






ORIGINAL STUDIES

12-Month outcomes of transcatheter tricuspid valve repair with the PASCAL system for severe tricuspid regurgitation

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Abstract

Objectives: We investigated the durability of tricuspid regurgitation (TR) reduction and the clinical outcomes through 12 months after transcatheter tricuspid valve repair (TTVr) with the PASCAL Transcatheter Valve Repair System.

Background: TTVr has rapidly developed and demonstrated favorable acute outcomes, but longer follow-up data are needed.

Methods: Overall, 30 patients (age 77 ± 6 years; 57% female) received PASCAL implantation from September 2017 to May 2019 and completed a clinical follow-up at 12 months.

Results: The TR etiology was functional in 25 patients (83%), degenerative in three (10%), and mixed in two (7%). All patients had TR severe or greater (massive or torrential in 80%) and heart failure symptoms (90% in NYHA III or IV) under optimal medical treatment. Single-leaflet device attachment occurred in two patients. Moderate or less TR was achieved in 23/28 patients (82%) at 30 days, which was sustained at 12 months (86%). Two patients underwent repeat TTVr due to residual torrential TR (day 173) and recurrence of severe TR (day 280), respectively.

One-year survival rate was 93%; 6 patients required rehospitalization due to acute heart failure. NYHA functional class I or II was achieved in 90% and 6-minute walk distance improved from 275 ± 122 m at baseline to 347 ± 112 m at 12-month ($+72 \pm 82$ m, $p < .01$). There was no stroke, endocarditis, or device embolization during the follow-up.

Conclusions: Twelve-month outcomes from this multicenter compassionate use experience with the PASCAL System demonstrated high procedural success, acceptable safety, and significant clinical improvement.

Abbreviations: 6MWD, six-minute walk distance; EuroSCORE, European System for Cardiac Operative Risk Evaluation; IQR, interquartile ranges; LV, left ventricle; NYHA, New-York Heart Association functional class; RA, right atrium; RV, right ventricle; SLDA, single-leaflet device attachment; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TTVr, transcatheter tricuspid valve repair.

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KEYWORDS

transcatheter tricuspid valve intervention, PASCAL, 12-month outcomes, severe tricuspid regurgitation, right-sided heart failure

1 | INTRODUCTION

Severe tricuspid regurgitation (TR) represents a critical unmet need due to its high incidence, adverse prognosis, and symptom burden.¹ TR deteriorates cardiac performance and leads to poor prognosis in heart failure patients.^{2,3} Severe TR is characterized by concomitant atrial fibrillation and/or right ventricular (RV) enlargement and may solitarily occur despite the absence of overt TR causes.³ According to current guidelines, surgical tricuspid valve repair is recommended concomitantly to other surgical valve interventions.^{4,5} Isolated surgical TR repair/replacement remains controversial due to high periprocedural mortality and lack of evidence regarding the efficacy of tricuspid surgery compared to medical therapy.⁶ Therefore, most patients are placed on conservative diuretic therapy, rather than surgical therapy, for alleviating heart failure symptoms.

Transcatheter tricuspid valve repair (TTVr) has rapidly developed as an alternative treatment modality, and several devices have emerged in the clinical setting.⁷⁻⁹ For example, the initial retrospective analysis from the TriValve registry consisting of high-risk patients with severe TR demonstrated a survival benefit compared to medical therapy in a propensity-matched analysis.¹⁰ Additionally, early compassionate use experiences with the PASCAL Transcatheter Valve Repair System (Edwards Lifesciences, Irvine, CA) also demonstrated promising results in severe mitral¹¹ and tricuspid regurgitation⁸; both indications have received CE mark approval.

This follow-up report outlines the 12-month outcomes from the multicenter, observational compassionate use experience of the PASCAL Repair System in high-risk patients with severe TR.

2 | METHODS

2.1 | Patients

This compassionate use experience included six centers from Germany and North America. In this analysis, the patients who received device implantation and a 12-month clinical examination were enrolled to elucidate the 12-month outcomes of TTVr with the PASCAL device. Thus, four patients were excluded from the initial cohort ($n = 28$) of the previous report⁸ due to no device implantation ($n = 2$) and lack of a 12-month clinical visit in the participating center ($n = 2$). In addition to the initial cohort, six patients who received the PASCAL implantation for severe TR thereafter were enrolled in this investigation. Overall, 30 patients who underwent TTVr with the PASCAL Repair System from September 2017 to May 2019 were included in this report of 1-year outcomes.

