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# Percutaneous pulmonary valve implantation within bioprosthetic valves

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**Aims** Replacement of bioprosthetic valves in the right ventricular (RV) outflow tract (RVOT) is inevitable due to acquired valvar dysfunction. Percutaneous pulmonary valve implantation (PPVI) may result in acceptable clinical improvement avoiding surgical reintervention. To report outcomes of PPVI in dysfunctional surgically implanted bioprosthetic valves.

**Methods and results** All children undergoing PPVI into a bioprosthetic pulmonary valve between October 2005 and February 2008 were reviewed. Acute haemodynamic changes were compared and an analysis of variance applied to assess changes in ventricular geometry and pressure over time. Fourteen children (seven males), median weight 57.8 kg and 14.7 years of age were identified, with an echocardiographic RVOT gradient of 59.6 $\pm$ 26.8 mmHg and a pulmonary regurgitation (PR) grade of 3.6 $\pm$ 0.8 (out of 4). Implantation was successful in all. Twenty-four hours after implantation, there was a significant improvement in RV pressure (RVP) (from 82.2 $\pm$ 15.6 to 59.4 $\pm$ 9.9 mmHg, $P < 0.001$) and degree of PR to 0.6 $\pm$ 0.9 ($P < 0.001$). Mean hospital stay was 2.0 $\pm$ 0.4 days. Freedom from reintervention was 92 and 89% at 1 and 2 years, respectively. Follow-up echocardiography (mean 12.9 $\pm$ 9.8 months) revealed a further reduction in RVP ($P < 0.001$) and RVOT gradients ($P < 0.001$) and an increase in left ventricular end-diastolic volume ($P = 0.01$) and aortic valve annulus diameters ($P < 0.001$).

**Conclusions** Percutaneous pulmonary valve implantation for RVOT dysfunction in a previously implanted prosthetic valve is feasible and safe. Short-term follow-up data are encouraging, yet longer-term information is required to determine if this form of palliation has a significant impact on management strategies.

**Keywords** Congenital heart disease • Interventional cardiology • Paediatric cardiac catheterization • Percutaneous pulmonary valves • Conduits

## Introduction

Right ventricular (RV) outflow tract (RVOT) dysfunction is a common problem after surgical repair of congenital heart disease.[1–3] Surgical revision may employ valved conduits, homografts, or bioprosthetic prosthetic valves. These implants can degenerate leading to obstruction, pulmonary regurgitation (PR), or both, and as a result often require multiple surgical revisions.[4–6] Recently, percutaneous pulmonary valve implantation (PPVI) has provided an option for non-surgical management.[7–8] This novel technique leads to a reduction of right ventricular pressure (RVP) and improvement in symptoms. In this study, we review our early results of PPVI in children who had a previously implanted bioprosthetic valve.

## Methods

### Study subjects

Medical and cardiac catheterization records of all children who underwent PPVI from October 2005 to February 2008 were retrospectively reviewed. Those who had received a valve implantation in other than a bioprosthetic valve were excluded. Ethics board approval was obtained and a waiver of consent granted due to the retrospective nature of the review. Follow-up was obtained on all children in 2008 and was 100%

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complete. Indications for the procedure included RV pressure overload from outflow tract obstruction (RVP-to-systemic pressure ratio >0.66), significant pulmonary insufficiency, RV dilation, or RV failure.[8]

## Procedural details of percutaneous pulmonary valve implantation

All cases were performed under general anaesthesia. Vascular access was achieved either from the femoral ($n = 11$) or internal jugular veins ($n = 3$). A standard right heart catheterization and haemodynamic study was performed with systemic arterial pressure monitoring. Right ventricular outflow tract and branch pulmonary artery (PA) angiography was performed before implantation to assess PR and determine appropriate site of stent deployment (*Figure 1*). The valve implant diameter (18, 20, or 22 mm) was chosen to be 1–2 mm greater than the internal diameter of the prosthesis, which itself was generally 3 mm less than the rated outer diameter (*Figure 2*). Technical details of PPVI have been described previously.[8] In brief, an ultra extra-stiff exchange guide wire (Cook, Inc., Bloomington, IN, USA) was positioned in either the right or the left PA, and a Melody™ transcatheter pulmonary valved stent mounted on the appropriate Ensemble™ delivery system (Medtronic, Inc., Minneapolis, MN, USA) advanced to straddle the prosthesis (*Figures 1* and *2*) and inflated in place. Angiography and haemodynamics were repeated after implantation. Valve dysfunction was categorized as predominantly stenotic (RVOT peak-to-peak pressure gradient >40 mmHg with less than moderate PR); predominantly regurgitant (more than moderate PR with a RVOT peak-to-peak pressure gradient <40 mmHg); or mixed (RVOT peak-to-peak pressure gradient >40 mmHg and more than moderate PR).

