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Original Article

Transcatheter Mitral Valve-in-Valve Implantation in Pediatric Patients

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ABSTRACT

Background: Transcatheter implantation of the Edwards Sapien 3 valve (Edwards Lifesciences, Irvine CA) within the bioprosthetic mitral valve (MV) is an established method of treatment in adults. However, it has not been well studied in the pediatric age group.

Methods: Transcatheter mitral valve-in-valve implantation was attempted in 4 symptomatic pediatric patients with a dysfunctional MV bioprosthesis implanted at an earlier stage due to severe MV stenosis or regurgitation. We reviewed our experience with MV implantation in this cohort.

Results: The mean age and weight of the patients at the time of the procedure were 11.4 years (range: 10-14 years) and 36 kg (range: 31-44 kg), respectively. The transmitral mean gradient dropped from a mean of 19.75 mm Hg (range: 15-22 mm Hg) to a mean of 1 mm Hg (range: 0-3 mm Hg) after the procedure. The mean fluoroscopy time

RÉSUMÉ

Introduction : L'implantation de la prothèse valvulaire Edwards Sapien 3 (Edwards Lifesciences, Irvine, CA) par cathéter dans la bioprothèse valvulaire mitrale (VM) est une méthode de traitement établie chez les adultes. Toutefois, cette méthode n'a pas fait l'objet d'études approfondies auprès d'enfants.

Méthodes : Une tentative d'implantation valvulaire mitrale de type *valve-in-valve* par cathéter a été réalisée chez quatre enfants symptomatiques qui avaient une bioprothèse VM dysfonctionnelle implantée antérieurement en raison d'une sténose VM ou d'une régurgitation grave. Nous avons passé en revue notre expérience d'implantation VM auprès de cette cohorte.

Résultats : L'âge et le poids moyens des patients au moment de l'intervention étaient respectivement de 11,4 ans (étendue : 10-14 ans) et de 36 kg (étendue : 31-44 kg). La moyenne du gradient moyen

It is well known that redo mitral valve (MV) surgeries are associated with unique clinical and technical difficulties in the pediatric age group.[1] Potential challenges of MV replacement (MVR) in this cohort include small size of the valve annulus, left atrium, and left ventricle, compared with that of the available prosthesis, with a potential risk for leaflet entrapment, left ventricular outflow tract obstruction (LVOTO), and conduction block.[2] Late complications of bioprosthetic and mechanical valves include morbidity associated with long-term anticoagulation, noncompliance with medications, lifestyle limitations, and an ongoing risk of endocarditis and arrhythmias.[3] Moreover, spontaneous valve degeneration is substantially higher in a cohort of young patients characterized by an overactive immune system. The degeneration rate of bioprosthetic valves at 10 years is almost 50% in patients below 35 years of age, compared with 10% in patients aged above 70 years, probably owing to age-related changes in immune function.[3] Furthermore, bioprostheses in the MV position exhibit higher spontaneous valve degeneration than aortic bioprostheses, owing to hemodynamic stress.[4,5] Children usually have a higher immuno-inflammatory initiated

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Ethics Statement: The institutional review board of the Prince Sultan Cardiac Centre (PSCC-R20034) approved the study, and it was conducted in accordance with the Declaration of Helsinki.

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was 55.25 minutes (range: 40-72 minutes), and the mean hospital length of stay was 4 days (range: 3-7 days). The patients' functional class improved from New York Heart Association class IV to class I during the follow-up period.

Conclusions: Transcatheter mitral valve-in-valve implantation can be performed safely for dysfunctional bioprosthetic MVs in the pediatric age group with favorable early and midterm outcomes. This procedure offers a viable alternative in patients who have high surgical risk or are deemed unfit for conventional surgery. However, we still recommend a long-term study of this approach in a large cohort, multicentre study.

transmitral a baissé. Elle est passée de 19,75 mmHg (étendue : 15-22 mmHg) à 1 mmHg (étendue : 0-3 mmHg) après l'intervention. La durée moyenne de la fluoroscopie était de 55,25 minutes (étendue : 40-72 minutes), et la durée moyenne du séjour à l'hôpital était de quatre jours (fourchette : 3-7 jours). La classification fonctionnelle des patients selon la New York Heart Association a montré une baisse. Les patients sont passés de la classe IV à la classe I durant la période de suivi.

