CLINICAL RESEARCH

Outcomes and safety of transcatheter pulmonary valve replacement in patients with large patched right ventricular outflow tracts

Résultats de l’implantation percutanée de valves pulmonaires chez les patients ayant des voies d’éjection droite patchées

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KEYWORDS
Congenital heart disease; Transcatheter pulmonary valve replacement;

Summary
Background. — Although globally accepted, the indication for implantation of the Melody\textsuperscript{®} (Medtronic Inc., Minneapolis, MN, USA) transcatheter pulmonary valve is limited to the treatment of haemodynamically dysfunctional right ventricular outflow tract (RVOT) with right ventricle to pulmonary artery (PA) obstruction. The use of the Melody valve for haemodynamically significant isolated pulmonary regurgitation has not been evaluated.

Abbreviations: LPA, left pulmonary artery; MPA, main pulmonary artery; MRI, magnetic resonance imaging; PA, pulmonary artery; RPA, right pulmonary artery; RV, right ventricle/ventricular; RVOT, right ventricular outflow tract.

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Melody® (Medtronic Inc, Minneapolis, Minnesota, États-Unis) was evaluated in a series of 13 patients with patched right ventricular outflow tract (RVOT) conduits < 22 mm in diameter as an alternative to surgical replacement [1–4]. The device is available in a single size (diameter of 18 mm; dilatable up to 22 mm). Since the first human case report, several published reports have demonstrated uniform efficacy and outcomes in selected populations [1–8]. With the rising volume of patients who are surviving complex congenital heart surgeries, there is now a need to broaden the indications for Melody valve implantation.

We report on the use of the Melody valve in patients with a patched right ventricular outflow tract with pulmonary regurgitation and absence of any obstruction, as a case series.

Methods

The data were derived from an ongoing prospective multicentre non-randomized trial (REVALV; Medico-economic Evaluation of a Non chirurgical Pulmonary Valve Replacement) to evaluate outcomes after Melody transcatheter pulmonary valve implantation in France; formal approval was given by the French Ministry of Health in May 2008. Patients with a dysfunctional RVOT conduit were identified and evaluated by investigators. All patients had a preinclusion evaluation that involved a clinical examination, a surface electrocardiogram, echocardiography, exercise testing and magnetic resonance imaging (MRI) or cardiac catheterization. The Melody valve was implanted using a standard transcatheter approach, with all procedures performed by experienced interventional cardiologists [9].

Background

Aim. — We evaluated the outcomes of Melody valve insertion in patients with a large patched RVOT.

Methods. — We analysed procedural and short-term outcomes data from 13 patients who underwent Melody valve implantation for a large RVOT with significant pulmonary regurgitation as the primary lesion. RVOT preparation was done in all patients using the Russian dolls technique and/or the PA jailing technique. Melody valve insertion was performed concomitantly in 10 patients and after 1 to 3 months in three patients.

Results. — All procedures were successful. The mean follow-up period was 30 ± 4 months after the procedure. There was no incidence of stent fracture, migration or embolization. Only one patient who underwent the jailing technique developed a significant paraprosthetic leak and is scheduled for redilatation of the Melody valve.

Conclusions. — Careful patient selection, balloon sizing and RVOT preparation with pre-stenting using the Russian dolls technique and/or the PA jailing technique are required to modify the RVOT for transcatheter valve implantation. Short-term follow-up showed competent valves with no stent fracture or migration and appears promising. Wider experience with long-term outcomes may be required to standardize the procedure in such a subset of patients.

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Résumé Bien que largement acceptées dans le monde, les indications de valvation percutanée sont limitées au traitement des dysfonctionnements de conduits prothétiques interposés entre le ventricule droit (VD) et l’artère pulmonaire (AP). L’utilisation de la valve Melody (Medtronic Inc, Minneapolis, Minnesota, États-Unis) n’a pas été évaluée pour les fuites pulmonaires isolées.

But. — Nous avons évalué le devenir de l’implantation de Melody chez des patients avec une voie VD-AP patchée et large.

Méthodes. — Nous avons analysé les données de procédure et le devenir à court terme de 13 patients ayant reçu une valve Melody. La voie VD-AP a été préparée chez tous les patients avant la valvulation par un proustenting en utilisant deux techniques (la technique des poupées russes et/ou la technique d’emprisonnement d’une AP). La valvulation a été simultanée chez huit patients et après un délai de un à trois mois chez trois.