## Echocardiography

Echocardiography was performed in all children before and within 24 h after PPVI, with peak instantaneous pressure gradients reported. The RVP was calculated from the tricuspid regurgitant jet, and the grade of PR determined by the appearance of the regurgitant jet on colour-flow Doppler mapping. The severity of PR was classified as 0 = none or trivial, 1 = mild (no retrograde diastolic flow in pulmonary trunk with detectable regurgitant jet in RV outflow), 2 = moderate (retrograde diastolic flow in main PA), or 3 = severe (additional retrograde diastolic flow in branch PA).[9] Right ventricular and left ventricular (LV) dimensions were measured echocardiographically. All echocardiograms were reviewed by single investigator (K.A.).

## Statistical analysis

Data are presented as medians, standard deviation, and ranges wherever appropriate. Statistical significance was taken as a *P*-value of <0.05. Differences before and after intervention were compared

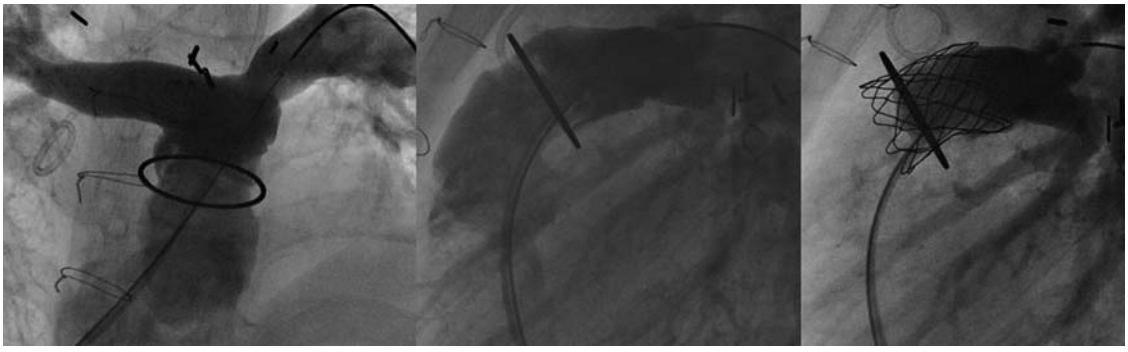

**Figure 1** Left panel: cranial-left anterior oblique projection of an angiogram performed above the pulmonary valve defining the confluence of the branch pulmonary arteries and distance of the valve from the pulmonary artery bifurcation. Middle and right panels: left lateral projections with injections above the valves before and after implantation. Note the absence of regurgitation after the valve implant.

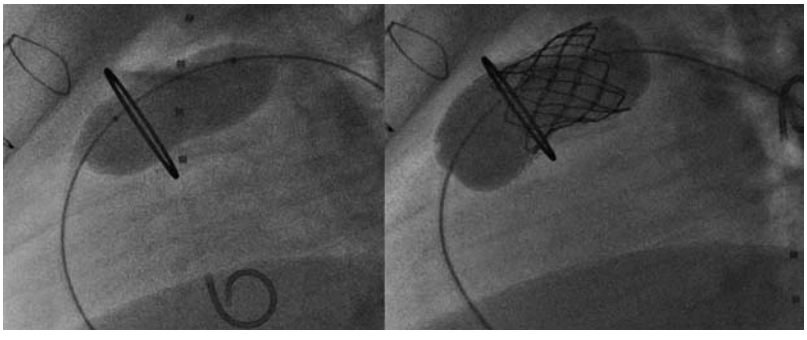

**Figure 2** Left panel: sizing balloon inflated across the bioprosthetic implant. Note that the fully expanded balloon is smaller than the opaque ring of the bioprosthetic valve, and right panel, during expansion of the Melody™ valve in the bioprosthetic valve ring.

