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Autologous Right Auricular Versus PTFE Cavopulmonary Lateral Tunnel: Influence of Surgical Technique on Arrhythmias

Sara C. Arrigoni, MD[1], Freek van den Heuvel, MD, PhD[2], Tineke P. Willems, MD, PhD[3], Nic J.G.M. Veeger, MD[4], Paul Schoof, MD, PhD[1], and Tjark Ebels, MD, PhD[5]

Abstract

Background: To compare the incidence of arrhythmias and the overall survival at long-term follow-up of the right auricular baffle technique (RA) versus Gore-Tex® (GT) baffle as intra-atrial cavopulmonary lateral tunnel, as well as the Nakata index and tunnel dimensions on cardiac magnetic resonance. **Methods:** Data were retrospectively collected. Serial 24-hour Holter recordings and cardiac magnetic resonance findings of the two groups were compared. **Results:** There was no significant difference in the estimated freedom from arrhythmias (87% at 10 years and 78% at 15 years vs 80% at 10 years and 70% at 15 years in RA and GT, respectively; $P = .44$) nor cumulative survival (86% at 10 years and 84% at 15 years vs 97% at 10 years and 81% at 15 years in RA and GT, respectively; $P = .8$). Also, no difference between the groups was observed in the Nakata index. The tunnel dimensions on cardiac magnetic resonance were significantly wider in the RA group. In reference to other potential risk indicators, using Cox proportional hazard regression analysis, only age (5 years or older at the time of total cavopulmonary connection) was associated with an increased risk for both arrhythmia and mortality. **Conclusions:** This study demonstrated that there was no difference in freedom from arrhythmias, Nakata index, or survival between the two groups. This study confirmed the growth potential of the right auricular tunnel. However, the growth of the tunnel did not influence the incidence of arrhythmias.

Keywords

arrhythmia, CHD, univentricular heart, Fontan, total cavopulmonary connection

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Introduction

Total cavopulmonary connection (TCPC) is currently the standard palliative treatment for children with univentricular circulation. Since Fontan and Kreutzer described the original technique of atrio-pulmonary anastomosis,[1,2] it has been modified, leading to improved particularly early outcome.[3,4] Arrhythmias, however, lead to a significant amount of morbidity by necessitating hospitalization and interventions.[5–7] Moreover, arrhythmias often cause further failure of the Fontan circulation and prompt conversion with either arrhythmia surgery or heart transplantation.[7,8] This is the so-called fourth step after the initial palliative procedures, Glenn anastomosis, and TCPC completion. Surgical technique may well be associated with the occurrence of these arrhythmias by damaging the sinus node or its blood supply and creating flutter circuits through atrial suture lines and scar tissue.[9–11] In 1989, we introduced a modified technique, right auricular (RA) intra-atrial baffle TCPC, in which it was not necessary to use any prosthetic material.[12] Our primary goal was to achieve a tunnel that had growth potential. In performing the operation, suture lines analogous to those in the Senning and Mustard operations were avoided in order to spare the sinus node. We postulated that this

[1] Department of Cardiothoracic Surgery, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands
[2] Department of Pediatric Cardiology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands
[3] Department of Radiology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands
[4] Department of Epidemiology, University Medical Centre Groningen, University of Groningen, Groningen, Netherlands
[5] Department of Cardiothoracic Surgery, University Medical Center Amsterdam, University of Amsterdam, Amsterdam, Netherlands

Corresponding Author:
Sara C. Arrigoni, Thoraxcentrum, University Medical Center Groningen, University of Groningen, Hanzeplein 1, 9700 RB, Groningen, the Netherlands.
Email: s.c.arrigoni@umcg.nl

Abbreviations

APF	additional pulmonary flow
BSA	body surface area
CMR	cardiac magnetic resonance
GT	Gore-Tex
ICV	inferior caval vein
LPA	left pulmonary artery
RA	right auricular
RPA	right pulmonary artery
SCV	superior caval vein
T	intracardiac tunnel
TCPC	total cavopulmonary connection

technique could be advantageous by preventing atrial arrhythmias. A lower incidence of arrhythmias was indeed reported 20 years ago after a maximal follow-up of 10 years.[12] The present study presents the long-term results of this technique, compared to the lateral intracardiac baffle technique using a vascular prosthetic baffle.

