

Percutaneous pulmonary valve implantation for free pulmonary regurgitation following conduit-free surgery of the right ventricular outflow tract



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ABSTRACT

Introduction: Pulmonary regurgitation (PR) following surgery of the right ventricular outflow tract (RVOT) is not innocent and leads to significant right heart dysfunction over time. Recent studies have demonstrated that percutaneous valves can be implanted in conduit free outflow tracts with good outcomes.

Objectives: To evaluate in patients with severe PR – anticipated to require future pulmonary valve replacement – the feasibility and safety of pre-stenting dilated non-stenotic patched conduit-free right ventricular outflow tracts before excessive dilation occurs, followed by percutaneous pulmonary valve implantation (PPVI).

Patients and methods: Twenty seven patients were evaluated, but only 23 were deemed suitable based on the presence of an adequate retention zone ≤ 24 mm defined by semi-compliant balloon interrogation of the RVOT. A 2 step procedure was performed: first the landing zone was prepared by deploying a bare stent, followed 2 months later by valve implantation.

Results: RVOT pre-stenting with an open cell bare metal stent (Andrastent XXL range) was performed at a median age of 13.0 years (range: 6.0–44.9) with a median weight of 44.3 kg (range: 20.0–88.0). Ninety six percent (22/23) of patients proceeded to PPVI a median of 2.4 months (range: 1.4–3.4) after initial pre-stent placement. Twenty one Melody valves and one 26 mm Edwards SAPIEN™ valve were implanted. Complications consisted of embolization of pre-stent (n = 1), scrunching (n = 4) and mild stent dislocation (n = 2). During follow-up, no stent fractures were observed and right ventricular dimensions decreased significantly.

Conclusions: Post-surgical conduit-free non-stenotic RVOT with free pulmonary regurgitation can be treated percutaneously with a valved stent if anatomical (predominantly size) criteria are met. In experienced hands, the technique is feasible with low morbidity.

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1. Introduction

Pulmonary regurgitation (PR) after transannular patching or even limited infundibulotomy is associated with late adverse events such as aneurysmal dilation of the right ventricular outflow tract (RVOT), right ventricular dysfunction, progressive tricuspid valve regurgitation, dysrhythmias and premature sudden death [1–3]. Surgical pulmonary valve replacement (PVR) is an efficient technique to avoid these late problems [4,5]. However, this strategy is not free of either early or late complications, requiring repeated re-interventions of increasing complexity and risk. Proper timing is therefore essential not only to reduce the number of sternotomies, but also to limit cumulative risk and keep long term morbidity as low as possible. The ideal timing of re-

intervention in order to allow a patient to experience a cardiac event-free existence as well as a normal life expectancy has yet to be determined and remains a hotly debated issue [6]. Current survival studies with long term follow-up of patient groups where current guidelines have been applied report on an ongoing excess mortality in every decade: this suggests that there is a margin for improvement and that current guidelines may require refinement [3,7].

Percutaneous pulmonary valve implantation (PPVI) may be of benefit in these patients [8,9]. PPVI is recognized as an acceptable method for right ventricular outflow tract valve implantation in selected patients, typically with a surgical conduit. However, the majority of patients that will eventually require a pulmonary valve do not have a surgical conduit as landing zone.

In recent publications, it was shown that PPVI is effective and safe in patients with conduit-free RVOTs [10–12]. The aim of this study was to determine the safety and feasibility of RVOT stenting and subsequent PPVI in patients with non-stenotic dilating RVOTs. This included

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assessment of right ventricular (RV) changes and determination of the limitations and complications of this strategy and also, to start accumulating data to compare the different strategies.

2. Methods

Patients were recruited from the outpatient clinics where they routinely present for annual evaluation. The main inclusion criterion for this ongoing, prospective study was severe pulmonary regurgitation (grade 3 or 4) in a conduit-free RVOT with progressive dilation of the right ventricle, where one would anticipate the need for a pulmonary valve in the near future. Such patients typically have no significant gradient across the RVOT. During the study period only the Melody valve (Medtronic, Minneapolis, MN, US) was considered because of reimbursement issues; due to the maximum indicated outer diameter of 24 mm, RVOT diameter at the level of the pulmonary valve had to measure between 18 and 21 mm on echocardiography to qualify for inclusion. The severity of PR was classified on color flow Doppler similar to our previous publication [10]. Patient records were used to obtain catheterization and follow-up data. Digital measurements of catheterization data were performed using an IMPAX® viewer (Agfa Heartlab®, Mortsel, Belgium). Cardiovascular magnetic resonance imaging (MRI) was performed in some cases, but information was not used for selection.

The study was conducted in accordance with local Ethics Committee guidelines; fully informed consent after extensive discussion of all different strategies was obtained from the patient and parents.

2.1. Cardiac catheterization and PPVI: technical aspects

All procedures were performed under general anesthesia. The catheterization procedure and valve implantation were similar to that previously described [9,10,13].

2.2. Interrogation of the RVOT

2.2.1. Angiography

Biplane angiography was performed in the RVOT by means of a Multi-Track™ angiographic catheter (NuMED, NY, USA) using the lateral projection for the pulmonary valve region, and a frontal view with extreme cranial angulation to demonstrate predominantly the pulmonary artery bifurcation.

2.2.2. Guide wires

A stiff exchange length guide wire was securely positioned in a distal pulmonary artery branch (e.g. E®-wire, JOTEC, Germany; Amplatz UltraStiff, COOK, Bloomington, USA; Lunderquist™, COOK, Bloomington, USA). It is helpful to put a curve on the wire matching the shape of the RVOT and pulmonary artery since this will facilitate balloon retrieval after stent placement by improving the inner curve.