Conclusions : L'implantation valvulaire mitrale de type *valve-in-valve* par cathéter peut être pratiquée de façon sûre chez les enfants porteurs d'une bioprothèse VM dysfonctionnelle dont les issues à court ou à moyen terme sont favorables. Cette intervention est une alternative viable pour ces patients dont le risque lié à l'intervention chirurgicale est élevé ou considérés inaptes à subir une intervention chirurgicale traditionnelle. Toutefois, nous recommandons encore une étude à long terme sur cette approche, voire une vaste étude multicentrique de cohorte.

process against the bioprosthetic valves, leading to earlier than usual valve degeneration.[6] In addition to that, failure of the fixed-size stented prostheses to match the growing MV annulus leads to inflow obstruction requiring frequent MV reoperation. [7-9] Although evidence indicates that clinical outcomes following MVR have improved due to the vast improvement in surgical techniques, the Society of Thoracic Surgeons database still describes high morbidity and early mortality associated with redo MV surgeries, as high as 11%.[1,4,10] Recently, transcatheter mitral valve-in-valve implantation (TMVI) has emerged as a novel therapy for dysfunctional MV bioprostheses.[11,12] Currently, the American Heart Association/American College of Cardiology guidelines for the management of adult patients with valvular heart disease have given valve-in-valve implantation a class IIb recommendation.[9] Only 2 case reports on TMVI in the pediatric age group are available in the literature to date.[11,13] Here, we report our experience with 4 pediatric patients who underwent TMVI in our centre. To our knowledge, this case series is the largest reported for this age group to date.

Methods

Patient population

From January 2017 to January 2020, four pediatric patients out of a total of 35 patients (adult and pediatric) underwent TMVI in our centre. The inclusion criteria were weight above 15 kg, left ventricular ejection fraction more than 35%, MV regurgitation $\geq$ grade 3+, and a New York Heart Association (NYHA) classification of grade III/IV. Exclusion criteria included the presence of other structural cardiac congenital anomalies or other associated valvular anomalies. The mean age and weight of the patients at the time of the procedure were 11.4 years (range: 10-14 years) and 36 kg (range: 31-44 kg), respectively. Details of their demographic data, underlying diagnosis, and previous procedures are presented in Table 1. All patients underwent bioprosthetic MVR secondary to rheumatic heart disease or MV prolapse. The MV was replaced by a Mosaic tissue valve (Medtronic. Minneapolis, MN), size 25 mm in 2 patients, and size 29 mm in 1 patient. One patient had a Hancock II (Medtronic. Minneapolis, MN), size 25 mm. At a mean postoperative follow-up interval of 49.25 months (range: 30-82 months), participating patients were noted to be symptomatic, with NYHA class III or IV secondary to progressive bioprosthetic dysfunction. This dysfunction was demonstrated with an echocardiographic increase in the transmitral mean Doppler gradient, with a mean of 19.75 mm Hg (range: 15-22 mm Hg; Tables 1 and 2).

Ethics and patient selection

Patient conditions were thoroughly discussed in the joint surgical and medical cardiology meeting. The procedure of

Table 1. Patient demographic data, diagnosis, and previous operations

Patient #	Age, y	Sex	Weight, kg	Previous diagnosis	Previous MV procedure	Other operations / interventions
1	11	Female	33	Rheumatic heart disease (mitral stenosis)	Mosaic bioprosthesis* size 25, ID 20.5	None
2	12	Female	31	MV prolapse (mitral stenosis)	Mosaic bioprosthesis* size 25, ID 20.5	None
3	10	Female	39	Rheumatic heart disease (mitral stenosis)	Hancock bioprosthesis* size 25, ID 20.5	Aortic valve repair
4	14	Female	44	Rheumatic heart disease (mitral stenosis and grade 1 regurgitation)	Mosaic bioprosthesis* size 29, ID 24	LA appendage plication during the same surgical procedure

ID, internal diamater provided by the manufacturer; LA, left atrial; MV, mitral valve.
* Medtronic (Minneapolis, MN).