Material and Methods

Study Design

The Institutional Review Board of the University Medical Center Groningen agreed to waive the need for an informed consent because data were collected as part of routine medical care and patients were not individually identifiable.

We selected from our institutional databases all patients who underwent a TCPC with the lateral intracardiac tunnel technique either by means of a Gore-Tex® vascular prosthetic baffle (GT group) or of a right auricular tunnel technique (RA group). The cohort of patients consists of 73 patients: 44 patients in the RA group and 29 patients in the GT group.

The operations were performed between 1989 and 2011. The Gore-Tex® baffle technique was used in those patients where the RA technique was not feasible because of the small size of the right auricle, precluding its use as a tunnel.

Data Collection and Patients Characteristics

Preoperative, operative, and postoperative data from all patients were collected retrospectively. Depending on their specific morphological diagnosis, patients were categorized into one of the four main groups: tricuspid atresia, pulmonary atresia with an intact ventricular septum, double inlet left ventricle, and miscellaneous. The miscellaneous category included hypoplastic left ventricle, hypoplastic tricuspid, or pulmonary valve in combination with a hypoplastic right ventricle, mitral valve atresia, unbalanced atrioventricular septum defect, and multiple ventricle septal defects. The palliative procedures included aorto-pulmonary shunt, pulmonary artery banding, Norwood stage I, and atrial septectomy.

Surgical Technique

The RA tunnel was performed as previously described.[12] The right auricle was separated from the rest of the atrium by means of two perpendicular incisions and thus a tissue flap of the right auricle was created. This tissue flap was then sutured to the junction of the inferior caval vein (ICV) and the right atrium as a baffle thus creating the cavopulmonary tunnel. The lateral tunnel was performed by using a Gore-Tex® vascular prosthesis as described by Van Doorn and De Leval.[13]

Follow-up

The follow-up was complete in all patients except for two patients who moved abroad: both patients were not included in the analysis although they were still alive according to their Social Security status. The median follow-up of the RA group was 19 years (95% confidence interval [CI]: 17.9-21.3). The median follow-up of the GT group was 11.8 years (95% CI: 8.5-19.1). The clinical follow-up was performed at regular yearly outpatient visits. Serial 24-hour Holter recordings were performed in 59 patients: 35 of the RA group and 24 of the GT group. Since 2000, the departmental protocol for Fontan patients consisted of serial Holter registrations every 2 years. Before 2000, Holter registration was performed only if indicated and that meant in case of symptoms. Holter tests were not done in 14 patients: 8 patients had died at follow-up, 3 patients had permanent pacemakers, 2 patients moved and lived abroad, 1 patient made outpatient clinic controls in another hospital, and for an unknown reason no Holter was performed.

Cardiac magnetic resonance (CMR) was performed in 39 patients. Five CMRs could not be used for the analysis: three because of the poor quality of the images and in two cases contrast-enhanced CRM was not performed. As a result, 19 CRMs of the RA group and 15 of the GT group were analyzed. CMR could not be performed in patients with a pacemaker and in one patient who suffered from claustrophobia.

Cardiac Magnetic Resonance

Cardiac magnetic resonance was performed using a commercially available 1.5 T scanner (Magnetom Aera, Siemens Medical Solutions, Erlangen, Germany). Cardiac magnetic resonance was done using the methods of short-axis multislice acquisition using breath-holding, ECG-triggered cine-MRI (using Mass 7.6 Medis Medical Imaging, Leiden, the Netherlands).

Diameters and cross-sectional areas were measured of ICV intracardiac tunnel (T), and both pulmonary arteries and superior caval vein (SCV). The diameters were measured as previously described.[14] The sum of the cross-sectional area (in mm^2) of the ICV and SVC (ICV+SVC) was calculated, as well as the sum of the cross-sectional areas of the tunnel and SCV (T+SCV) and of the right and left pulmonary artery (RPA+LPA). The Nakata index (in mm^2/body surface area) was calculated according to the Haycock formula.

For each patient, four ratios were calculated (ICV+SCV)/(RPA+LPA), T/(RPA+LPA), (T+SCV)/(RPA+LPA), and ICV/T.

