JACC: CARDIOVASCULAR INTERVENTIONS VOL. 18, NO. 8, 2025

ORIGINAL RESEARCH

STRUCTURAL

Transcatheter Pulmonary Valve Implantation Using Self-Expandable Percutaneous Pulmonary Valve System

3-Year CE Study Results

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ABSTRACT

BACKGROUND Pulmonary regurgitation is common during follow-up of patients after surgical repair of tetralogy of Fallot and other right ventricular outflow tracts (RVOTs). Many percutaneous pulmonary valves have been used but are limited to smaller RVOTs.

OBJECTIVES Since August 2016, a multicenter CE (Conformité Européenne) study was initiated to evaluate a self-expandable VenusP-valve. We aimed to report the acute and 3-year follow-up results.

METHODS A total of 81 patients with pulmonary regurgitation were recruited for VenusP-valve implantation and assessed for a 3-year period.

RESULTS In all patients, VenusP-valves were successfully implanted. The mean age was 26.5 ± 13.3 years and the mean weight 59.5 ± 15.6 kg. There was no early procedure-related or late mortality. One patient experienced guidewire perforation of a branch pulmonary artery, causing hemoptysis, and 1 had ventricular tachycardia, at the end of the procedure. During follow-up, 1 patient developed runs of ventricular tachycardia and needed an implantable cardioverter-defibrillator and ablation of the RVOT 5 months after valve implantation. One developed endocarditis 11 months after implantation. After medical treatment, the valve has continued to function normally. One patient developed thrombus on the distal flare 3 years after implantation and was treated with anticoagulants. During 3-year follow-up, valve function has remained satisfactory and right ventricular remodeling has occurred in all patients.

CONCLUSIONS We report the 3-year CE study results of percutaneous pulmonary valve implantation in patients with severe pulmonary regurgitation. The valve has shown promising safety and durability. Long-term evaluation is warranted. (JACC Cardiovasc Interv. 2025;18:1045–1056) © 2025 the American College of Cardiology Foundation. Published by Elsevier. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

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ISSN 1936-8798/$36.00 https://doi.org/10.1016/j.jcin.2024.12.031

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

MPA = main pulmonary artery

PA = pulmonary artery

PPVI = percutaneous pulmonary valve implantation

PR = pulmonary regurgitation

PRF = pulmonary regurgitant fraction

RV = right ventricular

RVEDVi = indexed right ventricular end-diastolic volume

RVOT = right ventricular outflow tract

Pulmonary regurgitation (PR) is common in patients after surgical repair of tetralogy of Fallot and other right ventricular outflow tracts (RVOTs).[1,2] Significant PR may result in progressive right ventricular (RV) dilation/dysfunction. In the past, this was dealt with by surgically replacing the pulmonary valve, however, multiple reoperations may be required during the lifetime, which may be associated with low mortality but significant morbidity.[3,4] To reduce the risks of reoperations, percutaneous pulmonary valve implantation (PPVI) using balloon-expandable valves has been developed and is a recognized alternative treatment.[5,6] A recent multicenter study has shown lower incidence of procedural complications using the SAPIEN valve (Edwards Lifesciences) compared with surgery.[7] The currently approved percutaneous valves in Europe, such as the Melody (Medtronic) and SAPIEN valves, have been used for 10 to 20 years with acceptable results but are limited by their size, as the largest valve available is 29 mm in diameter.[5,8-10] Patients with RVOTs larger than 29 mm have been excluded from PPVI.[10] Recently, self-expanding valves or a combination of self-expanding stent and balloon-expandable valves, such as the Harmony (Medtronic) and the Alterra prestent combined with SAPIEN valve (Edwards Lifesciences), have been used and have been approved by the Food and Drug Administration but have limited availability in Europe.[11,12]

The VenusP-valve (VenusMedtech) is a new self-expandable valve, designed to adapt to RVOTs unsuitable for the Melody and SAPIEN valves. An animal study and early clinical experience have shown excellent valve function.[13] Subsequently, the VenusP-valve has been used in Asia and Europe on a compassionate use basis with encouraging early and midterm results since initial use in 2013.[14-17]

Since August 2016, a multicenter CE (Conformité Européenne) study was undertaken to evaluate the VenusP-valve. The aim of this paper was to report the acute outcomes and 3-year follow-up results.

METHODS

PATIENTS. Between August 2016 and December 2021, a multicenter study evaluated the outcomes of VenusP-valve implantation. The distribution of study centers and patients are detailed in Table 1.

TABLE 1 Distribution of Study Centers and Patients

	Subjects Enrolled	Study Device Implanted
Eveline London Children's Hospital	19	19
Leeds General Infirmary	7	5
Mater Hospital and Our Lady's Hospital	9	9
Sidra Medicine & Weill Cornell Medicine	9	9
Queen Sirikit National Institute of Child Health	8	8
National Taiwan University Hospital	15	15
The Chinese University of Hong Kong	3	3
Deutsches Herzzentrum der Charité	6	5
University Hospitals Leuven	3	3
Instituto Dante Pazzanese de Cardiologia	5	5
Total	84	81

The study protocol was approved by respective Institutional Review Board or national research ethics committees. Informed consent was obtained from the patient or the legal representatives, depending on the age of the patient and capacity to consent.