All patients presented with New-York Heart Association (NYHA) functional class II to IV despite optimal medical therapy according to current guideline recommendations and were deemed at prohibitive surgical risk by the local heart team in consideration with clinical conditions. Eligible patients provided written consent and were included after acceptance from the corresponding national regulatory board on the basis of individual patient characteristics. No pre-specified inclusion or exclusion criteria were defined, given that this was a compassionate use experience with no study protocol. Patients were included if the operator judged that edge-to-edge leaflet repair would be feasible: in general, patients with a coaptation gap >15 mm, severe leaflet tethering, and pacemaker lead-induced TR were deferred from TTVr.

The primary outcome was the durability of TR reduction after PASCAL implantation, which was evaluated by longitudinal echocardiography data. At 30-day and 12-month follow-ups, NYHA functional class, six-minute walk distance (6MWD), and TR severity grade were assessed as major outcome parameters, along with major adverse cardiac and cerebrovascular events. Furthermore, echocardiographic parameters of right ventricular size and function were compared to baseline.

2.2 | TTVr with the PASCAL transcatheter valve repair system

Procedural details have been described previously.⁸ Briefly, the PASCAL Transcatheter Valve Repair System for TR is identical to the system used for treating mitral regurgitation. The system consists of a 22-Fr guide sheath, a steerable guide catheter, and a device delivery catheter which allow independent and atraumatic grasping of fragile tricuspid leaflets and device elongation for safe repositioning within the subvalvular apparatus. The PASCAL Repair System was introduced through a transfemoral approach into the right atrium. Once the device orientation was aligned to the failing coaptation, both paddles were opened and the clasp side was checked. Under guidance by transesophageal echocardiography, both leaflets responsible for the coaptation defect were grasped. After verification of stable leaflet insertion and grasp by both paddles, the PASCAL device was carefully deployed. After the procedure, patients without indications for oral anticoagulation received dual-antiplatelet therapy with aspirin and clopidogrel for a minimum of 1 month. Otherwise, patients continued oral anticoagulation without routine antiplatelet treatment. A representative case is shown in Figure 1.

In repeat TTVr procedures ($n = 2$), a conventional clipping device, that is, the MitraClip[®] XTR (Abbott Vascular, Santa Clara, CA), was selected instead of the PASCAL device due to its small device width,