End Points

Primary end point. Incidence of first arrhythmias: comparison between the GT group and the RA group. Tachyarrhythmias were defined as intra-atrial tachycardia and atrioventricular reentry tachycardia. Bradyarrhythmias were defined as atrial bradyarrhythmias and atrioventricular bradyarrhythmias.

The secondary end points. Comparison between the GT group and the RA group of:

(1) Overall survival
(2) Nakata index and the 4 ratios as described above.

Statistical Analysis

Statistical analysis was performed using IBM SPSS Statistics 23 (IBM Corporation, New York). Values are reported as mean ± standard deviation or as number with percentages.

To evaluate differences between the two treatment groups, for categorical variables, a chi-square test (exact when indicated) or Fisher exact test was used. For continuous data, a Student *t* test or Mann–Whitney *U* test (in case of a skewed distribution) was used.

Event-free survival was graphically depicted using the Kaplan–Meier method. Between-group differences were evaluated using the log-rank test. In addition, Cox proportional hazards modelling was used to estimate hazard ratios with 95% CIs of potential risk indicators for the occurrence of arrhythmias and overall survival. A two-tailed *P* value less than .05 was used to indicate statistical significance.

Results

Baseline patient characteristics are presented in Table 1. Patients of the GT group were older and had a larger body surface area (BSA). A previous bidirectional Glenn operation was performed more often in the GT group (72% vs 34% in the RA group, $P = .001$).

The median length of stay in the hospital (17 days) and ICU (3 days) was the same in both groups, as was the length of intubation (1 day) and the need for inotropic support (32%).

Incidence of Arrhythmias

There was no significant difference in the estimated freedom from arrhythmias at follow-up, either of tachyarrhythmias or bradyarrhythmias. The estimated cumulative freedom from arrhythmias was 87% at 10 years and 78% at 15 years in the RA group versus 80% at 10 years and 70% at 15 years in the GT group, $P = .44$ (Figure 1). The estimated cumulative freedom from tachyarrhythmias was 92% at 10 years and 83% at 15 years in the RA group versus 83% at 10 years and 73% at 15 years in the GT group ($P = .51$). The estimated cumulative freedom from bradyarrhythmias was 95% at 10 years and 92% at 15 years in the RA group versus 84% at 10 and 15 years in the GT group ($P = .6$).

Seven patients of the RA group and seven of the GT group received a pacemaker: four patients because of bradyarrhythmias, three because of sick sinus syndrome, and seven because of tachyarrhythmias.

Table 1. Baseline Patients' Characteristics.

	RA (44 patients)	GT (29 patients)	*P* Value
Gender	F 19 (43%)	F 13 (45%)	1
Cardiac anatomy			.13
Tricuspid atresia	21 (48%)	7 (24%)	
Pulmonary atresia	5 (11%)	7 (24%)	
DILV	8 (18%)	4 (14%)	
Miscellaneous	10 (23%)	11 (38%)	
Previous palliative operation	36 (82%)	22 (76%)	.538
Previous aorto-pulmonary shunt	21 (48%)	14 (48%)	.963
Previous pulmonary banding	14 (32%)	6 (21%)	.297
Previous Glenn operation	15 (34%)	21 (72%)	.001
Mean age at operation (years)	3.92 ± 1.71	7.31 ± 4.48	<.001
Mean BSA at operation (Haycock)	0.64 ± 0.11	0.89 ± 0.33	<.001

Abbreviations: BSA, body surface area; DILV, double inlet left ventricle; GT, Gore-Tex; RA, right auricular.

