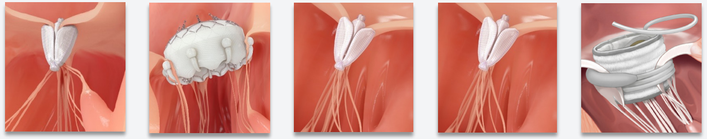
Building a body of clinical evidence

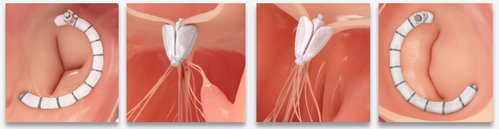
Edwards Lifesciences is committed to advancing and expanding treatment options for patients with tricuspid or mitral regurgitation.

5 pivotal trials
to transform the standard of care



THE CLASP II TR TRIAL | THE TRISCEND II PIVOTAL TRIAL | THE CLASP IID TRIAL | THE CLASP IIF TRIAL | THE ENCIRCLE TRIAL

4 EU postmarket studies
to build real-world evidence



TriBAND*
tricuspid system

TriCLASP*
tricuspid system

MiCLASP
mitral system

MiBand*
mitral system

4 early feasibility studies
to advance learnings

TRISCEND*
tricuspid system

Tricuspid EFS*
tricuspid system

SAPIEN M3*
mitral system

MISCEND*
mitral system

PASCAL Precision system is only approved for DMR in the US.

*CAUTION: Investigational devices. Limited by Federal (USA) law to investigational use. Except for PASCAL Precision for use in DMR patients, the devices are not available for marketing or commercial sale in the United States.

Explore the PASCAL system at Edwards.com/PASCAL

Important Safety Information

Edwards PASCAL Precision Transcatheter Valve Repair System

Indications: The PASCAL Precision transcatheter valve repair system (the PASCAL Precision system) is indicated for the percutaneous reduction of significant, symptomatic mitral regurgitation (MR ≥ 3+) due to primary abnormality of the mitral apparatus (degenerative MR) in patients who have been determined to be at prohibitive risk for mitral valve surgery by a heart team, which includes a cardiac surgeon experienced in mitral valve surgery and a cardiologist experienced in mitral valve disease, and in whom existing comorbidities would not preclude the expected benefit from reduction of the MR.

Contraindications: The PASCAL Precision system is contraindicated in patients with the following conditions: patients who cannot tolerate procedural anticoagulation or post procedural anti-platelet regimen; untreatable hypersensitivity or contraindication to nitinol alloys (nickel and titanium) or contrast media; active endocarditis of the mitral valve; rheumatic etiology for mitral regurgitation; evidence of intracardiac, inferior vena cava (IVC) or femoral venous thrombus.

Warnings: The devices are designed, intended, and distributed for single use only. There are no data to support the sterility, non-pyrogenicity, and functionality of the devices after reprocessing. Devices should be handled using standard sterile technique to prevent infection. Do not expose any of the devices to any solutions, chemicals, etc., except for the sterile physiological and/or heparinized saline solution. Irreparable damage to the device, which may not be apparent under visual inspection, may result. Do not use any of the devices in the presence of combustible or flammable gases, anesthetics, or cleaners/disinfectants. Do not use the devices if the expiration date has elapsed. Do not use if the packaging seal is broken or if the packaging is damaged for sterile devices. Do not use if any of the devices were dropped, damaged or mishandled in any way. Standard flushing and de-airing technique should be used during preparation and throughout procedure to prevent air embolism.

As with any implanted medical device, there is a potential for an adverse immunological response. Serious adverse events, sometimes leading to surgical intervention and/or death, may be associated with the use of this system ("Potential Adverse Events"). A full explanation of the benefits and risks should be given to each prospective patient before use. Careful and continuous medical follow-up is advised so that implant-related complications can be diagnosed and properly managed. Anticoagulation therapy must be determined by the physician per institutional guidelines.

Precautions: Prior to use, patient selection should be performed by a heart team to assess patient risk and anatomical suitability. After use, short-term anticoagulation therapy may be necessary after valve repair with the PASCAL Precision system. Prescribe anticoagulation and other medical therapy per institutional guidelines.

