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Authors: Sara Korabiewska-Pluta, Krzysztof Michalak, Joanna Młodawska, Monika Łubisz, Grażyna Brzezińska-Rajszys, Adam Koleśnik, Mario Carminati, Tomasz Moszura

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First-in-Central-Europe implantation of the self-expandable Pulsta valve in pulmonary position: Short-term results

Short title: Implantation of the Pulsta valve in pulmonary position in children

Sara Korabiewska-Pluta[1]*, Krzysztof Michalak[1]*, Joanna Młodawska[1], Monika Łubisz[1], Grażyna Brzezińska-Rajszys[2], Adam Koleśnik[2], Mario Carminati[3], Tomasz Moszura[1]

[1]Department of Cardiology, Polish-Mother's Memorial Hospital Research Institute, Łódź, Poland
[2]Cardiovascular Interventional Laboratory, The Children's Memorial Health Institute, Warszawa, Poland
[3]Department of Pediatric and Adult Congenital Cardiology and Cardiac Surgery, IRCCS Policlinico, San Donato Milanese, Italy
*Both authors equally contributed to the study.

Correspondence to:
Sara Korabiewska-Pluta, MD,
Department of Cardiology,
Polish Mother's Memorial Hospital Research Institute,
Rzgowska 281/289, 93–338 Łódź, Poland,
phone: +48 42 271 14 71,
e-mail: sara.korabiewska@gmail.com

WHAT'S NEW?

The initial outcomes of the novel transcatheter implantable Pulsta pulmonary valve are distinguished by its larger diameter in comparison to that of available valves. Significantly, its compatibility for implantation in the native outflow tract offers a less invasive alternative to open-heart surgery, particularly benefiting patients not previously considered for other types of transcatheter valves. We provide insight into the early evolution of echocardiographic parameters pertaining to the right ventricle following percutaneous pulmonary valve implantation.

Abstract

Background: Tetralogy of Fallot after complete correction constantly presents potential challenges in pediatric cardiology. In particular, patients with pulmonary regurgitation require ongoing monitoring, reoperation or catheter intervention during adolescence. The increasing demand for a wide spectrum of sizes and shapes of implantable prostheses led to the development of the self-expanding Pulsta® valve.

Aims: In this study, we evaluated postprocedural outcomes, focusing on pulmonary valve functionality and right ventricular (RV) parameters, using advanced echocardiographic techniques.

Methods: We reviewed five pediatric patients before and over a 6-month follow-up period after the procedure using three-dimensional echocardiography acquisition (3D transthoracic echocardiography), RV global longitudinal strain and tissue Doppler imaging.

Results: All procedures were successful, with good early effects and no complications. Postprocedural assessment of RV diameter and volume revealed a statistically significant reduction, and this promising trend continued during the follow-up period. However, in this cohort, the ejection fraction of the RV, which was initially within the normal range, showed a slight reduction immediately after the procedure, followed by a gradual return to normal values during the follow-up period. Similar statistically significant results in RV strain values were observed.

Conclusion: In the study group, the Pulsta® valve provided good early-term effectiveness and feasibility without adverse events, and the overall mortality rate was 0%, highlighting the potential benefits of this intervention as measured by echocardiographic parameters.

Key words: pediatric, percutaneous pulmonary valve implantation, pulmonary valve disease, right ventricular outflow tract, stent valve

INTRODUCTION

Tetralogy of Fallot is a congenital heart disease characterised by a ventricular septal defect, aortic overriding, infundibular pulmonary obstruction, and right ventricular (RV) hypertrophy [1]. Among the conditions considered in the differential diagnosis, the double outlet RV is characterised by significant displacement of the aorta towards the right. Complete correction of these defects using a transannular patch technique is associated with generally good outcomes. However, significant pulmonary regurgitation is common in adolescents because of the nature

of the surgical intervention [2]. Without further repair, severe pulmonary regurgitation causes RV failure and dilatation and eventually results in exercise intolerance, dyspnoea, and ventricular arrhythmias [3]. Unfortunately, repeated operations are associated with significant risks of morbidity and mortality. For many years, open-heart surgery was generally the only available procedure, with percutaneous intervention becoming a treatment possibility later. The initial options were the Melody and Edwards Sapien valves. Currently, the increasing demand for a wide spectrum of sizes and shapes of percutaneous prostheses has led to the development of new types of valves (i.e., the Pulsta valve, the Venus p-valve, and the Medtronic Harmony TPV) for routine intervention.

