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European Journal of Cardio-thoracic Surgery xxx (2011) xxx–xxx

 EUROPEAN JOURNAL OF
 CARDIO-THORACIC
 SURGERY

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The Contegra conduit in the right ventricular outflow tract is an independent risk factor for graft replacement[☆]

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Received 31 July 2010; received in revised form 20 November 2010; accepted 26 November 2010

Abstract

Objective: A large spectrum of congenital heart diseases requires valved conduits to establish an anatomical continuity between the right ventricle outflow tract (RVOT) and the pulmonary artery. The aim of the present study was to compare the incidence of graft replacement in patients receiving the Contegra conduit (bovine jugular vein graft) with that in patients receiving a homograft implanted in the RVOT. **Methods:** We reviewed a total of 347 conduits (Contegra 54; homografts 293) implanted in the RVOT from 1989 to 2003 in 323 patients (median age 12.7 years, range 4 days–69 years). Indications were Tetralogy of Fallot ($n = 148$), Ross operation ($n = 89$), truncus arteriosus communis ($n = 47$), pulmonary valve atresia ($n = 30$), double-outlet right ventricle ($n = 15$), transposition of the great arteries ($n = 12$), and endocarditis ($n = 6$). Follow-up was 99.4% complete (mean time: 5.9 years; range: 0–14.2 years). **Results:** Freedom from graft replacement at 1, 5, and 10 years of follow-up in the Contegra and homograft groups were $98.1 \pm 1.9\%$, $78.3 \pm 5.8\%$, and $63.5 \pm 7.2\%$ and $99.6 \pm 0.4\%$, $94.0 \pm 1.6\%$, and $81.4 \pm 3.4\%$, respectively (log-rank test, $p < 0.001$). Independent predictors of graft replacement of the whole sample population were: graft size ≤ 20 mm (hazard ratio (HR) 3.6), age ≤ 10.4 years (HR 3.0), the non-anatomical position of the graft (HR 2.9), and the use of the Contegra conduit (HR 2.5). The multivariable analysis carried out on the propensity-score-matched population confirmed three independent predictors of graft replacement: graft size ≤ 20 mm (HR 8.0), the non-anatomical position of the graft (HR 2.3), and the use of the Contegra conduit (HR 3.7). **Conclusions:** Besides size of the graft, age of the patients, and the non-anatomical position of the graft, the use of the Contegra conduit was found to be an independent risk factor for graft replacement in the RVOT. Patients receiving this conduit were more than twice as likely to undergo re-operation for graft replacement as those receiving a homograft.

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Keywords: Right ventricular outflow tract; Homograft; Allograft

1. Introduction

A large spectrum of congenital heart diseases requires valved conduits to establish an anatomical continuity between the right ventricle outflow tract (RVOT) and the pulmonary artery.

In 1966, Ross and Somerville [1] described the reconstruction of the RVOT with a homograft. Since then, aortic, but, especially, pulmonary homografts have been reported to offer excellent hemodynamic results when implanted in RVOT position [2].

Nonetheless, the valved human homografts do not represent the ideal conduit. They are not always sufficiently

available, and their life span is limited by a bio-degeneration process. In selected subgroups of patients, a high incidence of graft replacement because of homograft failure is observed.

In 1999, the Contegra bovine jugular valved conduit (Medtronic, Inc., Minneapolis, MN, USA) was proposed for the reconstruction of the RVOT. Because of its encouraging initial results in clinical trials [3,4], it gained quickly popularity as a possible alternative to the homograft.

The recent literature about early and the midterm results of the Contegra conduit implanted in the RVOT is controversial. Several studies have reported an unexpected occurrence of graft failure [5,6], while others have reported similar behaviors compared with homograft [7].

The aim of this study is therefore to analyze the long-term durability of this graft and to compare the incidence of graft replacement in patients receiving the Contegra conduit with that in patients receiving a homograft implanted in RVOT.

[☆] Presented at the 24th Annual Meeting of the European Association for Cardio-thoracic Surgery, Geneva, Switzerland, September 11–15, 2010.