Table 2. Procedure and results of transcatheter mitral valve implantation

Patient #	Implanted valve* size, mm	Transmitral gradient, pre (mm Hg)	Transmitral gradient, post (mm Hg)	NYHA class, pre	NYHA class, post	Fluoroscopic time, min	Minor / major complications
1	23	22	0	III	I	40	Mild pericardial effusion
2	23	22	3	III	I	55	None
3	23	15	1	III	I	72	None
4	26	20	0	VI	I	54	None

Approach used in all cases listed was via right femoral vein.
NYHA, New York Heart Association.
* Edwards Sapien 3 valve (Edwards Lifesciences, Irvine, CA).

valve-in-valve implantation in the nonaortic position was detailed for every patient as part of the informed consent process. The study was approved by the institutional review board of the Prince Sultan Cardiac Centre (IRB Number R20034), and patient consent to participate in the study was waived because of the retrospective nature of the research. Data on one of the patients included in this study were previously published as a case report.[13]

Patients recruited in this procedure included those who were symptomatic, with dysfunctional bioprosthetic valves with a weight above 20 kg. The primary outcome was successful implantation of the Edwards Sapien 3 valve (Edwards Lifesciences, Irvine CA), with no major complications. Secondary outcomes included acute and chronic relief of mitral stenosis or mitral regurgitation (MR) and related symptoms, survival, and any related adverse events.

Implantation procedure

Echocardiography. All valve-in-valve procedures were performed with a thorough echocardiographic assessment of valvular hemodynamics and the flow characteristics before, during, immediately following valve implantation and in the follow-up period. Transthoracic echocardiography was performed before the procedure, to evaluate the bioprosthesis morphology and function, as well as for routine measurements. Preprocedural transesophageal echocardiography (TEE) was conducted to confirm the absence of left atrial appendage thrombus and assess the functional status of the bioprosthetic valve. TEE was also used throughout the procedure. Additionally, 3-dimensional (3D) TEE aided in assessment of bioprosthetic valve function, the transseptal perforation, the positioning of the Edwards Sapein 3 valve, and postprocedural valve status (Fig. 1).

Technique. The procedure was performed with patients under general anesthesia, with continuous arterial monitoring. Three patients required transseptal perforation, and one patient had a prior atrial septal defect. Right femoral vein access was used, under TEE guidance, to perform transseptal puncture, as previously detailed.[11] Correct transseptal puncture location is important in TMVI, particularly with the Sapien system (Edwards Lifesciences, Irvine, CA), due to the relatively posterior flex point of the Commander system (Edwards Lifesciences, Irvine, CA). A posterior superior puncture, at or close to the fossa ovalis, permitted better coaxial deployment for the Commander system and decreased the orthogonal trajectory of the system upon deployment. After transseptal puncture, a 5 F diagnostic Judkins right