2.2.3. Delineation of the RVOT anatomy (Fig. 1)

Balloon-interrogation during low-pressure sub-maximal inflation and deflation was performed using a semi-compliant, mildly oversized balloon, e.g. a 23–25 mm Tyshak® balloon (NuMED, NY, USA) (Table 1). At nominal pressure the balloon typically stretched open the outflow tract almost completely without a significant indentation (Fig. 1B); the balloon at this point has a predetermined size which facilitates interpretation of diameters. Also, the absence of movement and mild indentation of the inflated interrogation balloon are important and comforting signs. If there was no or minimal indentation, simultaneous injection through the side-arm of a long Mullins sheath was carried out. This assists in further outlining the RVOT, provides evidence that the inflated balloon is securely seated (confirms probable stent fixation) and assesses the (un)likelihood of a paravalvular leak post valve

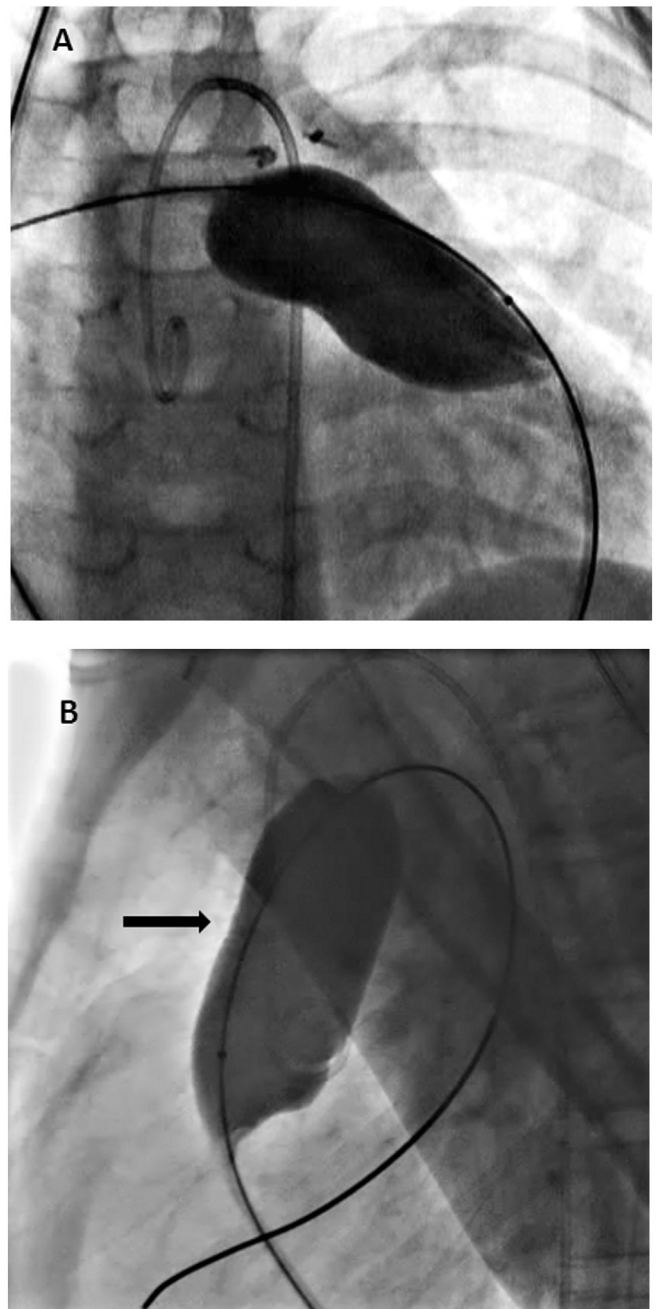


Fig. 1. Balloon interrogation of RVOT. A. Cranially tilted antero-posterior view of 23 mm Tyshak balloon inflated in RVOT patient 12, with mild indentation. B. Lateral view of 25 mm Tyshak balloon fully inflated in RVOT of patient 24. Note minimal indentation of future landing zone (arrow).

implantation. Simultaneous aortogram was performed during full inflation of the balloon to exclude coronary compression.

2.2.4. Pre-stenting the RVOT

2.2.4.1. Stent placement (Figs. 2 & 3). Open cell design, bare metal stents (Andrastent XXL series, Andramed, GmbH, Reutlingen Germany) were hand-crimped on balloon-in-balloon (BIB) balloons (NuMED, Hopkinton, NY, USA). More detail can be viewed in Table 1. BIB balloons were selected to be 2–4 mm larger than the retention zone or – most frequently – a BIB 24 mm was used if only mild indentation of a 25 mm Tyshak was observed. Ideally the length of the balloon should be matched to the stent; if too long, these large balloons will push themselves back due to the distal shoulders locked in the bifurcation. The Andrastent XXL

Table 1

Patient characteristics and procedural information. BIB, balloon-in-balloon delivery balloon; IP, infundibular patch; TA, transannular patch. PPVI: percutaneous pulmonary valve implantation; RVOT, right ventricular outflow tract; all diameters (diam) in mm. –, not available. *26 mm Edwards valve implanted. Patient 6 went for surgical pulmonary valve implantation after stent migration.

