Original article

Iberian experience with PASCAL transcatheter edge-to-edge repair for mitral valve regurgitation

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A B S T R A C T

Introduction and objectives: The PASCAL system is a novel device for transcatheter mitral valve repair based on the edge-to-edge concept. The unique features of this device might have a relevant impact on the repair outcomes. There are few data on clinical outcomes in real-life registries. The aim of this study was to report the early Iberian experience (Spain and Portugal) of the PASCAL system.
Methods: Procedural and 30-day outcomes were investigated in consecutive patients with symptomatic severe mitral regurgitation (MR) treated with the PASCAL system at 10 centers. Primary efficacy endpoints were technical success and degree of residual MR at discharge. The primary safety endpoint was the rate of major adverse events (MAE) at 30 days.
Results: We included 68 patients (age, 75 [68-81] years; 38% women; EuroSCORE II 4.5%). MR etiology was degenerative in 25%, functional in 65%, and mixed in 10%. A total of 71% of patients were in New York Heart Association (NYHA) functional class ≥ III. Technical success was achieved in 96% and independent capture was used in 73% of procedures. In the treated population, MR at discharge was ≤ 2+ in 100%, with no in-hospital deaths. At 30 days, the MAE rate was 5.9%, the all-cause mortality rate was 1.6%, 98% were in NYHA functional class ≤ II, and 95% had MR ≤ 2+ (*P* < .001).
Conclusions: Transcatheter mitral valve repair with the PASCAL system was safe and effective, with high procedural success and low rates of MAE. At 30 days, MR was significantly reduced, with a significant improvement in functional status.

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Experiencia ibérica con PASCAL para la reparación percutánea borde a borde en insuficiencia mitral

R E S U M E N

Introducción y objetivos: PASCAL es un dispositivo novedoso de terapia mitral transcatéter basada en la reparación borde a borde. Algunas características únicas podrían tener un impacto relevante en sus resultados. Hay pocos datos sobre los resultados clínicos en registros de la vida real. El objetivo de este estudio es publicar la experiencia ibérica precoz (centros de España y Portugal) del sistema PASCAL.
Métodos: Se incluyó prospectivamente a los pacientes tratados consecutivamente de insuficiencia mitral (IM) grave sintomática en 10 centros. El objetivo primario de eficacia fue el éxito técnico y el grado de regurgitación al alta. El objetivo primario de seguridad fueron los eventos adversos mayores (MAE) a 30 días.

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Resultados: Se incluyó a 68 pacientes (75 [68-81] años, 38% mujeres, EuroSCORE II 4,5%). La IM fue degenerativa en el 25% de los casos, funcional en el 65%, y mixta en el 10%. El 71% de pacientes estaban en clase funcional New York Heart Association (NYHA) ≥ III. El éxito técnico fue del 96% y la captura independiente se usó en el 73% de los procedimientos. Toda la población tratada obtuvo una IM al alta ≤ 2+ (100%) y no hubo muertes intrahospitalarias. A los 30 días, los MAE fueron del 5,9%, la mortalidad global del 1,6%, el 98% estuvieron en clase NYHA ≤ II y el 95% tuvieron IM ≤ 2+ (p < 0,001).
Conclusiones: El sistema PASCAL de terapia transcatéter mitral fue efectivo y seguro, con elevado éxito técnico y baja tasa de MAE. A los 30 días la IM se redujo significativamente, y hubo una mejoría en la clase funcional.

Abbreviations

MR: mitral regurgitation
NYHA: New York Heart Association
TEER: transcatheter edge-to-edge repair

INTRODUCTION

Mitral regurgitation (MR) is a highly prevalent and under-treated valvular heart disease, which carries a poor prognosis if left untreated.[1–3] Transcatheter edge-to-edge repair (TEER) using the MitraClip system (Abbott Vascular, United States) has been consolidated as an effective therapy for high-risk patients with MR, with high procedural safety and producing rapid recovery.[4–7] However, residual MR after TEER with MitraClip is not uncommon and is associated with worse outcomes.[8]

The PASCAL valve repair system (Edwards Lifesciences, United States) is a novel device for TEER. It offers special characteristic features including a central spacer, broad paddles made of pliable nitinol and the possibility of independent leaflet capture.[9] PASCAL Ace is a new device designed with a narrow profile. Pivotal studies[10] and German real-world experience[11,12] demonstrated a low complication rate and high survival with sustained MR reduction. The present study assessed the real-world experience of a postapproval patient cohort treated at Spanish and Portuguese tertiary care centers.