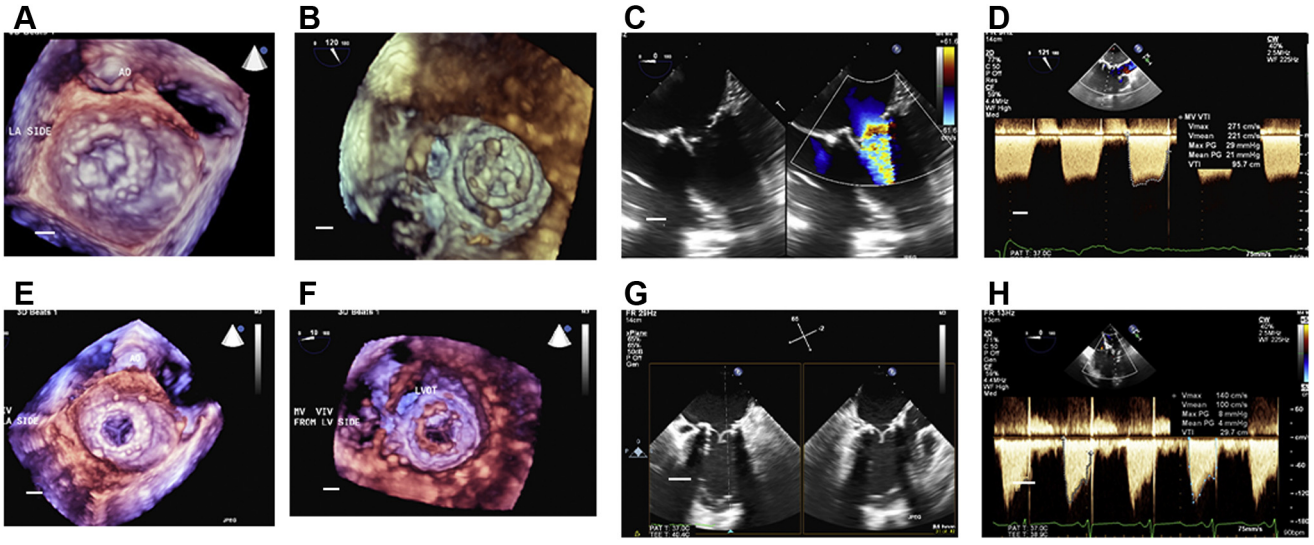

Figure 1. (**A**) Three-dimensional (3D) transesophageal echocardiography (TEE) for preimplantation calcified mitral valve (MV), left atrial view. (**B**) 3D TEE for preimplantation calcified MV, left ventricular view. (**C**) Two-dimensional (2D) echocardiography showing preimplantation color inflow Doppler. (**D**) TEE showing a preimplantation mitral inflow gradient of 24 mm Hg. (**E**) 3D TEE for the postimplantation mitral valve-in-valve, left atrial view. (**F**) 3D TEE for the postimplantation mitral valve-in-valve, left ventricular view. (**G**) 2D TEE with X-plane view of the mitral valve-in-valve. (**H**) 2D echocardiography showing a postimplantation inflow gradient with a mean of 4 mm Hg.

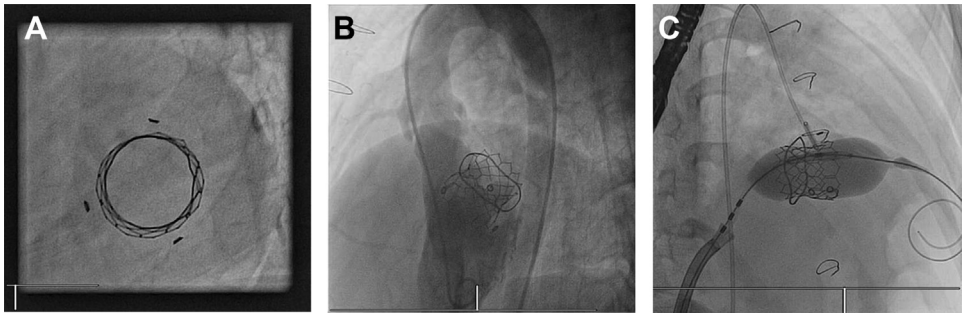

Figure 2. Still-frame fluoroscopy images. (**A**) Right anterior oblique view showing the E sheath retracted to the level of the inferior vena cava, with the Edwards Sapien 3 (Edwards Lifesciences, Irvine, CA) valve balloon inflated in position over the bioprosthetic mitral valve. (**B**) Left anterior oblique fluoroscopy showing the Edwards Sapien 3 valve in position within the bioprosthetic valve. Left ventriculogram using a pig tail showing no mitral valve regurgitation and no left ventricular outflow tract obstruction. (**C**) Extreme caudal view showing the Edwards Sapien 3 valve fully opened in position within the bioprosthetic valve.

catheter (JR5; Cordis, Santa Clara, CA) was introduced into the left atrium via the transseptal sheath. A stiff guide wire was secured in the left lower pulmonary vein through the JR5. An Atlas Gold PTA Dilation Catheter with a 12 by 20 mm balloon (Becton Dickinson, Franklin Lakes, NJ) was then used to balloon the interatrial perforation, which aided the passage of the valve balloon ensemble system. After performing the transseptal perforation, heparin 100 U/kg (maximum dose: 5000 IU) was given intravenously, to keep the activated clotting time at $>$ 250 seconds throughout the procedure. The patients were also covered with antibiotic prophylaxis.

After ballooning the interatrial septal defect, a JR5 or pigtail catheter (Cordis, Santa Clara, CA) was introduced into the left ventricle via the mitral prosthesis. Manipulation was performed carefully, to avoid entrapment within the paravalvular area, by avoiding crossing the valve with a wire. After crossing the defective valve, an extra stiff Safari guidewire (Boston Scientific, Marlborough, MA) was secured into the left ventricle through a 4 Fr Judkin right coronary catheter (Cordis, Santa Clara, CA).

