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ORIGINAL ARTICLE

Stentless xenografts as an alternative to pulmonary homografts in the Ross operation†

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Abstract

OBJECTIVES: Because of the limited availability of pulmonary homografts (PH), porcine stentless xenografts (SX) have been proposed as an alternative for pulmonary valve replacement in the Ross operation. However, it is unknown whether they have similar good long-term durability. Therefore, we compared mid- to long-term outcomes between those two right ventricular outflow tract (RVOT) substitutes.

METHODS: In 288 adults (>18 years) undergoing a Ross operation between 1991 and 2012, Freestyle® SX was used in 18 patients and a cryopreserved PH was used in 270 for RVOT reconstruction. Only patients with follow-up >2 years were included. According to the operative period, gender and age, 37 patients with PH could be matched with 17 SX patients. Clinical and echocardiographic follow-up were obtained. In a subset of patients (SX, $n = 11$ and PH, $n = 25$), a cardiac computed tomographic (CT) scan was performed to analyse graft calcification.

RESULTS: The mean follow-up period was 8.2 ± 4.0 (range 2–14.6 years). During this period, 3 patients died from cancer, 2 in the SX group and 1 in the PH group ($P = 0.15$). No patient needed RVOT reoperation. At follow-up, RVOT peak gradient was 21 ± 5.9 mmHg in the SX and 16.3 ± 8.7 in the PH groups ($P = 0.07$). Peak gradient >40 mmHg was observed in only 1 patient in the PH group. Mean RVOT regurgitation was 0.1 ± 0.4 in the SX group and 0.8 ± 0.6 in the PH group ($P = 0.008$). CT scan analyses showed progressive calcification mainly of the graft wall, while the valve remained relatively free of calcium. Patients with the SX presented significantly higher calcium scores than those with PH ($P = 0.01$).

CONCLUSIONS: In adult patients having the Ross operation, calcic degeneration is observed in both the PH and the SX used as pulmonary substitutes. Calcification progresses more rapidly in the SX compared with the PH. In both grafts, calcifications affect mainly the wall, while the valve remains relatively free of calcium. As a consequence, both grafts show good and similar haemodynamic outcomes at mid- to long-term follow-up. The Freestyle® SX can be considered as an acceptable alternative for RVOT reconstruction when PH is not available.

Keywords: Ross procedure • Pulmonary valve • Pulmonary homograft • Stentless bioprosthesis

INTRODUCTION

In young adults with aortic valve dysfunction, the Ross operation is an attractive alternative to prosthetic aortic valve replacement. Indeed, it offers an excellent long-term survival, without the need for life-long anticoagulation, with more physiological haemodynamics and good durability of the pulmonary autograft [1–3]. The cost of those benefits is a more complex surgical procedure in comparison with prosthetic valve implantation, and the need for the right ventricular outflow tract (RVOT) reconstruction. The cryopreserved pulmonary homograft (PH) is the most used substitute and is currently considered the gold standard in this indication. It has shown a good durability with 95% freedom from reintervention in adults and between 80 and 90% in children [1, 4–6]. The main disadvantage of homografts is their limited availability in all graft sizes. This has led surgeons to use other valved grafts for RVOT reconstructions [7]. Stentless xenografts (SX), originally developed to compete with aortic bioprostheses, have been suggested by several teams as an interesting option for RVOT reconstruction, with encouraging preliminary results [8–10]. Our group has used since 1998 the Freestyle® SX (Medtronic, Inc., Minneapolis, MN, USA) in selected adult patients undergoing Ross operations.

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The aim of this study was to review our experience with the Freestyle® in this indication and to compare this graft with the PH. The comparison of both substitutes was made on mid- to long-term clinical and haemodynamic outcomes and on the degree of calcic degeneration.

PATIENTS AND METHODS

Patients

Between 1991 and 2012, 288 adult patients underwent a Ross operation in our institution. Surgery was performed by two experienced surgeons (G.K. and J.R.). In 270 patients, the RVOT was reconstructed with a cryopreserved PH from the European Homograft Bank (EHB, International Association, Brussels, Belgium). The use of the SX for RVOT reconstruction was introduced in the year 1998 for adult patients in whom no appropriate size of the PH was available, or in a few patients in whom the decision to perform a Ross procedure was taken intraoperatively. A total of 18 SX were used during this period. Because mid- to long-term outcomes were analysed in this study, we included only patients with a follow-up >2-years (SX, $n = 17$ and PH, $n = 253$).