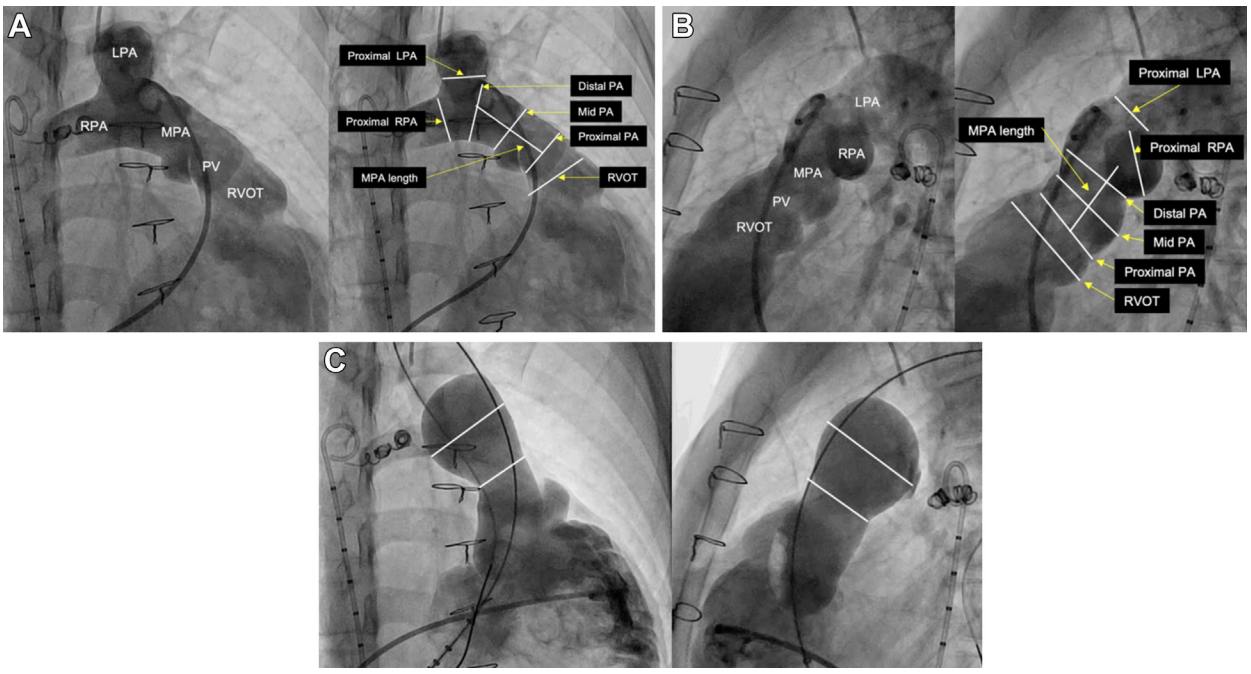
All patients underwent cardiac magnetic resonance (CMR) before the PPVI procedure for assessment of anatomical suitability and pulmonary regurgitant fraction (PRF). After excluding unsuitable patients on CMR, they proceeded to cardiac catheterization for hemodynamic assessment and measurements to determine the appropriate size of the percutaneous pulmonary valve, with additional angiograms performed to evaluate the main pulmonary artery (MPA) and RVOT (Figures 1A and 1B). Simultaneous balloon inflation was performed to interrogate expansibility of MPA (Figure 1C) and the possibility of coronary compression.

PERCUTANEOUS PULMONARY VALVE AND DELIVERY CATHETER SYSTEM. The VenusP-valve consists of 3 porcine pericardial leaflets hand sewn to a self-expanding nitinol stent (Figure 2A). It was designed for dilated patched conduit-free RVOTs. The frame includes a middle straight section and proximal and distal flares, for anchoring in the RVOT and pulmonary artery (PA) bifurcation. The proximal flare is completely covered by porcine pericardium, while the distal flare is uncovered and has an open-cell wire frame allowing access to the PA branches. The middle

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received July 7, 2024; revised manuscript received December 11, 2024, accepted December 17, 2024.

FIGURE 1 Measurement on Angiography



Measurements are made on the angiogram at the different levels shown. (A) Right ventricular angiogram, right anterior oblique projection. (B) Right ventricular angiogram, left lateral projection. (C) Balloon interrogation of the right ventricular outflow tract (RVOT) and main pulmonary artery (MPA). Interrogation with a compliant balloon with simultaneous right ventricular angiogram. Measurements are made of the waist(s) and the dilated part(s) on the balloon to help with choice of a valve. LPA = left pulmonary artery; PA = pulmonary artery; PV = pulmonary valve; RPA = right pulmonary artery.

section houses the valve. There are radiopaque gold markers at the level of the distal and proximal flares. The diameters of the middle section are 26 to 36 mm in 2-mm increments, and the lengths (of the straight section) are from 20 to 30 mm in 5 mm increments. The flares are 10 mm larger in diameter than the middle section. There are 2 small "ears" at the proximal flare, for attaching and loading the valve. The valve, when released in situ, has an expanded length varying between 52 mm (for the smallest diameter and length) and 61 mm for the largest.

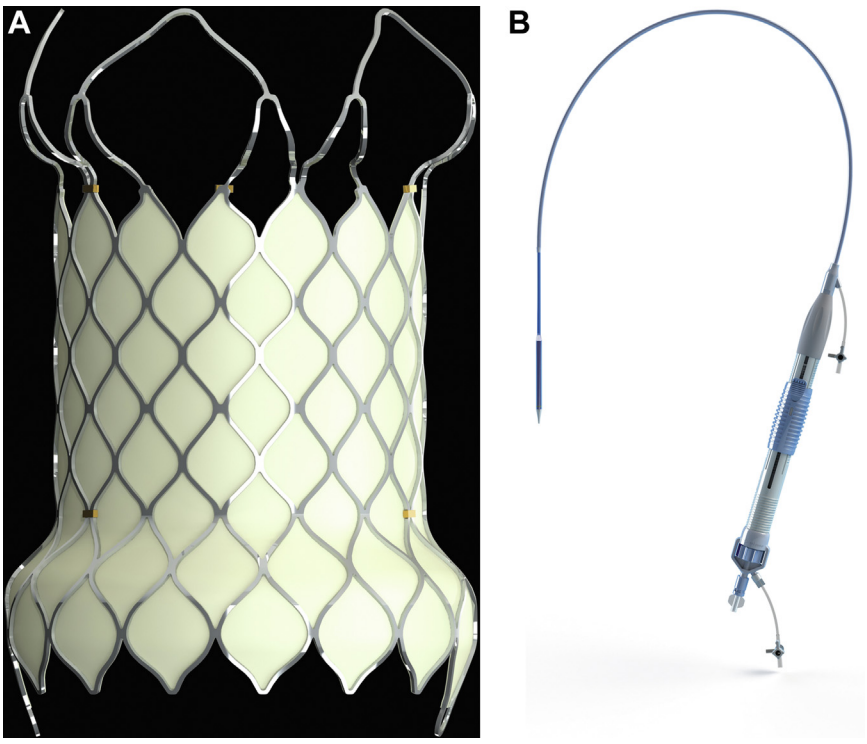
The Delivery Catheter System is 22-F to 24-F with a 12-F, 110-cm-long shaft, compatible with a 0.035-inch guidewire (Figure 2B). A distal capsule contains the loaded valve. The distal end has an atraumatic radiopaque nosecone. The valve is crimped with a crimping device and loaded under sterile ice/saline solution, and protected by a sheath, to maintain the valve in a crimped position.