The neo-trans-catheter Edwards Sapein 3 valve size and site of implantation were chosen per the valve-in-valve mitral mobile app, version 2.2, developed by the technology company UBQO (UBQO Ltd, London) and Dr Vinayak Bapat (http://www.ubqo.com/vivmitral). A 14 Fr Edwards e-sheath was then secured in the right femoral vein. An Edwards Sapien 3 Transcatheter Heart Valve (Edwards Lifesciences, Irvine, CA) was used in all patients. It was introduced through the e-sheath over the stiff wire and passed, under TEE and fluoroscopy guidance, across the dilated atrial septum and the dysfunctional bioprosthetic valve. Once the valve was in a target position, the sheath was retracted to the level of the inferior vena cave, and the balloon was slowly inflated, ensuring that the neo-implant did not extend beyond the dysfunctional prosthetic valve (Fig. 2). The aim was to achieve a prosthesis position such that its outer skirt was placed into the plane of the calcified mitral annulus or into the valvular plane of the bioprosthesis. This positioning was achieved by a slight protrusion, of approximately 10%-20%, of the prosthetic height into the left atrium (Videos 1 and 2). Before inflation, 3D TEE was also used to allow reconstruction of the left ventricular outflow tract (LVOT) from both sides (left ventricle and aortic valve), showing the precise location of the MV strut and confirming the absence of any clinically significant LVOTO. No pacing was used during our procedure. Details of the procedural aspects of the TMVI in adults were published previously.[14,15]

After implantation, valve performance was assessed with TEE, to assess the positioning of the newly implanted valve, its function, the transmitral gradients, any paravalvular leak (abnormal communication between the newly implanted transcatheter valve and the underlying bioprosthesis generating turbulent blood flow with varied clinical consequences),[16] and the presence of implanted valve regurgitation (Fig. 1, F-H). In addition, it was important to rule out any encroachment effect of the new valve on the LVOT. After the procedure, the catheters and guide wires were removed, and hemostasis was achieved via manual compression. The mean fluoroscopy time was 55.25 minutes (range: 40-72 minutes). All patients were extubated in the catheterization laboratory, and none of the patients required blood transfusion or intensive care unit admission. No major early or late complications occurred. One patient developed a small pericardial effusion post-procedure, possibly related to the catheter and wire manipulations, which spontaneously resolved on the second day postimplantation. The mean hospital length of stay was 4 days (range: 3-7 days). After the procedure, all patients were started on aspirin, 3 mg/kg per day, and clopidogrel, 0.2 mg/kg per day, for 6 months.

Results

An Edwards Sapien 3 valve (S3; Edwards Lifesciences, Irvine, CA) 23 mm in size was implanted in 3 patients, and a 26 mm valve was implanted in one patient. The pre- and postprocedure hemodynamics are described in Tables 2 and 3. The transmitral mean gradient decreased from a mean of 19.75 mm Hg (range: 15-22 mm Hg) to a mean of 1 mm Hg (range: 0-3 mm Hg) after the procedure. The newly implanted valve did not exceed the struts of the dysfunctional valve, and there was no paravalvular leak or LVOTO. Patients were followed up in the clinic after 30 and 90 days, and then annually or as required. Table 4 demonstrates the transmitral mean gradient during the clinical follow-up. All patients' symptoms improved from NYHA class III/IV to class I. No heart block or endocarditis was reported during follow-up.

Table 3. Pre– and post–valve implantation hemodynamic pressures

Patient #	Pre- or post- intervention	Pressure, mm Hg			
		RA A/V/mean	PA systolic/diastolic/mean	LA A/V/mean	LV systolic/LVEDP
1	Pre	10/11/9	55/32/40	33/32/28	92/6
	Post	7/9/8	Not done	11/15/12	104/12
2	Pre	13/16/13	65/37/50	31/42/32	93/10
	Post	14/15/12	Not done	18/24/17	103/14
3	Pre	Mean 5	52/27/36	Mean 24	93/9
	Post	Mean 6	44/20/29	Mean 11	114/10
4	Pre	6/5/4	45/24/32	33/52/29	96/9
	Post	Mean 5	31/9/18	14/6/9	99/10

A, a wave; FA, femoral artery; LA, left atrium; LV, left ventricle; LVEDP, left ventricular end diastolic pressure; PA, pulmonary artery; RA, right atrium; RV, right ventricle; RVEDP, right ventricular end diastolic pressure; V, v wave.