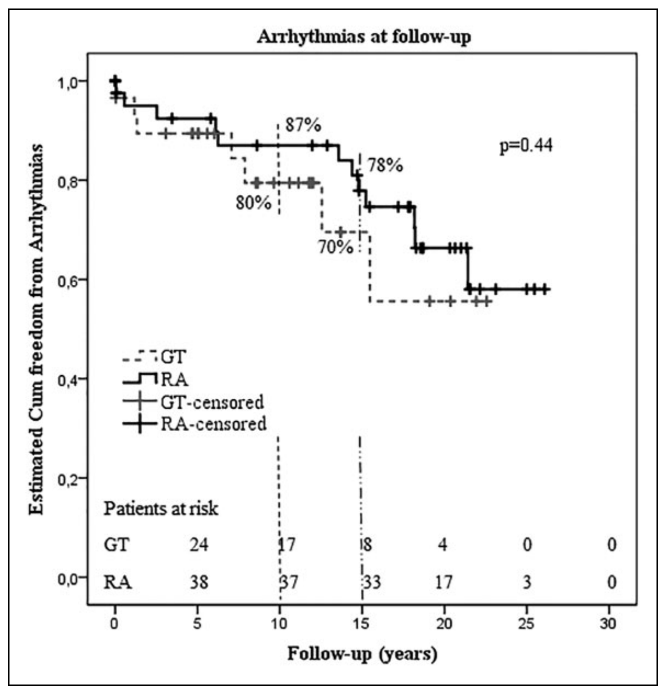

Figure 1. Arrhythmias at follow-up. Comparison between RA and GT group of estimated cumulative freedom from arrhythmias at 10- and 15-year follow-up. GT indicates Gore-Tex; RA, right auricular.

Table 2. Univariable Analysis of Freedom From Arrhythmias.

Risk Factors	Hazard Ratio (95% CI)	*P* Value
(A) Univariable Analysis		
Female gender	0.87 (0.35-2.14)	.75
RA group	0.68 (0.26-1.79)	.44
Cardiac anatomy		.34
Tricuspid atresia (reference)	1	
Pulmonary atresia	2.03 (0.48-8.54)	
DILV	2 (0.54-7.46)	
Miscellaneous	2.84 (0.89-9.02)	
Previous palliative operation	1.13 (0.38-3.41)	.83
Previous aorto-pulmonary shunt	0.57 (0.23-1.46)	.24
Previous pulmonary banding	1.75 (0.69-4.46)	.23
Previous Glenn operation	1.34 (0.5-3.57)	.56
Operation 1st period (1989-1996)	1.44 (0.5-4.18)	.5
Age at operation > 5 years old	3.29 (1.30-8.32)	.008
BSA > 0.7 (Haycock)	2.58 (0.95-7.05)	.06
(B) Univariable analysis patients at risk		
Age ≥ 5 years old		
RA group	0.48 (0.09-2.57)	.38
Age < 5 years old		
RA group	2.66 (0.34-21.2)	.34

Abbreviation: RA, right auricular.

Univariable analysis is shown in Table 2A. In this, The RA technique was not associated with the occurrence of arrhythmias. Age of 5 years or older and BSA > 0.7 at time of TCPC were univariately associated risk factors for arrhythmias. When considering the effect of surgical technique in the two age categories, some indication of heterogeneity of the effect of surgical technique was observed (Table 2B). The RA technique reduced the risk of arrhythmias in the older patients (hazard ratio 0.48, 95% CI [0.09-2.57]; $P = .38$) and increased the risk in the younger patients (hazard ratio 2.66, 95% CI [0.34-21.2]; $P = .34$); however, both ratios did not reach statistical significance.

CMR Analysis

There was no significant difference in the Nakata index between the two groups ($P = .92$). The Nakata index was higher than 200 in 58% of the RA group and 50% of the GT group. Figure 2 shows the ratios of the two groups. The mean ratio (ICV+SCV)/(RPA+LPA) was 2.89 ± 1.43 in the RA group versus 2.081 ± 0.97 in the GT group ($P = .064$). The mean ratio T/(RPA+LPA) was 3.51 ± 1.88 in the RA group versus 1.4 ± 1 in the GT group ($P < .001$). The mean ratio T+SCV/(RPA+LPA) was 4.1 ± 1.97 in the RA group versus 2.01 ± 1.14 in the GT group ($P = .001$). The mean ratio T/ICV was 0.69 ± 0.25 in the RA group versus 1.25 ± 0.51 in the GT group ($P < .001$).

Overall Survival

There was no significant difference in the estimated cumulative survival between the two groups: 87% at 10 years and 78% at 15 years in the RA group versus 80% at 10 years and 70% at 15 years in the GT group, $P = .44$ (Figure 3A).

When excluding the patients who died during the hospitalization for TCPC or within the first 30 postoperative days, the estimated cumulative survival between the two groups was 93% at 10 years and 90% at 15 years in the RA group versus 100% at 10 years and 83% at 15 years in the GT group, $P = .46$ (Figure 3B).

