

TR grade 2 or less achieved in ...



*... of PASCAL Ace implant patients**

*Wild, EuroPCR 2021



PASCAL
Platform



Cardioband
Tricuspid System
(TriBAND study)



EVOQUE Valve
(TRISCEND study)

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therapies for tricuspid regurgitation



Edwards

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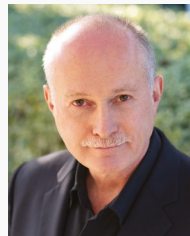
At Edwards Lifesciences, we recognise the unique challenges faced by cardiologists when treating patients with tricuspid regurgitation (TR). In this highly symptomatic and comorbid patient population, treatment options have historically been considered limited. Wide coaptation gaps, leaflet tethering, and the presence of pacemaker leads further complicate treatment choice, emphasising the need for treatment options that are tailored to a patient's individual requirements.

To address these challenges, Edwards Lifesciences has developed a range of transcatheter treatment approaches for patients with severe TR, including the PASCAL transcatheter valve repair system, the Cardioband tricuspid valve reconstruction system, and the EVOQUE tricuspid valve replacement system.*

This issue of *Transcatheter Mitral and Tricuspid Therapies Today* brings together the latest evidence on these treatment approaches in patients with TR, including real-world transcatheter tricuspid valve repair (TTVr) studies across different centres, the TriBAND study focussing on transcatheter annuloplasty, and the TRISCEND study on tricuspid valve replacement. Finally, we discuss how TTVr, annular reduction and tricuspid valve replacement may fit together in the emerging treatment landscape for TR.



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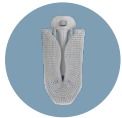
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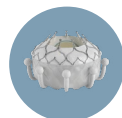
Real-world outcomes with the PASCAL Platform in TR



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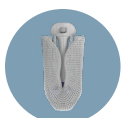
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PASCAL Platform in TR

Compassionate use experience with the PASCAL Platform in TR: One-year outcomes



Dr Nicole Karam

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Dr Nicole Karam is Associate Professor in the Department of Cardiology at the European Hospital Georges Pompidou, Paris. During a period at the Ludwig-Maximilians Universität (LMU) in Munich, Germany, Dr Karam became involved in the CLASP TR EFS study. She is also involved in the TRI-FR clinical trial.

Early data from a compassionate use study have demonstrated the safety and efficacy of the PASCAL platform in patients with clinically significant TR, including those with severe TR and large coaptation gaps (please read [TMTT Today #2](#) and [TMTT Today #4](#) for more information).^{1,2} Now, Dr Nicole Karam discusses one-year data from this study, alongside data from CLASP TR EFS (Edwards PASCAL Transcatheter Valve Repair System In Tricuspid Regurgitation Early Feasibility Study), which together demonstrate safety and durable TR reduction with the PASCAL platform in patients with severe TR.^{3,4}



My experience with the Edwards PASCAL platform was gained at LMU in Munich, where the technology was used first in the treatment of patients with mitral regurgitation (MR) and more recently for patients with TR. Comprising the PASCAL implant and the smaller PASCAL Ace implant, the PASCAL platform has a number of distinctive features that contribute specifically to good therapeutic and safety outcomes for patients with TR. First, the PASCAL implants contain a central spacer which fills the regurgitant orifice area and reduces the coaptation gap, and contoured paddles that are shaped to maximise leaflet coaptation and minimise leaflet stress during capture. Second, the implants can perform independent grasping and optimisation to allow the

user to ensure good capture of the leaflets, especially in difficult anatomies. Third, the implants are flexible due to their Nitinol frame and have a spring-based passive closing mechanism, enabling acute implant flexing and designed to reduce clinically significant leaflet damage. Finally, the ability to elongate the implants facilitates navigation

through the dense chordae of the tricuspid valve and reduces the risk of entanglement,⁵ especially with the smaller PASCAL Ace implant.

'The results were pretty impressive. At 30 days, there was procedural success and a reduction in TR to moderate or less in 82% of patients. 86% of patients had moderate TR or less at 12 months'
Dr Nicole Karam

Compassionate use study

In the compassionate use study, 30 patients with severe TR were treated with the PASCAL platform across six sites in Germany and North America. These patients had a mean age of 77 ± 6 years and 57% were female. Most patients

(83%) presented with functional TR, 10% had degenerative TR and 7% had TR of mixed aetiology. TR severity was severe (21% of patients), massive (36%) or torrential (43%), and the patients were highly symptomatic (mean EuroSCORE II was 5.7 ± 5.2 and 90% were in New York Heart Association [NYHA] functional class III or IV at baseline).³

On average, 1.6 ± 0.6 devices were implanted per patient, with most devices positioned in the anteroseptal commissure (53%) or anteroseptal and posteroseptal commissures (43%). Procedural success* in this very early experience with the PASCAL platform was high (83%).³

Patients treated with the PASCAL platform benefitted from sustained reductions in TR (Figure 1), with most patients (86%) achieving TR grade ≤ 2 at the 12-month follow up. The reduction in TR following implantation was durable in 89% of patients, based on a sustained TR reduction of at least one grade without reintervention. There was no difference in TR grade between the 30-day and 12-month follow ups in most patients; between 30 days and 12 months, TR reduction was unchanged in 64% of patients, improved in 21%, and worsened in 14%.³

In addition to significant TR reduction, patients treated with the PASCAL platform experienced sustained improvements in clinical symptoms, with 90% of patients achieving NYHA class I or II and 6-minute walk distance (6MWD) increasing by 72 ± 82 m (Figure 2).³

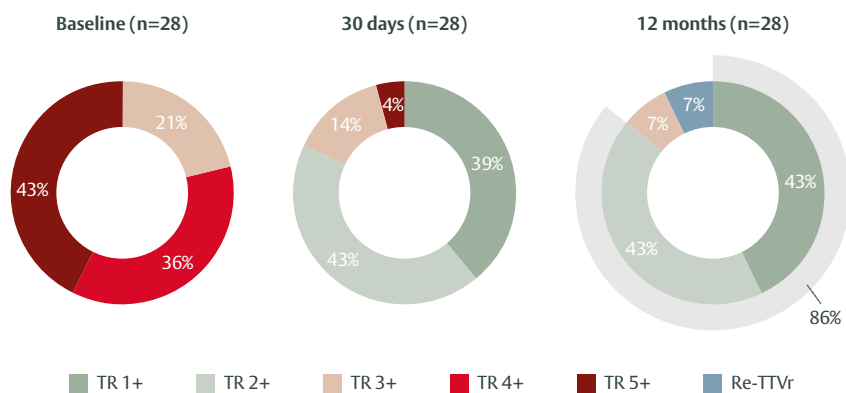


Figure 1. TR reduction and survival up to 12 months using the PASCAL repair system.³

Adapted from Kitamura M et al. 2021

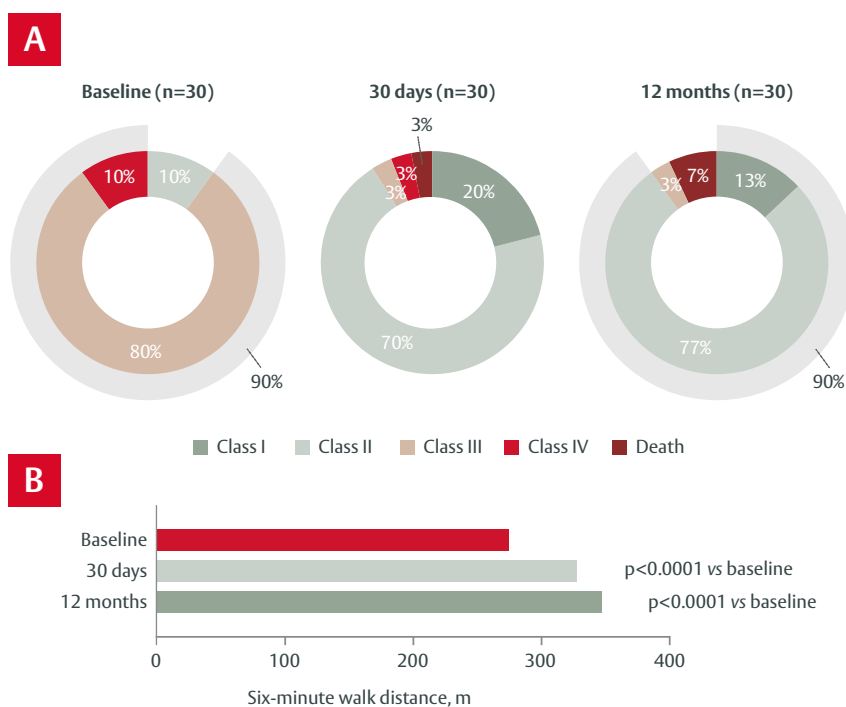


Figure 2. Functional outcomes following TTVr using the PASCAL repair system. (A) NYHA class; (B) 6-minute walk distance.³

