Early outcomes of percutaneous pulmonary valve implantation using the Edwards SAPIEN XT transcatheter heart valve system

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Funding

This work was supported by an unrestricted educational research grant that was provided by Edwards Lifescience, Nyon, Switzerland to IPPMed.

Competing Interests

Peter Bramlage is the representative of the Institute for Pharmacology and Preventive Medicine (IPPMed), Cloppenburg, Germany.

Keywords: pulmonary valve, congenital heart disease, percutaneous pulmonary valve implantation, SAPIEN XT

Journal: Int. J. Cardiol. **Article type:** Clinical Paper **Words:** 3,349 **Abstract:** 237

Figures: 0 **Tables:** 4 **Supp. tables: 1** **Supp. figures**: 2 **References:** 18

Version: 14.06.2017

ABSTRACT

Background: Patients with congenital or acquired heart defects affecting the pulmonary valve and right ventricular outflow tract (RVOT) commonly require multiple surgical interventions, resulting in significant morbidity. A less invasive alternative is percutaneous pulmonary valve implantation (PPVI). Though studies have previously reported the safety and efficacy of the early generation transcatheter heart valves (THVs), data on more recent devices are severely lacking.

Methods and Results: We performed a multinational, multicentre, retrospective, observational registry analysis of patients who underwent PPVI using the Edwards SAPIEN XT THV. Of the 46 patients that were enrolled, the majority had tetralogy of Fallot as the underlying diagnosis (58.7%), and stentless xenograft as the most common RVOT anatomy (34.8%). Procedural success rate was high (93.5%), with a low frequency of periprocedural complications and adverse events (6.5% and 10.9%, respectively). At 30 days post-procedure, NYHA class had improved significantly (90.6% were at NYHA I or II). The rate of moderate/severe pulmonary regurgitation had decreased from 76.1% at baseline to 5.0% at 30 days, and the calculated peak systolic gradient had decreased from 45.2 (SD ± 21.3) mmHg to 16.4 (SD ± 8.0) mmHg, with these values remaining low up to 2 years.

Conclusions: The data suggest the efficacy and safety of the SAPIEN XT THV in PPVI in common anatomies in patients with conduits, as well as those with native pulmonary valves or transannular patches. Continued data collection is necessary to verify long-term findings.

Clinicaltrials.gov identifier: NCT02302131

Keywords: pulmonary valve, congenital heart disease, percutaneous pulmonary valve implantation, SAPIEN XT

1 INTRODUCTION

Malfunctioning pulmonary valves and alterations of the right ventricular outflow tract (RVOT) are frequent in many congenital heart defects. Typical examples include Tetralogy of Fallot (ToF), double outlet right ventricle (DORV), pulmonary stenosis (PS), pulmonary atresia (PA), truncus arteriosus (TA), transposition of the great arteries (TGA) with PS (Rastelli's Operation), absent pulmonary valve syndrome (Miller-Lev-Paul), and the Ross Procedure for aortic valve disease.

Surgical correction involves the repair or replacement of the native RVOT using biological valves such as homografts, bioprostheses, or xenografts. These valve corrections frequently become dysfunctional within 3 to 20 years after the primary intervention, depending on patient's age and size. This results in the requirement for a further pulmonary valve replacement procedure. An emerging, less invasive treatment option that aims to reduce the considerable morbidity associated with repeat operations is percutaneous pulmonary valve implantation (PPVI).[1, 2]

Until recently, the Medtronic Melody and Edwards SAPIEN transcatheter heart valves (THVs) were the only registered devices for this purpose, with the Melody valve available in diameters of 18, 20, and 22 mm, and the Edwards SAPIEN valve being available in diameters of 23 and 26 mm.[3-6] On-going developments in THV design have led to the next generation SAPIEN XT being available in sizes of 20, 23, 26, and 29 mm (for further details see **Supplementary Table 1**); however, there is a clear need for data on the new valve technology. For this reason, we began to retrospectively collect the available data on SAPIEN XT implants in the pulmonic position, and to follow the identified patients within the structured environment of a multicentre registry. We aimed to describe patient experiences, and to document the feasibility and safety of using the SAPIEN XT THV for PPVI.

2 METHODS

Pulmonic XT is an investigator-initiated, multicentre, observational registry collecting data on patients undergoing PPVI using the SAPIEN XT technology (**Supplementary Figure 1**). The project was registered with clinicaltrials.gov in November 2014 and assigned the registration number NCT02302131. Enrolment was carried out either retrospectively or at the time of the procedure, with a retrospective and/or prospective follow-up, depending on the time of recruitment relative to implantation. All patients provided written informed consent and the respective ethics committees at each centre granted approval prior to patient documentation. The study was performed in accordance with the Declaration of Helsinki and its amendments.