Nine patients of the RA group died during follow-up. Three patients died within the first postoperative 48 hours because of acute circulatory failure. One patient with asplenia died because of Streptococcus sepsis. Five patients died because of chronic circulatory failure. Five patients of the GT group died during the follow-up. One patient died two weeks after the operation because of severe cyanosis and multi-organ failure. One patient died because of a hepatocellular carcinoma. Two patients died because of chronic cardiac failure and one patient died suddenly during the rehabilitation after a pacemaker implantation.

Univariable analysis is shown in Table 3. Also for mortality, the RA technique was not an associated risk factor. All patients who died during follow-up had a previous palliative operation and were all operated in the first operation period (1989-1996). Age of 5 years or older at time of TCPC was an associated risk factor for mortality. We investigated if the surgical technique could influence mortality in the two age subgroups (Table 3B). In the subgroup of patients younger than 5 years, all fatalities were observed in the RA group (point estimate of hazard rate not estimated). In the subgroup of patients of 5 years or older, no significant difference in mortality was observed.

Comment

Freedom from arrhythmias does not differ between our two operative groups and does not differ from the literature.[15–17] Our hypothesis that the RA technique could be advantageous by preventing atrial arrhythmias was not confirmed at long-term follow-up. A lower incidence of atrial arrhythmias after the extracardiac cavopulmonary connection has been reported if compared to the intra-atrial tunnel.[18,19] These findings seem to indicate a relationship between the suture load and scar tissue in the atrium and the atrial arrhythmias, as shown in experimental models.[20,21] Avoiding those suture lines by using an extracardiac conduit instead of an intra-atrial tunnel could then reduce the incidence of arrhythmias. However, several studies showed no difference in arrhythmias incidence between extracardiac and intra-atrial tunnel, suggesting that there could be other surgical and non-surgical risk factors for postoperative arrhythmias.[22–24]

The only associated risk factors for arrhythmias at univariate analysis were age of 5 years or older and BSA > 0.7 at the time of TCPC. The higher incidence of arrhythmias in patients who underwent the TCPC at an older age, in the era when a bidirectional Glenn was not yet customary, could be related to the longer cardiac volume overload and the consequent atrial and ventricular dilatation. It is clear that the bidirectional Glenn or a single-stage TCPC reduces the cardiac volume overload, but that also depends on *Qp*/*Qs*. However, we have to consider other

