

Original article

Pediatrics Spanish Registry of Percutaneous Melody Pulmonary Valve Implantation in Patients Younger Than 18 Years



Ruth Solana-Gracia,^{a,b,*} Fernando Rueda,^c Pedro Betrián,^d Federico Gutiérrez-Larraya,^e María Jesús del Cerro,^f Manuel Pan,^g Juan Alcívar,^h José Félix Coserria,ⁱ José Manuel Velasco,^j and José Luis Zunzunegui^{b,k}

^aUnidad de Cardiología Infantil, Hospital Universitario Infanta Leonor, Madrid, Spain

^bInstituto de Investigación Sanitaria Gregorio Marañón, Madrid, Spain

^cUnidad de Cardiología Infantil, Hospital Universitario A Coruña, A Coruña, Spain

^dServicio de Cardiología, Hospital Universitario Vall d'Hebron, Barcelona, Spain

^eServicio de Cardiología Infantil, Hospital Universitario La Paz, Madrid, Spain

^fServicio de Cardiología Infantil, Hospital Universitario Ramón y Cajal, Madrid, Spain

^gServicio de Cardiología, Hospital Universitario Reina Sofía, Córdoba, Spain

^hServicio de Cardiología, Hospital Universitario de Cruces, Bilbao, Vizcaya, Spain

ⁱServicio de Cardiología Infantil, Hospital Virgen del Rocío, Sevilla, Spain

^jInstituto Pediátrico del Corazón, Hospital Universitario 12 de Octubre, Madrid, Spain

^kUnidad de Cardiología Infantil, Hospital Universitario Gregorio Marañón, Madrid, Spain

Article history:

Received 19 April 2017

Accepted 6 July 2017

Available online 16 October 2017

Keywords:

Percutaneous valve implant

Congenital heart disease

Structural catheterization

Pediatrics

ABSTRACT

Introduction and objectives: A decade has passed since the first Spanish percutaneous pulmonary Melody valve implant (PPVI) in March 2007. Our objective was to analyze its results in terms of valvular function and possible mid-term follow-up complications.

Methods: Spanish retrospective descriptive multicenter analysis of Melody PPVI in patients < 18 years from the first implant in March 2007 until January 1, 2016.

Results: Nine centers were recruited with a total of 81 PPVI in 77 pediatric patients, whose median age and weight were 13.3 years (interquartile range [IQR], 9.9–15.4) and 46 kg (IQR, 27–63). The predominant cardiac malformation was tetralogy of Fallot (n = 27). Most of the valves were implanted on conduits, especially bovine xenografts (n = 31). The incidence of intraprocedure and acute complications was 6% and 8%, respectively (there were no periprocedural deaths). The median follow-up time was 2.4 years (IQR, 1.1–4.9). Infective endocarditis (IE) was diagnosed in 4 patients (5.6%), of which 3 required surgical valve explant. During follow-up, the IE-related mortality rate was 1.3%. At 5 years of follow-up, 80% ± 6.9% and 83% ± 6.1% of the patients were free from reintervention and pulmonary valve replacement.

Conclusions: Melody PPVI was safe and effective in pediatric patients with good short- and mid-term follow-up hemodynamic results. The incidence of IE during follow-up was relatively low but was still the main complication.

© 2017 Sociedad Española de Cardiología. Published by Elsevier España, S.L.U. All rights reserved.

Registro español de implante percutáneo de la válvula pulmonar Melody en menores de 18 años

RESUMEN

Introducción y objetivos: Pasada 1 década desde el primer implante percutáneo de la válvula pulmonar (IPVP) Melody en España, se exponen sus resultados en cuanto a la función valvular y las complicaciones a corto y medio plazo.

Métodos: Análisis descriptivo retrospectivo y multicéntrico nacional de los IPVP Melody en pacientes menores de 18 años desde el primer implante (de marzo de 2007 hasta el 1 de enero de 2016).

Resultados: Se reclutaron 9 hospitales que contaban un total de 81 IPVP en 77 pacientes, cuyas medianas [intervalo intercuartílico] de edad y peso eran 13,3 [9,9–15,4] años y 46 [27–63] kg respectivamente. La enfermedad cardíaca más frecuente fue la tetralogía de Fallot (n = 27) y el sustrato anatómico más común, el conducto valvulado de yugular bovina (n = 31). Las incidencias de complicaciones intraprocedimiento y agudas fueron del 6 y el 8% (no hubo muertes periprocedimiento). La mediana del tiempo de seguimiento fue 2,4 [1,1–4,9] años. Se diagnosticó endocarditis infecciosa (EI) a 4 pacientes (5,6%), de los que 3 precisaron el explante de la válvula. En el periodo de seguimiento, la mortalidad fue

Palabras clave:

Implante percutáneo de válvula

Cardiopatía congénita

Intervencionismo estructural

Pediatría

* Corresponding author: Unidad de Cardiología Infantil, Hospital Universitario Infanta Leonor, Avda. Gran Vía del Este 80, 28031 Madrid, Spain.

E-mail address: ruth.solana@salud.madrid.org (R. Solana-Gracia).

del 1,3%, relacionada con EI. A los 5 años de seguimiento, el $80 \pm 6,9\%$ y el $83 \pm 6,1\%$ de los pacientes estuvieron libres de reintervención y recambio valvular pulmonar respectivamente.

Conclusiones: El IPVP en pacientes pediátricos es una opción válida con buenos resultados hemodinámicos a corto y medio plazo. La incidencia de EI durante el seguimiento fue relativamente baja, si bien es la principal complicación que tener en cuenta.