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2. Methods

2.1. Patients

In total, 347 conduits (Contegra 54; homografts 293) implanted in the RVOT from 1989 to 2003 in 323 patients (median age 12.7 years, range 4 days–69 years) were retrospectively reviewed. The study was restricted to patients, who survived to 30 days after the graft implantation surgery. Indications for RVOT surgery were Tetralogy of Fallot ($n = 148$), Ross procedure ($n = 89$), truncus arteriosus communis ($n = 47$), pulmonary valve atresia ($n = 30$), double-outlet right ventricle ($n = 15$), transposition of the great arteries ($n = 12$), and endocarditis ($n = 6$). Follow-up was 99.4% complete (mean time: 5.9 years; range: 0–14.2 years).

Table 1 summarizes the baseline characteristics of the sample populations. Patients receiving the Contegra were younger, had a higher proportion of graft implanted in non-anatomical position, lower proportion of redo, shorter clamp times, and smaller graft sizes compared with patients receiving homografts. Differences in terms of age and graft size between the two groups may reflect the low availability of the homograft under 16 mm diameter. Differences in terms of clamp times may reflect the differences in diagnosis between the groups. In fact, a larger proportion of patients receiving the homograft presented with aortic valve stenosis or regurgitation treated by the Ross procedure, which is a more time-consuming procedure.

In Table 2, the baseline characteristics of a propensity-score-matched population are listed (see below).

2.2. Homograft

The implanted homografts were cryopreserved aortic ($n = 45$, 15.4%) and pulmonary ($n = 248$, 84.6%) valve conduits processed by the European Homograft Bank (EHB, Brussels, Belgium). No ABO blood group or gender matching was realized.

They are dissected and decontaminated in a low-grade antibiotic solution containing cefoxitin 240 mg ml⁻¹, lincomycin 120 mg ml⁻¹, polymyxin B 100 mg ml⁻¹, and vancomycin 50 mg ml⁻¹. They are immersed in a 10% dimethylsulfoxide solution and left for 30 min in wet ice to allow penetration of dimethylsulfoxide into the tissue. Cooling rate is 1 °C min⁻¹ down to -40 °C, and 5 °C min⁻¹ down to -100 °C and is electronically monitored. Then the tissue is transferred into liquid nitrogen at a temperature below -150 °C and stored for a maximum of 3 years [2]. The grafts were transported in a cooler of liquid nitrogen to the operating theatre and thawed in a water bath before use.

2.3. Contegra

The Contegra conduit is a heterologous bovine jugular vein graft with a trileaflet venous valve and natural sinus slightly larger in diameter than its lumen.

A final sterilization step is performed using a proprietary sterilant that contains 1% glutaraldehyde and 20% isopropyl alcohol, and in which the conduit is preserved and packaged until use (www.fda.gov). The Contegra was available in our department in sizes between 12 and 22 mm since January 2000.

Table 1. Baseline characteristics of the whole sample population.

	Total cases ($n = 347$)	Homograft group ($n = 293$)	Contegra group ($n = 54$)	<i>p</i> Value	Standardized difference of the mean
Age (years)	Median 12.7 (5.1–22.5) Mean 14.7 ± 11.9	Median 13.4 (5.7–24.0) Mean 15.5 ± 12.1	Median 10.4 (2.5–15.8) Mean 10.6 ± 9.4	0.009	44.6%
Age ≤ 10.4 years	42.9% (149)	41.9% (123)	48.1% (26)	0.4	
Female sex	36.9% (128)	36.2% (106)	40.7% (22)	0.54	
Indications					
TOF	42.7% (148)	42.0% (123)	46.2% (25)		
Ross	25.7% (89)	27.3% (80)	16.7% (9)		
TAC	13.5% (47)	11.6% (34)	24.1% (13)		
PVA	8.6% (30)	9.6% (28)	3.7% (2)		
DORV	4.3% (15)	4.1% (12)	5.6% (3)		
TGA	3.5% (12)	3.4% (10)	3.7% (2)		
Endocarditis	1.7% (6)	2.0% (6)	0% (0)		
Graft in non-anatomical position	17.9% (62)	15.7% (46)	29.6% (16)	0.020	
Redo	47.0% (163)	52.9% (155)	14.8% (8)	<0.001	
Clamp time (min)	Median 71.5 (45–108) Mean 75.3 ± 37.8	Median 75.0 (46–112) Mean 79.9 ± 36.8	Median 56.5 (29–74) Mean 50.6 ± 33.7	<0.001	82.7%
Graft size (mm)	Median 22 (19–24) Mean 20.1 ± 4.2	Median 22.5 (20–24) Mean 21.4 ± 4.1	Median 20.0 (14–22) Mean 18.6 ± 4.0	<0.001	67.8%
Graft size ≤ 20 mm	35.4% (121)	32.3% (93)	51.8% (28)	0.009	
Graft sizes (mm)		7–10: $n = 5$ 11–14: $n = 23$ 15–18: $n = 27$ 19–22: $n = 89$ 23–26: $n = 136$ 27–29: $n = 8$ Missing data: 5	12: $n = 10$ 14: $n = 4$ 16: $n = 5$ 18: $n = 2$ 20: $n = 7$ 22: $n = 26$ Missing data: 0		