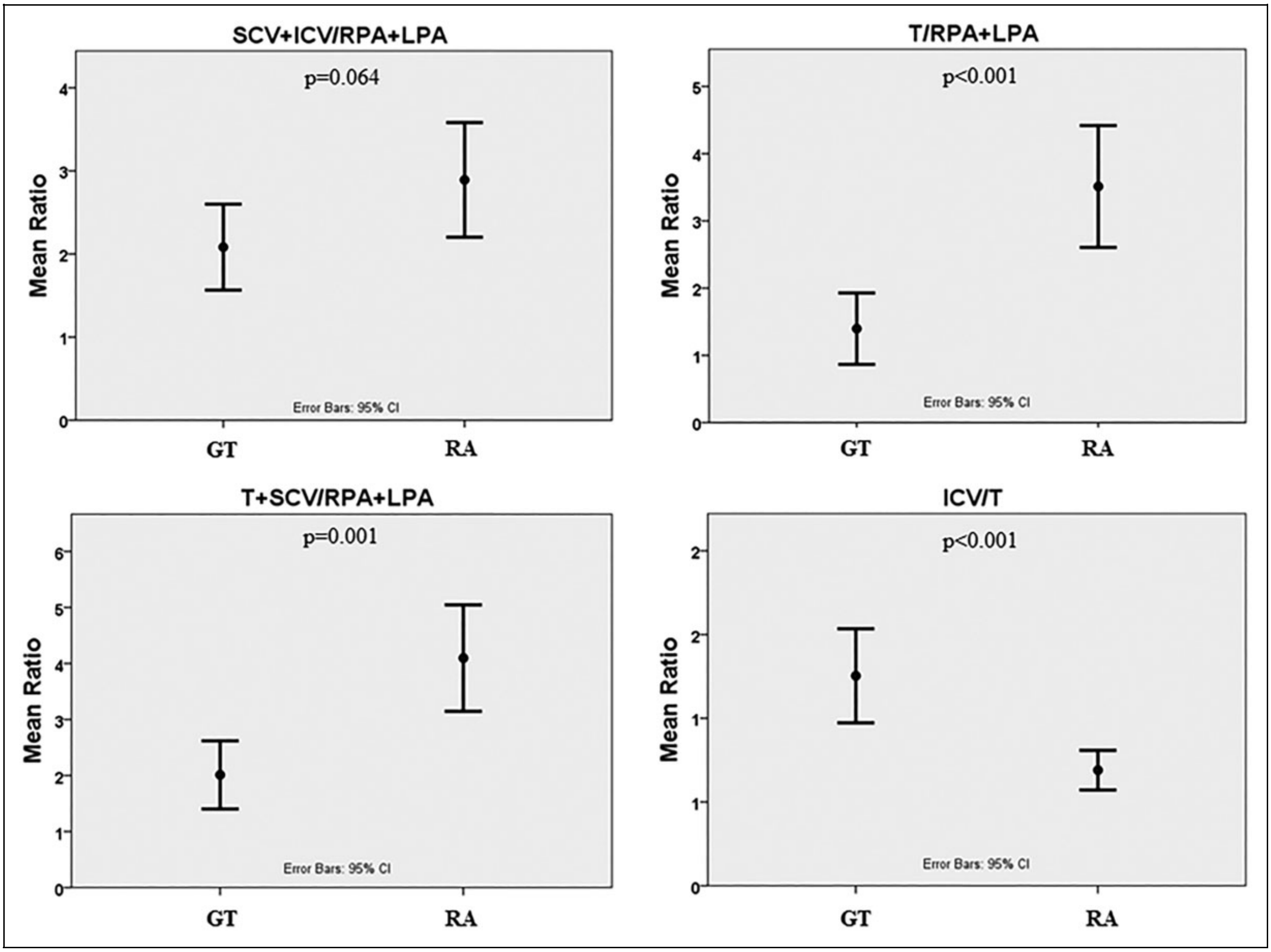

Figure 2. Ratios at CMR. Comparison between RA and GT group of the four ratios measured by cardiac magnetic resonance. CMR indicates cardiac magnetic resonance; GT, Gore-Tex; RA, right auricular.

factors that influence cardiac volume load, such as patients who underwent a bidirectional Glenn with additional pulmonary flow (APF) through a pulmonary banding, a patent pulmonary stenosis, or aorto-pulmonary collaterals. Because there was no significant difference in previous Glenn or APF in the two age subgroups ($P = .19$), we presume that the older age alone at the time of TCPC did influence the cardiac volume overload. Older patients have mostly a larger BSA; therefore, it is not unexpected that BSA > 0.7 is a risk factor for arrhythmias as well.

In our study, there was no difference in the Nakata index between the groups. Nakata identified a low PA index (<200) as a risk factor for postoperative circulatory failure and premature mortality in Fontan patients.[25] Chowdhury et al confirmed the results of Nakata and reported that only a low Nakata index was significantly associated with the presence of severe intimal lesions, abnormal smooth muscle extension, intra-acinar pulmonary arterial thrombus, and smaller intra-acinar pulmonary arteries by histomorphometric analysis of lung tissue from patients undergoing cavopulmonary procedures.[26] However, other studies reported that small pulmonary artery size did not affect the midterm results of Fontan operation.[27,28] Moreover, the Nakata index could be influenced by pulmonary vascular development prior to TCPC and could still affect Nakata index at late follow-up.

All three ratios in which the tunnel area was normalized for bodily size were significantly higher in the RA group. These findings confirm the growth of the tunnel by the RA technique. Mostly, the mean ratio T/(RPA+LPA) (3.51 $\pm$ 1.88) and (T+SCV)/(RPA+LPA) (4.1 $\pm$ 1.97) in the RA group proved that the tunnel cross-sectional area of the RA group was significantly wider than the GT group. This growth is excessive when compared to the pulmonary arteries and negatively influences the hemodynamic resistance of the Fontan circuit. In fact, according to Poiseuille's law, the increased cross-sectional area of the tunnel results in a decreased blood flow velocity in the tunnel itself and an increased blood flow velocity in the structures of the Fontan circuit with smaller cross-sectional areas, more specifically the pulmonary arteries or the ICV.