In the following case, we present the short-term results of the first implantation of the Pulsta® valve in the pulmonary position in Central Europe. We reviewed all pediatric patients who underwent this procedure and who underwent advanced echocardiographic techniques to evaluate early outcomes over a 6-month follow-up period.

The aim of this study was to test the hypothesis that the pulmonary valve prosthesis will improve the functionality of the RV, leading to reductions in both the diameter and volume of the RV.

METHODS

Study group

The study was designed for patients with severe pulmonary regurgitation with or without additional stenosis within the native RV outflow tract (RVOT) who underwent percutaneous Pulsta valve implantation in the pulmonary position in the Cardiology Department of the Polish Mother's Memorial Hospital in 2023. All requirements were explained, and the informed consent form was dated and signed after the study was approved by the Ethics Committee. The clinical investigation of the PULSTA Transcatheter Pulmonary Valve System is ongoing, and it is currently being applied for CE marking in Europe (the ClinicalTrials.gov website with the ID number: NCT03983512).

Qualification for the procedure was performed using multimodality imaging techniques, and initial echocardiography with detailed assessment of pulmonary valve function, diameter, RV function and volume was performed to confirm that the patient required intervention. The inclusion criteria were patients with a body weight greater than 30 kg, severe pulmonary regurgitation, and a main pulmonary artery size less than or equal to 30 mm. Computed tomography angiography and magnetic resonance imaging were subsequently performed to

determine the size and anatomy of the RVOT, pulmonary artery, and RV indexed end-diastolic volume and function and to calculate the pulmonary regurgitant fraction (Table 1).
With this information, the manufacturing company provided suitable valve sizes for use in patients on the day of the procedure.

The procedure was performed as a single-centre clinical trial in Poland using the Pulsta® valve. The pulmonary valve was successfully implanted in 5 (2 female and 3 male patients aged 13–16 years) of seven prequalified adolescent patients. Valve deployment was not attempted in 2 patients because of significant paravalvular leakage upon balloon inflation when the size of the main pulmonary artery was measured (TYSHAK 30 × 40 mm). An initial group of five patients were included in this prospective study and were monitored during the 6-month follow-up period.

The Pulsta® valve and interventional procedure

The Pulsta® valve is a self-expandable knitted nitinol-wire stent with valve leaflets made from porcine pericardial tissue and a delivery system suitable for percutaneous pulmonary valve implantation in pediatric patients [4] (Figure 1). The native RVOT is accessed through blood vessels, mainly femoral veins. The valve leaflets undergo chemical treatment processes such as decellularization, treatment with alpha-galactosidase, anticalcification and detoxification. The valve diameter ranges from 18 to 32 mm with 2 mm increments. Both ends of the valve are flared to 4 mm wider than the outer diameter for stable valve adaptation to various RVOT geometries. The total length of the valve is 28 to 38 mm according to the outer diameter.

All procedures were performed with the patients under general anesthesia and fluoroscopic guidance. Pretreatment with intravenous antibiotics (cefazolin) and anticoagulants (heparin 100 UI/kg) was provided and the controlled activated coagulation time with heparin was calculated before valve implantation [5]. The Pulsta® valve delivery system consists of a catheter shaft and handle. The usable length of the catheter shaft is 110 cm, and the outer diameter of the valve loading area sheath is 18 or 20 French, depending on the valve model. The atraumatic tapered tip at the end of the distal area of the catheter allows easy entrance to the blood vessel, and the hook in the valve prevents the valve from bouncing off abruptly, allowing for controlled deployment and safe positioning to the target site. The two X-ray markers at the proximal and distal ends indicate the target position of the crimped valve. The handle has a knob for precise operation and a slider fixed in the inner case, which partially develops the crimped Pulsta valve, pressing and pulling the fixed slider deploys the valve to the