DORV: double outlet right ventricle; PVA: pulmonary valve atresia. TAC: truncus arteriosus communis; TGA: transposition of great arteries; TOF: Tetralogy of Fallot. Graft in non-anatomical position: DORV, TAC.

Table 2. Baseline characteristics of propensity score-matched population.

	Total cases (n = 82)	Homograft group (n = 41)	Contegra group (n = 41)	p Value	Standardized difference of the mean
Age (years)	Median 7.8 (1.8–15.9) Mean 10.3 ± 10.9	Median 5.9 (1.7–18.2) Mean 10.5 ± 11.7	Median 9.5 (1.5–15.8) Mean 10.1 ± 10.3	0.9	3.6%
Age ≤ 10.4 years	58.5% (48)	63.4% (26)	53.7% (22)	0.5	
Female sex	42.7% (35)	43.9% (18)	41.4% (17)	1	
Graft in non-anatomical position	22.0% (18)	17.0% (7)	26.8% (11)	0.4	
Redo	20.7% (17)	21.9% (9)	19.5% (8)	1	
Clamp time (min)	Median 66 (47.0–79.0) Mean 63.29 ± 32.0	Median 67.0 (56.55–79.5) Mean 68.6 ± 30.2	Median 62.0 (44.0–76.0) Mean 57.9 ± 30.8	0.4	35.1%
Graft size (mm)	Median 20.0 (14.0–22.0) Mean 18.6 ± 4.5	Median 19 (154.3–23.0) Mean 18.8 ± 4.8	Median 20.0 (14.0–22.0) Mean 18.3 ± 4.2	0.4	11.1%
Graft size ≤ 20 mm	55.5% (45)	56.1% (23)	53.7% (22)	0.8	

The conduits were rinsed 3 times for 5 min in normal saline solution before use.

2.4. Surgical technique

Implantations were done during support with cardiopulmonary bypass and moderate hypothermia or normothermia. The surgical procedures were carried out under cardioplegic heart arrest or fibrillating heart. The conduits were kept as short as possible. The distal anastomosis was performed using 4/0 or 5/0 continuous Prolene sutures. Care was taken to prevent the purse-string effect. If needed, the incision to the left or right pulmonary artery was extended to allow proper fitting of the interposed graft. The proximal anastomosis was performed using a 4/0 suture at the level of the crista supraventricularis in the case of ventriculoarterial concordance (anatomic position) and to the anterior free wall of the right ventricle in the case of non-concordance (non-anatomic position). In the homograft group, the anastomosis to the right ventricle was sometimes enlarged with a right-ventricular outflow hood of xenopericardium.

In the Contegra group, the distal part of the conduit was cut at the level of the commissures and sewed in on a circumferentially cut pulmonary artery bifurcation. In this case, care was also taken to avoid the purse-string effect. The proximal part of the conduit was cut with a redundant anterior flap to construct the hood of the outflow tract. Transesophageal echocardiography was performed routinely in the operating room.

2.5. Follow-up

Patients did not receive any antiaggregation or anticoagulation therapy. All patients were followed up by our referring pediatric or congenital cardiologists. Patients were seen routinely 6 weeks after surgery and then every 6 months. In case of pathologic findings, the patients were asked to return earlier. An instantaneous peak gradient ≥ 50 mmHg was considered as a severe stenosis. A pulmonary valve regurgitation grade 3 (on a scale of 4) or more was considered severe. The follow-up mean time of the whole sample population was 5.9 years (0–14.2 years), and it was 99.4% complete. For the homograft and Contegra groups, the follow-up mean times were 5.9 years (0–14.2 years) and 6.0 years (0–10.4 years), respectively.

