



Mid-Term Outcomes Following Percutaneous Pulmonary Valve Implantation Using the “Folded Melody Valve” Technique

Zakaria Jalal¹, MD, PhD; Estíbaliz Valdeolmillos², MD; Sophie Malekzadeh-Milani, MD; Andreas Eicken, MD, PhD; Stanimir Georgiev³, MD; Michael Hofbeck, MD; Ludger Sieverding, MD; Marc Gewillig⁴, MD, PhD; Caroline Ovaert⁵, MD, PhD; Helene Bouvaist, MD; Xavier Pillois, PhD; Jean-Benoit Thambo, MD, PhD*; Younes Boudjemline, MD, PhD*

BACKGROUND: The folded valve is a manual shortening of the Melody device, which has been validated as a valuable therapeutic option for the management of dysfunctional right ventricular outflow tracts needing a short valved stent. In this article, we aimed to evaluate, in a multicenter cohort, the mid-term outcomes of patients in whom a percutaneous pulmonary valve implantation was performed using the folded valve technique.

METHODS: A 2012 to 2018 retrospective multicenter study was performed in 7 European institutions. All patients who benefit from percutaneous pulmonary valve implantation with a folded Melody valve were included.

RESULTS: A total of 49 patients (median age, 19 years [range 4–56], 63% male) were included. The primary percutaneous pulmonary valve implantation indication was right ventricular outflow tract stenosis (n=19; 39%), patched native right ventricular outflow tracts were the most common substrate (n=15; 31%). The folded technique was mostly used in short right ventricular outflow tracts (n=28; 57%). Procedural success was 100%. After a median follow-up of 28 months (range, 4–80), folded Melody valve function was comparable to the immediate postimplantation period (mean transvalvular peak velocity=2.6±0.6 versus 2.4±0.6 m/s, *P*>0.1; only 2 patients had mild pulmonary regurgitation). Incidence rate of valve-related reinterventions was 2.1% per person per year (95% CI, 0.1%–3.9%). The probability of survival without valve-related reinterventions at 36 months was 90% (95% CI, 76%–100%).

CONCLUSIONS: The folded Melody valve is a safe technique with favorable mid-term outcomes up to 6.5 years after implantation, comparable with the usual Melody valve implantation procedure. Complications and reinterventions rates were low, making this technique relevant in selected patients.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: incidence ■ probability ■ pulmonary valve ■ retrospective ■ stent

Percutaneous pulmonary valve implantation (PPVI) has emerged in the last 2 decades as an effective and less invasive alternative to surgical valve replacement for the treatment of dysfunctional right ventricular outflow tracts (RVOTs).^{1,2} Currently, 2 dedicated devices

are used on a larger scale, including the Melody valve (Medtronic, Minneapolis, MN) and the Sapien XT valve (Edwards Lifescience, Irvine, CA). The Melody device consists of a bovine jugular venous valve, sutured within a bare-metal platinum-iridium stent (CP stent, NuMED,

Correspondence to: Zakaria Jalal, MD, PhD, University Hospital of Bordeaux, Ave Magellan, 33600 Pessac, France. Email jalalzakaria1@gmail.com

*J.-B. Thambo and Y. Boudjemline contributed equally.

For Sources of Funding and Disclosures, see page 379.

© 2021 The Authors. *Circulation: Cardiovascular Interventions* is published on behalf of the American Heart Association, Inc., by Wolters Kluwer Health, Inc. This is an open access article under the terms of the [Creative Commons Attribution Non-Commercial-NoDerivs](https://creativecommons.org/licenses/by-nc-nd/4.0/) License, which permits use, distribution, and reproduction in any medium, provided that the original work is properly cited, the use is noncommercial, and no modifications or adaptations are made.

Circulation: Cardiovascular Interventions is available at www.ahajournals.org/journal/circinterventions

WHAT IS KNOWN

- The folded valve is a manual shortening of the Melody device, which has been shown to be feasible in complex right ventricular outflow tracts needing a short valved stent.
- However, data on the delayed impact of this device modification were lacking.

WHAT THE STUDY ADDS

- Our study showed favorable mid-term outcomes following folded Melody valve implantation up to 6.5 years after the procedure.
- Valve-related reinterventions rate of 2.1% per person per year, which is comparable to unmodified Melody valve outcomes.
- Further studies are needed to assess outcomes after similar valve modifications, such as Melody implantation in the mitral valve.

Nonstandard Abbreviations and Acronyms

| | |
|-------------|---|
| IE | infective endocarditis |
| MSF | melody stent fracture |
| PPVI | percutaneous pulmonary valve implantation |
| RV | right ventricle |
| RVOT | right ventricular outflow tract |

Inc, Hopkinton, New York), which can be expanded up to 22 mm (inner diameter). The Sapien XT is a bovine pericardial valve sutured in a cobalt-chromium stent, which is available at 23, 26, and 29 mm (outer diameters).³ The stent length differs between these 2 devices: Melody's length is 24.6 mm when expanded to 22 mm whereas the Sapien's length ranges between 14.3 and 19.1 mm when expanded to 23 and 29 mm, respectively.^{4,5} These 2 devices are therefore complementary as their design allows operators to cover a large range of RVOT diameters and anatomies.

However, while the Melody received CE marking in 2006 and FDA approval in 2010, the Sapien XT received both CE mark and FDA approval for PPVI in 2016. Therefore, until the Sapien valve became widely available, operators only had the Melody valve at their disposal. With this valve, to treat a wide variety of RVOT anatomies and lesions, several teams reported either off-label use or advanced techniques to achieve PPVI in small, large, or complex RVOTs.^{6–8} Among these procedural modifications, we described in 2014 the folded valve technique, which consists in shortening the Melody valved stent by folding its extremities, to implant the device in RVOTs with complex anatomy which might be at risk of PPVI-related complications.^{9,10} After this first descriptive case series, reporting favorable procedural and early results in

10 patients, the technique has been extended and performed by other centers. However, some concerns were raised about the delayed outcomes of the valve following this modification. In this article, we aimed to evaluate, in a multicenter cohort, the mid-term outcomes of patients in whom the folded valve technique was performed.

METHODS

Study Protocol

The data that support the findings of this study are available from the corresponding author upon reasonable request.

In this retrospective multicenter study, we reviewed data of patients who underwent PPVI using the folded valve technique between April 2012 and June 2018 in European centers accepting to collaborate to this survey. Data were collected anonymously and retrospectively from medical records focusing on demographic characteristics, procedural data, and both early and mid-term follow-up data. All participating centers had exhaustive computerized databases for data collection of consecutive patients. The implantation of a Melody valve using the folded valve technique was performed according to operators' preferences. As previously described, the main indications of this technique were (1) short RVOT with early pulmonary bifurcation (ie, expected landing zone shorter than the length of the fully deployed Melody valved stent, according to the manufacturer's data, depending on the size of the delivery system to be used), (2) bioprosthetic valves, (3) coronary arteries proximity, and (4) prevention of sternal compression (ie, by implanting a shorter valved stent away from the sternum, to decrease stent fracture risk). The study was approved by the institutional review board of each participating center. Informed consent was obtained from patients and/or parents/guardians as appropriate.