The rotating handle at the proximal end of the delivery system is connected to a slide knob. To load the crimped valve, the knob is turned anticlockwise, and to deploy the valve, it is turned clockwise.

STUDY OUTCOME. Patients 12 to 70 years of age with moderate or greater PR were enrolled. Active infection requiring current antibiotic therapy and history of active endocarditis were excluded. The primary safety endpoints included valve/procedure-related deaths or reoperations at 12 months and major adverse cardiac and cerebrovascular events at 1 month. The primary performance endpoint was evaluated based on valve placement success, hemodynamic measurements at 1 month, PR improvement during follow-up, and structural deterioration at 6 months.

PROCEDURAL STEPS FOR PPVI. The technique has been described in detail in previous studies.[14-17] All the procedures were performed under general anesthesia using both femoral veins and a femoral artery. Heparin 100 U/kg was given after obtaining access, and the activated clotting time was maintained at >250 seconds during the procedure. After detailed hemodynamic assessment, RVOT and PA dimensions were reassessed from angiograms in right anterior oblique/cranial and lateral views. A 260-cm long

FIGURE 2 VenusP-Valve System



The VenusP-valve system consists of 2 parts: the percutaneous pulmonary valve and the VenusP-valve delivery system. (A) The percutaneous pulmonary valve consists of a self-expanding nitinol stent with a tri-leaflet porcine pericardium tissue valve. (B) VenusP-valve delivery system.

0.035-inch Lunderquist extra-stiff guidewire (Cook Medical) was positioned in a distal left or right lower PA. Balloon interrogation was performed with a compliant, low-pressure 34-mm-diameter/4-cm-long Amplatzer Sizing Balloon Catheter (St. Jude Medical) or a similar atrial septal defect sizing balloon, before the final valve selection. Selected valve diameter was 2 to 4 mm larger than the balloon waist diameter, while length was based on the distance from the RVOT-to-PA bifurcation. After rinsing the valve in normal saline for at least 15 minutes, it was manually crimped under cold normal saline onto a 20-F to 22-F delivery system. The delivery system/valve assembly was passed through a 22-F Check-Flo Performer Extra Large Introducer (Cook Medical) and placed in the proximal left PA and occasionally in right PA depending on the anatomy. In the latter part of the study, in some institutions, DRYSEAL Flex Introducer sheaths (W.L. Gore & Associates) up to 26-F were used. The distal flare was exposed by slow clockwise rotation of the knob and was withdrawn and positioned in the distal MPA. The valve was adjusted slowly, with frequent pulmonary angiograms via a separately placed 5-F or 6-F pigtail catheter in the MPA, until the valve was fully released. After valve deployment, the RV/PA pressures and MPA angiography were repeated. Hemostasis was achieved with a Perclose ProGlide 6-F Suture-Mediated Closure System (Abbott Vascular) or manual pressure, when the patients were smaller.

The patients received therapeutic heparin or low molecular weight heparin for 24 hours, after which oral aspirin 5 mg/kg/day and clopidogrel 75 mg once daily were given for 6 months, and then aspirin indefinitely. Prophylactic antibiotics were given. The patients were assessed 1 day after the procedure or before discharge, and at 1 month, 3 to 6 months, and yearly. Follow-up included clinical evaluation, electrocardiography, chest radiography, and transthoracic echocardiography. Fluoroscopy was performed in right anterior oblique/cranial and lateral projections 3 to 6 months later, to evaluate for fractures, and CMR was repeated approximately 6 months after the procedure.

TABLE 2 Baseline Characteristics (N = 81)

Age, y	26.5 ± 13.3
Weight, kg	59.5 ±15.6
Male	42 (51.9)
Smoking	4.8 (4)
Renal insufficiency	1.2 (1)
Diabetes requiring therapy	2.5 (2)
Hypertension requiring medication	4.9 (4)
Original congenital heart diseases	
Tetralogy of Fallot	77.7 (63)
Pulmonary stenosis	8.6 (7)
Pulmonary atresia with/without ventricular septal defect	6.2 (5)
Aortic stenosis with Ross operation	4.9 (4)
Noonan syndrome with RVOT repair	1.2 (1)
Endocardial cushion defect and RVOT repair	1.2 (1)
Number of previous open-heart surgeries	1.3 ± 0.6 (81)[a]

Values are mean ± SD, % (n), or mean ± SD (n). [a]Two patients had no records of numbers of previous open-heart surgeries.
RVOT = right ventricular outflow tract.