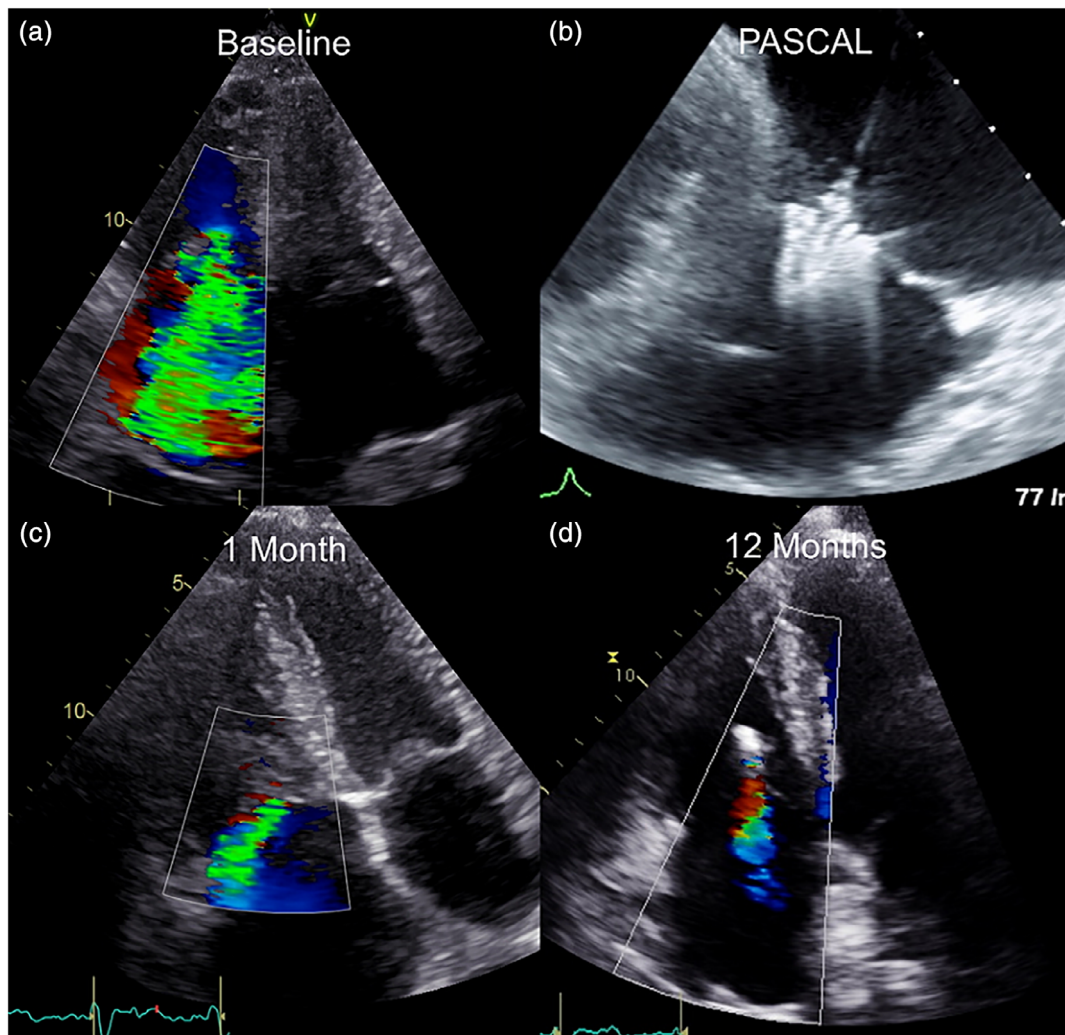


FIGURE 1 A representative case of TTVr with the PASCAL Transcatheter Valve Repair System. A 70-year-old man with severe TR suffered from severe right-sided heart failure and pulmonary hypertension (a). PASCAL implantation and successful TR reduction to mild (b). Mild residual TR was observed at 30 days (c) which further improved through 12 months (d). TR, tricuspid regurgitation; TTVr, transcatheter tricuspid valve repair [Color figure can be viewed at wileyonlinelibrary.com]

in order to minimize the interference to the device implanted with a potential risk of further device detachment.

2.3 | Echocardiography

All patients underwent transthoracic echocardiography according to current guidelines by the European Association of Cardiovascular Imaging and American Society of Echocardiography.^{12,13} TR severity grade was evaluated using the 5-grade scheme: none/trace, mild, moderate, severe, massive, and torrential, as recently proposed.¹⁴ To determine the 12-month durability of TR reduction, paired echocardiography was compared at baseline vs. 30-day and 12-month follow-up visits. All echocardiograms were performed by an experienced operator in the local echocardiography laboratory.

Systolic function of the left ventricle (LV) and RV and TR parameters were obtained at baseline of the index hospitalization. The

coaptation gap was measured at the maximal position perpendicular to the septal leaflet tip. The tricuspid annular diameter (septo-lateral), the mid-RV diameter, and the tricuspid annular systolic plane excursion (TAPSE) were evaluated to assess the RV remodeling after TR reduction.

To determine the 12-month durability of TR reduction, paired echocardiography was compared at baseline versus 30-day and 12-month follow-up visits ($n = 28$), wherein two patients were excluded due to death prior to the 12-month follow-up. Durable TR reduction was defined as a reduction of TR with a moderate or less grade on echocardiography through 12 months after TTVr.

2.4 | Statistical analysis

Continuous variables are expressed as mean \pm standard deviation if normally distributed, or as a median and interquartile ranges (IQR)

TABLE 1 Study population

	N = 30
Age, years	77 ± 6
Female, n (%)	17 (57)
EuroSCORE II, %	5.7 ± 5.2
STS score, % ^a	4.4 ± 2.8
NYHA functional class III or IV, n (%)	27 (90)
Coronary artery disease, n (%)	9 (30)
Previous myocardial infarction, n (%)	0 (0)
Coronary artery bypass, n (%)	3 (10)
Percutaneous coronary intervention, n (%)	5 (17)
Pulmonary hypertension, n (%) ^b	11 (37)
Previous valvular intervention, n (%)	11 (37)
Transtricuspid PM/ICD lead, n (%)	1 (3)
Chronic lung disease, n (%)	6 (20)
Chronic kidney disease, n (%)	21 (70)
Atrial fibrillation, n (%)	28 (93)
Loop diuretic agent, n (%)	30 (100)
Aldosterone antagonist, n (%)	20 (67)
N-terminal pro B-type natriuretic peptide, ng/L	1,679 [1087–2,495]
Left ventricular ejection fraction, %	59 ± 8
< 50%, n (%)	1 (3)
Right ventricular end-diastolic diameter, mm	44 ± 9
Tricuspid annular diameter, mm	49 ± 10
Coaptation gap, mm	7.1 ± 2.9
Coaptation gap >10 mm	6 (20)
Tricuspid annular systolic plane excursion, mm	16.2 ± 3.5
Etiology of TR	
Functional, n (%)	25 (83)
Degenerative, n (%)	3 (10)
Mixed, n (%)	2 (7)
Baseline TR grade	
Torrential TR, n (%)	13 (43)
Massive TR, n (%)	11 (37)
Severe TR, n (%)	6 (20)
Details of the procedure	
Number of devices implanted	1.6 ± 0.6
One device, n (%)	13 (43)
Two devices, n (%)	16 (53)
Three devices, n (%)	1 (3)
Commissure position treated, per patient	
Antero-septal, n (%)	16 (53)
Anterior-septal and postero-septal, n (%)	13 (43)
Postero-septal, n (%)	1 (3)
Procedural success, n (%)	25 (83)

Note: Data are shown as N (%), mean ± SD, or median [interquartile ranges].

