TMTT Today

Your source for information on Edwards' innovations in transcatheter mitral and tricuspid therapies

Issue #11 – April 2024

The power of atraumatic clasp and closure*

PASCAL implants *enhance leaflet capture with atraumatic reclasp capabilities*

The CLASP IID trial
1-year outcomes with the PASCAL system[1]

96% MR ≤2+
77% MR ≤1+

Also inside:

- Edwards reusable accessories: A stable foundation for PASCAL Precision system procedures
- PASCAL implants: Assessing the effect of multiple clasping attempts on valve leaflets[2]
- Tips and tricks for your MR patients

*Performance and design data on file and marketing evaluation.

Edwards

Dear Reader,

You may remember that back in *TMTT Today* issue 9, we presented early data from the CLASP IID randomised controlled trial (RCT) and the CLASP IID registry up to 6 months' follow-up.[3,4] Now, we are delighted to present the 1-year outcomes from both studies, which continue to demonstrate high survival, significant and sustained mitral regurgitation (MR) reduction, and sustained functional and quality-of-life benefits for patients with severe, symptomatic degenerative MR who are at prohibitive surgical risk and were treated with the PASCAL repair system. The data also highlight that the PASCAL repair system is suitable for treating a wide range of patients, including those with complex anatomies.[1,5] This versatility is also illustrated in the four PASCAL platform case studies we share in this issue, in which experts describe their approaches to treating patients with diverse aetiologies and valvular anatomies.

As highlighted in the case studies, a key feature of the PASCAL Precision system is that it enables users to clasp and reclasp the valve leaflets multiple times to optimise leaflet capture.* Preserving leaflet integrity during multiple clasping attempts is important, because leaflet damage could result in residual or worsening severe MR or worsening haemodynamic status.[6] Professor Dabit Arzamendi examines data from an independent *ex vivo* study that support atraumatic clasp and closure with the PASCAL Precision system, showing no clinically relevant leaflet tissue damage even after repeated leaflet captures.[2,7]

This issue also celebrates the launch of the Edwards reusable accessories, which are designed to enhance procedures with the PASCAL Precision system while reducing the amount of waste post procedure. Our Director of Engineering in Research and Development, Michelle Chu, describes the hard work and collaboration that went into developing these accessories, and cath lab staff and physicians share what they like about using them.

Enjoy reading!

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*Performance and simulation data on file.

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Developing the Edwards Reusable Accessories for transcatheter edge-to-edge repair

As part of its commitment to innovation in transcatheter edge-to-edge repair (TEER), Edwards Lifesciences has developed the Edwards reusable accessories. Here, Michelle Chu talks us through the development story and explains how the accessories were designed to enhance procedures with the PASCAL Precision system.

Michelle Chu
Director of Engineering, Edwards Lifesciences

Michelle Chu is Director of Engineering in Research and Development (R&D) at Edwards Lifesciences. She joined the Transcatheter Mitral and Tricuspid Therapies R&D team after 8 years in the Transcatheter Heart Valve team as a valve engineer on the SAPIEN valve platform. She focuses on developing next-generation devices for the PASCAL platform. Prior to the reusable accessories, she led the development and commercialisation of the PASCAL stabilizer rail system (SRS).

"Being a good listener is a vital skill for my colleagues and I in the R&D department at Edwards Lifesciences. Only by truly listening to feedback from physicians and other cath lab staff can we discover what would make the biggest differences to their practice. One of the key requests from physicians was improved stability during TEER procedures, so, in 2021, we launched the PASCAL SRS to reduce unintended catheter movements during PASCAL repair system procedures. We then turned our attention to the stability of the platform used during TEER procedures. This platform might seem simple, but it took around 2 years of development – with attention to even the smallest details – to produce new and improved accessories that we were confident would meet our users' needs. In 2023, we launched the Edwards reusable platform, along with the reusable cradle and reusable plate (Figure 1).

The development process involved multiple departments, usability studies, field surveys, concepts, build iterations and simulated uses, during which we identified five key design requirements – stability, adjustability, compactness, sustainability and compatibility with the PASCAL Precision system and a pipeline of future innovation.

Stability

Physicians rated this as the most important feature of a platform, and so we designed the platform – and the cradle – with 50% glass-filled polypropylene for a good balance between rigidity, durability and weight compared with the more commonly used polymer or metal. The platform weighs approximately 4 kg, and each leg has a rubber foot, so the platform is not easily knocked out of place. The cradle enables the disposable SRS to be mounted on to the platform and keeps it stationary during the procedure.[8]

During our research, we observed that the flatness of operating tables varied between hospitals. A solid, flat surface is needed to provide a stable foundation for the

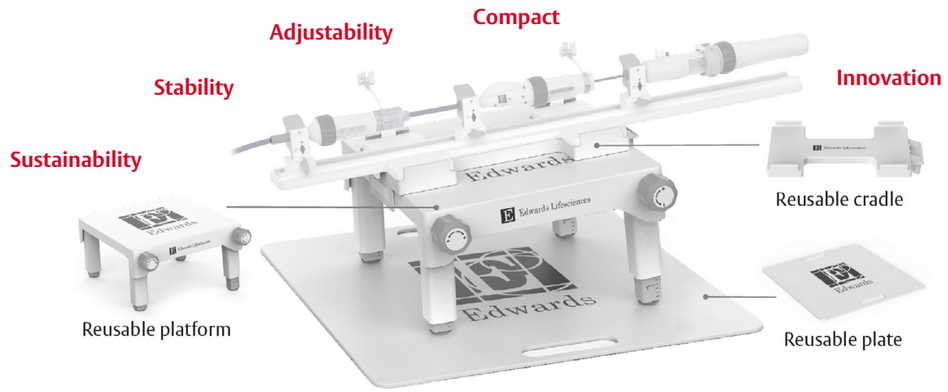

Figure 1. Edwards reusable platform, reusable cradle and reusable plate for TEER procedures with the PASCAL Precision system.[8]

TEER, transcatheter edge-to-edge repair.

platform, so we designed a reusable plate to sit under it. The reusable plate is made from acrylonitrile butadiene styrene, a rigid and durable material suited to the manufacturing of large flat plates.

Adjustability

Many physicians were interested in being able to customise the accessory set-up to each patient, such as tilting the platform to reduce stress on the patient's access site and enable a more direct approach. Our reusable platform features a unique linear drive mechanism, so users can customise the height and angle for each patient by turning the two knobs at the front to adjust the four legs. The height of the platform can vary from approximately 18 cm to 28 cm, with continuous increments, and the front-facing knobs mean that users do not have to reach over the patient to see or adjust the knobs.

Compactness

Hospitals often lack storage space, so we knew that easy-to-store accessories were vital. Our reusable platform is the first in the market to feature folding legs for compact storage. The platform's size means it can easily be moved and repositioned during set-up, and we maximised its working surface area relative to the overall footprint, so it can also support additional procedural devices, such as intracardiac echocardiography catheters, during TEER procedures.

Sustainability

The environmental impact of our products is important to us – and to users. We are all concerned about the volume of single-use plastic we use, and we recognised opportunities for improvement with the accessories used to support TEER procedures.

For example, the disposable tables used for TEER procedures result in around 1 kg of plastic waste after each procedure. The environmental impact is huge if you multiply that by the number of procedures every month. Our reusable platform can be used many times,* thereby effectively reducing the amount of plastic waste from the cath lab.

> Edwards Lifesciences cares about the environment, so we have been focusing our attention on the sustainability of our products.
>
> Michelle Chu

*Please refer to Edwards Reusable Accessories Instructions for Use for more information on visual and functional assessment before each use.

Innovation

We want physicians and cath lab staff to have a consistent and user-friendly experience across all our products. Therefore, our ultimate goal is to have one set-up for all transcatheter mitral and tricuspid procedures. The reusable accessories are compatible with the PASCAL Precision system and a pipeline of future innovation.

Conclusions

Edwards reusable accessories provide a stable foundation for your PASCAL Precision system TEER procedures. Compact and adjustable, the reusable platform can be moved and adjusted for individual patients' needs, before being neatly stored at the end of the procedure.

Designed with environmental sustainability in mind, these accessories can be used over and over again, enabling hospitals to reduce their plastic waste post procedure. They are compatible with the PASCAL Precision system and a pipeline of future innovation, offering the potential to simplify set-up and inventory management at hospitals.

