The freestyle valve as a right ventricle to pulmonary artery conduit. A systematic review and meta-analysis

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ABSTRACT

Introduction: Reconstruction of the right ventricular outflow tract is the most commonly performed valve repair/replacement procedure in congenital cardiac surgery. There is an ongoing shortage of homografts, and existing bioprosthetic options suffer from substantial rates of structural valve deterioration over time. The Medtronic Freestyle valve is used extensively in the aortic position, but little data is available on its performance in the pulmonary position.

Methods: A systematic review and meta-analysis of primary studies reporting echocardiographic and clinical outcomes, including reintervention and functional status, associated with the Freestyle valve in the pulmonary position for both Ross and congenital surgery.

Results: 13 observational studies including 334 patients with a mean follow-up of 34 months (range 10-98 months) fulfilled the eligibility criteria and were included in the review. Structural valve deterioration occurred in 4.8% (95% confidence interval 0.8-10.6%) of patients. Reintervention was required in 1.1% (95% confidence interval 0.0-3.3%). Freedom from symptoms of heart failure occurred in 97.7% (94.6-99.7%). The results did not change substantially when analysed according to Ross or congenital surgery.

Conclusions: The Freestyle valve performs well at short-term follow-up and provides a viable alternative when homografts are unavailable. Further long-term studies are required to better assess its role in right ventricular outflow tract reconstruction.

Keywords: pulmonary valve replacement, right ventricular outflow tract reconstruction, freestyle valve, tetralogy of Fallot, Ross procedure.

INTRODUCTION

Pulmonary valve replacement (PVR) or right ventricular outflow tract reconstruction (RVOTR) is the most common valve replacement/repair procedure performed in the Society of Thoracic Surgeons (STS) Congenital database, comprising 16% of procedures performed in the adult congenital population.

There is a growing population of children surviving well into adulthood with repaired congenital heart disease and the number of PVR/RVOTR procedures required will grow with this population. Since Ross performed the first RVOTR using an aortic homograft in 1966 (1), the search for the optimal conduit choice has been the subject of much debate. Whilst a cryopreserved homograft is the gold standard, calcification and homograft failure remain an issue, with only 40-75% of homografts remaining free from structural valve deterioration (SVD) at 10 years in the congenital population (2, 3). Alternative bio-
prostheses face similar longevity problems (4, 5).

An alternative is the Medtronic Freestyle valve, derived from a porcine aortic root, decellularised using glutaraldehyde and treated with alpha-amino oleic acid to minimize xenograft calcification. Potential benefits include its stentless design, the possibility to achieve a greater effective orifice area, the availability in a range of sizes (19-29 mm), and the lack of requirement for lifelong anticoagulation. Comparative outcomes however, remain uncertain.

The aim of this study, therefore, was to systematically review all of the primary publications describing the outcomes associated with using the Freestyle valve for RVOTR in both the Ross procedure and in congenital heart disease, primarily to determine short-term rates of structural valve dysfunction and reintervention, and functional status. These outcomes were compared to those outcomes with homografts and alternative bioprostheses.

METHODS

A review of available literature was undertaken via online searches of the major clinical databases: Medline, Pubmed, Cochrane database and Google Scholar. The search terms used were - “Freestyle” OR “Xenograft” OR “Stentless”, AND “Pulmonary Valve Replacement” OR “Right Ventricular Outflow Tract”. The search years included ranged from January 1980 to October 2014. Bibliographies, from included papers, were assessed for suitable references in an attempt to avoid missing potentially useful material.

Publications were eligible for inclusion if they presented original data on Freestyle valves in the pulmonary position. Review articles and opinion pieces, isolated case reports and animal studies were excluded because they lacked any outcomes of interest.

All publications deemed suitable for inclusion on the above criteria were reviewed separately by two authors (BD and DA) to ensure suitability and disagreements resolved by consensus. Level of evidence for each study was recorded.