2.6. Indications for graft explantation

The first indication to replace the graft was the presence of severe stenosis or regurgitation associated with at least one of the following: reduction in exercise tolerance, dilatation of the right ventricle, presence of tricuspid insufficiency, or presence of arrhythmias. The second indication was diagnosis of endocarditis. All patients presenting with severe distal stenosis of the graft underwent balloon dilation and stenting. In case of persistent stenosis, surgical treatment was required. No trans-catheter valve was implanted in this sample population.

2.7. Analysis of data

Continuous variables were expressed as median (25th and 75th percentiles), and mean ± standard deviation. Dichotomous categorical variables were indicated as absolute frequency (percentage). When appropriate, Student's *t*-test for independent samples, Mann–Whitney *U*-test, chi-square test, and Fisher's exact test were used in the univariable analysis to study the differences in baseline characteristics between the homograft and the Contegra groups.

Unadjusted long-term rates of freedom from graft replacement were calculated using the Kaplan–Meier method. The log-rank test was used to compare the curves of freedom from graft replacement of the two groups.

As the goal of the study was to determine the longevity of the grafts, we excluded, from the original sample population, the patients who did not survive the first postoperative month because of competing risk. In particular, 10 patients over 333 (3.0%), two in the Contegra group and eight in the homograft group, died in the first postoperative month.

Further, to simplify our analysis, we used the variable 'non-anatomical position of the graft', which groups the diagnosis of truncus arteriosus communis and double-outlet right ventricle.

The covariates 'age of the patients' and 'size of the graft' were studied as dichotomic variables. Hence, a receiver operating characteristic (ROC) curve analysis was carried out for both covariates, inserting as classification variable 'graft replacement'. The obtained pivot values (10.4 years of age and 20 mm of size graft) were used as cut off values for the dichotomization procedure.

All operative data listed in Table 1 were entered in a backward logistic Cox regression multivariable model with ‘graft replacement’ as dependent variable. From this model, the independent predictors of graft replacement of the whole sample population were obtained.

Parallely, a propensity score matching was used to reduce the selection bias related to the retrospective nature of this study. Propensity score was defined as the conditional probability of belonging to the Contegra group versus the homograft group, given the covariates. Hence, all operative data listed in Table 1 were studied by univariable analysis to identify factors predictive of group membership. Variables predictive of group membership with a p values ≤ 0.15 (age of the patient, size of the graft, redo prevalence, not anatomical position of the graft prevalence, and clamp times) were entered into a backward logistic multivariable regression model with ‘graft type’ (1 = Contegra, 0 = homograft) as dependent variable. From this model, the propensity score was computed for each patient. The final model had an area under the ROC curve of 0.86. A nearest neighbour 1:1 matching within a calliper width of 0.1 was used. From this procedure, 41 matched pairs of patients were obtained. Their baseline characteristics are listed in Table 2. To assess the balance in terms of covariate distributions between the two groups, the significance tests (p values) and the standardized difference of the mean were used. The

same statistical steps mentioned above were used to identify the independent predictors of graft replacement in this propensity-score-matched population.

By definition, any variable that, according to the multivariable Cox regression analysis, was associated with the event showing a p -value ≤ 0.05 was considered a predictor of graft replacement. The hazard ratio (HR) values are shown with 95% confidence intervals (CIs). The proportionality assumption was tested for each independent variable with Kaplan–Meier curves.

Statistical analyses were performed using MedCalc for Windows (version 9.3.7.0; MedCalc Software, Mariakerke, Belgium) and Statistical Package for Social Sciences (SPSS) 17 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

Two patients, one of each group, were lost during follow-up. At the end of the observation phase, 53 patients (15.3%) underwent graft replacement.

Thirty-six (12.3%) events were registered in the homograft group. Causes of graft replacement in this group were wall calcification of the homograft ($n = 33$), resulting in increasing peak systolic gradients and considered as expression of graft degeneration and endocarditis ($n = 3$).