> We want users to be able to apply the same familiar set-up across our products, so they can focus their time and energy on the procedure.
>
> Michelle Chu

What do users think?

The true judgement of the success of the Edwards reusable accessories lies with the users, so we asked cath lab staff and physicians to share their experience.

> The Edwards reusable accessories are easier to set up than the accessories we used to use. Plus, they are easy to clean and store.
>
> **Giovanna Di Battista,**
> **San Donato Hospital, Milan, Italy**

> I am pleased to have the Edwards reusable accessories rather than disposable plastics. They are functional and user friendly.
>
> **Lauren Connolly,**
> **Royal Brompton Hospital, London, UK**

> The Edwards reusable platform is really stable and can be adjusted, which helps make the procedure simpler and safer. The pressure on the groin at the point of entry is reduced, so it is less traumatic for the patient.
>
> **Dr Adam Rdzanek,**
> **Medical University of Warsaw, Poland**

> The Edwards reusable platform is very easy to adjust once in position. The large knobs are easy to reach and turn. The platform can be tilted to reduce stress at the vascular access site, which is particularly useful for patients with low body weight.
>
> **Dr Nedy Brambilla,**
> **San Donato Hospital, Milan, Italy**

PASCAL Repair System in patients with degenerative MR

One-year outcomes from the CLASP IID randomised controlled trial and the CLASP IID registry

Treating patients with degenerative MR is challenging due to a lack of effective medical therapy and an elderly patient population for whom surgical risk is often high. Mitral valve TEER (M-TEER) presents an alternative treatment for these patients, and currently, two devices are available in Europe for this approach. Early data from the CLASP IID RCT, comparing outcomes with the PASCAL repair system and the MitraClip system, were previously published[3] and are summarised in *TMTT Today* issue 9. In this article, Professor Philipp Lurz highlights 1-year outcomes from the trial, including a significant reduction in MR that is maintained throughout follow-up.[1] Additionally, Professor Ralph Stephan von Bardeleben discusses 1-year outcomes from the CLASP IID registry, emphasising the safety and performance of TEER with the PASCAL repair system in patients with more complex valve anatomy than those included in the RCT.[5]

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Professor Dr med. Philipp Lurz

Mainz University Medical Center, Germany

Professor Philipp Lurz, an interventional cardiologist, is the Director of the Center for Cardiology at the Mainz University Medical Center. He is Principal Investigator of the MiCLASP registry and an investigator in the CLASP IID/IIF RCT, as well as in trials for multiple other therapies.

Professor Dr med. Ralph Stephan von Bardeleben

Mainz University Medical Center, Germany

Professor Ralph Stephan von Bardeleben is an interventional cardiologist and Head of the Center of Structural Heart Disease Interventions and the Heart Valve Center in Mainz. He is a Principal Investigator for the CLASP IID/IIF RCT and a Steering Committee member for the TRISCEND II study. Professor von Bardeleben specialises in percutaneous valve therapy and has been involved in many other clinical trials, including REPAIR, TRI-REPAIR and MiCLASP.

CLASP IID (NCT03706833) is a prospective, multicentre, multinational RCT comparing the safety and effectiveness of the PASCAL repair system with the MitraClip system in patients with significant, symptomatic degenerative MR (grade 3+ or 4+) who are at prohibitive risk for surgery. It is a noninferiority trial with primary endpoints of safety (based on a composite major adverse event [MAE] rate comprising cardiovascular mortality, stroke, myocardial infarction, new need for renal replacement therapy, severe bleeding and non-elective mitral valve reintervention at 30 days) and effectiveness (based on the proportion of patients with MR ≤2+ at 6 months). Secondary effectiveness endpoints were MR ≤2+ and MR ≤1+ rates at 1 year.[1]

Patients were enrolled in the CLASP IID RCT if they were deemed suitable for treatment with the PASCAL repair system and the MitraClip system by a central screening committee and echocardiographic core laboratory. Patients considered suitable for treatment with the PASCAL repair system but not with the MitraClip system, based on complex anatomy,[a] were considered for the CLASP IID registry. Inclusion and exclusion criteria for the CLASP IID RCT and the CLASP IID registry are outlined in *TMTT Today* issue 9.

CLASP IID RCT outcomes

Patients were randomised 2:1 to treatment with either the PASCAL repair system (n=204) or the MitraClip system (n=96). No significant differences in baseline characteristics were observed between the two groups in patients with procedure attempted (PASCAL repair system n=199, MitraClip system n=95). In the PASCAL repair system group, 78.9% of patients were treated with the first-generation PASCAL repair system and 21.1% were treated with the latest-generation PASCAL Precision system. In the MitraClip system group, 68.4% of patients received a newer generation (G4) implant, 30.5% received the earlier generation of implant and 1.1% received a combination.[1]

One-year results from the CLASP IID RCT confirm the safety and performance of M-TEER with the PASCAL repair system. The Kaplan–Meier freedom from MAE at 1 year was 84.7% for the PASCAL repair system and 88.3% for the MitraClip system (p=0.471). The proportion of patients achieving MR ≤2+ was sustained from discharge to 1 year with both the PASCAL repair system (97.9% *vs* 95.8%; p=0.125) and the MitraClip system (96.8% *vs* 93.8%; p=0.375;

[a]Based on the anatomical considerations in the special patient populations section of the current MitraClip system Instructions for Use.[9]

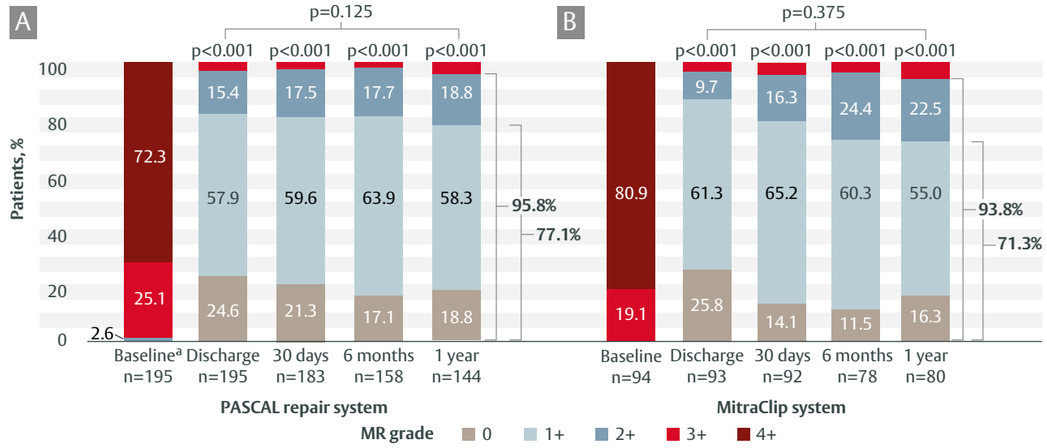


Figure 2. MR severity following treatment of patients with degenerative MR using (A) the PASCAL repair system and (B) the MitraClip system in the CLASP IID RCT.

Chart shows unpaired analysis; p values relative to baseline were calculated from paired analysis using the Wilcoxon signed rank test, and p values between discharge and 1 year for MR ≤2+ were calculated using the exact McNemar's test.
[a]TOE was used for baseline qualification of 5 patients.
MR, mitral regurgitation; RCT, randomised controlled trial; TOE, transoesophageal echocardiography.
Adapted from Zahr F *et al*. 2023.[1]

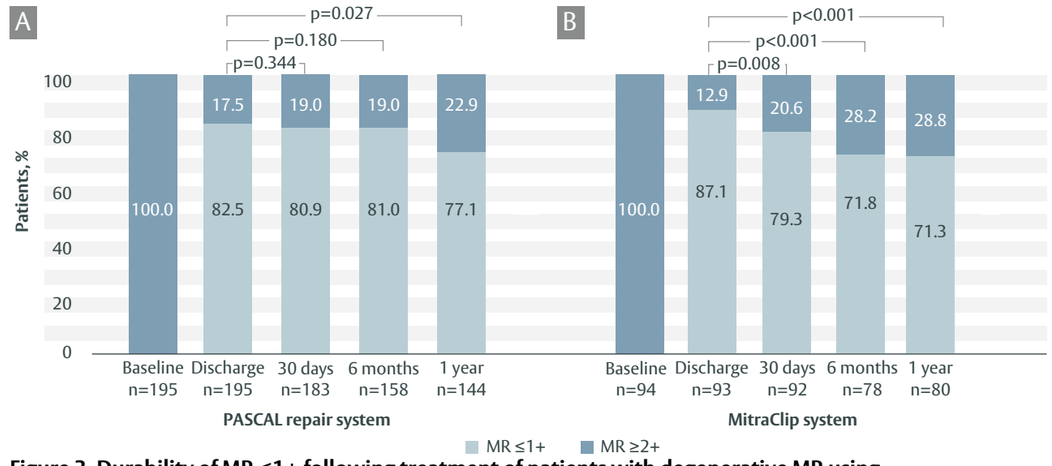


Figure 3. Durability of MR ≤1+ following treatment of patients with degenerative MR using (A) the PASCAL repair system and (B) the MitraClip system in the CLASP IID RCT.