Discussion

MVR in the pediatric age group has proven to be challenging, with relatively high rates of reintervention.[11] Xenograft and homograft valves in children are well known to deteriorate over time, with an almost inevitable need for rereplacement.[17,18] Compared with mechanical valves, which are less prone to degeneration, very close monitoring for anticoagulation is needed with xenograft and homograft valves.[19] Studies have described the incidence of repeat MVR in patients with bioprosthetic valves as being 2.3% to 2.5% per patient-year in children.[20] Reports of 10-year freedom from valve failure or reoperation in children after MVR range from 50% to 56%.[8] Furthermore, a multi-institutional study from a Pediatric Cardiac Care Consortium of 45 cardiac centres suggests that the median longevity for prosthetic MVs in children aged 5 years or less undergoing MVR is 12.7 years,[21] implying that half of the patients required MVR 12.7 years after initial MVR. Additionally, morbidity associated with redone MV surgeries includes the need for pacemakers in 9% of cases, and heart failure in more than 27% of cases.[20]

Data suggest that annular growth actually continues after MVR,[20,22,23] indicating that the child will outgrow the valve. However, fixed-sized prostheses cannot accommodate somatic growth in patients. Thus, the concept of an expandable bioprosthetic valve is appealing. Transcatheter valves have the potential to enlarge to match somatic growth on subsequent procedures, thus limiting the number of redo surgeries needed to accommodate this enlargement as the patient grows and allowing sufficient time until a fitting adult-size prosthesis can be implanted. We acknowledge that most, if not all, MVs repaired or replaced during childhood eventually may have to be re-replaced at some time later in life. Nonetheless, TMVI allows delay of the inevitable reoperation.

In adults, the Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) have recently added transcatheter valve-in-valve implantation as an option for the management of dysfunctional bioprostheses in high–surgical risk patients.[24] With the possible need for several redo surgeries for these patients, we felt that it was reasonable to explore the use of TMVI as a means to delay or replace the inevitable redo surgery in the pediatric age group.

However, experience with TMVI in the pediatric population is still very limited. Recently, a multicentre study reported the surgical replacement of a MV with a Melody valve (Medtronic, Minneapolis, MN) in a cohort of pediatric patients.[17] Designed as a temporary device to replace failing pulmonary valves, the Melody valve had more-adequate performance under systemic pressures in the study. However, almost one third of these patients developed degeneration within the first 2 years postprocedure.[17] We elected to use the Edwards Sapien 3 valve rather than the Melody valve because, compared to the Edwards Sapien 3 valve, the Melody valve stent is more liable to fracture during higher cyclic compressive stresses,[25] making the Melody valve more likely to collapse if implanted in the MV position. In addition, the Melody valve is longer than the Edwards Sapien 3 valve, making it higher risk to LVOTO when implanted in the MV position.[26] In 2016, Murphy et al.[27] published the first case of an 11-year-old patient with a failed mechanical mitral prosthesis requiring hybrid implantation of a 26-mm Edwards Sapien 3 valve mounted on a MEMO 3D (Sorin Group, Milan, Italy) annuloplasty ring (Sorin Group, Milan, Italy).[27] Momenah et al. published the first case of transcatheter TMVI of an Edwards Sapien 3 in the pediatric age group,[13] a case included in this series.

More-complex cases, such as Shone complex and congenital mitral stenosis, are being operated on at a younger age, making the MV vulnerable to early repair and thus increasing the need for redo surgeries. We believe that the hybrid-transcatheter Melody valve is useful in providing valvular competence in small children with irreparable or failed MV repair, because it can be sequentially dilated, on a short-term basis, until the child can receive a traditional prosthesis (> 19 mm).[18,28] However, data are still limited on the off-label use of the Melody valve, its longevity in this position, and the effect of repeated dilatation on its function and durability. The Edwards Sapien valve can be used after the surgical bioprosthesis has been implanted and shows signs of degeneration, owing to its larger internal diameter and stronger stent, which allow it to withstand systemic pressures. The 1-year outcomes of mitral valve-in-valve procedures using the Edwards Sapien 3 transcatheter heart valve in 1529 patients did not describe valve stent fracture, as compared to use of the Melody valve in the mitral position, with which stent fracture has been reported.[29,30]