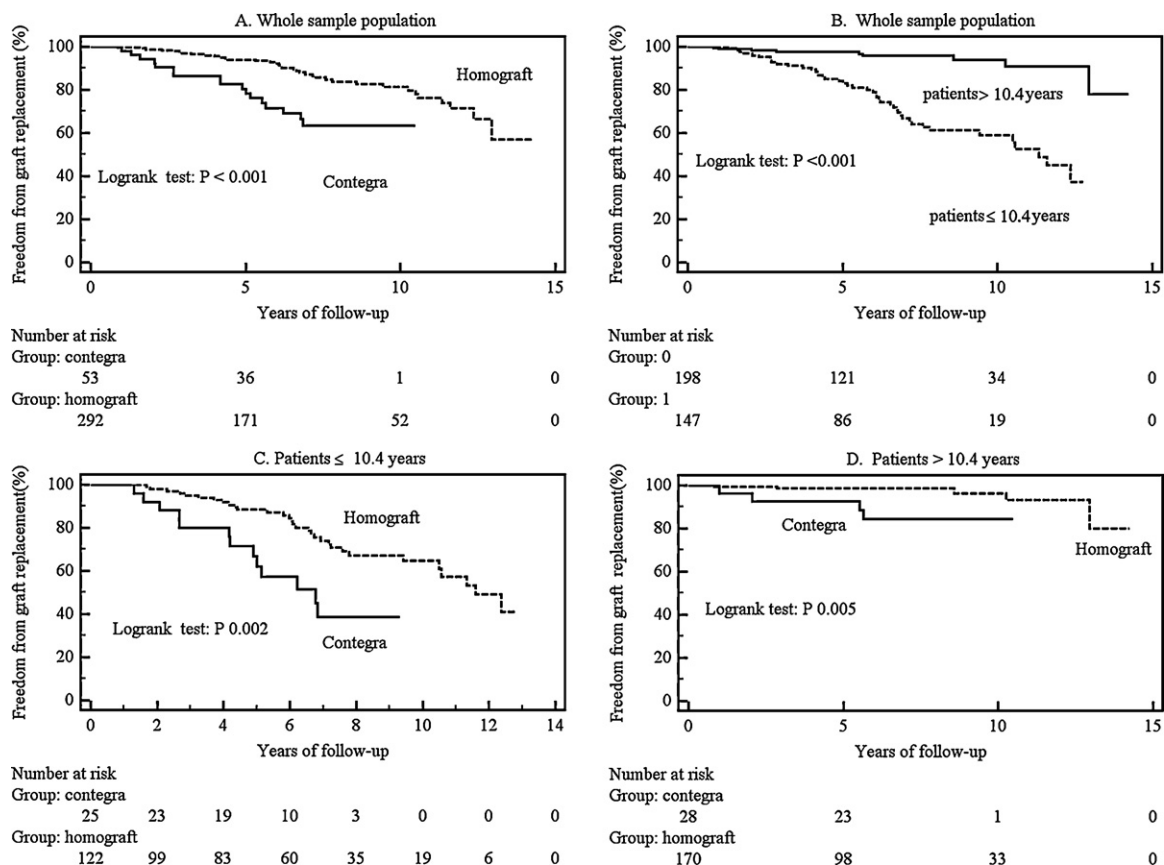


Fig. 1. (A) Unadjusted Kaplan–Meier freedom from graft replacement curves of the whole sample population after reconstruction of the RVOT with homograft or Contegra. (B) Unadjusted Kaplan–Meier freedom from graft replacement curves of two groups of age: >10.4 years (Group 0) and ≤ 10.4 years (Group 1). (C) Freedom from graft replacement curves of the Contegra and the homograft patients aged ≤ 10.4 years old. (D) Freedom from graft replacement curves of the Contegra and the homograft patients aged > 10.4 years old. For every graph the result of the log-rank test of comparison of the two curves is showed.

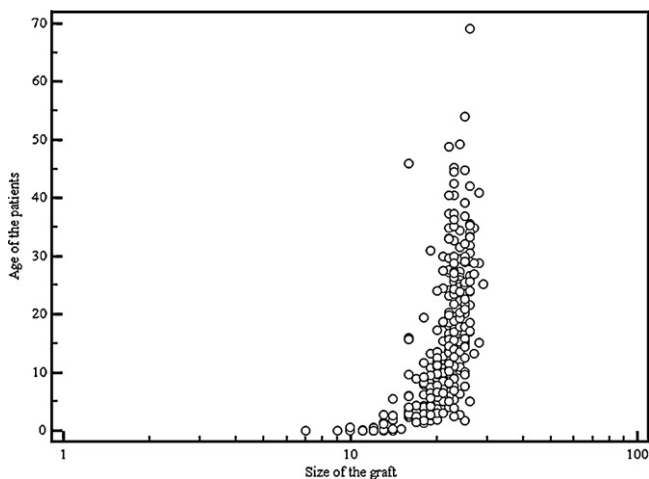


Fig. 2. Scatter diagram of the logarithmic relationship between age of the patients and size of the graft implanted in the RVOT.