The principal factors influencing the PH degeneration are: young recipient age, young donor age, length of cryopreservation, homograft size and the duration since implantation [2, 6, 11]. To compare the results of SX and PH, we selected a subgroup of PH patients who had characteristics similar to those of SX patients. The selection criteria were based on patient-related factors involved in graft degeneration: recipient age at implantation (±24 months) and duration since implantation (±12 months). For morphometric reasons, gender was used as a third selection criterion. For each SX patient, one or more PH patients meeting the criteria were selected, knowing that a certain percentage would deny undergoing the imaging studies proposed for the study. Following these criteria, we were able to select a subgroup of 37 PH patients. These 37 PH and the 17 SX patients represent the study cohort. Homograft-related factors, like donor age and length of cryopreservation, were not used for matching as obviously no correspondence existed in the SX group. For the same reason, the graft size was not used as selection criterion, because the labelled size of the two grafts does not represent the same measures (PH size = internal diameter and SX size = external diameter).

Patient characteristics and operative data were collected from patient charts and operative notes. The institutional ethics committee approved the study protocol.

Operative techniques

The Ross procedure was performed in a relatively standard way. The details of our technique were described in a previous work [12]. The techniques of autograft implantation included 'inclusion cylinder' and 'freestanding root'. As mentioned in a previous paragraph, PHs were the first choice for RVOT reconstruction. The largest size available at the homograft bank was generally implanted. Both the proximal and distal anastomoses were performed with running sutures of Prolene 4/0. A small piece of Teflon felt was used only to tie the running suture on the RVOT. Care was taken to avoid PH torsion and purse string effect at the distal anastomosis. For SX implantation, the technique was similar. The largest size available for the SX (27 and 29 mm) was systematically used.

Follow-up

Clinical follow-up was conducted through either outpatient visits or telephone follow-up by a research nurse. Information on survival status and valve-related complications, including thromboembolism, haemorrhage, endocarditis, reoperation and cardiovascular symptoms, was obtained. The closing interval for the study was between March and August 2012. Clinical follow-up was 100% complete. Mean follow-up was 7.3 ± 3.5 (range 2–14.5) years in the SX group and 8.6 ± 4.1 (range 2–14.6) years in the PH group ($P = 0.28$). The distribution of patients regarding the operative period was balanced: 28% ($n = 15$) had <5 years of follow-up, 37% ($n = 20$) had 5–10 years of follow-up and 35% ($n = 19$) had >10 years of follow-up.

Echocardiographic analysis

Transesophageal echocardiography was systematically performed intraoperatively, and transthoracic echocardiography (TTE) was obtained before discharge and at regular intervals during the follow-up. For patients followed in another institution or having no recent TTE, we asked them to perform this examination in our institution. Echographic data were obtained with the commercially available ultrasound systems: SONOS® 7500 and more recently the iE33 xMATRIX® (Philips Healthcare, Cleveland, OH, USA) with a second harmonic broadband, wide angle matrix array transducer (3.5/1.7 MHz).

All patients underwent a comprehensive examination, including M-mode, two-dimensional echocardiography, as well as conventional and colour Doppler examinations from parasternal and apical views. Transvalvular pulmonary gradients were calculated from the continuous Doppler waves, using the Bernoulli equation. The degree of regurgitation was evaluated by colour-flow Doppler mapping and staged as absent, mild, moderate or severe. The annulus size of the pulmonary graft was measured on a long-axis view at the level of the pulmonary valve insertion. The right ventricle (RV) assessment was performed through the apical four-chamber view: basal, mid-cavity and longitudinal diameters were measured. The RV function was estimated by measuring the fractional area change.

Discharge and last follow-up TTE were blinded reviewed by one cardiologist experimented in echocardiography (J.M.). TTE was available for analysis in 14 (82%) patients in the SX group (2 deaths and 1 patient denied to undergo TTE) and in 36 (97%) in the PH group (1 death). The mean TTE follow-up was 7.1 ± 3.8 years in the SX group and 8.1 ± 4.2 years in the PH group ($P = 0.47$).

Computed tomographic scanner acquisition and analysis

A computed tomographic (CT) scan was proposed to all patients included in the study. A CT scan was performed using a Brilliance® iCT256 scanner (Philips Healthcare). Serial images were prescribed over the heart and acquired using a prospectively

electro-cardiographically gated acquisition. Tube current was 900 mA and voltage, 100 kV. Images were acquired using 0.5-mm section thickness and reconstructed to 0.9-mm thickness. All scans were blinded reviewed on a dedicated workstation using a dedicated software (HeartBeatCS®, Philips Medical Systems, Cleveland, OH, USA) by one experienced operator (B.G.). A degree of pulmonary valve and tube calcification was quantified both using the Agatston [13] Score and Volume Score. CT scans were available in 11 (65%) patients in the SX group (2 deaths and 4 denied to undergo a CT scan) and in 25 (68%) in the PH group (1 death and 11 denied to undergo a CT scan). In this subgroup of patients, the mean follow-up was 7.8 ± 3.9 years in the SX group and 8.8 ± 4.1 years in the PH group ($P = 0.47$).