No.	Surgical procedure	Age at pre-stent (y)	Weight (kg)	RVOT pre-stent						PPVI			
				ECHO		Angio	Interrogation	Andrastent XXL	BIB	Fluoroscopy	Ensemble	Time	Fluoroscopy time (min)
				RVOT min diam	RVOT min diam	Balloon diam	Length	Balloon (diam)	Time (min)	Diam	After pre-stent (mo)		
1	TA	7.2	21	15	15.7	20	39	22	14.0	22	2.4	15.0	
2	TA	12.3	34	19	16.7	23	39	24	9.3	22	1.6	11.0	
3	TA	6.0	20	18	18.5	20	39	22	8.1	22	2.3	11.0	
4	TA	7.3	26	17	18.0	23	39	18	12.7	20	1.9	18.9	
5	TA	16.5	88	21	23.1	25	43	25	22.7	24*	3.4	9.0	
6	IP	8.6	26	22	19.0	25	30	24	10.0	NA	NA	10.0	
7	TA	12.2	45	20	23.0	25	39	24	4.9	22	2.7	6.5	
8	TA	9.7	38	19	18.0	25	39	24	14.4	22	2.3	12.0	
9	TA	13.1	46	20	17.1	20	39	20	23.0	20	2.8	40.0	
10	TA	11.9	38	17	14.0	23	48	22	15.4	22	2.2	22.1	
11	IP	14.0	58	17	24.0	25	57	24	11.0	22	3.3	15.8	
12	TA	9.2	36	18	22.0	23	43	24	8.0	22	1.9	12.3	
13	TA	7.0	29	19	19.0	23	39	24	19.0	22	2.1	18.9	
14	TA	8.3	21	19	22.0	23	39	22	14.4	22	3.0	20.4	
15	IP	17.9	70	21	21.0	25	43	24	10.0	22	1.9	9.2	
16	TA	44.9	80	20	19.0	23	48	24	35.0	22	1.4	8.8	
17	TA	20.8	78	22	22.9	25	43	24	14.0	22	3.0	26.2	
18	TA	6.5	24	20	20.0	25	39	24	11.0	22	3.0	17.0	
19	IP	13.7	42	22	21.0	25	39	24	8.5	22	2.4	9.7	
20	TA	10.3	40	21	21.1	25	39	22	12.2	22	2.5	10.8	
21	TA	16.3	80	20	24.0	25	43	24	18.5	22	2.1	10.1	
22	IP	10.7	36	20	18.0	25	43	24	11.6	22	2.1	13.5	
23	TA	15.3	43	19	22.0	25	57	25	22.0	22	1.9	18.0	

shortens 5–15% at 20–24 mm distention (bench testing) and was chosen long enough to leave no redundant RVOT. Stents placed in a conduit-free non-stenotic RVOT tend to move proximally during inflation.

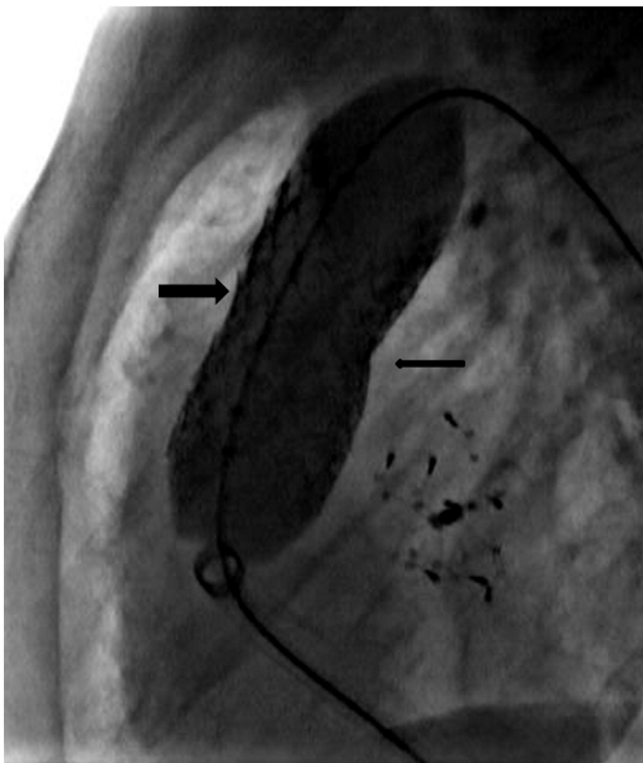


Fig. 2. Implantation of pre-stent in RVOT. Andrastent 39XXL mounted on 22 mm BIB balloon with outer balloon inflated. Note nice indentation posteriorly which will assist in keeping stent secure (small arrow). Open cells act as anchors by hooking onto surrounding tissue (thick arrow).

During stent mounting the outer balloon was slightly inflated to create mild shoulders proximal and distal to the stent – the distal shoulder assists progress in the long sheath during difficult passage and the proximal shoulder prevents the stent from sliding-off. As we gained experience, we started deployment more distally in the main pulmonary artery in order to ensure that proximal movement is compensated for and that the stent is positioned across the intended retention zone. Once the stent was in the desired position and uncovered, BIB balloons were sequentially inflated using hand insufflation as only low pressure is required to open and anchor the stent. This allows maximal control during deployment, with the balloon being inflated until the stent is anchored onto the wall or retention area: this is visually confirmed by either seeing an indentation in the stent, or seeing the cells splay open and hook into the walls or, rarely, by means of a control angiogram through the side-arm of the sheath to observe complete occlusion of the RVOT by the inflated balloon–stent unit. If required, the 24 mm BIB was slightly overinflated up to 25–26 mm (off-label). It is important to keep the tip of the long sheath close to the balloon since this will allow the operator to stabilize the system and limit the stent from being milked back.

2.2.4.2. Balloon retrieval after RVOT stent placement (Fig. 4). The balloon should be carefully retrieved as it may cause displacement or embolization of the stent. If concerned ($n = 2$), we placed a second guide wire using a balloon tipped catheter through the stent, advanced another long sheath into the stent and removed the dilator – this enabled the operator to “push” with the second sheath stabilizing the stent and keeping it in place while withdrawing the original balloon. In general, we considered these newly implanted stents insufficiently stable to allow the manipulations typically required for pulmonary valve implantation at this point. Therefore, a period of 2 months was allowed for a tissue ingrowth to secure the stent [14].

