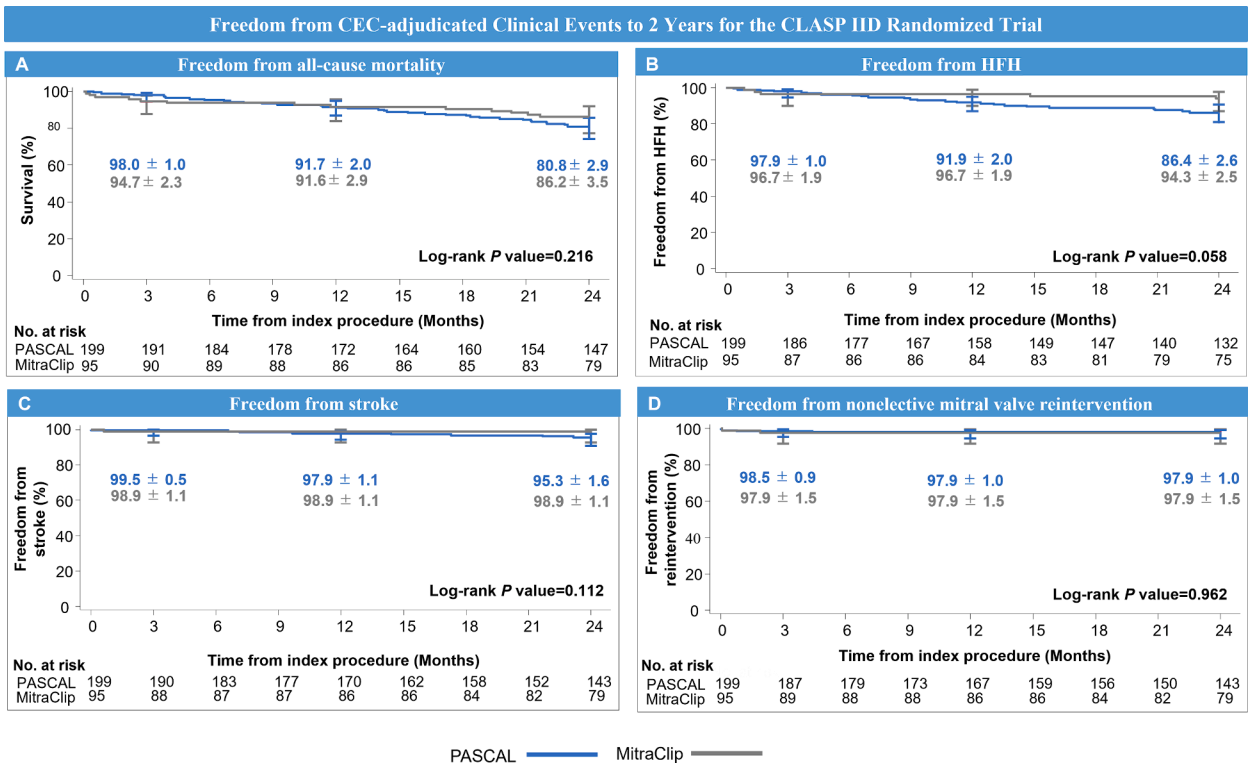


Graph shows unpaired analysis for NYHA functional class. *P* values for intragroup comparisons were calculated from paired analysis using the Wilcoxon signed rank test. *P* values for intergroup comparison of NYHA functional class I/II were calculated using Fisher exact test. The EuroQol 5-Dimensions 5-Level (EQ-5D-5L) graph shows unpaired analysis (mean ± SD). The *P* value for intragroup comparison was calculated from paired analysis using Student's *t*-test, and the *P* value for intergroup comparison was calculated with analysis of covariance (ANCOVA) model adjusted for baseline values as covariates. CLASP IID = Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial.

In the registry cohort, 83.7% (41/49) of patients were in NYHA functional class I/II at 2 years ($P < 0.001$ vs baseline). The overall KCCQ score improved significantly by 12.3 points [95% CI: 5.8-18.8 points] ($P < 0.001$ vs baseline) and the EQ-5D-5L VAS increased by 6.9 points (95% CI: 0.8-13.0 points) ($P = 0.028$ vs baseline) (**Figure 1**, Supplemental Figure 4).

