European Journal of Cardio-Thoracic Surgery 43 (2013) 325–334
doi:10.1093/ejcts/ezs264 Advance Access publication 9 May 2012

ORIGINAL ARTICLE

Long-term results of the arterial switch operation for ventriculo-arterial discordance

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Received 19 January 2012; received in revised form 28 February 2012; accepted 23 March 2012

Abstract

OBJECTIVES: The arterial switch operation (ASO) has become the standard surgical procedure for transposition of the great arteries (TGA) or variants with an excellent early outcome. However, there are concerns regarding neopulmonary stenosis, neoaortic regurgitation (neoAR) associated with neoaortic root dilatation and coronary artery disease.

METHODS: A total of 220 early survivors of the ASO were included in this retrospective study between November 1987 and June 2011. The median age and weight at operation were 13 days (0–1768 days) and 3.52 kg (1.69–19 kg), respectively. The indications for the ASO included TGA with intact ventricular septum in 113 patients, TGA with ventricular septal defect in 90 and Taussig–Bing anomaly in 17 patients. The median follow-up period was 103.2 months (0.4–277.4 months). Statistical analyses with the Kaplan–Meier and Cox proportional hazards models were performed.

RESULTS: The actuarial late survival rate and freedom from reoperation at 23 years were 96.6 ± 1.3 and 81.9 ± 3.8%, respectively. Twenty-four (10.9%) patients underwent reoperations for right ventricular outflow tract obstruction in 10 patients, neoAR in four and coronary artery stenosis in three, etc. Freedom from neoAR of Grades IV, III and II at 23 years was 90.2 ± 6.6, 70.9 ± 9.6 and 20.3 ± 5.5%, respectively. The risk factors for neoAR were size discrepancy of the great arteries, aortic root dilatation after the ASO and follow-up duration after the ASO. NeoAR was significantly correlated with the size of aortic sinus and aortic sinotubular junction over time. Freedom from pulmonary stenosis (PS) of ≥36 and ≥20 mmHg at 23 years was 34.8 ± 18.0 and 17.7 ± 9.6%, respectively. The risk factors for PS were Taussig–Bing and arch anomalies. Coronary artery evaluation was performed in 95 (43.2%) patients with angiography, computed tomography or single-photon emission computed tomography, and five (5.3%) patients had abnormal coronary morphology or perfusion. Three patients underwent reoperation for coronary artery stenosis, and two had reversible perfusion defects in various regions, which were clinically not significant. Freedom from coronary events was 88.1 ± 6.4% at 22 years. A risk factor for coronary events was the single coronary artery.

CONCLUSIONS: The survival and functional outcomes of the ASO were excellent in the long-term. Strict serial surveillance is required to evaluate the long-term functional outcome of the ASO, particularly in a high-risk anatomy.

Keywords: Arterial switch operation • Transposition of the great arteries • Taussig–Bing anomaly • Aortic regurgitation • Pulmonary stenosis

CONGENITAL

INTRODUCTION

The arterial switch operation (ASO) has become the standard surgical procedure for transposition of the great arteries (TGA) or variants with an excellent early outcome. The current operative mortality is low and the late results are satisfactory [1, 2]. However, although called an anatomical repair, the result obtained after the ASO is far from being truly anatomical. There are many potential late problems regarding aortic regurgitation (AR) associated with aortic root dilatation, coronary artery disease, progressive left ventricular dysfunction and pulmonary stenosis (PS) [3, 4].

Since a neopulmonary trunk needs to be reconstructed in a nonanatomical position, neopulmonary stenosis is a frequent finding, but it rarely has clinical consequences [5]. Most obstructions of the neopulmonary trunk are located at the neopulmonary anastomotic site and are clearly related to inadequate growth [4]. The ability of the neoaortic valve to function without incompetence and the ability of the coronary anastomoses to grow are also concerns as the follow-up lengthens. Progressive neoaortic regurgitation (neoAR) associated with neoaortic root dilatation is probably the result of a multifactorial process for which the aortic root geometry and the surgical technique are some of the mechanisms involved [6]. The incidence of coronary events is relatively low, but coronary lesions are progressive [4].