© 2017 Sociedad Española de Cardiología. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

Abbreviations

IE: infectious endocarditis
PPVI: percutaneous pulmonary valve implantation
RV: right ventricle
RVOT: right ventricular outflow tract

INTRODUCTION

Advances in cardiac surgery, percutaneous catheterization, intensive care, and noninvasive imaging techniques have improved life expectancy and reduced the number of congenital heart disease-related reinterventions.¹ Accordingly, and due to the harmful effects of chronic dysfunction of the right ventricular (RV) pulmonary valve, the recent focus of clinical practice has been to shorten intervention times.²

Percutaneous pulmonary valve implantation (PPVI) was described for the first time in 2000.³ It is now fairly widely accepted and more than 10 000 such implants have thus far been performed worldwide. The characteristics of the valve and implant system are described in Figure 1. Various devices are currently in use but only the Melody valve (Medtronic; Minnesota, United States) had been approved by the relevant regulatory bodies (CE 9/2006 and FDA 01/2010) at the study start date.

The main aim of our study was to present the Spanish experience with Melody PPVIs in pediatric patients and, as a secondary objective, to evaluate its changes over time in terms of valve functioning and any short-to-mid-term complications.

METHODS

This study comprised a descriptive, retrospective, and multicenter analysis of the Melody PPVI in individuals younger than 18 years from March 2007 (date of the first implant in Spain) to January 1, 2016. The Cardiac Catheterization Working Group of the Spanish Society of Pediatric Cardiology and Congenital Heart Disease developed a questionnaire that was subsequently completed by all centers with pediatric PPVI experience. The study was performed in accordance with the Spanish Law on Data Protection 15/1999. Patient follow-up was completed on May 15, 2016.

Major complications were defined as those with clinical impact, those that endangered the patient's life, and those that required surgical or percutaneous treatment (eg, coronary compression, cardiac structure perforation, embolization of prosthetic material). All other complications were considered minor.⁴ Intraprocedural complications were events occurring from patient catheterization to transfer to intensive care; acute complications were those that occurred up to 72 hours afterward.

Statistical Analysis

Statistics/Data Analysis 13.1 (Stata, StataCorp LP, United States) was used for the statistical analysis. Normally distributed

quantitative variables are expressed as mean \pm standard deviation; those with a nonnormal distribution are expressed as median [interquartile range]. Nominal variables are expressed as numbers and percentages; the Student *t* test was used to compare differences between pre- and postimplantation means. The chi-square test, Wilcoxon test, and Mann-Whitney *U* test were used as required to compare categorical variables. All tests were 2-sided and a *P* value less than .05 was considered statistically significant. Analysis of event-free survival was performed using Kaplan-Meier curves. Factors associated with an event (reintervention/endocarditis) during follow-up were included in univariable Cox regression analysis and were considered significant at $P \leq .05$.

RESULTS

Since the first implant in Spain until January 1, 2016, a total of 173 Melody valves were implanted in 16 hospitals; of these, 81 were used for PPVI in 77 pediatric patients (Table 1). One patient underwent a double implantation because he had a double right ventricular outflow tract (RVOT) (conduit + native RVOT) and 3 patients required a second Melody valve (2 via the valve-in-valve technique and the other after explantation of the initial valve and surgical reconstruction of the RVOT).

To homogenize the data, the results of the 78 primary implantations (77 patients) were analyzed. Clinical descriptions of the patients and the procedure are provided in Table 2 and Table 3, respectively. The modern technique of pretesting² was used in all procedures, except for implantations performed for a dysfunctional surgical valve prosthesis (6 patients) or for the initial experiences (7 patients).

In terms of periprocedural complications, there were no incidences of coronary compression or death. The most serious intraprocedural complication was an iatrogenic aortopulmonary window in 1 patient undergoing Jatene surgery (11 years old, 66 kg), which was initially resolved using percutaneous implantation of an 11-mm muscular ventricular septal defect closure device with subsequent elective surgical closure of the residual shunt. The remainder of the complications were mild (Table 3) and were resolved with conservative treatment. In the first postimplantation hours, one 16-year-old patient with tetralogy of Fallot had transient angina not related to mechanical interference of the prosthesis with the origin of the coronary arteries (evaluated using computed tomography and angiography), but to systolic compression of the intramyocardial coronary segment of the anterior descending artery; the situation was resolved using beta-blocker therapy.

In total, because 3 patients moved to their area of origin (which was different from that of the implanting hospital), 75 patients completed follow-up. The median follow-up time was 2.4 [1.1–4.9] years. In the final follow-up echocardiography, the mean peak pulmonary valve gradient was 25.0 ± 26.5 mmHg, 3 patients (4%) had $>$ grade II pulmonary regurgitation, and 1 (1.3%) had mild perivalvular leak.

Thirteen patients required some type of reintervention: 8 balloon overdilations (3 without pretesting of the RVOT), 5 explantations (3 due to infectious endocarditis [IE] and 2 due to