2.1 Centres

Based on information provided by the core group of participating centres and Edwards Lifesciences, we estimated that approximately 23 centres globally (excluding the United States) had performed at least one PPVI using SAPIEN XT technology, with an approximate total of 92 patients receiving the valve (estimated range 77 to 120). We approached all 23 centres in November 2014 to initiate data collection. These included centres in Europe (Belgium, Switzerland, Germany, Netherlands, UK, Sweden, Italy, France), the Middle East (Israel, Saudi Arabia), North America (Canada), and Australia.

2.2 Patients

Patients with a clinical indication for PPVI who had undergone or were undergoing the procedure using the SAPIEN XT THV were eligible, provided that they supplied signed data release and informed consent. So as to cover the broadest possible spectrum of patients undergoing PPVI, no exclusion criteria were stipulated.

2.3 Endpoints

The endpoints of this registry were selected in order to evaluate the feasibility and safety of implanting a SAPIEN XT THV in the pulmonic position. The procedural and clinical outcome data collected were based on the standards of care for PPVI at each individual participating site. Examinations may include (but are not limited to) physical assessments, ECG, exercise testing, laboratory results, X-rays, angiograms, CT/MRI scans, and transthoracic and/or transoesophageal echocardiography.

Short-term outcomes included right ventricular (RV) and pulmonary artery (PA) pressures, maximum flow velocity RVOT, degree of pulmonary regurgitation, peak gradients, procedural success, and length of hospitalisation (from admission to discharge). Long-term outcomes included changes in New York Heart Association (NYHA) class; peak oxygen consumption (VO_2); anaerobic threshold (AT); device function; and evidence of structural valve deterioration, including stent fracture. Safety outcomes were device malfunction; arrhythmia; coronary compression; neurologic impairment; conduit/RVOT rupture; stent dislocation/THV dislocation; bleeding complications; need for surgical correction; endocarditis of the implanted valve; and any cardiovascular events, including death, myocardial infarction, coronary compression, pulmonary embolism, and stroke/transient ischemic attack (TIA).

2.4 Data collection

Authors collectively designed a case report form to accommodate the broadest possible spectrum of clinical situations in which PPVI may be indicated. Data collection was paper-based, with investigators transferring the obtained data (via letter, fax, or email) to the coordinating centre at the Institute for Pharmacology and Preventive Medicine (IPPMed, Cloppenburg, Germany). Double data entry was carried out by data managers to transfer the information to the *Pulmonic XT* database.

Follow-up time points were defined as follows: 30 days (post intervention up to and including 30 days), 6 months (more than 30 days and up to and including 6 months), 1 year (more than 6 months and up to and including 1 year), and 2 years (more than 1 years and up to and including 2 years).

2.5 Statistics

For categorical variables (e.g. gender) frequency distributions are given. For numerical variables (e.g. patient age) means with standard deviations (SD) and medians with ranges are given. Statistical analysis was performed using SPSS Statistics 23.0 (SPSS, Inc., Chicago, IL).

3 RESULTS

A total of eight centres participated in the registry. Five of the 23 approached centres were unresponsive to the invitation to participate, five declined participation, and five did not deliver data. Up until May 31st 2017, the 8 participating centres provided data on a total of 46 patients (range 1 to 21 patients per centre). This corresponds to 50.5% of the 91 patients estimated to have received an implant up to this time point. Follow-up was 89.1% at day 30 (n=41), 65.2% at 6 months (n=30), 41.3% at 1 year (n=19), and 41.3% at 2 years (n=19). Three patients died during the extended follow-up (>30 days).

3.1 Patient characteristics

At baseline, the mean age was 29.0 (SD ± 14.1) years (range 9-64 years, median 27.5 years) and 28.3% were female (13/46) (**Table 1**). The majority of patients (27/46; 58.7%) had ToF as the underlying primary diagnosis, followed by 5 patients with truncus arteriosus (10.9%) and 4 patients who had undergone a Ross Procedure (8.7%). Of the two patients with simple PS as a primary diagnosis, one also had tricuspid stenosis and an atrial septal defect. The most frequent RVOT anatomy prior to valve implantation was stentless xenograft (16/46; 34.8%). Further anatomies were homograft (8/46; 17.4%), transannular patch (6/46; 13.0%), native outflow tract (5/46; 10.9%) and others (such as Carpentier-Edwards, Hancock etc.; 11/46; 23.9%). The majority of patients were either NYHA class II (52.4%) or NYHA III (35.7%).