Abbreviations: EuroSCORE, European System for Cardiac Operative Risk Evaluation; NYHA, New-York Heart Association; PM/ICD, pacemaker or implantable cardioverter defibrillator; TR, tricuspid regurgitation; STS, Society of the Thoracic Surgeons.

^aSTS score was calculated as the risk of an isolated mitral valve repair.

^bPulmonary hypertension was defined as estimated pulmonary artery systolic pressure ≥ 50 mmHg.

(first to third quartiles) if non-normally distributed. Distributions of each variable were tested using a Shapiro–Wilk test. Categorical variables are expressed as counts (percentages). Kaplan–Meier curves were described to elucidate survival outcomes through 12 months. Related samples were analyzed by a one-way repeated measures analysis of variance test if all the groups were normally distributed, or Friedman's two-way analysis of variance by ranks if at least one group was non-normally distributed. If the overall result was significant, post-hoc tests with a Bonferroni's correction were performed for each pair. Alluvial plots were processed with the statistical analysis software R (ver. 4.0.2, R Core Team, 2020). A two-tailed *p*-value of .05 was considered statistically significant. All statistics were performed by SPSS ver. 21 (IBM Corporation, Armonk, NY).

3 | RESULTS

Baseline characteristics and procedural details are summarized in Table 1. A total of 30 consecutive patients (77 ± 6 years, 57% women) were considered to be at high surgical risk with a European System for Cardiac Operative Risk Evaluation (EuroSCORE) II score of 5.7 ± 5.2%. The etiology of TR was functional in 25 patients (83%), degenerative in three (10%), and mixed in two (6.7%).

All patients had severe or greater TR at baseline: 43% in torrential TR, 37% in massive TR, and 20% in severe TR. Procedural success (implantation of at least 1 device with post-procedural TR of a moderate or less grade, with no device-related complication, mortality or conversion to surgery) was achieved in 25 patients (83%), wherein a total of 48 devices were implanted (1.6 ± 0.6 devices and max. Three devices, per patient). A sequential leaflet insertion by independent claspings was performed for 42 (88%) devices in 27 patients (90%). A single-leaflet device attachment (SLDA) was observed in two patients (6.7%); one occurred during the procedure, and another within 48 hours after the procedure. In the other 3 patients with post-procedural severe or greater TR, TTVr resulted in a TR reduction of at least 1 grade from baseline massive or torrential TR with an acceptable device deployment without evidence of injuries to leaflets and the surrounding structures. Hence, baseline torrential TR decreased to severe TR in 2 patients, and in another patient, a suboptimal TR reduction (massive TR to severe TR) was accepted because a sufficient RA pressure reduction (mean 25 to 17 mmHg, v wave 30 to 15 mmHg) was achieved, while the TV inflow gradient increased to 3 mmHg after two devices deployment. During the index procedure, no patient died or required bailout surgery.