Adapted from Kitamura M et al. 2021

'We started with 90% of patients in NYHA class III–IV. By the end of the study we had 90% of patients in NYHA class I–II, so great functional results'

Dr Nicole Karam

* Implantation of at least 1 device with post-procedural TR of a moderate or less grade, with no device-related complications, mortality or conversion to surgery

Table 1. Major adverse events following TTVr using the PASCAL repair system.³

Major adverse events (N=30)	n (%)
Cardiovascular mortality	2 (6.7)
Stroke	0
Endocarditis	0
Rehospitalisation due to heart failure	6 (20)
Single-leaflet device attachment	2 (6.7)
Recurrent severe tricuspid regurgitation	2 (6.7)
Repeat tricuspid valve intervention	2 (6.7)

Adapted from Kitamura M *et al.* 2021

'We had a great improvement in 6-minute walking distance at 12 months'

Dr Nicole Karam

Safety outcomes following the procedure were very good (Table 1), with 93% survival at 12 months and no cases of stroke or infectious endocarditis.³ Two patients died after the procedure, one at 29 days with an acute single-leaflet device attachment, the second at 167 days and had severe pulmonary hypertension at baseline.³

CLASP TR Early Feasibility Study – 6 months' follow-up

CLASP TR EFS was a prospective, single-arm, multicentre, US study evaluating the safety and performance of the PASCAL platform in 63 symptomatic patients with severe functional or degenerative TR.⁴

Patients had a similar profile to those included in the compassionate use study. They had a mean age of 78 ± 9 years, were highly symptomatic (70% were NYHA functional class III or IV, 89% had atrial fibrillation/flutter and 53% had pulmonary hypertension), and 96% had severe or greater TR at baseline (29% with massive TR, 40% with torrential TR). Most patients (65.5%) received the PASCAL

implant, 29% received the PASCAL Ace implant and 5.5% received both devices.⁴

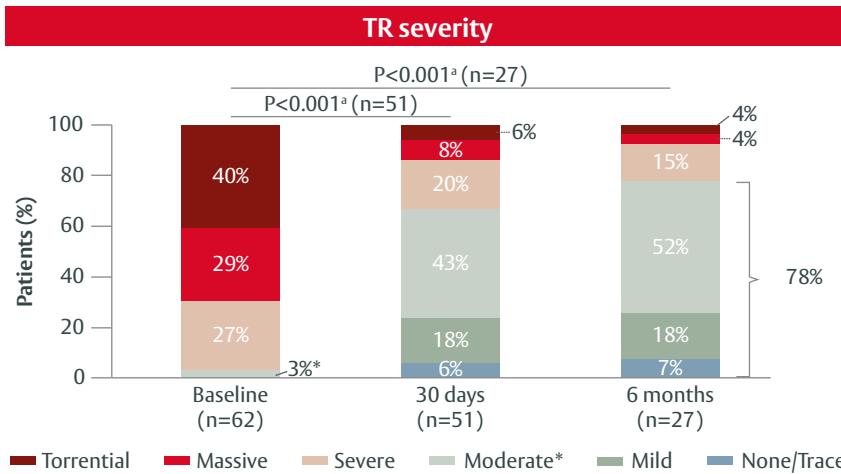
The rate of implant success* was 91% in the intent-to-treat population. In the treated population, mean device time was 159 min and procedural† (98%) and clinical success‡ (87%) were both high. In six patients, the leaflets were not captured due to complex anatomy, but the implants were successfully retrieved with no adverse consequences.⁴

TR severity was significantly reduced within 30 days of the PASCAL platform procedure and, as seen in the compassionate use study, this reduction was sustained at six months (Figure 3). After six months, 78% of patients had mild-to-moderate TR, 89% had achieved at least a one-grade reduction in TR, and 70% had achieved at least a two-grade reduction. Significant reductions in proximal isovelocity surface area effective regurgitant orifice area (PISA EROA) and vena contracta width were also observed at 30 days and maintained at six months (Figure 3).⁴

* Implant deployed as intended and delivery system retrieved as intended at the time of the patient's exit from the cardiac catheterisation laboratory

† Implant success with at least one grade reduction in TR at the end of the procedure without surgical or percutaneous intervention prior to hospital discharge

‡ Procedural success without major adverse events at 30 days



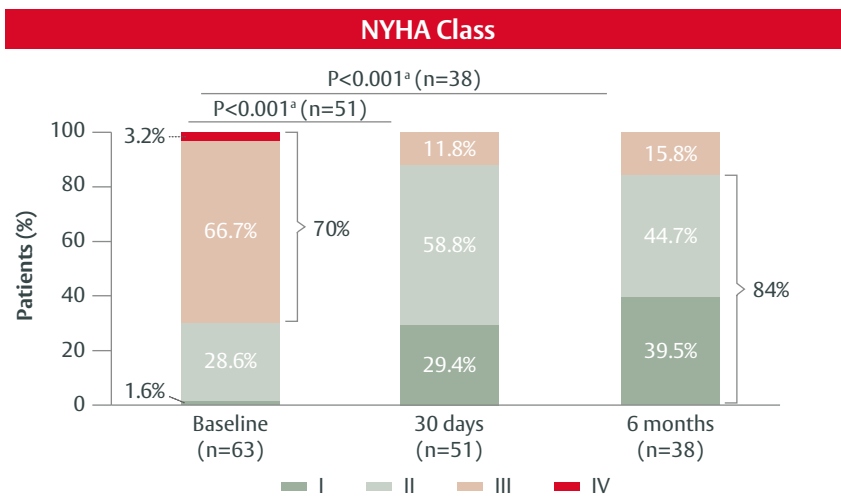
Change from baseline	PISA EROA (Δcm ²)	Vena contracta width (Δcm)
30 days	↓ 0.34*	↓ 0.71*
6 months	↓ 0.43*	↓ 0.74*

*p<0.001 vs baseline (paired T-test)

Figure 3. Echocardiographic outcomes at 6 months by Core Lab in the CLASP TR EFS study.⁴

*Two patients initially considered to have severe TR at baseline by transoesophageal echocardiography (TEE) were reclassified as moderate TR by transthoracic echocardiography (TTE)

Adapted from Eleid M 2021



Change from baseline	6MWD (Δm)	KCCQ score (Δpoints)
30 days	↑ 63*	↑ 17*
6 months	↑ 39	↑ 18*

*p<0.001 vs baseline (paired T-test)

Figure 4. Clinical, functional, and quality-of-life outcomes in the CLASP TR EFS study.⁴

Adapted from Eleid M 2021

These improvements in TR severity and echocardiographic outcomes were matched by sustained improvements in functional and quality-of-life outcomes (Figure 4). At six months, most patients (84%) achieved NYHA class I or II, and there was a 39 m improvement in 6MWD and an 18-point improvement in Kansas City Cardiomyopathy Questionnaire (KCCQ) score from baseline.⁴

Conclusion

Together, the results from the Compassionate Use study and CLASP EFS show that patients with symptomatic TR treated with the PASCAL repair system have significant and durable TR reduction, with improvements in clinical, functional, and quality-of-life outcomes at 6–12 months.^{3,4} The effectiveness of the PASCAL repair system for patients

with severe, symptomatic TR will be further evaluated in a randomised pivotal trial, CLASP II TR (NCT04097145), which is currently enrolling.