3.2 Procedural characteristics

There was a strong preference for the transfemoral access route (93.5%), with a jugular access route selected for only three patients (6.5%; **Table 2**). The RVOT was pre-stented in 42 patients , with 19 being stented before and 22 stented on the day of the procedure (no information on the time of stenting in one patient). The majority received one stent (69.6%) and the most frequently chosen stent type was a CP bare stent (38.1%). Before pre-dilation, the minimal RVOT diameter was 16.6 (SD ± 4.6) mm, increasing to 22.8 (SD ± 3.3) mm after pre-dilation. The 26 mm SAPIEN XT was the most frequently chosen valve size (n=26; 56.5%), followed by the 23 mm valve (n=10; 21.7%) and 29 mm valve (n=8; 17.4%), with only 4.3% (n=2) receiving the smallest 20 mm valve. In 23.9% of patients (11/46), the SAPIEN XT was implanted into a previously implanted bioprosthesis (Symbion in 3 patients, Mitroflow in 2, Carpentier-Edwards Perimount in 2, and Medtronic in 1, other in 3). In these 11 patients, the principal diagnosis was ToF alone (5 patients), followed by history of Ross Procedure (2), pulmonary atresia with VSD (1) and without VSD (1), truncus arteriosus (1), and pulmonary stenosis (1). Mean total procedural time was 147.8 (SD ± 55.0) minutes, with a fluoroscopy time of 38.4 (SD ± 30.1) minutes and a mean contrast volume of 171.5 (SD ± 134.4) ml.

3.3 Periprocedural and long-term outcomes

Procedural success, defined as a single valve implanted in the intended location, was 93.5% (**Table 3**). An example of a successfully implanted valve can be seen in **Supplementary Figure 2**. Periprocedural complications were transient in one patient, with a significant paravalvular leak that was managed without a need for conversion to surgery but with a new stent and a SAPIEN XT 26 mm valve. The patient was clinically stable (NYHA class I) at follow-up, with trivial pulmonary regurgitation. In another two patients, conversion to surgery was necessary due to valve dislocation. In a retrospective analysis, valve dislocation occurred due to inadequate measurement of the pre-stented outflow tract, resulting in an inadequate valve size within a large RVOT. No periprocedural mortality occurred.

Three deaths occurred during follow-up, but were not valve-related: one at 3 months due to life-threatening comorbidities, and the other at 5 months due to multiple organ failure resulting from complications after surgical aortic valve replacement for severe aortic insufficiency, which had already been apparent prior to PPVI.

3.4 Functional outcomes

After PPVI, an improvement in heart failure was seen (**Table 4**). While 38.1% of patients enrolled in the registry were at NYHA class III–IV prior to intervention, this declined to 13.0% 6 months after the procedure. Accordingly, an improvement of pulmonary and tricuspid regurgitation was noted, with no or trivial pulmonary regurgitation in 92.5% of patients at follow-up day 30, and 85.7% after two years. The peak systolic gradient ($4Vmax^2$) over the pulmonary and tricuspid valves decreased markedly after PPVI; however, peak systolic gradients over the RVOT remained substantially lower than baseline at 2 years. Results regarding oxygen consumption and anaerobic threshold were difficult to interpret owing to small patient numbers.

4 DISCUSSION

There are few published reports on use of the SAPIEN XT THV in PPVI for patients with pulmonary valve and RVOT dysfunction. The data gathered in the present registry suggest that implantation of this device in a wide range of given anatomies and different diameters of the RVOT leads to substantial improvements in haemodynamic profiles, with low complication rates. Thus, the SAPIEN XT appears to have a high level of procedural safety and efficacy when implanted in the pulmonary position in an international, real-world setting.

4.1 Haemodynamics

A significant reduction in the proportion of patients experiencing moderate/severe pulmonary regurgitation was seen following PPVI (5.0% at day 30 compared to 76.1% at baseline) which persisted up to 2 years. This marked drop is consistent with that reported in previous studies[2-5, 7, 8], and supports the case for the long-term efficacy of PPVI with the SAPIEN XT. Concurrently, the mean peak systolic RVOT gradient at 30 days post-PPVI in the present study had dropped by 29 mmHg relative to baseline. This is similar to the magnitude of post-procedural improvement seen by a number of other studies (reductions of between 18 and 30 mmHg)[2-5, 8-10], including one solely evaluating PPVI in patients undergoing valve-in-valve procedures.[7] Of these studies, those assessing long-term hemodynamic outcomes also reported a continued, progressive reduction in this gradient over the subsequent 6–12 months.[3, 5, 7, 9] In the present study, the peak systolic gradient ($4Vmax^2$) remained markedly lower than the baseline value at all follow-ups. The finding that the mean peak RVOT gradient was 16.4 mmHg at 30 days is particularly encouraging given recent evidence that a post-procedural RVOT gradient below 25 mmHg is associated with longer periods of freedom from intervention[10], and a reduction in conduit gradient is an independent predictor for increased exercise capacity.[11] Our findings are therefore consistent with the idea that PPVI results in a marked, sustained improvement in cardiac flow for patients with a range of underlying aetiologies and RVOT anatomies (including those with existing bioprostheses), and provides evidence for the medium-term efficacy of the SAPIEN XT.