target site. The crimper and pusher are used to load the Pulsta valve into the delivery sheath (Figure 2). The delivery system is compatible with a stiff guidewire. The Pulsta valve, storage solution, and delivery system were sterile. The valve must be rinsed with room temperature sterile saline solution during the procedure before implantation (for a total of 9 minutes in 3 separate solutions). The Pulsta valve can be partially deployed, and the position of the valve can be adjusted before the device is released [3]. The Pulsta® valve size was selected according to the measurements of the sizing balloon (with an outer diameter of 18–32 mm, a flare diameter of 22–36 mm, a length of 28–38 mm, and a delivery system size of 18–20 French).

The procedure starts with ultrasound-guided cannulation of the right femoral vein and left femoral artery. The right atrial and ventricular pressures were measured, and after the tricuspid valve was crossed with the pigtail catheter, initial angiography was performed. Before proceeding to valve implantation, coronary artery risk compression was excluded during main pulmonary artery (MPA) occlusion with a TYSHAK 30 × 40 mm balloon catheter and simultaneous aortography (in the left lateral and antero-posterior C-arm positions). A Lunderquist guidewire was positioned in the right pulmonary artery, with preferential RAO 40 and cranial C-arm positions for valve deployment. Next, an 18–20 Fr sheath was inserted percutaneously from the femoral vein to the distal pulmonary artery trunk after scrupulous valve preparation (rinsing and crimping of the valve) and was deployed in the selected landing zone (Supplementary material, *Video S1*). After valve implantation, the RV and pulmonary artery (PA) pressures were measured again to determine the pressure gradient across the implanted valve, and the final main PA angiogram was performed. No significant periprocedural complications were noted in any patient.

Study protocol

All five patients who underwent valve implantation underwent a preoperative echocardiographic study prior to implantation and 4 times after the procedure — the first study was performed one day after implantation and 1, 3 and 6 months after the procedure. The echocardiographic study focused on the RV and pulmonary valve (Figure 3), and each case included the following:

- RV m-mode diameter in the parasternal short axis;
- RV 2D diameter in parasternal long axis;
- RV diameters in the apical four-chamber view (base, middle and length);

- RV end-diastolic and end-systolic volume and fractional area change in the apical four-chamber view;
- RV strain (base, mid and apical);
- Tricuspid annular plane systolic excursion;
- RV tissue Doppler imaging (TDI) parameters (e'; a'; s) and MPI measured from the TDI curve;
- RV end-diastolic volume, end-systolic volume and ejection fraction (3D reconstruction);
- Pulmonary valve function (flow speed, regurgitation, leaflet movement, symmetry of the stent, diameter) in the high parasternal short axis;
- 3D reconstruction of the MPA and pulmonary valve.

Ethics

The informed consent form was obtained from the patients and their parents. Ethical committee approval was achieved from Polish Mother's Memorial Hospital (No. 11/2023).

Statistical analysis

All quantitative variables are presented as the median and interquartile range. All qualitative variables are presented as percentages. All echocardiographic quantitative variables were checked with the Friedmann test to establish the statistical significance of the observed differences and Wilcoxon test for *post hoc* analyses. A *P*-value less than 0.05 was considered significant.

RESULTS

All the implantation procedures were successful, with full deployment of the stent. On postprocedure angiography, pulmonary regurgitation was graded trivial or less in all patients (Supplementary material, *Video S2*). There was no pressure gradient through the valve in any case. There were also no serious device-related adverse events. During echocardiographic assessment of the Pulsta valve, we noticed that the valve was truly echo-friendly, and it was easy to obtain high-quality images irrespective of patient weight and age (Figure 4). In two patients, abnormal movement of leaflets was detected; one of the leaflets did not close completely in early diastole, which resulted in wide early diastolic regurgitation. After the early diastole leaflets are fully coapted, the regurgitant jet vanishes. This abnormality was not

observed in every cardiac cycle, and the regurgitant jet was assessed as mild (Supplementary material, *Video S3*).