METHODS

Study design and population

This article covers the initial experience of transcatheter edge-to-edge mitral valve repair with the PASCAL system in the Iberian Peninsula (Spain and Portugal). This was a multicenter study collecting individual data from an unselected all-comer population from 10 hospitals with initial access to the PASCAL and PASCAL Ace systems for the treatment of severe symptomatic MR from October 2019 to September 2021.

Demographics, baseline and procedural characteristic and clinical/echocardiographic outcomes at follow-up were prospectively collected in a dedicated, shared database at each participating center. All procedures were performed under general anesthesia and guided by transesophageal echocardiogram (TEE) and fluoroscopy. Periprocedural complications were noted during the index hospitalization. The study was conducted in accordance with the institutional ethics committee of each participating center, and all patients provided signed informed consent for the procedure.

Endpoints and definitions

Standardized definitions of all patient-related variables, clinical diagnoses, and in-hospital complications and outcomes were based on the Mitral Valve Academic Research Consortium criteria unless indicated otherwise.[13] MR was assessed using standard 2-dimensional color Doppler methods and were graded using a 4-class grading scheme: mild, moderate, moderate-severe, and severe.

The primary efficacy endpoints were technical success (device successfully deployed as intended, delivery system successfully retrieved without procedural mortality or need for surgery or reintervention) and severity of MR at discharge in the treated population.

The main safety endpoint was freedom from major adverse events (MAE) at 30 days, including all-cause mortality, cardiac tamponade, emergent surgery, vascular complications, severe bleeding (major, extensive, life-threatening, or fatal bleeding), stroke, and myocardial infarction.

Secondary endpoints included the severity of MR at discharge on an on-treatment basis (at least 1 PASCAL device implanted, alive and without reintervention), device success (at 30 days, defined as successful device implantation, MR ≤ 2+, mean gradient < 5 mmHg and freedom from mortality, stroke, unplanned surgical or interventional procedures, and device failure), clinical success (as defined in the CLASP[14] approval trial as successful device implantation, MR ≤ 2+, and freedom from mortality, stroke, unplanned surgical or interventional procedures, and device failure at 30 days), reintervention, and change in clinical evaluation of New York Heart Association (NYHA) functional class during follow-up.

Statistical analysis

Results are presented as mean ± standard deviation for continuous normally distributed variables, median [interquartile range] for continuous nonnormally distributed data, and as number (percentages) for categorical data. Analysis of normality was performed with the Kolmogorov-Smirnov and Shapiro-Wilks test. Categorical data and proportions were compared using the chi-square or Fisher exact test. Comparisons of continuous variables were analyzed using the unpaired *t*-test and the Mann-Whitney U-test as appropriate. The McNemar paired-test and Wilcoxon matched-pairs signed-rank test were used to compare differences resulting from treatment as appropriate. An alpha error level of .05 was established and Stata 12.1 software (College Station, United States) was used for all analyses.

RESULTS

Patient population and baseline characteristics

A total of 68 patients (median age 75 years, 62% men) with symptomatic MR underwent transcatheter mitral valve repair

Table 1
Baseline characteristics

Baseline characteristics	Total (n = 68)	Functional MR (n = 44)	Degenerative MR (n = 17)
Age, y	75 [68-81]	72 [66-77]	84 [76-87]
Women	26 (38)	18 (41)	6 (35)
BSA	1.79 ± 0.18	1.79 ± 0.17	1.76 ± 0.20
Hypertension	57 (84)	36 (82)	15 (88)
Diabetes mellitus	22 (32)	17 (39)	3 (18)
Atrial fibrillation	40 (59)	26 (59)	10 (59)
CAD	30 (44)	19 (43)	6 (35)
PCI	22 (32)	14 (32)	5 (29)
CABG	9 (13)	4 (9)	3 (18)
Stroke/TIA	9 (13)	2 (5)	3 (18)
CKD	22 (32)	16 (36)	5 (29)
Previous valvular intervention	5 (7)	2 (5)	2 (12)
EuroSCORE II, mean	4.5 ± 3.6	4.6 ± 3.9	3.5 ± 2.6
STS, mean	4.1 ± 3.0	4.0 ± 3.4	4.2 ± 1.9
NYHA ≥ III	48 (71)	34 (77)	9 (53)
Previous heart failure admission	38 (56)	28 (64)	6 (35)
Medical treatment			
Beta-blockers	51 (75)	37 (84)	9 (53)
ACE-I /ARB	35 (52)	21 (48)	10 (59)
Sacubitril/Valsartan	24 (35)	22 (50)	0 (0)
Nitrates/Hidralazine	10 (15)	7 (16)	0 (0)
CRT	9 (13)	8 (18)	1 (6)

ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blockers; BSA, body surface area; CABG, coronary artery bypass graft; CAD, coronary artery disease; CKD, chronic kidney disease; CRT, cardiac resynchronization therapy. NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons Score; TIA, transient ischemic attack.
Data are expressed as No. (%), mean ± standard deviation, or median [interquartile range].

between October 2019 and November 2021. Baseline characteristics and center distribution are summarized in table 1 and figure 1. Patients were considered at high surgical risk, expressed by a mean EuroSCORE II of 4.5% and a relevant burden of comorbidities: 44% of patients had concomitant coronary artery disease, 13% had undergone surgical revascularization, and 7% had previous valve intervention. The prevalence of atrial fibrillation (59%) and chronic renal failure (32%) was high, most patients (71%) were in NYHA functional class III or IV and 38 patients (56%) had had a previous heart failure hospitalization in the last year.

Baseline echocardiographic parameters are shown in table 2. Most patients (96%) had moderate to severe (3+) or severe (4+) MR at baseline. MR etiology was classified as functional in 44 patients (65%), degenerative in 17 patients (25%), and mixed in the remaining 7 patients (10%). Median left ventricular ejection fraction was 43% and effective regurgitant orifice area 0.38 [0.30-0.49] cm^2. Optimal guideline-directed medical therapy in secondary MR was achieved in a high number of patients: 84% of patients were treated with beta-blockers, 98% with angiotensin inhibition (angiotensin converting enzyme inhibitors/angiotensin II receptor blockers/angiotensin receptor-neprilysin inhibitors, [ACE-I/ARB/ARNI:]), and 18% were treated with cardiac resynchronization therapy (CRT).

Procedural and intrahospital outcomes

Procedural outcomes are summarized in table 3. One PASCAL device was implanted in 52 patients (76%) and 2 devices in 16 patients (24%). Overall, technical success was achieved in 65 patients (96%). The procedure was aborted without PASCAL implantation in 3 patients (4%). One patient with a short posterior
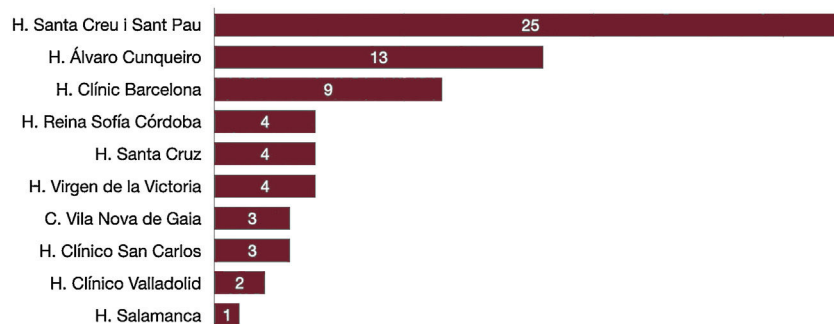

Figure 1. Distribution of cases performed by centers.