4.2 Functional status

Concurrent with improvement in hemodynamic dysfunction, a large improvement in NYHA class was observed following PPVI, with the proportion of patients in class III or IV falling from 38.1% to just 9.4% at day 30. Furthermore, a trend towards an increasing proportion of patients falling within NYHA class I was apparent up to 2 years. In support of our findings, several other studies have also reported a dramatic shift of patients from higher to lower NYHA classes following PPVI, accompanied by a long-term persistence of this finding.[3, 4, 8, 10, 12] The only decline in NYHA class that has been reported was identified as being due to stent fracture or recurrent RVOT obstruction[8], neither of which was encountered in the present study. Thus, despite limited patient numbers, we can be reasonably confident that PPVI with the SAPIEN XT results in both short- and mid-term improvements in functional status. Future data analysis including a greater number of patients at later follow-ups will help to confirm this.

The increased diameter of the RVOT after PPVI enables a significant increase of cardiac output under exercise conditions, translating into a measurable increase in exercise capacity. On the other hand, in patients with predominant pulmonary regurgitation, PPVI will result in a reduced RV volume, but very often no considerable change in exercise capacity. In our cohort, the majority (35/46) showed moderate / severe pulmonary regurgitation as the leading pathophysiology, therefore no major change in exercise capacity could be anticipated.

4.3 Periprocedural complications and events

A high procedural success rate (93.5%) and low rates of periprocedural complications and adverse events (approximately 6.5% and 10.9%, respectively) were observed in the present study. These are similar to those reported previously for SAPIEN devices.[3, 4, 12, 13] In terms of procedural complications, one incident of device malfunction resulting in a significant paravalvular leak that was managed without a need for conversion to surgery and two episodes of valve dislocation (4.4% of patients) requiring conversion to surgery were observed; in retrospect, these dislocations may have been preventable, and may be attributed to a learning curve. The rate of valve dislocation compares favourably to the rates reported in previous studies by Haas et al. and Kenny et al. using the SAPIEN THV (8.8% and 13.6%, respectively).[3, 4] In addition, the remaining adverse events reported herein are minimal and included only arrhythmia requiring pacing, drugs, or cardioversion (4 patients). There was however one report of significant bleeding at the groin catheter insertion site. Other authors have previously reported additional complications and events such as transient cerebral plexus palsy, pulmonary haemorrhage, ventricular fibrillation, and stent or THV migration[3, 4]; none of which were seen in the current study. Standardisation of complication/event reporting would aid comparisons in future studies. In any case, all events and complications in the present study were successfully resolved without further complications, and the 3 deaths that occurred at >30 days post-PPVI were considered unrelated to the procedure or device used. This may lend further evidence as to the safety of the SAPIEN XT.

Stent fracture has been a significant concern for PPVI, though has been more often associated with the Melody valve.[2, 9, 14, 15] One study reported as much as 18% of patients experiencing this complication up to one year, even after pre-stenting.[16] Conversely, studies have consistently reported no stent fractures in patients treated with SAPIEN valves[3, 4, 12, 13], which was also the case in the present study. This suggests that the SAPIEN XT has the same superior device integrity as previous models and may be preferable to Melody valves in patients at risk of stent fracture, such as those with severely obstructed RVOT conduits.[14]

The high mortality associated with coronary compression following valve deployment in PPVI makes it a particular cause for concern, especially as Morray et al. reported that approximately 5% of patients are at risk.[17] In the present study, no patients experienced coronary compression, despite the diverse range of underlying diagnoses (including a large number of patients with ToF) and inter-subject diversity. This reflects improvements in pre-implantation procedures that have enhanced the safety and predictability of PPVI. Future studies to identify patients most at risk of developing arrhythmias would further improve the safety outcomes of PPVI.