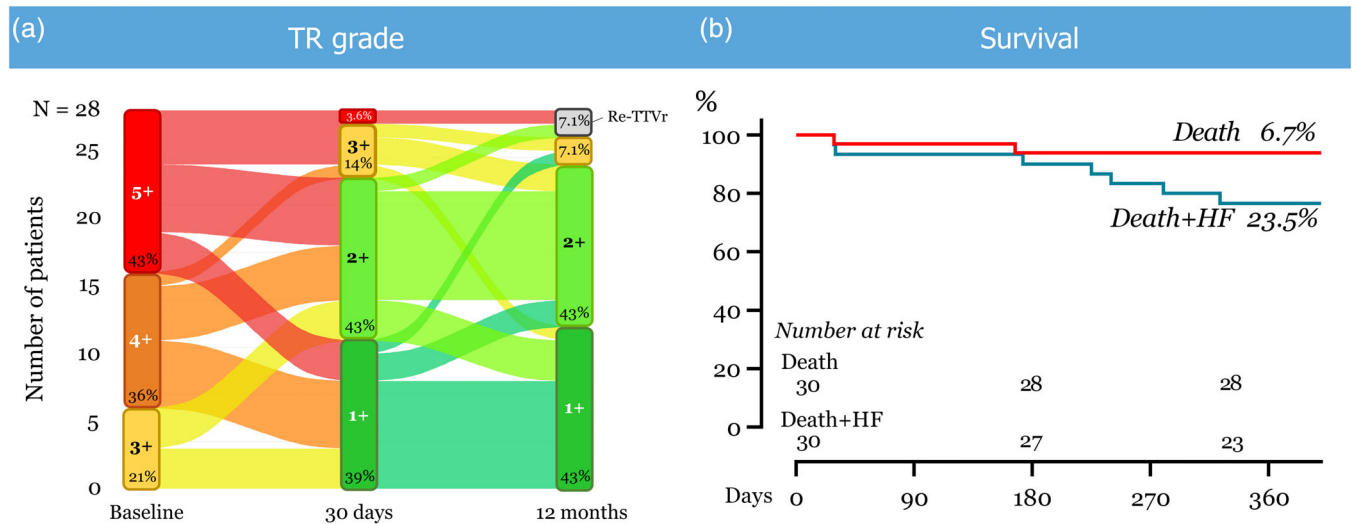


FIGURE 2 (a) TR reduction (b) Kaplan–Meier curves after the index procedure for severe TR. HF, heart failure; TR, tricuspid regurgitation [Color figure can be viewed at wileyonlinelibrary.com]

3.1 | Durability of TR reduction

Of the 30 patients, TR severity was evaluable in 28 patients at 12-month follow-up. Data were not available for two patients due to death prior to the 12-month follow-up schedule. TR reduction was durable in 89% of patients (25/28), demonstrating a sustained TR reduction of at least 1 grade without reintervention at 12 months. Moderate or less TR without reintervention was achieved in 86% (24/28) at 12 months, compared to 82% (23/28) at 30 days.

Comparing 30-day and 12-month TR severity, 21% (6/28) of patients showed further TR reduction, while 14% (4/28) showed worsening TR: two with moderate TR from mild TR at 30-day and two with a recurrence of severe or greater TR. The other patients (64%) had unchanged TR reduction from the 30-day to 12-month follow-up. Overall, there was no significant difference in TR grade between 30 days and 12 months ($p = .96$). An alluvial plot of TR grade through 12 months demonstrated consistent TR reduction achieved by the PASCAL implantation (Figure 2(a)).

3.2 | Functional and clinical outcomes

At 12 months, 28 patients (93%) were alive, and rehospitalization due to heart failure was experienced by 6 patients (20%) (Figure 2(b)). At 12 months, 27 of 30 patients (90%) were in NYHA functional classes I or II (Figure 3(a)), and 6MWD significantly improved from 275 ± 122 m at baseline to 328 ± 115 m at 30 days ($+53 \pm 53$ m, $p < .0001$) and 347 ± 112 m at 12 months ($+72 \pm 82$ m, $p < .0001$) (Figure 3(b)). There was no significant difference between 30 days and 12 months ($+17 \pm 51$ m, $p = .48$).

Repeat TTVr was performed in two patients (6.7%): one for remaining torrential TR at 173 days due to SLDA within 48 hr and one for recurrence of severe TR at 280 days. Both procedures

achieved stable device deployment without further device-related complications; however, severe TR remained in the SLDA case and moderate TR was achieved in the recurrent TR case.

Clinical outcomes at 30-day follow-up are summarized in Table 2. Two patients died due to cardiovascular reasons; one patient with an acute SLDA died presumably of cardiac deterioration (POD 29), and another patient who had presented with severe pulmonary hypertension at baseline was repeatedly admitted after 22 and 166 days due to heart failure decompensation. In the latter case, invasively assessed pulmonary systolic pressure was 76 mmHg with severe RV dysfunction (TAPSE 16 mm and RV fractional area change 30% with an RV/LV ratio > 1). Despite achieving a durable TR reduction (baseline torrential TR to moderate TR at 30-day) by TTVr, TAPSE reduced from 16 mm at baseline to 9 mm at 30 days, while the pulmonary artery pressure was unchanged with an increase of NTpBNP from 2094 ng/L to 3,396 ng/L at 30 days. The patient died 167 days after the TTVr due to terminal heart failure. Including this case, rehospitalization due to heart failure was observed in six patients and the mean duration from the index procedure to the rehospitalization was 212 ± 103 days (Supplemental Table 1).

Patients who experienced major adverse events ($n = 7$) were younger (74 ± 8 vs. 78 ± 4 years, $p = .032$), and had a higher frequency of torrential TR at baseline (71% vs. 35%), a larger mid-RV diameter (47 ± 5 vs. 43 ± 10 mm, $p = .047$), and a higher TV inflow gradient (1.3 mmHg [IQR 1.1–1.5] vs. 1.0 mmHg [IQR 1.0–1.0], $p = .019$) than those without events ($n = 23$). No other differences were found in 6MWD, LV ejection fraction, TAPSE and TR gradient (Supplemental Table 2).

