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Long-Term Comparison Between Pulmonary Homograft Versus Bioprosthesis for Pulmonary Valve Replacement in Tetralogy of Fallot

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Background—Tetralogy of Fallot repair results in late occurrence of pulmonary regurgitation, which requires pulmonary valve replacement in a large proportion of patients. Both homografts and bioprostheses are used for pulmonary valve replacement as uncertainty remains on which prosthesis should be considered superior. We performed a long-term imaging and clinical comparison between these 2 strategies.

Methods and Results—We compared echocardiographic and clinical follow-up data of 209 patients with previous tetralogy of Fallot repair who underwent pulmonary valve replacement with homograft (n = 75) or bioprosthesis (n = 134) between 1995 and 2018 at a tertiary hospital. The primary endpoint was the composite of pulmonary valve replacement reintervention and structural valve deterioration, defined as a transpulmonary pressure decrease ≥50 mm Hg or pulmonary regurgitation degree of ≥2. Mixed linear model and Cox regression model were used for comparisons. Echocardiographic follow-up duration was longer in the homograft group (8 [interquartile range, 4–12] versus 4 [interquartile range, 3–6] years; P < 0.001). At the latest echocardiographic follow-up, homografts showed a significantly lower transpulmonary systolic pressure decrease (16 [interquartile range, 12–25] mm Hg) when compared with bioprostheses (28 [interquartile range, 18–41] mm Hg; mixed model P < 0.001) and a similar degree of pulmonary regurgitation (degree 0–4) (1 [interquartile range, 0–2] versus 2 [interquartile range, 0–2]; mixed model P = 0.19). At 9 years, freedom from structural valve deterioration and reintervention was 81.6% (95% CI, 71.5%–91.6%) versus 43.4% (95% CI, 23.6%–63.2%) in the homograft and bioprosthesis groups, respectively (adjusted hazard ratio, 0.27; 95% CI, 0.13–0.55; P < 0.001).

Conclusions—When compared with bioprostheses, pulmonary homografts were associated lower transvalvular gradient during follow-up and were associated with a significantly lower risk of reintervention or structural valve degeneration. (J Am Heart Assoc. 2019;8:e013654. DOI: 10.1161/JAHA.119.013654.)

Key Words: bioprosthesis • homograft • pulmonary heart disease • regurgitation • structural valve degeneration • tetralogy of Fallot

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart disease, accounting for the 7% to 10% of all congenital heart disease, with an incidence of 4 to 5 per 10 000 births.1 The surgical repair includes a pulmonary valvotomy and, depending on the anatomical features, placing a transannular patch to relieve the right ventricular (RV) outflow tract; and the common sequela of this procedure is pulmonary valve regurgitation. Pulmonary regurgitation is initially well tolerated. However, over the years, RV volume overload leads to RV dilatation and subsequent symptoms of RV failure, life-threatening arrhythmias, and reduced survival.2,3

Although pulmonary valve replacement (PVR) is the standard treatment for this condition, controversy still exists about which prosthesis should be used. Homografts have been considered as the first choice for a long time.4,5 Despite bioprosthesis being readily available, being easier to be implanted, and having shown excellent results in the aortic position,6 their durability for PVR remains controversial.2,7 Mechanical prostheses are rarely used because of the increased risk of thrombosis in pulmonary valve position and patient’s choice.8

Long-term comparisons between homografts and bioprostheses were needed to clarify which prosthesis should be preferred for PVR in patients with TOF.9 Therefore, we compared long-term results after PVR with pulmonary homografts versus bioprosthesis using a 20-year single-center cohort.

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Accompanying Tables S1 through S4 and Figures S1 through S5 are available at https://www.ahajournals.org/doi/suppl/10.1161/JAHA.119.013654

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Clinical Perspective

What Is New?

- Although bioprostheses have become the first choice for pulmonary valve replacement at many centers, we demonstrated that, in our experience, homografts are associated with a lower incidence of structural valve degeneration and/or need for reintervention and lower transvalvular gradient.

What Are the Clinical Implications?

- Homografts should be considered as a first choice in patients undergoing pulmonary valve replacement.