Graph shows unpaired analysis; p values were calculated with paired analysis using the McNemar's test.
MR, mitral regurgitation; RCT, randomised controlled trial.
Adapted from Zahr F *et al*. 2023.[1]

Figure 2). In the PASCAL repair system group, the proportion of patients achieving MR ≤1+ was sustained from discharge to 30 days (82.5% *vs* 80.9%, p=0.344) and to 6 months (81.0%, p=0.180), but decreased to 77.1% at 1 year (p=0.027; Figure 3A). In contrast, in the MitraClip system group, 87.1% of patients achieved MR ≤1+ at discharge, which declined to 79.3% at 30 days (p=0.008), 71.8% at 6 months (p<0.001) and 71.3% at 1 year (p<0.001; Figure 3B), according to Professor Lurz, these results demonstrate the safety of TEER using the PASCAL repair system and an initial and sustained improvement in MR at 1 year.

Clinical and functional outcomes were also encouraging at 1 year following treatment, comments Professor Lurz. Freedom from all-cause mortality was comparable in both groups: 91.2% with the PASCAL repair system and 91.6% with the MitraClip system. Both groups also saw similar significant improvements in New York Heart Association (NYHA) functional class (change in proportion of patients in class I/II of +53.6% with PASCAL repair system and +44.2% with MitraClip system; p<0.001 for both) and Kansas City Cardiomyopathy Questionnaire (KCCQ) score (PASCAL repair system +15.2 points; MitraClip system +15.1 points; p<0.001 for both) from baseline to 1 year. Finally, numerical improvements were seen in 6-minute walk distance (PASCAL repair system +15.5 m, p=0.101; MitraClip system +22.6 m; p=0.121).[1]

Together, these results confirm that the initial reduction to MR ≤2+ was sustained at 1 year following treatment with both devices, leading to a robust improvement in clinical and functional status and quality of life in patients with severe, symptomatic degenerative MR who were at prohibitive risk for surgery. These outcomes are especially encouraging as enrolling centres had more experience with the MitraClip system than the PASCAL repair system.

CLASP IID registry outcomes

Due to anatomical considerations described in the special patient populations section of the MitraClip Instructions for Use,[9] 98 patients were ineligible for randomisation in the CLASP IID RCT. They were, however, suitable for treatment with the PASCAL repair system, and their outcomes were studied in the CLASP IID registry.

Even in this elderly population with complex anatomy (Figure 4), clinical outcomes demonstrate the safety and performance of M-TEER with the PASCAL repair system in patients with severe, symptomatic degenerative MR who were at prohibitive risk for surgery (Figure 5).[5] Almost 90% of patients were alive at 1 year, explains Professor von Bardeleben, which, given the baseline mean age of 81 years, is very high.

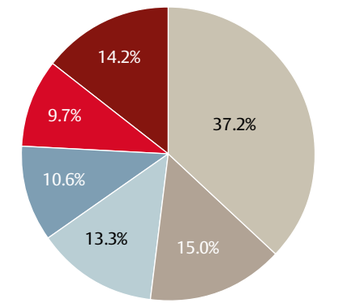


Figure 4. Distribution of 113 anatomical complexities in patients in the CLASP IID registry.

[a]Other includes presence of significant cleft or perforation in the clasping area (6.2%), moderate to severe calcification in the clasping area (3.5%), leaflet mobility length <8 mm (3.5%), history of endocarditis and significant tissue defects in the leaflet (0.9%).
Adapted from Smith RL *et al.* 2023.[5]

Composite MAEs	83.5%
All-cause mortality	89.3%
Cardiovascular mortality	94.6%
Heart failure hospitalisation	91.5%

Figure 5. Kaplan–Meier freedom from various clinical outcomes at 1 year in the CLASP IID registry.[5]

MAE, major adverse event.

Significant MR reduction was achieved at 1 year, with 93.2% of patients achieving MR ≤2+ and 57.6% achieving MR ≤1+ (Figure 6). Post-procedural transmitral valve gradients remained low and stable, with a mean of 4.3 mmHg at 1 year (p=0.230 *vs* discharge). Additionally, related echocardiographic measures improved, including significant decreases in both left ventricular end-diastolic volume (−19.1%) and left ventricular end-systolic volume (−12.4%) *versus* baseline (p<0.001).[5] This is the first study to demonstrate remodelling in these elderly patients, emphasises Professor von Bardeleben.

Patients also benefited from meaningful improvements in functional capacity and quality of life. At 1 year, 78.3% of patients were in NYHA class I/II, compared with 30.7% at baseline (p<0.001; Figure 7), and 6-minute walk distance increased by 22.4 m *versus* baseline (p=0.206; paired analysis). Overall, KCCQ score increased on average by 14.8 points (p<0.001 *vs* baseline; paired analysis).[5]

Overall, these results from the CLASP IID registry demonstrate favourable safety, significant and sustained MR reduction, and meaningful functional and quality of life improvements at 1 year in patients at prohibitive surgical risk with degenerative MR ≥3+ and complex mitral valve anatomy.[5]

Conclusion

Together, the results from the CLASP IID RCT and CLASP IID registry illustrate the value of the PASCAL repair system in successfully treating a wide range of patients with severe, symptomatic degenerative MR at prohibitive surgical risk. Both studies demonstrated high survival, significant and sustained MR reduction and meaningful benefits in functional and quality-of-life outcomes.[1,5]

Our population is ageing, notes Professor von Bardeleben, and society must enable a better quality of life for elderly citizens. In his view, functional and quality-of-life improvements, together with evidence of remodelling, indicate that M-TEER reverses heart failure in patients with degenerative MR, and therefore the procedure is likely to be the most impactful transcatheter therapy for at least the next 5 years.

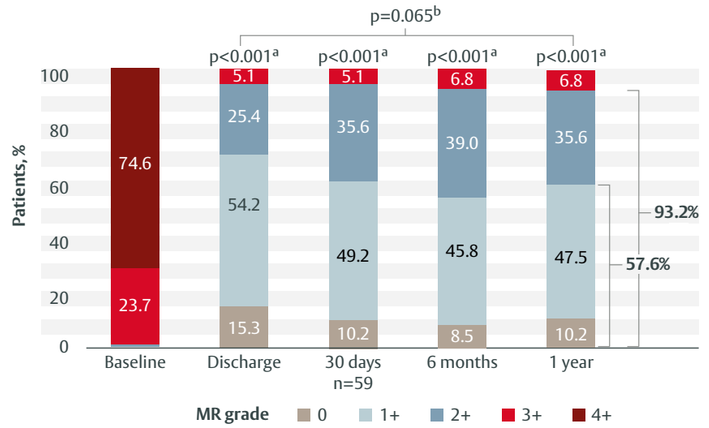


Figure 6. MR reduction with the PASCAL repair system in patients with significant symptomatic degenerative MR and complex anatomy precluding use of the MitraClip system (CLASP IID registry).