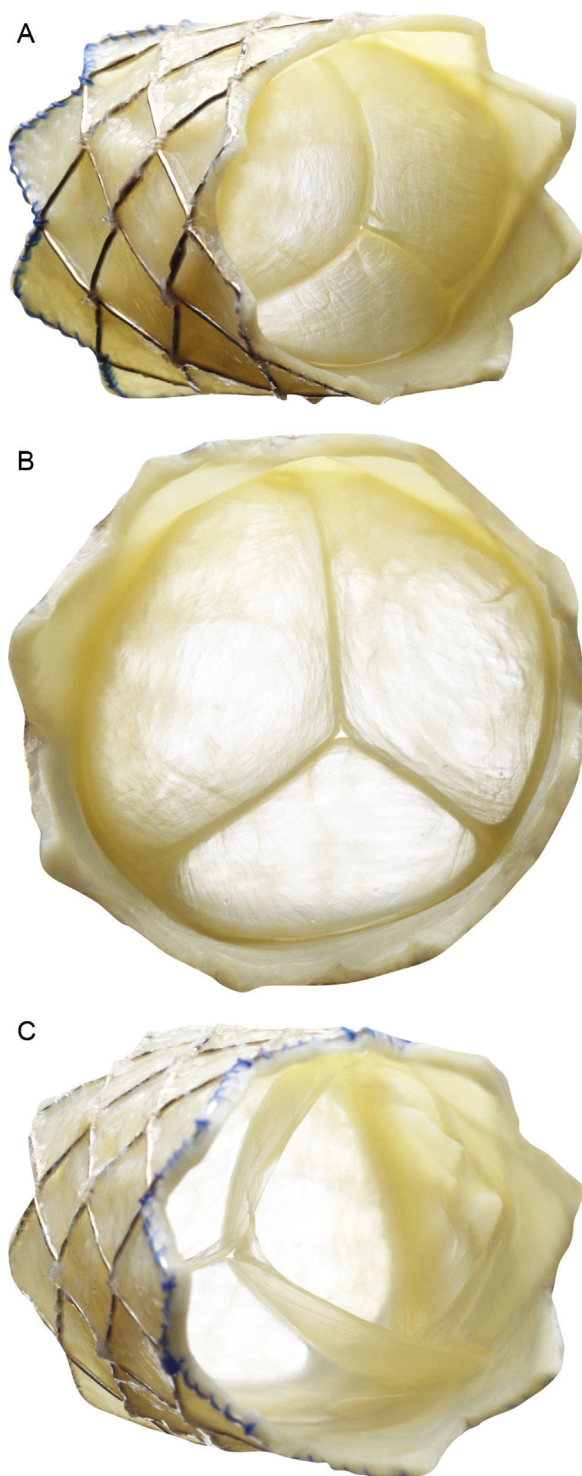


Figure 1. Description of the Melody percutaneous pulmonary valve (Medtronic Inc.; Minneapolis, Minnesota, United States). The valve consists of a 34-mm bare-metal platinum-iridium stent (CP stent, NuMED Inc.; Hopkinton, New York, United States) with a hand-sewn valved segment of bovine jugular vein. A: frontolateral view. B: frontal view. C: view from the distal end. The device is crimped over a balloon-in-balloon catheter and released via a long modified 22-Fr sheath (Ensemble Delivery System, Medtronic Inc.), available in external balloon diameters of 18, 20, and 22 mm. The balloon-in-balloon technique permits 2-step valve release and its repositioning once the lower-size balloon is inflated.

Table 1

List of National Hospitals With Experience in Melody Percutaneous Pulmonary Valve Implantation, in Order of Year of First Implantation

Hospital	First year	Implantations
Hospital Universitario Gregorio Marañón, Madrid	2007	38
Hospital Universitario Reina Sofía, Córdoba	2007	5
Hospital Universitario Vall d'Hebron, Barcelona	2008	10
Hospital Universitario La Paz, Madrid	2009	7
Hospital Universitario de Cruces, Bilbao	2011	5
Hospital Universitario Ramón y Cajal, Madrid	2012	6
Complejo Hospitalario Universitario A Coruña	2013	6
Hospital Universitario Virgen del Rocío, Sevilla	2013	3
Hospital Universitario 12 Octubre, Madrid	2014	1
Total		81

loss of stent integrity caused by fracture and/or sternal compression), and 2 valve-in-valve implantations (due to valve dysfunction secondary to fracture). Accordingly, $97\% \pm 2\%$, $95\% \pm 3\%$, and $80\% \pm 7\%$ of patients were reintervention-free (ie, balloon over-dilation, valve-in-valve implantation, or explantation) at 1, 2, and 5 years, respectively. There were no significant differences between patients in terms of weight (reference, 30 kg), anatomical substrate, or type of preimplantation RVOT lesion. The event-free survival times for the various events are shown in Figure 2. After 1, 2, and 5 years of follow-up, $97\% \pm 2\%$, $93\% \pm 3.5\%$, and $83\% \pm 6\%$ of patients were pulmonary valve replacement-free (percutaneous or surgical), respectively (Figure 3). There was 1 death (1.3%), related to IE.

There were 4 cases of IE (affecting 5.6% of the total population) (Table 4): 1 occurring at an early stage in a patient with a history of preimplant endocarditis with the same bacterium; 3 patients required surgical extraction of the valve, performed 9, 19, and 78 days after diagnosis (corresponding to 814, 418, and 178 days after implantation). At the 5-year follow-up, 92% of patients were disease-free, giving a mean IE incidence of 1.8% per patient-year.

DISCUSSION

The durability of surgical RVOT interventions for complex congenital heart diseases varies considerably according to patient age and the type of material used.^{5,6} One of the studies with the largest sample size reported a mean intervention-free survival of 11.2 years for adult-sized conduits (> 18 mm).⁷ Right ventricular outflow tract dysfunction occurs without warning over time due to diverse mechanisms: pulmonary regurgitation, somatic growth, stenotic anastomosis, valvular stenosis, conduit kinking, sternal compression, intimal proliferation, calcification, and aneurysmatic dilatation.⁸ Right ventricular outflow tract reconstruction can be performed with low mortality but can be associated with high morbidity, particularly given the need for surgical reinterventions. The strategy of choice for PPVI is to minimize reinterventions without compromising ventricular volume or function. The main controversial aspects are the time of RVOT valve placement and the choice between PPVI and surgery. Given the intrinsic complexity of congenital heart disease, due to its rarity and variability, no studies have directly compared PPVI with surgery, which is why descriptive multicenter studies are the main source of information available.