Methods

Because of the sensitive nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to University Hospitals of Bristol at lucia.cocomello@uhbristol.nhs.uk. The present retrospective analysis was approved by the audit board at University Hospital of Bristol, and informed consent was waived. A total of 219 patients with repaired TOF who underwent first-time PVR with either homografts or bioprosthesis valves between 1995 and 2018 at the Bristol Heart Institute were reviewed. The type of implanted valve was chosen on the basis of the surgeon’s assessment and homograft availability. Indications for the first PVR intervention were generally pulmonary regurgitation with symptom or with severe RV dilatation. Patients receiving mechanical valve (n=1), Contegra valve (n=1), aortic homograft (n=4), and transcatheter valve (n=4) were excluded from the analysis.

Study End Points

The primary end point was to compare long-term freedom from PVR reintervention (surgical or transcatheter PVR) or structural valve degeneration (SVD) in patients receiving homografts versus bioprostheses. SVD was defined as a transpulmonary valve systolic pressure decrease ≥50 mm Hg or significant pulmonary regurgitation (3+) at echocardiographic examination.7,10,11 Information about reintervention and SVD was also obtained from outpatient and inpatient clinical letters. All-cause mortality was also investigated, and late mortality was obtained from the Office of National Statistics.

Moreover, existing echocardiographic examination reports were used to compare echocardiographic measurements in the homograft and bioprosthesis groups preoperatively, early (within 1 year) and at the latest follow-up echocardiographic examination. Velocity across the pulmonary valve was derived from continuous wave Doppler echocardiography, and peak systolic pressure gradient was estimated using the modified Bernoulli equation. Pulmonary regurgitation was graded into 5 categories: 0, absent; 1, trivial; 2, mild; 3, moderate; and 4, severe. Finally, to determine the effect of PVR on RV volume (indexed for body surface area) changes after surgery, data from available preoperative and follow-up cardiac magnetic resonance imaging (MRI) examinations were reviewed and analyzed.

Statistical Analysis

Categorial and continuous variables were presented as proportion or median and interquartile range, respectively. Clinical and echocardiographic data of patients treated with homografts versus bioprostheses were compared using χ² statistics for categorical variables (or the Fisher exact tests for analyses with a cell count <10) and Wilcoxon rank sum (Mann–Whitney) test for continuous variables. Kruskal-Wallis test was used when multiple groups were compared (tableone R package). To assess the effect of type of prosthesis on transpulmonary systolic pressure decrease and pulmonary regurgitation over the time, a mixed linear model for repeated measurement was used, forcing the interaction term between treatment and time to follow-up and other risk factors (age, sex, body mass index, and prosthesis size) as fixed terms and individual patient as random effect (lme4 R package). Results were graphically presented (ggplot2 R package) by plotting echocardiographic measurements over the time and adding a smoothed conditional regression line. The same analysis was used to investigate the effect of time and type of prosthesis on RV volumes at cardiac MRI examination.

Kaplan-Meier method and log-rank test were used to compare freedom from the composite of PVR reintervention and/or SVD in the 2 groups. Multivariable Cox regression analysis was used to calculate the effect of prosthesis type (homograft versus bioprosthesis) on the risk for PVR reintervention and/or SVD. Competing risk framework was used in this analysis to account for those patients who died without primary event (pulmonary valve reintervention/degeneration) (riskRegression R package). Covariates included in the model were as follows: age; sex; chromosomal abnormality; smoking history; left ventricular ejection fraction <50%; body surface area; concomitant procedures, including tricuspid valve repair, RV outflow tract reconstruction, and pulmonary artery plasty; time from original repair; and long-term antiplatelet therapy after surgery (>6 months). Stepwise regression, based on Akaike information criterion, was used to identify a subset of variables in the data set, resulting in the best performing model (lowest prediction error). The same analysis was repeated to assess the effect of valve choice on mortality.
The following variables were tested as treatment effect modifiers on the primary outcome by subgroup analysis and interaction term: age ($\leq 10, 11–19$, and $\geq 20$ years), long-term antiplatelet therapy (>6 months), and different eras (1995–2009 versus 2010–2018). An $\alpha$ of 0.05 was used as the cutoff for significance. All statistical analyses were performed using R Statistical Software, version 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria).