Echocardiographic core laboratory assessed MR severity by transthoracic echocardiography. Baseline qualification for one patient used transoesophageal echocardiography. Complex anatomy judgement based on the anatomical considerations in the special patient populations section of the current MitraClip system Instructions for Use.[9]
Graph shows paired analysis; [a]p values calculated using the Wilcoxon signed rank test; [b]calculated for MR ≤1+ by exact McNemar's test.
MR, mitral regurgitation; RCT, randomised controlled trial.
Adapted from Smith RL *et al.* 2023.[5]

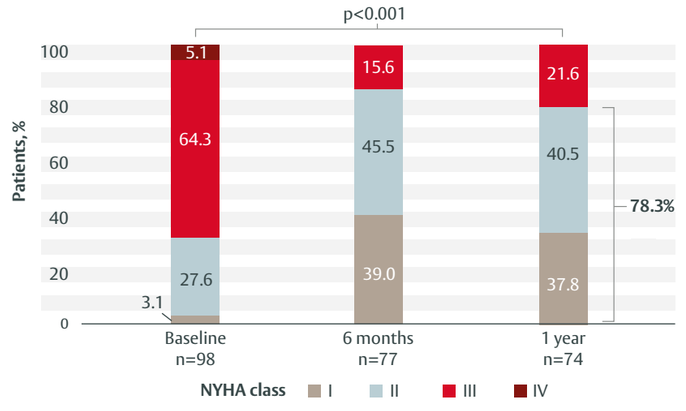


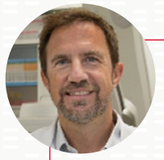
Figure 7. NYHA functional class at baseline and following treatment with the PASCAL repair system in patients with significant symptomatic degenerative MR and complex anatomy precluding use of the MitraClip system (CLASP IID registry).

Graph shows unpaired analysis. p value calculated from paired analysis using the Wilcoxon signed rank test. Complex anatomy judgement based on the anatomical considerations in the special patient populations section of the current MitraClip system Instructions for Use.[9]
MR, mitral regurgitation; NYHA, New York Heart Association.
Adapted from Smith RL *et al.* 2023.[5]

Atraumatic clasp and closure of the PASCAL and PASCAL Ace implants

PASCAL Precision System: Assessing the effect of multiple clasping attempts on the mitral and tricuspid valves

The PASCAL Precision system enables users to perform multiple attempts to clasp the leaflets, if required, to optimise the final placement of the PASCAL or PASCAL Ace implants.[2,7] Physicians may wonder if multiple clasping attempts eventually induce leaflet tissue damage, thereby potentially impacting valve function. Here, Professor Dabit Arzamendi explains how the impact of multiple clasping attempts on the leaflets has been studied, demonstrating that leaflet integrity is preserved, even under extreme repeated clasp and closure circumstances.



Professor Dabit Arzamendi

Department of Cardiology, Hospital Sant Pau, Barcelona, Spain

Professor Dabit Arzamendi in an interventional cardiologist at the Hospital Sant Pau in Barcelona. His specialities include percutaneous aortic, mitral and tricuspid valve treatments, intracardiac septal defect repair and complex coronary interventions.

> The PASCAL Precision system allows multiple clasping attempts, using both independent and/or simultaneous clasping to optimise leaflet capture or reposition the implant when aiming to achieve an optimal outcome. This is possible because of several features of the device that ensure atraumatic clasp and closure. Both clasps on the PASCAL and PASCAL Ace implants have a single row of retention elements with horizontal orientation at the distal end of the clasp (Figure 8). This retention element configuration is advantageous because it aligns with collagen fibres in the leaflet and targets the mid-point of the leaflet consisting of dense fibrosa tissue, rather than the soft spongiosa tissue on the free edge of the leaflet.[10,11] In addition, the nitinol construction of the PASCAL and PASCAL Ace implants allows for spring-like closure to conform to native anatomy and dynamic flexing during the cardiac cycle (Figure 8). The native state of the implant is in the closed position. The paddles constantly apply a passive force towards the spacer, and the clasps constantly apply a downward force on the inner paddle to maintain leaflet capture. During the cardiac cycle, outward forces are applied to the paddles, causing them to flex. Over time, sufficient tissue in-growth minimises paddle flexing. Overall, these implants are designed to preserve the leaflets, even in complex cases where multiple attempts to clasp the leaflets are needed.
>
> Can we be confident that the leaflets do not sustain damage that impacts their ability to function? Based on the results from an *ex vivo* study,[2] I believe the answer is yes.

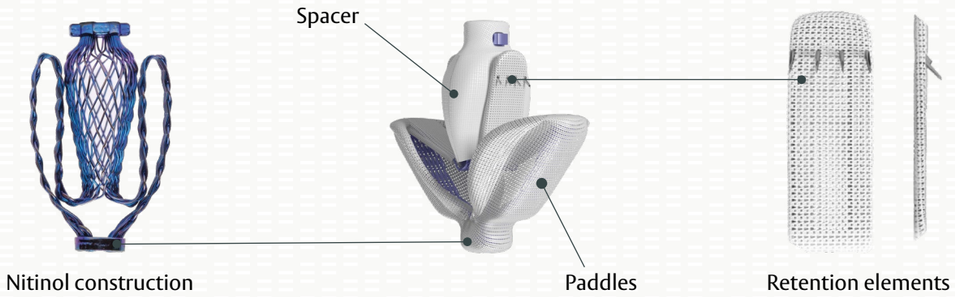


Figure 8. The PASCAL implant has a single row of retention elements to clasp, reclasp and preserve leaflets and a nitinol construction to conform to native anatomy and flex during the cardiac cycle.

The experimental set-up: An *ex vivo* specialised steady flow model using cadaver hearts to simulate *in vivo* tissue conditions and interactions

To better represent the native properties of human mitral and tricuspid valve leaflets, this study, performed in partnership with the CVPath Institute (Gaithersburg, MD, USA), used human cadaver hearts (n=9). To allow for testing and optimal visualisation, both atria were opened to expose the tricuspid and mitral valves. Afterwards, the heart was sutured to a ring holder to keep it in place in the specialised model set-up, and a pump was used to generate forward pressure in the ventricle to increase ease of capture.[2,7]

To assess the impact that multiple leaflet capture attempts may have on the leaflets, each mitral and tricuspid valve was marked into two parts: the experimental side and the control side. For the experimental side, an extreme scenario was created, with 15 leaflet captures and closing attempts using either the PASCAL or PASCAL Ace implants.

For the control side, instead, up to two captures and closing attempts were performed (Figure 9). For the mitral valve, the anterior and posterior leaflets were evaluated; for the tricuspid valve, the anterior and septal leaflets were evaluated. Immediately after the procedure, the leaflets were excised and photographed digitally. Since there is no available standard to assess clinically relevant injury to the leaflets, leaflet tissue damage was evaluated using a semi quantitative scoring system developed by CV Path, comprising two different types of visual analysis: 1) extent of surface roughening (graded 0–4); and 2) leaflet damage gross score (scored 0–5; Table 1). A clinically relevant injury was defined as a leaflet damage gross score of 4 or 5, because this may have a significant negative impact on the degree of regurgitation.[2,7]

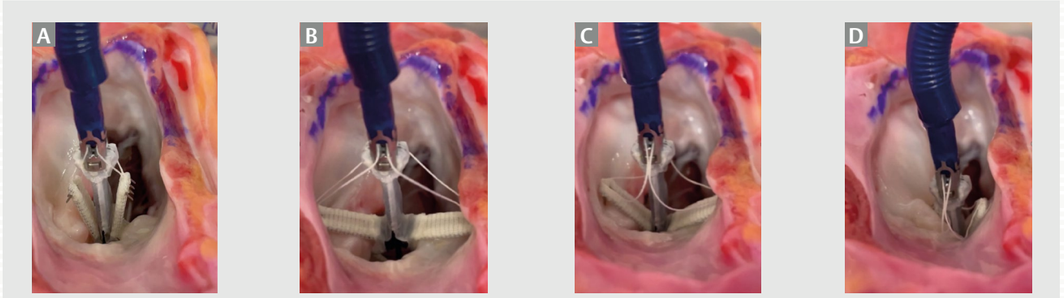


Figure 9. Leaflet capture and device closure for the experimental set-up: A) leaflet on paddles in capture-ready position; B) clasps down; C–D) closure of device, tension release to maximum 3 mm, measured on marked implant catheter.

Table 1. Leaflet damage scoring system.[7]

Beige colouring represents leaflet injury defined to be clinically relevant.