3.3 | RV remodeling through 12-month follow-up

Changes in echocardiographic parameters were compared in consecutive patients through 12-month follow-up visits (Table 3). Through

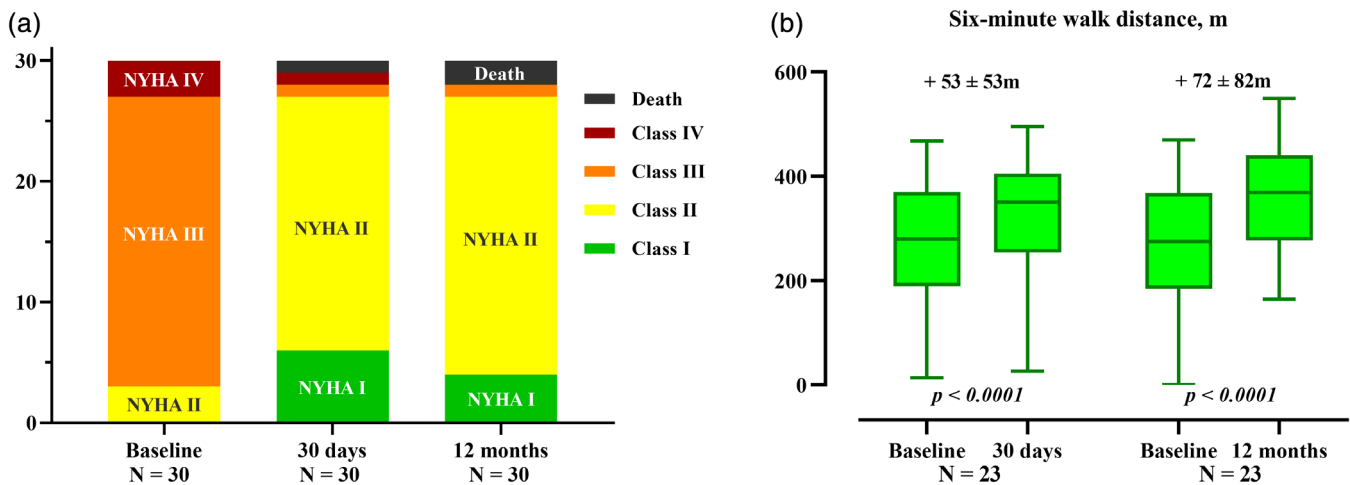


FIGURE 3 Changes in New York Heart Association functional class and 6-minute walk distance. (a) 12-month follow-up of the NYHA functional class. (b) Changes in 6-minute walk distance. Data are presented as box plots (25th centile, median, and 75th centile) and whisker (fifth centile, median, and 95th centile). NYHA; New-York Heart Association [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 2 Clinical outcomes at 12-month follow-up

Major adverse events	N = 30
Cardiovascular mortality	2 (6.7) ^{a,b}
Infectious endocarditis	0
Stroke	0
Rehospitalization due to heart failure	6 (20.0) ^a
Single-leaflet device attachment	2 (6.7) ^{b,c}
Conversion to surgery	0
Recurrent severe tricuspid regurgitation	2 (6.7)
Repeat tricuspid valve intervention	2 (6.7) ^c

Note: Data are shown as N (%). Major adverse events were defined as mortality, rehospitalization due to heart failure, single-leaflet device attachment, conversion to surgery, recurrent severe tricuspid regurgitation, repeat tricuspid valve intervention, infectious endocarditis and stroke.

^aOne patient was readmitted on days 22 and 166 and died on day 167 following the second hospitalization due to heart failure.

^bOne patient with an acute single-leaflet device attachment during the index procedure died on day 29.

^cOne patient underwent repeat intervention due to remaining torrential tricuspid regurgitation with a single-leaflet device attachment within 48 hours.

12 months, the septo-lateral tricuspid annular diameter decreased from 47 ± 8 to 40 ± 6 mm and the mid-RV diameter from 44 ± 10 to 35 ± 6 mm. The TV inflow gradient increased from 1.0 mmHg [IQR 1.0–1.0] to 1.5 mmHg [IQR 1.0–2.0] at 30 days and 1.4 mmHg [IQR 1.0–3.0] at 12 months. There was no patient with a TV inflow gradient above 3.5 mmHg during the follow-up. The RV/right atrium (RA) systolic gradient increased through 12 months ($p = .014$), wherein 6 of 22 patients (27%) presented $>50\%$ and at least 10 mmHg increase from baseline without 12-month adverse events. The TAPSE was unchanged through 12 months ($p = .16$). These RV parameters did not significantly change from 30 days to 12 months.