According to the 2010 European guidelines, in general, the following patients should be treated: symptomatic patients with a RV pressure > 60 mmHg and/or moderate/severe pulmonary regurgitation, asymptomatic patients with pulmonary stenosis or severe pulmonary regurgitation with impaired exercise capacity or progressive dilation or systolic dysfunction of the RV, progressive

Table 2

Characteristics of the 78 Percutaneous Pulmonary Valve Implantations in 77 Patients Younger Than 18 Years

Clinical characteristics		Type of heart disease		Anatomical substrate	
Age, y	13.3 [9.9–15.4]	Tetralogy of Fallot	27 (35)	Contegra	31 (40)
Weight, kg*	46 [27–63]	PA + VSD	14 (18)	Homograft	18 (23)
Men	46 (59)	AoS (Ross)	8 (10)	Native RVOT	16 (21)
NYHA functional class		TGA + PS	7 (9)	Su prosthesis	7 (9)
I	40 (51)	Double outlet RV	6 (8)	Labcor	4 (5)
II	32 (41)	PA with intact septum	6 (8)	Others	2 (2.5)
III	6 (8)	Truncus arteriosus	5 (6)		
No. of previous operations		TGA (Jatene)	3 (4)		
1	28 (36)	Others	2 (3)		
2	24 (31)				
≥ 3	26 (33)				
Type of RVOT lesion					
Mixed	40 (51)				
PS	22 (28)				
PR	16 (21)				

AoS, aortic stenosis; NYHA, New York Heart Association; PA, pulmonary atresia; PR, pulmonary regurgitation; PS, pulmonary stenosis; RV, right ventricle; RVOT, right ventricular outflow tract; Su, surgical; TGA, transposition of the great arteries; VSD, ventricular septal defect.

Data are expressed as No. (%) or median [interquartile range].

* 22 patients (28%) weighed less than 30 kg; mean, 22 (range, 12–29.5) kg.

tricuspid regurgitation, pulmonary gradient > 80 mmHg, or sustained atrial or ventricular tachycardias.⁹ In 2011, the American Heart Association recommended (IIa B) that PPVI be considered in patients with a conduit between the RV and the pulmonary artery with moderate/severe pulmonary stenosis or pulmonary regurgitation, according to the inclusion/exclusion criteria of each valve.¹⁰

Several countries have now published national prospective registries of the Melody PPVI, with excellent short- and mid-term results (Table 5).^{4,11–15} The procedure has been considered successful (Melody implanted in the desired location, mild or minor residual pulmonary regurgitation, an RV-pulmonary artery gradient < 35 mmHg, absence of explantation 24 hours after the procedure)¹⁶ in 93% to 99% of cases.^{4,14,17} As in our study, there was

a significant reduction in the RV/aorta pressure ratio^{4,12–15} and a general improvement in hemodynamic parameters¹⁷ and New York Heart Association functional class.^{13,14,16} However, our series is the first to specifically analyze the results obtained in a pediatric population, including those weighing less than 20 to 30 kg and with various anatomical substrates for the implant.

The overall reported rate of periprocedural complications is about 6% with a 2.7% rate of major complications (conduit rupture, pulmonary artery perforation, tricuspid valve injury, valve dislodgement, coronary artery compression, or pulmonary artery obstruction) and a 11.9% rate of minor complications.¹⁶ Our series shows rates of acute major complications of 2.6% (n = 2, aortopulmonary window and tricuspid valve injury) and of minor

Table 3

Procedure Characteristics of 78 Primary Percutaneous Pulmonary Valve Implantations

Procedure characteristics (general anesthesia with assisted ventilation)		Intraprocedural complications (n = 5; 6.4%)		Acute complications (n = 6; 8%)	
Prestenting	65 (83.3)	2	Mild ETT bleeding	2	Nonsustained VT
Two-step approach	10 (15.4)	1	SVT	1	Femoral thrombosis
Difference between them (mo)	7.9 ± 7.1	1	Moderate iatrogenic TR	1	Pulmonary edema
Ensemble size		1	Aortopulmonary window	1	Mild pneumothorax
18 mm	12 (15.4)			1	Angina (systolic compression of intramyocardial AD segment)
20 mm	29 (37.2)				
22 mm	37 (47.4)				
RV/aorta pressure*					
Before	0.70 ± 0.23				
After	0.43 ± 0.13				
RV-PA gradient (mmHg) after	10 ± 14.8				
Residual PR	1 (1.3)				
Residual leak	1 (1.3)				
Hospitalization ≤ 3 d	58 (77)				
NYHA after*					
I	62 (83)				
II	13 (17)				

AD, anterior descending coronary artery; ETT, endotracheal tube; NYHA, New York Heart Association; PA, pulmonary artery; PR, pulmonary regurgitation; RV, right ventricle; SVT, supraventricular tachycardia; TR, tricuspid regurgitation; VT, ventricular tachycardia.

Values represent No. (%) or mean ± standard deviation.

* $P < .01$ vs the situation before the percutaneous pulmonary valve implantation.