TABLE 3 Procedure Characteristics (N = 81)

Transfemoral access	100 (81)
Balloon sizing (shape)	
Minimum MPA diameter, mm	27.5 ± 3.5 (78)
Maximum MPA diameter, mm	31.2 ± 3.7 (79)
MPA length, mm	38.3 ± 8.9 (81)
RVOT diameter, mm	32.2 ± 6.9 (81)
Fluoroscopy duration, min	25.2 ± 18.7 (81)
Procedure duration, min	21.7 ± 13.6 (81)
Technical success (at exit from catheter laboratory)[a]	100 (81)
Freedom from mortality	100 (81)
Successful access, delivery of the device, and retrieval of the delivery system	100 (81)
Correct positioning of a single VenusP-valve into correct anatomical location	100 (81)
Freedom from surgery or intervention related to the device or to a major vascular or access related, or cardiac structure complication	100 (81)
Freedom from coronary compression/obstruction	100 (81)

Values are % (n) or mean ± SD (n). A total of 84 patients were enrolled; 81 patients were implanted with the VenusP-valve and 3 patients were not implanted. The reason for 3 patients not implanted with VenusP-valve: 3 had borderline anatomy but were taken to the catheter laboratory for assessment; they were then considered to have unfavorable RVOT anatomy and diameter of the valve annulus >32 to 34 mm at catheterization (n = 1) or risk of coronary artery compression (n = 1), and in 1 patient with a large aneurysm of the MPA, it was decided that there was no safe anchoring point for a valve. These patients were excluded. [a]Technical success is adapted from the transcatheter aortic valve replacement definition (Valve Academic Research Consortium-3).
MPA = main pulmonary artery; RVOT = right ventricular outflow tract.

STATISTICAL ANALYSIS. Continuous variables are expressed as mean ± SD and categorical variables are presented as number and percentage. The range includes the maximum and minimum values. A comparison of parameters before and after pulmonary valve implantation was analyzed using the Wilcoxon signed rank test. A P value of <0.05 was considered statistically significant. Statistical analyses were performed using SPSS 29.0 (IBM).

RESULTS

PATIENT ENROLLMENT. In the 10 centers, 84 patients were evaluated with CMR. Three patients were unsuitable for the VenusP-valve. Thus, 81 underwent successful implantation of the VenusP-valve. All completed the follow-up at 1 year, 80 (98.7%) completed the 2-year follow-up, and 79 (97.5%) completed 3-year follow-up.

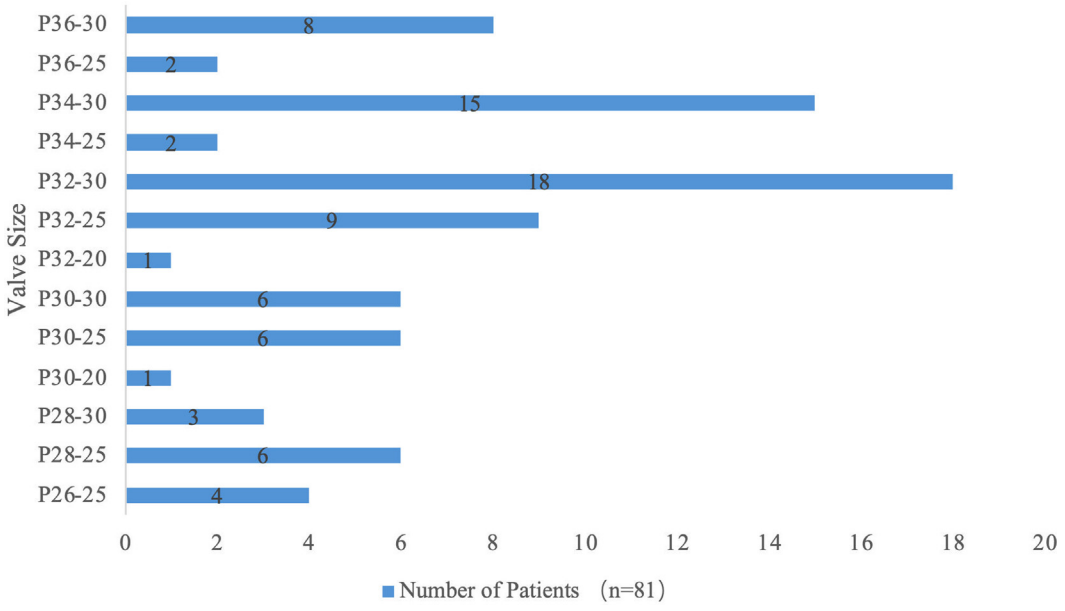
BASELINE AND DEMOGRAPHIC CHARACTERISTICS. Table 2 shows the baseline characteristics. The majority of patients had undergone surgical repair of tetralogy of Fallot (n = 63 [77.7%]). The number of previous open-heart operations was 1.3 ± 0.6.

PROCEDURE CHARACTERISTICS. Table 3 shows the procedure characteristics. All 81 patients underwent VenusP-valve implantation using femoral venous access. The sizes of the VenusP-valve implanted are summarized in Figure 3. Of 81 patients with successful valve implantation, 68 (84.0%) received valves >30 mm diameter. The procedures were technically successful in 100% of patients.

EARLY COMPLICATIONS. There was no early (defined as up to time of discharge from hospital) procedure-related mortality (Table 4). In 1 patient, guidewire perforation of left lower lobe PA occurred with the Lunderquist guidewire during the initial balloon interrogation, causing hemoptysis. VenusP-valve implantation was completed, but because of persistent hemoptysis over the subsequent days, the patient needed surgical exploration of the lung. In 1 patient, runs of ventricular tachycardia occurred at end of the procedure, needing a single direct current shock of 100 J. One patient developed contrast nephropathy, which resolved with medical treatment. One patient developed pleuritic chest pain 2 days after valve implantation and was hospitalized for 4 days until the pain resolved. No cause was found.

LATE COMPLICATIONS. There was no late mortality (defined as after discharge from the hospital). In 1 patient, 8 days after discharge, the valve leaflets appeared thickened on echocardiography, and microthrombus deposition on the leaflets was suspected. This was treated with anticoagulation with

FIGURE 3 Implanted Valve Size Distribution



Product specification in the format PXX-YY. P = pulmonary valve; XX = outer diameter straight section; YY = straight section length.