4.4 Generations of Edwards SAPIEN valves

The number of patients for whom PPVI is deemed appropriate has been severely limited by both anatomical substrate and the restricted availability of heart valve sizes.[6] In a study by Lurz et al. in 2008, 5% of patients did not meet the morphological criteria for PPVI due to incompatible RVOT dimensions.[15] In the present study, the 26 mm valve was most frequently used. This size was already available in the previous SAPIEN range and was recognised as a welcome extension to the Melody valve, which had previously only been expandable to sizes of 18–22 mm.[4] However, 17.4% (8/46) of patients in the present study benefitted from the availability of a 29 mm valve, a newly available size with the SAPIEN XT range. This confirms the potential for larger valves to permit PPVI in a significant number of patients with larger outflow tracts, as was previously suggested by Demkow et al.[13] On the other hand, 2 patients were treated with a 20 mm valve, thereby extending the potential use even to patients with smaller RVOTs. Further extension of the available valve sizes may open up the opportunity for PPVI to even more patients in future.

The most recent SAPIEN 3 valve has recently received FDA approval for the aortic position. This valve is also available in 23, 26, and 29 mm sizes, and offers further potential advantages, such as an outer skirt for minimisation of paravalvular leakage, and an improved frame design to allow smaller crimping and higher radial strength. A recent study comparing the SAPIEN 3 and SAPIEN XT THVs for transcatheter implantation in the aortic position has reported that the newest model is associated with reduced platelet activation and a lesser degree of aortic regurgitation.[18] Future real-world studies will examine its potential benefits in the pulmonary position (NCT02777892).

4.5 Study limitations

The number of patients enrolled in this registry is small. This is a commonly encountered limitation in studies assessing PPVI, which is due to the relative novelty of the procedure and the limited availability of patients. This was further complicated in the present study by the reluctance of sites to participate.

There is presently little registry data available regarding the long-term effects of PPVI with the SAPIEN XT on haemodynamics and functionality. Therefore, the sustainability of the initial positive results is uncertain. However, our findings compare well to earlier published results of PPVI with the SAPIEN valve[2-5], suggesting validity. The on-going collection of data at later time points will help to clarify longitudinal trends in the present study, while future studies with larger cohorts will add value to our findings.

As a largely retrospective study, uncertainty over the reliability of procedural data is an inherent limitation, and not all data was available for each patient. The latter was particularly evident regarding exercise capacities. However, this problem is unavoidable in a real-world setting as the relative rarity of patients meeting entry requirements would result in either an excessively long prospective trial period or insufficient patient numbers. Therefore, future studies when the SAPIEN XT is more widely utilised for PPVI are necessary to investigate aspects such as improvements in oxygen consumption.

The observational nature of the present study led to a lack of PPVI procedure standardisation throughout the different centres, implying that results may have been influenced by the various management approaches. Further, because patients were retrospectively documented in this registry, there were no information captured on patients excluded because of the proximity of the coronary arteries to the RVOT. However, the observational design may offer several potential advantages over a controlled study, such as the opportunity to gain an insight into the safety and efficacy of the valve in real-world clinical practice.

5 CONCLUSIONS

In those patients we were able to document, the SAPIEN XT had a good safety profile and a high level of efficacy in terms of haemodynamic and functional improvement. This appears at least comparable to the previous SAPIEN valve, with a potentially reduced complication rate. The availability of an additional valve size for implantation in the pulmonary position has allowed PPVI to be successfully carried out in patients with a larger conduit diameter for whom the procedure would otherwise have been impossible. Continued data collection and initiation of larger registries in future will add weight to our findings.

6 AUTHOR CONTRIBUTIONS

All authors, led by Nikolaus A. Haas (NH), Peter Bramlage (PB), and Michael Mullen (MM), were involved in the conception and design of the study. PB drafted the manuscript, and all authors have revised the article for important intellectual content. All authors gave final approval of the version to be submitted.

6.1 Principal investigators

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6.2 Centres with enrolled patients (Investigators)

Bad Oeynhausen, Germany 21 patients (Nikolaus A. Haas); Vancouver, Canada 7 pts (Ronald Giacomo Carere); Zürich, Switzerland 5 pts (Oliver Kretschmar); Toronto, Canada 5 pts (Eric Horlick); Munich, Germany 3 pts (Peter Ewert); Quebec, Canada 2 pts (Josep Rodés-Cabau); Gent, Belgium 2 pts (Daniël de Wolf), Gasthuisberg, Leuven, Belgium 1 patient (Marc Gewillig)

7 ACKNOWLEDGEMENTS

Helen Sims (IPPMed Barcelona) provided editorial support during the preparation of this manuscript. Andrea Gansz (IPPMed Cloppenburg) managed the conduct of the project.