The purpose of this study is to review the long-term outcomes in early survivors of the ASO and to analyse the risk factors for reoperation, AR, PS and coronary events.

MATERIALS AND METHODS

Study population

A total of 258 consecutive patients underwent ASO for the TGA and Taussig–Bing anomaly between November 1987 and June 2011. There were 38 early deaths and 220 early survivors of the ASO were included in this retrospective study.

The median age and weight at operation were 13 days (0–1768 days) and 3.52 kg (1.69–19 kg). TGA with intact ventricular septum was present in 113 (51.4%), TGA with ventricular septal defect (VSD) in 90 (40.9%) and Taussig–Bing anomaly in 17 (7.7%) patients. The coronary arterial pattern was usual in 165 (75%) patients. Before the ASO, 113 (51.4%) patients underwent palliative procedures including balloon atrial septostomy in 95 patients, pulmonary artery (PA) banding in 20, arch repair in 11, Blalock–Taussig shunt in 10 and atrial septectomy in nine patients.

Operative technique and operative data

All the operations were performed by three surgeons under the conditions of moderately hypothermic cardiopulmonary bypass (CPB). The Lecompte manoeuvre was performed in 193 (87.7%) patients. A variety of surgical techniques were employed for the PA reconstruction. For the initial cases, we used two free pericardial patches to reconstruct the sinus portion of the neoPA. Alternatively, a direct anastomosis was made without any patch material. Beginning in 1996, a single pantaloon patch was used in almost all patients in the study. Repair of a VSD was usually performed through the right atrium using the standard techniques. When tension in the coronary anastomosis was suspected, the trap-door technique for the coronary artery transfer was applied in 110 (50.0%) patients. The mean CPB time and the aortic cross-clamp (ACC) time were 179.5 ± 61.9 and 101.3 ± 40.3 min. After the ASO, the sternum could not be closed in six patients and mechanical circulatory support was required in nine patients. The median follow-up period was 103.2 months (0.4–277.4 months).

Echocardiographic evaluation

Echocardiographic evaluations were performed preoperatively, immediately postoperatively and before discharge. A follow-up echocardiography was scheduled for between 6 months and 1 year postoperatively. Thereafter, the echocardiographic follow-up was performed on an annual basis.

We measured the internal diameter of the great arteries at the level of the annulus, using echocardiography. The size discrepancy of the great arteries was evaluated as the ratio of the size of the pulmonary annulus to the aortic annulus (Ao) preoperatively. The presence and quantity of AR were evaluated by colour Doppler imaging and graded as none (0), trivial (I), mild (II), moderate (III) or severe (IV) depending on the ratio of the width of the regurgitant jet to the diameter of the left ventricular outflow tract [7]. We evaluated the dilatation of the neoaortic root at the three different levels of measurement with the calculation of these *Z*-values of Ao, aortic sinus (AS) and aortic sinotubular junction (SJ) diameters. AS and SJ diameters were indexed using the ratio to Ao. SJ diameters were also indexed using the ratio to AS. Aortic root measurements and assessment of AR were taken from the original echocardiographic reports.

Statistical analysis

Statistical analysis was performed using SPSS version 19.0 software (SPSS Inc., Chicago, IL, USA). All descriptive data were expressed as mean values ± standard deviation or median with ranges, as appropriate. The χ^2 test was used to compare categorical variables and the *t* tests were used for continuous variables. Estimated survival and freedom from events including reoperation, AR, PS and coronary events were determined by the Kaplan–Meier method. The subgroups were compared using the log-rank test. Variables were evaluated using the likelihood-ratio test in the Cox proportional hazards regression model. Hazard ratios with 95% confidence intervals were constructed for the significant multivariable predictors. The gradual increases of neoaortic root size, degree of AR and PS over time after the ASO were assessed using the Pearson correlation coefficient. The relationships between neoaortic root size and degree of AR were assessed using the Spearman rank correlation coefficient. A *P*-value of <0.05 was set as the level of statistical significance.