TABLE 4 Cumulative Rate of Complications

SAE	30 d	6 mo	1 y	2 y	3 y
Death	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Reoperation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Myocardial infarction	0 (0)	0 (0)	0 (0)	1.2 (1)	1.2 (1)
Vascular injury[a]	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Stroke	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Pulmonary embolism	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Device migration/ embolization	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Valvar thrombus	1.2 (1)	1.2 (1)	1.2 (1)	1.2 (1)	2.5 (2)
Thromboembolism	1.2 (1)	1.2 (1)	1.2 (1)	1.2 (1)	1.2 (1)
Bleeding	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Device migration/ embolization	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Paravalvar leak	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Endocarditis	0 (0)	0 (0)	1.2 (1)	1.2 (1)	1.2 (1)
Nonstructural dysfunction	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Explant	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Hemolysis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Arrhythmias	2.5 (2)	2.5 (2)	2.5 (2)	2.5 (2)	2.5 (2)
MACCE	0 (0)	0 (0)	0 (0)	1.2 (1)	1.2 (1)

Values are % (n). [a]Vascular injury is defined as injury needing unplanned vascular grafting intervention. MACCE is defined as death, myocardial infarction, reoperation, vascular injury needing an unplanned vascular grafting intervention, stroke, and pulmonary embolism.

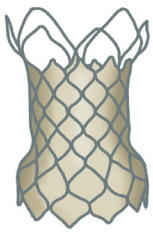
MACCE = major adverse cardiac and cerebrovascular event(s); SAE = serious adverse event(s).

complete resolution. Blood cultures were negative. One patient, 46 years of age, developed a wide complex tachycardia 4 weeks after valve implantation. This was treated with amiodarone and dual-chamber implantable cardioverter-defibrillator and RVOT ablation 5 months after valve implantation. One patient developed deep vein thrombosis 1 week after the procedure and was treated with anticoagulation. One patient had colonic polyps and hemorrhoids a year after valve implantation and 3 years later underwent hemorrhoidectomy. One patient needed treatment for non-ST-segment elevation myocardial infarction (because of coronary artery disease) 18 months after valve implantation. One 17-year-old, with habitual nail biting, had fever for 3 weeks and vegetation was noted on the valve 11 months after implantation. Blood cultures grew *Streptococcus mitis*, and the endocarditis was successfully treated with 6 weeks of antibiotics. The valve is functioning normally 3 years later. In 1 patient, 18 years of age, a thrombus was noted on the distal flare 3 years after implantation on routine assessment. This was successfully treated with heparin and warfarin and later changed to dual antiplatelets (aspirin and clopidogrel), with complete resolution of the thrombus. The valve has continued to function normally.

CENTRAL ILLUSTRATION **Acute and 3-Year Outcomes After Implantation of the Self-Expandable VenusP-Valve in Patients With Severe Pulmonary Regurgitation (N = 81)**

Acute and 3-Year Outcomes After Implantation of the Self-Expandable VenusP-Valve in Patients With Severe Pulmonary Regurgitation, N = 81

A) Unique Features of the VenusP-Valve



Six golden markers
Precise valve positioning

Broad valve size range
Wide patient population coverage

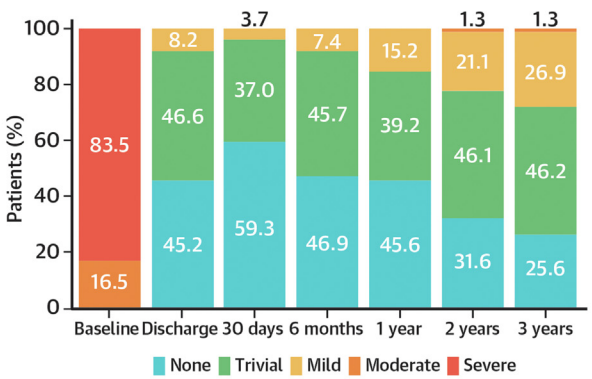
Self-expanding valve
No pre-stenting or balloon expansion

Strong anchoring capabilities
Easy valve deployment

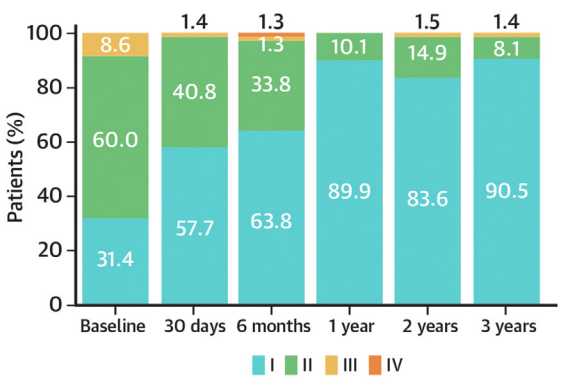
B) Acute (In-Hospital) Outcomes

- 100% Technical success at exit from catheterization laboratory (VARC-3)
- 100% Patients ≤ mild regurgitation
- 0% In-hospital MACCE, mortality, or reintervention