Data was extracted from the included studies into a prespecified case report form. The primary outcome of interest was rates of structural valve deterioration as defined by Akins et al. (6) in their joint STS/AATS/EACTS report. Secondary outcomes of interest included reintervention (defined as percutaneous balloon valvuloplasty, percutaneous PVR or surgical revision) and functional status (defined according to New York Heart Association class or modified Ross score).

Meta-analysis was undertaken where sufficient data existed to pool studies, using a fixed effects or random effects model depending on study heterogeneity.

We defined a priori two subgroups: one group that underwent RVOTR as part of a Ross procedure and another group that underwent RVOTR as surgical management of congenital heart disease.

Two statistical models, namely, fixed effects and random effects models, were used depending on study heterogeneity. Fixed effects models were used if the between study variance was less than 0, whilst a random effects model was used, where the between study variance was larger than 0.

A search for comparative series of alternative bioprostheses and homografts was also performed to allow for comparison with the results of our meta-analysis.

RESULTS

A total of 435 papers were initially retrieved with the search strategy described above, of which 13 retrospective case reports and animal studies were excluded because they lacked any outcomes of interest.
trials or prospective series were identified (Figure 1).
One study presented their data only as a Kaplan Meier curve and so could not be analysed with the other 12 studies but was reviewed separately. The twelve papers included in the meta-analysis yielded data on 311 patients with a mean follow-up of 33.6 months. Of the 12 studies, 2 reported on solely paediatric patients, 3 reported solely on adult patients and 7 reported data on both paediatric and adult patients. Seven of the papers solely reviewed cohorts of patients that RVOTR were performed on as part of a Ross procedure, while the other 5 papers were from series of predominantly congenital cases (Table 1).

**Figure 1** - Flow diagram of the included studies.

**Structural valve deterioration.** Twelve studies (n=311) reported echocardiographic data on SVD at 34 months follow-up (range 10-98 months). The mean rate of SVD was 4.8% (95% confidence interval (CI) 0.8-10.6%). Analyzing Ross recipients separately (7 studies, n=137), the pooled rate of SVD was 7.1% (95% CI 0.2-19.3%) at 45 months follow-up. For congenital recipients (5 studies, n=174 patients) the pooled rate of SVD was 3.5% (95% CI 0.9-7.3%) at 18 months.

Heterogeneity between studies was high, so random effects modeling was used for this analysis.

**Reintervention data.** Reintervention was reported in twelve studies (n=311) with a
mean follow-up of 34 months. Reintervention occurred in nine patients (mean 1.1%, 95% CI 0.0-3.3%).

Analyzing Ross recipients separately (7 studies, n = 137), the rate of reintervention was 2.1% (95% CI 0.0-6.4%) at 45 months. The 5 congenital series (n = 174) were also analysed separately and had a mean rate of reintervention of 1.0% (95% CI 0.1-3.7%) at 18 months.

Heterogeneity between studies was low, so fixed effects modeling was used for this analysis.

In the whole cohort, the mean time to reintervention was 28 months. The indications for reintervention were subvalvar stenosis due to pannus and stricture formation at the proximal suture line (n = 7) and true valvular stenosis (n = 2). Five of these reinterventions were percutaneous (2 balloon valvuloplasties, 3 percutaneous valve replacements), and 4 were open surgical conduit replacements.

In comparison, Lee et al. (5) reported only 31% freedom from reintervention in their cohort of 23 patients with a mean of 91 months follow-up. They did not state what proportion of reinterventions were due to
SVD, but did describe that three cases were due to conduit compression by the overlying sternum.

**Functional status.** Eight of the twelve studies (n = 214) provided data on the functional status of their patients with a mean follow-up of 36 months. Freedom from the symptoms of heart failure was 97.7% (95% CI 94.6-99.7%). In the Ross population (n = 53), it was 91.7% (95% CI 81.2-98.9%). In the congenital population (n = 161), it was 97.6% (95% CI 94.2-99.7%). Heterogeneity between studies was low, so fixed effects modeling was used for this analysis (Table 2).