### Results

The study population consisted of 209 patients with previous TOF repair who underwent PVR with homograft ($n=134$) between 1995 and 2018. From 1995 to 2006, homografts only were used, whereas bioprostheses became the preferred choice more recently (Figure 1). The most frequently used bioprosthetic valves were Perimount valve ($n=56$) and Hancock Medtronic ($n=62$), whereas Matrix ($n=13$), St Jude Epic ($n=1$), and Sheth (n=2) valves were used in remaining cases. Demographic and operative data and medication at discharge in the 2 groups are summarized in Table 1. Patients receiving homografts were more likely to present a smaller body surface area, a lower incidence of concomitant tricuspid valve repair, and a shorter time from initial repair to PVR.

### Echocardiographic Findings

Preoperative, early, and latest follow-up echocardiographic examination findings are reported in Table 2. Echocardiographic follow-up duration was longer in the homograft group (8 [interquartile range, 4–12] versus 4 [interquartile range, 3–6] years; $P<0.001$). At the latest follow-up, transpulmonary systolic pressure decrease was significantly lower in the homograft group (16 [interquartile range, 11.56–25.52] versus 28 [interquartile range, 18.12–40.75] mm Hg; $P<0.001$), despite a longer follow-up duration in the homograft group. Homografts showed a statistically significant, but not clinically relevant, higher pulmonary regurgitation degree at early follow-up, but this difference was no longer present at latest follow-up. Mixed models (Table 3, Figure 2) for repeated measurement showed that homografts were independently associated with a significantly lower transpulmonary systolic pressure decrease ($-8.9\pm2.5$ mm Hg; $P<0.001$) and a comparable degree of pulmonary regurgitation ($0.2^\circ\pm0.2^\circ$; $P=0.19$) when compared with bioprostheses. Prosthesis size was negatively associated with systolic pulmonary pressure decrease, but we found no significant interaction between the effect of homograft and prosthesis size ($P=0.11$; Figure S1). Other predictors of increased transpulmonary systolic pressure decrease were a longer duration of follow-up and a larger body surface area. Male sex was associated with a marginally nonsignificant increased transpulmonary pressured decrease. When the analysis was stratified according to the type of bioprosthesis used (Tables S1 and S2), we found that Hancock (33 [interquartile range, 19–42] mm Hg; $P=0.001$) and other types of bioprostheses (44 [interquartile range, 30–

### Table 1. Baseline Characteristics in Patients Receiving Homograft Versus Bioprosthesis

| Characteristics | Homograft | Bioprosthesis | $P$ Value |
|-----------------|-----------|---------------|-----------|
| No.             | 75        | 134           | ...       |
| Age, median (IQR), y | 23 (12–35) | 24 (18–34) | 0.16 |
| Male, n (%)     | 40 (53.3) | 78 (58.2)     | 0.59      |
| Chromosomal abnormality, n (%) | 6 (8.0)  | 17 (12.7)     | 0.42      |
| Smoking history, n (%) | 14 (18.7) | 26 (19.4) | 1.0       |
| LVEF <50%, n (%) | 8 (10.7)  | 24 (17.9)     | 0.23      |
| BSA, mean (SD), m² | 1.59 (0.44) | 1.72 (0.30) | 0.02 |
| Concomitant TVR, n (%) | 3 (4.0)   | 21 (15.7)     | 0.02      |
| Concomitant reconstruction, n (%) | 10 (13.3) | 15 (11.2) | 0.81 |
| Concomitant PA plasty, n (%) | 16 (21.3) | 29 (21.6) | 1.0 |
| Time from repair, median (IQR), y | 20 (12–27) | 22 (16–31) | 0.02 |
| Long-term antiplatelet therapy, n (%) | 31 (41.3) | 55 (41.0) | 1 |

BSA indicates body surface area; IQR, interquartile range; LVEF, left ventricular ejection fraction; PA, pulmonary artery; TVR, tricuspid valve repair.
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57] mm Hg; \( P<0.001 \) but not Perimount (25 [interquartile range, 17–32] mm Hg; \( P=0.15 \)) were associated with a significantly increased transpulmonary systolic pressure decrease over time when compared with homografts (16 [interquartile range, 12–26] mm Hg). On the other hand, Hancock valves were associated with 0.5 reduction in the pulmonary regurgitation degree (\(-0.5 \pm 0.2\) mm Hg; \( P=0.005 \)) when compared with homografts (Figure S2).