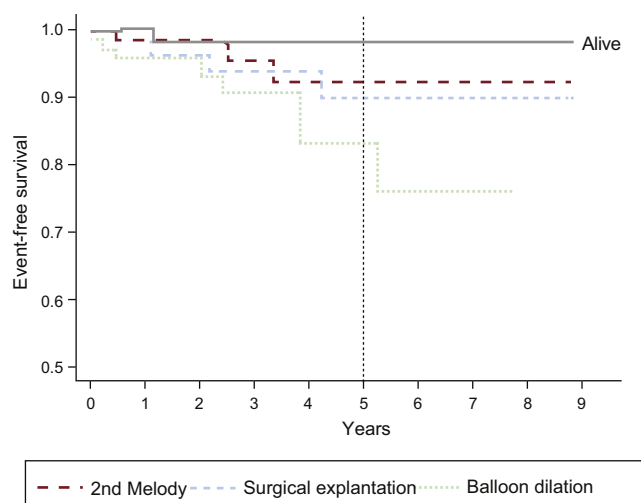


Figure 2. Kaplan-Meier event-free survival curve. At 5 years (mean \pm standard error), 98% \pm 1.8% of patients were still alive, 93% \pm 4.2% were second Melody percutaneous pulmonary valve implantation-free, 88% \pm 5.6% were explantation-free, and 86% \pm 5.8% were balloon catheter overdilation-free.

complications of 3.8%. Prediction of coronary compression risk is one of the most difficult steps in the procedure and this complication is the event most frequently associated with death in the catheterization laboratory. An estimated 5% to 6% of all possible PPVI candidates have coronary anatomy that is susceptible to compression during implantation.^{4,11} Additionally, there is greater risk of RVOT rupture/tear in highly calcified conduits and homografts.¹⁸ Fortunately, none of these events occurred in our patients.

During the short- and mid-term follow-up, the overall mortality ranged from 0% to 5% and it was generally not related to the device,¹⁶ except in severe cases of IE. The most frequent cause of percutaneous or surgical reintervention was reestenosis of the valve stent, caused by late recoil or by loss of radial force secondary to fracture.¹⁶ The risk factors for the development of fractures are younger age, a significant pre- and postprocedural RV-pulmonary artery gradient, lower conduit diameter on angiography, stent recoil or graft compression, and valve position directly under the sternum.^{19,20} Hence, the importance of RVOT conditioning with pretesting before the implantation. The development of significant pulmonary regurgitation due to injury to the valve cusps is a rare condition typically associated with IE.^{21,22} Generally, the valve dysfunction- or reintervention-free survival exceeds 90%, 80%, and 70% at 1, 2, and 4 years, respectively,^{14,19,23} as seen in our study. Specifically, the US Investigational Device Exemption Trial reported 5-year reintervention- and explantation-free survivals of 76% \pm 4% and 92% \pm 3%, respectively. The factors associated with reintervention are a high residual gradient (mean gradient $>$ 25 mmHg)^{13,23} or stent

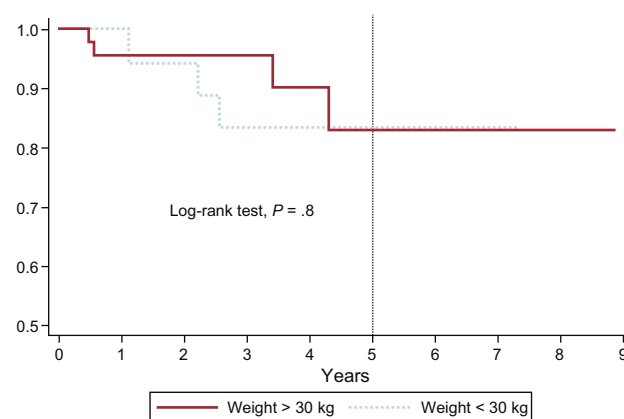


Figure 3. Pulmonary valve replacement-free survival curve (percutaneous or surgical) in patients weighing more than 30 kg and less than 30 kg. At 1, 2, and 5 years of follow-up, there was no need for valve replacement in a mean \pm standard error of 100%, 95% \pm 0.05%, and 84% \pm 0.09% in patients weighing less than 30 kg vs 96% \pm 0.03%, 96% \pm 0.03%, and 83% \pm 0.09% in those weighing more than 30 kg. Differences were not statistically significant.

compression/recoil immediately after valve release.¹⁸ On the other hand, protective factors are pretesting,^{13,18} which stabilizes the RVOT, and operator experience.²³ Pretesting can be performed in the same procedure or 2 or 3 months beforehand to allow endothelial growth and better stent fixation.²⁴ Retrospective analysis of a national surgical pulmonary valve implantation series²⁵ showed a 5-year replacement-free survival due to prosthesis dysfunction in patients younger than 20 years of about 90% (although our series includes the initial experience with PPVI without pretesting for RVOT conditioning in 7 patients).

The mid-term risk of IE has been estimated at 2.4% per patient-year,²¹ although more than half of infections do not directly affect the valve cusps and most respond to antibiotic therapy. Regardless, IE is the main cause of surgical explantation and death due to sepsis.^{4,11,21} The possible pathophysiological mechanisms involved include turbulence caused by high residual gradient, in situ thrombosis, and poor adherence to prophylactic antibiotics.^{4,26} This risk is not exclusive to PPVI; an example is given by the series of Oliver et al.,²⁵ with a postoperative IE incidence of 11.5% during a median follow-up of 7 years. Bovine jugular tissue is generally associated with greater infectious risk than other biological or synthetic prosthetic material.^{27,28} A recent in vitro study reported that its manipulation during percutaneous procedures can cause histological changes and microfractures.²⁹ Accordingly, these patients should be treated with lifelong antiplatelet therapy with aspirin and undergo a dental evaluation before the PPVI. Our series showed an IE incidence slightly lower than that seen in the literature, undoubtedly related to the lower weight of our patients (fewer dental and dermatologic problems) and because 19% of the native RVOTs were conduit-free.