RESULTS

Late survival

There were seven (3.2%) late deaths due to respiratory problems in four patients, sequelae of brain injury in one and arrhythmia in two patients. All late deaths occurred within 16 months (2.5–15.2 months). The actuarial late survival rates were 97.1 ± 1.2% at 1 year, 96.6 ± 1.3% at 5 years, 96.6 ± 1.3% at 10 years, 96.6 ± 1.3% at 15 years, 96.6 ± 1.3% at 20 years and 96.6 ± 1.3% at 23 years (Fig. 1A).

Reoperation

During the entire follow-up period, 24 (10.9%) patients underwent reoperations. Freedom from reoperation was 95.5 ± 1.5% at 1 year, 92.5 ± 1.9% at 5 years, 86.5 ± 2.9% at 10 years, 81.9 ± 3.8% at 15 years, 81.9 ± 3.8% at 20 years and 81.9 ± 3.8% at 23 years. Reoperation-free late survival was 92.7 ± 1.8% at 1 year, 89.2 ± 2.2% at 5 years, 83.4 ± 3.0% at 10 years, 79.0 ± 3.8% at 15 years, 79.0 ± 3.8% at 20 years and 79.0 ± 3.8% at 23 years (Fig. 1A).

The indications for reoperation included right ventricular outflow tract obstruction in 10 patients, neoAR in four, supravalvar aortic stenosis in four, residual VSD in four, coronary artery stenosis in three, tricuspid regurgitation in three, subaortic stenosis in two, residual arch obstruction in two, mitral regurgitation in two, complete atrioventricular block in three, aortic root dilatation in one and atrial flutter in one.

Risk factors of reoperation

Multivariate analysis indicated that arch anomaly, CPB time, post-ASO PS and post-ASO coronary events were independent predictors for reoperation (Table 1).