Primary End Point Analysis

After a median follow-up time of 10 (interquartile range, 5–13) and 4 (interquartile range, 2–7) years for patients treated with homograft and bioprosthesis, respectively, a total of 11 homografts (3 endocarditis and 8 SVD) and 11 bioprostheses (2 endocarditis and 9 SVD) required reintervention. Overall, SVD was observed in 10 and 25 homografts and bioprostheses, respectively. Freedom from SVD/reintervention on the pulmonary valve at 3, 5, and 9 years was 95.7% (95% CI, 91.0%–100.0%) versus 87.2% (95% CI, 80.8%–93.5%), 89.5% (95% CI, 82.2%–96.9%) versus 79.0% (95% CI, 70.1%–88.0%), and 81.6% (95% CI, 71.5%–91.6%) versus 43.4% (95% CI, 23.6%–63.2%) in the homograft and bioprosthesis groups, respectively (log-rank \( P=0.002 \); Figure 3). After adjusting for other risk factors, pulmonary homografts were an independent predictor of freedom from reintervention/SVD (adjusted hazard ratio [HR], 0.27; 95% CI, 0.13–0.55; \( P=0.001 \); Table S3). Homografts were superior to bioprostheses regardless of patient age (interaction \( P=0.61 \)), although the benefit from homografts was larger in patients aged between 11 and 19 years (HR, 0.15; 95% CI, 0.02–1.2) and \( \geq 20 \) years (HR, 0.32; 95% CI, 0.13–0.77) than in patients aged \( \leq 10 \) years (HR, 0.81; 95% CI, 0.08–8.13) (Figure S3). Homografts were superior to bioprostheses in patients with (HR, 0.14; 95% CI, 0.02–1.23) and without (HR, 0.40; 95% CI, 0.19–0.85) long-term antplatelet therapy (interaction \( P=0.76 \)). However, the use of long-term antplatelet therapy was associated with a lower risk of SVD/reintervention in the overall population (HR, 0.28; 95% CI, 0.13–0.64; \( P=0.002 \)) and in patients who received homograft (HR, 0.23; 95% CI, 0.05–0.99; \( P=0.04 \)) and bioprosthesis (HR, 0.30; 95% CI, 0.12–0.8; \( P=0.02 \); Figure S4). The effect of homograft was not significantly influenced by eras of surgery (\( P=0.77 \)). When compared with homografts, Hancock and other valves were significantly associated with a significantly increased risk of reintervention/SVD, whereas Perimount valves were associated with a nonsignificant increased risk (Table S4, Figure S5). No hospital death was recorded. Overall survival rates at 9 years were 90.6% (95% CI, 83.4%–97.9%) versus 99.2% (95% CI, 97.8%–100.0%) in the homograft and bioprosthesis groups, respectively, with no significant difference between the 2 groups after multivariate adjustment (log-rank test \( P=0.08 \); adjusted \( P=0.14 \)).

Table 2. Echocardiographic Data at Baseline, at 1-Year Follow-Up, and at Latest Follow-Up

| Variable | Homograft | Bioprosthesis | \( P \) Value |
|----------|-----------|---------------|--------------|
| Preoperative data | | | |
| No. | 75 | 134 | … |
| TV regurgitation degree (0–4) | 2 (1–2) | 2 (1–2) | 0.95 |
| TV regurgitation pressure decrease, mm Hg | 39 (31–62) | 30 (25–42) | 0.003 |
| PV regurgitation degree (0–4) | 4 (3–4) | 4 (3–4) | 0.08 |
| PV systolic pressure decrease, mm Hg | 24 (16–38) | 19 (14–31) | 0.12 |
| Early follow-up data (within 1 y) | | | |
| No. | 65 | 129 | … |
| TV regurgitation degree (0–4) | 1 (1–2) | 1 (1–2) | 0.50 |
| TV regurgitation pressure decrease, mm Hg | 39 (31–62) | 29 (21–36) | 0.62 |
| PV regurgitation degree (0–4) | 1 (0–2) | 0 (0–1) | <0.001 |
| PV systolic pressure decrease, mm Hg | 18 (12–27) | 22 (16–31) | 0.01 |
| Latest follow-up available data | | | |
| No. | 48 | 87 | … |
| Follow-up duration, y | 8 (4–12) | 4 (3–6) | <0.001 |
| TV regurgitation degree (0–4) | 1 (1–2) | 1 (1–2) | 0.96 |
| TV regurgitation pressure decrease, mm Hg | 30 (25–41) | 32 (25–45) | 0.23 |
| PV regurgitation degree (0–4) | 1 (0–2) | 2 (0–2) | 0.52 |
| PV systolic pressure decrease, mm Hg | 16 (12–25) | 28 (18–41) | <0.001 |