Statistical analysis

Categorical variables were reported as absolute numbers and percentages and compared with Pearson's χ^2 test. Continuous variables were expressed as mean ± standard deviation or median (inter-quartile range) if not normally distributed. The normal distribution of continuous variables was tested with the Kolmogorov–Smirnov test. Variables of normal distribution were compared by two-tailed Student's *t*-test, otherwise the non-parametric Mann–Whitney *U*-test was used. Statistical significance was considered for a *P*-value ≤0.05. For correlation studies, correlation coefficients were calculated between datasets for the linear, cubic, polynomial, exponential and logarithmic models. The model with the highest correlation coefficient was retained, namely the exponential model for Fig. 4 and the linear model for Fig. 5. For estimation of the regression lines, the software used the method of least squares, and the best-fit curve for the model chosen is the one with the minimal sum of the deviations squared from the set of data. The strength of the correlation was estimated by Spearman's Rho test and was considered as weak for a Rho <0.4, moderate between 0.4 and 0.7 and strong >0.7. The statistical analysis was performed with SPSS v15.0 (IBM Inc., Chicago, IL, USA).

RESULTS

Patient's demographic and preoperative characteristics are listed in Table 1. No statistically significant differences were found between the two groups in terms of age, gender, body surface area, symptomatology, type of aortic valve dysfunction and left ventricular ejection fraction.

Operative results

In the SX group, the first two patients received a 27-mm valve, and then a 29-mm valve was implanted in the 15 following patients. In the PH group, the mean size of the PH implanted was 25 ± 1.5 (range 23–28) mm. Techniques of autograft implantation, associated procedures and operative times were similar in both groups (Table 2). There was no hospital mortality. Major postoperative complications are listed in Table 2.

Long-term clinical outcomes

During the follow-up period, 3 patients died, all from cancer (SX, $n = 2$ and PH, $n = 1$; $P = 0.15$). No patient needed RVOT reintervention for SX or PH dysfunction. At last follow-up, all patients were in NYHA Class I or II, with no difference between the two groups (SX, Class I = 10, Class II = 5 and PH, Class I = 27, Class II = 9; $P = 0.79$).

Table 1: Patients preoperative characteristics

Variables	Stentless xenografts (17)	Pulmonary homografts (37)	*P*-value
Age (years ± SD, [range])	48.6 ± 8.2 [36–57]	46.4 ± 5.8 [34–55]	0.28
Sex (males)	13 (76.5%)	31 (83.8%)	0.52
Body surface area (m^2)	2.0 ± 0.2	2.0 ± 0.2	0.47
Previous surgery	2 (11.8%)	3 (8.1%)	0.66
Clinical status			
New York Heart Association I	2 (11.8%)	11 (29.7%)	
New York Heart Association II	10 (58.8%)	15 (40.5%)	0.30
New York Heart Association III	5 (29.4%)	11 (29.7%)	
Aortic valve pathology			
Aortic stenosis	2 (11.8%)	12 (32.4%)	
Aortic regurgitation	7 (41.2%)	8 (21.6%)	0.17
Mixed (aortic stenosis + aortic regurgitation)	8 (47%)	17 (46%)	
Aortic valve disease aetiology			
Congenital	11 (64.7%)	27 (73%)	
Tricuspid degenerative	3 (17.6%)	4 (10.8%)	
Rheumatic	1 (5.9%)	2 (5.4%)	0.97
Endocarditis	1 (5.9%)	2 (5.4%)	
Valve prosthesis failure	1 (5.9%)	2 (5.4%)	
Left ventricular function			
Left ventricle ejection fraction >50%	14 (82.3%)	34 (91.9%)	
Left ventricle ejection fraction 30–50%	2 (11.8%)	2 (5.4%)	0.58
Left ventricle ejection fraction <30%	1 (5.9%)	1 (2.7%)	

Echocardiographic results

The discharge and follow-up TTE results are presented in Table 3. Despite a relative difference in the mean labelled size of SX and PH implanted, the annulus diameter and peak gradient were similar at discharge between the two types of pulmonary substitutes. From discharge to follow-up, both groups showed an increase in peak gradient; however, the gradient remained, in the majority of patients, in an acceptable clinical range. Peak gradient >40 mmHg was observed in only 1 patient from the PH group ($P = 0.49$). The peak gradient increased slightly more in the SX compared with the PH group, but the difference between the two groups was not statistically significant (Table 3 and Fig. 1). At follow-up, RVOT regurgitation was nil in 79% and Grade 1 in 21% in the SX group; and in the PH group, regurgitation was nil in 31%, Grade 1 in 58% and Grade 2 in 11% ($P = 0.008$).