2.2.4.3. PPVI. At the second catheterization, we used a balloon-tipped catheter to re-enter the original RVOT stent to ensure that the guide wire remained free of the stent cells. Once again we recommend pre-

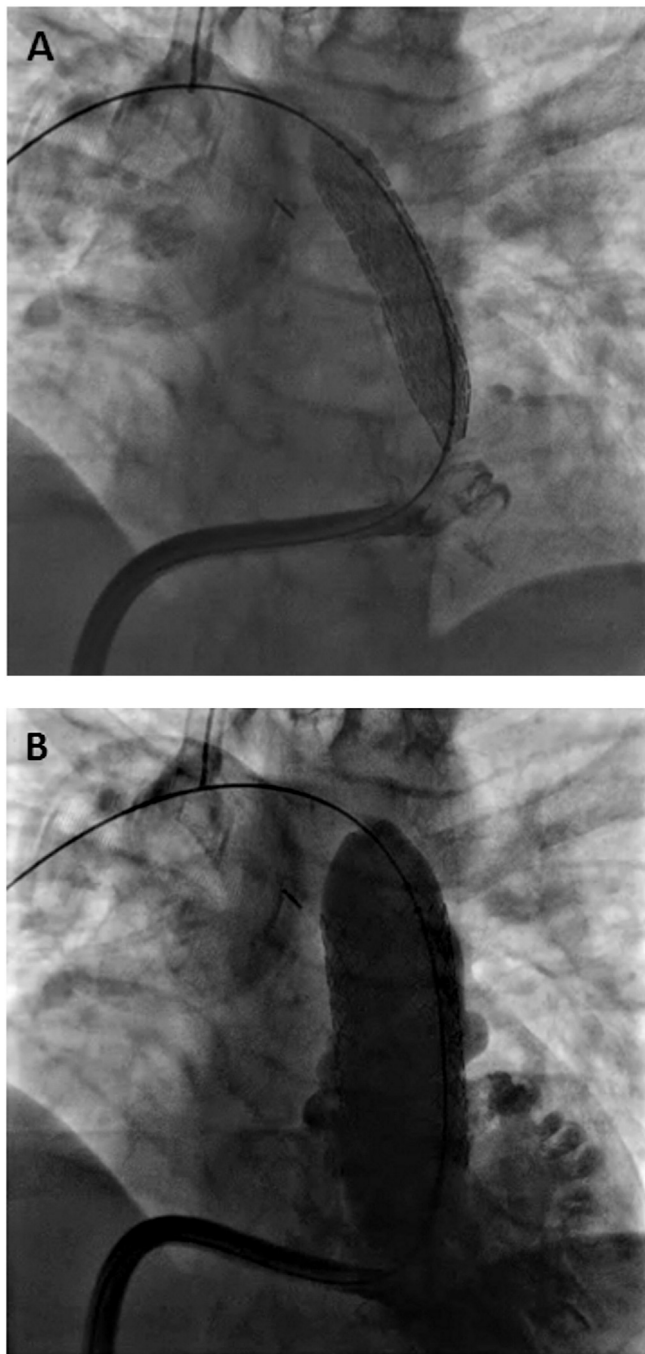


Fig. 3. Pre-stent RVOT with Andrastent 57XXL in patient 24. A. Inner balloon of 24 mm Balloon-in-balloon (NuMED, USA) BIB inflated and in good position. B. Outer balloon insufflated. Stent pushed slightly back by BIB due to the smaller diameter of the right pulmonary artery and encroachment on bifurcation. Also notice how close the long sheath is positioned to BIB balloon in order to allow the operator to stabilize or push system forwards during inflation. Angiography performed via long sheath illustrates good apposition of stent to RVOT walls.

bending the wire, but at a more acute angle with the intention to facilitate passage on the way in. If a stent protruded too much into the RVOT and passing of the Ensemble could potentially be difficult, the proximal end was flared open ($n = 2$). Alternatively, a covered (closed cell) stent can be placed to prevent hooking of the valved stent delivery system onto the open cells of the previously placed RVOT stent ($n = 2$); or, it may be used to decrease the internal diameter of the stented RVOT in order to ensure good fixation of the percutaneous pulmonary valve ($n = 2$). A jugular approach will allow the Ensemble to enter the

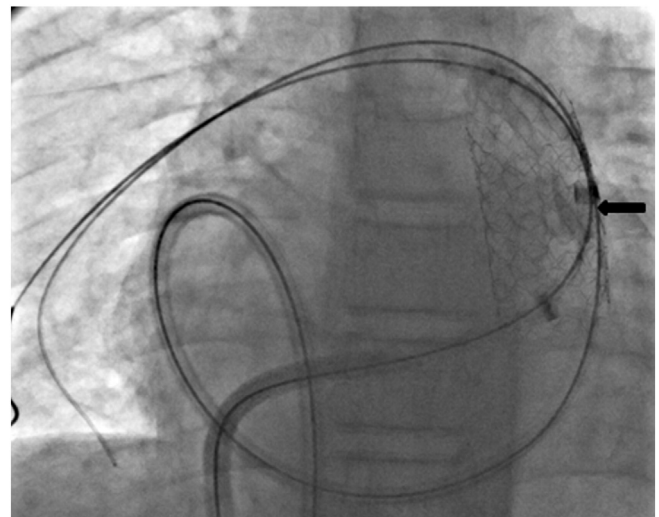


Fig. 4. Stabilizing RVOT stent for balloon retrieval in patient 23. Due to difficulty during retrieval stent was stabilized by exerting pressure with a second long sheath (arrow).

RVOT stent more centrally with less friction on the lateral walls of the RVOT. The valved stent should be fully expanded to ensure complete contact with the RVOT stent. If required, the 22 mm Ensemble BIB may be slightly further expanded up to 24 mm by adding more volume (off-label use).

2.2.4.4. Follow-up. Patients were re-evaluated clinically, electrocardiographically and echocardiographically after 1, 3, 6 and 12 months, and annually thereafter. Magnetic resonance imaging (MRI) was performed after 3 months. Chest roentgenogram is performed after 6 and 12 months, and annually thereafter for 3 years, if indicated.