Moreover, in a mechanistic reasoning, a wider tunnel could promote the atrial arrhythmias because of the dilatation of the

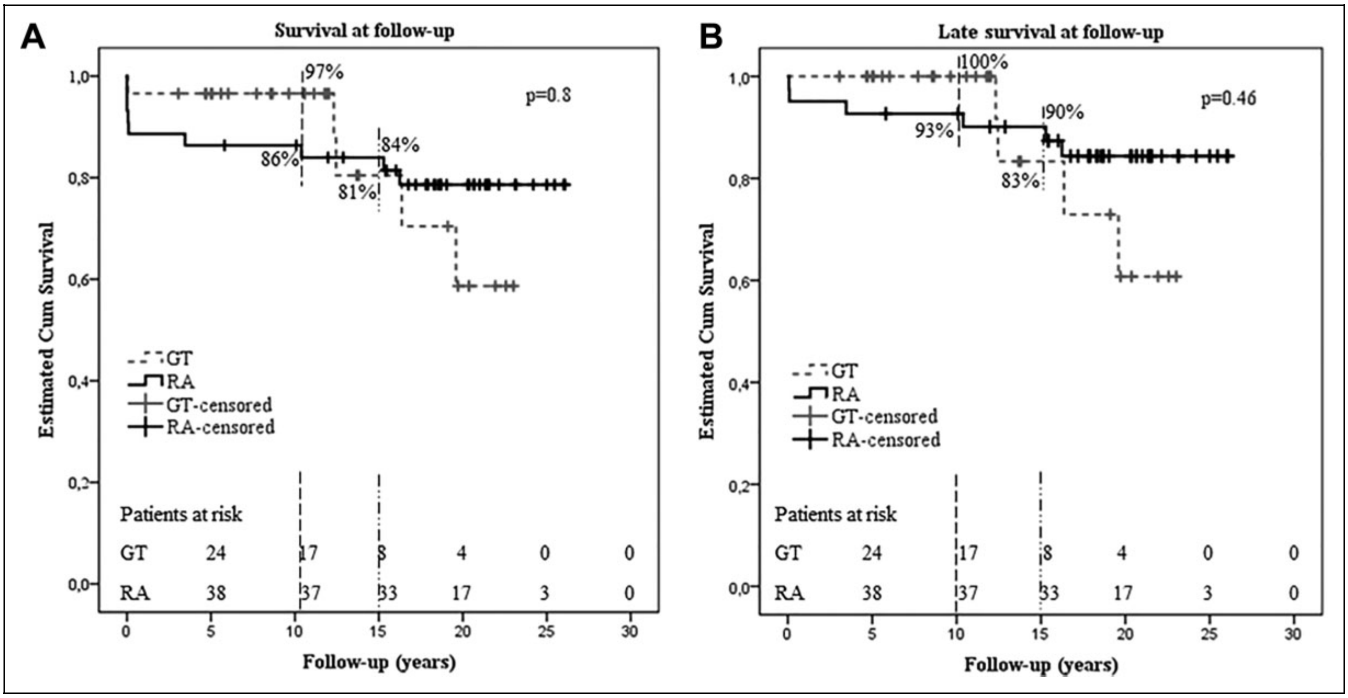

Figure 3. Overall survival at follow-up. (A) Comparison between RA and GT group of estimated cumulative survival at 10 and 15 years follow-up. (B) Comparison between RA and GT group of estimated cumulative "late" survival at 10- and 15-year follow-up, excluding in-hospital and 30-postoperative day mortality. GT indicates Gore-Tex; RA, right auricular.

Table 3. Univariable Analysis of Overall Survival.

Risk Factors	Hazard Ratio (95% CI)	*P* Value
(A) Univariable Analysis		
Female gender	0.43 (0.13-1.37)	.14
RA group	0.87 (0.29-2.64)	.80
Cardiac anatomy		.37
Tricuspid atresia (reference)	1	
Pulmonary atresia	3.36 (0.67-16.85)	
DILV	2.41 (0.49-11.93)	
Miscellaneous	3.05 (0.72-12.89)	
Previous palliative operation	Not estimable	.04
Previous aorto-pulmonary shunt	1.98 (0.66-5.90)	.21
Previous pulmonary banding	1.49 (0.50-4.44)	.48
Previous Glenn operation	0.37 (0.10 -1.37)	.12
Operation 1st period (1989-1996)	not estimable	.005
Age at operation > 5 years old	3.07 (1.07-8.79)	.028
BSA > 0.7 (Haycock)	2.34 (0.7-7.83)	.16
(B) Univariable analysis patients at risk		
Age $\geq$ 5 years old		
RA group	0.61 (0.12-3.20)	.55
Age < 5 years old		
RA group	Not estimable	.12