using a Mann–Whitney test (two sided) due to the small sample size and non-normal distribution. We modelled follow-up echocardiographic derived variables (ventricular dimensions, valve annulus, and estimated pressures) using a linear regression model adjusted for repeated measures over time. Given the fact that measurements closer together in time are more closely correlated, we used an autoregressive covariance structure with a generalized estimation equations model (PROC GENMOD). All echocardiographic derived variables were entered into the model separately and tested at univariate level. All statistical analyses were performed using SAS statistical software v9.1 (The SAS Institute, Cary, NC, USA).

# Results

## Baseline characteristics

Of the 30 PPVI that occurred during this time period, 13 children and 1 adolescent had a previously implanted prosthetic valve, either a Hancock™ porcine valves ($n = 12$; valve diameter 18 mm $n = 1$, 21 mm $n = 1$, 22 mm $n = 3$, 23 mm $n = 1$, 25 mm $n = 5$, or 26 mm $n = 1$, Medtronic, Minneapolis, MN, USA) or Symbion™ valves ($n = 2$, 23 mm or 25 mm, Symbion, Inc., Salt Lake City, UT, USA) (*Table 1*). Mean age was 15.4 ± 2.0 years (range 13.0–19.0 years) and weight 56.8 ± 7.5 kg (range 42.2–71.1 kg). Fallot's tetralogy or one of its variants was the most common intracardiac lesion. Time from prosthetic valve implantation to PPVI was a mean 10.4 ± 4.0 years (range 3.7–18.2 years). Valve dysfunction was categorized as predominantly stenotic in 2; predominantly regurgitant in 2; and mixed in 10 children.

**Table 1 Cohort characteristics ($n = 14$)**

| | |
|---|---|
| **Gender** | **M: 7, F: 7** |
| Primary diagnosis | Tetralogy of Fallot ($n = 4$)<br>Pulmonary atresia with VSD ($n = 3$)<br>Truncus arteriosus ($n = 4$)<br>Double outlet right ventricle ($n = 2$)<br>Aortic insufficiency ($n = 1$) |
| RVOT morphology | Hancock conduit ($n = 11$)<br>Native outflow tract with valve implantation ($n = 3$) |
| Type of prosthetic valve | Symbion ($n = 2$)<br>Hancock ($n = 12$) |
| Time from prosthetic valve implantation to PPVI | 10.4 ± 4.0 years |
| Age (range) | 15.4 ± 2.0 (13.0–19.0) years |
| Body weight (range) | 56.8 ± 7.5 (44.2–71.1) kg |
| BSA (range) | 1.6 ± 0.1 (1.4–1.8) $m^2$ |
| Indications | Predominant stenosis ($n = 2$)<br>Predominant regurgitation ($n = 2$)<br>Combined lesion ($n = 10$) |
| Clinical symptoms | Exercise intolerance ($n = 5$)<br>Dyspnoea ($n = 2$)<br>Chest pain ($n = 1$)<br>Arrhythmia ($n = 1$)<br>Asymptomatic ($n = 5$) |

On chest roentgenography, calcium could be seen on the valve leaflets in 10 children. In two children with Symbion™ (Symbion, Inc.) valve, one was stented and the other balloon dilated at an earlier procedure.