CLINICAL OUTCOMES. The KM estimate for survival at 2 years was 80.8% (95% CI: 74.4%-85.8%) for the PASCAL group and 86.2% (95% CI: 77.5%-91.8%) for the MitraClip group ($P = 0.216$) (**Figure 3**). The numerical difference in survival was driven by noncardiovascular deaths. At 2 years, there were a total of 51 deaths, 38 in the PASCAL group (21 due to cardiovascular causes and 17 due to noncardiovascular causes) and 13 in the MitraClip group (9 due to cardiovascular causes and 4 due to noncardiovascular causes) (Supplemental Table 5). The primary reasons for noncardiovascular deaths were cancer, infection, and trauma in the PASCAL group and infection in the MitraClip group (Supplemental Table 5A). The KM estimates for freedom from cardiovascular mortality were 88.6% (95% CI: 82.9%-92.5%) in the PASCAL group vs 90.4% (95% CI: 82.3%-94.9%) in the MitraClip group, respectively ($P = 0.666$) (**Central Illustration**); freedom from nonelective mitral valve reintervention (either percutaneous or surgical), a prespecified endpoint, was 97.9% (95% CI: 94.6%-99.2%) vs 97.9% (95% CI: 91.7%-99.5%) ($P = 0.962$). The KM estimates for freedom from any mitral valve reintervention, including elective and nonelective, and details on the types of reinterventions are provided in Supplemental Table 6. The KM estimates for freedom from stroke were 95.3% (95% CI: 90.8%-97.6%) vs 98.9% (95% CI: 92.5%-99.8%) ($P = 0.112$) and the KM estimate for freedom from HFH was 86.4% (95% CI: 80.3%-90.7%) vs 94.3% (95% CI: 86.8%-97.6%) ($P = 0.058$), respectively (**Figure 3**). In a post hoc Cox proportional hazards regression analysis (Supplemental Table 7), the following covariates were significant for HFH at 2 years in the adjusted model: history of hypertension, ventricular tachycardia/fibrillation, anemia and other noncardiovascular conditions; enrollment at a site with high annualized HFH rate; baseline NYHA functional class ≥III; baseline left atrial volume; and MR ≥2+ at

FIGURE 3 Clinical Outcomes at 2 Years for the CLASP IID Randomized Trial



Freedom from (A) all-cause mortality, (B) heart failure hospitalization (HFH), (C) stroke, and (D) nonelective mitral valve reintervention at 2 years. Graph shows Kaplan-Meier estimate ± SE and error bars represent 95% CI. CEC = clinical events committee; CLASP IID = Edwards PASCAL TrAnScatheter Valve RePair System Pivotal Clinical Trial.

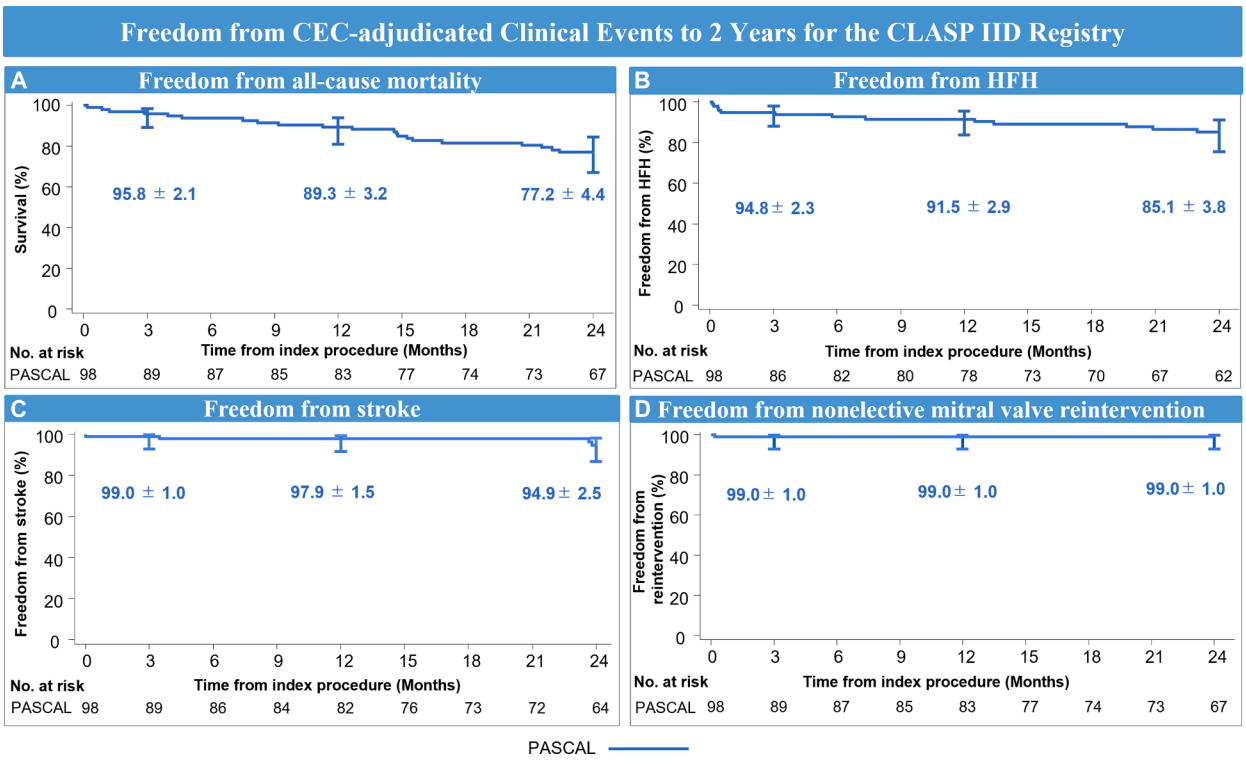
discharge. Treatment group assignment was not a significant factor for HFH in the unadjusted model or the adjusted model. In both groups, the annualized HFH rate decreased significantly from 1 year preprocedure to 2 years postprocedure. In the PASCAL group, the annualized HFH rate decreased significantly by 77.1% from 0.42 HFH per patient-year preprocedure to 0.1 HFH per patient-year at 2 years postprocedure ($P < 0.001$). In the MitraClip group, the annualized HFH rate decreased significantly by 93.9% from 0.47 HFH per patient-year preprocedure to 0.03 HFH per patient-year at 2 years postprocedure ($P < 0.001$) (Supplemental Figure 5).