Résultats. — Toutes les procédures ont été réalisées avec succès. Le suivi moyen après la procédure était de 30 plus ou moins quatre mois. Aucun patient n’a eu de fracture de stent, de migration ou d’emboïlisation de stents. Seul un patient du groupe « emprisonnement » a développé une fuite paraprosthetique et est planifié pour une redilatation de la valve Melody.

Conclusions. — Une sélection soigneuse des patients, une calibration au ballonnet et une préparation de la voie VD-AP sont nécessaires pour pouvoir insérer une valve Melody aux patients ayant des voies VD-AP patchées. A court terme, la valve est compétente sans fracture de stent ni embolisation. Les techniques utilisées pour le proustenting sont prometteuses. Une expérience plus large est nécessaire pour standardiser la procédure et avoir plus de recul.

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Figure 1. Angiograms showing calibration of right ventricular outflow tract (RVOT) and pulmonary artery (PA) for selection of patients. (A and B) Angiograms in four-chamber (A) and lateral (B) views without balloon with a marked catheter. (C) Angiogram showing inflation of a balloon catheter in the RVOT and simultaneous injection in the Mullins sheath. (D) Angiogram showing inflation of a balloon catheter in the left PA and simultaneous injection in the Mullins sheath. Measurements are made according to the diameter of the balloon at the level of the expected landing zone.

tomography. Prospective patients were further evaluated by conventional cardiac catheterization to assess the degree of haemodynamic derangement and by RVOT angiography to define the RVOT and pulmonary artery (PA) morphology and thereby establish a strategy prior to Melody valve placement (Table 1). Balloon calibration was done in all patients for accurate sizing, using low pressure and compliant balloons. RVOT and individual PA diameters were measured at baseline and with balloon inflation (Fig. 1). All patients were screened to look for the position of the coronary arteries in regard to the RVOT, the right PA (RPA) and the left PA (LPA) (aortogram).

If stenosis was the primary indication and the right ventricle (RV)/aorta systolic pressure ratio was greater than 0.66, the patient was considered for standard pulmonary valve insertion. Elsewhere, one of two techniques or a combination of the two was used, as described below (Fig. 2).

### Preparation of the right ventricular outflow tract (RVOT) for melody valve insertion

**Pulmonary artery (PA) jailing technique**

The smallest or stenosed PA branch was used as an anchor for multiple stents and subsequently for Melody valve insertion. When the diameter of a PA branch was < 22 mm and the RVOT was > 22 mm, stenting was started from that PA branch all the way to the RVOT with overlapping uncovered stents, thus jailing the opposite PA (PA jailing technique). This novel

<table>
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<th>Table 1 Inclusion criteria.</th>
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<tr>
<td>Age ≥ 5 years</td>
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<td>Weight ≥ 20 kg</td>
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<tr>
<td>Non-circumferential RVOT conduit OR history of patch enlargement of the RVOT and/or one PA ≤ 26 mm in diameter in systole on MRI</td>
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</table>

MRI: magnetic resonance imaging; PA: pulmonary artery; RVOT: right ventricular outflow tract.
technique was utilized only if the main PA (MPA), RPA or LPA diameter measured \(< 25\) mm, otherwise the patient was deemed anatomically unsuitable for the jailing technique.

Uncovered bare-metal stents with open-cell design were used for this application (MaxLD 36 mm, ev3, Irvine, CA, USA). The first stent was crimped over a BIB balloon (Numed Inc., Hopkinton, NY, USA) and deployed in the suitable branch PA. The same balloon was used for deploying additional stents of same type and length below the first one, going all the way to the RVOT. An overlap of 50% was achieved. After deployment of the last stent, an MPA angiogram was performed to look for patency of the contralateral vessel (Figs. 3 and 4).