Table 2
Baseline echocardiographic variables

Echocardiographic variables	Total (n = 68)	Functional MR (n = 44)	Degenerative MR (n = 17)
LVEF	43 [30-60]	35 [26-55]	60 [55-69]
LVEDD, mm	59 ± 9	62 ± 9	52 ± 5
LVESD, mm	46 ± 12	50 ± 12	37 ± 6
MR severity ≥ 3+	65 (96)	41 (93)	17 (100)
MR mechanism			
Functional	44 (65)		
Degenerative	17 (25)		
Mixed	7 (10)		
EROA, cm²	0.38 [0.30-0.49]	0.39 [0.32-0.50]	0.36 [0.28-0.55]
sPAP by echo, mmHg	48 ± 13	48 ± 14	48 ± 11
Mitral valve area, cm²	5.4 [4.5-6.3]	5.4 [4.4-6.2]	5.5 [5.1-7.0]
Mitral mean gradient, mmHg	1.7 ± 0.9	1.8 ± 1.0	1.6 ± 0.7

EROA, effective regurgitant orifice area; LVEDD, left ventricle end-diastolic diameter; LVEF, left ventricle ejection fraction; LVESD, left ventricle end-systolic diameter; MR, mitral regurgitation; sPAP, systolic pressure pulmonary artery.
Data are expressed as No. (%), mean ± standard deviation, or median [interquartile range].

Table 3
Procedural and in-hospital data

Procedural data	Total (n = 68)
Number of PASCAL per patient	
1	52 (76)
2	16 (24)
Type of PASCAL Ace/P10Ace	
Ace	22 (33)
P10	43 (64)
Both	2 (3)
Optimization	47 (73)
Technical success	65 (96)
Technical complications	
Partial detachment	0
Total detachment	0
Leaflet tear	1 (1)
Chordae rupture	0
MitraClip switch	1 (1)
Major adverse events	
Death	0
Cardiac tamponade	0
Emergent surgery	1 (1)
Vascular complications	0
Major bleeding	0
Stroke	2 (3)
Myocardial infarction	0
MR severity ≤ 2+ at discharge	65 ± 100
Mean gradient (mmHg) at discharge	2.7 ± 1.3
Admission days	2 [1-3]

MR, mitral regurgitation.
Data are expressed as No. (%), mean ± standard deviation, or median [interquartile range].

leaflet had a tear with severe MR and underwent surgical repair. The second patient had leaflet tip calcification precluding appropriate PASCAL closure; the device was removed and a MitraClip was subsequently implanted. The third patient had worsening MR after leaflet clasping due to mitral valve distortion and the device was ultimately not released. Independent clasp

optimization was applied in 47 patients (73%). Median procedural time was 121 [IQR: 83-168] minutes. There were no cases of intraprocedural single leaflet device attachment. Median length of stay after the procedure was 2 IQR: 1-3] days. There were no in-hospital deaths. In the treated population, residual MR at discharge was ≤ 2+ in 100% of the patients and ≤ 1+ in 77%. The mean transmitral gradient increased from 1.7 mmHg at baseline to 2.7 mmHg at discharge (*P* = .0001). Transmitral gradient was significantly lower in patients treated with a single device than in those requiring 2 devices (2.4 vs 3.5 mmHg, *P* = .0037). A mean gradient ≥ 5 mmHg was observed in 10% of patients (n = 6) and was not related to the number of devices (3 patients treated with 1 device, *P* = .27) nor to the type of device (4 patients treated with PASCAL, 1 treated with ACE, and 1 treated with both devices, *P* = .10).

Follow-up outcomes

Thirty-day survival status was available in all patients (median follow-up time 223 [IQR: 105-439] days). Clinical success was achieved in 86.7% (59 of 68 patients). The primary safety endpoint, defined as a freedom from composite MAE rate at 30 days, occurred in 64 of 68 patients (94%). One patient died from cardiovascular causes due to sudden death at 30 days and another patient died from cardiovascular causes at 12 months of follow-up. The Kaplan-Meier survival curve of freedom from mortality is shown in figure 2. In-hospital stroke occurred in 2 patients and 1 patient had surgical conversion due to leaflet tear. At 30 days, 96% of patients were in NYHA class I or II and 95% of patients had MR ≤ 2+, with significant clinical and echocardiographic improvement from baseline (*P* = .001, figure 3).

At 12 months, 5 patients were hospitalized for cardiovascular causes with a Kaplan-Meier curve for survival and cardiovascular hospitalization of 13.85% (figure 2).