^a Wilcoxon signed-rank test; 6MWD, 6-minute walk distance; KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA Class, New York Heart Association TR, tricuspid regurgitation



PASCAL Platform in TR

Real-world outcomes with the PASCAL Platform in TR



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Professor Dr Jörg Hausleiter is Professor of Medicine and the Deputy Clinic Director at the Ludwig-Maximilians Universität (LMU) in Munich. Professor Hausleiter has been Principal Investigator in many clinical trials, including TRICuspid, BRIGHT, MiCLASP, TRILUMINATE and CLASP IID/IIIF.



Dr med. Mirjam Wild

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Dr Mirjam Wild is a Research Fellow in the Valvular Heart Team at LMU University Hospital in Munich and recently completed a fellowship in the Structural Heart Team at Bern University Hospital, Switzerland. Dr Wild's research interests include new devices and treatment strategies for percutaneous mitral and tricuspid valve interventions, and cardiovascular imaging.

The PASCAL platform, comprising the PASCAL and PASCAL Ace implants, received its CE mark for TR in May 2020 and has been shown to be an effective and safe treatment option for patients with TR.^{3,4,6} Professor Jörg Hausleiter and Dr Mirjam Wild now describe their single-centre experience from the LMU University Hospital in Munich, a high-volume centre with extensive experience in edge-to-edge repair, showing similar outcomes with the PASCAL and PASCAL Ace implants in patients with TR.⁷

The PASCAL platform has a number of specific features that are key to the successful treatment of patients with TR,^{1,3} including a high degree of flexibility, which enhances manoeuvrability when accessing the tricuspid valve.⁸ Independent grasping is also well established with the PASCAL platform and, along with the central spacer and broad paddles, allows the user to bridge large coaptation gaps with minimal leakage.^{1,8}

The nitinol construction of the PASCAL platform provides flexibility for the implants to move with the leaflets during the cardiac cycle, reducing stress on the leaflets.^{1,8}

While many of the key features of the PASCAL platform are shared between the PASCAL and PASCAL Ace implants, the PASCAL Ace implant has a narrower central spacer and profile, which helps with navigation of the device through the subvalvular apparatus.⁸ This is especially useful in the tricuspid valve, which has a dense network of thin, fragile chordae.⁹ In general, the benefit of having multiple implants with different features is to broaden the spectrum of patients who can be treated, leading to a more tailored approach in which the individual patient's anatomy can be considered.

“The big advantage of having multiple implants with different features is that you broaden the spectrum of patients who can be treated. A more tailored approach can be used which takes account of the patient's anatomy”

Professor Jörg Hausleiter

Munich single-centre experience

At the LMU University Hospital in Munich, we routinely treat patients with TR using the PASCAL platform, either with the PASCAL or the PASCAL Ace implant. We have conducted a prospective data collection and analysis of all patients treated with the PASCAL Ace implant since October

2020, and a descriptive analysis and comparison with a comparable patient cohort treated with the PASCAL implant. In this analysis, 78 patients with TR were treated with the PASCAL platform, including 50 with the PASCAL implant and 28 with the PASCAL Ace implant. There was a high technical success rate with both implants

(ranging from 95–100%) and no significant difference in the mean number of devices implanted per patient (PASCAL implant 1.8; PASCAL Ace implant 1.5).⁷

“There was a high technical success rate with both implants”

Professor Jörg Hausleiter

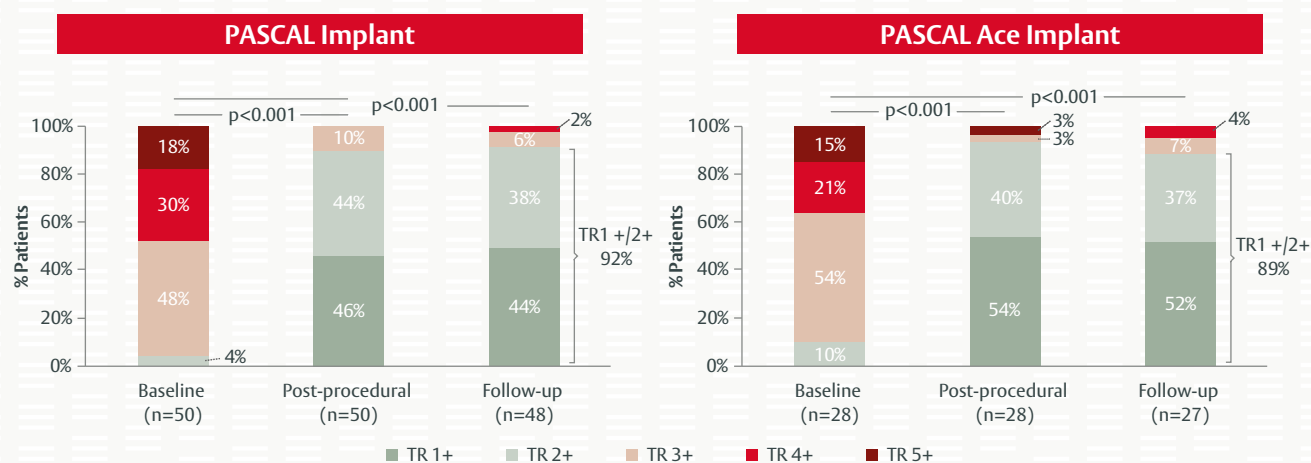


Figure 5. Impact of PASCAL and PASCAL Ace implantation on TR severity in patients with severe TR or greater⁷

Wild M. EuroPCR 2021. Reproduced with permission

TR severity was significantly reduced in patients treated with the PASCAL and the PASCAL Ace implants (Figure 5). While over 90% of patients had TR severity $\geq 3+$ at baseline, mild-to-moderate TR ($\leq 2+$) was achieved in 92% of patients receiving the PASCAL implant and in 89% of patients receiving the PASCAL Ace implant at the 30-day follow up. Similarly, patients demonstrated a significant improvement in heart failure symptoms and NYHA functional class with both the PASCAL and PASCAL Ace implants (Figure 6). There were no device-related procedural complications with the two implants and only one patient had a single-leaflet device attachment.⁷

Overall, we found no significant difference in the extent to which the PASCAL and PASCAL Ace implants reduced TR severity and improved clinical outcomes in patients with severe TR.⁷



The safety profile with the PASCAL platform was very good. There were no relevant procedural complications that were device-related

Professor Jörg Hausleiter



Conclusion

Our single-centre experience at the LMU in Munich adds further evidence of the efficacy and safety of the PASCAL platform in treating patients with severe or greater TR.⁷ With the availability of different devices for TTVr, including the PASCAL and PASCAL Ace implants that make up the PASCAL platform, there is an opportunity to adapt TTVr treatments to individual patients based on their specific anatomies. However, before clear conclusions can be drawn in this regard, additional studies are required to determine which patients are most suitable for each treatment approach.