The RV diameter (m-mode, short parasternal axis) measured before the procedure ranged between 21 and 31 mm (median 25 mm; IQR 23.5–26 mm); these values decreased significantly (median 18 mm; range 16.5–22.7 mm; IQR 17.5–21 mm) during the follow-up period (Supplementary material, *Table S1*); $P = 0.03$; Friedman test. Similarly, statistically significant differences were observed in the RV end-diastolic volume index, RV end-diastolic area and RV mid diameter in the apical four-chamber view. However, the differences in RV diameter in 2D parasternal long-axis view and RV base diameter were not significant.

Looking at the systolic function of the RV, the ejection fraction was initially within the normal range (median 59.8%; IQR 52%–60%). After the procedure, it fell below the normal range in most patients (3/5) (median 40%; IQR 39.7%–45.7%), but returned to the normal range during the follow-up period (median 54%; IQR 49.2%–54%). Although this difference was not statistically significant, the initial decrease and subsequent improvement in the base, middle, and apical strain values, as well as the S value in TDI, were statistically significant (Supplementary material, *Table S2*). Changes in other parameters related to the RV systolic function (TAPSE, RV ejection fraction) did not reach statistical significance (Supplementary material, *Table S3*).

Among the diastolic parameters (e', a' and MPI), e' was significantly reduced after intervention, with a subsequent improvement during follow-up.

DISCUSSION

Transcatheter pulmonary valve implantation has changed the postoperative course of many complex congenital heart defects. Compared with repeated open heart surgeries, a definitely less invasive treatment is a great alternative. It usually leads to earlier improvement in pulmonary valve dysfunction, prevents more serious complications, such as ventricular arrhythmias and significant RV dilatation, and improves the quality of life of patients.

In patients with congenital heart disease associated with significant pulmonary stenosis, where the transannular patch is initially necessary for successful repair, the native RVOT typically widens, pulmonary regurgitation becomes hemodynamically significant, and valve repair is inevitable. This underscores the necessity for a broad spectrum of transcatheter valves of different sizes and possibly low-profile delivery systems.

Compared with available valves, the Pulsta valve offers a relatively low profile and a larger diameter. Its self-expandable stents allow for implantation in the native outflow tract,

even with atypical geometry, as they can adjust to the MPA and RVOT. Additionally, the Pulsta valve size is precisely selected based on patient-specific computed tomography in virtual reality to determine the optimal size. In contrast, other self-expandable valves, such as the Venus p-valve and the Medtronic Harmony TPV, have a different deployment concept. These valves feature two wide anchoring parts on both ends of the stent, which secure the valve in place by positioning one fragment in the RVOT and the other in the distal pulmonary trunk. Self-expandable stents, on the other hand, may not be a suitable option for severe pulmonary stenosis because the stent may not have enough radial force to relieve the stenosis, and additional balloon dilatation may be necessary [3]. As presented in this initial study, this valve has excellent short-term functionality and durability when deployed in patients with dysfunctional native pulmonary valves.

After pulmonary valve implantation, we observed a reduction in the diameter and volume of the RV, which was clearly visible from the first control examination after valve implantation. This effect persisted during the follow-up control period. After the procedure, a slight reduction in RV systolic function was present, and it tended to improve during the following follow-up period. It was statistically significant for of all base to apex strain values. The lower systolic function may be explained by the reduced RV preload, resulting in lower stretching of muscle fibres, which is expected to be restored to normal values when RV remodelling occurs. Notably, diastolic function initially decreased after implantation but recovered during the follow-up period and was even better than that before the procedure.

The Pulsta valve in our series of patients allows good high-resolution visualisation of all structures — leaflets and stents. Our team, experienced in echocardiographic assessment of various types of biological valves, unanimously obtained this information as the first subjective impression upon reviewing the echo clips. Two patients had abnormal motion of the leaflets with incomplete closure during early diastole; such a pattern presented once in a few cardiac cycles, which resulted in mild, short regurgitation. The limitations of these findings were due to the small size of the study group. This observation requires further investigation through extended follow-up to determine whether this abnormality increases in the future.