DISCUSSION

We report the first Iberian experience of TEER with the PASCAL device in patients with symptomatic functional and degenerative MR. The main findings of the study are: *a)* technical success was achieved in 96%, and MR in the treated population was reduced to
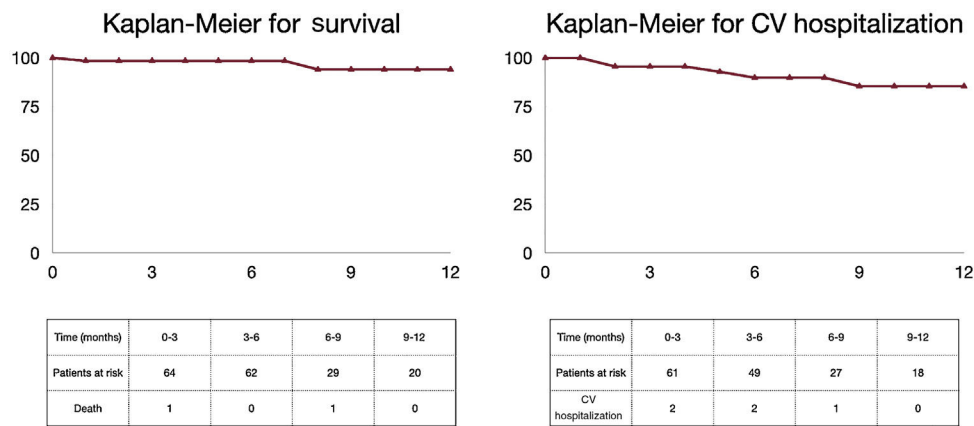
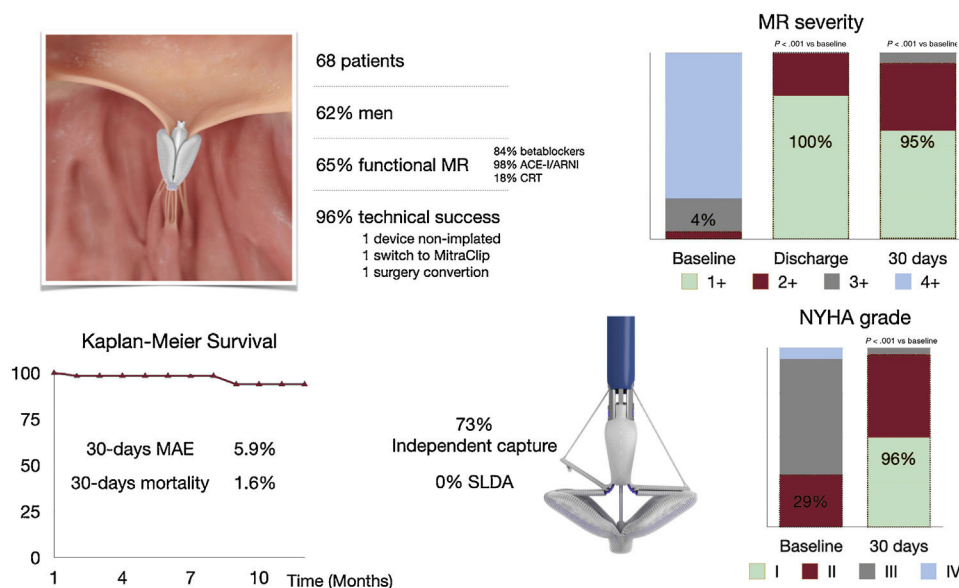**Figure 2.** Kaplan-Meier curve for survival and cardiovascular hospitalization. CV, cardiovascular.

Figure 3. Central Illustration. Iberian experience with PASCAL for transcatheter mitral regurgitation repair. Baseline characteristics, procedural results, and follow-up. ACE-I/ARB/ARNI, angiotensin converting enzyme inhibitors/angiotensin II receptor blockers/angiotensin receptor-neprilysin inhibitors; CRT, cardiac resynchronization therapy; MAE, major adverse events; MR, mitral regurgitation; NYHA, New York Heart Association; SLDA, single leaflet device attachment.

grade ≤ 2+ at discharge in 100% and to grade ≤ 1+ in 77% of patients; *b)* all-cause mortality and the MAE rate at 30 days were low at 1.6% and 5.9%, respectively; and *c)* the main reasons for technical failure were aborted procedures or a change to the MitraClip device due to worsening of MR (n = 2) or posterior leaflet tear (n = 1).