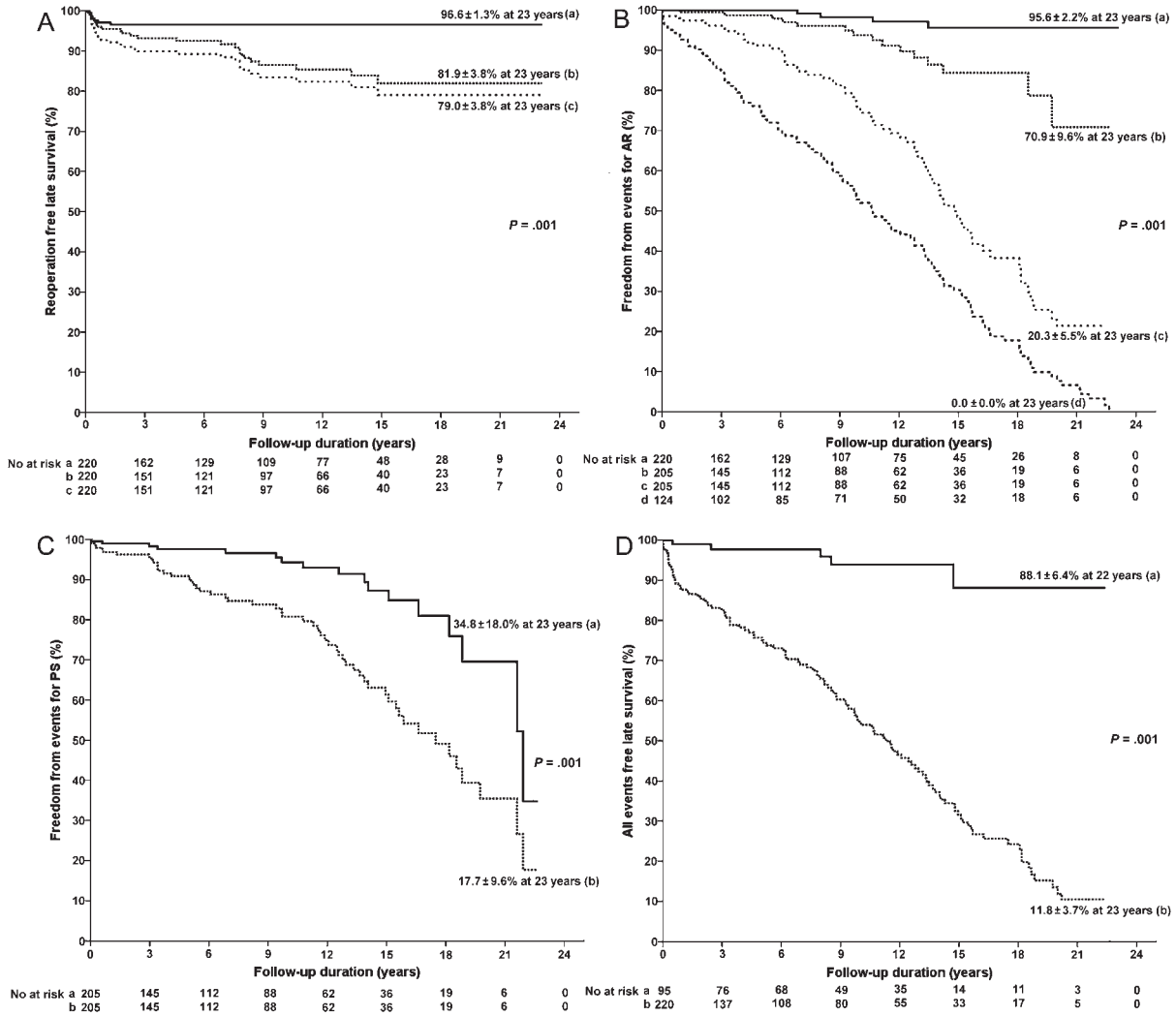

Figure 1: (**A**) The Kaplan–Meier curves for reoperation-free late survival. (a): late survival, (b): freedom from reoperation, (c): reoperation-free late survival. (**B**) The Kaplan–Meier curves for freedom from reoperation for AR, AR and aortic root dilatation. a: freedom from reoperation for AR, (b): freedom from AR of Grade III, (c): freedom from AR of Grade II, (d): freedom from aortic root dilatation (aortic root *Z*-value >0). (**C**) The Kaplan–Meier curves for freedom from PS. (a): freedom from PS ≥36 mmHg, b: freedom from PS ≥20 mmHg. (**D**) The Kaplan–Meier curves for freedom from events. (a): freedom from coronary events, (b): all events-free late survival. Events include reoperation, AR Grade II, PS ≥20 mmHg and coronary events. AR: aortic regurgitation; PS: pulmonary stenosis.

Follow-up echocardiographic and clinical results

The last follow-up echocardiography was performed at a median of 87.5 months (0.1–271.8 months) after the ASO. At the last follow-up echocardiography ($n = 205$), neoAR of Grade IV was present in three (1.5%) patients, neoAR of Grade III in 15 (7.3%) and neoAR of Grade II in 75 (36.6%) patients. At the last follow-up echocardiography ($n = 205$), PS (peak pressure gradients ≥36 mmHg) at main PA was present in 17 (8.3%) and PS (peak pressure gradients ≥20 mmHg) in 48 (23.4%) patients. At the last follow-up echocardiography, the mean left ventricular ejection fraction and the fraction of shortening were 63.4 ± 7.8% (range: 39–81%) and 34.8 ± 5.2% (range: 22.3–49.5%). At the last follow-up, 211 (95.9%) patients met the criteria for the New York Heart Association functional Class I.