Data are presented as median (interquartile range). PV indicates pulmonary valve; TV, tricuspid valve.

| Table 3. Risk Factors for Trans-PPD and PVR (0°–4°) After Pulmonary Valve Replacement (Mixed Linear Model for Repeated Measurement) |
|-------------------------------------------------|----------|------------|----------|
| Risk Factors | End Point | PPD, mm Hg | \( P \) Value | PVR, ° | \( P \) Value |
| Homograft | –8.9 ± 2.5 | <0.001 | 0.2 ± 0.2 | 0.19 |
| Follow-up duration | 1.1 ± 0.3 | 0.001 | 0.1 ± 0.2 | <0.001 |
| Valve size | –1.9 ± 0.7 | 0.006 | –0.02 ± 0.05 | 0.61 |
| Age | –0.1 ± 0.1 | 0.21 | –0.01 ± 0.006 | 0.01 |
| Body surface area | 11.8 ± 3.6 | 0.001 | –0.25 ± 0.25 | 0.31 |
| Male | 3.4 ± 1.8 | 0.06 | –0.04 ± 0.13 | 0.74 |
| Homograft/time | –1.0 ± 0.4 | 0.02 | –0.08 ± 0.03 | 0.02 |

PPD indicates pulmonary systolic pressure decrease; PVR, pulmonary valve regurgitation.
Cardiac MRI Findings

Cardiac MRI findings are summarized in Table 4. A total of 21 and 85 patients with homograft and bioprosthesis, respectively, underwent baseline cardiac MRI. Of those patients, 17 and 40, respectively, underwent cardiac MRI follow-up; and 9 and 16, respectively, among those had late cardiac MRI follow-up. We observed a significant reduction of indexed end-diastolic and end-systolic RV volumes in both patients treated with homografts or bioprostheses, with no significant difference between the 2 groups. Repeated measures mixed model confirmed that type of prosthesis (homograft versus bioprosthesis) did not significantly influence the reduction in RV volumes (indexed end-diastolic RV volume, $-8.5\pm7.8$ mL/m² $[P=0.27]$; indexed end-systolic RV volume, $-3.1\pm5.1$ mL/m² $[P=0.53]$; Figure 4).

Discussion

Little published data are available directly comparing the performance of bioprosthetic valves with homografts in the pulmonary position, with conflicting findings reported.\textsuperscript{7,11–13} The present long-term follow-up study following PVR with homografts versus bioprostheses in patients previously treated for TOF found that pulmonary homografts were associated with lower transvalvular gradients and lower incidence of SVD and need for reintervention. This effect was more pronounced among patients aged $>10$ years, although the number of patients aged $\leq10$ years was small to draw conclusion.

Both strategies achieved significant reduction in RV volumes, as shown by cardiac MRI examination. Among bioprostheses, Perimount was associated with a lower
transvalvular gradient and a lower incidence of SVD and need for reintervention. Similar degrees of pulmonary regurgitation with homografts and bioprostheses were observed at late follow-up.

To our knowledge, this is the largest comparison of echocardiographic, cardiac MRI, and clinical outcomes between pulmonary homografts and bioprostheses. In a previously published small series, Fiore et al \(^{11}\) compared 15 homografts with 18 bovine pericardial and 49 porcine stented bioprostheses. They reported no significant differences between the 3 groups in terms of transpulmonary valve gradients and a significantly higher incidence of valve dysfunction with homografts (54%) when compared with bovine pericardial valves (5.5%) and porcine valves (19%). However, it is not possible to draw a definitive conclusion from this report because of the small number of patients receiving homografts.

Batlivala et al \(^{12}\) reported on 84 cryopreserved homografts and 170 bioprosthetic valves. At 10 years, freedom from moderate or severe pulmonary regurgitation was 61% and freedom from moderate or severe stenosis was 74%, with no difference between the 2 cohorts. However, the homograft group in this study contained 50 aortic homografts, which have previously been shown to deteriorate more rapidly in the pulmonary position. \(^{14}\) The only 4 aortic homografts in our study population were intentionally excluded from the final analysis.