Procedural Data

All procedures were performed under general anesthesia, with or without endotracheal intubation and ventilation through a femoral approach. PPVI procedure was performed as previously described.¹⁰ Briefly, a preprocedural detailed hemodynamic assessment was done in all patients, with measurements of right atrial, right ventricle (RV), PA and aortic (Ao) pressures. Balloon interrogation of the RVOT with simultaneous aortic root or selective coronary artery angiograms were performed to assess the proximity of the valve landing zone with the coronary arteries or aorta. The indications for the use of the folded valve technique were recorded, followed by valve implantation. The folded valve modification has been already reported.¹⁰ Briefly, the terminal Melody stent struts on either sides of the Melody valve were folded over itself from inside out on a 10-mL syringe to obtain a length reduction of the device. Up to 2 extremities of the Melody can be folded artificially changing a CP8Z34 to a CP8Z28 if one extremity is folded, or to a CP8Z22 where both extremities are folded. Of note, the expected lengths of the Melody after partial and complete folding after full inflation at 22 mm were respectively 20.9 and 16.7 mm. The decision to go for partial folding or complete folding was decided by the operator based on the length of the landing zone. The crimping and loading of the Melody valve onto the Ensemble delivery

system (Medtronic, Minneapolis, MN), as well as valve deployment, were achieved using standard technique.⁴ The valve was post-dilated with high pressure balloons in case of significant residual gradient. Hemodynamic and angiographic assessments were repeated after PPVI. All patients received heparin and antibiotic prophylaxis during and after the procedure, according to institutional protocol.

Follow-Up

Patients' follow-up was performed according to each local protocol. Follow-up work up included clinical assessment (NYHA functional class), transthoracic echocardiography, chest X-ray, and cardiac magnetic resonance imaging when appropriate. Adverse events included all-cause mortality, catheter-based or surgical cardiac reinterventions, infective endocarditis (IE) (presumed or definite according to modified Duke criteria), melody stent fractures (MSFs) (graded according to previously validated classification¹¹) or symptomatic arrhythmias. Delayed complications were defined as occurring beyond 1 month after PPVI.

Statistical Analysis

Continuous variables are expressed as mean (SD) or median (range) and categorical variables as percentages and numbers of patients. Student paired *t* test was used for comparisons of quantitative data. Time to event outcomes was analyzed using standard Kaplan-Meier analysis. A *P*<0.05 was considered statistically significant. Data analysis was performed using the STATA software (StataCorpLP, College Station, TX).

RESULTS

Patient Population

A total of 49 patients (median age: 19 years [range, 4–56]; 63% male) were included from 7 centers (University Hospital of Bordeaux [n=9], Grenoble [n=1], Marseille [n=1], and Paris [n=20]—France; German Heart Center Munich [n=14] and Tuebingen University Children's Hospital (n=3)—Germany; University Hospitals Leuven (n=1)—Belgium). Underlying congenital defect was mostly Tetralogy of Fallot with or without pulmonary atresia (33 patients, 68%). The primary PPVI indication among patients was RVOT stenosis in 19 (39%), pulmonary regurgitation in 11 (22%), and mixed lesion in 19 (39%). Patched native RVOTs were the substrate in 15 patients (31%). The remaining patients presented with homografts, prosthetic conduits, or bioprostheses with a mean diameter of 19.8±3.8 mm. Patient baseline characteristics are summarized in Table 1.

Procedural Details

Indications for using the folded valve technique were short RVOT in 28 (57%), bioprosthetic valves in 13 (27%), coronary arteries proximity in 5 (10%), prevention of retrosternal compression in 2 (4%), and for increasing

Table 1. Patients' Baseline Characteristics

| | |
|--------------------------------------|-----------|
| Age at PPVI, y | 19 (4–56) |
| Sex (male) | 31 (63) |
| Body surface area, m ² | 1.4±0.4 |
| Underlying defect | |
| Tetralogy of Fallot/PA-VSD | 33 (68) |
| Common arterial trunk | 510 |
| Aortic valve disease, Ross procedure | 36 |
| TGA | 24 |
| Pulmonary valve agenesis | 24 |
| Other | 48 |
| Primary RVOT lesion | |
| Stenosis | 19 (39) |
| Regurgitation | 1122 |
| Mixed | 19 (39) |
| RVOT substrate | |
| Native | 1531 |
| Conduit | 1327 |
| Bioprosthesis | 1122 |
| Homograft | 1020 |
| Original substrate diameter, mm | |
| Homograft/conduits | 19±5 |
| Bioprostheses | 21±3 |
| Preprocedural TTE | |
| RV systolic pressure, mm Hg | 69.9±22 |
| RVOT peak velocity, m/s | 3.9±0.87 |
| RVOT gradient, mm Hg | 33±17 |
| PR moderate or severe | 29 (59) |

Values are mean±SD, median (range) or n (%). PA-VSD indicates pulmonary atresia with ventricular septal defect; PPVI, percutaneous pulmonary valve implantation; PR, pulmonary regurgitation; RV, right ventricle; RVOT, right ventricular outflow tract; TGA, transposition of the great arteries; and TTE, transthoracic echocardiography.

device's outer diameter in 1 patient (2%) with large RVOT (Figure 1). Procedural success was 100%. RVOT pre-stenting was performed in 43 (89%), with a mean stent length of 32±6.8 mm, while post-dilatation of the valve was performed in 22 patients (45%) with high-pressure balloons (size diameter range between 18 and 24 mm). In case of coronary proximity, all patients had a short pre-stent (CCP 8Z28, n=1; CP8Z22+LD max 26 mm, n=1; CP8Z22, n=1; EV LD max-26, n=2), so that the folded valve would be implanted within this framework without overlapping (Figure 2). No major procedural complication occurred.

Significant reduction of the invasively measured peak RV-to-PA gradient, RV systolic pressure and RV/Ao ratio were observed from 34.6±17.8 to 11.8±11.5 mm Hg, 60.3±19.3 to 41.1±16 mm Hg, and 0.68±0.22 to 0.38±0.14, respectively (*P*<0.001). Trivial pulmonary regurgitation was found in 5 patients (10%) while the remaining had no valvular leakage. Procedural features are displayed in Table 2.