Russian dolls technique

If the PAs were large and unsuitable for anchoring, then multiple stents with decremental diameters were deployed in the RVOT region to reduce its size and allow proper seating of the Melody valve (Fig. 5). Again, only patients with MPAs \(\leq 26\) mm were included. For this technique, the stent of choice was a high-profile stent (CP 8Z45 or 8Z39 covered and uncovered, Numed Inc.). The stent was manually crimped on a balloon catheter (25 mm, Balt, Montmorency, France; BIB 24 and 22 mm; Numed Inc.) and placed in the RVOT. The balloon was chosen according to the MPA diameter; for example, if the RVOT measured 24 mm, a 25 mm balloon was chosen. Additional stents were subsequently inserted using balloons of smallest diameter with a decrement of 1 to 2 mm until 22 mm. To obtain a ‘conduit of sufficient length and strength’, stents were placed to cover the entire length of the RVOT with an overlap \(\geq 50\%\).

Combined technique

In patients with large MPAs (24–26 mm) and one PA \(< 22\) mm, a jailing technique was used, as described previously. The distance between the implanted stent and the MPA wall was measured. If this distance was \(> 2\) mm, one or two additional covered stents mounted on a 22 mm BIB balloon (CP 8Z39, Numed Inc.) were placed within the previously implanted stents in the MPA (Russian dolls technique). The additional overlapping stents used in this technique, together with the anchorage in the PA branch, would thus reduce the RVOT size.
and allow secure and proper seating of the Melody valve with decreased risk of paraprosthetic leak.

**Melody valve insertion**

Melody valve implantation was performed either concomitant to or 1 to 3 months after the ’bare-metal stent preparation’. The insertion was accomplished using the standard implantation technique. Prestenting allowed a good landing zone for the Melody device, ensuring immediate and long-term stability. For the Russian dolls technique, the stiff wire may be parked in any PA branch before Melody valve insertion. However, while using the jailing technique, extreme care was exercised to position the stiff guide wire.
in the jailed PA to identify the MPA bifurcation and thereby prevent accidental and possibly catastrophic covering of a PA branch. The guide wire was placed in the jailed PA and the stent struts dilated with balloon inflation to facilitate advancement of the delivery system. If this could not be achieved due to difficult angulation or other technical reasons, the wire was parked in the stented PA and extreme care was exercised to prevent any degree of occlusion to the jailed PA by the stent covering of the Melody valve. The valve was inserted by a standard technique using a 22 mm Ensemble catheter (Medtronic Inc.). The valve was positioned within the prestented region as low as possible and well below the MPA bifurcation. Postdilatation of the Melody valve using a balloon of appropriate diameter (22 or 24 mm) was done to reduce the amount of paraprosthetic leak. Table 2 gives the final external diameter of the Melody valve postdilatation with a 22 mm balloon catheter, as it appears in the manufacturer’s instructions for use. Haemodynamic and angiographic assessments were repeated at the end of the procedure. All patients received intravenous heparin and antibiotic prophylaxis during and after the procedure according to institutional protocol.

**Results**

Following clinical and non-invasive screening, 15 prospective patients were considered for cardiac catheterization evaluation prior to Melody pulmonary valve implantation. After careful evaluation in the cardiac catheterization laboratory, two patients were considered as candidates for surgery due to inappropriate anatomy and the remaining patients satisfied the inclusion criteria for possible Melody valve insertion (Fig. 6). The excluded patients had both MPA and PA branches > 26 mm in diameter after careful balloon sizing.

The diameter of the MPA on MRI varied from 16 to 26 mm. The diameters of the LPA and RPA on MRI varied from 11 to 26 mm. After balloon calibration, the diameters were > 24 mm in three patients. The diameter of the RPA or LPA was < 22 mm in five patients. A PA branch stenosis was present in two patients. For a large RVOT and large PA, the method of choice was the Russian dolls technique; this method was utilized in six patients. For a large RVOT with favourable PA dimensions, the jailing technique was preferred; this method was utilized in three patients. A combination was used in two patients to allow adequate preparation of the RVOT before Melody valve insertion. The remaining two patients had the Melody valve placed using a conventional technique.

Multiple bare-metal stents (1–4, with a median of 3) were used in each patient, with no stent migration or embolization noted in any patient but one. One patient from the Russian dolls technique group did have a secondary dislodgement; the stent moved from its original position during the advancement of the Ensemble delivery system during valve implant. The stent was secured in its initial position using two additional bare-metal stents and we proceeded successfully with the Melody valve insertion.