Abbreviation: RA, right auricular.

atrial component resulting in a higher wall tension. Subsequent atrial dilatation and fibrosis can result in the dispersion of electrical conductivity, allowing the development of atrial reentrant arrhythmias, as demonstrated in older patients with large atriopulmonary connections.[5,29] Therefore, dilatation of the tunnel could increase the risk of development of arrhythmias. However, the diameters of the tunnel were not measured at the time of the operation and the tunnel sizes could have been different from the beginning. Therefore, we could not evaluate the progression of tunnel dilatation. Nonetheless, a wider atrial tunnel can be associated with a higher wall tension, which could be associated with the development of arrhythmias.

The analysis of the Nakata ratios is a simplification of the complicated hemodynamics of the Fontan circuit. In fact, we should consider also the lack of elasticity of the blood vessels that contributes to the flow velocity. The Fontan physiology leads to abnormal vascular patterns, as described in the histopathologic data of pulmonary histology[30] and the high concentration of vascular endothelial growth factor in patients with a cavopulmonary circulation modifies the features of the vascular wall.[31,32] Moreover, such as in the pulmonary bifurcation, the angles between the branches influence the resistance to the blood flow.[33,34] Branching of the blood vessel is somewhat similar to the vascular tree: in both cases, the relationship between branching angles and its radii determine the pressure and the flow in the branches.[35] To make a thorough estimation of the flow in the different level of the Fontan circuit, we should consider all these variables.

In reference to mortality, there was no significant difference in the estimated cumulative survival between the two groups. Patient's older age at the time of TCPC was an associated risk factor for mortality at univariate analysis. The higher mortality in patients who underwent the TCPC at an older age could be explained with the longer chronic cyanosis and the related organ hypoxia that could influence the clinical outcome. Operation period was an associated risk factor for mortality too. In fact, all patients who died at follow-up were operated in the first period between 1989 and 1996. Of course, the difference in length of the follow-up can influence the survival, increasing the risk of late Fontan complications and mortality. However, one-third of all deaths (4 of 14 patients) occurred within 30 postoperative days or during the hospitalization for TCPC (early mortality) and in all cases pulmonary vascular hypertensive crises were reported. The early mortality in the first period was 5.48%: 6.2% in the RA group and 3.45% in the GT group ($P = .53$). No early mortality occurred in the second period (1997-2011). In the beginning of the 90s, nitric oxide for the treatment of pulmonary hypertension was not routinely available in our center and this definitively influences the clinical course of these patients. Moreover, the standard performance of cardiac catheterization prior to TCPC completion was not yet introduced in our center. Therefore, it was difficult to identify patients at risk for elevated postoperative pulmonary resistance. We could then presume that late mortality could reasonably have a stronger relation with the surgical technique and its long-term complications. However, even in late mortality analysis, there was no significant difference in the estimated cumulative late survival between the two groups.

The univariable analysis for the age subgroup (see Table 3B) did not show any significant difference in survival compared to GT and RA group in patients of 5 years or older. All patients younger than 5 years who died during follow-up were in the RA group.

The main limitation of this study is that it is a single-center retrospective study and no randomization was performed. Furthermore, the limited number of our group of patients does not provide enough statistical power to reach significance. Patients' selection was affected by the size of the right auricle that had to be large enough to perform an RA technique.

To conclude, long-term follow-up confirmed the growth potential of the RA-TCPC. However, excessive growth of the RA tunnel could have a negative effect on the hemodynamics of the Fontan circuit. Furthermore, the RA–TCPC cannot prevent the development of arrhythmias and the growth of the tunnel could theoretically even facilitate its occurrence. The surgical technique did not influence the cumulative survival. Because patient's age at the time of TCPC was an associated risk factor for arrhythmias and mortality at univariable analysis, the timing of the operation is essential for the clinical outcome.

Declaration of Conflicting Interests

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