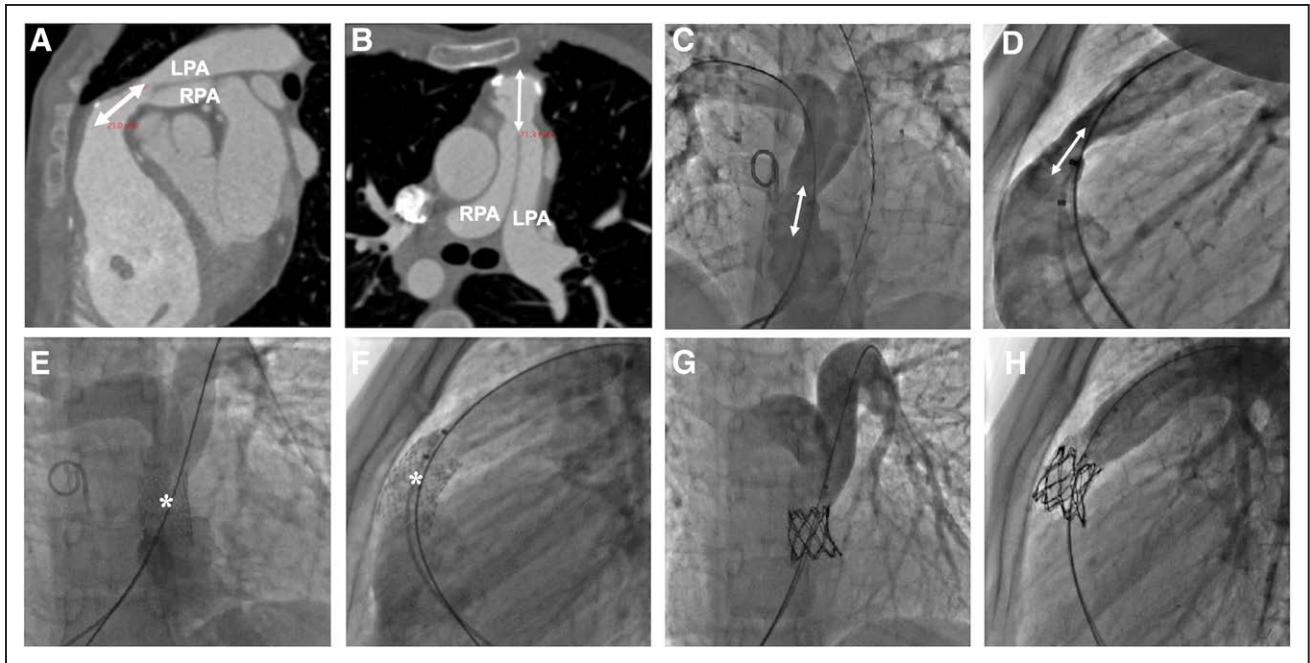


Figure 1. Folded Melody valve implantation in a short right ventricular outflow tract (RVOT) with early pulmonary artery (PA) bifurcation.

Twelve-year-old patient with operated common arterial trunk presenting with stenotic lesion of 14-mm Contegra conduit. **A–D**, Cardiac computed tomography reconstructions (**A** and **B**) and angiograms (**C** and **D**) showing severe conduit stenosis with short landing zone (white arrows) before PA bifurcation; **E** and **F**, angiograms showing RVOT prestenosis with a 26-mm Intrastent LD Max (ev3 Endovascular, Inc, Plymouth, MN; white asterisk); **G** and **H**, Final angiogram after folded Melody valve implantation showing good valve function without PA jailing. LPA indicates left pulmonary artery; RPA, right pulmonary artery; and RVOT, right ventricular outflow tract.

Follow-Up

Follow-up data were available for all but 2 patients who were lost of follow-up (47/49, 96%). After a median follow-up duration of 28 months (range, 4–80), resulting in a total of 137 patient-years, all patients were alive and the great majority was free of symptoms (NYHA I in 40/47 patients [85%], NYHA III in 1 patient [2%]).

At last follow-up, transthoracic echocardiography evaluation showed a mean transvalvular peak velocity, RVOT gradient and RV systolic pressure of 2.6 ± 0.6 m/s, 15 ± 12 , and 39.5 ± 15.6 mm Hg, respectively, which was comparable with immediate postimplantation values (2.4 ± 0.6 m/s, 13 ± 11 , and 35.8 ± 8.3 mm Hg, respectively, $P > 0.1$). In addition, all but 2 patients were free of pulmonary regurgitation (a trivial regurgitation was observed in the latter).

Overall, 7/49 patients underwent reinterventions during the follow-up, giving an incidence rate of 5.1% per person per year (95% CI, 1.9%–7.7%). The probability of reintervention-free survival at 12, 24, and 36 months was 98% (95% CI, 93.5%–100%), 90% (95% CI, 79.3%–99.8%), and 85% (95% CI, 68.1%–100%), respectively (Figure 3). Among those patients, 4 patients underwent transcatheter interventions unrelated with the Melody valve, including PA angioplasty ($n=2$) and/or stenting ($n=2$). The 3 remaining patients had valve-related complications that led to reinterventions. The incidence rate

of valve-related reinterventions was 2.1% per person per year (95% CI, 0.1%–3.9%). The probability of survival without valve-related reinterventions at 12, 24, and 36 months was 98% (95% CI, 93.5%–100%), 95% (95% CI, 87.4%–99.9%), and 90% (95% CI, 76%–100%), respectively (Figure 3).

Reasons for reinterventions are as followed: IE occurred in 2 patients giving an incidence rate of 1.4% per person per year (95% CI, 0.2%–3.3%) in this population. Both had positive blood cultures with a significant increase of Melody valve gradient. Of them, one patient was shown to have a folded Melody type 1 stent fracture (Figure 4). Of note, this patient had a prestenosis (36-mm Intrastent LD Max [ev3 Endovascular, Inc, Plymouth, MN]) during the folded valve implantation. This patient was first managed by antibiotic treatment associated transcatheter RVOT balloon dilatation. He underwent a Melody valve-in-valve implantation 3 years later because of a mixed residual lesion. The other patient with IE required medical antibiotic therapy followed by surgical Melody explant and pulmonary valve replacement.