With both [PASCAL] implants, at least 90% of patients had moderate or less TR immediately after the procedure and at 30-day follow-up, indicating very good efficacy

Professor Jörg Hausleiter

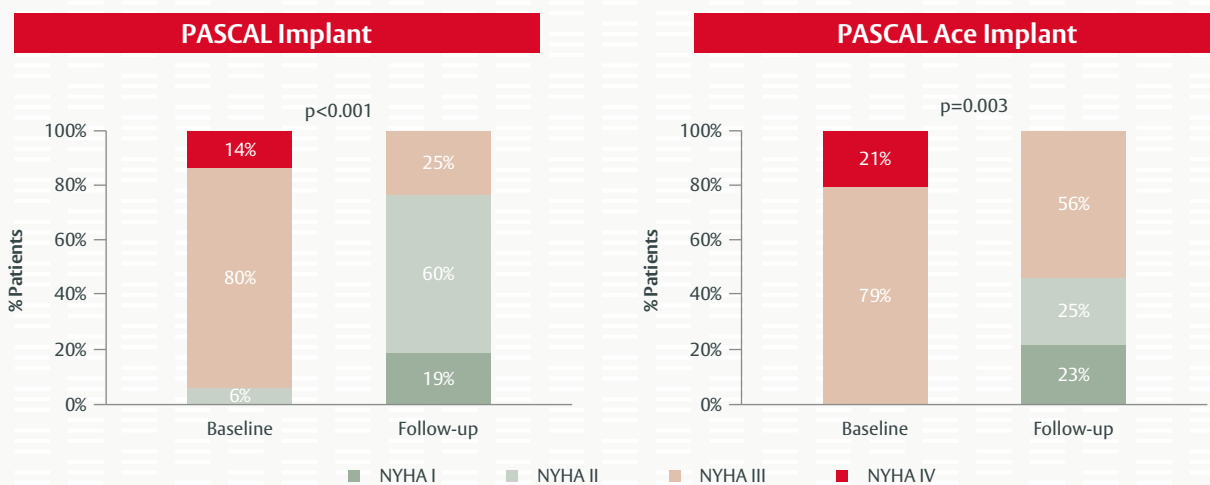


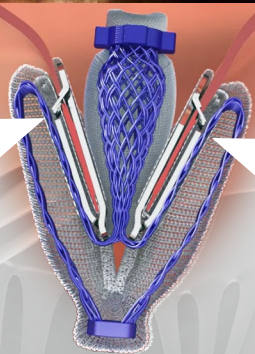
Figure 6. Impact of PASCAL and PASCAL Ace implantation on NYHA class in patients with severe TR or greater⁷

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Reason #12

Passive Closure ...

... designed
to flex with
movement



One more reason to adopt the PASCAL Repair System

The PASCAL repair system benefits from a passive closure mechanism that is designed to flex with movement.^{1,2}

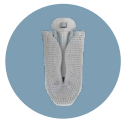
The shape of the PASCAL implant's Nitinol inner frame means that a balanced spring force is applied which is a smart way to maintain the captured leaflet, as the implant acutely flexes with the natural movement of each heartbeat.^{1,2}

¹ Edwards Lifesciences. Data on file: PASCAL Ace Implant component design enhancement. 2020.

² Masiero G, Rodinò G, Tarantini G. Percutaneous "edge-to-edge" leaflet repair in patients with secondary mitral valve regurgitation. *Mini-invasive Surg.* 2020; 4: 71.



Edwards



PASCAL Ace implant in TR

Single-centre experience with the PASCAL Ace Implant System for the treatment of TR



**Professor
Dr med.
Philip Raake**

Klinik für Kardiologie,
Universitätsklinikum
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Professor Philip Raake is Head of the Cardiac Catheter Laboratory of Internal Medicine III at Universitätsklinikum Heidelberg. Professor Raake has been Investigator or Principal Investigator in a number of clinical trials including CLASP IID/ IIF, TriCLASP, EXPAND G4 and RESHAPE-HF2.

A growing body of evidence supports the efficacy and safety of the PASCAL platform in the treatment of patients with severe TR.^{3,4,7,10}

The PASCAL Ace implant is particularly well suited for treatment of TR, benefiting from a narrow profile and implant elongation that facilitates its navigation through the dense chordae of the tricuspid valve without becoming entangled.⁸ Here, Professor Philip Raake describes his single-centre experience using the PASCAL Ace implant in patients with serious TR at the Universitätsklinikum, Heidelberg.^{11,12}

We started using the PASCAL platform at our centre in 2019 to treat patients with MR, but now use it routinely in both the MR and TR settings. The PASCAL Ace implant is our preferred option for all our PASCAL TTVr procedures as its narrow profile and small central spacer help with manoeuvrability through the subvalvular apparatus.⁸

Of 11 patients successfully treated with the PASCAL Ace implant in

our centre, three had severe TR (TR 3+), six had massive TR (TR 4+) and two had torrential TR (TR 5+) at baseline (Figure 7).^{11,12}

Following the procedure, there was a significant improvement in TR severity (p=0.001), with 10/11 patients achieving mild-to-moderate TR (TR ≤2+).^{11,12}

Patients also showed significant reductions in NYHA class (p=0.008), right atrial volume (p=0.004) and right ventricular end-diastolic diameter (p=0.013) following the procedure.^{11,12}

'Due to its independent grasping capability and small size, the PASCAL Ace implant is our preferred device for the treatment of patients with TR'
Professor Philip Raake

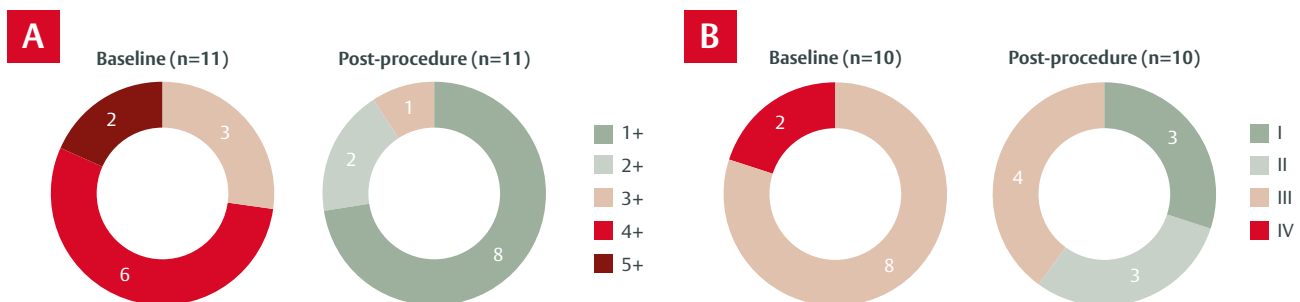


Figure 7. Pre- and post-procedural TR (A) and NYHA class (B) in patients with TR treated with the PASCAL Ace implant^{11,12}

Raake P. EuroPCR 2021. Reproduced with permission

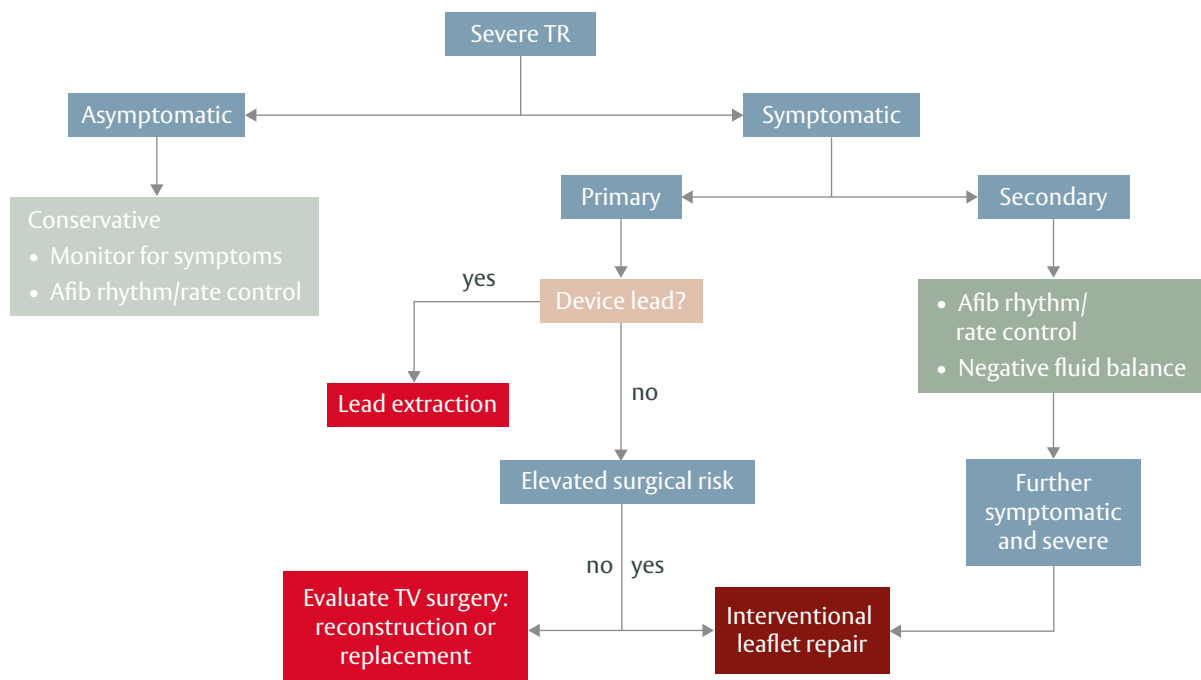


Figure 8. Algorithm for treatment of symptomatic severe-to-torrential TR at the Universitätsklinikum, Heidelberg¹²

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As experienced users of the PASCAL platform for the treatment of MR, we found the PASCAL Ace implant to

'We are very satisfied with the PASCAL Ace implant. The steering is very intuitive, and the device has a high safety standard'
Professor Philip Raake

be intuitive to use in patients with TR, and we had no issues in learning how to use the new implant. The most challenging aspect is imaging of the tricuspid valve, so it is important to work with a good echocardiographer. We also now use the PASCAL Stabilizer Rail System (SRS) during implantation as this makes the procedure more comfortable

for the user and allows more precise positioning of the implant (to know more on the PASCAL Stabilizer Rail System, see [TMTT Today #5](#)).