In the registry cohort, the KM estimates for survival, freedom from cardiovascular death, nonelective mitral valve reintervention (either percutaneous or surgical), stroke, and HFH were 77.2% (95% CI: 67.1%-84.5%), 84.0% (95% CI: 74.5%-90.2%), 99.0% (95% CI: 93.0%-99.9%), 94.9% (95% CI: 86.9%-98.1%), and 85.1% (95% CI: 75.7%-91.1%), respectively (**Figure 4**). The annualized HFH rate decreased significantly from 0.57 HFH per patient-year preprocedure to 0.14 at 2 years postprocedure ($P < 0.001$), a reduction of 76.0% (Supplemental Figure 6).

DISCUSSION

The CLASP IID Trial is the first randomized controlled trial comparing the safety and effectiveness of the PASCAL system and the MitraClip system for the treatment of symptomatic, moderate-to-severe or severe DMR in prohibitive surgical risk patients. At 2 years, the principal findings from the study were as follows. First, there was no significant difference between the PASCAL group and MitraClip group in echocardiographic outcomes including MR reduction or mean transmitral gradients. A significant reduction in MR severity was achieved, with 1-year outcomes sustained to 2 years. Second, there was no significant difference between the 2 groups in clinical outcomes, including survival, cardiovascular death, HFH, stroke, or nonelective mitral valve reintervention at 2 years. Third, patients in both the PASCAL

FIGURE 4 Clinical Outcomes at 2 Years for the CLASP IID Registry



Freedom from (A) all-cause mortality, (B) heart failure hospitalization, (C) stroke, and (D) nonelective mitral valve reintervention at 2 years. Graph shows Kaplan-Meier estimate ± SE, and error bars represent 95% CI. Abbreviations as in Figure 3.

and MitraClip groups experienced a similar significant and sustained improvement in functional status (as assessed with NYHA functional class) and quality of life (as assessed with the KCCQ overall score and EQ-5D-5L VAS) at 2 years. Fourth, 2-year outcomes in the anatomically complex CLASP IID Registry patients show that the PASCAL system was successful in treating DMR in a diverse range of mitral valve anatomies that were historically considered challenging for M-TEER.