The third patient presented with asymptomatic severe obstruction of the folded Melody during a planned out clinic consultation 24 months following PPVI. She was still under antiplatelet regimen, according to local protocol. transthoracic echocardiography revealed a significant increase of transvalvular peak

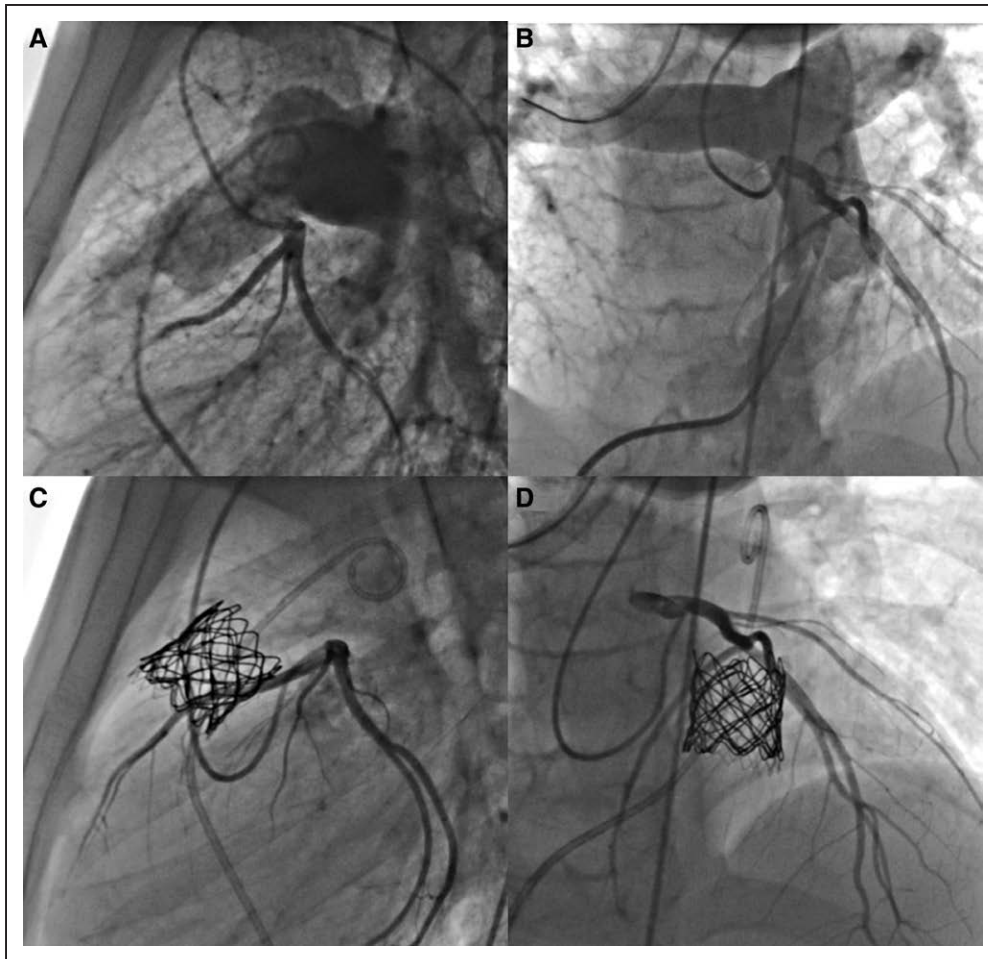


Figure 2. Folded Melody valve implantation in right ventricular outflow tract (RVOT) with coronary artery proximity.

A and B, Simultaneous RVOT and selective coronary angiograms showing a close proximity between the coronary arteries and distal RVOT. **C and D,** Selective coronary angiogram after folded Melody valve implantation showing coronary artery patency.

gradient, without signs of IE nor valvular thrombus. No stent fracture was observed on chest X-rays, suggesting an early valve degeneration or a noninfective complication such as subacute valve thrombosis. The patient underwent an emergent catheterization and was managed by valve-in-valve Melody implantation (the new valve was not folded, as first Melody was used as a landing zone) with excellent result (Figure 5). The last follow-up, 26 months later, revealed a normal function on the new Melody valve (transvalvular peak velocity, 2.3 m/s; RVOT gradient, 12 mmHg, without pulmonary regurgitation). Detailed description of patients with valve-related reinterventions is displayed in Table 3.

DISCUSSION

In this article, we report the mid-term-outcomes of PPVI using the folded Melody valve technique, in a multicenter series of 49 patients followed up to 6.5 years. After initial report of this modified implantation technique in 2014, we sought to evaluate how the manual folding of the Melody valved stent impacted patients' outcomes,

with a focus on potentially induced device-related complications. Our results showed that the folded Melody function was preserved during follow-up, with only a mild progression of transvalvular gradient and excellent valve competence in the great majority of patients. Moreover, in our cohort, freedom from valve-related reintervention was 90% at 3 years, with a cumulative rate of valve-related complications of 2.1% per person per year, which is not higher than those observed following unmodified Melody valve implantation.

Indications of the Folded Melody Valve

This technique has been developed to allow safe PPVI in complex anatomies by implanting a valved stent that is shorter than the Melody valve. The feasibility of this technique has already been reported. From a technical point of view, the folding of the Melody valve was always feasible, without disrupting the valve function on inspection. The folded Melody loading was mostly quickly done, although one must admit that it is more difficult than loading an unfolded valve. Some operators used an umbilical tape to

Table 2. Procedural Features of Folded Melody Valve Implantation

| Indications of folded valve technique | |
|--|-----------|
| Short RVOT | 28 (57) |
| Bioprostheses | 13 (27) |
| Coronary proximity | 5 (10) |
| Prevention from retrosternal compression | 2 (4) |
| Increase valve outer diameter | 1 (2) |
| Basal hemodynamics | |
| RV-PA systolic gradient, mm Hg | 34.6±17.8 |
| RV/Ao ratio | 0.68±0.22 |
| Moderate/severe pulmonary regurgitation | 29 (63) |
| Presenting before PPVI | |
| No stent | 6 (12) |
| 1 stent | 35 (72) |
| 2 stents | 7 (14) |
| 3 stents | 1 (2) |
| Final hemodynamics | |
| RV-PA systolic gradient, mm Hg | 11.8±11.5 |
| RV/Ao ratio | 0.38±0.14 |
| Mild pulmonary regurgitation | 5 (10) |

Values are mean±SD or n (%). Ao indicates aortic; PA, pulmonary artery; PPVI, percutaneous pulmonary valvular implantation; RV, right ventricle; and RVOT, right ventricular outflow tract.

make the loading easier. In one patient, device covering with the Ensemble system was impossible because of unusual thickness of the Melody. One Z was “unfolded” to its original configuration, thereby reducing the device’s thickness. As previously described in our first series, the main indications of this technique were (1) short RVOT with early pulmonary bifurcation, (2) bioprosthetic valves, (3) coronary arteries proximity, and (4) prevention of sternal compression.¹⁰ In this multicenter study, the main

indication was a short RVOT with early PA bifurcation. Indeed, in such anatomies with a short landing zone, the operator has to deal with the risk of implanting the valve too proximal (with the risk of ventricular embolization or mechanically induced ventricular arrhythmias) or too distal (with the risk of jailing one PA).^{12,13} Using the folded technique in complex substrates with short landing zones appears to be the most relevant indication of this technique. The second indication of the folding technique is the treatment of dysfunctional supported bioprosthetic valves. In this setting, having a shorted valved stent has 2 advantages: (1) avoid the protrusion of the proximal stent struts in the RV, which may increase the risk of arrhythmias¹² and (2) prevent from stent fracture by implanting the Melody within the supporting bioprostheses framework.¹⁴ We know that this latter theoretical advantage might be a matter of debate, as stent fracture rate is very low following PPVI in bioprostheses.¹⁴ However, we think that preventing device induced ventricular arrhythmias is reason enough to implant a folded valve within bioprostheses substrates. Moreover, similar modifications of the Melody have been described for surgical mitral implantation of this device. In this indication, to avoid sub aortic stenosis due to Melody stent protrusion, various techniques of device shortening have been described, including the folding technique.^{15,16} As Melody implantation in mitral valves is currently expanding, our article may provide additional information regarding the absence of significant impact of the folding technique on device outcome.