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9 TABLES

Table 1: Patient characteristics

	n/N (%) / mean ± SD / median (range)
Age [years]	29.0 ± 14.1
	27.5 (9–64) (N = 46)
Female gender	13/46 (28.3)
Weight [kg]	71.3 ± 20.5
	68.7 (22–110) (N = 46)
Height [cm]	167.8 ± 13.8
	172.5 (130–189) (N = 46)
Prior endocarditis	4/43 (9.3)
Underlying diagnosis	
ToF	27/46 (58.7)
Pulmonary atresia with VSD	3/46 (6.5)
Pulmonary atresia without VSD	3/46 (6.5)
Truncus arteriosus	5/46 (10.9)
Hx of Ross Procedure	4/46 (8.7)
TGA	2/46 (4.3)
Pulmonary stenosis	2/46 (4.3)
RVOT anatomy prior to valve implantation	
Native RVOT / PS	5/46 (10.9)
Transannular patch	6/46 (13.0)
Homograft	8/46 (17.4)
Stentless xenograft	16/46 (34.8)
Others (Carpentier-Edwards, Hancock etc.)	11/46 (23.9)

Legend: n, number of patients with variable; N, number of patients with data available; ToF, Tetralogy of Fallot; TGA, Transposition of the great arteries; DORV, double-outlet right ventricle; RVOT, right ventricular outflow tract; PS, pulmonary stenosis; SD, standard deviation

Table 2: Procedural characteristics

	n/N (%)/ mean ± SD / median (range)
General anaesthesia	18/46 (39.1)
Access	
Transfemoral	43/46 (93.5)
Jugular	3/46 (6.5)
RVOT pre-stenting	
Stent placed at the time of the procedure	22/45 (48.9)
Stent placed before day of procedure	19/45 (42.2)
Number of stents implanted	
0	4/46 (8.7)
1	32/46 (69.6)
2	10/46 (21.7)
Type of stent	
CP bare stent	16/42 (38.1)
CP covered stent	10/42 (23.8)
Andramed	10/42 (23.8)
Other	6/42 (14.3)
Minimal diameter before pre-dilation [mm]	16.6 ± 4.6
	17.0 (6–25) (N = 37)
Minimal diameter after pre-dilation [mm]	22.8 ± 3.3
	23.0 (11–28) (N = 34)
SAPIEN XT THV size implanted	
20 mm	2/46 (4.3)
23 mm	10/46 (21.7)
26 mm	26/46 (56.5)
29 mm	8/46 (17.4)
Valve in valve (previously implanted bioprothesis)	11/46 (23.9)
Length of procedure [min]	147.8 ± 55.0
	139.5 (45–291) (N = 44)
Fluoroscopy time [min]	38.4 ± 30.1
	33.5 (5.0–113.0) (N = 40)
Contrast volume [ml]	171.5 ± 134.4
	129.5 (25–470) (N = 42)

Legend: n, number of patients with variable; N, number of patients with data available; RVOT, right ventricular outflow tract; CP, Cheatham Platinum; SD, standard deviation

Table 3: Periprocedural outcomes

	n/N (%)
Procedural success*	43/46 (93.5)
Procedural complications	
Device malfunction	1/46 (2.2)
Dislocation of valve during implantation requiring subsequent surgical intervention	2/46 (4.4)
Procedural adverse events	
Arrhythmia with pacing, drugs or cardioversion	4/45 (8.9)
Myocardial infarction	0/46 (0.0)
Pulmonary embolism	0/46 (0.0)
Rupture requiring emergency stenting or surgery	0/46 (0.0)
Coronary compression	0/46 (0.0)
Significant bleeding	1/46 (2.2)
Significant neurologic impairment	0/46 (0.0)
Periprocedural death	0/46 (0.0)

Legend: n, number of patients with variable; N, number of patients with data available; SD, standard deviation. *Defined as single valve implanted in intended location.