Table 4
Description of Patients Diagnosed With Infectious Endocarditis

Bacteria	Diagnosis after implantation, d	Patients' Characteristics					Explantation
		Weight, kg	Sex	Substrate	Pretest	Residual gradient after (mmHg)	
<i>Streptococcus epidermidis</i>	100	58	M	Homograft	No	0	Yes
<i>Haemophilus influenzae</i> *	805	27	W	Homograft	Yes	10	Yes
<i>S. viridans</i>	959	27	W	Homograft	Yes	5	No
<i>S. mitis</i>	399	18	M	Contegra	Yes	0	Yes
		<i>P</i> = .25	<i>P</i> = .74	<i>P</i> = .52	<i>P</i> = .56	<i>P</i> = .99	

M, man; W, woman.

* Only patient of the 4 patients with endocarditis confirmed to have discontinued antiplatelet therapy 6 months after the implantation.

Table 5
 Characteristics of the Main Registries of Melody Percutaneous Pulmonary Valve Implantation: Prospective and Multicenter Observational Studies

Publication	Patients, n	Age, y	Weight, kg	Fallot/PA + VSD	RVOT lesion indication	RV-PA conduit	Prevalence	Follow-up time	Hospitalization time, d	Complications	Death	Endocarditis	Explantation	Balloon dilatation	Valve-in-valve
2011, Germany Eicken et al. ¹¹	102	21.5 [16.2-30.1]	63 [54.2-75.9]	61 (60)	Not described	100% (79% homograft)	96 (94)	352 [99-390] d	2	2 major (2%) 1 LCA compression 1 transient complete AVB	1 (1%)	1 (1) <i>Staphylococcus aureus</i>	1 (1)	8 (7.8)	4 (3.4)
2013, Italy Butera et al. ⁴	63 (implantations, 61)	24 [11-65]	60 [30-140]	39 (62)	30 Mixed 21 PS 12 PR	100% (33% homograft, 28% bioprosthesis)	53 (87)	2.4 y	5 [3-45]	9 major + minor (14%) 1 valve embolization 1 VF 3 vascular access 1 mild ETT bleeding 2 transfusions 1 conduit tear	4 (6.5%)	2 (3.3) <i>Staphylococcus aureus</i>	2 (3.3)	Not described	2 (3.3)
2014, France Fraisie et al. ¹²	64	21.4 [10.5-77.3]	Not described > 25 kg	32 (50)	67% Mixed 21.9% PS 12.9% PR	100% (subtypes not described)	62 (97)	4.6 [0.2-5.2] y	3 [2-5]	Minor (17%) 7 homograft tears 1 ETT bleeding 1 false femoral artery aneurysm 1 inguinal hematoma 1 transfusion for access site bleeding	3 (4.5%) 2 IE 1 CHF	4 (6.3) <i>Staphylococcus epidermidis</i> <i>Streptococcus sanguinis</i> <i>Staphylococcus haemolyticus</i>	3 (4.7)	Not described	0
2015, United States Cheatham et al. ¹³ (2010, McElhinney et al., ¹⁴ Zahn et al. ¹⁵)	150 (implantations, 136)	19 [7-53]	Not described > 25 kg	77 (51)	80 (53) PR 39 (26) PS 31 (21) Mixed	100% (74% homograft, 21% bioprosthesis)	49 (36)	4.5 [0.4-7] y	1-7	8 major + minor (6%) 1 conduit rupture 1 coronary artery dissection 1 conduit tear 1 SVT (cardioversion) 1 hypercapnia 1 femoral thrombosis 2 guidewire perforations of lobar artery	5 (3.7)	14 (10.3) (unknown)	11 (8.1)	6 (4.4)	20 (14.7)

AVB, atrioventricular block; CHF, congestive heart failure; ETT, endotracheal tube; IE, infectious endocarditis; LCA, left coronary artery; PA, pulmonary artery; PR, pulmonary regurgitation; PS, pulmonary stenosis; RV, right ventricle; RVOT, right ventricular outflow tract; SVT, sustained ventricular tachycardia; VF, ventricular fibrillation; VSD, ventricular septal defect.
 Unless otherwise indicated, the data represent No. (%) or median [interquartile range].

Resolution of RVOT dysfunction via PPVI has also been associated with reverse remodeling of the RV,^{11,12,14,30} better left ventricular filling,³⁰ and even improved tricuspid regurgitation.³¹

Percutaneous pulmonary valve implantation also modifies the ventricular electrophysiological substrate³² and, in the acute postimplantation period, new arrhythmias develop in 7% to 15% of patients, generally extrasystole or nonsustained ventricular tachycardia.^{32,33} Such arrhythmias are considered transient phenomena that spontaneously resolve, generally in the first 6 months, particularly in smaller patients and those requiring conservative treatment (and beta-blockers should be tried). Another possibly associated mechanism would be placement of the endoprosthesis so that it touches the RVOT muscle. In our series, 2.6% of patients had episodes of nonsustained ventricular tachycardia during the acute postprocedural period; these patients were treated with beta-blockers for 12 to 18 months and had a favorable course.

As mentioned above, PPVI is officially approved for patients weighing more than 30 kg with dysfunctional surgical RVOT conduits with diameters of 18 to 22 mm for Melody valves and 23 to 26 mm for SAPIEN valves (Edwards Lifescience LLC; California, United States). However, it is estimated that just 20% of patients with congenital heart disease and RVOT dysfunction meet these criteria. Thus, most patients would be candidates for off-label PPVI.² In our series, such patients comprised 47.4% (37 of 78), due to placement in a different anatomical substrate of the conduit (n = 23) and/or due to weight < 30 kg (n = 22).