2.3. Statistical analysis

Data was analyzed using standard statistical software (SPSS for windows, SPSS Inc., IBM Company, Chicago, Illinois, US, version 18). A Student-t test was used to compare normally distributed data. Continuous data were expressed as medians with the minimum and maximum values. A p -value < 0.05 was considered significant.

3. Results

During a three year period ranging from November 2010 to May 2013, 27 patients were interrogated for bare metal pre-stenting; 4 patients were deemed unsuitable because of lack of indentation ($n = 2$) or the presence of significant flow around an inflated 25 mm RVOT interrogation balloon ($n = 2$). No patient was excluded because of potential coronary artery compression. The remaining 23 patients (16 males and 7 females) form the basis of this report: these include 3 patients who were previously described (8). All patients had undergone surgery for tetralogy of Fallot at a median age of 0.5 years (range: 0.2–12); 18/23 (80%) had received a limited transannular patch during initial repair, and the remainder had an infundibular patch.

3.1. RVOT pre-stent

RVOT pre-stenting was performed at a mean age of 13.0 years (range: 6.0–44.9) with a median weight of 44.3 kg (range: 20.0–88.0) and height of 143.7 cm (range: 100–192), respectively. Patient and procedural characteristics can be viewed in Table 1. There was no significant gradient across the RVOT before initial stent placement (median 9 mm Hg; range: 0–23). Due to the distensibility of the RVOT, and because the available valved stent could reach maximally 24 (to 25) mm, a 25 mm Tyshak balloon was typically used for

interrogation. Only Andrastent XXLs were used (30–57XXL) and, as operator experienced increased, larger outflow tracts treated (Table 1). Stents were mounted on 18–24 mm BIB balloons and delivered through a 14 F long Mullins sheath (COOK Medical, Bloomington, USA). In 2 patients (nos. 5 & 23) the BIB was over expanded to 25–26 mm. All stents were implanted via the femoral venous route, except in patient no. 5 where the right jugular vein was used since the femoral veins were inaccessible. Fluoroscopy lasted a median of 14.3 min (range: 4.9–35.0) and radiation dose a median of 7522.2 μGym^2 (range: 164.0–19,015.0).

3.2. PPVI

Ninety six percent (22/23) of patients proceeded to PPVI a median of 2.4 months (range: 1.4–3.4) after initial stent placement. Twenty one Melody valves (Medtronic, Minneapolis, MN, US) were implanted: nineteen ($n = 19$) on a 22 mm and two ($n = 2$) on a 20 mm Ensemble system. In patient no. 5 a 26 mm Edwards SAPIEN™ valve (Edwards Life Sciences Inc., Irvine, CA, US) was implanted due to concerns regarding the diameter of the RVOT. The most common route for valve insertion was via the femoral veins ($n = 19$), right jugular vein ($n = 2$) and subxyphoidal hybrid procedure ($n = 1$, patient no. 5). In patient no. 9, access was changed to the jugular venous route after difficulties with delivery were encountered with the transfemoral route. A covered 45 mm 8 Zig Cheatham Platinum stent (CCP) mounted on a 24 mm BIB balloon was placed before Melody valve implantation during the same session in patients 5 and 17 to reduce the diameter of the RVOT, since during implantation of the initial pre-stent, a 24 mm BIB balloon was overinflated to ensure secure seating of the stent. Fluoroscopy lasted a median of 15.3 min (range: 6.5–40.0) and radiation dose a median of 3956.9 μGym^2 (range: 872.0–12,972.0).

Pre-discharge echocardiography showed gradients less than 10 mm Hg in all patients, and none or trivial pulmonary regurgitation; 1 patient had a minimal paravalvular leak.

3.3. Follow-up

After 3 months M-mode right ventricular end diastolic dimension (RVEDD) decreased an average of 20% ($p < 0.005$) from a median z score of 3.9 (range: 1.8–5.2) before valve implantation to a median z score of 2.3 (range: –0.5–3.8) ($p < 0.001$). Left ventricular end diastolic dimension remained essentially unchanged. Paired magnetic resonance imaging before and after was available for only 7 patients and showed that right ventricle end diastolic volumes decreased significantly from a median of 118.4 ml/m² (range: 88.4–156.1) to 104.1 ml/m² (range: 81.9–129.3) ($p = 0.05$) and left ventricular volumes improved from 77.0 ml/m² (range: 69.1–147) to 88.6 ml/m² (range: 79–157) ($p = 0.037$) (Fig. 5). Subjective exercise capabilities also improved: upon specific request all patients reported specific physical activities that could be performed easier or faster than before pulmonary valve implantation.

No stent fractures of the Melody CP stent were observed on chest radiography at 6 months and yearly after implantation. Valve function remained very stable during the short follow-up of 14–42 months without a significant increase of gradient nor regurgitation (mean gradient 16 mm Hg, range 5–30; median PR 0, range 0–1).

3.4. Complications

All patients were hemodynamically stable throughout the procedures and there were no periprocedural deaths or coronary artery compromise. In one patient (no. 6), the RVOT stent migrated into the right ventricle after placement and the patient was sent for surgery. This occurred early in the series and in retrospect was avoidable. In 2 patients (nos. 17 & 23) the stent migrated proximally while withdrawing the BIB; the Andrastent remained in satisfactory position and both patients later proceeded to Melody valve implantation. Crumpling of the stent