Finally, follow-up TTE's showed similar RV dimensions between the two groups. Basal diameter was 44 ± 7 in SX vs 45 ± 7 mm in PH ($P = 0.6$), mid-cavity diameter was 33 ± 6 in SX vs 34 ± 7 mm in PH ($P = 0.85$) and longitudinal diameter was 76 ± 4 in SX vs 79 ± 7 mm in PH ($P = 0.3$). The RV fractional area change was also similar between groups (SX, 51 ± 7% and PH, 48 ± 6%; $P = 0.15$).

Table 2: Operative data and postoperative results

Variables	Stentless xenografts (17)	Pulmonary homografts (37)	*P*-value
CPB time (min)	152 ± 26	154 ± 27	0.79
Cross-clamping time (min)	127 ± 19	127 ± 17	0.98
Autograft implantation			
Inclusion cylinder	6 (35.3%)	14 (37.8%)	0.86
Free standing root	11 (64.7%)	23 (62.2%)	–
Pulmonary substitute size (mm)[a]	27 ($n = 2$) 29 ($n = 15$)	25 ± 1.5 –	– –
Concomitant procedures			
AAR with Dacron graft	4 (23.5%)	7 (18.9%)	0.98
Mitral valve repair	1 (5.9%)	4 (10.8%)	0.94
CABG	1 (5.9%)	2 (5.4%)	0.57
Subaortic membrane resection	1 (5.9%)	0 (0%)	0.69
Postoperative complication			
Mortality	0	0	–
Reoperation for bleeding	1 (5.9%)	1 (2.7%)	0.84
Pericardial effusion	0 (0%)	4 (10.8%)	0.39
Myocardial infarction	0 (0%)	1 (2.7%)	0.69
Permanent pace maker implantation	1 (5.9%)	0 (0%)	0.69

AAR: ascending aortic replacement; CABG: coronary artery bypass graft; CPB: cardiopulmonary bypass.
[a]In the SX group: all patients received a 29-mm (larger available size) size, except 2 who received 27 mm; In the PH group: the number represents the mean inner diameter of the inflow given by the tissue bank.

Computed tomographic scanner results

The CT scan analyses showed that calcification affects essentially the wall of the grafts, while the valves remain relatively free of calcium (Fig. 2). Overall, patients in the SX group presented significantly higher calcium scores compared with those in the PH group (Table 3). The difference between the groups is observed already in the mid-term follow-up interval and increases in the long-term follow-up intervals (Fig. 3). Correlation analyses showed that graft calcification increases exponentially with time in both grafts, with a more rapid progression in the SX group (Fig. 4). Between the calcium score and peak gradient, a linear correlation was found in each group (Fig. 5). The near-to-horizontal slopes of the correlation lines, related to the a coefficient in the line equations (SX, $a = 0.001$ and PH, $a = 0.002$), are consistent with the relatively low degree of calcification observed in the valve cusps (Fig. 2).

DISCUSSION

In his initial experience with the Ross procedure during the 1970s, Donald Ross had used aortic homografts and other autologous tissues to reconstruct the RVOT [7]. One decade later, PHs were introduced, and their superior results compared with aortic homografts made them the gold standard for this indication [14]. However, the shortage of suitable homografts in

Table 3: Postoperative echocardiographic and CT scan results

	Discharge TTE			Follow-up TTE			CT scan		*P*-value[b]
	Annulus diameter (mm)	Pulmonary regurgitation	Peak gradient (mmHg)	Pulmonary regurgitation	Peak gradient (mmHg)	Peak gradient increase (mmHg)	Calcium volume (mm^3)[a]	Agatston Score[a]	
Stentless xenografts	21.6 ± 1.5	0	11.9 ± 4.5	0.1 ± 0.4	21 ± 5.9	9.5 ± 5.5	2782 [671–5666]	1213 [829–7286]	0.17; <0.001
Pulmonary homografts	22.3 ± 1.6	0.2 ± 0.2	9.4 ± 4.9	0.8 ± 0.6	16.3 ± 8.7	5.4 ± 8.8	351 [211–936]	398 [196–1322]	0.006; 0.007
P-value	0.26	0.28	0.14	0.008	0.07	0.16	0.006	0.015	–