Zubairi et al \(^{13}\) compared the performance of 56 cryopreserved pulmonary homografts with 113 bioprosthetic valves. No difference in reoperation was observed between the 2 groups, with freedom of reoperation of 93% at 5 years and 71% at 10 years. However, a higher proportion of children aged <10 years received a homograft and younger age (<3 years) was identified as a risk factor for homograft failure.

Our findings are supported by another report by Bell et al \(^{7}\) on patients aged 10 to 20 years, who presented freedom from SVD at 10 years in 85% and 53% with homografts (n=131) and bioprostheses (n=57), respectively. Bioprostheses were associated with a 5-fold increase in risk of SVD when compared with homografts (HR, 5.64; 95% CI, 2.11–15.07; \(P<0.001\)). Subgroup analysis demonstrated no statistical difference in the performance of bovine and porcine bioprostheses, despite a trend toward better performance of the bovine bioprosthesis.

We found that homografts provided lower transvalvular gradients regardless of the annulus size, and it has been proposed that improved RV outflow tract hemodynamic conditions contribute to the beneficial effect of homografts. Von Knoebelsdorff-Brenkenhoff et al \(^{15}\) described variable flow hemodynamic outcomes after aortic valve replacement using mechanical, stented, or nonstented xenografts. Additional studies focused on comparison of the flow hemodynamics after aortic root replacement either with a mechanical valved conduit or by applying the valve-sparing techniques. \(^{16–18}\) Both studies concluded that valve-sparing techniques improved flow hemodynamic parameters compared with xenograft valve conduits, which could potentially lead to reduced stress and deterioration of the morphologically normal trileaflet valve, compared with a xenograft. Unfortunately, no 4-dimensional flow MRI data are available for assessing RV outflow tract flow.

**Table 4.** Cardiac MRI Findings in Patients Treated With Homograft Versus Bioprosthesis and Results of Mixed Model

| Variable                          | Homograft | Bioprosthesis | \(P\) Value |
|----------------------------------|-----------|---------------|-------------|
| Preoperative data                |           |               |             |
| No.                              | 21        | 85            | ...         |
| Indexed RV EDV, mL/m²            | 150 (119–164) | 150 (135–169) | 0.33        |
| Indexed RV ESV, mL/m²            | 76 (62–90) | 74 (61–88)    | 0.91        |
| Follow-up MRI data               |           |               |             |
| No.                              | 17        | 40            | ...         |
| Follow-up duration, y            | 4.7 (2.4–8.9) | 2.1 (1.2–4.4) | 0.045       |
| Indexed RV EDV, mL/m²            | 104 (87–112) | 106 (84–131)  | 0.08        |
| Indexed RV ESV, mL/m²            | 53 (42–59) | 53 (38–74)    | 0.21        |
| Late follow-up MRI data          |           |               |             |
| No.                              | 9         | 16            | ...         |
| Follow-up duration, y            | 7.9 (7.3–8.8) | 6.5 (5.0–8.2) | 0.14        |
| Indexed RV EDV, mL/m²            | 107 (98–112.25) | 114 (95–131) | 0.57        |
| Indexed RV ESV, mL/m²            | 58 (52–75) | 59 (43–74)    | 0.61        |

Data are presented as median (interquartile range). MRI indicates magnetic resonance imaging; EDV, end-diastolic volume; ESV, end-systolic volume; RV, right ventricular.

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dynamics with different pulmonary valve prosthesis. Studies using imaging techniques, such as 4-dimensional cardiac MRI, are beginning to shed light on the hemodynamics in patients with TOF. Using this technique, it has been observed that patients with repaired TOF and pulmonary regurgitation presented with misaligned hemodynamic forces in the left ventricle and higher diastolic RV forces along the direction of regurgitant flow, compared with healthy controls.\textsuperscript{19} Changes in kinetic energy and intracardiac vorticity have also been observed in patients with TOF using 4-dimensional cardiac MRI, suggesting the potential for a novel noninvasive biomarker.\textsuperscript{20–22} A recent case report suggests the role for 4-dimensional cardiac MRI in assessing patients with TOF before and after valve replacement,\textsuperscript{23} yet data on RV outflow tract flow dynamics with different pulmonary valve prostheses are still lacking.

Finally, we have found that long-term antiplatelet therapy was associated with a significantly lower risk of SVD and reintervention regardless the type of valve used and, therefore, this treatment should be strongly recommended after PVR unless contraindication exists.