In Heidelberg, we use an algorithm to assess whether patients with severe-to-torrential TR require, and are candidates for, interventional treatment (Figure 8).¹² Patients are first assessed on whether their condition has been fully optimised with regard to the treatment of underlying conditions (e.g. atrial fibrillation). Patients who continue to have high-grade TR after optimisation and who are also symptomatic (i.e. with shortness of breath, leg oedema or ascites) are then considered for interventional treatment. Those patients who

have a pacemaker lead across the tricuspid valve, which could be causing their TR are assessed by a surgeon. In remaining patients, a transoesophageal echocardiogram is used to check for feasibility of interventional leaflet repair. The acceptance rate for interventional treatment of TR in Heidelberg is approximately 50%, as 50% of patients are not optimised or no longer have symptomatic high-grade TR following optimisation.

'The PASCAL SRS is a real improvement over the original stabiliser. It is more comfortable for the user, it is easier to use and it is more precise'
Professor Philip Raake

Case study

Professor Raake described the case of a patient with functional MR and secondary TR who was treated in Heidelberg using both a PASCAL implant and PASCAL Ace implant (Figure 9).¹² Initially, the patient was treated for moderate-to-severe functional MR using a PASCAL implant. Within the same procedure, the patient was treated for massive TR with a PASCAL Ace implant, placed in the anteroseptal commissure. Following claspings of the anterior and septal leaflets using the PASCAL Ace implant, a suboptimal result was obtained. Leaflets were therefore released from the clasps and the implant was repositioned more centrally within the tricuspid valve. Adjustment of the clocking device and reclaspings of the leaflets resulted in improved TR reduction. The dual MR and TR procedure, from puncture of the groin to closure, was completed in 45 minutes and resulted in an MR reduction from moderate-to-severe to mild, and a TR reduction from massive to trace. The patient also showed improvements in NYHA class and exercise capability following the procedure. This case highlights the effectiveness of the PASCAL and PASCAL Ace implants in treating patients with combined MR and TR.

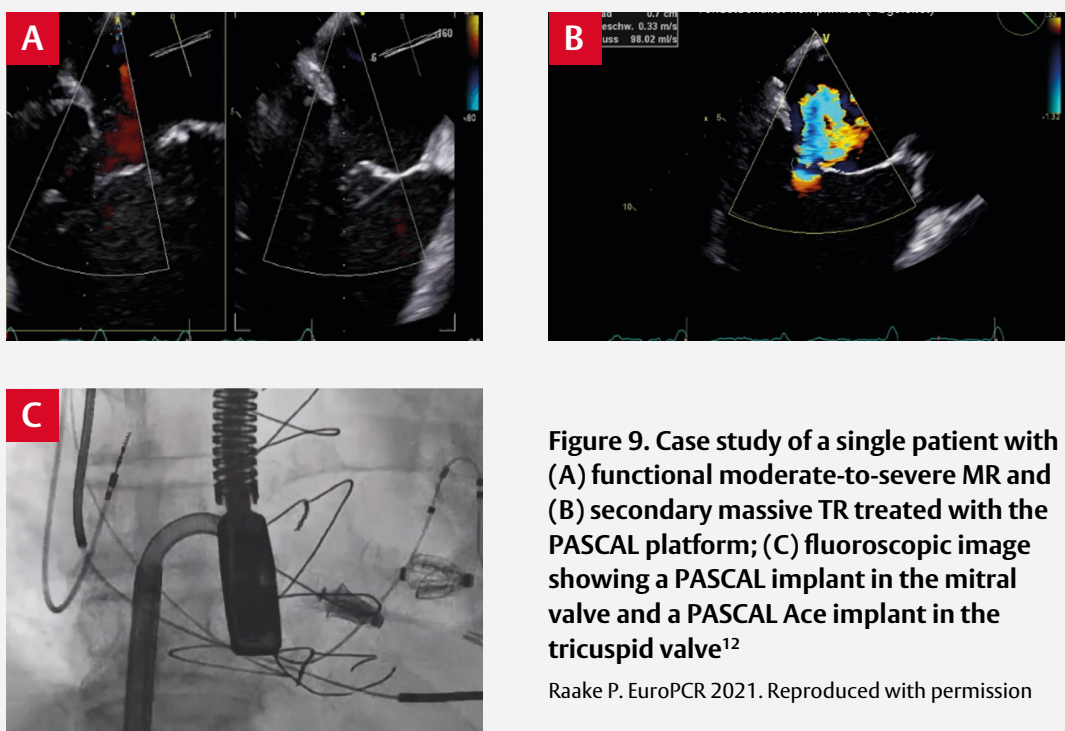


Figure 9. Case study of a single patient with (A) functional moderate-to-severe MR and (B) secondary massive TR treated with the PASCAL platform; (C) fluoroscopic image showing a PASCAL implant in the mitral valve and a PASCAL Ace implant in the tricuspid valve¹²

Raake P. EuroPCR 2021. Reproduced with permission

Conclusion

This single-centre experience supports the efficacy of the PASCAL Ace implant in reducing TR severity and improving clinical outcomes in patients with severe TR.^{11,12} The PASCAL Ace implant shares key features of the PASCAL

implant that are important for clinical success, including independent leaflet capture and a central spacer to bridge coaptation gaps with minimal leakage while minimising leaflet stress.⁸ In addition, its narrower profile allows it to be confidently and safely extracted from the

tricuspid valve or repositioned if entanglement occurs, further contributing to chordal safety.⁸ The efficacy and safety of the PASCAL Ace implant for the treatment of TR is being further evaluated in prospective randomised trials, including CLASP II TR (NCT04097145).



Cardioband Tricuspid System in TR

Cardioband Tricuspid Valve Reconstruction System: 30-day outcomes from the TriBAND study

As the first commercially available transcatheter therapy for the treatment of tricuspid heart valve disease and the only transcatheter annuloplasty solution,¹³ the Edwards Cardioband tricuspid valve reconstruction system provides an alternative treatment approach to leaflet repair for patients with TR.^{14,15} Here, Professor Georg Nickenig describes 30-day outcomes from the TriBAND study, an ongoing European, single-arm, multicentre, prospective, post-market study designed to assess the safety and effectiveness of the Cardioband tricuspid system in patients with chronic, symptomatic, functional TR.¹⁶



Professor Dr med. Georg Nickenig
Universitätsklinikum Bonn, Germany

Professor Georg Nickenig is Professor and Chair of the Department of Internal Medicine and Polyclinic II at Universitätsklinikum Bonn. Professor Nickenig has been Principal Investigator in many clinical trials, including AHEAD, bRIGHT, MiCLASP, MiBAND, TriBAND, TRI-REPAIR, TRILUMINATE and TRICI-HF.