Seventeen (32.0%) events were registered in the Contegra group. Causes of graft replacement in this group were stenosis of the distal anastomosis ($n = 10$), endocarditis ($n = 4$), and graft degeneration ($n = 3$), characterized by graft wall calcification without leaflet impairment. In one case, the distal stenosis was associated with valve degeneration.

In the Contegra conduit explanted because of stenosis of the distal anastomosis, an excessive amount of neo-intima composed by spindle cells was observed in this segment of the graft.

No primary regurgitation of the graft (dysfunction not related to the dilatation of the conduit caused by distal anastomosis) was diagnosed.

According to the Kaplan–Meier analysis, freedom from graft replacement for any cause at 1, 5, and 10 years of follow-up in the Contegra and homograft groups were $98.1 \pm 1.9\%$, $78.3 \pm 5.8\%$, and $63.5 \pm 7.2\%$ and $99.6 \pm 0.4\%$, $94.0 \pm 1.6\%$, and $81.4 \pm 3.4\%$, respectively (log-rank test: $p < 0.001$; Fig. 1(A)).

Kaplan–Meier analysis showed that the population aged ≤ 10.4 years presented lower freedom from graft replacement when compared with patients > 10.4 years (Fig. 1(B)). Further, within both age groups, patients receiving the homograft present a higher freedom from graft replacement compared with those receiving the Contegra conduit (Fig. 1(C) and (D)).

The variables ‘graft size’ and ‘age of the patients’ were related in a logarithmic fashion (Fig. 2). Independent predictors of graft replacement of the whole sample population were: graft size ≤ 20 mm (HR 3.6), age ≤ 10.4 years (HR 3.0), the non-anatomical position of the graft (HR 2.9), and the use of the Contegra conduit (HR 2.5) (Table 3).

Table 3. Independent predictors of graft replacement of the whole sample population.

Predictors	Hazard ratio	95% Confidence interval	p Value
Graft size ≤ 20 mm	3.6	1.5–8.9	0.005
Age ≤ 10.4 years	3.0	1.2–7.7	0.02
Non-anatomical position	2.9	1.4–4.7	0.0003
Contegra conduit	2.5	1.6–5.2	0.003

Table 4. Independent predictors of graft replacement of the propensity score-matched population.

Predictors	Hazard ratio	95% Confidence interval	p Value
Graft size ≤ 20 mm	8.0	2.3–28.1	0.001
Contegra conduit	3.7	1.3–10.4	0.01
Non-anatomical position	2.3	1.0–5.3	0.05

The multivariable analysis carried out on the propensity-score-matched population confirmed three independent predictors of graft replacement: graft size ≤ 20 mm (HR 8.0), the non-anatomical position of the graft (HR 2.3), and the use of the Contegra conduit (HR 3.7) (Table 4).

4. Discussion

Since its clinical introduction in 1999, the Contegra graft seemed to have the appropriate characteristics to replace the homograft for the reconstruction of the RVOT in complex congenital heart diseases in the pediatric and adult population. In particular, due to its ready availability in a wide range of sizes, this graft was at the center of a growing interest, even if the recent literature about early and the midterm results of the Contegra conduit implanted in the RVOT is still controversial.

According to our analysis, the independent predictors of graft replacement for the whole sample population were age ≤ 10.4 years, size of the graft ≤ 20 mm, the non-anatomical position of the graft, and the use of the Contegra conduit. The first two risk factors, age of the patient and size of the graft, were strongly interrelated. This result is consistent with the literature [8,9] reporting that the smaller the diameter of the conduit, the higher is the risk to undergo graft replacement or graft failure. The inverse relation between age and risk of graft replacement is the most visible expression of outgrowing. This could be defined as a phenomenon present in all growing patients, which produces, after few years from the reconstruction of the RVOT, a patient/graft mismatch. The third risk factor, non-anatomical position of the graft, is an expression of the underlying diagnosis. Double-outlet right ventricle and truncus arteriosus communis are typical cases where the graft is placed in a non-anatomical position. Therefore, according to our analysis, patients with the above-mentioned diseases have a higher risk to undergo graft replacement when compared with patients undergoing Ross operation, correction of Tetralogy of Fallot, pulmonary valve atresia, and transposition of the great arteries. These data confirmed the results of a previous analysis we have carried out on a sample population undergoing homograft implantation in the RVOT [2]. The fourth risk factor is the Contegra conduit implantation. Patients receiving this conduit were more than twice as likely to undergo graft replacement as those receiving a homograft. This result was consistent with the study of Niemantsverdriet et al. [10] comparing Contegra and homograft. In this large trial, 194 patients undergoing primary RVOT reconstruction with an aortic homograft ($n = 111$), pulmonary homograft ($n = 48$), Contegra conduit ($n = 23$), and synthetic conduits ($n = 12$) were analyzed; the median follow-up period was 4.7 years. Conduit failure was