C) 3-Year Outcomes: Pulmonary Regurgitation



D) 3-Year Outcomes: NYHA Functional Class

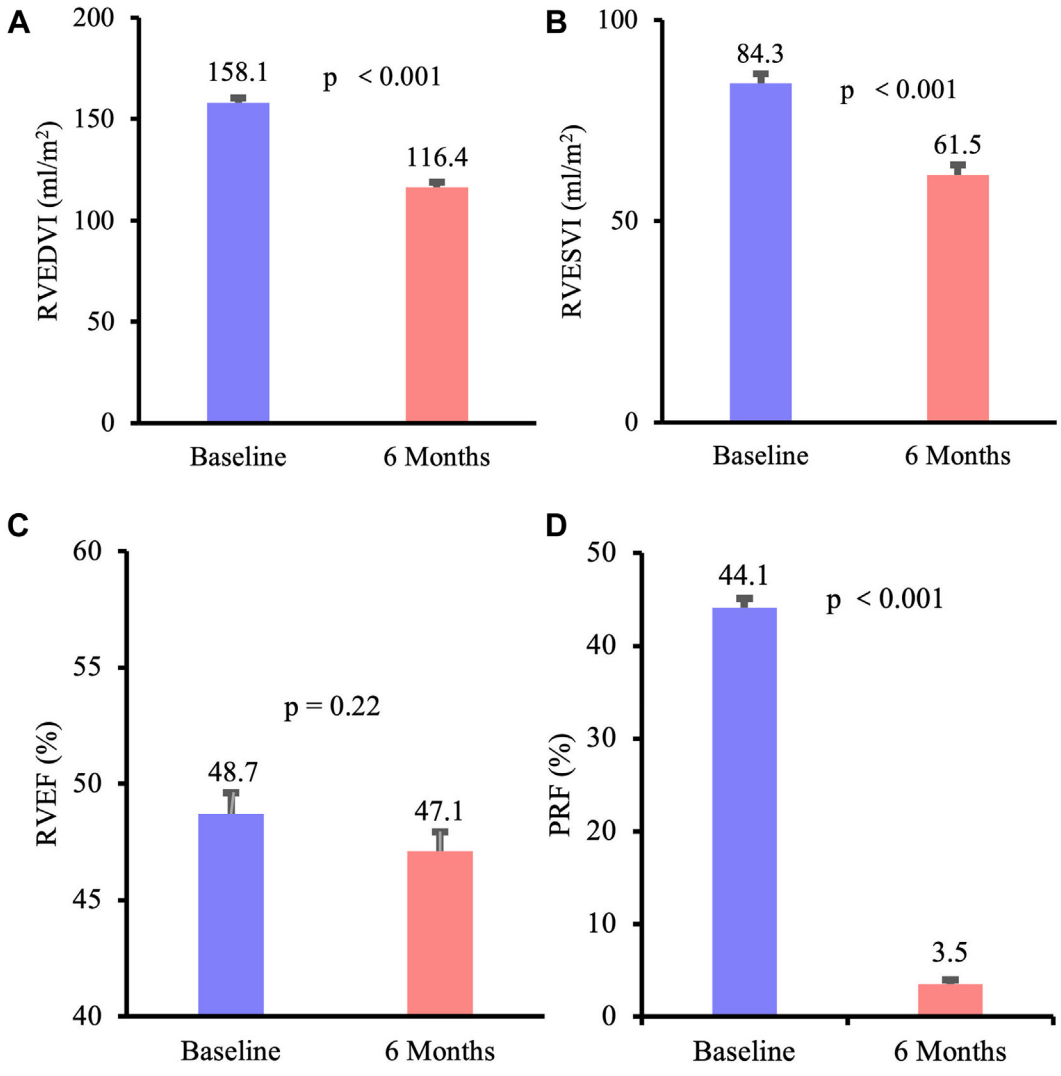


- The acute outcomes following implantation showed that the valve performed well in all patients
- Pulmonary regurgitation decreased from 100% of patients with moderate or greater regurgitation before valve implantation to only 1 patient (1.3%) with moderate regurgitation after 3 years
- At late follow-up, >90% patients were in NYHA functional class I

Qureshi SA, et al. JACC Cardiovasc Interv. 2025;18(8):1045–1056.

The VenusP-valve demonstrates excellent safety and efficacy in both acute outcomes and 3-year follow-up results. (A) The VenusP-valve is a self-expanding valve that does not require prestenting or balloon expansion, featuring 6 golden markers for precise valve positioning, strong anchoring capabilities, and a broader range of valve sizes. (B) The acute outcome following implantation showed that the valve performed well in all patients. (C) Pulmonary regurgitation decreased from 100% of patients with moderate or greater regurgitation before valve implantation to only 1 (1.3%) patient with moderate regurgitation after 3 years. (D) At late follow-up, >90% of patients were in NYHA functional class I. MACCE = major adverse cardiac and cerebrovascular event(s); VARC-3 = Valve Academic Research Consortium-3.

FIGURE 4 Cardiac Magnetic Resonance Assessment for Right Ventricular Remodeling



Comparison of right ventricular assessment parameters between baseline and 6 months after valve implantation shows that the right ventricle had achieved remodeling at 6-month follow-up, as shown by significant decreases in (A) indexed right ventricular end-diastolic volume (RVEDVI), (B) right ventricular end-systolic volume index (RVESVI), and (D) pulmonary regurgitant fraction (PRF) compared with baseline ($P < 0.001$). (C) The right ventricular function remained good, with right ventricular ejection fraction (RVEF) remaining stable ($P = 0.22$).

FOLLOW-UP. During follow-up of up to 3 years, there was no late mortality (Table 4). The cumulative incidence of major adverse cardiac and cerebrovascular events was 1.2%, of endocarditis was 1.2%, and of valve thrombus was 2.5% (Table 4).

Prior to valve implantation, on echocardiography, 83.5% of patients had severe and 16.5% had moderate PR (Central Illustration). There was significant improvement in PR at subsequent follow-up with only 1 patient having moderate regurgitation at 2 and 3 years follow-up due to valve leaflet prolapse. At 2- and 3-year follow-up, only 1 patient had an increase to moderate PR due to valve leaflet prolapse. The mean pressure gradient was 13 ± 10 mm Hg before valve implantation and 9.8 ± 7.2 mm Hg at 3-year follow-up. NYHA functional class was also improved with more than 90% patients in class I.