I. Leaflet damage score	II. Grade of surface roughening
Score 0 = no discernible damage	Grade 0 = no roughening
Score 1 = small (≤1 mm in size) with up to ½ leaflet thickness damage as defined by disruption in leaflet surface of surface disruption of collagen on the atrial surface, or ≤1 mm full leaflet thickness tear	Grade 1 = minimal irregularity of the valve
Score 2 = 1–5 mm in size but <½ leaflet thickness damage/ disruption of collagen on the atrial surface	Grade 2 = imprints of the device visible on the surface of the valve
Score 3 = 2–5 mm in size but >½ leaflet thickness damage/ disruption of collagen on the atrial surface	Grade 3 = deep imprint of the device easily visible
Score 4 = 2–5 mm in size with full leaflet thickness damage or tear, which may or may not require repair	Grade 4 = surface tears visible
Score 5 = >5 mm in size and/or full leaflet thickness tear, which would require repair	

Results: No clinically relevant tissue injury, even under extreme experimental conditions

The main findings of this study are represented in Figures 10–12. Gross image evaluation of the leaflets in the region that interacts with the retention elements indicated no cases of clinically relevant injury, in either the experimental or control side, for both the mitral and tricuspid valves (Figure 10). As would be expected, the experimental side (extreme scenario) consistently resulted in higher leaflet injury than the control side (Figures 11 and 12).

However, clinically non-significant surface imprints and superficial damage (<5 mm) were observed on the atrial side of the leaflet only, while the ventricular side was unaffected by repetitive capture and closure.[7] This confirms that the observed superficial tissue injuries are related to the retention elements, and highlights the atraumatic properties of the clasp.

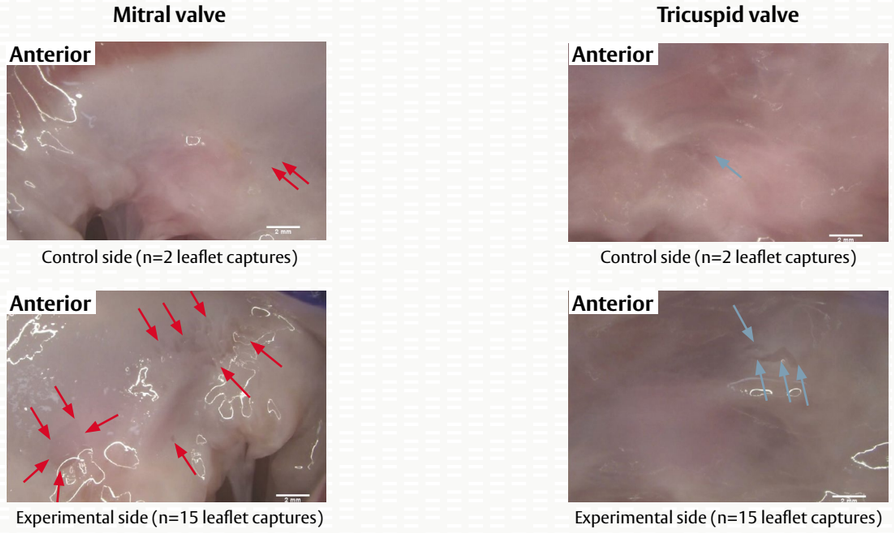


Figure 10. Representative gross images of excised mitral and tricuspid leaflets under the dissection microscope. The leaflet damage was photographed in the region of the leaflets that interacts with the four retention elements lining each clasp.[2,7]

Arrows indicate small surface imprints and damages (<5 mm) visible only on the atrial side of the leaflet. For the mitral valve, both anterior and posterior leaflets were evaluated; for the tricuspid valve, anterior and septal leaflets were evaluated.

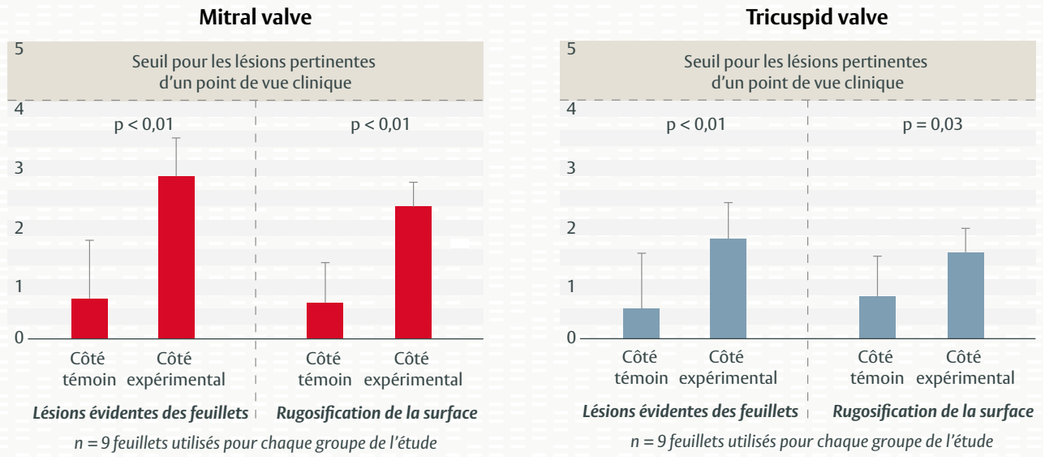


Figure 11. Multiple clasping was performed with either the PASCAL or the PASCAL Ace implants. Leaflet damage was assessed on excised leaflets under the dissection microscope, revealing no clinically relevant injury for either the mitral or tricuspid valve.[2,7]

p values were obtained using Wilcoxon rank-sum test to compare data.
Tests were performed using either the PASCAL implant (n=5 for the mitral valve, n=3 for the tricuspid valve) or the PASCAL Ace implant (n=4 for the mitral valve, n=6 for the tricuspid valve). Observers were three internal, one external.

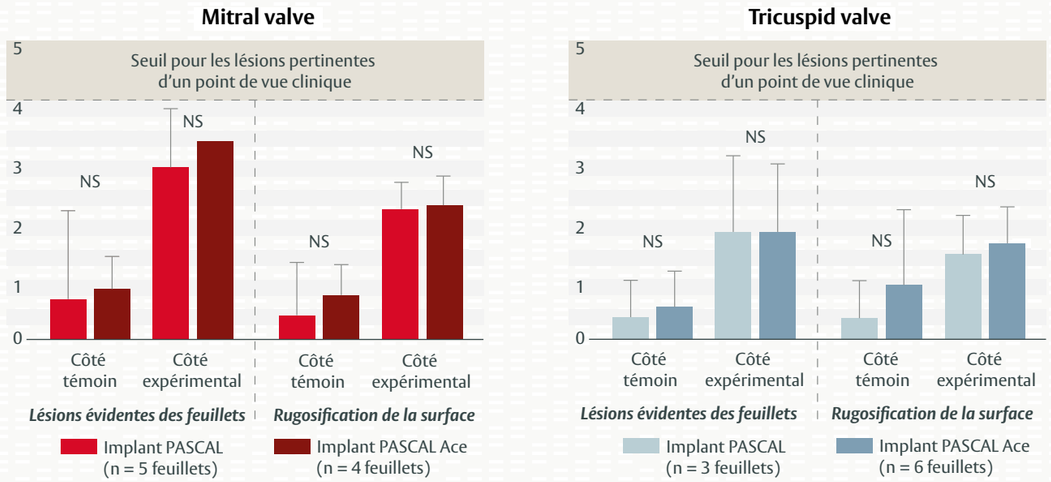


Figure 12. No clinically relevant injury with either the PASCAL or the PASCAL Ace implants after multiple clasping was performed on the mitral or tricuspid valve. Leaflet damage was assessed on excised leaflets under the dissection microscope.[2,7]

Significance was obtained using the Wilcoxon rank-sum test to compare data. Observers were three internal, one external.