This is the first report of 2-year echocardiographic outcomes with contemporary M-TEER devices for the treatment of DMR, as assessed by an independent echocardiography core laboratory. The findings reveal significant and sustained reduction in the severity of MR in both the PASCAL and the MitraClip groups over a period of 2 years. Additionally, the reduction in MR translated into significant and clinically meaningful improvements in functional status and quality of life, which were also maintained to 2 years. Previously, the EVEREST trial (Endovascular Valve Edge-to-Edge Repair Study) reported long-term echocardiographic outcomes of M-TEER with the first-generation MitraClip system, rendering those outcomes less meaningful in the present era.[10] The real-world EXPAND (The MitraClip® EXPAND Study of the Next Generation of MitraClip® Devices) and EXPAND G4 (MitraClip EXPAND G4 Study) registries reported echocardiographic core laboratory assessed outcomes of M-TEER with the third-generation NTR/XTR MitraClip devices and fourth-generation MitraClip G4 system, respectively.[11,12] However, reports from the EXPAND and EXPAND G4 registries were limited by a 1-year follow-up duration, retrospective echocardiographic assessments, and recategorization of a significant proportion of baseline echocardiograms to MR 2+ following echocardiography core laboratory assessment.

Moderate or less residual MR (MR ≤2+) has traditionally been considered a reasonable outcome in high surgical risk DMR patients undergoing M-TEER.[9] In low surgical risk DMR patients evaluated in the National Institutes of Health-funded PRIMARY (Percutaneous or Surgical Repair In Mitral Prolapse

And Regurgitation for ≥60 Year-Olds; NCT05051033) trial of M-TEER vs surgery, adequacy of MR correction, defined as MR <2+ is one of the primary endpoints. In a recent STS/ACC TVT (Society of Thoracic Surgery/American College of Cardiology Transcatheter Valve Therapy) national registry analysis of 19,088 patients with moderate-to-severe or severe DMR undergoing M-TEER with the MitraClip device, the lowest mortality at 1 year was observed in patients with mild or less MR (MR ≤1+).[13] Even the presence of moderate residual MR, compared with mild residual MR, was associated with increased mortality and heart failure admissions at 1 year. Residual MR severity of mild or less after M-TEER for DMR was noted in 65.7% of patients at 30 days in the STS/ACC TVT registry, 79.2% of patients at 1 year in the EXPAND registry, and 88.8% of patients at 1 year in the EXPAND G4 registry.[11,12] In the CLASP IID Trial, the proportion of patients achieving MR ≤1+ was not statistically different between the PASCAL and MitraClip groups (77.2% for PASCAL and 67.8% for MitraClip). In this study, 21.1% of patients were treated with the contemporary PASCAL Precision system, and more than two-thirds of the patients were treated with the MitraClip G4 system (69.5%), respectively. The use of MitraClip G4 system in the EXPAND G4 registry was associated with an improvement in MR reduction compared with the older third-generation NTR/XTR devices used in the EXPAND registry. Similarly, the use of the newer PASCAL Precision system is expected to elevate the likelihood of attaining mild or less residual MR.[14] Although the threshold for acceptable residual MR after surgical mitral valve repair is lower, the CLASP IID Trial and Registry outcomes were achieved in an octogenarian, highly comorbid patient population unsuitable for surgery. As the field of M-TEER evolves with the REPAIR MR (Percutaneous MitraClip Device or Surgical Mitral Valve Repair in Patients With Primary Mitral Regurgitation Who Are Candidates for Surgery) and PRIMARY trials evaluating outcomes in a broader group of patients, including younger and lower surgical risk patients, achieving higher rates of mild-or-less residual MR should be more attainable.

With transcatheter mitral valve replacement developing as an option for the treatment of MR, improved understanding of the mitral valve anatomies associated with optimal M-TEER outcomes is important. Before the CLASP IID Registry, prospective data on M-TEER outcomes in complex anatomy patients was limited. Two-year results of the CLASP IID Registry demonstrated significant and sustained MR reduction with 91.9% at MR ≤2+ and 64.9% at MR ≤1+, respectively. Additionally, significant reduction in LV dimensions along with improvements in functional and quality-of-life outcomes were sustained. Of note, these results were similar to the typical, noncomplex anatomy patients in the randomized cohort, and were achieved with low reintervention rates, confirming that DMR patients with a broad range of mitral valve anatomies can be treated successfully and durably with the PASCAL system.