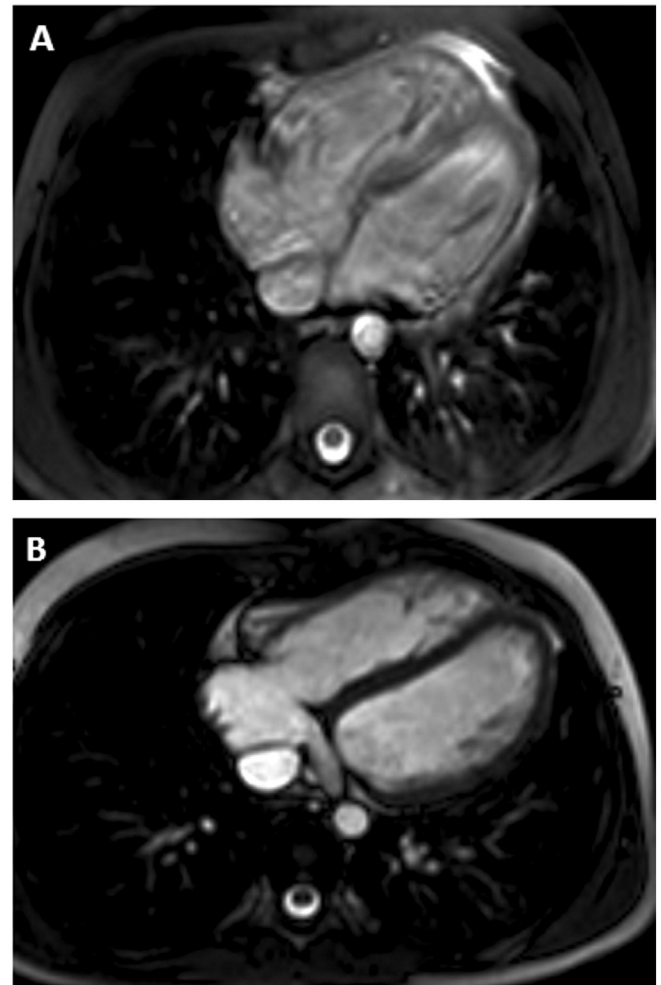


Fig. 5. Four chamber MRI imaging. MRI before (A) and following (B) pulmonary valve implantation. Decrease in volume of right ventricle and increase in left ventricular volume.

during valved stent insertion was observed in 4 patients (nos. 5, 9, 12 and 22) (Fig. 6). In patient 5 (SAPIEN valve), the pre-stent was implanted with the BIB balloon overinflated to 25 mm; at that point in our experience we opted not to use a Melody valve because of recommended maximum size. We first tested passage with the Sapien delivery system – this resulted in scrunching the stent. Consequently, we decided on a hybrid approach from subxyphoidal 2 months later which allowed easy deployment after reopening the pre-stent with a covered CP stent. In the other 3 patients, scrunching occurred during advancement of the Ensemble delivery system, but this did not preclude optimal positioning for valve implantation. In patient 23 (pre-stenting up to 26 mm) the landing zone was first trimmed down to 24 mm by means of a covered CP stent. The Melody valve was then deployed using a 22 mm Ensemble. However, after withdrawal of the Ensemble, the Melody migrated proximally (insufficient expansion) but remained within the original pre-stent. The Melody valve was subsequently further expanded using a 24 mm BIB and was safely secured.

4. Discussion

Results of this study show that PPVI in young patients with dilating, conduit free non-stenotic RVOTs is feasible. Creation of an adequate landing zone by pre-stenting the RVOT makes the subsequent PPVI procedure safe and predictable.

Ninety six percent of stents were safely implanted in the conduit free RVOTs. This finding is in agreement with recent reports showing that stents can be securely positioned in larger outflow tracts with a waist

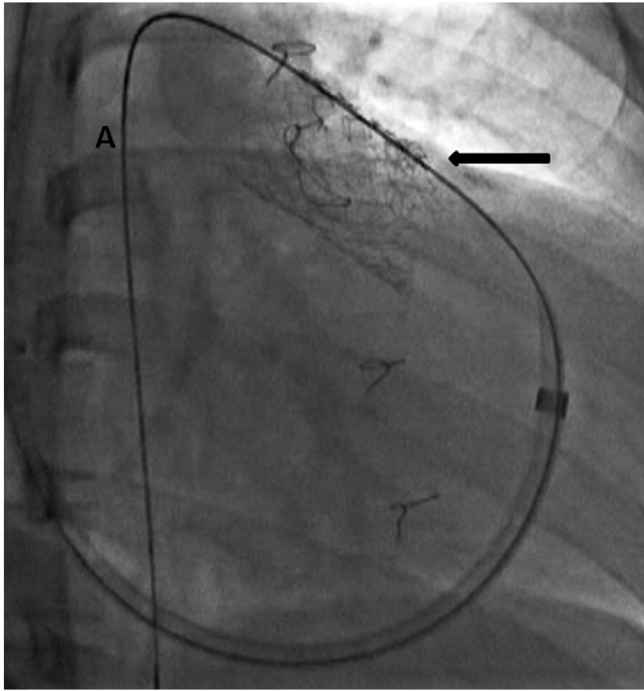


Fig. 6. Frontal projection of crumpled stent. At reentry of the stent 2 months after initial deployment in patient 5, crumpling of prestent occurred (arrow).

[10,11]. It should be emphasized that this study was carried out in younger patients using a different strategy – earlier stenting for a progressively dilating RVOT with the aim to prevent large aneurysmal dilation of the RV and RVOT with the intention to normalize “early” right ventricular volumes. Our results demonstrate that stents can be safely secured if a stretched retention zone of ≤ 24 mm exists during semi-compliant balloon interrogation of the RVOT.

A potential disadvantage of RVOT stent placement is that pulmonary regurgitation persists or may even be aggravated, but none of our patients became symptomatic; pulmonary regurgitation is known to be well tolerated for a limited period [15]. A stent in the RVOT is expected to fix the size and prevent further dilation of that zone; this maneuver may delay the need for pulmonary valve implantation for months or years, but this possibility was not explored in the current study.

4.1. Follow-up

During our short term follow-up, right ventricular dimensions and volumes reduced in all patients – a finding reported in other studies [11]. Furthermore, subjective parameters of exercise ability improved during short term follow-up. These and other outcomes will receive attention in the course of the ongoing phase of this study.