Valve selection of new prostheses for degenerated surgical valves is relatively simple using the ViV app. However, the selection of valves for mitral rings is more nuanced, due to the lack of consensus regarding proper ring sizing. None of our

Table 4. Clinic follow-up findings

	Pre-procedural		Immediate post-procedure	1-month follow-up			3-month follow-up			12-month follow-up			Last clinic follow-up	
Patient	MV mean gradient by echo	RVSP	mean gradient by echo	MV mean gradient	RVSP	NYHA class	MV mean gradient	RVSP	NYHA class	MV mean gradient	RVSP	NYHA class	Duration, months	Mean gradient by echo
1	27	100	3	11	40	I	10	40	I	10	40	I	21	10
2	25	30	7	10	23	I	9	23	I	9	30	I	17	12
3	23	110	6	12	30	I	14	30	I				7	12
4	25	60	5	6	30	I	7	35	I				3	7

Values are mm Hg, unless otherwise indicated.

MV, mitral valve; NYHA, New York Heart Association; RVSP, right ventricular systolic pressure.

patients had a mitral ring. In our series of patients, there was no need to fracture the bioprosthetic valve, because the valve stenosis was due to valve degeneration and was not a result of patient−prosthesis mismatch, and all were of adequate size to accommodate the S3 valve. Most bioprosthetic valves, including the Mitroflow (Sorin Group, Arvada, CO), Magna, Magna Ease (Edwards Lifesciences, Irvine, CA), Mosaic (Medtronic, Inc, Minneapolis, MN), and Biocor Epic (St. Jude Medical, Minneapolis, MN) surgical valves, can be successfully fractured using a high-pressure balloon 1 mm larger than the labeled valve size, whereas the Trifecta (Abbott, St Paul, MN) and Hancock II (Medtronic, Minneapolis, MN) surgical valves cannot be fractured.[14] One patient in our cohort had a Hancock II valve that could accommodate an Edwards Sapien 3 valve.

Thorough echocardiographic assessment is crucial before considering the TMVI procedure, to avoid LVOTO. Mitral valve-in-valve−induced LVOTO with hemodynamic compromise is a serious complication with limited treatment options, and can be fatal; therefore, it should be avoided. Bioprostheses with bovine pericardial leaflets are at particular risk of creating an LVOTO, because the leaflets are positioned higher up the stent frame, thus resulting in greater transcatheter heart valve frame coverage in the LVOT. Preprocedure assessment included the MV annulus, at the hinge points of the valve leaflets, in the lateral and antero-posterior planes from the apical 4-chamber and parasternal long-axis views, respectively. Correct anatomic imaging planes using a true commissural view showing the P1-A2-P3 scallops and a perpendicular on-axis long-axis view depicting the A2-P2 scallops have been proposed for more adequate assessment and can provide a major and minor mitral diameter and a complex 3D mitral geometry. Important to note is that papillary muscle and chordae anatomy should be assessed for the presence of false bands and for direct insertion of papillary muscles. In addition, because LVOTO potentially occurs in the subaortic region (Sub A) with expansion of the valve, we tend to use the "SubA:MV" ratio, which is the ratio of the subaortic region in systole, (A), to the actual antero-posterior mitral annulus dimension, both measured from the parasternal long-axis view. A ratio of > 0.5 is less likely to cause LVOTO.[29] Although we did not do this, some experts recommend using multidetector computed tomography to identify the trigone to trigone distance, the true internal diameter of the surgical valve and the LVOT tract anatomic morphology.[31,32] Prominent septal hypertrophy and a narrow aorto-mitral angle increase the risk of subsequent LVOTO.[30] Echocardiography and computed tomography scans can assist in measuring the aorto-mitral-annular angle, defined as the angle formed at the intersection of lines running through the intercommissural diameter of the mitral annulus and the centre of the aortic annulus. Acute angles < 115 degrees may increase the risk of LVOTO after deployment of a balloon-expandable valve.[31] Preprocedural virtual valve implantation, using 3D printing or 3D reconstruction software to calculate the neo-LVOT area after valve implantation, can help to avoid such complications. Some studies suggest that a neo-LVOT area of 250 mm^2 or smaller is associated with a risk of LVOTO.[31] Multidetector computed tomography may also be crucial to identify the anatomy of the left circumlex artery. This artery crosses between the coronary sinus and the mitral annulus in 80% of patients, and special consideration is needed to avoid impingement on this artery during inflation.[33] Dedicated specialized software for annular sizing, stabilization, and sealing of the new device within the 3D configuration for the MV and the existing prosthesis is key for the development and advancement of TMVI.[32]