Few articles discuss PPVI in patients younger than 5 years, given that the technique is limited by the high profile of the sheath (22–24 Fr). Good short-term hemodynamic results were obtained in a series of 25 patients published in 2010 (median age, 8 years; median weight, 21.4 kg).³⁴ The incidence of major complications was 16% but the only complication associated with lower weight was abdominal hematoma development. Thus, femoral venography is recommended if access is obtained at this site, as well as use of jugular access for patients weighing less than 20 kg, to obtain a favorable RV curvature and to not overdilate the conduit more than 110% of the initial size. During a median follow-up of 16 months in 22 patients, there was 1 surgical conduit replacement, 2 fractures treated with valve-in-valve PPVI, and 2 cases of endocarditis. Other authors theorize that younger patients benefit most from the hemodynamic effects of PPVI in terms of reverse remodeling of the RV and maximal oxygen consumption.³⁵

In addition, various studies have shown good hemodynamic results for the Melody PPVI over native or patch-extended RVOT^{36,37} and over surgical bioprosthetic valves.³⁸ In the case of the latter, the 2-year reintervention-free survival was higher than 90% and there were no procedure-related deaths.

Good results have also been obtained after implantation of a second Melody valve by the valve-in-valve technique, as long as there were no external obstacles impeding correct valve expansion (eg, sternal compression).³⁹

CONCLUSIONS

The results of Melody PPVI in pediatric patients in Spain show that it is a viable, successful, and safe technique, even in those weighing less than 30 kg or with native RVOT. The short- and mid-term hemodynamic results are excellent and there is low morbidity and mortality. The incidence of IE was relatively low, possibly related to the younger age and absence of conduits in many of our patients. We consider our work to be a gateway to new prospective studies involving interhospital collaboration that include adult patients and shed light on the ventricular remodeling data and life expectancy of these patients.

ACKNOWLEDGMENTS

Cardiac Catheterization Working Group of the Spanish Society of Pediatric Cardiology and Congenital Heart Disease.

CONFLICTS OF INTEREST

J.L. Zunzunegui is a proctor for the Medtronic percutaneous pulmonary valve implant.

WHAT IS KNOWN ABOUT THE TOPIC?

- The classic treatment strategy for RVOT dysfunction, established 4 decades ago, has been interposition of surgical prosthetic material between the ventricle and pulmonary artery. During their clinical course, the treated patients required frequent surgical replacements due to growth and degeneration of this material over time. Subsequent advances with the arrival of percutaneous treatment have progressed from high-pressure balloon angioplasty and stent placement to PPVI. Numerous studies now show that PPVI is viable and achieves excellent results.

WHAT DOES THIS STUDY ADD?

- Our study shows the national experience with the Melody PPVI in pediatric patients, focusing on valve functioning during follow-up and the possible development of complications, particularly endocarditis.

REFERENCES

- Prieto R, Yotti R, Ávila P, Álvarez T, Gil-Jaurena JM, Fernández-Avilés F. Selección de lo mejor del año 2016 en cardiopatías congénitas. *Rev Esp Cardiol*. 2017;70:299–300.
- Ansari MM, Cardoso R, Garcia D, et al. Percutaneous pulmonary valve Implantation. Present status and evolving future. *J Am Coll Cardiol*. 2015;66:2246–2255.
- Bonhoeffer P, Boudjemline Y, Saliba Z, et al. Percutaneous replacement of pulmonary valve in a right-ventricle to pulmonary-artery prosthetic conduit with valve dysfunction. *Lancet*. 2000;356:1403–1405.
- Butera G, Milanese O, Spadoni I, et al. Melody transcatheter pulmonary valve implantation. Results from the registry of the Italian Society of Pediatric Cardiology. *Catheter Cardiovasc Interv*. 2013;81:310–316.
- Yuan SM, Mishaly D, Shinfeld A, Raanani E. Right ventricular outflow tract reconstruction: valved conduit of choice and clinical outcomes. *J Cardiovasc Med (Hagerstown)*. 2008;9:327–337.
- Oosterhof T, Meijboom FJ, Vliegen HW, et al. Long-term follow-up of homograft function after pulmonary valve replacement in patients with tetralogy of Fallot. *Eur Heart J*. 2006;27:1478–1484.
- Homann M, Haehnel JC, Mendler N, et al. Reconstruction of the RVOT with valved biological conduits: 25 years' experience with allografts and xenografts. *Eur J Cardiothorac Surg*. 2000;17:624–630.
- Wells WJ, Arroyo Jr H, Bremner RM, Wood J, Starnes VA. Homograft conduit failure in infants is not due to somatic outgrowth. *J Thorac Cardiovasc Surg*. 2002;124:88–96.
- Baumgartner H, Bonhoeffer P, De Groot NM, et al. ESC guidelines for the management of grown-up congenital heart disease. *Eur Heart J*. 2010;31:2915–2957.
- Feltes TF, Bacha E, Beekman 3rd RH, et al. American Heart Association Congenital Cardiac Defects Committee of the Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; Council on Cardiovascular Radiology and Intervention; American Heart Association. Indications for cardiac catheterization and intervention in pediatric cardiac disease: a scientific statement from the American Heart Association. *Circulation*. 2011;123:2607–2652.
- Eicken A, Ewert P, Hager A, et al. Percutaneous pulmonary valve implantation: two-centre experience with more than 100 patients. *Eur Heart J*. 2011;32:1260–1265.