Our findings are derived from unselected real-world patients. In this initial experience, the suitability criteria for PASCAL were similar as previously used for MitraClip therapy.

Some special features differentiate the MitraClip and PASCAL devices:

- The central spacer seems to generate less leaflet tension in the mitral valve, and it could be useful in MR with atrial or ventricular tethering.
- Independent capture of leaflets. The independent capture allows 1 leaflet to be released while the other is captured. Until the development of the PASCAL system, capture of leaflets had been simultaneous and when trying to optimize the capture of one there was a risk of losing the other. The new G4 MitraClip system also incorporates this special feature. However, differences between the aggressivity of leaflet capture in the MitraClip system can reduce its use, reported in 49% of its initial experience.[15]

Baseline population characteristics were comparable with other real-world data from the German registry,[11,12] rather than the pivotal CLASP trial,[10,14] targeting a highly comorbid population with a mean EuroSCORE II of 4.5% and advanced NYHA functional class, > 70% in class III-IV.

Our results are in line with previous efficacy endpoints reported with the PASCAL repair system. The CLASP study achieved 95% technical success with MR ≤ 2+ in 96% of the patients at 30 days and real-world data from the German registry showed a technical success of 96% with residual MR ≤ 2+ in 93% of the patients. The results of this experience confirmed the safety profile of the PASCAL Repair system, with zero procedural mortality and a low rate of 30-day MAE (5.9%), similar to that reported in the CLASP and German studies (8.3% and 4.1%, respectively). Of note, there were no cases of intraprocedural single leaflet device attachment (1% in the German registry), which may be due to a higher rate of

independent clasp optimization (after initial simultaneous clasping) in the present series (73% vs 48% in the German study).

Importantly, there was a significant NYHA functional class improvement at 30 days (96% NYHA I-II), which is much higher than that observed in the German registry (72%), CLASP study (81%), or in our first reported experience with TEER with MitraClip in 2014[16] (81%).

Learning effect

Since our first publication, the learning curve achieved with MitraClip in terms of patient selection and increased procedural experience may have strongly impacted on the positive results obtained with PASCAL in the present study. Indeed, patient selection has changed after the COAPT and Mitra-FR trials, which showed that patients with severe secondary MR with EROA > 0.3 cm^2 and LVESD < 70 mm under optimal medical treatment were more likely to benefit from TEER. Our data confirm these findings, with a median EROA value of 0.39 cm^2 [IQR: 0.32-0.50 cm^2], a mean LVESD of 50 mm and optimal guideline-directed medical therapy: 84% patients with beta-blockers, 98% with ACE-I/ARB/ARNI, and 18% with cardiac resynchronization therapy.

In addition, increased procedural skills over time have led to a significant reduction in transseptal puncture-related complications (0% vs 3% in our initial experience with MitraClip), as well as a lower ratio of devices required per patient ($\geq$ 2 devices required in 39% in MitraClip early-generation vs 24% in the present study).

Limitations

The present study was observational in nature. Because the study was designed as a registry, all echocardiographic and clinical data were site reported and lacked independent adjudication by a core laboratory or an event committee. The absence of a randomized control group limits conclusions and the results for efficacy and safety should be regarded in the context of the early phase of the learning curve with a new device.

CONCLUSIONS

Transcatheter mitral valve repair with the PASCAL device was safe and effective for treating severe MR, with a high technical success rate, a low rate of procedural complications, and sustained reduction in MR severity at 30 days. Larger studies with a longer-term follow-up are warranted.

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AUTHORS' CONTRIBUTIONS

C.-H.P. Li: concept/design, data collection, data analysis/interpretation, drafting article, critical revision of article, approval of article, statistics. R. Estevez-Loureiro: concept/design, data collection, critical revision of article, approval of article. X. Freixa: data collection, critical revision of article, approval of article. R. Teles: data collection, critical revision of article, approval of article. A. I. Molina-Ramos: data collection, approval of article. M. Pan: data collection, critical revision of article, approval of article. L. Nombela: data collection, critical revision of article, approval of article. B. Melica: data collection, critical revision of article, approval of article. I. J. Amat-Santos: data collection, critical revision of article, approval of article. I. Cruz-González: data collection, critical revision of article, approval of article. Ll. Asmarats: doncept/design, data analysis/interpretation, critical revision of article, approval of article, statistics. R. Alarcón: data collection, critical revision of article, approval of article. L. Sanchis: data collection, critical revision of article, approval of article.