Limitations

As with every experimental model, the cadaver heart and *ex vivo* set-up model used in this study have several limitations. In terms of the heart, tissue fragility due to post-mortem autolysis may have exaggerated leaflet tissue damage. On the other hand, the simplified set-up lacked dynamic motion, and the forward flow pressure provided by the pump was below physiological pressures. This may have underestimated the extent of leaflet damage that may occur *in vivo*.[2,7]

Conclusion and physician perspective

In this *ex vivo* study using a human cadaver heart model, semi-quantitative analysis revealed no clinically relevant injury in either the experimental or control sides for both the mitral and tricuspid valves. Any tissue injury resulting from multiple clasping attempts was minimal to mild and present on the atrial side only. The experimental side (extreme situation; subjected to 15 captures) tended to have a higher degree of leaflet injury compared with the control side (subjected up to two captures only); however, even on the experimental side, no clinically relevant injury was reported.[2,7]

Of course, we should always try to obtain a good result at the first clasping attempt; however, this study should reassure operators that optimisation through reclasping is low risk and may dramatically improve the result. In fact, my team optimises implant placement in more than 90% of our procedures because the benefit to our patients is clear. We do more clasping attempts in patients with prolapses. We try to get the whole prolapsing tissue inside the implant, but, sometimes, because of the force of the regurgitation, being precise is difficult. My advice is to try to optimise the placement of a PASCAL or PASCAL Ace implant in a physiological manner, avoiding tension and rotation. If in any doubt, with the leaflets inside the implant, quickly open and close the clasps to reduce the tension.

With the PASCAL platform, optimisation through reclasping is low risk and may help operators achieve better outcomes.

Professor Dabit Arzamendi

Tips and tricks for your patient with MR

Observation of an indirect annuloplasty effect when treating severe functional mitral regurgitation with the PASCAL implant

Case study 1

Dr Sebastian Rosch recently transitioned from his cardiology residency at Heart Center Leipzig to the Center for Cardiology at University Medical Center Mainz. His research primarily focuses on investigating haemodynamic changes in heart failure with preserved ejection fraction and examining the haemodynamic impact of interventional treatments for mitral and tricuspid valve diseases.

Dr Thilo Noack is a senior consultant for cardiac surgery and a heart valve interventionalist in the University Department of Cardiac Surgery at the Heart Center Leipzig. He has extensive experience in all aspects of heart valve interventions and is a strong advocate of the multidisciplinary heart team. His areas of expertise include all types of heart valve interventions, heart valve surgery and complete arterial coronary revascularisation.

The patient

A 66-year-old man in NYHA class III had severe ischaemic cardiomyopathy resulting from advanced coronary disease. The patient's medical history consisted of multiple percutaneous coronary interventions and a cardiac resynchronisation as part of a multimodal heart failure therapy. His left ventricular ejection fraction (LVEF) was severely reduced at 18%. Due to severe ventricular and annular dilatation, we observed a ventricular functional eccentric MR. Considering the patient's severely elevated perioperative risk, the joint decision of our interdisciplinary heart team was for M-TEER.

The challenge

Major challenges in this case were the severely reduced left ventricular function, the massively dilated ventricle and the resulting restriction of both the anterior and posterior mitral valve leaflets (Figure 13). M-TEER in these anatomies may result in elevated postinterventional mean transmitral pressure gradients, which are associated with mortality[12] and therefore need to be prevented.

The approach

Considering the challenges for this patient, we aimed for a two device strategy to achieve residual mild MR. However, to obtain this optimal outcome, we needed to ensure a resulting low transmitral pressure gradient. We hypothesised that the flexible nitinol scaffold of the PASCAL implant would minimise the risk of elevated gradients.

Since we treated this patient in September 2019, before the release of the PASCAL Ace implant, we used the PASCAL implant. Nowadays, we would probably have chosen the PASCAL Ace implant because of the complex subvalvular apparatus in this patient.

The procedure

After transseptal puncture, we inserted the first PASCAL implant in the left atrium and then evaluated an appropriate clasp location within the mitral valve (i.e. sufficient MR reduction, enough space

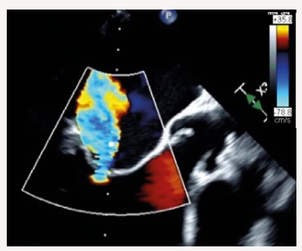


Figure 13. Peri-procedural transoesophageal echocardiography of the mitral valve before implantation.

left for the second device, no relevant mean transmitral gradients). After achieving this, we released the PASCAL implant. We placed the second implant medial to the first device, further optimising the M-TEER result (Figure 14). Here, we optimised leaflet clasping, and hence MR reduction, in a few attempts using the implant's independent leaflet capture mechanism.

We were very happy with the procedure, which resulted in significant MR reduction, with residual mild MR (Figure 15A) and a mean transmitral pressure gradient of 2.1 mmHg at discharge. Besides the convincing procedural result, we also observed a significant acute intraprocedural reduction of the anterior–posterior diameter (from 4.13 cm to 3.95 cm), as well as a reduction in the annular circumference and area.This annuloplasty-like effect is thought to be associated with improved clinical response to M-TEER, particularly in patients with functional MR (FMR),[13,14] and, indeed, this patient had improved NYHA class and reduced N-terminal-pro B type natriuretic peptide at follow-up. Importantly, we observed a durable result at 1 year: the residual MR was still mild (Figure 15B) and the mean transmitral gradient remained unchanged, with no adverse events.

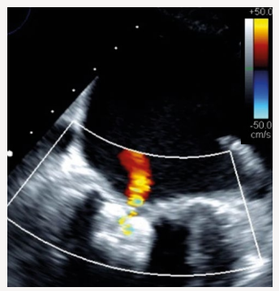


Figure 14. Peri-procedural transoesophageal echocardiography after implantation of the second PASCAL implant.

Key tips

In our experience TEER is effective in two ways for patients with FMR: leaflet approximation and indirect annuloplasty. Consider both when planning your strategy.

Recently, we published a prospective, observational, single-centre study comparing mitral valve geometry changes in patients with FMR following TEER using either the PASCAL repair system or the MitraClip system. The anatomic mitral valve orifice area (AMVOA) was significantly reduced in both groups. The AMVOA in mid and late diastole was larger in patients treated with the PASCAL repair system.[15] This might be relevant as AMVOA reduction has been associated with increased postinterventional transmitral gradient, which was associated with adverse long-term outcomes.[12,15] Importantly, both systems showed a significant and comparable reduction in anterior–posterior diameter, annular circumference and annular area. At 1-year follow-up, a durable result with 90% of patients having MR ≤1+ and evidence for left ventricular reverse remodeling following M-TEER using the PASCAL repair system was observed.[15]

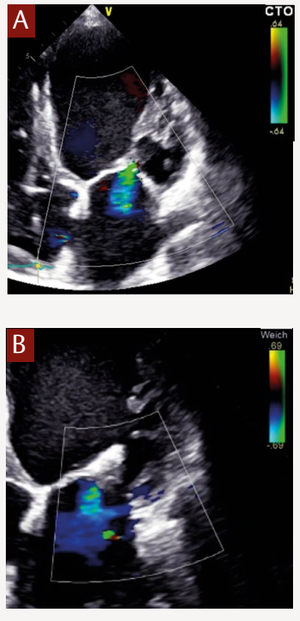


Figure 15. Post-procedural transthoracic echocardiography of the mitral valve at discharge (A) and at 1-year follow-up (B).

Rosch S *et al.* 2023

Treating mitral regurgitation of mixed aetiology with the PASCAL Precision system and the PASCAL Ace implant

Case study 2

Dr med. Sebastian Barth is Chief Senior Consultant in the Department of Cardiology at the Rhön-Klinikum Campus Bad Neustadt in Germany. His research interests include interventional cardiology and transcatheter therapies of the aortic, mitral and tricuspid valves. He has performed around 170 M-TEER procedures with the PASCAL repair system and PASCAL Precision system.

The patient

We admitted an 87-year-old male with progressive heart failure symptoms, left heart decompensation and permanent atrial fibrillation. On admission, he was in poor clinical condition, and echocardiography confirmed severe MR of mixed aetiology, due to atrial annulus dilatation and billowing of both mitral valve leaflets (Figure 16). Considering the patient's frailty and age, the Heart Team decided upon a M-TEER procedure.

The challenge

Treating MR of mixed aetiology is particularly challenging. The complex anatomical conditions make it difficult to predict whether a single implant will be enough to considerably reduce the MR. Additionally, particularly in non-centrally located pathologies, entangling the implant in the subvalvular chords is a risk.

The approach

We decided to use the PASCAL Precision system for this procedure because accurate and intuitive control, accompanied by predictable release of the system, was a prerequisite for coping with this patient's complex anatomy. In addition, the full elongation capabilities of the PASCAL implants facilitate navigation through the subvalvular chordae, which was important in this case. We suspected that we might need to use more than one implant, so we opted for the PASCAL Ace implant with its narrower design profile. Our initial strategy was to start with a central position of the first implant, then see if another was required.