## Immediate haemodynamic results

Percutaneous pulmonary valve implantations were performed through the femoral vein in 12 children and the internal jugular vein in 2 (*Figure 3*). Right ventricular pressures fell acutely from 62.2 ± 21.1 (range 34.0–110.0 mmHg) to 42.4 ± 11.4 mmHg (range 29.0–60.0 mmHg), $P < 0.005$, RVOT pressure gradients from 36.7 ± 19.4 (range 7.0–81.0 mmHg) to 12.9 ± 7.3 mmHg (range 2.0–32.0 mmHg), $P < 0.05$, and the ratio of RVP to aortic pressure (AoP) fell from 72 ± 19% (range 47–113%) to 45 ± 10% (range 32–61%), $P < 0.001$. Only one child had an RV to PA pressure gradient >25 mmHg after implant. There was no significant change in RV end-diastolic pressure [9.8 ± 4.8 (range 4.0–22.0 mmHg) to 9.3 ± 2.9 mmHg (range 4.0–14.0 mmHg), $P = 0.6$]. Angiography in the main PA after implantation showed significant improvement of PR (*Figure 1*). Mean fluoroscopy time was 31.3 ± 8.5 min (range 20.0–50.0 min).

## Procedural complications and hospital stay

One child (7.1%) was found to have a femoral artery pseudoaneurysm after the procedure, managed with a thrombin injection and a hospital stay of 3 days. All other children were discharged from hospital within 2 days of the procedure.

## Immediate echocardiographic findings

Echocardiograms within 24 h of PPVI revealed a significant reduction in RVPs from before the procedure [82.2 ± 15.6 (range 50.0–110.0 mmHg) to 61.0 ± 10.0 mmHg, (range 48.0–80.0 mmHg), $P < 0.01$] and RVOT gradients [59.6 ± 26.8 (range 19.0–106.0 mmHg) to 41.0 ± 19.1 mmHg (range 21.0–96.0 mmHg), $P < 0.05$, *Figure 4*]. Additionally, a significant improvement in the grade of PR, summarized in *Figure 5*, was documented, 10 children having Grade 3 before and 11 children having Grade 0 after the implant (3.6 ± 0.8 to 0.6 ± 0.9, $P < 0.001$).

## Time-related changes in echocardiographic data

Time-related changes in echocardiographic variables are shown in *Figure 6*. Estimated RVPs and RVOT pressure gradients were noted to fall gradually ($P < 0.001$) with time. At latest follow-up (mean 12.9 ± 9.8 months), mean RVP was 52.1 ± 14.4 mmHg, RVOT gradient 28.9 ± 12.7 mmHg, and RVP/AoP ratio 48 ± 15%. Also observed was an increase in aortic valve annulus diameters ($P < 0.001$) and LV end-diastolic dimensions ($P = 0.01$). There was no change in the degree of PR compared with immediately after the implant.

## Reintervention

During the study period, balloon dilation for an obstructed implant was performed in two children at 0.99 and 1.9 years after the procedure. Body weights at PPVI were 58.7 and 63 kg, and both

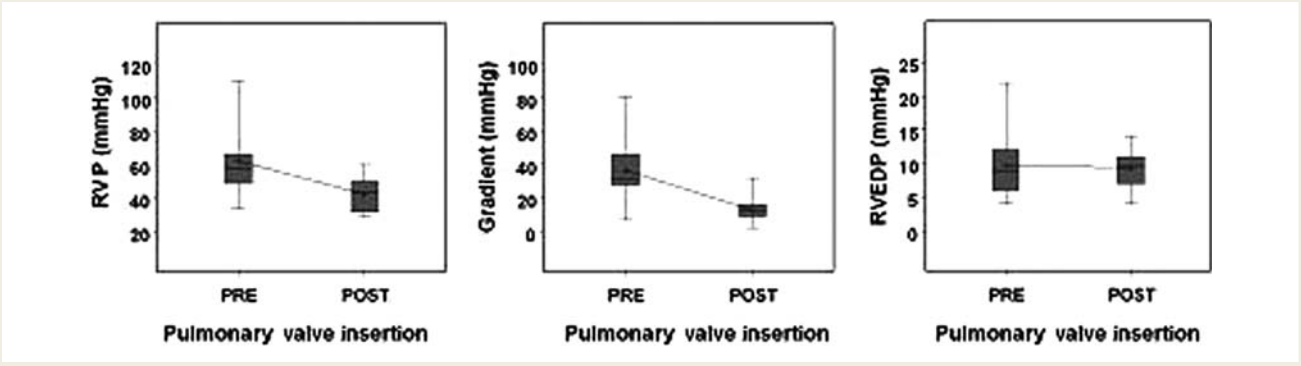


**Figure 3** Change in haemodynamics before and after percutaneous pulmonary valve implantation (PPVI). Plots (median = bold line, box= upper and lower limits, respectively, whiskers represent range, the mean is shown by black dot and adjoining line). Left panel: right ventricular (RV) systolic pressure (RVP). Middle panel: RV to pulmonary artery gradient. Right panel: RV end-diastolic pressure (RVEDP).