Table 4: Functional outcome after PPVI

	Baseline	Day 30	Month 6	Year 1	Year 2
NYHA class					
Class I	4/42 (9.5)	20/32 (62.5)	15/23 (65.2)	10/14 (71.4)	9/13 (69.2)
Class II	22/42 (52.4)	9/32 (28.1)	5/23 (21.7)	4/14 (28.6)	1/13 (7.7)
Class III	15/42 (35.7)	2/32 (6.3)	2/23 (8.7)	0/14 (0.0)	3/13 (23.1)
Class IV	1/42 (2.4)	1/32 (3.1)	1/23 (4.3)	0/14 (0.0)	0/13 (0.0)
Peak systolic gradient over RVOT [mmHg]	45.2 ± 21.3 (N = 34)	16.4 ± 8.0 (N = 26)	20.5 ± 8.1 (N = 15)	14.7 ± 9.9 (N = 6)	26.1 ± 10.6 (N =10)
Pulmonary regurgitation					
None/trivial	3/46 (6.5)	37/40 (92.5)	27/29 (93.3)	13/18 (72.2)	12/14 (85.7)
Mild	8/46 (17.4)	1/40 (2.5)	1/29 (3.4)	3/18 (16.7)	2/14 (14.3)
Moderate	8/46 (17.4)	2/40 (5.0)	1/29 (3.4)	2/18 (16.7)	0/15 (0.0)
Severe	27/46 (58.7)	0/40 (0.0)	0/29 (0.0)	0/18 (0.0)	0/15 (0.0)
RVSP across tricuspid valve [mmHg]	59.6 ± 19.0 (N = 38)	35.0 ± 9.3 (N = 33)	35.2 ± 15.1 (N = 20)	33.8 ± 9.8 (N = 12)	32.6 ± 12.7 (N = 13)
Tricuspid regurgitation					
None/trivial	16/46 (34.8)	24/39 (61.5)	10/30 (33.3)	5/17 (29.4)	6/17 (35.3)
Mild	22/46 (47.8)	10/39 (25.6)	16/30 (53.3)	10/17 (58.8)	9/17 (52.9)
Moderate	6/46 (13.0)	4/39 (10.3)	3/30 (10.0)	2/17 (11.8)	2/17 (11.8)
Severe	2/46 (4.3)	1/39 (2.6)	1/30 (3.3)	0/17 (0.0)	0/17 (0.0)
Peak oxygen consumption [ml O_2/min/kg bodyweight]	30.0 ± 25.6 (N = 9)	-	15.8 ± 7.5 (N = 4)	26.5 ± 7.5 (N = 6)	22.4 ± 8.2 (N = 9)

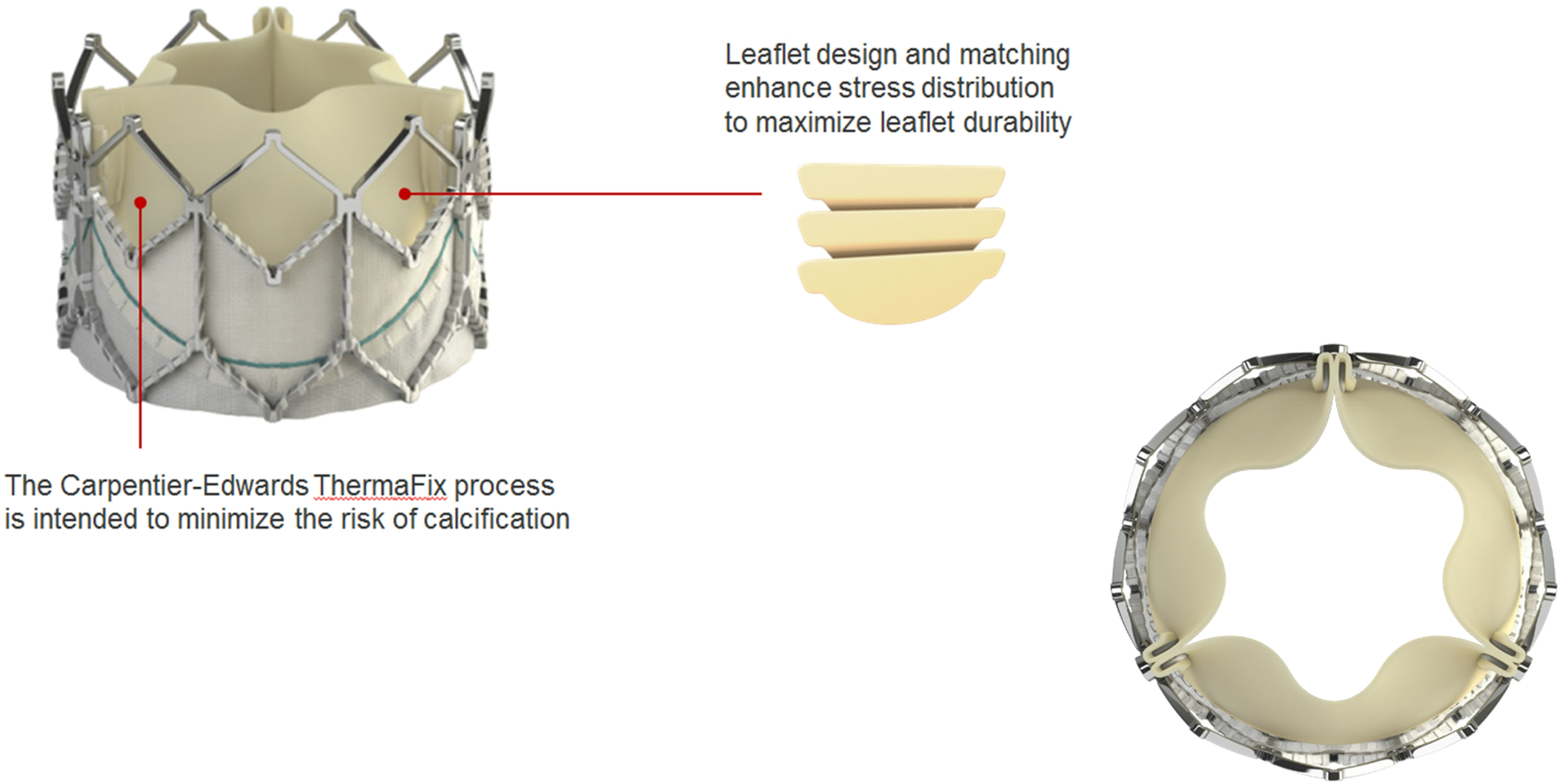
Anaerobic threshold [ml/min/kg]	14.6 ± 10.0 (N = 5)	-	13.3 ± 0.6 (N = 3)	17.0 ± 6.0 (N = 6)	18.5 ± 6.2 (N = 6)