The procedure

We followed our initial strategy of implanting a PASCAL Ace implant centrally. After our first grasping attempt (Figure 17A), we wanted to adjust the implant laterally to ensure an optimal result. We reopened the clasp, but it remained attached to the anterior mitral leaflet. To resolve this, we elongated the implant and detached it atraumatically from the leaflet (Figure 17B). Our second grasping attempt gave an improved result (Figure 17C), and we did not need a second implant.

The procedure was successful (Figure 17D): the patient's MR was reduced from severe to trace, and he was discharged home 4 days after the procedure. At 3-month follow-up, the MR reduction was sustained, and the patient had improved from NYHA functional class III at baseline to class II.

Figure 16. Transoesophageal echocardiography (A) and 3D echocardiography (B) of the mitral valve at admission.

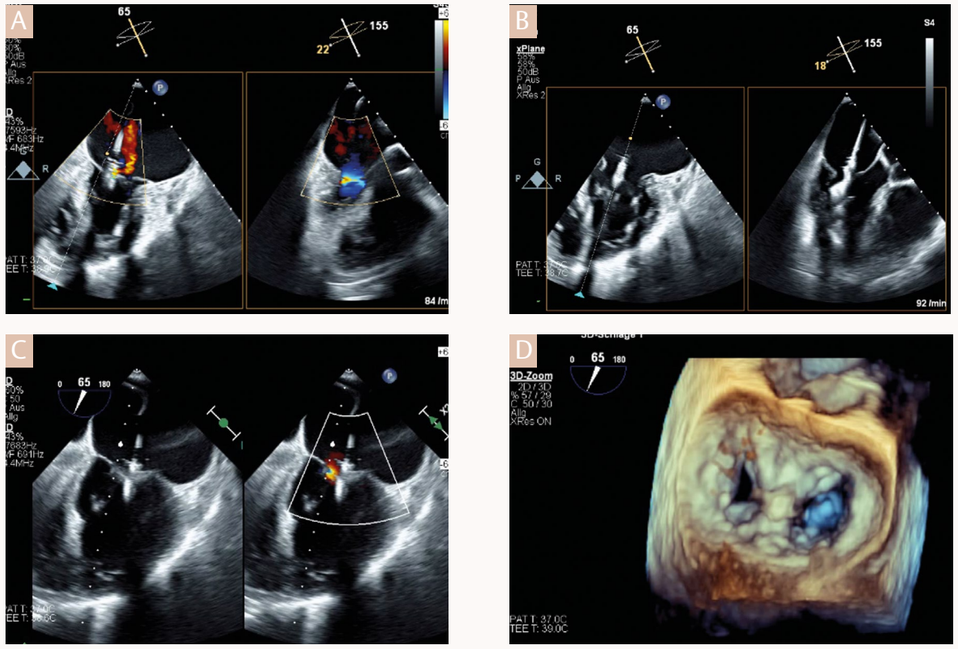


Figure 17. Transoesophageal echocardiography of the first grasping attempt (A), the disengagement of the PASCAL Ace implant from the anterior mitral leaflet by elongation (B), the second grasping attempt (C) and 3D echocardiography after final positioning of the PASCAL Ace implant (D).

Key tips

I particularly recommend the PASCAL Precision system for complex anatomies with eccentric and multiple MR jets. This case illustrated two of its key advantages: the independent grasping and the ability to elongate the implant.

A particular advantage of the PASCAL Precision system is that the device can be navigated through the subvalvular chordae by elongation.

Dr Sebastian Barth

Treating functional mitral regurgitation with the PASCAL Precision system and the PASCAL implant

Dr med. Claudia Walther is a senior consultant in the Department of Interventional Cardiology at CCB Frankfurt, Germany. She specialises in heart failure, acute myocardial infarction, interventional cardiology and functional coronary diagnostics. Dr Walther has performed around 600 TEER procedures, of which about 100 used the PASCAL repair system or PASCAL Precision system.

The patient

A 69-year-old male was referred to our centre with signs of decompensated heart failure. We already knew him from a previous myocardial infarction and ongoing ischaemic cardiomyopathy. He had multiple comorbidities, including peripheral arterial disease, diabetes, arterial hypertension and atrial fibrillation. After surgery for colon cancer earlier this year, his condition deteriorated, resulting in an LVEF of around 25% and MR grade 3. The patient had a EuroSCORE II of 5.4%, putting him at moderate surgical risk, but because of his cardiomyopathy and comorbidities, the Heart Team chose a transcatheter approach.

The challenge

We often see patients with ischaemic cardiomyopathy and this Carpentier type 3b tethering of the posterior leaflet. However, the challenge here was the restrictive posterior leaflet with pseudo prolapse of the anterior leaflet causing functional, but also eccentric, MR (Figure 18). We know from the COAPT trial that patients with FMR have good outcomes regarding hospitalisation and mortality, but this patient had a left ventricular diameter of 70–74 mm, which is on the boundary of COAPT inclusion criteria. However, we decided to proceed with TEER.

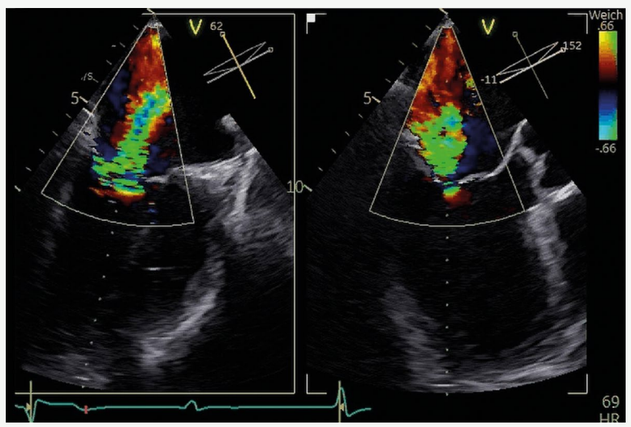


Figure 18. Pre-procedural echocardiography of the mitral valve showing a large, eccentric jet.

The approach

The FMR went over the whole coaptation line from medial to lateral, so we decided upon a one device strategy in the A2/P2 region. We chose to use the PASCAL Precision system because it enables us to recapture the leaflets and optimise implant positioning without the fear of losing a leaflet. In this case, we had almost no leaflet coaptation, so we chose the PASCAL implant with its wider spacer and larger paddles than the PASCAL Ace implant. We hoped that this implant would minimise tension on the leaflets and, obviously, reduce the MR.

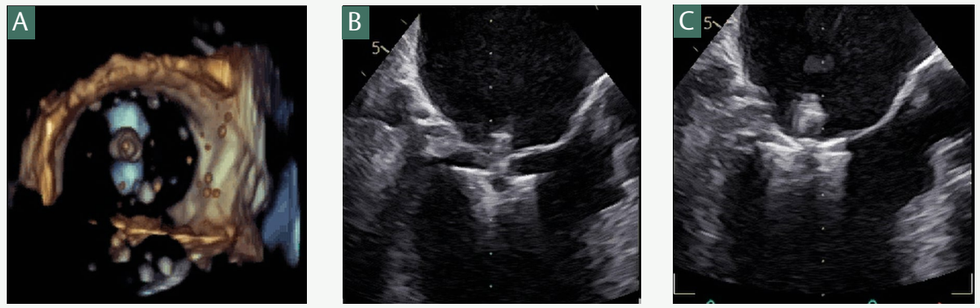


Figure 19. Echocardiography showing clocking of the PASCAL implant in the A2/P2 region in 3D view (A), open PASCAL implant with mitral valve leaflets on the paddles (B) and capture-ready PASCAL implant with clasps down (C).

The procedure

After a straightforward transeptal puncture, we followed our planned one-device strategy. Optimising the posterior leaflet was foremost in my mind, and we managed this easily with the PASCAL Precision system. First, I simultaneously clasped the leaflets, then switched to independent clasping to grasp more of the posterior leaflet (Figure 19). Notably, we measured haemodynamics during the procedure and saw the left atrial V wave pressure drop by 10 mmHg when we closed the implant. This was helpful when deciding if we should release it. We managed to reduce the patient's MR to a trace level, so I was really happy with the result (Figure 20).