12. Fraisse A, Aldebert P, Malekzadeh-Milani S, et al. Melody transcatheter pulmonary valve implantation: results from a French registry. *Arch Cardiovasc Dis.* 2014;107:607–614.
13. Cheatham JP, Hellenbrand WE, Zahn EM, et al. 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.
14. McElhinney DB, Hellenbrand WE, Zahn EM, et al. Short- and medium-term outcomes after transcatheter pulmonary valve placement in the expanded multicenter US Melody valve trial. *Circulation.* 2010;122:507–516.
15. Zahn EM, Hellenbrand WE, Lock JE, McElhinney DB. Implantation of the Melody transcatheter pulmonary valve in patients with a dysfunctional right ventricular outflow tract conduit: early results from the U.S. clinical trial. *J Am Coll Cardiol.* 2009;54:1722–1729.
16. Armstrong AK, Balzer DT, Cabalka AK, et al. One-year follow-up of the Melody transcatheter pulmonary valve multicenter post-approval study. *J Am Coll Cardiol Interv.* 2014;7:1254–1262.
17. Wagner R, Daehnert I, Lurz P. Percutaneous pulmonary and tricuspid valve implantations: an update. *World J Cardiol.* 2015;7:167–177.
18. Boudjemline Y, Malekzadeh-Milani S, Patel M, et al. Predictors and outcomes of right ventricular outflow tract conduit rupture during percutaneous pulmonary valve implantation: a multicenter study. *EuroIntervention.* 2016;11:1053–1062.
19. McElhinney DB, Cheatham JP, Jones TK, et al. 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.
20. Nordmeyer J, Khambadkone S, Coats L, et al. Risk stratification, systematic classification, and anticipatory management strategies for stent fracture after percutaneous pulmonary valve implantation. *Circulation.* 2007;115:1392–1397.
21. McElhinney DB, Benson LN, Eicken A, et al. Infective endocarditis after transcatheter pulmonary valve replacement using the Melody valve: combined results of 3 prospective North American and European studies. *Circ Cardiovasc Interv.* 2013;6:292–300.
22. Buber J, Bergersen L, Lock JE, et al. Bloodstream infections occurring in patients with percutaneously implanted bioprosthetic pulmonary valve: a single-center experience. *Circ Cardiovasc Interv.* 2013;6:301–310.
23. Lurz P, Coats L, Khambadkone S, et al. Percutaneous pulmonary valve implantation: impact of evolving technology and learning curve on clinical outcome. *Circulation.* 2008;117:1964–1972.
24. Boshoff DE, Cools BL, Heying R, et al. Off-label use of percutaneous pulmonary valved stents in the right ventricular outflow tract: time to rewrite the label? *Catheter Cardiovasc Interv.* 2013;81:987–995.
25. Oliver JM, Garcia-Hamilton D, González AE, et al. Risk factors for prosthetic pulmonary valve failure in patients with congenital heart disease. *Am J Cardiol.* 2015;116:1252–1256.
26. Patel M, Iserin L, Bonnet D, Boudjemline Y. Atypical malignant late infective endocarditis of Melody valve. *J Thorac Cardiovasc Surg.* 2012;143:e32–e35.
27. Van Dijk I, Budts W, Cools B, et al. Infective endocarditis of a transcatheter pulmonary valve in comparison with surgical implants. *Heart.* 2015;101:788–793.
28. Jalal Z, Galmiche L, Lebeaux D, et al. Selective propensity of bovine jugular vein material to bacterial adhesions: An in-vitro study. *Int J Cardiol.* 2015;198:201–205.
29. Jalal Z, Galmiche L, Beloin C, Boudjemline Y. Impact of percutaneous pulmonary valve implantation procedural steps on leaflets histology and mechanical behaviour: An in vitro study. *Arch Cardiovasc Dis.* 2016;109:465–475.
30. Secchi F, Resta EC, Cannao PM, et al. Four-year cardiac magnetic resonance (CMR) follow-up of patients treated with percutaneous pulmonary valve stent implantation. *Eur Radiol.* 2015;25:3606–3613.
31. Jones TK, Rome JJ, Armstrong AK, et al. Transcatheter pulmonary valve replacement reduces tricuspid regurgitation in patients with right ventricular volume/pressure overload. *J Am Coll Cardiol.* 2016;68:1525–1535.
32. Nguyen HH, Shahnavaz S, Van Hare GF, Balzer DT, Nicolas R, Avari Silva JN. Percutaneous pulmonary valve implantation alters electrophysiologic substrate. *J Am Heart Assoc.* 2016;5:e004325.
33. Loar RW, Qureshi AM, Miyake CY, Valdes SO, Kim JJ, De la Uz CM. Percutaneous pulmonary valve implantation-associated ventricular tachycardia in congenital heart disease. *J Interv Cardiol.* 2016;29:639–645.
34. 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.
35. Borik S, Crean A, Horlick E, et al. Percutaneous pulmonary valve implantation: 5 years of follow-up: does age influence outcomes? *Circ Cardiovasc Interv.* 2015;8:e001745.
36. Boshoff DE, Cools BL, Heying R, et al. Off-label use of percutaneous pulmonary valved stents in the right ventricular outflow tract: time to rewrite the label? *Catheter Cardiovasc Interv.* 2013;81:987–995.
37. Meadows JJ, Moore PM, Berman DP, et al. 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.
38. Gillespie MJ, Rome JJ, Levi DS, et al. Melody valve implant within failed bioprosthetic valves in the pulmonary position: a multicenter experience. *Circ Cardiovasc Interv.* 2012;5:862–870.
39. Nordmeyer J, Coats L, Lurz P, et al. Percutaneous pulmonary valve-in-valve implantation: a successful treatment concept for early device failure. *Eur Heart J.* 2008;29:810–815.