Seventy-nine (97.5%) patients had CMR examination, while in the other 2 patients CMR was contraindicated. These were performed a mean of 186.8 days (range 142-266 days) after valve implantation. Before the procedure, the indexed

TABLE 5 Stent Fractures

Patient and Detail	Stent Fracture Classification	Stent Fracture Classification
1. 3 strut fractures in proximal flare	Minor	Type I
2. Single strut fracture at RVOT end of stent	Minor	Type I
3. Single strut fracture at RVOT end of stent	Minor	Type I
4. 5 strut fractures identified toward RVOT end of proximal flare	Minor	Type I
5. Single strut fracture at RVOT end of stent	Minor	Type I
6. Single strut fracture at RVOT end of stent	Minor	Type I
7. Single strut fracture at RVOT end of stent	Minor	Type I
8. 4 strut fractures in proximal flare	Minor	Type I
9. Single frame fracture in proximal flare	Minor	Type I
10. 2 wire fractures, at RVOT-MPA	Minor	Type I
11. 6 wire fractures at RVOT end of stent	Minor	Type I

Abbreviations as in Table 3.

right ventricular end-diastolic volume (RVEDVi) was 158.1 ± 21.3 mL/m^2 (range 113.0-213.0 mL/m^2) and the indexed RV end-systolic volume was 84.3 ± 20.8 mL/m^2 (range 45.0-134.0 mL/m^2) (Figure 4A). At 6-month follow-up, the RVEDVi had reduced to 116.4 ± 22.6 mL/m^2 (range 59.6-181.0 mL/m^2) ($P < 0.001$) and the indexed RV end-systolic volume had reduced to 61.5 ± 15.4 mL/m^2 (range 31.6-100.0 mL/m^2) ($P < 0.001$) (Figure 4B). The RV ejection fraction was 48.7% ± 8.1% (range 28.0%-69.8%) at baseline and 47.1% ± 7.4% (range 30%-67%) after valve implantation ($P = 0.22$) (Figure 4C). The PRF was 44.1% ± 8.7% (range 11.2%-66.9%) at baseline and had reduced to 3.5% ± 3.7% (range 0%-17.4%) ($P < 0.001$) after valve implantation (Figure 4D).

Fluoroscopy was performed in 76 (93.8%) of 81 patients (remainder having a chest radiography) 3 to 6 months after valve implantation to evaluate for stent fractures, which were identified in 11 (13.6%) patients and were usually single wire fractures, occurring at the proximal flare (Table 5). However, all the stent fractures were minor[18] and type I,[19] and there was no Doppler evidence of valvar malfunction. There was no increased propensity for wire fractures in any particular valve size. Comparing the PRF between the fracture and intact subgroups at 6-month follow-up, there was no significant difference (3.6% ± 2.6% vs 3.5% ± 3.8%; $P = 0.886$) (Figure 5A). During 3-year follow-up, the mean gradient remained unchanged with no significant difference between the fracture and intact stent subgroups (baseline: 11.9 ± 7.0 mm Hg vs 13.2 ± 10.4 mm Hg; at 1-month follow-up: 13.3 ± 15.1 mm Hg vs 10.4 ± 8.0 mm Hg; at 6-month follow-up: 8.5 ± 3.4 mm Hg vs 10.9 ± 7.5 mm Hg; at 1-year follow-up: 7.1 ± 4.6 mm Hg vs 11.5 ± 9.1 mm Hg; at 2-year follow-up: 9.3 ± 5.0 mm Hg vs 11.6 ± 7.6 mm Hg; at 3-year follow-up: 7.9 ± 5.0 mm Hg vs 10.1 ± 7.5 mm Hg) (all $P > 0.05$) (Figure 5B).

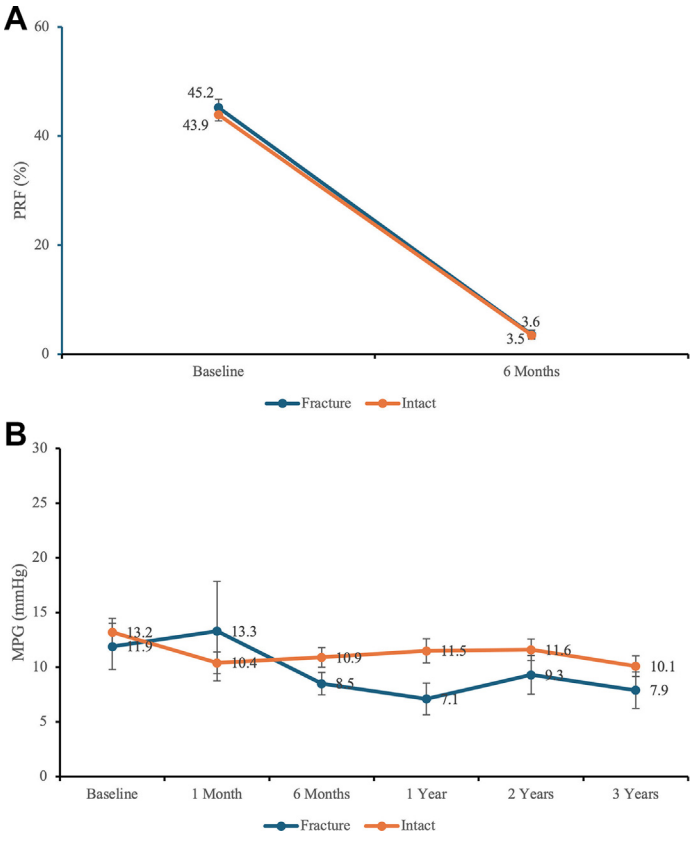
DISCUSSION

VenusP-valve is a major advance for patients with dilated RVOTs and severe PR after previous transannular patched repair. Patients with RVOTs of >30 mm were previously considered unsuitable for PPVI. In the last few years, various self-expanding valves/stents have been evaluated, predominantly in the United States.[11,12] Since 2013, the VenusP-valve has been implanted worldwide on a compassionate use basis in large RVOTs with favorable results.[13-17] Subsequently, a CE multicenter study was initiated to evaluate early and medium-term performance.

One of the important steps for VenusP-valve implantation is preprocedural anatomical measurements for selection of suitable patients. Maximum diameters of the RVOT, MPA, and PA branches and proximity of the coronary artery to the landing zone were assessed. The valve diameter chosen should be 2- to 4-mm larger than the balloon waist. The length of the middle section of the frame should match the distance from the RVOT-to-PA bifurcation. Depending on the morphology of the RVOT and MPA, the VenusP-valve can be used for balloon waists up to diameters between 32 and 34 mm. This valve can conform to the dilated RVOT, reducing the risk of migration. The anchoring points can be the proximal and distal flares or the straight section at the valve annulus, or all 3 points. The technique of valve deployment has been described.[13-17] Previous CMR and computed tomography scanning may help in selecting patients, and a more detailed assessment is needed to determine the appropriate valve size, such as RVOT balloon interrogation. With further developments in imaging, it may be possible to select patients based on computed tomography scanning.