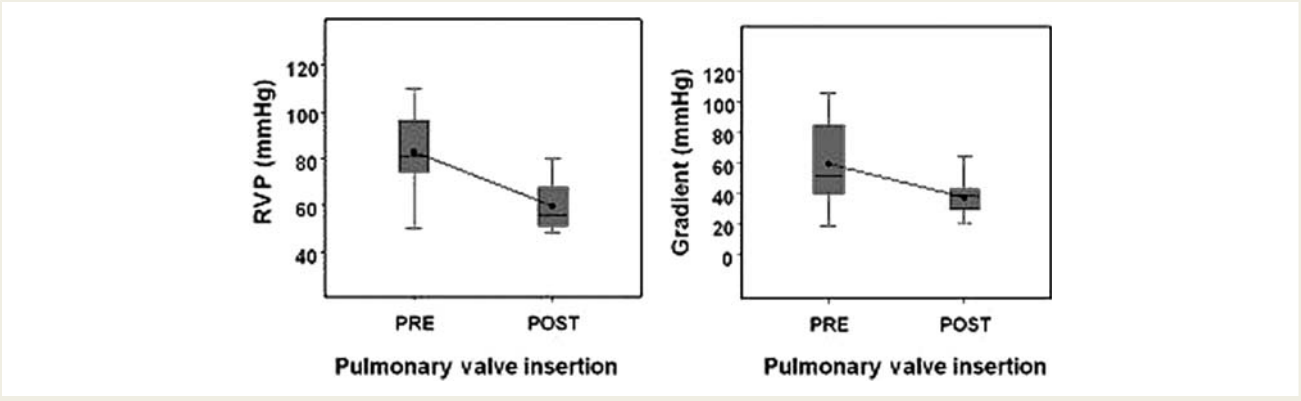


**Figure 4** Echocardiographic estimates before and after PPVI. Plots and abbreviations as in *Figure 3*. Left panel: RVP and right panel: RV outflow tract gradient.

children had previously implanted Hancock valves (25 and 18 mm). In the latter child, no change in RVOT gradient occurred and this child underwent surgical replacement, as they had outgrown the maximal outflow diameter that could be achieved. The other child had good result with the pressure gradient falling from 40 to 20 mmHg. Freedom from re-intervention was $100 \pm 0$, $91.7 \pm 7.8$, $81.5 \pm 12.0$, and $81.5 \pm 12.0$%, at 3, 12, 25, and 32 months, respectively. No stent fracture was identified during the study period by chest roentgenography.

## Discussion

Surgical revision the RVOT, either with a prosthetic valve or an RV to PA valved conduit can be accomplished with low mortality.[1] However, such implants have a limited lifespan and expose the child to multiple open heart procedures. Percutaneous bare metal stent implantation within such conduits or prosthetic valves has emerged as a palliative therapy for such RV stenotic lesions[10,11] but exposes the ventricle to the detrimental effects of PR. As such, it is clinically useful only for a limited time period. Percutaneous pulmonary valve implantation has recently been introduced as an additional catheter-based intervention to address conduit dysfunction,[7,8] whether stenotic, regurgitant, or mixed. In a recent study, Lurz *et al.*[12] reported their experience in 155 PPVI procedures where 7% ($n = 11$) of the valve stents were implanted in bioprosthetic valves. As such, no study has directly assessed acute and follow-up haemodynamics specific to this subgroup, as in this cohort. In all 14 children, valved stents were successfully implanted. There was excellent relief of both regurgitant and stenotic lesions, despite the slightly reduced internal dimension of the outflow, compared with the *in situ* valve. In this regard, the competency of the bovine valve Melody™ valve is a continuum from 14 to 22 mm and becomes advantageous in this setting. Additionally, these data noted a time-related improvement in non-invasive estimated RVP and RVOT gradient, as reported by Rodés-Cabau *et al.*[13] Those authors speculated that the mechanism of delayed haemodynamic improvement was due to oedema or haematoma after stent implantation, clearly not applicable in this situation. Also noted was an increase in LV end-diastolic and aortic valve annulus dimensions, corresponding to improved forward flow and a decrease in RV dimensions. This unique observation suggests that repeated