**RESULTS**

**Alternatives.** There are a number of alternative bioprostheses available for RVOTR. A review of all available prosthetic options was also performed to allow for comparison between the many available alternatives (see table 3). There is a shortage of truly long-term data available, however 5-year results are available for most bioprostheses. Across all bioprostheses a 5-year failure rate of 10-40% exists, with failure rates at 10 years climbing to 25-60% (Table 3).

**DISCUSSION**

To our knowledge, this is the first systematic review and meta-analysis of the performance of the Medtronic Freestyle valve in the pulmonary position. Several important findings bear further consideration. First, our results suggest that the Freestyle valve has a low incidence of SVD, reintervention and symptoms of heart failure, and compares well with alternative bioprostheses at similar relatively short duration of follow-up. Proximal suture line pannus was noted in a small minority of cases. This is an atypical failure mode for RV-PA conduits and it may relate to the stiffness of the Freestyle root wall in comparison to the mobility of the muscular RVOT leading to anastomotic site tension.

Second, long-term follow-up data for the Freestyle valve in the pulmonary position is limited. Only 3 studies (5, 7, 8) have truly long-term data on the performance of the Freestyle valve and display markedly different results. Dohmen (7) and Hechadi (8) had no SVD or Reintervention at 60 and 98 months follow-up respectively, while Lee (5) describes a 69% rate of Reintervention at 90 months. Further studies are required to truly determine the long-term outcomes of this valve in the pulmonary position.

Third, the promising findings potentially increasing options for RVOTR may stimulate competition within the industry and provide the impetus to reduce the cost of these bioprostheses; a cost-effectiveness analysis may provide further useful data to guide clinicians.

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**Table 3 - Alternative bioprostheses.**

<table>
<thead>
<tr>
<th>Bioprosthesis</th>
<th>SVD at 3 years</th>
<th>SVD at 5 years</th>
<th>SVD at 10 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Homografts</td>
<td>12% (19)</td>
<td>40% (2)</td>
<td>25-60% (2, 3)</td>
</tr>
<tr>
<td>Bovine pericardial</td>
<td>11% (20)</td>
<td>22% (4)</td>
<td></td>
</tr>
<tr>
<td>Contegra</td>
<td>20-27% (21, 22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edwards Prima</td>
<td>20% (23)</td>
<td>7% (24)</td>
<td></td>
</tr>
<tr>
<td>Edwards porcine conduit</td>
<td>0% (25)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hancock II</td>
<td>4.17% (26, 27)</td>
<td>50% (5)</td>
<td></td>
</tr>
<tr>
<td>Melody</td>
<td>2.10% (28-30)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perimount</td>
<td>11.26% (27, 31)</td>
<td>20% (5)</td>
<td></td>
</tr>
<tr>
<td>Toronto SPV</td>
<td>10.5% (32)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SVD = Structural Valve Deterioration.
Finally, this study has a number of limitations. The meta-analysis did not include any randomized controlled trials of the Freestyle valve, the patient numbers were low and the duration of follow-up relatively short, precluding definitive conclusions in comparing valve outcomes. Nevertheless, early results with the Freestyle valve compare favourably with available alternatives. The included studies were also heterogeneous in nature with a mixture of pediatric and adult patients, and no data on valve sizes used was available. We did however identify a priori subgroups for analysis and did not find substantial differences upon analysis according to Ross or congenital procedure, although mean length of follow-up differed between these two groups.

CONCLUSION

Pulmonary valve replacement or right ventricular outflow tract reconstruction using the Freestyle valve is associated with satisfactory short-term echocardiographic and clinical outcomes, including functional status and freedom from reintervention at over 2 years. Freestyle valves may be a reasonable alternative to homografts or other bioprostheses, particularly when homografts are not readily available. Determination of the optimal valve, however, is currently limited by lack of long-term comparative data and this review has identified a significant need for long-term data on the Freestyle valve in the pulmonary position.

REFERENCES


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