One of the patients with LPA stenosis who underwent the jailing technique using the stentor valve as an anchor required elective recatheterization 48 hours after valve

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**Figure 5.** Angiograms demonstrating the Russian dolls technique in a patient with single right pulmonary artery (PA). (A and B) Angiogram in oblique view during diastole (A) and systole (B) showing the change of diameter during the cardiac cycle. (C) Bare-metal stent insertion to reduce the diameter of the PA. (D) Final result showing excellent function of the Melody valve.
Table 2  Sizing information adapted from the manufacturer’s instructions for use of the Melody valve implant.

<table>
<thead>
<tr>
<th>Delivery system size (outer balloon)</th>
<th>Outer balloon applied pressures atm</th>
<th>Corresponding valve outside diameter (mm)</th>
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<tr>
<td>Size 18 mm (9 mm × 3.5 cm/19 mm × 4 cm)</td>
<td>1 2 3 4 RBP&lt;sup&gt;a&lt;/sup&gt;</td>
<td>17.93 18.57 19.42 20.06&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Size 20 mm (10 mm × 3.5 cm/20 mm × 4 cm)</td>
<td>1 2 3 4 RBP&lt;sup&gt;a&lt;/sup&gt;</td>
<td>19.65 20.70 21.73 22.42&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Size 22 mm&lt;sup&gt;b&lt;/sup&gt; (11 mm × 3.5 cm/22 mm × 4 cm)</td>
<td>1 2 3 RBP&lt;sup&gt;a&lt;/sup&gt;</td>
<td>21.80 22.79 24.06&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

atm: atmosphere; RBP: rated burst pressure = maximum applied pressure.
<sup>a</sup>Do not exceed these pressure values for either the inner or outer balloon of the delivery system size.
<sup>b</sup>Note the external diameter of the device after inflation at 22 mm.

implantation due to persistent elevated isosystemic systolic LPA and RV pressures. The jailed RPA was angiographically patent but the flow was preferably directed towards the hypoplastic LPA. The stent jailing the RPA was crossed and the stent struts were dilated using non-compliant balloon inflation. Systolic RV and PA pressures reduced to 40 mmHg immediately after the procedure.

Timing of Melody valve implantation and follow-up

The valve implantation was performed concomitantly to the RVOT preparation procedure in 10 patients and 1 to 3 months later in three patients. In all patients in whom the procedure was intended, implantation was successfully completed using a single Melody valve over a 22 mm delivery system. There was no stent migration or valve displacement during the procedure or after 32 ± 4 months (5–42 months) of follow-up. The valve showed good competence with no paraprosthetic leaks, stent fractures or elevation of RV/PA pressures on last follow-up. None of these patients required urgent or delayed surgery. Follow-up echocardiography and MRI did not reveal significant pulmonary regurgitation or paraprosthetic leaks, except in one patient. One patient who underwent the jailing technique experienced a significant paraprosthetic leak and is scheduled for repeat dilatation of the Melody valve.

Discussion

Although it has been previously shown that the Melody valve can be implanted in patients with chronic pulmonary valve regurgitation in the presence of a RVOT patch, this indication remains controversial and is generally considered as a contraindication to such a procedure [1–8]. Moreover, among the four patients reported by Momenah et al. [7], all but one had mixed lesions with significant RV to PA obstruction. In our study, all patients had pulmonary regurgitation as the primary lesion rather than obstruction.

RVOT prestenenting has been shown to reduce Melody fracture and is recommended prior to Melody implantation [9]. The importance of RVOT prestenenting in patients with patch enlargement and dynamic translated motion deserves special emphasis. Moreover, prestenenting provides a stable circumferential platform and a great means of scaffold for Melody valve stability. In the given population, several important technical considerations are highlighted. Abnormal haemodynamics and complex anatomy play a major role in decision-making and technique selection. In the presence of elevated RV systolic pressure with a significant RV to PA gradient, percutaneous pulmonary valve insertion can be safely accomplished using a standard technique, with pre-procedure coronary angiography in selected cases. For all other types of dysfunctional RVOTs, the standard technique alone may not be useful and careful anatomical evaluation is required to define the possible strategy. Besides the conventional Melody implantation, we used two other types of techniques or a hybrid of both to make the RVOT suitable for Melody insertion; these were the Russian dolls technique and the jailing technique. Careful preprocedure patient screening was mandatory before proposing suitability and type of technique. Calibration of the MPA and its branches (i.e. MPA, RPA and LPA) with a balloon catheter was necessary before deciding if a platform for Melody could be made. During the study period, out of more than 100 patients screened, most were excluded by non-invasive assessment
(MRI) and only a small proportion of patients were considered for catheterization assessment. Two patients out of 15 were excluded after balloon sizing due to unsuitable anatomy.