Potential Adverse Events: Below is a list of the potential adverse effects (e.g., complications) associated with the use of the PASCAL Precision system: death; abnormal lab values; allergic reaction to anesthetic, contrast, heparin, Nitinol; anemia or decreased hemoglobin (may require transfusion); aneurysm or pseudoaneurysm; angina or chest pain; anaphylactic shock; arrhythmias – atrial (i.e. atrial fibrillation, Supraventricular tachycardia); arrhythmias – ventricular (i.e. ventricular tachycardia, ventricular fibrillation); arterio-venous fistula; atrial septal injury requiring intervention; bleeding; cardiac arrest; cardiac failure; cardiac injury, including perforation; cardiac tamponade/pericardial effusion; cardiogenic shock; chordal entanglement or rupture that may require intervention; coagulopathy, coagulation disorder, bleeding diathesis; conduction system injury which may require permanent pacemaker; deep vein thrombosis (DVT); deterioration of native valve (e.g., leaflet tearing, retraction, thickening); dislodgement of previously deployed implant; dyspnea; edema; electrolyte imbalance; emboli/embolization including air, particulate, calcific material, or thrombus; endocarditis; esophageal irritation; esophageal perforation or stricture; exercise intolerance or weakness; failure to retrieve any PASCAL Precision system components; fever; gastrointestinal bleeding or infarct; heart failure; hematoma; hemodynamic compromise; hemolysis; hemorrhage requiring transfusion or intervention; hypertension; hypotension; implant deterioration (wear, tear, fracture, or other); implant embolization; implant malposition or failure to deliver to intended site; implant migration; implant thrombosis; infection; inflammation; LVOT obstruction; mesenteric ischemia; multi-system organ failure; myocardial infarction; native valve injury; native valve stenosis; nausea and/or vomiting; need for open surgery (conversion, emergent or nonemergent reoperation, explant), nerve injury neurological symptoms, including dyskinesia, without diagnosis of TIA or stroke; non-neurological thromboembolic events; pain; papillary muscle damage; paralysis; PASCAL Precision system component(s) embolization; peripheral ischemia; permanent disability; pleural effusion; pulmonary edema; pulmonary embolism; reaction to anti-platelet or anticoagulation agents; renal failure; renal insufficiency; respiratory compromise, respiratory failure, atelectasis, pneumonia – may require prolonged ventilation; retroperitoneal bleed; septal damage or perforation; septicemia, sepsis; skin burn, injury or tissue changes due to exposure to ionizing radiation; single leaflet device attachment (SLDA); stroke; syncope; transient ischemic attack (TIA); urinary tract infection and/or bleeding; valvular regurgitation; vascular injury or trauma, including dissection or occlusion; vessel spasm; ventricular wall damage or perforation; worsening native valve regurgitation / valvular insufficiency; worsening of heart failure; wound dehiscence, delayed or incomplete healing.

References

1. Zahr F, Smith RL, Gillam LD, et al. One-year Outcomes from the CLASP IID Randomized Trial for Degenerative Mitral Regurgitation. J Am Coll Cardiol Intv 2023; Oct 26; [Epub Ahead of Print].
2. Smith RL, Lim SD, Gillam, LD, et al. One-year Outcomes of Transcatheter Edge-to-Edge Repair in Anatomically Complex Degenerative Mitral Regurgitation Patients. J Am Coll Cardiol Intv 2023; Oct 26; [Epub Ahead of Print].
3. Spargias K, Lim DS, Makkar R, et al. Three-year outcomes for transcatheter repair in patients with mitral regurgitation from the CLASP study. Catheter Cardiovasc Interv. 2023 Jul;102(1):145-154. doi: 10.1002/ccd.30686. Epub 2023 May 13.

CAUTION: Federal (United States) law restricts this device to sale by or on the order of a physician. See instructions for use for full prescribing information.