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CONFLICTS OF INTEREST

WHAT IS KNOWN ABOUT THE TOPIC?

- The PASCAL system is safe and effective: the CLASP study achieved 95% technical success with MR $\leq$ 2+ in 96% of the patients at 30 days and real-world data from the German registry showed technical success of 96% with residual MR $\leq$ 2+ in 93% of the patients. MAE previously reported in CLASP and German studies were 8.3% and 4.1%, respectively.
- The PASCAL system allows independent capture of leaflets, and it was used in 48% of patients in the real-world data from the German registry.

WHAT DOES THIS STUDY ADD?

- The Iberian experience confirms the safety and effectiveness of the Pascal system: technical success was 96%, and MR in the treated population was reduced to grade $\leq$ 2+ at discharge in 100% and to grade $\leq$ 1+ in 77% of the patients. All-cause mortality and the MAE rate at 30 days were low at 1.6% and 5.9%, respectively.
- The main reasons for technical failure were aborted procedures or a change to the MitraClip device due to worsening of MR (n = 2) or posterior leaflet tear (n = 1).
- The independent capture rate was 73%, which was higher than in previous publications.
- The Iberian patient profile is adjusted to the COAPT trial with a high rate of optimal medical treatment.

REFERENCES

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. *Lancet.* 2006;368: 1005–1011.
2. Iung B, Baron G, Butchart EG, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on valvular heart disease. *Eur Heart J.* 2003;24:1231–1243.
3. Dziadzko V, Clavel MA, Dziadzko M, et al. Outcome and undertreatment of mitral regurgitation: a community cohort study. *Lancet.* 2018;391:960–969.
4. Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med.* 2011;364:1395–1406.
5. 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;66:2844–2854.
6. Obadia J-F, Messika-Zeitoun D, Leurent G, et al. Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation. *N Engl J Med.* 2018. NEJ-Moa1805374.
7. Stone GW, Lindenfeld J, Abraham WT, et al. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. *N Engl J Med.* 2018;379:2307–2318.
8. Reichart D, Kalbacher D, Rübsamen N, et al. The impact of residual mitral regurgitation after MitraClip therapy in functional mitral regurgitation. *Eur J Heart Fail.* 2020;22:1840–1848.
9. Praz F, Spargias K, Chrissoheris M, et al. Compassionate use of the PASCAL transcatheter mitral valve repair system for patients with severe mitral regurgita-tion: a multicentre, prospective, observational, first-in-man study. *Lancet.* 2017;390:773–780.
10. Webb JG, Hensey M, Szerlip M. et al., 1-Year Outcomes for Transcatheter Repair in Patients With Mitral Regurgitation From the CLASP Study. *JACC Cardiovasc Interv.* 2020;13:2344–2357.
11. Mauri V, Besler C, Riebisch M, et al. German Multicenter Experience With a New Leaflet-Based Transcatheter Mitral Valve Repair System for Mitral Regurgitation. *JACC Cardiovasc Interv.* 2020;13:2769–2778.
12. Schlegel P, Crespo López P, Kreusser MM, et al. PASCAL-based mitral valve repair in an all-comer population: acute and mid-term clinical results. *ESC Hear Fail.* 2021;8:3530–3538.
13. 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;66:308–321.
14. Lim DS, Kar S, Spargias K, et al. Transcatheter Valve Repair for Patients With Mitral Regurgitation: 30-Day Results of the CLASP Study. *JACC Cardiovasc Interv.* 2019;12:1369–1378.
15. Chakravarty T, Makar M, Patel D, et al. Transcatheter Edge-to-Edge Mitral Valve Repair With the MitraClip G4 System. *JACC Cardiovasc Interv.* 2020;13: 2402–2414.
16. Carrasco-Chinchilla F, Arzamendi D, Romero M, et al. Initial Experience of Percu-taneous Treatment of Mitral Regurgitation With MitraClip® Therapy in Spain. *Rev Esp Cardiol.* 2014;67:1007–1012.