defined as either conduit replacement or other conduit surgery to relieve conduit obstruction or regurgitation. According to the multivariable analysis, the implantation of Contegra conduit was one of the independent risk factors for conduit failure (HR 2.8, $p = 0.03$).

The analysis of a propensity-score-matched population confirmed three of the four above-mentioned independent predictors of graft replacement: size of the graft ≤ 20 mm, the non-anatomical position of the graft, and the use of the Contegra conduit.

In the present study, we observed that the prevalent cause of homograft failure is graft degeneration, while the prevalent cause of Contegra failure is stenosis of the distal anastomosis associated with excessive amount of neo-intima composed by spindle cells.

These data are consistent with several previous studies. Shebani et al. [11] have documented a conduit specific freedom from re-intervention (catheter or surgical) of 66% at 38 months. In 9 cases over 10, the re-intervention was due to an acquired stenosis involving the distal anastomosis of the conduit. This outcome, predominantly occurring in 12- and 14-mm conduits, was associated with histopathological findings of elastic-fiber proliferation and calcification on top of the neo-intimal and thrombus layer covering the entire conduit.

Göber et al. [12] showed that 15.8% of the patients, after a mean follow-up of 18 months, presented with acquired stenosis of the distal anastomosis of the conduit, associated with the histological finding of granulomatous inflammation. One patient had severe fibrosis of the intimal layer with lymphocytic infiltrates and, in another patient, a strong foreign body reaction within the whole conduit was observed with lymphocytic and mastocytic infiltrates. Kadner et al. [13] reported the formation of stenotic membranes at the distal anastomosis of the Contegra conduit, requiring graft removal in 2 of 67 conduits at 8 and 12 months after implantation. These membranes were partially covered by granulation tissues, with infiltration of lymphocytes and macrophages predominantly in the adventitia and in the internal lumen of the graft.

By contrast, several studies did report on the promising early-term results of the Contegra graft [3,14–16] implanted in the RVOT.

Midterm results were studied by Breyman et al. [8], who have analyzed, in a large multicenter trial, 165 patients with RVOT reconstruction with Contegra. The mean follow-up time was 4.1 years (range 0–7 years). Of the original sample population, 18 patients did not survive the first postoperative month (10.9%). From the remaining 147 patients, 10 (6.8%) were lost at follow-up and 27 (18.4%) conduits were explanted during the observation phase. Causes of explantation were: peripheral pulmonary arteries stenosis (40.8%), technical reasons (18.5%), endocarditis (14.8%), valve degeneration (11.1%), thrombus (7.4%), outgrowth (3.7%), and dilatation (3.7%). The authors stated that these values were corresponding to a 74% freedom from explantation at 7 years.

In our study, freedom from graft replacement at 10 years of follow-up in the Contegra group was 63.5%. Differently to the study of Breyman et al. [8], we decided, in our analysis, to exclude from the original sample population the patients

who did not survive the first postoperative month (3.0%), because of competing risk. Further, in our study, only one patient receiving the Contegra (1.9%) was lost at follow-up. For these reasons, we opine that the percentage of patients needing graft replacement in the Breyman study may be underestimated.

5. Conclusions

Our results show that the most important determinant for the graft longevity is the size of the graft. In terms of freedom from graft replacement, the sample population receiving a homograft had better outcomes when compared with that one receiving the Contegra. In particular, our patients receiving the Contegra were more than twice as likely to undergo re-operation for graft replacement than those receiving a homograft.

The higher incidence of the Contegra failure in our study was mostly related to the stenosis of the distal anastomosis. In conclusion, the present study suggests that the homograft is still the gold standard for RVOT surgery.