Patients with TR usually present at our hospital several years into their disease, and often when their TR has become severe or even torrential. These patients typically have high perioperative risk and limited treatment options. The leading pathology among our patients is dilation of the tricuspid annulus, causing malcoaptation of the tricuspid leaflets. A device that targets the dilated tricuspid annulus is a logical treatment solution for TR. The Cardioband tricuspid system reduces the size of the tricuspid annulus, facilitating leaflet coaptation and restoring the tricuspid valve to a more functional state.¹⁶

In the TriBAND study, 61 patients with symptomatic, moderate-to-torrential TR were treated with the Cardioband tricuspid system. Patients had a mean age of 79 ± 6 years and most (75%) were female.

The Cardioband tricuspid system was deployed successfully* in 97% of patients. Procedural success rate¹ was 83.9%.¹⁶

Despite the very sick patient population, 80% of those who received the Cardioband tricuspid system had no major adverse events at 30 days. Of the 61 patients enrolled in the study, one patient (1.6%) died within 30 days from procedure-related renal failure and seven patients (11.5%) had severe bleeding, although

none of the severe bleeding events were fatal. All patients with severe bleeding were receiving oral anticoagulation or antiplatelet therapy for atrial fibrillation at baseline. There were no cases

of stroke or major cardiac structural complications after the procedure.¹⁶

'The leading pathology of TR is dilation of the tricuspid annulus. Therefore, a device that treats the dilated annulus directly is a logical device to use for the treatment of TR'

Professor Georg Nickenig

'Technical and procedural success with the Cardioband tricuspid system were both very high. In almost every patient, we were able to place the device where we wanted'
Professor Georg Nickenig

'Despite the very sick patient population, 80% of those who received the Cardioband tricuspid system had no major adverse events at 30 days'
Professor Georg Nickenig

* Device deployed as intended and the delivery system successfully retrieved as intended at the time of the patient's exit from the cardiac catheterisation laboratory

¹ Procedural success defined as device success with 30% TR reduction in PISA EROA post-procedure relative to baseline, and without the need for intervention prior to discharge (per patient)

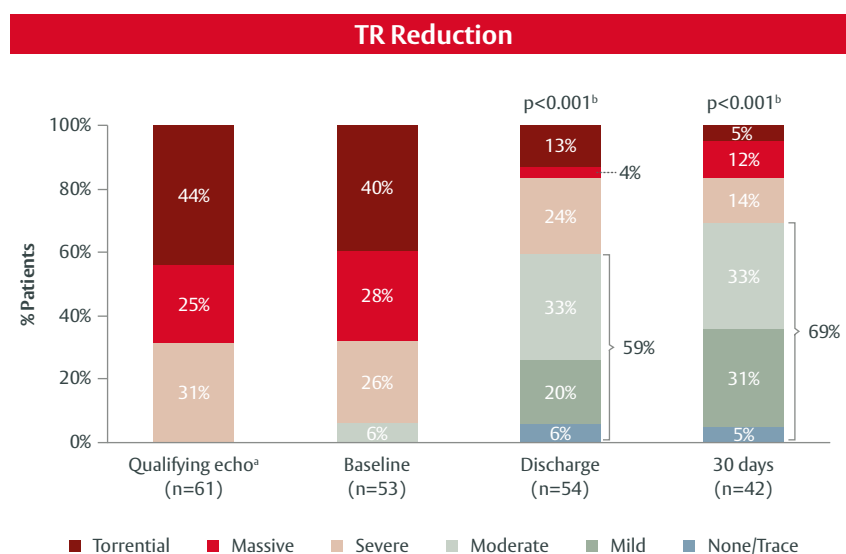
The Cardioband tricuspid system demonstrated encouraging efficacy in this patient population. The septolateral annular diameter reduced by 20% between baseline and 30 days, based on Core Lab measurements, and there was a significant reduction in TR grade (Figure 10). While 94% of patients had severe, massive or torrential TR at baseline, 59% had moderate or lower TR at discharge, increasing to 69% at 30 days. In addition, at least one-grade improvement in TR was achieved in 78% of patients at discharge and in 85% of patients at 30 days.¹⁶ These improvements in TR were mirrored in the clinical performance of patients. While 85% of patients were NYHA class III–IV at baseline, 74% of patients were NYHA class I–II at 30 days (Figure 11). Similarly, patient quality of life significantly improved following the procedure, with overall KCCQ score increasing by 17 points between baseline and 30 day follow up (Figure 11).¹⁶ There was also evidence of right heart remodelling after implantation of the Cardioband tricuspid system, as evidenced by significant reductions in right ventricular end-diastolic diameter, right atrial volume, and inferior vena cava diameter between baseline and 30 days (Figure 13).¹⁶

'At least a one-grade improvement in TR was achieved in 78% of patients at discharge and in 85% of patients at 30 days following implantation'

Professor Georg Nickenig

Annular reduction	
	Annular reduction
Discharge (n=54)	↓ 19%*
30 days (n=42)	↓ 20%*

*p<0.001 vs baseline (paired T-test, baseline vs discharge [n=50], baseline vs 30 days [n=38])



^aSite-reported, ^bWilcoxon signed-rank test, baseline vs discharge (n=51), baseline vs 30 days (n=39). TR: tricuspid regurgitation.

Figure 10. Annular and TR reduction following implantation of the Cardioband tricuspid system¹⁶

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The learning curve with the Cardioband tricuspid system was similar to that of leaflet repair devices.* The main challenge for new users of the Cardioband tricuspid system is learning how to image the annulus from the anterior, lateral and posterior aspects of the tricuspid valve. In addition, it is important to assess the proximity of the right coronary artery to the annulus as this may determine whether patients are suitable candidates

for the procedure. During implantation, the user deploys anchors to secure the device in place and can then adjust the device by cinching so that it reduces the annular diameter, thereby reducing TR. This real-time adjustment capability allows confirmation of the procedural results through echocardiography before finalising the procedure.¹⁵

*Professor Georg Nickenig: personal communication.

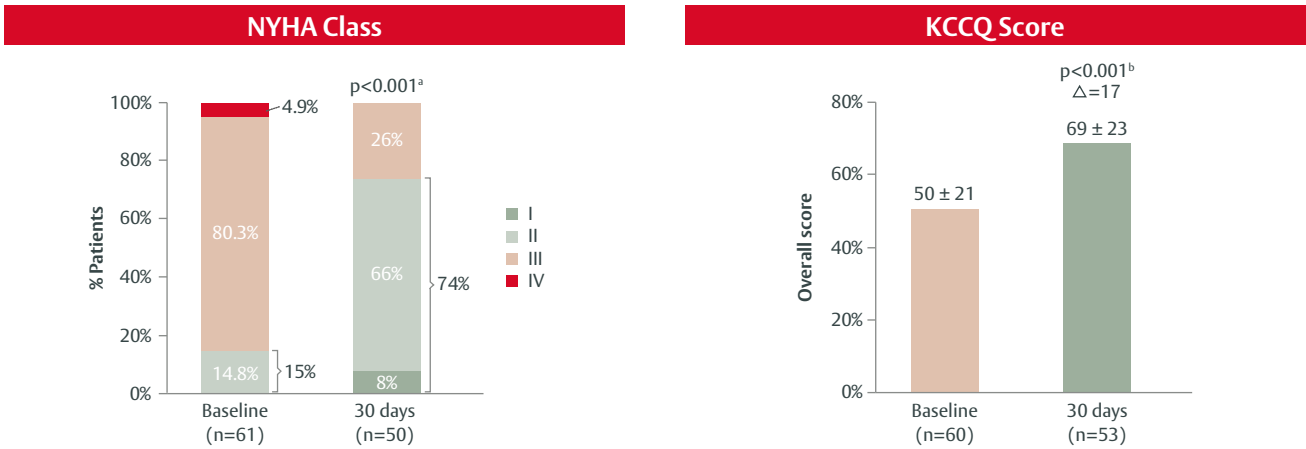


Figure 11. Functional and quality of life outcomes at 30 days following implantation of the Cardioband tricuspid system¹⁶

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Δ and p-value presented for paired analysis; p-value calculated using ^aWilcoxon signed-rank test, baseline vs 30 days (n=50), and ^bStudent's T-test, baseline vs 30 days (n=52). KCCQ, Kansas City Cardiomyopathy Questionnaire; NYHA Class, New York Heart Association.