**Limitations**

The main limitation of our analysis is its observational nature. Despite the fact that we used multivariable adjustment, other unmeasured factors not included in the model can have influenced our results. Second, patients receiving a bioprosthesis were more likely to have had their operations recently when compared with those receiving homografts, resulting in unequal follow-up times and cohort effects by which patients receiving a bioprosthesis were likely to benefit from more recent advances in surgical and medical technologies. We have used a mixed model to account for difference in follow-up duration, and estimates were unchanged. Furthermore, this potential bias is likely to have favored the bioprosthesis group and, therefore, to have attenuated our effect estimates, thus supporting our final conclusions. It is suggested that velocity propagation may differ between homografts and bioprostheses, and a lower cutoff for SVD has been suggest for homografts.\textsuperscript{24} However, the value of a lower threshold for homografts has not been clinically validated; and a peak gradient of 50 mm Hg is still widely regarded as the cutoff for surgical reintervention, regardless of type of prosthesis.\textsuperscript{7,10,11} Finally, we found an excess of deaths in the homograft group, which was not statistically significant after multivariable adjustment. Moreover, the present analysis is largely underpowered to detect a difference in survival.

**Conclusions**

The present findings suggest that pulmonary homografts outperformed bioprosthetic valves when implanted in the pulmonary position in patients with pulmonary regurgitation.
with previous TOF repair, with a larger effect in patients aged ≥10 years. On the basis of this observation, pulmonary homografts may be considered as first choice in this population. However, other factors should be considered in the choice of prosthesis, including the conundrum with availability of good quality homografts and the role of the transcatheter, within previous failed PVR. 25

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Disclosures

Dr Bucciarelli-Ducci is a consultant for Circle Cardiovascular Imaging (Calgary, Canada). The remaining authors have no disclosures to report.

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Supplemental Material
Table S1. Baseline characteristics in patients receiving homograft vs different types of bioprostheses.

|                           | Hancock       | Homograft     | Other         | Perimount     | P-value |
|---------------------------|---------------|---------------|---------------|---------------|---------|
| **n**                     | 62            | 75            | 16            | 56            |         |
| Age, years (median [IQR]) | 26 [19-36]    | 23 [12-35]    | 28 [24-37]    | 20 [17-31]    | 0.04    |
| Male n(%)                 | 41 (66.1)     | 40 (53.3)     | 7 (43.8)      | 30 (53.6)     | 0.27    |
| Chromosomal abnormality n(%) | 4 (6.5)  | 6 (8.0)       | 4 (25.0)      | 9 (16.1)      | 0.08    |
| Smoking history n(%)      | 14 (22.6)     | 14 (18.7)     | 2 (12.5)      | 10 (17.9)     | 0.80    |
| LVEF<50%                  | 12 (19.4)     | 8 (10.7)      | 1 (6.2)       | 11 (19.6)     | 0.28    |
| BSA, m² (mean [SD])       | 1.78 (0.29)   | 1.59 (0.44)   | 1.70 (0.33)   | 1.65 (0.29)   | 0.02    |
| Concomitant TVR n(%)      | 16 (25.8)     | 3 (4.0)       | 1 (6.2)       | 4 (7.1)       | <0.001  |
| Concomitant RVOT reconstruction n(%) | 10 (16.1) | 10 (13.3) | 1 (6.2) | 4 (7.1) | 0.41 |
| Concomitant PA plasty n(%) | 12 (19.4) | 16 (21.3) | 2 (12.5) | 15 (26.8) | 0.60 |
| Time from repair (median [IQR]) | 23.9 [18.6-33] | 19.75 [11.9-26.9] | 24.4 [20.4-33.1] | 18.7 [14.7-26.4] | 0.005 |
| Long-term antiplatelet therapy n(%) | 25 (40.3) | 31 (41.3) | 4 (25.0) | 26 (46.4) | 0.50 |

BSA: body surface area; TVR: tricuspid valve repair; RVOT: right ventricular outflow tract; PA: pulmonary artery.
Table S2. Echocardiographic data at 1 year follow-up and at latest follow-up in patients receiving Homograft vs different types of bioprosthesis.