4 | DISCUSSION

In this multicenter, compassionate use experience from six tertiary care centers in Germany and North America, we report 12-month outcomes of TTVr with the PASCAL Repair System. The main findings show 93% survival rate and sustained TR reduction through 12 months (moderate or less TR in 86%). At 12 month follow-up, 26% of patients treated by TTVr experienced clinical adverse outcomes of death or HF rehospitalization. Sustained improvement in clinical symptoms was also observed, with NYHA class I or II in 90% and a 6WMD increase of $+72 \pm 82$ m. No additional safety events related to the PASCAL device were documented during the follow-up. Overall, these findings support the durable efficacy and safety of TTVr with the PASCAL device.

4.1 | Durable TR reduction with the PASCAL Transcatheter valve repair system

The high rate of durable TR reduction confirms the early experience with the PASCAL Repair System, and demonstrates that the encouraging initial results translated into a durable reduction of TR with favorable long-term outcomes.⁸ Nevertheless, a few patients experienced recurrent severe TR within 12 months, which was associated with advanced right-sided cardiac enlargement. Importantly, no injury to leaflets and their adjacent anatomies were documented, and there was no further SLDA beyond the index hospitalization. These findings have emphasized the importance of secure leaflet grasping at the index procedure, while also maintaining optimal guideline-derived medical treatments.

Compared with a previous multicenter prospective TRILUMINATE trial using the TriClip[®] (Abbott Vascular, Santa Clara, CA),⁹ procedural success (moderate or less TR) was more frequently documented in the present study (82% vs. 57%), even though patients with large

TABLE 3 Echocardiographic RV parameters after TTVr with the PASCAL® implantation

	Baseline		30 days		12 months		Baseline versus 30 days		Baseline versus 12 months		30 days versus 12 months	
	N	Values	N	Values	N	Values	p value	p value	p value	p value		
Tricuspid annular diameter, mm	17	47 ± 8 (34, 65)	17	40 ± 7 (24, 52)	17	40 ± 6 (28, 48)	.002	.003	.003	1.0		
Mid-RV diameter, mm	18	44 ± 10 (29, 62)	18	39 ± 8 (26, 52)	18	35 ± 6 (26, 47)	.085	<.001	<.001	.62		
TAPSE, mm	19	16.8 ± 4.1 (8.0, 25.0)	19	15.0 ± 3.5 (8.0, 22.0)	19	16.0 ± 4.2 (7.9, 22.0)	Overall ANOVA test p = .16					
Tricuspid valve inflow gradient, mmHg	25	1.0 [1.0–1.0] (1.0, 1.8)	25	1.5 [1.0–2.0] (1.0, 3.2)	25	1.4 [1.0–3.0] (1.0, 3.5)	.022	.014	.014	1.0		
RV/RA systolic gradient, mmHg	16	22 [17–31] (14, 43)	16	28 [25–44] (21, 59)	16	31 [25–37] (21, 72)	.040	.031	.031	1.0		

Note: Data are shown as mean ± SD or median [interquartile ranges] (min., max.). One-way repeated measure ANOVA (if all groups were normally distributed) or Friedman's test (if at least one group was not normally distributed) were performed, and post-hoc tests with Bonferroni's correction if *p* value < .05 in the overall analysis.

Abbreviations: RA, right atrium; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation.

coaptation defects and a higher TR grade (massive or torrential TR 80% vs. 68%) were treated in the PASCAL experience. In a previous MitraClip® evaluation, a large coaptation gap was a strong predictor for procedural failure of TTVr.¹⁵ Despite treating highly challenging anatomies in the majority of patients in this experience, durable TR reduction was achieved, which we attribute to the unique features of the PASCAL device. Hence, sequential leaflet capture with the PASCAL device enables movement of the lateral leaflet to the septal leaflet to bridge the coaptation gap, and a central spacer provides a synergetic effect in coaptation enhancement. The elastic device material lessens the traction stress on the target leaflets and avoids valve injuries. These advantageous device features might have facilitated the durable efficacy in TTVr. Nevertheless, when compared with the TRILUMINATE trial, the findings should be carefully interpreted, because the present experience was conducted retrospectively, without a central echocardiography laboratory or clinical events committee.

4.2 | Clinical outcomes through 12 months

Cooperating with the durable TR reduction, the mid-term mortality was low (1-year 6.7%), comparable to previous studies.^{7,9} The favorable outcomes could be explained by clinical characteristics of the population; most patients presented with preserved LV ejection fraction (97%) and prevalence of pulmonary hypertension was relatively low (37%). Hence, the majority of the population had isolated TR without underlying left-sided cardiac disease. In such condition, the hemodynamic benefits from mitigating RV volume overload would have been optimally obtained, which might have improved the clinical course of HF.