Case study

Professor Nickenig described the case of a 68-year-old female patient who presented with massive TR and severe heart failure (NYHA class III–IV). The patient had been repeatedly hospitalised due to decompensation for heart failure and massive oedema, and also suffered from dyspnoea, fatigue and diminished resilience. Her EuroSCORE and logistic EuroSCORE values were 4% and 15%, respectively. The patient also presented with several comorbidities, including moderate-to-severe reduced left-ventricular ejection fraction, atrial fibrillation, MR and severe lung disease due to bronchiectasis and long-standing asthma bronchiale. She was considered a poor candidate for open-heart surgery, so a catheter-based treatment approach using the Cardioband tricuspid system was selected.

Following implantation of the Cardioband tricuspid system approximately 18 months ago, the patient had a sustained reduction in TR, from massive to mild-to-moderate, with no sign of recurrence (Figure 12). Additionally, the septolateral diameter of the annulus reduced from 44 mm to 30 mm following the procedure, indicating an improvement in both anatomy and haemodynamics. Her exercise capacity and quality of life were also increased in accordance with outcomes from the TriBAND study, and NT-proBNP, a marker for heart failure, was reduced over time.

This case highlights the positive impact of Cardioband tricuspid system implantation on TR, anatomy, haemodynamics and clinical outcomes in a difficult-to-treat patient with massive TR.

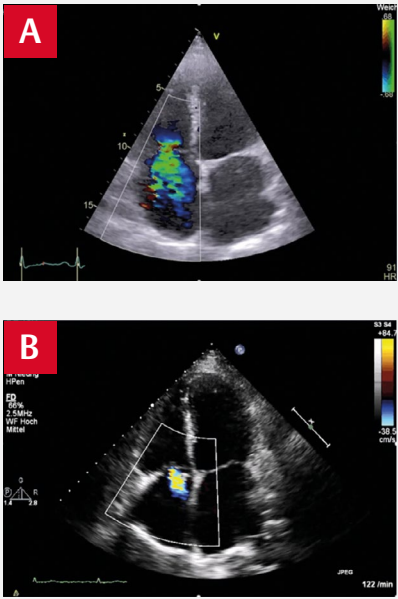
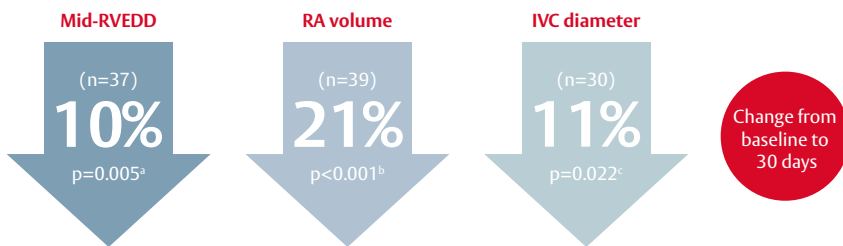


Figure 12. Transthoracic echocardiograms before (A) and after (B) implantation of the Cardioband tricuspid system

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Change from baseline to 30 days

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Δ and p-value presented for paired analysis; p-value calculated using Student's T-test, baseline vs 30 days
^a(n=37), ^b(n=39), ^c(n=30).
 EDD: end diastolic diameter, IVC: inferior vena cava, RA: right atrium, RV: right ventricle.

Figure 13. Early evidence of right heart remodelling following implantation of the Cardioband tricuspid system¹⁶

Conclusion

The Cardioband tricuspid system is a novel, transfemoral annular reduction therapy for the treatment of functional TR. This approach directly targets dilation of the tricuspid annulus, the leading pathology in patients with TR. Early outcomes from the ongoing TriBAND study indicate

that the Cardioband tricuspid system offers a safe and effective treatment option for patients with moderate-to-severe TR, causing significant TR reduction, evidence of right heart remodelling, and improvements in functional status and quality of life at 30 days post-implantation.¹⁶ These findings

confirm reproducibility of the positive outcomes demonstrated in the TRI-REPAIR study,^{14,17} and support the Cardioband tricuspid system as a valuable component of a growing toolbox of therapies for patients with TR, along with leaflet repair and emerging valve replacement technologies.

Reason #1
Improved quality of life



One more reason to adopt the PASCAL Repair System

At Edwards Lifesciences, we strive to design solutions that first and foremost benefit patients. The PASCAL repair system improves functional status, exercise capacity and quality of life for patients with severe tricuspid regurgitation.

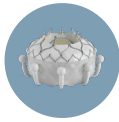
After implantation:

- NYHA Class I or II was achieved in 90% of patients at 12 months, compared with 10% with Class II, 80% with Class III and 10% with Class IV at baseline¹
- Average distance in the 6MWT increased by 53 m at 30 days and by 72 m at 12 months¹
- Mean KCCQ overall score improved by 17 points at 30 days and by 18 points at 6 months²



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EVOQUE Tricuspid Valve Replacement System for TR

TRISCEND study: First-in-human experience with the EVOQUE Tricuspid Valve Replacement System

Tricuspid valve replacement is being investigated as a potential treatment approach for patients with TR, alongside transcatheter tricuspid leaflet repair and direct annuloplasty. Here, Dr Susheel Kodali and Professor Rebecca Hahn discuss the EVOQUE system and describe 30-day outcomes from the TRISCEND study, an ongoing single-arm, prospective, multicentre study evaluating the safety and performance of the system in patients with symptomatic moderate (or worse) TR.¹⁸



Dr Susheel Kodali
Columbia University
Medical Center,
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Dr Susheel Kodali is Director of the Structural Heart & Valve Center at New York-Presbyterian/CUMC. Dr Kodali has been Principal Investigator in many clinical trials, including ALIGN-AR, CLASP IID/IIF, CLASP II TR, CLASP TR EFS, PARTNER II, TAVR UNLOAD, TRILUMINATE, TRISCEND and TRISCEND II.

Many patients with TR have anatomical challenges, such as wide coaptation gaps, tethering, or the presence of pacemaker leads across the tricuspid valve. Any or all of these factors can make them unsuitable for tricuspid leaflet repair and/or annuloplasty. For these patients, tricuspid valve replacement may be a suitable option as it can accommodate larger coaptation gaps and pacemaker leads. The EVOQUE tricuspid valve replacement system is a low profile, 28F transfemoral, fully percutaneous delivery device comprising a nitinol frame with bovine pericardial leaflets (Figure 14).^{18,19}

The valve uses atraumatic anchors to engage leaflets, chords and the annulus to achieve secure placement. Three different EVOQUE valve sizes (44, 48 and 52 mm) are designed to accommodate treatment of a wide range of tricuspid pathologies and anatomies.¹⁸

While the EVOQUE system is not yet approved for commercial use, the TRISCEND study is a first-in-human study that builds on the compassionate use experience, assessing the performance and safety of the EVOQUE valve in a population with symptomatic, moderate or greater TR.¹⁸



Professor Rebecca Hahn
Columbia University
Medical Center,
New York, USA

Professor Rebecca Hahn is Director of Interventional Echocardiography at New York-Presbyterian/Columbia University Medical Center (CUMC) and Professor of Clinical Medicine at Columbia College of Physicians and Surgeons. Professor Hahn has been an Investigator or Principal Investigator in a number of clinical trials, including CLASP IID/IIF, SCOUT, TRISCEND and TRISCEND II.