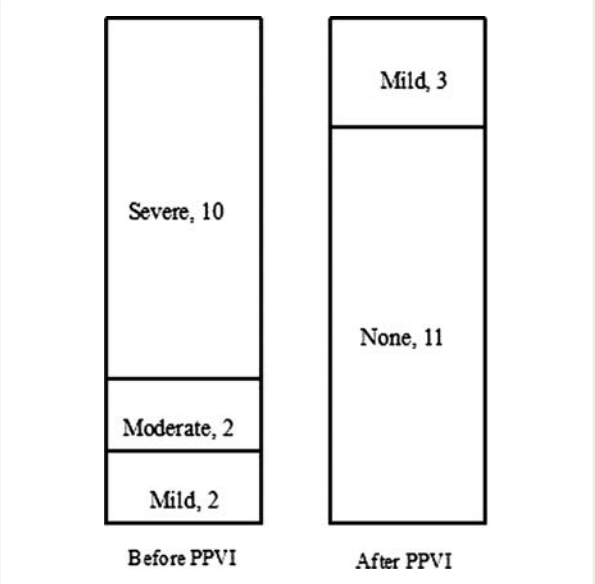


**Figure 5** Change of degree of pulmonary regurgitation from the echocardiogram before and after PPVI. Abbreviations as in *Figure 3*.

estimates of gradient and flow data are necessary to judge the effectiveness of PPVI, with haemodynamic changes occurring over several months. Finally, a note of caution must be exercised in applying this technology as a treatment strategy in this situation. As the bioprosthetic valves have rigid non-dilatable sewing rings, the internal (haemodynamic area) dimension being about 3 mm less than the rated size of the valve. With PPVI, there is a further reduction in the haemodynamic orifice due to the added thickness of the valved stent (metal stent plus bovine vein graft). Thus, normalization of RVP and elimination of the outflow gradient are unlikely. As such, in the growing child with a small valve, long lasting haemodynamic improvement should not be anticipated, although acute recovery from RV pressure or volume overload can be achieved. This is similar to the observations by Nordmeyer *et al.*,[14] where a second PPVI (inserted for device dysfunction into a homograft) resulted in clinically important pressure and gradient reduction. This may have been accomplished by a slight increase in homograft diameters affected by the implant, not possible in a bioprosthetic valve. In this study, the majority of children had primarily mixed lesions, which responded favourably with a clinically significant reduction (but not normalization) in RVP and RVOT gradients. The absence of PR was an important component of this clinical response. However, the longevity of this response in the