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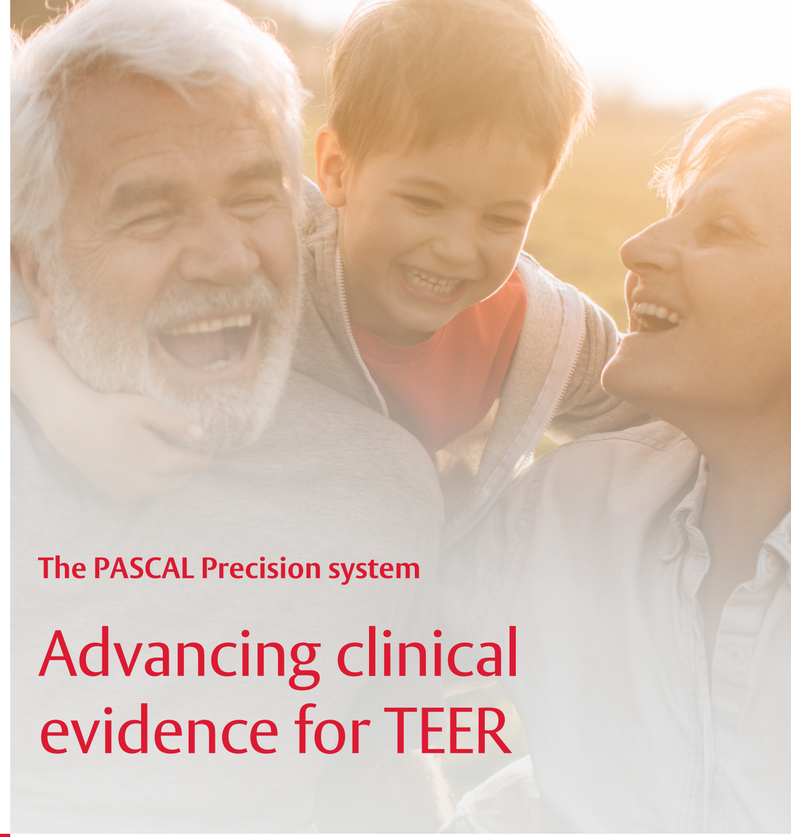


The PASCAL Precision system

Advancing clinical evidence for TEER

Compelling evidence for patients with clinically significant degenerative mitral regurgitation (DMR)

The CLASP IID trial, CLASP IID registry and CLASP study form a body of evidence supporting the safety, efficacy and durability of TEER for patients with significant DMR (MR 3+ or 4+).

Edwards

PASCAL system body of clinical evidence

THE CLASP IID TRIAL

The CLASP IID Trial: The first head-to-head trial in transcatheter edge-to-edge repair (TEER) for patients with DMR

The CLASP IID trial is the first **randomized controlled** trial to directly compare the safety and effectiveness of **two contemporary** TEER therapies for patients deemed suitable for both the PASCAL system and MitraClip system.

- 54 sites in U.S., Canada, Europe
- Most users were new to the PASCAL system, all were experienced with MitraClip
- Study oversight included independent Echocardiographic Core Laboratory, Central Screening Committee, Clinical Events Committee and Data Safety Monitoring Board

The CLASP IID trial met its primary safety and effectiveness endpoints with the PASCAL system demonstrating a low MAE rate at 30 days and significant MR reduction at 6 months.[1]

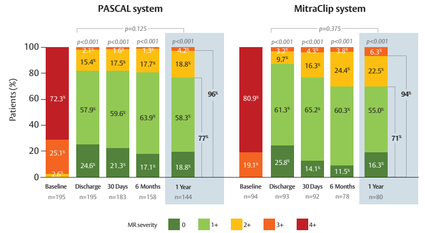
	PASCAL system	MitraClip system
Composite MAE rate* at 30 days	4.6% (9/195)	5.4% (5/93)
MR ≤ 2+ at 6 months	97.9% (186/190)	95.7% (88/92)

*Composite MAEs include cardiovascular mortality, stroke, myocardial infarction, new need for renal replacement therapy, severe bleeding, and non-elective mitral valve re-intervention (either percutaneous or surgical).