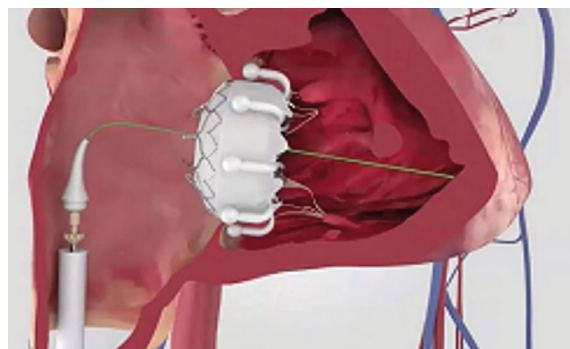
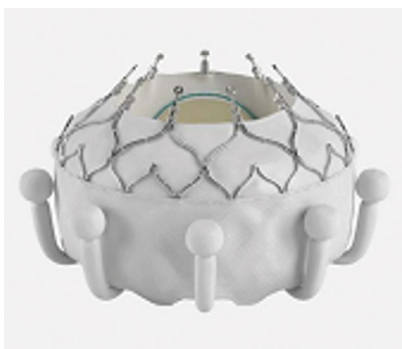
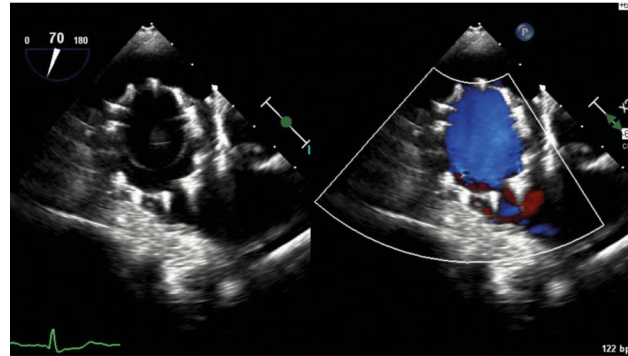
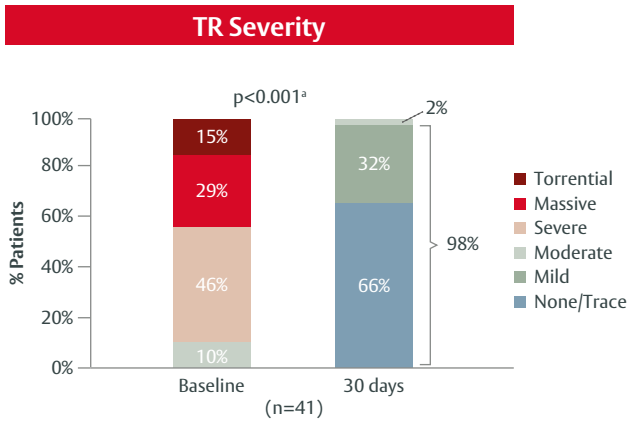


Figure 14. EVOQUE tricuspid valve replacement system¹⁸

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Case study showing no residual TR in a patient after implantation with the EVOQUE valve. Image courtesy of Dr Susheel Kodali.

^aWilcoxon signed-rank test

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Figure 15. TR severity at baseline and 30 days after EVOQUE valve implantation in the TRISCEND study¹⁸

The mean age of patients was 79 years and most (77%) were women. Most of the 56 patients who received the EVOQUE valve had a number of comorbid conditions (91% had atrial fibrillation, 79% had pulmonary hypertension, and 66% had chronic kidney disease at baseline).¹⁸ Despite the very sick patient population, there was a high rate of both device*

(98%) and procedural[†] (94%) success with the EVOQUE system, and these rates were consistent across multiple study sites. From an operator's perspective, the procedure was very reproducible, with mean device time of only 70 minutes.¹⁸

At 30-days post-implantation, 77.4% of patients (41/53) had no major adverse events. In total, 23% of patients (12/53) had a severe bleeding event but none of these events was fatal or considered life-threatening.¹⁸

There was an improvement in TR severity ($p<0.001$) in patients following implantation of the EVOQUE valve (Figure 15). While 46% of patients had severe TR, 29% had massive TR and 15% had torrential TR at baseline,

almost all (98%) achieved a reduction in TR severity to none/trace or mild by the 30-day follow up. All patients (100%) achieved at least

a one-grade reduction in TR at 30 days, and 95% achieved at least a two-grade reduction.¹⁸

In addition to the reduction in TR severity, there was an improvement in quality of life following the procedure,

'After starting with moderate, severe, massive or torrential TR, 98% of patients had mild TR or better after the procedure'
Professor Rebecca Hahn

'The device was deployed successfully in 98% of patients and with 94% procedural success'
Professor Rebecca Hahn

* Device deployed and delivery system is retrieved as intended at the time of the patient's exit from the cardiac catheterisation laboratory

† Procedural success defined as device success without clinically significant paravalvular leak at the time of discharge (paravalvular leak data not available for 3 patients)

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'Quality of life improved with KCCQ score increasing by 19 points'

Dr Susheel Kodali

implantation of the EVOQUE valve (Figure 16). Most patients (77%) achieved NYHA class I or II at 30 days after the procedure, and 6MWD improved by 46 m between baseline and 30 days.¹⁸

as demonstrated by a 19-point improvement in KCCQ score between baseline and 30 days ($p < 0.001$) (Figure 16).¹⁸ There were also improvements in patients' functional outcomes, including NYHA class ($p < 0.001$) and 6MWD ($p = 0.001$), following

'Following the procedure, patients went from not being ambulatory to having a normal quality of life'

Dr Susheel Kodali

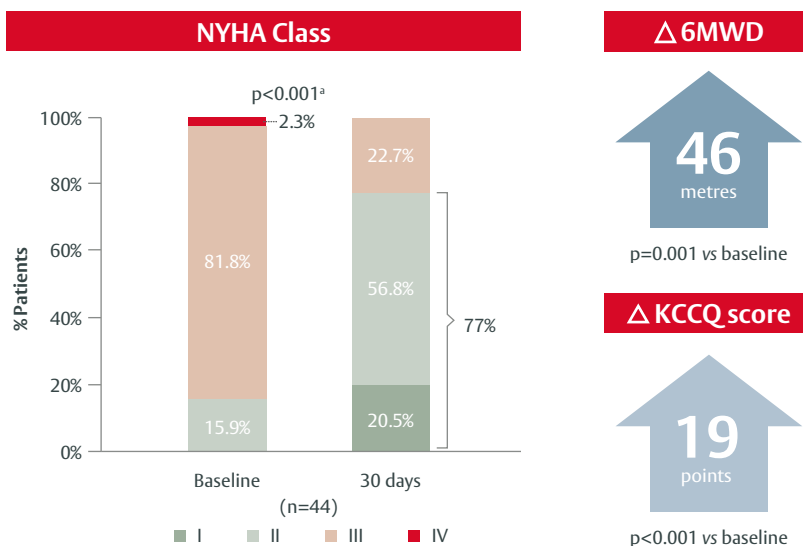


Figure 16. Effect of EVOQUE valve transplantation on functional outcomes and quality of life in the TRISCEND study¹⁸

^aWilcoxon signed-rank test

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Conclusions

Early experience with the EVOQUE system in the TRISCEND study has demonstrated technical feasibility, safety, significant TR reduction and symptomatic improvement in patients with moderate or greater TR.¹⁸ Despite the very sick patient population in this study, early

results indicate significant improvements in quality of life, clinical and functional outcomes in patients after receiving the EVOQUE valve.¹⁸ Tricuspid valve replacement shows potential as a treatment option for patients with TR, alongside annular reduction and tricuspid valve repair technologies.

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Conclusion

At Edwards Lifesciences, we are committed to improving the lives of patients with severe TR and recognise the need for treatment options that are tailored to a patient's individual requirements. A growing evidence base, reported in this edition of *Transcatheter Mitral and Tricuspid Therapies Today*, now supports our triple-pronged approach to the development of transcatheter treatments for TR, which includes tricuspid valve repair, annular reduction and tricuspid valve replacement.

Several studies and real-world experiences support the efficacy and safety of the PASCAL platform as a routine treatment for patients with severe TR, with impressive quality of life and functional improvements.^{3,4} Now, early outcomes from the TriBAND study show similar benefits of annular reduction using the Cardioband tricuspid system,¹⁶ confirming earlier data from the TRI-REPAIR study.^{14,17} Finally, while the EVOQUE system* has not yet received a CE mark, early experience with this technology in the TRISCEND study suggests feasibility of tricuspid valve replacement and the potential to provide significant improvements in quality of life, clinical and functional outcomes.¹⁸

With this range of complementary technologies, we are moving towards a treatment landscape that may provide individualised treatment options for patients with severe TR.



Ask your questions...

We can be reached at TMTT-Today@edwards.com to answer your questions about the Edwards' Mitral and Tricuspid Portfolio

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