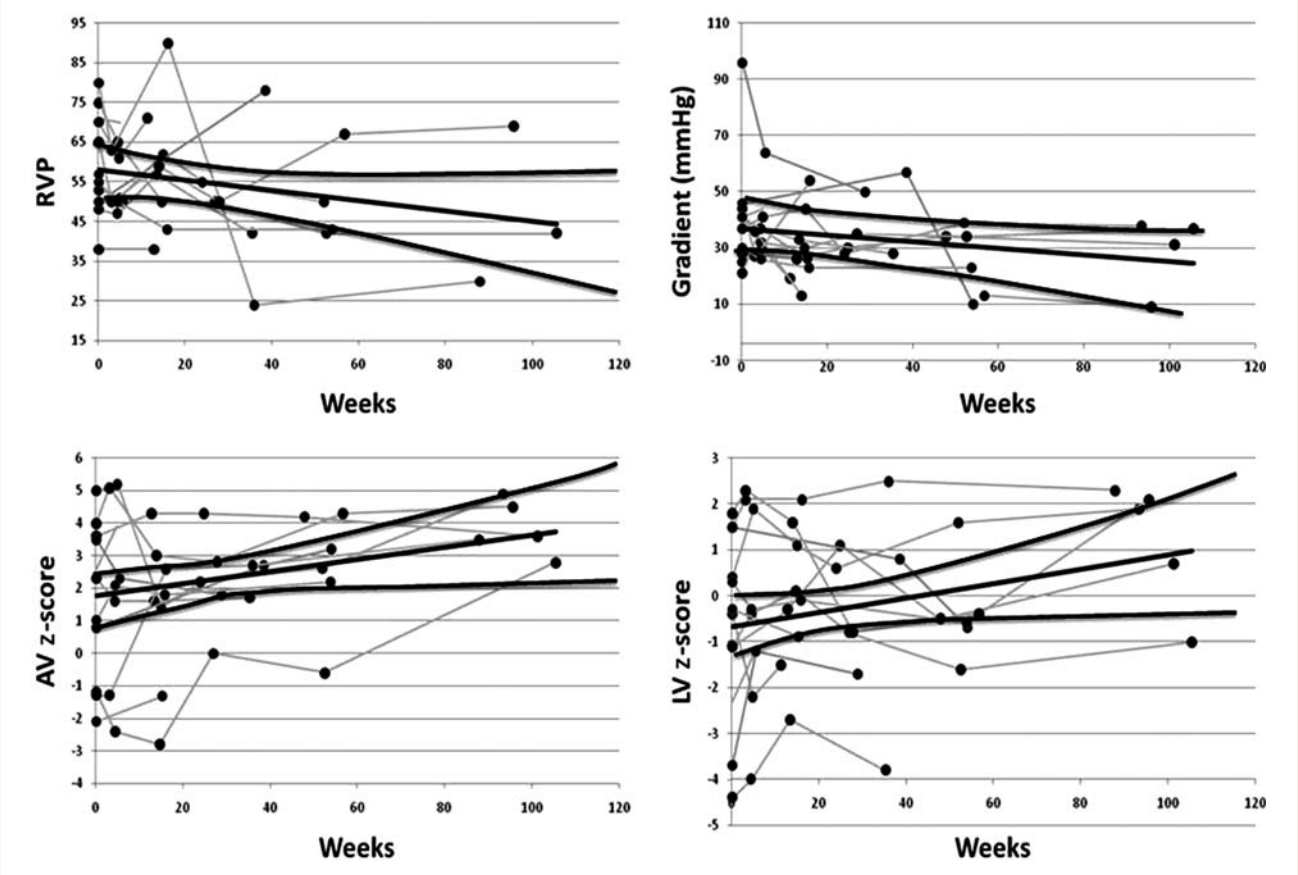


**Figure 6** Upper left panel: time-related change, in estimated RV systolic pressure, upper right panel: estimated RVOT gradient, lower left panel: aortic valve z-score, and lower right panel: left ventricular dimension z-scores for each patient (connected dots). Heavy lines, regression mean and confidence intervals. Abbreviations as in *Figure 3*.

growing child is a concern. In this regard, encouragingly, we observed a gradual reduction in RV and gradients over time, the cause not clearly obvious, and may well be multifactorial, with varying times courses. For example, time-dependent alterations in ventricular volumes may differentially affect stroke output and thus generated chamber pressures and gradients, despite a fixed RVOT diameter. Alternatively, dynamic subpulmonary obstruction, due to acute relief in outflow tract obstruction, may affect chamber pressures and outflow gradients and resolve with time. Finally, stent fractures were not observed in this cohort, in part due to the position of the bioprosthetic valve, away from the sternum, other extravalvular compressive forces (i.e. the aorta), and the rigid ring within which the valve was seated.

## Study limitation

This was a retrospective study and suffers the biases of such investigations. The timing of PPVI was not standardized but dependent upon the varied management approaches of a number of clinic physicians. We therefore limited our investigation of outcomes in the population who underwent PPVI. In addition, the sample size is small and the follow-up period short. Therefore, mid- and long-term performance and utility for late device function remain to be investigated.

**Conflict of interest:** none declared.

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