[a]Median [interquartile range].
[b]Compare pulmonary regurgitation and peak gradients between discharge and follow-up TTE within the SX and PH groups.
CT: computed tomography; TTE: transthoracic echocardiography.

paediatric patients, the lack of human tissue availability at some periods or in some countries and the PH failure due to structural degeneration have led to the consideration of other alternatives for RVOT reconstruction [7]. Accordingly, SXs appeared attractive because of their availability and their anticalcification treatments.

In this study, we analysed the mid- to long-term results of the Freestyle® SX used in adult patients having the Ross operation. We showed that RVOT can be safely reconstructed with the SX. In comparison with PH, the SX showed similar clinical outcomes with no need for reintervention after a mean follow-up of 8 years. Over time, transvalvular gradients increased in both grafts, but remained in acceptable clinical ranges in most patients. In comparison with the PH, the SX presented a slightly greater increase in transvalvular gradients, but a lower increase in regurgitation. Calcic degeneration occurred in both grafts and involved predominantly the wall of the graft, leaving the cusps relatively free of calcium. Calcifications progressed more rapidly and severely in the wall of the SX than in the PH.

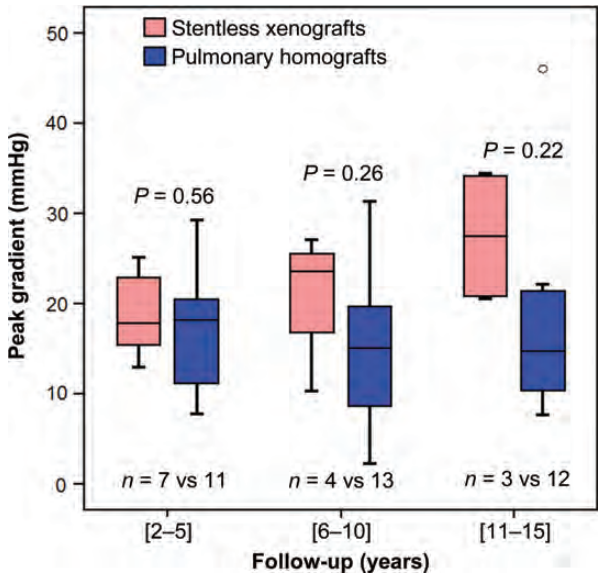

Figure 1: Box plot illustrating the evolution of the peak gradient along in three different periods of follow-up.

Like other bioprostheses, the PH is subject to structural degeneration due to immune reactions from the host [15]. The PH dysfunction, mainly stenosis, resulting from that degeneration occurs more frequently and earlier after implantation in children in comparison with adults, in patients receiving smaller PH, in PH from younger donor age and in PH with shorter duration of cryopreservation [2, 6, 11]. Following several large series, after one decade, the freedom from PH reintervention ranges from 93 to 100% in adults and from 80 to 90% in children [1, 4–6, 12, 16]. Regarding the other RVOT substitutes, aortic homografts in the pulmonary position did worse in comparison with PH with freedom from reintervention of 70% after 5 years only in a predominantly paediatric population [14]. The bovine jugular vein (Contegra®, Medtronic, Inc.), developed essentially to provide small conduits for children, showed freedom from reintervention at 10 years ranging from 70 to 90% depending on the conduit size [17, 18]. In comparison with PH, bovine jugular veins seemed to do as well or even better, in children <2 years [17–19].

Regarding the use of SXs in the Ross, few data are available in the literature. The studies include small series (<20 patients) that show all good short-term results in adults, or in children, with no need for reintervention after a mean follow-up of 3 years [8–10]. This study is the first to bring mid- to long-term follow-up data with clinical, haemodynamic and calcic degeneration analysis of the SX compared with the PH. While CT scan analyses showed more severe calcification in the SX, echocardiographic analyses showed relatively similar deterioration of valve function over time in both groups. Relevant valve regurgitation, which is