Mid-Term Function of the Folded Melody Valve

After the first description of the folded valve technique, some concerns were raised about the device late outcome after this modification. One potential issue of Melody valve

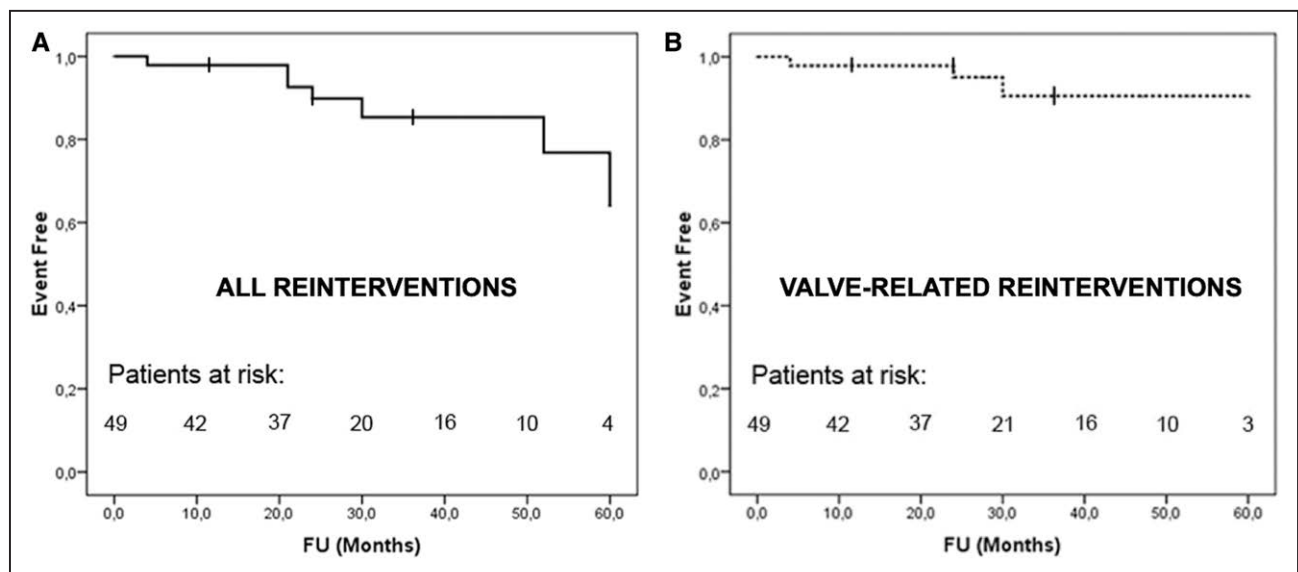


Figure 3. Kaplan-Meier curves of reinterventions-free survival among the study period. Plots of reintervention-free survival for all-cause reinterventions (A) and valve-related interventions (B). FU indicates follow-up.

Downloaded from http://ahajournals.org by on June 25, 2021

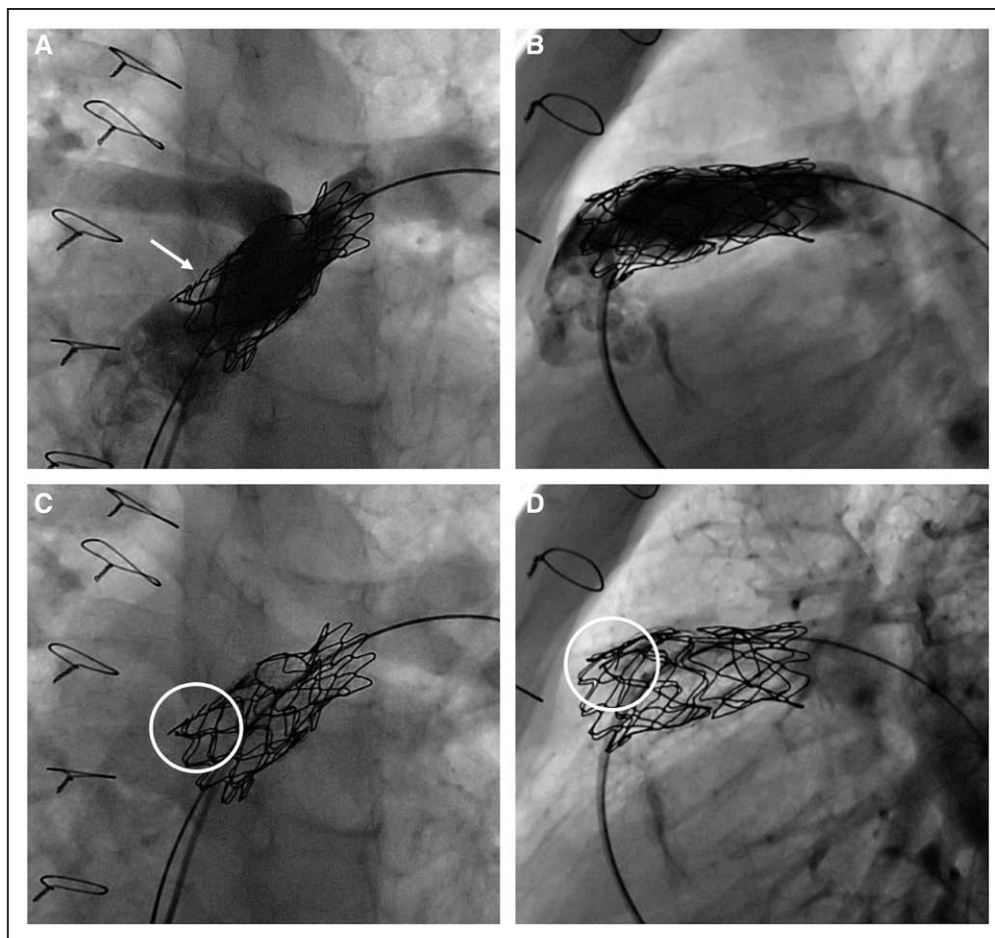


Figure 4. Stent fracture following folded Melody valve implantation.