We observed no stent fractures or stent compressions; the rounded shape remained preserved in all patients. The absence of stent compression-fracture is important for the longevity and long-term function of the valves. This observation is quite different compared to Melody valves implanted in shrunken homografts and other conduits: in our group of patients the RVOT is large and dilated and the place for the stent-valve was already provided – we consider it unlikely that the heart or surrounding tissues would exert significant localized compressing forces on the stents.

4.2. Complications

Overall, complications could be managed. The stent which migrated could have been avoided and occurred during the early learning curve.

Factors leading to the embolization included selection of a too short stent as well as incorrect positioning.

4.3. Changes of management strategies

Early surgical repair of tetralogy of Fallot remains the treatment of choice [1]. In the 1960s, postoperative death was predominantly related to residual stenosis, while pulmonary regurgitation was considered well tolerated [16,17]. However, after an event free period of 2 to 3 decades, patients started presenting with episodes of ventricular tachycardia and sudden death [1,3]. It then became clear that pulmonary regurgitation (PR) was not indefinitely tolerated but caused a progressive deterioration of right ventricular function and electrical stability [18]. Patients were initially considered for pulmonary valve implantation only when they became symptomatic, but it soon became clear that this strategy yielded suboptimal results. Several studies showed that a pulmonary valve at that stage allowed little if any recuperation of RV size and mechanical dysfunction, with persistence of electrical instability [19–23].

Pulmonary valve implantation at an earlier stage was clearly indicated. The perfect treatment should consist of valve replacement with a valved conduit of adult dimensions with no procedural risk and perfect long-term function of the valve. However, this perfect solution in patients with tetralogy of Fallot was not available in the nineties: operative risk was low but not zero, and all valved conduits had a limited lifespan requiring several surgical replacements with a progressive difficulty-morbidity-risk [24]. Thus, avoiding a “too early” replacement and ideal timing became important in order to reach the ultimate end-point: reach old age without cardiac events and with adequate exercise performance. Assessing strategies with such distant end-points is difficult. The search for the best surrogate end-point or predictive marker for irreversible or late dysfunction started: RV size, RV systolic or diastolic function, regurgitant fraction, exercise capacity etc. Currently, the marker most commonly used is RV size measured with MRI volumetrics with a current end diastolic threshold of 160–170 ml/m² [24]. Pulmonary valve implantation just below this marker predicts some (but incomplete) diminishing of RV size; however, this threshold has not been shown to be predictive or associated with a good survival free of cardiac events until old age. Several authors now advocate more restrictive volumes in the guidelines since it appears that the nearer to normal (average: 79 ± 14 ml/m²) right ventricular volumes return after PVR, the better the right ventricular substrate can remodel with lengthier electrical stability [24–30]. As clinicians, we should remain open-minded: we should not repeat the errors of the late 1980s when we presumed that any degree of PR would be well tolerated for a lifetime. Equally so, we must remain critical towards the current “guidelines” which have some logic background, but only consider upper limits of tolerance without knowledge of late outcome.

In the meantime, the therapeutic options have changed markedly: percutaneous pulmonary valve implantation at low (and progressively decreasing) risk is possible with valves that, if implanted under ideal conditions, are very competitive with good longevity [31]. This brings us back to the initial ideal treatment strategy: instead of seeing how far one can allow the RV to be damaged before compromising life expectancy and ventricular function, one might aim for pulmonary valve implantation when an adult sized valve can be implanted, provided this happens at near zero risk and with virtual perfect late outcomes. Such strategy allows to (hopefully) avoid going beyond the ill-defined point of irreversible damage to the RV. Conversely, earlier initial pulmonary valve implantation will induce different nature and timing of re-interventions, which over a lifetime may or may not be beneficial. With the current imperfect solutions, different strategies need to be explored, keeping in mind that the answer pertaining to the final outcome can only be expected in 3 to 4 decades.

4.4. Limitations

Due to the cross-sectional nature and small patient numbers of this specific subgroup, patients were not randomly assigned or compared to surgery; sample size is small and the current follow-up is short. However, the main objective of the initial phase of the study was to assess the feasibility and safety of our strategy. Paired MRI volumetric data were available in only a limited number of patients. This is due to the nature of the local referral and re-imburement system. Formal exercise testing was not performed in a structured fashion but was not the primary endpoint of this study and is now being prospectively collected. We also did not take into account other percutaneous valves now available since study was initiated before CE approval for those were obtained.

5. Conclusions

Post-surgical conduit-free non-stenotic RVOT with free pulmonary regurgitation can be stented and a pulmonary valve implanted percutaneously if anatomical (predominantly size) criteria are met. In experienced hands, the technique is safe with acceptable morbidity. Early results on functional class and RV size are promising. However, the long term superiority of any treatment strategy will only be answered in the decades to come.

Conflict of interest

Marc Gewillig is a proctor for NuMED, Medtronic and Edwards.