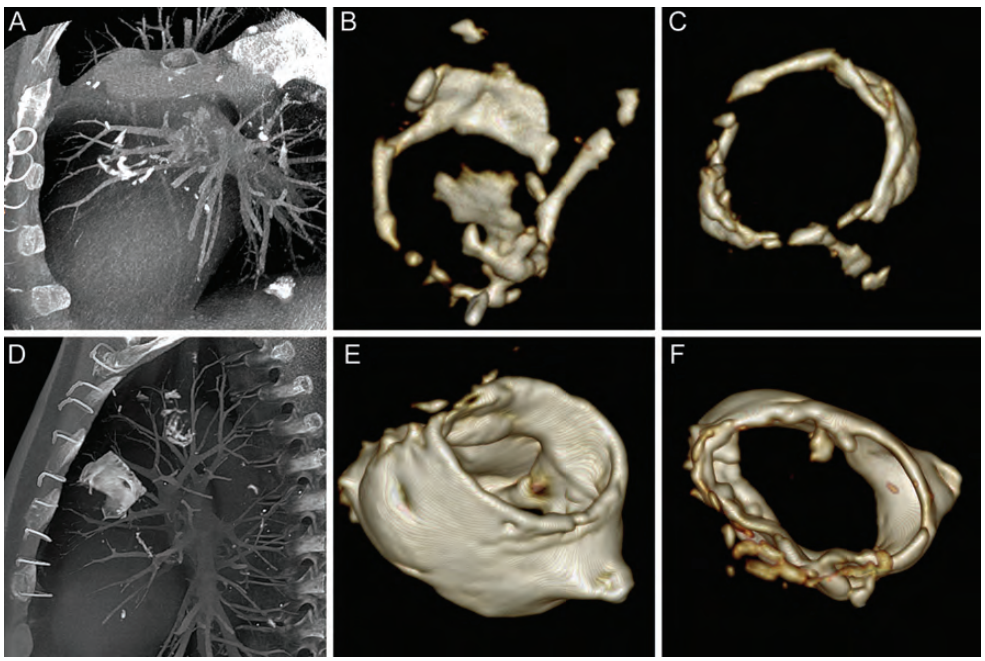

Figure 2: (**A**) Volume intensity projection (VIP) image of a calcified PH implanted 8 years ago; (**B**) volume rendering image of the calcified PH (anterior view); (**C**) volume rendering image of the calcified PH (inferior view); (**D**) VIP image of a SX xenograft implanted 12 years ago; (**E**) volume rendering image of the calcified SX (anterior view) and (**F**) volume rendering image of the calcified SX (inferior view).

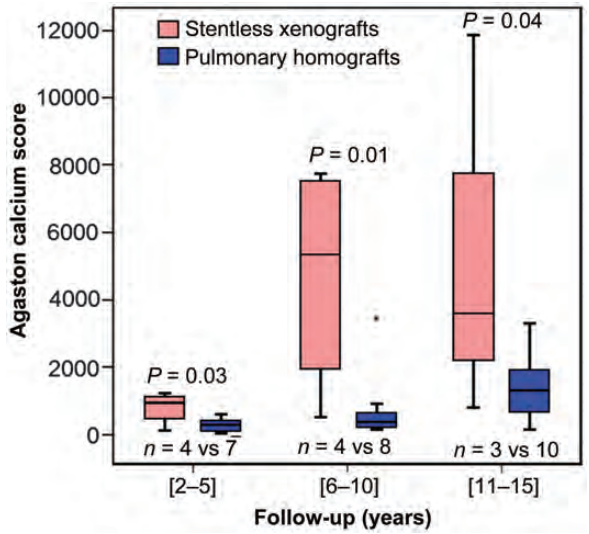

Figure 3: Box plot illustrating the evolution of the Agatston Calcium Score along in three different periods of follow-up.

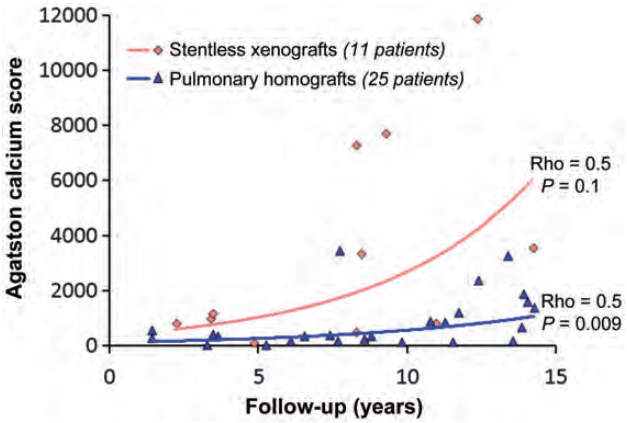

Figure 4: Exponential correlation between Agatston Calcium Scores and follow-up in pulmonary homografts and stentless xenografts.