In the randomized cohort, there was no significant difference between the PASCAL and MitraClip groups in clinical outcomes including freedom from all-cause mortality, cardiovascular mortality, stroke, nonelective mitral valve reintervention or HFH at 2 years. All-cause mortality was numerically higher in the PASCAL group, attributed to a higher incidence of noncardiovascular deaths. The numerically higher rate of HFH in the PASCAL group may be due to the small sample size of the study and differing attrition rates in the 2 treatment groups at 2 years. This observed difference is unlikely to be related to the device, given that echocardiographic outcomes and reintervention rates were similar in both groups. Additionally, based on the post hoc regression analysis, treatment assignment was not a significant factor for HFH risk at 2 years. Some of the predictors of HFH identified in the regression analysis, including baseline NYHA functional class >3 and MR ≥2+ at discharge, were also associated with risk of HFH in other M-TEER studies.[15] Continued follow-up will be important to evaluate longer-term differences.

The SLDA rates in both the randomized and registry cohorts were low and comparable to other contemporary M-TEER studies.[11,12] The SLDA rate in the PASCAL group was numerically higher than in the MitraClip group, and this may be related to limited operator experience with the PASCAL system. Chordal entrapment was rare, with 1 case in the MitraClip group where the device became entangled during repositioning and none in the PASCAL group. The PASCAL system's elongation feature and smooth low-profile were designed to enable navigation in chordal-dense areas; hence, the absence of entrapment events is encouraging.

Since the Food and Drug Administration approval of the PASCAL system, the commercial availability of 2 M-TEER systems offers operators a choice. Device-selection decisions may be driven by individual operator preference, and the distinct features of the 2 devices in relation to patient anatomy. For example,

the elongation and bailout feature of the PASCAL system may be well-suited for use in chordal-dense commissures. Operators may use the MitraClip system in patients who require a smaller device or have a short posterior leaflet. In conclusion, these results show that M-TEER remains a safe and effective treatment and having multiple device options will enable tailoring interventions to individual patient needs.

STUDY LIMITATIONS. In the CLASP IID Trial, treatment allocation was unblinded, possibly contributing to a bias in outcomes assessment. Rigorous study oversight and independent event adjudication was implemented to mitigate this bias. The trial was not powered to discern differences between treatment groups outside of the primary endpoints. The 2:1 randomization ratio of PASCAL vs MitraClip patients presents limitations especially at later timepoints due to patient attrition. The proportion of patients with completed 2-year assessments was lower in the PASCAL group, which might have been coincidental or a chance occurrence. Reasons for missing visits include patients' unwillingness or inability to travel to investigational sites or visits to non-investigational sites. Sensitivity analysis for MR reduction was performed using multiple imputation method and the estimates were consistent with the unpaired analysis indicating robustness of the outcomes. Meaningful analysis of outcomes by device iterations and utilization in specific anatomies is limited by sample size and availability bias due to the later introduction of the PASCAL Precision system and PASCAL Ace.

CONCLUSIONS

Two-year outcomes from the CLASP IID Randomized Trial and Registry, the only prospective, clinical events committee and core lab-adjudicated study evaluating contemporary M-TEER therapies, reinforce M-TEER as a valuable treatment option for prohibitive risk DMR patients. In patients with a broad range of mitral valve anatomies, including those who were ineligible for randomization due to anatomical complexities, treatment with the PASCAL system was associated with robust and durable MR reduction accompanied with favorable ventricular remodeling and significant improvements in functional status and quality of life. These results confirm the sustained safety and effectiveness of the PASCAL system in treating a broad population of DMR patients.

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PERSPECTIVES

WHAT IS KNOWN? One-year results from the CLASP IID Trial, the first randomized trial to compare 2 M-TEER therapies, showed that the PASCAL system was safe, effective, and non-inferior to the MitraClip system in prohibitive surgical risk patients with DMR. Complementary outcomes in the CLASP IID Registry demonstrated the value of the PASCAL system in anatomically complex DMR patients.

WHAT IS NEW? Two-year results from the CLASP IID Trial and Registry provide the longest follow-up from a rigorous, echocardiography core laboratory and clinical events committee-adjudicated study of contemporary M-TEER. In the CLASP IID Trial, favorable clinical, echocardiographic, functional, and quality-of-life outcomes were maintained to 2 years, reinforcing M-TEER as a valuable treatment option for prohibitive-risk DMR patients. In the CLASP IID Registry, treatment with the PASCAL system resulted in similar outcomes, including durable MR reduction, favorable ventricular remodeling, and significant functional and quality-of-life improvements. These results confirm the sustained safety and effectiveness of the PASCAL system in treating a broad population of DMR patients.

WHAT IS NEXT? Patient follow-up will continue to 5 years, providing long-term M-TEER outcomes.