The procedure was performed in the setting of an infective endocarditis with obstructive lesion of the valve. **A** and **B**, Angiograms showing moderate pulmonary regurgitation and valvular obstruction. Proximal stent fracture is visible (white arrow). **C** and **D**, Contrast-free fluoroscopies showing folded Melody stent fracture (white circles).

folding was the impact on valvular function durability. One of the most notable findings of this study was that the Melody TPV continued to function well, with little progression of RVOT obstruction and excellent valve competence in the majority of patients, out to at least 6.5 years after

implantation. One could argue that folding the valve could compromise valvular function. However, due to the length of the CP stent, folding of the extremities does not touch the commissures or leaflets at the top or at the base of the valve. There was no compromise on the integrity and competence

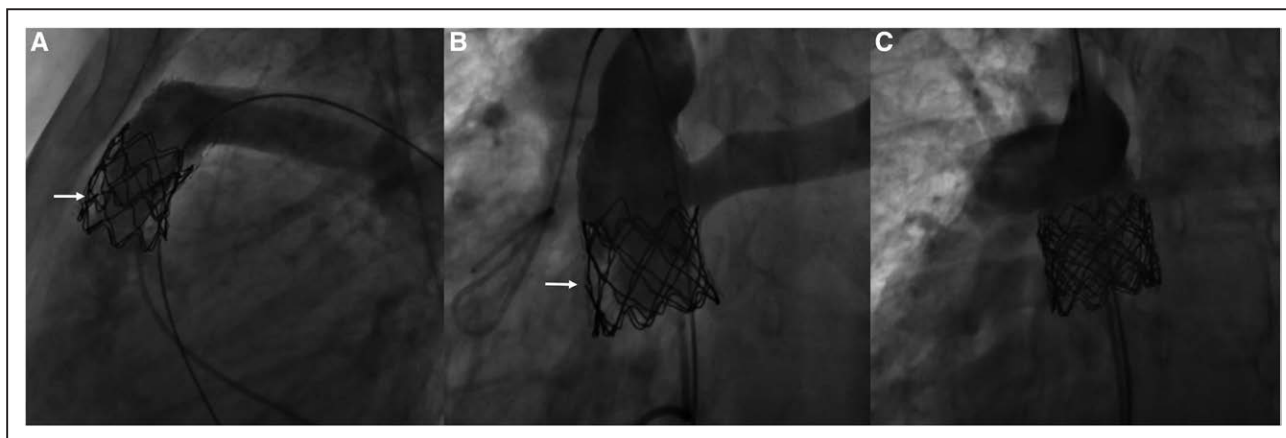


Figure 5. Valve-in-valve procedure following severe noninfectious obstruction of a folded Melody.

A and **B**, Angiograms showing moderate pulmonary regurgitation and valvular obstruction with contrast-media filling defect (white arrows) at the level of the valve, without stent fractures. **C**, Angiographic result following Melody valve in valve implantation.

Table 3. Details of the 3 Patients Who Had a Valve-Related Reintervention During Follow-Up

| | Patient 1 | Patient 2 | Patient 3 |
|--------------------------------------|-----------------------------|------------------------------|---|
| Age at PPVI | 10 | 11 | 26 |
| Sex | M | M | F |
| Underlying defect | Aortic stenosis | TOF | TGA/VSD/PS |
| | Ross procedure | | |
| RVOT substrate/diameter | Conduit/18-mm | Bioprosthesis 15-mm | Native |
| Primary lesion | Stenosis | Stenosis | Mixed |
| Indication of folded valve technique | Short RVOT | Bioprosthesis | Short RVOT |
| Basal RV-PA peak gradient | 49 | 40 | 48 |
| Postprocedural RV-PA peak gradient | 15 | 24 | 5 |
| Type of complication | IE | IE | Uncertain diagnosis |
| | MSF grade 1 | | Subacute thrombosis or valve degeneration |
| Delay PPVI to complication, mo | 24 | 4 | 24 |
| Complication features | <i>Streptococcus oralis</i> | <i>Kytococcus schroeteri</i> | Severe stenosis without IE nor MSF |
| | Portal of entry not found | No portal of entry | |
| | Valvular stenosis | Valvular stenosis | |
| Management | RVOT balloon dilatation | Surgical explant | Valve-in-valve |
| | Valve-in-valve | | |
| Outcome | Favorable | Favorable | Favorable |

IE indicates infective endocarditis; MSF, melody stent fracture; PA, pulmonary artery; PPVI, percutaneous pulmonary valvular implantation; RV, right ventricle; RVOT, right ventricular outflow tract; TGA/PS/VSD, transposition of the great arteries with pulmonary stenosis and ventricular septal defect; and TOF, Tetralogy of Fallot.

of the cusps, which must always be checked on the bench before implanting the valve. The excellent postimplantation performance of the folded valve were already observed in our preliminary work.¹⁰ This is further confirmed by the present article results, showing a favorable valvular function in the midterm, which is comparable to that observed in large series conducted with the Melody valve.^{17,18} Indeed, our series showed that valve-related reinterventions was 2.1% per person per year, whereas folded Melody valve function remained unchanged 44/47 patients at their last follow-up.

Valve-Related Complications and Reinterventions

The modification of the valve stent induced by the folding technique raised fears of potential increase in complications rates, especially about stent fractures or IE.

The modifications in stress distribution due to the folding of distal stents struts remain unclear as it has not been assessed in vitro. The results of these studies are not in favor of a stent integrity compromise and increased risk of MSF. In our series, only 1 patient presented stent fracture during follow-up. The impact of the latter on valve function was difficult to evaluate as this patient also had IE, which led to an obstruction of the valve. Furthermore, the rate of MSF in our series was not higher than the previously reported data, in which the MSF incidences ranged from 21% to 33% regardless to the type of RVOT substrate or presence of a presten.^{11,17–20} MSF-associated risk factors

were the presence of valve behind the chest wall or clearly compressed, while prestenting was shown to be the most important protective factor against fractures. Although our population is not strictly comparable to the previously cited studies, the very low incidence of stent fractures observed in this article suggests at least that Melody valve folding does not increase the risk of MSF.

Since the first articles which reported cases of severe IE following Melody valve implantation, multiple studies from various institutions have confirmed this important adverse outcome with an annualized incidence of 2.3% to 4%.^{17,21,22} The role of bovine jugular vein substrate, as well as other risk factors including age ≤ 12 years at implant or and high residual postimplant gradient ≥ 15 mmHg have been widely discussed.^{21–24} In our series, the IE annualized incidence was 1.4% per person per year (95% CI, 0.2%–3.3%). Similarly to MSF incidence, the rate of IE in our cohort seems in line with the previously reported data in larger series. Furthermore, the 2 patients who developed IE during follow-up had other well-recognized risk factors as they were males, young, and had a significant residual gradient following implantation (Table 3). Based on these observations, the folded Melody does not seem to have an increased risk of IE.