While the Russian dolls technique was always an option with a large RVOT, we electively used the jailing technique (or hybrid) when possible because we believe it offers a more stable and secure platform for fixing the valve implant. However, this latter technique was only possible in half of the patients with low RV systolic pressure.

The choice of stent is crucial for both techniques. With the Russian dolls technique and the aim of reducing the MPA...
diameter, high-profile stents should be used. For the jailing technique, it is important to use an open-cell non-covered stent to anchor the PA branch and maintain uninterrupted flow in the contralateral jailed PA branch. There was a single patient with a large RVOT who had a significant paraprosthetic leak after the jailing technique. After this case we utilized the hybrid approach, combining the jailing technique with placement of additional high-profile stents in the RVOT prior to Melody valve implantation. These techniques can be utilized either with the Melody valve or the SAPIEN pulmonic valve (Edwards Lifesciences, Irvine, CA, USA). The advent of and experience with the SAPIEN pulmonic valve may be very interesting as it is also available in larger diameters. Unfortunately, we were unable to test the utility of this valve for large RVOTs, as the device is currently available only for investigational use in France.

Procedural complications

The procedure carries a risk of embolization at various steps and thus each manoeuvre must be done carefully. The measurement of PA diameters, selection of balloon catheter, first stent implantation, manipulation inside the stent after implantation and advancement of the delivery system for valve implantation are some very important steps that merit special attention. Stent displacement occurred in a single patient; the previously placed bare-metal stent moved from its position during advancement of the Ensemble catheter. With partially inflated balloon support, the stent was pulled back and redeployed at the suitable location. Another stent was deployed over this stent. We thought that this occurred secondary to underestimation of the size of the initial balloon catheter. A third stent was therefore placed to sufficiently reduce the PA diameter prior to the placement of the Melody valve. Complications like these can be limited by various measures. First and foremost, patient selection with balloon calibration and sizing should be performed carefully in multiple projections. This will also help with selection of the balloon to be used for stent placement. Secondly, a staged approach with RVOT preparation and valve implantation performed in two separate sessions, 1 to 3 months apart, is favoured. We believe this allows enough time for tissue scaffold, thereby reducing the RVOT/MPA width and thus the risk of embolization. However, most of the patients in our study had a one-step procedure with excellent results. The staged approach should be considered especially in patients with a large RVOT diameter (26 mm) to begin with where multiple stents are required before Melody implant, in patients where the Russian dolls technique has been applied and in patients with complex RVOT anatomy where advancement of the sheath for bare-metal stent implant is difficult and/or where difficulties in advancing the Ensemble delivery catheter are predicted.

Follow-up

All patients showed good valve function on follow-up. Only one patient developed a paravalvular leak that was greater than trivial during follow-up. Besides a detailed echocardiogram, all patients underwent an X-ray examination to rule out stent fracture or displacement. No stent fracture was seen in any patient until the last follow-up. With good RVOT preparation, we are confident that even if it occurs late it may not have an impact on the risk of secondary embolization or valve function. Unlike a prostatic conduit, the implant is presumably fixed to the wall of the PA fairly quickly, as seen in experimental work.

Study limitations

This paper is a description of a series of patients without statistical analysis, from which no general conclusion can be drawn. The report describes only a small number of patients; more must be studied before such patients can be considered as candidates for percutaneous valve insertion with current devices.

Conclusion

Surgically repaired tetralogy of Fallot with transannular patch plasty and a large RVOT with haemodynamically significant regurgitation may be considered for percutaneous pulmonary valve implantation. Careful patient selection, balloon sizing and RVOT preparation with pretesting using the Russian dolls technique and/or the PA jailing technique are required to modify the RVOT for transcatheter valve implantation. Short-term follow-up showed competent valves with no stent fracture or migration and appears promising. Wider experience with long-term outcomes may be required to standardize the procedure in such a subset of patients.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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