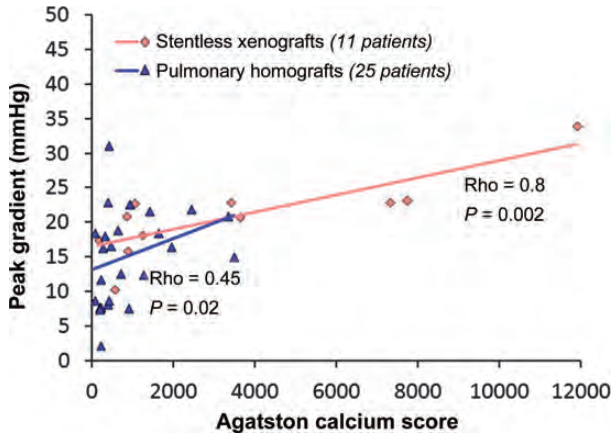

Figure 5: Linear correlation between peak gradients and Agatston Calcium Scores in pulmonary homografts (line equation: $y = 0.002x + 13.1$) and stentless xenografts (line equation: $y = 0.001x + 16.6$).

a typical mode of failure of the SX in the aortic position, was not observed in this study, probably because the low pressure in the right heart does not have the strength to tear the leaflets weakened by structural degeneration like it does in the left heart [20].

We found that calcic degeneration increased with time, essentially on the wall of the grafts and more rapidly in the SX group. These findings explain the relatively preserved valve function in both the groups and confirm in the human the observations made by Flameng *et al.* [21] in an experimental study. In that study, the authors compared structural degeneration of aortic homografts, PHs and different types of SXs (porcine and bovine) implanted in the pulmonary position of adolescent sheep. They found severe calcifications in the wall portion of the porcine xenografts irrespective of the antimineralization treatment. Aortic homografts walls also showed more calcium than PHs. Leaflet calcification or pannus was mild and similar between aortic, PHs and porcine xenografts. In this study, the bovine jugular vein showed wall calcifications, but leaflets were free of calcification or pannus. Finally, the bovine pericardial conduit (Pericarbon®, Sorin Group, Milan, Italy) showed no calcifications, but extensive pannus overgrowth with leaflet retraction. In a randomized study comparing aortic homografts and Freestyle® in the aortic position, El-Hamamsy *et al.* showed at long-term greater calcifications of aortic homografts in the long term [22]. However, their data and ours suggest similar calcification rates of the Freestyle® either on the aortic or the pulmonary position.

The Freestyle® SX is fixed with glutaraldehyde at zero pressure on the cusps and exposed to alpha-amino oleic acid as antimineralization treatment. PHs are exposed to antibiotics and then cryopreserved without chemical fixation. In both the SX and PH, structural degeneration is related to a certain degree of immune and inflammatory reaction [15, 20]. It has been demonstrated that the mineralization process in bioprosthetic valves is initiated within the nonviable connective tissue cells devitalized, but not removed, by glutaraldehyde or cryopreservation pretreatments [23]. For this reason, human decellularized pulmonary valves (e.g. Synergraft SG®, CryoLife, Inc., Kenesaw, GA, USA) have been developed to offer the potential for better performances due to the reduced degree of rejection [24]. These new grafts showed encouraging short- to mid-term results; [25] however, long-term data are necessary to confirm whether they offer better durability compared with non-decellularized homografts.

Limitations of the study

One limitation of this cohort study is that patients were not randomized for the choice of the pulmonary valve substitute. The comparison between the groups was based on a selection of PH patients meeting some of the criteria reported to influence bioprosthesis degeneration. As such, other patient-related factors or factors like duration of cryopreservation, donor age and graft size can have influenced the results obtained in this study. However, despite the graft size not being used for matching, interestingly, both groups showed a similar mean internal diameter of the graft after implantation.

Despite the long period of recruitment (1998–2010), the technique of implantation and preparation of the graft remained the same over this period. Variability related to the measurement methods, or materials, was minimized by reanalysing the source data (echographic images) by one-blinded experimented operator and by performing new follow-up evaluations (echo and CT scan).

The statistical power of the study was evaluated with compromise *post hoc* power analyses using GPower3 Software (Universitat Kiel, Germany). With a significance set at 0.05 and an error probability ratio at 1, the analysis revealed that, for the sample size and effect size, the power was 0.82 to detect differences in gradients and 0.89 to detect differences in calcium scores. In clinical studies, a power >0.8 is generally recommended.