Folded Melody or Sapien Valve?

The Melody and Sapien devices are complementary as their design allows operators to cover a large range of

RVOT diameters (16–29 mm). In addition, the Sapien stent's length is shorter, ranging between 14.3 and 19.1 mm when expanded to 23 and 29 mm, respectively; while Melody varies between 28.8 and 24.6 mm when expanded to 18 and 22 mm, respectively. The folding modification of the Melody valve leads to a theoretical maximum reduction in stent's length of 7.9 mm. Therefore, a 22-mm folded Melody has a length of 16.7 mm, which is quiet similar to the 23-mm Sapien. Our technique was developed in 2012 to make more patients amenable to PPVI, at a time where the Sapien device was not widely available.¹⁰ This allowed for treating several patients with satisfactory results and favorable midterm outcome, as shown in this article. Since 2016, the SAPIEN XT valve received both CE marking and FDA approval for PPVI indications. The multicenter studies reporting results PPVI with Sapien showed encouraging results.^{5,25} Therefore, in situations where the folded Melody was used, the Sapien valve became an alternative option due to its design. Despite the absence of detrimental impact of folding a Melody, as demonstrated in this work, it seems safer to implant a nonmodified valve like the Sapien in selected cases. In the meantime, several patients in our cohort had small RVOT diameters (minimal size=14 mm) where a 23 mm Sapien could not be a good option. In such selected cases, if there is a need of a short valved stent, we are convinced that a folded Melody should be considered to perform a safe PPVI.

Limitations

Our work has several limitations because of its retrospective nature, which inherently makes it susceptible to certain biases. As expected in a multicenter work, with no standardized follow-up of the patients, some data were lacking or incompletely collected. However, the main end point data regarding delayed outcomes were available for 100% of our series. The other limitation of our work is the lack of control group to be compared with our folded Melody cohort. We have considered this option; however, this latter was not possible from a methodological point of view. A control group with nonfolded Melody valve would not have been comparable as the folded technique is precisely used when a conventional Melody valve implantation is not feasible. Another control group would have been composed by Sapien valve implantations in similar substrates, however, due to the recent approval of this device, the follow-up duration of this group would have been too short, and therefore, irrelevant in terms of mid-term outcomes evaluation.

Conclusions

The folded Melody valve is a safe technique allowing patients with complex RVOTs to benefit from PPVI. Although this modification raised fears of potential

increase in complication rates, our study showed favorable mid-term outcomes comparable with the usual Melody valve implantation procedure. The folded Melody continued to function well, with little progression of RVOT obstruction and excellent valve competence in the majority of patients, out to at least 6.5 years after implantation. Complications and reinterventions rates were low, making this technique relevant in selected patients.

ARTICLE INFORMATION

Received June 14, 2020; accepted December 17, 2020.

Affiliations

Bordeaux University Hospital (CHU), Department of Pediatric and Adult Congenital Cardiology, Pessac, France (Z.J., E.V., J.-B.T.). IHU Liryc, Electrophysiology and Heart Modeling Institute, Fondation Bordeaux Université, Pessac-Bordeaux, France (Z.J., E.V., X.P., J.-B.T.). INSERM, Centre de recherche Cardio-Thoracique de Bordeaux, U1045, France (Z.J., E.V., X.P., J.-B.T.). Department of Congenital and Pediatric Cardiology, Centre de Référence Malformations Cardiaques Congenitales Complexes–M3C, Necker Hospital for Sick Children, Assistance Publique des Hôpitaux de Paris, Pediatric Cardiology, France (S.M.-M.). Department of Pediatric Cardiology and Congenital Heart Disease, German Heart Center Munich at the TU Munich, Germany (A.E., S.G.). Department of Pediatric Cardiology, University Children's Hospital, Tuebingen, Germany (M.H., L.S.). Department of Pediatric Cardiology, University Hospitals Leuven, Belgium (M.G.). Department of Pediatric Cardiology and Congenital Heart Disease, AP-HM, Timone enfants, Hôpital de la Timone, Provence-Alpes-Côte d'Azur, France (C.O.). Cardiology Department, CHU Grenoble, France (H.B.). Cardiac Catheterization Laboratories, Sidra Heart Center, Sidra Medicine, Doha, Qatar (Y.B.).

Sources of Funding

Drs Jalal and Thambo were supported by the French Government as part of the "Investments of the future" program managed by the National Research Agency (ANR) (grant reference ANR-10-IAHU-04).

Disclosures

Drs Jalal, Eicken, Gewillig, and Thambo have a modest conflict of interest as expert witnesses for Medtronic, Inc. The other authors report no conflicts.

REFERENCES

- Bonhoeffer P, Boudjemline Y, Saïba Z, Merckx J, Aggoun Y, Bonnet D, Acar P, Le Bidois J, Sidi D, Kachaner J. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. *Lancet*. 2000;356:1403–1405. doi: 10.1016/S0140-6736(00)02844-0
- McElhinney DB, Hellenbrand WE, Zahn EM, Jones TK, Cheatham JP, Lock JE, Vincent JA. Short- and medium-term outcomes after transcatheter pulmonary valve placement in the expanded multicenter US melody valve trial. *Circulation*. 2010;122:507–516. doi: 10.1161/CIRCULATIONAHA.109.921692
- Aboulhosn J, Levi DS. Percutaneous pulmonary valve implantation: is earlier valve implantation better? *Circ Cardiovasc Interv*. 2015;8:e002260. doi: 10.1161/CIRCINTERVENTIONS.115.002260
- Jalal Z, Thambo JB, Boudjemline Y. The future of transcatheter pulmonary valvulotomy. *Arch Cardiovasc Dis*. 2014;107:635–642. doi: 10.1016/j.acvd.2014.07.046
- Plessis J, Hascoët S, Baruteau A, Godart F, Le Gloan L, Warin Fresse K, Tahhan N, Riou JY, Guyomarch B, Petit J et al. Edwards SAPIEN transcatheter pulmonary valve implantation: results from a French Registry. *JACC Cardiovasc Interv*. 2018;11:1909–1916. doi: 10.1016/j.jcin.2018.05.050.
- Berman DP, McElhinney DB, Vincent JA, Hellenbrand WE, Zahn EM. Feasibility and short-term outcomes of percutaneous transcatheter pulmonary valve replacement in small (<30 kg) children with dysfunctional right ventricular outflow tract conduits. *Circ Cardiovasc Interv*. 2014;7:142–148. doi: 10.1161/CIRCINTERVENTIONS.113.000881