6. Limitations

Analyzing the factor ‘graft replacement’ could be jeopardized by its subjective nature. The indication to replace a graft is based on the quantitative evaluation of gradients, and on the qualitative clinical evaluation of the patient. Re-intervention is a medical decision and therefore biased.

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Appendix A. Conference discussion

Dr C. Schreiber (Munich, Germany): In my mind, these findings add to the confusion. There are centers which have fascinating results with the Contegra, and there are centers like yours. I am happy to hear what Reza will say. He is the invited discussant.

Dr R. Hosseinpour (Seville, Spain): The objective of this work is essentially to compare the longevity of two imperfect valved conduits, longevity being measured by the timing of conduit replacement.

There are three main findings in this study. I will just repeat them very briefly. First, young age was the strongest predictor. Of course, we know that this is strongly related to graft size in that the smaller the conduit, the sooner it is likely to need replacement. And this is thought to be due to the patient outgrowing the graft.

Second, non-anatomical placement of the conduit is also a predictor of earlier replacement. This, too, is in keeping with the existing knowledge.

Third, use of the Contegra is also a predictor of earlier replacement.

Now, this is where controversy begins, because as you just heard, there have been other works with contradictory evidence on this issue. But it is, nevertheless, the meat of your work. It is, as the title suggests, what your work is about.

Now, in this respect, there is a weakness in your study which may be very misleading, and that is that conduit size was not included in the multivariable analysis. This is immensely important because we know that small conduit size is a predictor of earlier replacement, and it is conceivable and likely that the Contegras used in your series were significantly smaller than the homograft. This is the case in many centers.

And I suspect it was also the case in yours because you found that the commonest cause of homograft failure in your series was degeneration, but in the Contegra group, it was distal stenosis not degeneration, which may suggest a size issue.

Now, that is fine. In fact, one of the attractions of the Contegra compared to the homograft is the fact that it is available in smaller sizes. That is fine. But then we cannot compare them to the homografts if the homografts are bigger.

Now, in your manuscript you mentioned that you did not include conduit size in your analysis because this information was not available in five cases, but your study includes 347 patients. I do not think that incomplete data in 5 cases would undermine your study significantly.

Are you able to comment whether such a bias existed in your work, or not, based on just eyeballing what happens day to day in your unit? Is there a tendency towards this bias?

Dr Urso: I have explained before that from a statistical point of view, it was not possible to insert two variables. Age of the patients and size of the graft represent the same statistical domain. So in a multivariable model, all of the covariates have to be tested to see if they are multicollinear or not.

If they are multicollinear, both of them cannot be inserted in the model because otherwise the statistical model is not stable.

So we should have inserted, instead of the age of the patient, the size of the graft, offsetting the fact that there are five patients with a missing value.

And the final results should not change. The final result we have suggests age of the patient and the size of the graft to be independent predictors. So it was just the statistical methodology.

Regarding the other question, I agree with you, our two groups were not homogenous from a statistical point of view. Patients receiving the Contegra were younger than the patients receiving a homograft.

For this reason, we did a multivariable analysis and as explained in the article, we also did a propensity score analysis. We implemented our model with the propensity score, and were able to obtain the same three predictors.

Of course, this kind of statistical adjustment can never be better than a randomized trial. Only a randomized trial can perfectly obtain two groups with two perfect homogenous distinct covariates.

From a statistical point of view, we did our best to adjust for these covariates.

Dr H. Najm (Riyada, Saudi Arabia): We have also had a fabulous result with a Contegra graft.

My question to you is, what is the technique for the distal anastomosis? We have recognized that mode of failure in the Contegra is a distal restriction, and there are two techniques which we adopted very early in our experience that we believe minimized that, which is everting suture on the distal anastomosis so it is endothelium to endothelium. That is number one.

Number two is we do not oversize the Contegras because they are pulsatile, and sometimes if you oversize them, you get shear forces into small pulmonary arteries and that creates intimal hyperplasia and causes stenosis.

The third technique, is the washing technique of the Contegras which are very long conduits. And if they are washed for a short period of time, some of the glutaraldehyde might be still be stuck within the lumen, and you may leave some of that and that could cause stricture at the anastomotic site.

Have any of these thoughts been put into looking at your data?

Dr Urso: Yes. I think we sized the Contegra appropriately. Our distal suture is the same as we do with the homograft, a standard 5-0 Prolene continuous suture. Anyway your suggestion could be taken into consideration.