CONCLUSION

This study reported, for the first time in Central Europe, encouraging results for the implantation of the Pulsta® valve in patients with tetralogy of Fallot and a double outlet RV repaired using the transannular patch technique. Percutaneous pulmonary valve implantation using the Pulsta valve resulted in good early-term effectiveness without serious adverse events. The valve has

predictable and sustained performance, particularly in patients with a dilated RVOT and dysfunctional pulmonary grafts. Significant improvements in pressure gradients, pulmonary regurgitation, and RV volume and function were noted. Although these findings are promising, continued data collection and larger studies are warranted to confirm our results.

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/polish_heart_journal.

Article information

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Table 1.

Patient data	Qualification data

Initials	Age, years	Weight, kg	Initial CHD	Degree of pulmonary regurgitation (TTE), I–III	Pulmonary pressure gradient (TTE), mm Hg	RVEDVi (TK), ml/m^2	MPA diameter (TK), mm	Clinical symptoms, ±
AW	10	30	DORV	III	22	149	25	–
PM	16	48.5	TOF	III	45	124	25	+
RK	14	35	TOF	III	18	119	22	–
WA	13	43	TOF	III	4	115	24	+
WF	15	42	TOF	III	4	108	25	–

Abbreviations: CHD, congenital heart disease; DORV, double outlet right ventricle; MPA, main pulmonary artery; RVEDVi, right ventricular end-diastolic volume index; ToF, tetralogy of Fallot; TTE, transthoracic echocardiography

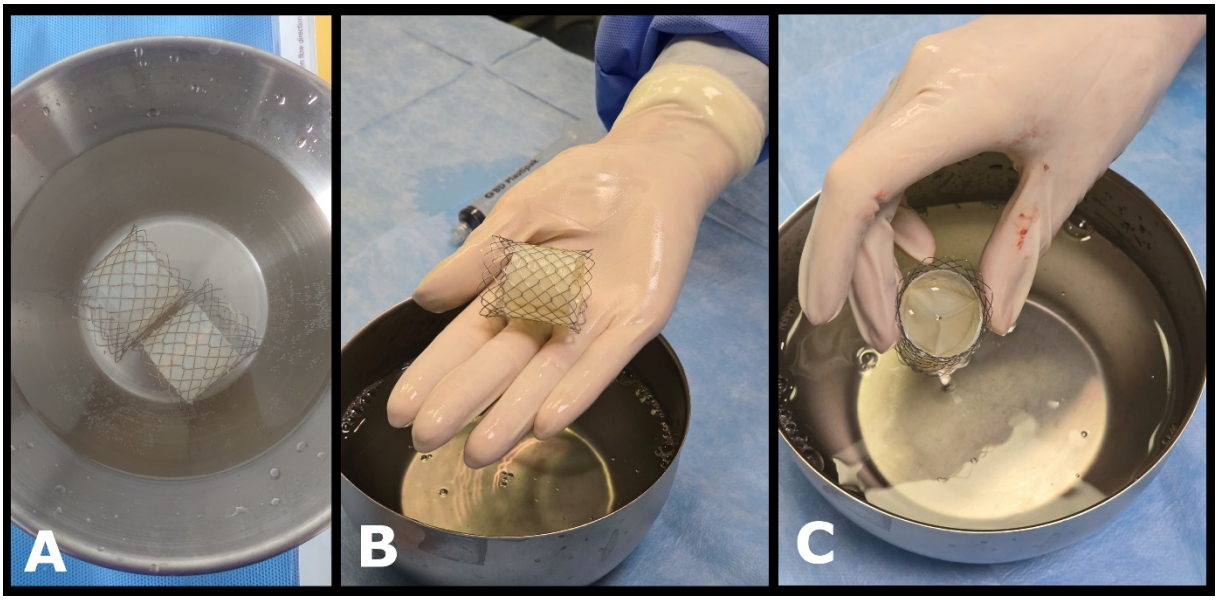

Figure 1. The Pulsta® Transcatheter Pulmonary Valve System. **A.** Two valves from preprocedural training. **B.** Pulsta valve nitinol frame in full length with symmetrical flares. **C.** Perfect coaptation of valve leaflets on the nitinol body frame