Several procedural issues should be considered during pediatric TMVI. First, the appropriate use of valve type, size, and implantation is crucial to successful implantation procedures. In our cohort, we preferred the use of the Edwards Sapien 3 valves. These valves have a lower profile e-sheath (14-F and 16-F sheaths), owing to the wide strut angles, with good expanding properties that allow TMVI to be performed in pediatric patients with smaller vessels. They are also less prone to regurgitation and paravalvular leak compared to the Edwards Sapien XT (Edwards Lifesciences, Irvine, CA) valves, because of an additional outer skirt at the distal part of the Edwards Sapien 3 valves.[34] The Edwards Sapein 3 valve was designed with a frame geometry that provides stronger radial force.[34] We believe that this aspect of the structure was important for withstanding mechanical annular forces and limiting strain-related mechanical failure. Furthermore, although the S3 valves are 15% longer than the Edwards Sapien XT (Edwards Lifesciences, Irvine, CA) valves, the difference in the cell geometry between the inflow and the outflow causes the S3 valve frame to foreshorten more from the ventricular side,[34] thereby reducing the risk of LVOTO. However, during deployment, the implanted MV should not exceed the struts of the defective surgical valve, to avoid the risk of embolization or LVOTO. The use of the valve-in-valve app helped to define the anchor point,

preventing protrusion of the implanted valve into the LVOT. It also assists in the selection of the size of the Sapien valve, based on the internal diameter of the previously implanted surgical bioprosthetic valve.

Second, to avoid the risk of left ventricular perforation or aneurysm, the use of a double curved wire (Safari Wire, Boston Scientific, Marlborough, MA) is desirable. Third, any paravalvular leak can be overcome by further inflation of the implanted valve. However, high-pressure balloons should be used cautiously to avoid the risk of fracture of the implanted surgical bioprosthetic valve annulus, which might lead to compression of the circumflex coronary artery or complete heart block. Finally, the valve should be mounted on the balloon for implantation via an antegrade approach, opposite to the mounting technique used in the transcatheter aortic valve implantation (TAVI) procedure.

All patients in our cohort were started on aspirin, 3 mg/kg per day, and clopidogrel, 0.2 mg/kg per day, for 6 months. This antiplatelet regimen is the same as that used for Sapien 3 implantation in other valve positions, which is important because valve thrombosis has been estimated to be approximately 2% per year with the balloon-expandable Sapien valve in the mitral position.[35,36] We tend not to undercoagulate, due to the high incidence of thrombosis after TMVI, especially in the pediatric age group, during the first 3 months after implantation.[36,37]

TMVI holds potential advantages, compared to regular surgical replacement. The short hospital length-of-stay, with minimal complications, is encouraging. The gradient across the percutaneous valve immediately after implantation and during short-term follow-up was acceptable. One of the drawbacks is the high cost of the percutaneous valves, but the procedure has the advantage of the short hospital length-of-stay and the avoidance of anticoagulation therapy, which require multiple follow-ups, and close follow-up of the international normalized ratio. More studies are needed to compare the longevity of the percutaneous valves in the mitral position, long-term outcomes, associated complications, and incidence of fractures and endocarditis, compared to those with the surgical redo bioprosthetic valves.

Limitations

The major limitation of the study is its retrospective nature, with its inherent referral and selection biases. Another limitation is the small number of patients, which may be considered acceptable for this newly introduced technique. Of particular interest, this retrospective study reported techniques and work-ups in a selective cohort.

Conclusions

TMVI implantation can be performed safely for degenerative MV bioprostheses and with favorable clinical and hemodynamic early and midterm outcomes in the pediatric age group. This procedure can offer a viable option in patients who have high surgical risk or are not fit for conventional surgery. However, we recommend that the long-term data from this approach be analyzed and reported in a large cohort multicentre study.

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Supplementary Material

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