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References

- [1] G.E. Sarris, et al., Results of reparative surgery for tetralogy of Fallot: data from the European Association for Cardio-Thoracic Surgery Congenital Database, *Eur. J. Cardiothorac. Surg.* 42 (5) (2012) 766–774 (discussion 774).
- [2] Y. d'Udekem, et al., Tetralogy of Fallot: transannular and right ventricular patching equally affect late functional status, *Circulation* 102 (19 Suppl. 3) (2000) III116–III122.
- [3] E.J. Hickey, et al., Late risk of outcomes for adults with repaired tetralogy of Fallot from an inception cohort spanning four decades, *Eur. J. Cardiothorac. Surg.* 35 (1) (2009) 156–164 (discussion 164).
- [4] H.W. Kim, et al., Long term results of right ventricular outflow tract reconstruction with homografts, *Korean J. Thorac. Cardiovasc. Surg.* 44 (2) (2011) 108–114.
- [5] S.M. Yuan, et al., Right ventricular outflow tract reconstruction: valved conduit of choice and clinical outcomes, *J. Cardiovasc. Med. (Hagerstown)* 9 (4) (2008) 327–337.
- [6] T. Geva, Indications for pulmonary valve replacement in repaired tetralogy of Fallot: the quest continues, *Circulation* 128 (17) (2013) 1855–1857.
- [7] J.A. Cuyppers, et al., Unnatural history of tetralogy of Fallot: prospective follow-up of 40 years after surgical correction, *Circulation* 130 (22) (2014) 1944–1953.
- [8] T.S. Momenah, et al., Extended application of percutaneous pulmonary valve implantation, *J. Am. Coll. Cardiol.* 53 (20) (2009) 1859–1863.
- [9] P. Bonhoeffer, et al., Percutaneous insertion of the pulmonary valve, *J. Am. Coll. Cardiol.* 39 (10) (2002) 1664–1669.
- [10] D.E. Boshoff, et al., Off-label use of percutaneous pulmonary valved stents in the right ventricular outflow tract: time to rewrite the label? *Catheter. Cardiovasc. Interv.* 81 (6) (2013) 987–995.
- [11] M. Demkow, et al., Percutaneous pulmonary valve implantation preceded by routine pretesting with a bare metal stent, *Catheter. Cardiovasc. Interv.* 77 (3) (2011) 381–389.
- [12] Y. Boudjemline, et al., Outcomes and safety of transcatheter pulmonary valve replacement in patients with large patched right ventricular outflow tracts, *Arch. Cardiovasc. Dis.* 105 (8–9) (2012) 404–413.
- [13] S. Khambadkone, et al., Percutaneous pulmonary valve implantation in humans: results in 59 consecutive patients, *Circulation* 112 (8) (2005) 1189–1197.
- [14] M. Gewillig, L. Mertens, L. Stockx, Percutaneous fenestration of the atrial septum with a stent: an experimental study, *Cor Europeum* 4 (1995) 122–125.
- [15] J.L. Gibbs, et al., Right ventricular outflow stent implantation: an alternative to palliative surgical relief of infundibular pulmonary stenosis, *Heart* 77 (2) (1997) 176–179.
- [16] B.G. Barratt-Boyes, J.M. Neutze, Primary repair of tetralogy of Fallot in infancy using profound hypothermia with circulatory arrest and limited cardiopulmonary bypass: a comparison with conventional two stage management, *Ann. Surg.* 178 (4) (1973) 406–411.
- [17] E. Zaragoza-Macias, K.K. Stout, Management of pulmonic regurgitation and right ventricular dysfunction in the adult with repaired tetralogy of Fallot, *Curr. Treat Options Cardiovasc. Med.* 15 (5) (2013) 575–586.
- [18] B. Bouzas, P.J. Kilner, M.A. Gatzoulis, Pulmonary regurgitation: not a benign lesion, *Eur. Heart J.* 26 (5) (2005) 433–439.
- [19] J.G. Murphy, et al., Long-term outcome in patients undergoing surgical repair of tetralogy of Fallot, *N. Engl. J. Med.* 329 (9) (1993) 593–599.
- [20] G. Nollert, et al., Long-term survival in patients with repair of tetralogy of Fallot: 36-year follow-up of 490 survivors of the first year after surgical repair, *J. Am. Coll. Cardiol.* 30 (5) (1997) 1374–1383.
- [21] M.A. Gatzoulis, et al., Risk factors for arrhythmia and sudden cardiac death late after repair of tetralogy of Fallot: a multicentre study, *Lancet* 356 (9234) (2000) 975–981.
- [22] J. Therrien, G.R. Marx, M.A. Gatzoulis, Late problems in tetralogy of Fallot—recognition, management, and prevention, *Cardiol. Clin.* 20 (3) (2002) 395–404.
- [23] J. Therrien, et al., Pulmonary valve replacement in adults late after repair of tetralogy of Fallot: are we operating too late? *J. Am. Coll. Cardiol.* 36 (5) (2000) 1670–1675.
- [24] T. Geva, Repaired tetralogy of Fallot: the roles of cardiovascular magnetic resonance in evaluating pathophysiology and for pulmonary valve replacement decision support, *J. Cardiovasc. Magn. Reson.* 13 (2011) 9.
- [25] E.W. Cheung, W.H. Wong, Y.F. Cheung, Meta-analysis of pulmonary valve replacement after operative repair of tetralogy of Fallot, *Am. J. Cardiol.* 106 (4) (2010) 552–557.
- [26] T. Oosterhof, et al., Preoperative thresholds for pulmonary valve replacement in patients with corrected tetralogy of Fallot using cardiovascular magnetic resonance, *Circulation* 116 (5) (2007) 545–551.
- [27] A. Frigiola, et al., Physiological and phenotypic characteristics of late survivors of tetralogy of Fallot repair who are free from pulmonary valve replacement, *Circulation* 128 (17) (2013) 1861–1868.
- [28] H. Tandri, et al., Normal reference values for the adult right ventricle by magnetic resonance imaging, *Am. J. Cardiol.* 98 (12) (2006) 1660–1664.
- [29] C.H. Lorenz, The range of normal values of cardiovascular structures in infants, children, and adolescents measured by magnetic resonance imaging, *Pediatr. Cardiol.* 21 (1) (2000) 37–46.
- [30] A. Frigiola, et al., Biventricular response after pulmonary valve replacement for right ventricular outflow tract dysfunction: is age a predictor of outcome? *Circulation* 118 (14 Suppl.) (2008) S182–S190.
- [31] M.J. Gillespie, et al., Sutureless mitral valve replacement: initial steps toward a percutaneous procedure, *Ann. Thorac. Surg.* 96 (2) (2013) 670–674.