REFERENCES

1. Lim DS, Smith RL, Gillam LD, et al. Randomized comparison of transcatheter edge-to-edge repair for degenerative mitral regurgitation in prohibitive surgical risk patients. *JACC Cardiovasc Interv*. 2022;15(24):2523–2536. https://doi.org/10.1016/j.jcin.2022.09.005

2. Hausleiter J, Lim DS, Gillam Linda D, et al. Transcatheter edge-to-edge repair in patients with anatomically complex degenerative mitral regurgitation. *J Am Coll Cardiol*. 2023;81(5):431–442. https://doi.org/10.1016/j.jacc.2022.11.034

3. Zahr F, Smith RL, Gillam LD, et al. One-year outcomes from the CLASP IID randomized trial for degenerative mitral regurgitation. *JACC Cardiovasc Interv*. 2023;16(23):2803–2816. https://doi.org/10.1016/j.jcin.2023.10.002

4. Smith RL, Lim DS, Gillam LD, et al. One-year Outcomes of transcatheter edge-to-edge repair in anatomically complex degenerative mitral regurgitation patients. *JACC Cardiovasc Interv*. 2023;16(23):2820–2832. https://doi.org/10.1016/j.jcin.2023.10.020

5. Edwards Lifesciences. Edwards PASCAL Precision Transcatheter Valve Repair System: Instructions for Use. Accessed May 5, 2024. https://www.accessdata.fda.gov/cdrh_docs/pdf22/P220003D.pdf

6. Abbott. MITRACLIP® CLIP DELIVERY SYSTEM. Accessed May 12, 2023. https://www.accessdata.fda.gov/cdrh_docs/pdf10/P100009c.pdf

7. Marcoff L, Koulogiannis K, Aldaia L, et al. Echocardiographic outcomes with transcatheter edge-to-edge repair for degenerative mitral regurgitation in prohibitive surgical risk patients. *JACC Cardiovasc Imaging*. 2024;17(5):471–485. https://doi.org/10.1016/j.jcmg.2023.09.015

8. Stone GW, Vahanian AS, Adams DH, et al. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 1: clinical trial design principles: a consensus document from the Mitral Valve Academic Research Consortium. *J Am Coll Cardiol*. 2015;66(3):278–307. https://doi.org/10.1016/j.jacc.2015.05.046

9. Stone GW, Adams DH, Abraham WT, et al. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions: a consensus document from the Mitral Valve Academic Research Consortium. *J Am Coll Cardiol*. 2015;66(3):308–321. https://doi.org/10.1016/j.jacc.2015.05.049

10. Feldman T, Kar S, Elmariah S, et al. Randomized comparison of percutaneous repair and surgery for mitral regurgitation: 5-year results of EVEREST II. *J Am Coll Cardiol*. 2015;66(25):2844–2854. https://doi.org/10.1016/j.jacc.2015.10.018

11. Kar S, von Bardeleben RS, Rottbauer W, et al. Contemporary outcomes following transcatheter edge-to-edge repair. *JACC Cardiovasc Interv*. 2023;16(5):589–602. https://doi.org/10.1016/j.jcin.2023.01.010

12. von Bardeleben RS, Mahoney P, Morse MA, et al. 1-Year outcomes with fourth-generation mitral valve transcatheter edge-to-edge repair from the EXPAND G4 study. *JACC Cardiovasc*

Interv. 2023;16(21):2600–2610. https://doi.org/10.1016/j.jcin.2023.09.029

13. Makkar RR, Chikwe J, Chakravarty T, et al. Transcatheter mitral valve repair for degenerative mitral regurgitation. *JAMA*. 2023;329(20):1778–1788. https://doi.org/10.1001/jama.2023.7089

14. von Stein P, Stolz L, Haurand JM, et al. Outcomes and impact of device iterations in mitral valve transcatheter edge-to-edge repair: the REPAIR study. *JACC Cardiovasc Interv*. 2025;18(5):573–586. https://doi.org/10.1016/j.jcin.2024.11.016

15. Kessler M, Rottbauer W, von Bardeleben R. Impact of heart failure hospitalizations on clinical outcomes after mitral transcatheter edge-to-edge repair: results from the EXPAND study. *JACC Cardiovasc Interv*. 2024;26(7):1495–1503.

KEY WORDS CLASP IID, degenerative mitral regurgitation, DMR, MitraClip system, Mitral valve transcatheter edge-to-edge repair, M-TEER, PASCAL system

APPENDIX For an expanded Methods section and supplemental figures and tables, please see the online version of this paper.