Coronary artery compression is a concern with PPVI, especially with the balloon-expandable valves.[14,17,20] In our study, this was assessed by CMR and during the balloon interrogation before

FIGURE 5 Comparison of PRF and MPG Between Fracture and Intact Subgroups



(A) Comparison of the pulmonary regurgitant fraction (PRF) between the fracture and intact subgroups showed no significant difference in PRF, which had significantly decreased in both the fracture and intact groups. (B) Comparison of the mean pressure gradient (MPG) between the fracture and intact subgroups showed that the MPG remained within the normal range and stable, with no significant difference in both the fracture and intact groups.

valve implantation. The lower radial force of the framework may not cause coronary artery compression after implantation, although continuous evaluation is recommended. Although 1 patient had non-ST-segment elevation myocardial infarction 2 to 3 years after implantation, this was due to progression of coronary artery disease, having undergone coronary artery stenting more than 2 years previously.

Stent fractures are also important to evaluate after PPVI. Although fractures may be visible on chest radiographs, they are best seen on fluoroscopy. In a study of Melody valve implantation, stent fractures occurred in stenosed conduits in 25% at 2-year follow-up.[19] Prestenting before Melody valve implantation has reduced this incidence.[21] The nitinol skeleton of the VenusP-valve allows conformation to the MPA curvature with less stress on the framework and less compression on the stent in the dilated RVOTs than in stenotic calcified conduits. However, because the proximal flare is placed in the infundibular region, there are compressive forces and so stent fractures may be expected. Stent fractures have been reported in 27%, all in the proximal flare, and the majority single wire fractures.[17] Serial fluoroscopy in that study did not show further fractures. In our CE study, fractures have been noted in 13.6% of patients in the first 6 months, usually single strut fractures and were only seen on careful fluoroscopy, rather than on chest radiographs. Despite the fractures, the valves have functioned normally without increase in the gradients during follow-up.

Endocarditis is an important issue with all PPVIs. Recently, a multicenter study from China reported 5 (9.1%) of 55 patients with endocarditis up to 5 years after VenusP-valve implantation.[22] Endocarditis occurred in only 1 (1.2%) patient in our CE study, a much lower incidence compared with other studies, and merits further consideration.[23,24] Although some of the centers in this CE study also contributed their data to the study of Morgan et al,[17] the patients in the CE study were completely different. Therefore, longer-term follow-up will be important for defining the incidence of endocarditis.

Thrombus formation occurred in 2 (2.5%) patients. In 1 patient, thrombus occurred on the distal flare 3 years after implantation, despite being on aspirin therapy. This was treated with heparin and warfarin for 45 days, followed by continuous dual antiplatelet therapy with aspirin and clopidogrel. In another patient, leaflet thickening with an increase in gradient occurred, and so platelet deposition was considered as a factor, and treated with anticoagulation for 6 months and then antiplatelet therapy. Both these patients had been on the normal dual antiplatelet therapy. However, possible microthrombus deposition in valve leaflets may occur (despite dual antiplatelet therapy), causing them to become thickened, when evaluated on computed tomography scanning.[25] It is not clear whether stent strut fractures are better evaluated by computed tomography scanning rather than by fluoroscopy, so further evaluation is needed for the role of computed tomography scanning and using anticoagulation after VenusP-valve implantation for 3 to 6 months and antiplatelet therapy indefinitely after this period.

Arrhythmias have also become important after different valve implantations, whether balloon expandable or self-expanding.[26] The shape of the proximal flare of the VenusP-valve is such that

theoretically the edges of the flare are less likely to protrude into the infundibular muscle. However, tachyarrhythmias are a leading cause of morbidity and mortality in patients with repaired tetralogy of Fallot,[27] and so all valves are likely to contribute to arrhythmias. Therefore, longer-term follow-up is needed.

This study has confirmed the results of the earlier studies showing excellent valve function in the early and medium terms. We have confirmed good RV remodeling (reduction of the RVEDVi and abolition of PR) on follow-up CMR and transthoracic echocardiography, confirming similar results reported with other self-expanding valves.[28] Doppler echocardiography has its limitations for routine assessment of the severity of PR,[29] whereas CMR assessment is more accurate and reliable. However, reliable information on the serial Doppler systolic velocity across the transcatheter pulmonary valves provides clues about its function and durability. Therefore, some useful hemodynamic information can be obtained during the follow-up.

STUDY LIMITATIONS. The main limitations of the study are the relatively small number of patients and short period of follow-up. Long-term data would provide more evidence of the durability of the valve.

CONCLUSIONS

This CE study reports the results of VenusP-valve implantation during 3-year follow-up in patients with severe PR after previous repair of RVOT. The VenusP-valve has expanded the scope of PPVI and has shown promising safety and durability in the 3-year follow-up. Further long-term evaluation is warranted.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

The study was supported by VenusMedtech (Hangzhou), China. Drs Qureshi, Jones, Pushparajah, Kenny, Promphan, Thomson, Bentham, Gewillig, Berger, and Hijazi have served as a consultant/proctor for VenusMedtech. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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PERSPECTIVES

WHAT IS KNOWN? PR is common after surgical repair of many congenital heart defects, which may need multiple reoperations for valve replacement during the lifetime of patients, and PPVI may help reduce the number of reoperations.

WHAT IS NEW? Balloon-expandable valves have a limited range of sizes, which preclude a majority of patients, whereas this study shows that larger-diameter RVOTs can be treated by catheter techniques, increasing the role of PPVI.

WHAT IS NEXT? Longer-term follow-up is needed together with larger studies to assess the durability of the VenusP-valve so that it can be applied to a larger population of patients.

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KEY WORDS **percutaneous pulmonary valve implantation, pulmonary regurgitation, VenusP-valve**