|                  | Hancock | Homograft | Other | Perimount | P-value |
|------------------|---------|-----------|-------|-----------|---------|
| **1-year follow-up** |         |           |       |           |         |
| n                | 61      | 65        | 15    | 53        |         |
| TV regurgitation degree (0-4) | 1 [1-2] | 1 [1-2] | 2 [1-2] | 1 [1-2] | 0.48    |
| TV regurgitation pressure drop (mmHg) | 29[25-43] | 39[31-62] | 31 [26-39] | 31 [27-37] | 0.72 |
| PV regurgitation degree (0-4) | 0 [0-0] | 1 [0-2] | 1 [0-2] | 1 [0-2] | <0.001 |
| PV systolic pressure drop (mmHg) | 29 [21-34] | 18 [12-27] | 22 [12-31] | 17 [14-22] | <0.001 |
| **Latest follow-up available** |         |           |       |           |         |
| n                | 31      | 48        | 14    | 42        |         |
| follow-up duration (years) | 4 [1-5] | 7 [4-12] | 7 [4-8] | 4 [3-6] | <0.001 |
| TV regurgitation degree (0-4) | 1 [1-2] | 1 [1-2] | 2 [1-2] | 2 [1-2] | 0.80 |
| TV regurgitation pressure drop (mmHg) | 31 [21-43] | 30 [25-41] | 47 [36-52] | 32 [26-36] | 0.03 |
| PV regurgitation degree (0-4) | 1 [0-2] | 1 [0-2] | 2 [1-3] | 2 [1-2] | 0.10 |
| PV systolic pressure drop (mmHg) | 33 [19-42] | 16 [12-26] | 43.56 [30-57] | 25 [17-32] | <0.001 |

Data are presented as median and inter-quantile range; TV: tricuspid valve; PV: pulmonary valve
Table S3. Risk factors for structural valve deterioration (SVD)/reintervention of the pulmonary valve substitute (prosthesis type as Homograft vs bioprosthesis) identified by Cox regression model.

| Variable                                | Hazard Ratio | 95% CI          | p-value  |
|-----------------------------------------|--------------|-----------------|----------|
| Homograft (bioprosthesis as ref)        | 0.27         | [0.13;0.55]     | < 0.001  |
| Age (per 1-year increase)               | 0.96         | [0.93;1.00]     | 0.055    |
| male sex                                | 2.07         | [1.06;4.03]     | 0.03     |
| BSA                                     | 0.36         | [0.12;1.03]     | 0.06     |
| Concomitant TVR                         | 0.18         | [0.04;0.93]     | 0.04     |
| Long-term antiplatelet therapy          | 0.28         | [0.12;0.63]     | 0.002    |

CI: confidence interval; BSA: body surface area; TVR: tricuspid valve repair
Table S4. Risk factors for structural valve deterioration (SVD)/reintervention of the pulmonary valve substitute including different types of bioprostheses identified by Cox regression model.

| Variable                    | Units    | Hazard Ratio | 95%CI          | p-value |
|-----------------------------|----------|--------------|----------------|---------|
| Type of valve               |          |              |                |         |
| Homograft                   | Ref      |              |                |         |
| Hancock                     | 4.26     | [1.74;10.45] | 0.001          |         |
| other                       | 8.20     | [3.19;21.12] | < 0.001        |         |
| Perimount                   | 2.03     | [0.80;5.18]  | 0.13           |         |
| Age (per 1-year increase)   |          |              |                |         |
| male sex                    | 2.20     | [1.09;4.43]  | 0.02           |         |
| BSA                         | 0.37     | [0.13;1.07]  | 0.07           |         |
| Concomitant TVR             | 0.10     | [0.02;0.58]  | 0.01           |         |
| Long-term antiplatelet therapy | 0.31     | [0.14;0.71]  | 0.005          |         |

CI: confidence interval; BSA: body surface area; TVR: tricuspid valve repair
Figure S1. Relationship between trans-pulmonary systolic pressure drop over the time patients receiving homografts and bio-protheses stratified by prosthesis size.
Figure S2. Relationship between trans-pulmonary systolic pressure drop (left) and pulmonary regurgitation degree (right) over the time patients receiving homografts and different type of bio-protheses.
Figure S3. Freedom from structural valve deterioration (SVD)/reintervention in patients receiving homografts vs bioprostheses stratified by age.
Figure S4. Freedom from structural valve deterioration (SVD)/reintervention in patients receiving homografts vs bioprostheses stratified by long term (>6 months) antiplatelet therapy following surgery.
Figure S5. Freedom from structural valve deterioration (SVD)/reintervention in patients receiving homografts vs bioprostheses stratified by eras of surgery.