The most frequent cause of HF rehospitalization was related to a recurrence of severe or greater TR requiring further treatments. In two patients, repeat TTVr was feasible with a technical success; however, TR reduction for the SLDA case was suboptimal, resulting in residual severe TR (Supplement Table 1). On the other hand, a few patients experienced episodes of HF rehospitalization despite optimal results achieved. Although the mechanisms still remains unclear, baseline severe pulmonary hypertension appears to be one of the important factors for survival after TTVr. Thereby, a long-standing RV pressure overload might have deteriorated RV systolic function.

Indeed, the adverse events during the follow-up were associated with more advanced RV remodeling (mid RV diameter 47 ± 5 vs. 43 ± 10 mm, *p* = .047) (Supplement Table 2). This may be an important finding that advanced RV cavity size is associated with mortality or HF rehospitalization after TTVr. In this moment, no conventional echocardiographic markers of RV dysfunction have proven to be useful outcome predictors in patients undergoing TTVr.¹⁶

4.3 | Effects on the right-sided cardiac chamber and its function

A facilitated reduction of TR volume mitigates RV volume overload and leads to RV size reduction, which further improves left-sided

cardiac hemodynamics.^{17,18} An immediate elimination of RV volume overload might have led to a slight reduction of TAPSE at 30 days, despite having no significant differences through 12 months. Indeed, a reduction of the RV diameter was observed after TTVr, and remained until 12 months. Despite no relation to adverse events, the RV/RA systolic gradient increased after TTVr in a considerable amount of patients. The mechanisms could be a decrease of RA pressure and an increase of RV stroke volume by TR reduction. This finding has been similarly observed in a previous investigation using invasive hemodynamic measurements.¹⁹ In addition, providing that the RA pressure is ventricularized due to a large coaptation defect, early terminated blood inflow from the RA to the RV could mask the increased RV/RA systolic gradient, leading to a discrepancy between the echo-based estimation and the actual pulmonary systolic pressure.²⁰ In such condition, RV/RA systolic gradient may increase after RA pressure improved by TTVr. Therefore, in particular for TTVr candidates with massive or torrential TR, an invasive evaluation for right-sided cardiac function is vital to elaborate the pathophysiology.

Altogether, TTVr with the PASCAL Repair System achieved favorable hemodynamic ameliorations, and consistently improved heart failure symptoms and physiological performances in patients with severe TR, which might be associated with the extent of the remodeling in the tricuspid annulus and the RV chamber.

5 | LIMITATIONS

Despite being designed as a multicenter observational study, several limitations should be acknowledged. First, this study was conducted in tertiary care centers, and the procedures were performed by experienced operators. Therefore, this result might not be translatable to centers with less experience. Second, it appears likely to choose candidates with large coaptation gaps due to potential advantages from PASCAL's independent clasps and the central spacer, which might have caused a considerable selection bias toward more complex anatomies of severe TR. Indeed, one-fifth of the population had a coaptation gap of ≥ 10 mm, which has been usually excluded from TTVr using conventional edge-to-edge repair devices. Finally, the study population was relatively small, and the echocardiographic follow-up was performed in each participating center without a central echocardiographic laboratory. Therefore, these findings should be verified by future studies with larger cohorts.

6 | CONCLUSIONS

TTVr with the PASCAL Repair System is associated with durable TR reduction at 12 month follow-up, with low rates of mortality and HF hospitalization. Despite advanced baseline HF symptoms, consistent improvements in clinical symptoms (NYHA and δ WMD) and favorable RV reverse remodeling were sustained at long-term follow-up. The pivotal randomized CLASP TR study will further define the clinical impact of PASCAL TTVr compared with medical therapy.

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CONFLICT OF INTEREST

Dr. Philipp Lurz is a consultant for Abbott, Edwards Lifesciences, and Medtronic. Dr. Neil P. Fam has received speaking honoraria from Abbott Vascular, and is a consultant for Edwards Lifesciences. Dr. Kim A. Connelly has received speaking honoraria from Abbott Vascular. Drs. Daniel Braun and Michael Nabauer have received speaking honoraria from Abbott Vascular. Dr. Ralph Stephan von Bardeleben has received speaking honoraria from Abbott Vascular and Edwards Lifesciences. Dr. Jörg Hausleiter has received speaking honoraria and research support from Abbott Vascular and Edwards Lifesciences; and is a consultant for Edwards Lifesciences. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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