Key tips

In my opinion, the PASCAL Precision system is easy to use, even for people new to TEER. If you worry about entanglement in chordae, the PASCAL Precision system is forgiving because you can elongate the implant for easy navigation.

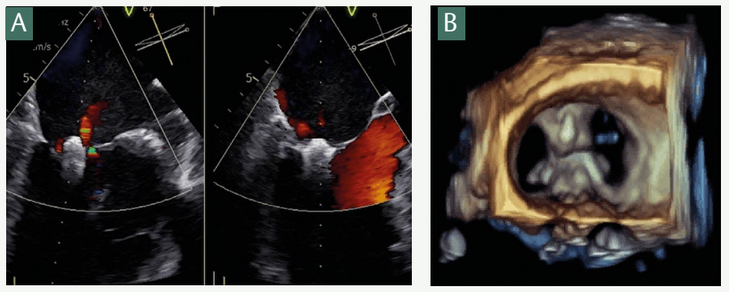


Figure 20. Post-procedural echocardiography showing trace MR (A) and the double orifice in 3D view (B).

> We had almost no leaflet coaptation, so we chose the PASCAL implant with its wider spacer and larger paddles than the PASCAL Ace implant. We hoped that this implant would minimise tension on the leaflets and, obviously, reduce the MR.
>
> **Dr Claudia Walther**

Treating mitral and tricuspid regurgitation in a two-stage approach with the PASCAL repair system

Prof. Dr med. Maurizio Taramasso is a specialist in cardiac surgery at the Heart Center Hirslanden Zurich in Switzerland. His main interests include surgical and transcatheter treatments of valvular heart disease and heart failure. He has performed over 1,000 TEER procedures on the mitral valve, of which about 70 used the PASCAL repair system or PASCAL Precision system.

The patient

A hospitalised 80-year-old female in NYHA class IV with recurrent decompensations was referred to the Heart Team. She had a history of previous hospitalisations, long-standing atrial fibrillation and chronic coronary artery disease. Despite guideline-directed medical therapy, recompensation was not possible. She had severe FMR, torrential tricuspid regurgitation (TR), severe biatrial dilatation and moderate right ventricular dysfunction (Figure 21). Considering the patient's clinical condition and comorbidities, the Heart Team recommended a transcatheter approach.

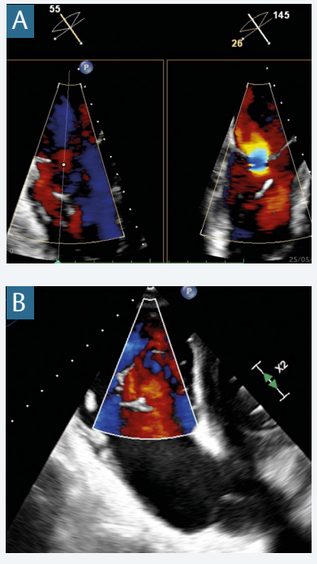


Figure 21. Pre-procedural echocardiograms, showing severe MR (A) and torrential TR with a large coaptation gap (B).
MR, mitral regurgitation;
TR, tricuspid regurgitation.

The challenge

The tricuspid coaptation gap was huge (Figure 21B), lessening the chance of procedural success of tricuspid TEER.

The approach

Our strategy was a staged procedure: M-TEER first, then recompensation and tricuspid TEER as the second stage. If the tricuspid coaptation gap had been smaller, we might have considered a concomitant procedure.

The procedure

We kept to our staged strategy; first, implanting a PASCAL Ace implant in the mitral position (Figures 22A and 22B). Since the main aetiology was atrial FMR in the context of atrial fibrillation (with mostly annular dilatation), we chose the PASCAL Ace implant in order to better stabilise the annular dimensions by pulling more on the leaflets. After 4 weeks of patient rehabilitation, echocardiography confirmed the success of the mitral valve repair, with only mild MR remaining (Figures 22C and 22D). In addition, we saw improved leaflet coaptation in the tricuspid valve (Figure 23). Therefore, we proceeded with stage 2, implanting a PASCAL Ace implant in the anterior–septal position of the tricuspid valve. We placed it as far as possible from the commissure without leaving a residual jet between the implant and commissure (Figure 24A). We then implanted a second PASCAL Ace implant more centrally (Figure 24B). The result was good: TR was reduced to mild, and the patient was asymptomatic at 3 months' follow-up.

Key tips

The PASCAL Precision system is user friendly, and single-operator intervention is possible. It is ideal for commissural lesions.

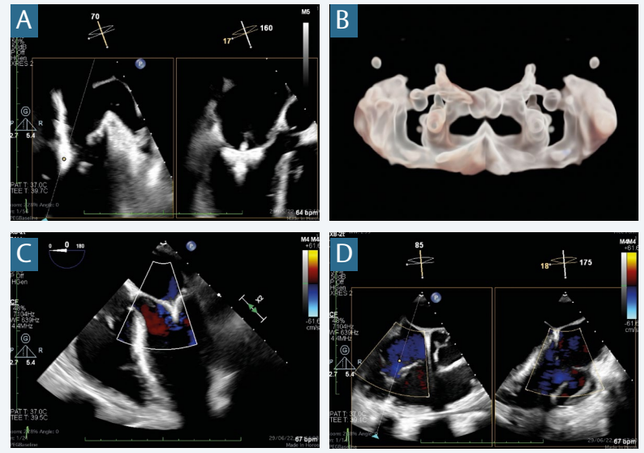


Figure 22. Echocardiograms of the mitral valve, showing the PASCAL Ace implant in position during the procedure (A and B) and after 4 weeks of patient rehabilitation (C and D).

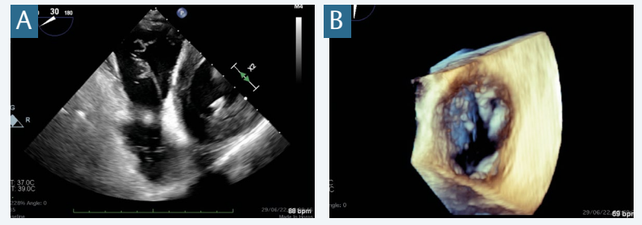


Figure 23. Echocardiograms of the tricuspid valve 4 weeks after mitral valve repair, showing improved leaflet coaptation.

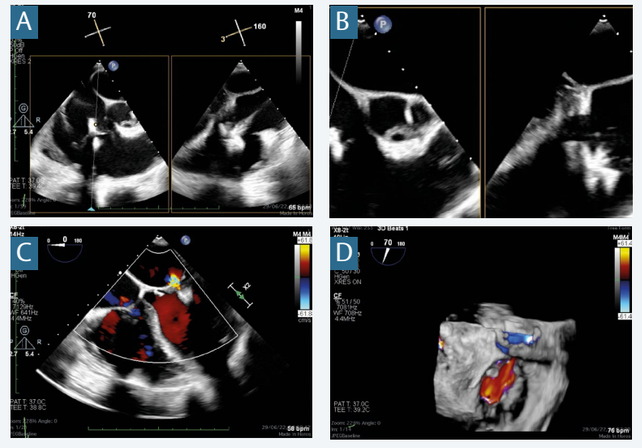


Figure 24. Echocardiograms of the tricuspid valve after the placement of the first (A) and second (B) PASCAL Ace implants, and the final result (C and D).

We chose a PASCAL Ace implant in the mitral position to better stabilise the annular dimensions.
Professor Maurizio Taramasso

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Conclusion

This issue reinforces that the PASCAL platform is effective at treating MR in a diverse range of patients.[1,5] Importantly, it preserves leaflet integrity, even after multiple clasping attempts to optimise leaflet capture.[2,7] The Edwards reusable accessories should further enhance procedures with the PASCAL Precision system, while reducing hospitals' plastic waste post procedure.

Ask your questions...

We can be reached at TMTT-Today@edwards.com to answer your questions about the portfolio of therapies for transcatheter mitral and tricuspid valve therapies.

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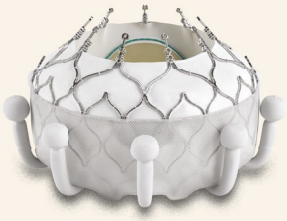

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