Legend: Values are expressed as n / N; mean ± SD; %; range; MRI: magnetic resonance imaging; RV: right ventricular; EF: ejection fraction

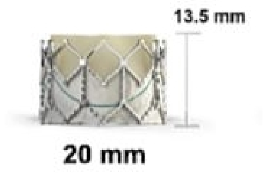
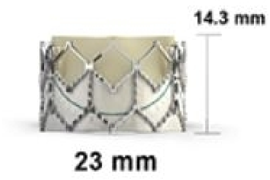
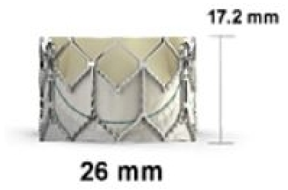
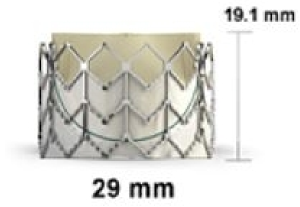
SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1: Native RVOT after balloon dilatation of a native and severe PS. Initially severe Pulmonary regurgitation. Prestenting performed with an Andrastent followed by implantation of a 26 mm SAPIEN XT valve.

Supplementary Figure 2: Edwards SAPIEN XT transcatheter heart valve for PPVI.


Leaflet design and matching enhance stress distribution to maximize leaflet durability
The Carpentier-Edwards ThermaFix process is intended to minimize the risk of calcification

Supplementary Table 1: Comparison of SAPIEN XT Balloon-Expandable Transcatheter Heart Valve (Model 9300TFX) Parameters

	SAPIEN XT (20 mm)	SAPIEN XT (23 mm)	SAPIEN XT (26 mm)	SAPIEN XT (29 mm)
				
Tissue Thickness	0.3-0.4	0.3–0.4 mm	0.3–0.4 mm	0.4–0.5 mm
Frame height (expanded)	13.5 mm	14.3 mm	17.2 mm	19.1 mm
Frame height (crimped)	16 mm	17 mm	20 mm	22 mm
Frame shortening (deployment)	2 mm	3 mm	3 mm	3 mm
Fabric Skirt Height	6 mm	6 mm	8 mm	11 mm
Delivery system	NovaFlex+	NovaFlex+	NovaFlex+	NovaFlex+
Delivery system volume	11 ml	17 ml	22 ml	33 ml
Rates burst pressure	7 atm	7 atm	7 atm	7 atm

eSheath profile (internal diameter, unexpanded)	16-F (5.3 mm)	16-F (5.3 mm)	18-F (5.9 mm)	20-F (6.6 mm)
eSheath profile (outer diameter, unexpanded)	6.7	6.7 mm	7.2 mm	8.0 mm
Guidewire Compatibility	0.035’’	0.035’’	0.035’’	0.035’’
Minimum Access Vessel Diameter	6.0 mm	6.0 mm	6.5 mm	7.0 mm

Legend: None