Patients sustained significant MR reduction with the PASCAL system

Echocardiographic Core Laboratory assessment at 1 year[1]

77%
sustained MR ≤ 1+ at 1 year with the PASCAL system[1]



The PASCAL system demonstrated high survival rates and significant improvements in functional capacity and quality of life outcomes at 1 year

91%
freedom from all-cause mortality at 1 year[1]

88%
of patients achieved NYHA Class I/II at 1 year[1]

THE CLASP IID REGISTRY

The CLASP IID Registry: A first-of-its-kind registry to evaluate the PASCAL system in DMR patients with complex anatomy

A prospective, multicenter, multinational, single-arm registry within the construct of the CLASP IID trial. This registry studied prohibitive surgical risk patients deemed suitable for PASCAL only* with significant symptomatic DMR and complex mitral valve anatomy and assessed safety, echocardiographic and clinical outcomes of the PASCAL transcatheter valve repair system.

*Based on the anatomical considerations in the special patient populations section of the current MitraClip Instructions for Use (IFU)

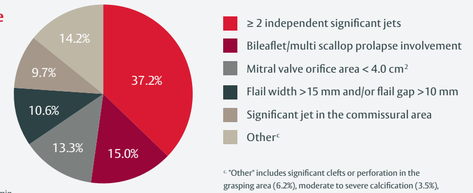
Anatomical complexity criteria[2]

The PASCAL system treated elderly patients with multiple comorbidities and a broad range of mitral valve anatomy

Baseline Characteristics	n=98
Age (years)	81 ± 7
Atrial fibrillation	69%
Renal insufficiency[a]	43%
Pulmonary hypertension[b]	57%

a. Estimated glomerular filtration rate < 60 ml/min to ≤ 25 ml/min
b. Pulmonary artery systolic pressure ≥ 30 mmHg

Baseline anatomical complexity of enrolled patients

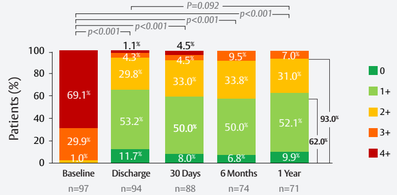


c. "Other" includes significant clefts or perforation in the grasping area (6.2%), moderate to severe calcification (3.5%), leaflet mobility length < 8 mm (3.5%), history of endocarditis and significant tissue defects in the leaflet (0.9%)

DMR patients with complex anatomy showed sustained MR reduction

Echocardiographic Core Laboratory assessment at 1 year[2]

62%
sustained MR ≤ 1+ at 1 year[2]



The PASCAL system demonstrated high survival rates and significant improvements in functional and quality of life outcomes in DMR patients with complex anatomy

89%
freedom from all-cause mortality at 1 year[2]

78%
of patients achieved NYHA Class I/II at 1 year[2]

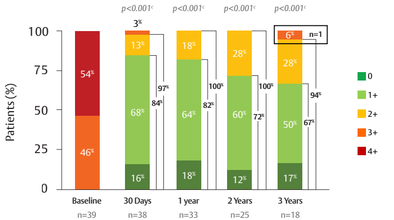
THE CLASP STUDY

The CLASP study: The first international, multicenter study to evaluate the safety and clinical outcomes of the PASCAL system

A prospective multi-center study providing 3-year outcomes of the PASCAL system in patients with clinically significant MR.

Echocardiographic Core Laboratory assessment at 1 year[3]

67%
sustained MR ≤ 1+ at 3 years with the PASCAL system[3]



The PASCAL system demonstrated a high safety profile and significant improvements in functional and quality of life outcomes at 3 years

92%
freedom from all-cause mortality in DMR patients at 3 years[3]

100%
of DMR patients achieved NYHA Class I/II at 3 years[3]

Conclusion

- **The CLASP IID randomized trial** confirms the safety and effectiveness of the PASCAL system for prohibitive surgical risk DMR patients.
- **The CLASP IID Registry** demonstrates the safety and performance of the PASCAL system in prohibitive-risk DMR patients with complex anatomy historically considered unsuitable for M-TEER.
- 3-year outcomes from **the CLASP study** confirm the safety and durability of the PASCAL system in patients with clinically significant MR.