7. Meadows JJ, Moore PM, Berman DP, Cheatham JP, Cheatham SL, Porras D, Gillespie MJ, Rome JJ, Zahn EM, McElhinney DB. Use and performance of the Melody transcatheter pulmonary valve in native and postsurgical, nonconduit right ventricular outflow tracts. *Circ Cardiovasc Interv.* 2014;7:374–380. doi: 10.1161/CIRCINTERVENTIONS.114.001225
8. Boudjemline Y. Percutaneous pulmonary valve implantation: what have we learned over the years? *EuroIntervention.* 2017;13:AA60–AA67. doi: 10.4244/EIJ-D-17-00501
9. Malekzadeh-Milani S, Patel M, Boudjemline Y. Folded Melody valve technique for complex right ventricular outflow tract. *EuroIntervention.* 2014;9:1237–1240. doi: 10.4244/EIJV9I10A207
10. Jalal Z, Malekzadeh-Milani S, Hofbeck M, Al Najashi K, Thambo JB, Boudjemline Y. A new percutaneous pulmonary valve implantation technique for complex right ventricular outflow tracts: the “folded melody valve”. *Catheter Cardiovasc Interv.* 2015;85:604–610. doi: 10.1002/ccd.25747
11. Nordmeyer J, Khambadkone S, Coats L, Schievano S, Lurz P, Parenzan G, Taylor AM, Lock JE, Bonhoeffer P. Anticipatory management strategies for stent fracture after percutaneous pulmonary valve implantation. *Circulation.* 2007;115:1392–1397. doi: 10.1161/CIRCULATIONAHA.106.674259
12. Priromprintr B, Silka MJ, Rhodes J, Batra AS. A prospective 5-year study of the frequency of arrhythmias during serial exercise testing and clinical follow-up after Melody valve implant. *Heart Rhythm.* 2016;13:2135–2141. doi: 10.1016/j.hrthm.2016.07.023
13. Nageotte SJ, Lee JW, El-Said HG, Moore JW, Ratnayaka K. Transcatheter electrosurgery rescue: jailed pulmonary artery following Melody pulmonary valve replacement. *JACC Cardiovasc Interv.* 2020;13:e21–e22. doi: 10.1016/j.jcin.2019.08.051
14. Gillespie MJ, Rome JJ, Levi DS, Williams RJ, Rhodes JF, Cheatham JP, Hellenbrand WE, Jones TK, Vincent JA, Zahn EM, et al. Melody valve implant within failed bioprosthetic valves in the pulmonary position: a multicenter experience. *Circ Cardiovasc Interv.* 2012;5:862–870. doi: 10.1161/CIRCINTERVENTIONS.112.972216
15. Pluchinotta FR, Piekarski BL, Milani V, Kretschmar O, Burch PT, Hakami L, Meyer DB, Jacques F, Ghez O, Trezzi M, et al. Surgical atrioventricular valve replacement with Melody valve in infants and children. *Circ Cardiovasc Interv.* 2018;11:e007145. doi: 10.1161/CIRCINTERVENTIONS.118.007145
16. Jalal Z, Seguela PE, Iriart X, Roubertie F, Quessard A, Kreitmann B, Thambo JB. Hybrid Melody valve implantation in mitral position in a child: usefulness of a 3-dimensional printed model for preprocedural planning. *Can J Cardiol.* 2018;34:812.e5–812.e7. doi: 10.1016/j.cjca.2018.02.011
17. Nordmeyer J, Ewert P, Gewillig M, AlJufan M, Carminati M, Kretschmar O, Uebing A, Dähnert I, Röhle R, Schneider H, et al. Acute and midterm outcomes of the post-approval MELODY Registry: a multicentre registry of transcatheter pulmonary valve implantation. *Eur Heart J.* 2019;40:2255–2264. doi: 10.1093/eurheartj/ehz201
18. Cheatham JP, Hellenbrand WE, Zahn EM, Jones TK, Berman DP, Vincent JA, McElhinney DB. Clinical and hemodynamic outcomes up to 7 years after transcatheter pulmonary valve replacement in the US melody valve investigational device exemption trial. *Circulation.* 2015;131:1960–1970. doi: 10.1161/CIRCULATIONAHA.114.013588
19. Cabalka AK, Hellenbrand WE, Eicken A, Kreutzer J, Gray RG, Bergersen L, Berger F, Armstrong AK, Cheatham JP, Zahn EM, et al. Relationships among conduit type, pre-stenting, and outcomes in patients undergoing transcatheter pulmonary valve replacement in the prospective North American and European Melody valve trials. *JACC Cardiovasc Interv.* 2017;10:1746–1759. doi: 10.1016/j.jcin.2017.05.022
20. McElhinney DB, Cheatham JP, Jones TK, Lock JE, Vincent JA, Zahn EM, Hellenbrand WE. Stent fracture, valve dysfunction, and right ventricular outflow tract reintervention after transcatheter pulmonary valve implantation: patient-related and procedural risk factors in the US Melody Valve Trial. *Circ Cardiovasc Interv.* 2011;4:602–614. doi: 10.1161/CIRCINTERVENTIONS.111.965616
21. McElhinney DB. Reflection and rationalization: making sense of the literature on endocarditis after transcatheter pulmonary valve replacement. *Circ Cardiovasc Interv.* 2017;10:e004983. doi: 10.1161/CIRCINTERVENTIONS.117.004983
22. Malekzadeh-Milani S, Houeijeh A, Jalal Z, Hascoet S, Bakloul M, Aldebert P, Piéchaud JF, Heitz F, Bouvaist H, Dauphin C, et al; French working group of Cardiac Catheterization in Congenital Heart Disease Patients. French national survey on infective endocarditis and the Melody™ valve in percutaneous pulmonary valve implantation. *Arch Cardiovasc Dis.* 2018;111:497–506. doi: 10.1016/j.acvd.2017.10.007
23. Jalal Z, Galmiche L, Lebeaux D, Villemain O, Brugada G, Patel M, Ghigo JM, Beloin C, Boudjemline Y. Selective propensity of bovine jugular vein material to bacterial adhesions: an in-vitro study. *Int J Cardiol.* 2015;198:201–205. doi: 10.1016/j.ijcard.2015.07.004
24. Sharma A, Cote AT, Hosking MCK, Harris KC. A systematic review of infective endocarditis in patients with bovine jugular vein valves compared with other valve types. *JACC Cardiovasc Interv.* 2017;10:1449–1458. doi: 10.1016/j.jcin.2017.04.025.
25. Kenny D, Rhodes JF, Fleming GA, Kar S, Zahn EM, Vincent J, Shirali GS, Gorelick J, Fogel MA, Fahey JT, et al. 3-year outcomes of the Edwards SAPIEN transcatheter heart valve for conduit failure in the pulmonary position from the COMPASSION multicenter clinical trial. *JACC Cardiovasc Interv.* 2018;11:1920–1929. doi: 10.1016/j.jcin.2018.06.001