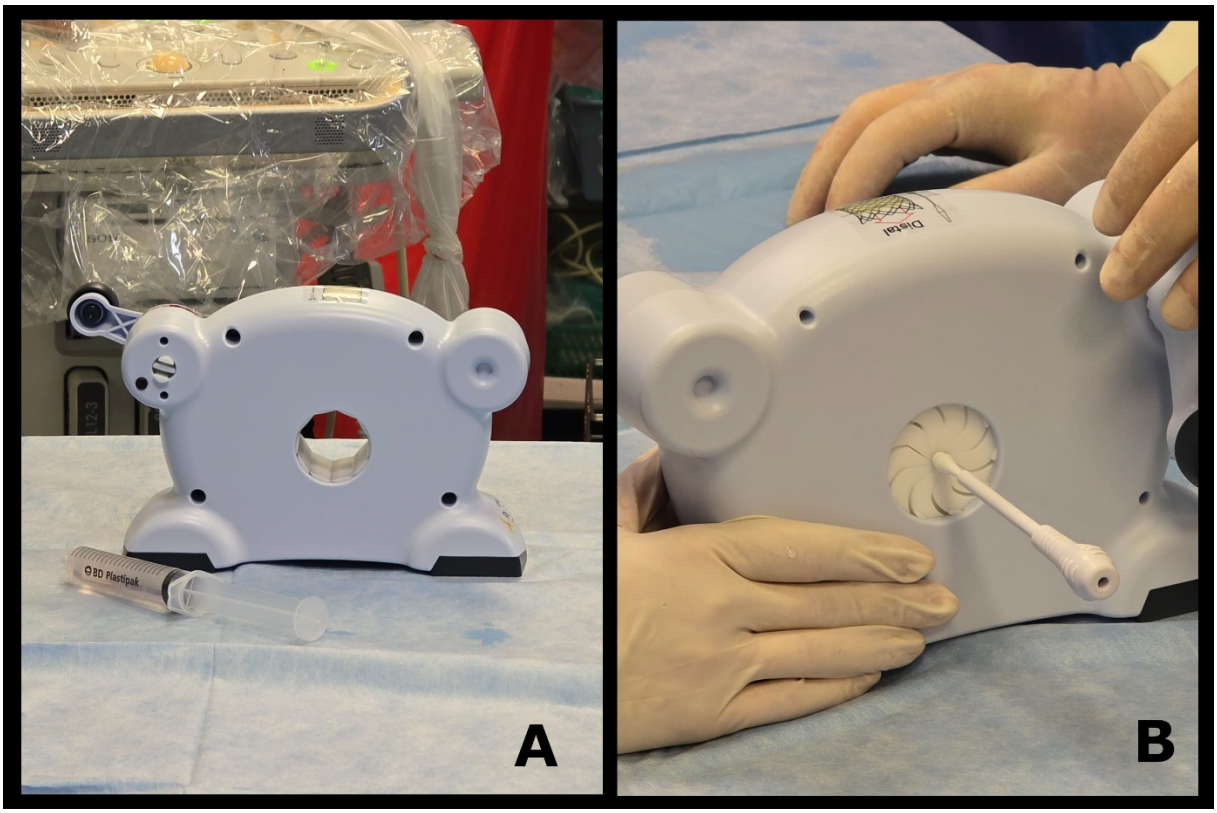

Figure 2. The crimper (**A**). The valve crimped onto the delivery system (**B**)