CONCLUSION

In adult patients having the Ross operation, calcic degeneration is observed in both PHs and Freestyle® SXs used as pulmonary substitutes. Calcification progresses exponentially, with a more rapid increase in SXs compared with PHs. In both grafts, calcifications affect mainly the wall, while the valve remains relatively free of calcium. As a consequence, both grafts showed good and similar haemodynamic outcomes at mid- to long-term follow-up. Considering these data, the Freestyle® SX can be considered as an acceptable alternative for RVOT reconstruction in the Ross procedure when a PH is not available. Further analyses are mandatory, particularly to determine whether the greater degree of calcic degeneration observed in SX will cause severe dysfunction in the longer term.

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APPENDIX. CONFERENCE DISCUSSION

Dr W. Hargrove *(Philadelphia, PA, USA)*: First, I'd say this is an observational study. I'm a little skeptical about making statistical analysis when you have so few patients. I know you did a type of propensity matching, but with 17 in one group and 37 in the other, I'm not sure; again, I'm not a statistician, but I'm not sure about that other than observation.

I have three questions. The first question is: What, if any, anatomical modifications of the xenograft did you need to make to place it into the right ventricular outflow tract to fit better? Two, based on your analysis of the calcium

scores and the CT scans, do you think possibly the cell-depleted xenografts may become the new Holy Grail? And finally, if you needed a Ross procedure next week, what would you tell the surgeon that you wanted to have placed in your right ventricular outflow tract?

Dr Hechadi: Excuse me, I didn't understand the two last questions. Can you repeat.

Dr Hargrove: The first, based on your analysis of the calcium score, you mentioned it somewhat in your discussion about the cell-depleted xenografts perhaps calcifying less, do you think this will be a better alternative than the standard xenograft? And the final is: If you needed a Ross procedure yourself, what would you tell the surgeon you wanted placed in your right ventricular outflow tract?

Dr Hechadi: In our centre, the institutional attitude is to use pulmonary homografts systematically for Ross procedures. So stentless xenografts were placed only when the Ross procedure was not initially planned or in the emergency cases. That's why we have few patients; we systematically use pulmonary homografts. So it's clear here that stentless xenografts calcify more, and we propose it just as an alternative. Pulmonary homografts remain the gold standard for this indication and the stentless xenografts are proposed only if the pulmonary homografts are not available or not available in suitable sizes.

Dr L. De Kerchove *(Brussels, Belgium)*: I'm one of the coauthors of this study. If I can add some information to the question asked by my colleague from Philadelphia.

Concerning your first question, do we trim the xenograft for implantation? No, we don't trim it. As it is, it fits relatively well to reconstruct the RVOT. The decellularized homograft is one of the options for the future. We actually have only short- and mid-term follow-up regarding the function of those substitutes in the right ventricular outflow tract. We lack the long-term results, so it's difficult to compare the clinical results with the cellularized homografts that we actually used. Those give quite good results, especially in the adult population.

So what is our actual approach for RVOT reconstruction? Dr. Hechadi told you, homografts; we are quite happy with them and in Brussels, we have a very nice homograft bank which provides us with a lot of very good homografts. And this is actually our first choice. If a lack of homografts is the case in your country, your institution, a xenograft is a substitute that can be used with so far good clinical long-term results.

Dr H. Schaefers *(Homburg/Saar, Germany)*: I would like to address the last aspect. If I recall the data correctly, the mean gradient across the outflow tract increased in an almost linear fashion. And in the group 10 to 15 years, which is a relatively wide window, it was close to 30 mmHg. You briefly mentioned the results of the statistical test, which, because of the variability, did not show a statistical significance. On the other hand, I would think that after 10–15 years, for an operation that should have a long durability, a mean gradient of 30 mmHg is definitely clinically relevant. Would you like to comment?

Dr Hechadi: I don't think so, because the peak gradient of 30 mmHg is not too high. The indication for reoperation for RVOT is a peak gradient of 70 mmHg. We were speaking here about peak gradients. We don't speak about mean gradients.

Dr S. Takamoto *(Tokyo, Japan)*: In your slide, the peak pressure gradient through the pulmonary xenograft is increased in the longer follow-up time. If it is increased to a critical level, 50 mmHg, how do you treat the patient?

Dr Hechadi: In these patients, in the stentless group there was no reoperation because the highest peak gradient we had in our series was about 36 mmHg. In the homograft group, we had some reoperations. In the others, there was about 20% of reoperations because they had peak gradients >70 mmHg. But in the stentless group we didn't have reoperations at all.

For reoperations, it was standard surgical re-replacement by a pulmonary homograft. We didn't use the Melody valve or anything like that.