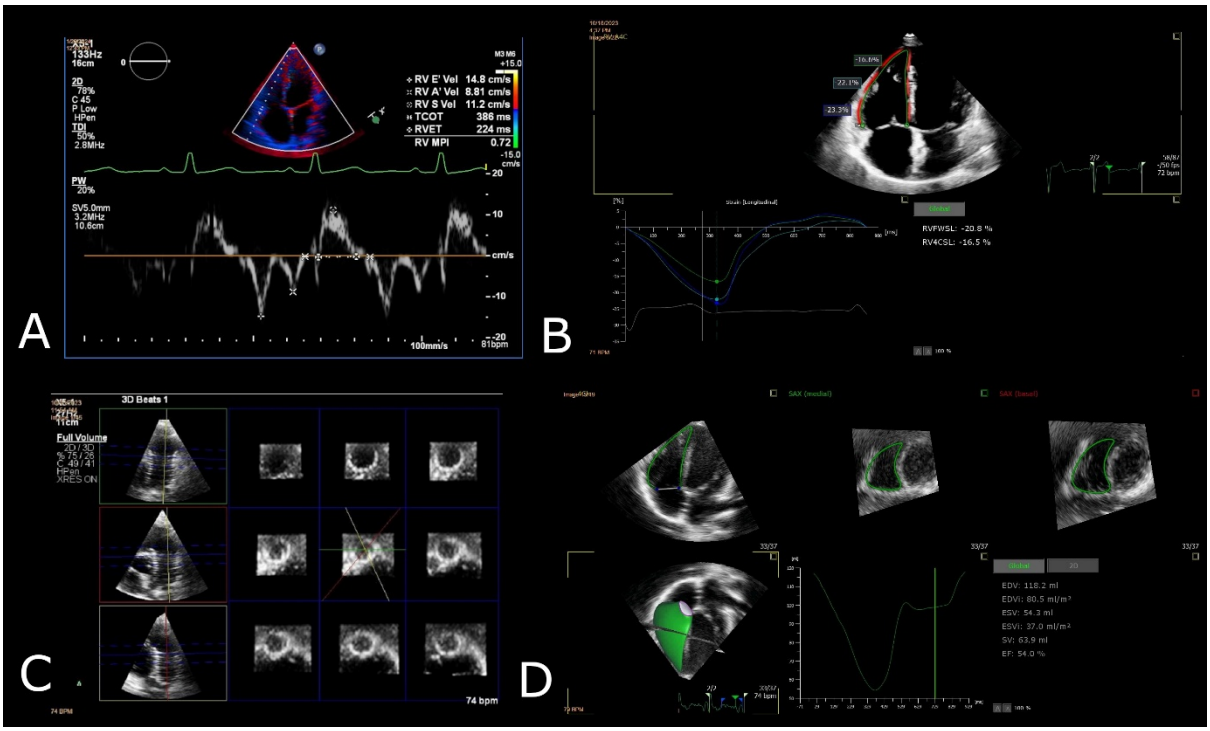

Figure 3. Tissue Doppler imaging assessment of right ventricular systolic and diastolic function

(**A**). Strain analysis of the right ventricle free wall (**B**). Multislice 3D analysis of the implanted Pulsta valve (**C**). Right ventricle 3D imaging with volume and systolic function assessment (**D**)

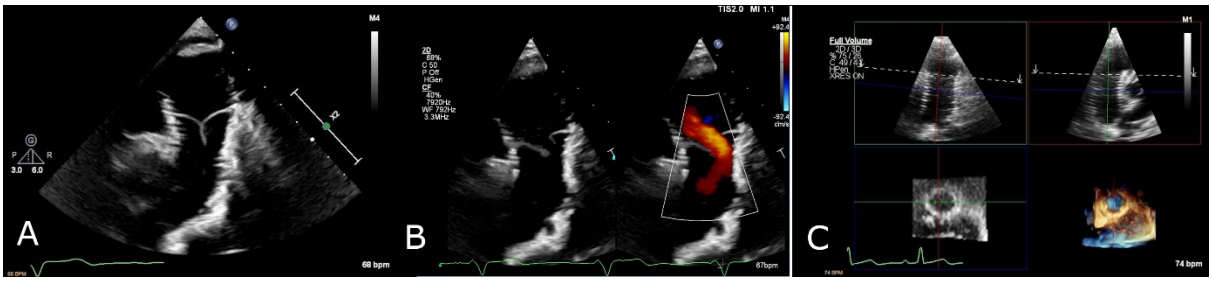

Figure 4. The Pulsta® valve in echocardiographic assessment. **A.** 2D parasternal view. **B.** Mild pulmonary regurgitation in color Doppler. **C.** Multiplane 3D reconstruction of the implanted valve