Risk factors of neoaortic regurgitation

Freedom from reoperation for AR was 100.0 ± 0.0% at 1 year, 100.0 ± 0.0% at 5 years, 98.3 ± 1.2% at 10 years, 95.6 ± 2.2% at 15 years, 95.6 ± 2.2% at 20 years and 95.6 ± 2.2% at 23 years, respectively. Freedom from neoAR of Grade IV was 100.0 ± 0.0% at 1 year, 100.0 ± 0.0% at 5 years, 100.0 ± 0.0% at 10 years, 96.7 ± 2.3% at 15 years, 90.2 ± 6.6% at 20 years and 90.2 ± 6.6% at 23 years, respectively. Freedom from neoAR of Grade III was 99.4 ± 0.6% at 1 year, 98.7 ± 0.9% at 5 years, 93.8 ± 2.3% at 10 years, 84.4 ± 4.3% at 15 years, 70.9 ± 9.6% at 20 years and 70.9 ± 9.6% at 23 years, respectively. Freedom from neoAR of Grade II was 97.4 ± 1.2% at 1 year, 91.2 ± 2.3% at 5 years, 75.4 ± 3.9% at 10 years, 48.6 ± 5.2% at 15 years, 20.3 ± 5.5% at 20 years and 20.3 ± 5.5% at 23 years, respectively. Freedom from aortic root dilatation (aortic root *Z*-value >0) was 92.7 ± 2.4% at 1 year, 75.3 ± 3.9% at 5 years,

Table 1: Risk factors for reoperation

Variable	Univariable			Multivariable		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Sex	1.174	0.465–2.964	0.734			
Age	0.999	0.997–1.002	0.552			
Body weight	0.880	0.640–1.211	0.433			
Diagnosis (TB vs TGA)	**3.623**	**1.217–10.779**	**0.021**			
Diagnosis (VSD)	1.908	0.834–4.363	0.126			
Arch anomaly	**4.232**	**1.650–10.850**	**0.003**	**6.984**	**1.367–35.671**	**0.019**
LVOTO	2.095	0.282–15.556	0.470			
RVOTO	1.532	0.206–11.360	0.677			
GA relation (side-by-side)	**5.808**	**2.131–15.827**	**0.001**			
GA size discrepancy	2.618	0.840–8.157	0.097			
Usual coronary artery	0.566	0.242–1.324	0.190			
Single coronary artery	2.423	0.825–7.112	0.107			
Preoperative PR	1.016	0.326–3.166	0.978			
Staged operation	0.901	0.402–2.019	0.800			
Preoperative PA banding	0.817	0.192–3.476	0.784			
Preoperative shunt	0.045	0.000–103.518	0.433			
Preoperative arch repair	**3.461**	**1.025–11.688**	**0.046**			
Cardiopulmonary bypass time	**1.011**	**1.006–1.016**	**0.001**	**1.014**	**1.004–1.024**	**0.004**
Aortic cross-clamp time	**1.018**	**1.007–1.029**	**0.001**			
Coronary artery transfer (trapdoor)	2.261	0.964–5.304	0.061			
PA reconstruction (pantaloon)	**0.398**	**0.177–0.895**	**0.026**			
Hospital stay	1.010	0.992–1.028	0.293			
Follow-up duration	0.997	0.991–1.004	0.437			
Postoperative AR	0.903	0.399–2.045	0.807			
Postoperative aortic root dilatation	2.341	0.920–5.959	0.074			
Postoperative pulmonary stenosis	**5.003**	**2.189–11.434**	**0.001**	**13.189**	**2.303–75.532**	**0.004**
Coronary event	**4.677**	**1.348–16.224**	**0.015**	**58.383**	**5.159–660.697**	**0.001**
Postoperative left ventricular EF	**0.935**	**0.884–0.988**	**0.017**			
Functional status	0.753	0.101–5.583	0.781			

HR: hazard ratio; CI: confidence interval; TB: Taussig–Bing; TGA: transposition of the great arteries; VSD: ventricular septal defect; LVOTO: left ventricular outflow tract obstruction; RVOTO: right ventricular outflow tract obstruction; GA: great artery; PR: pulmonary regurgitation; PA: pulmonary artery; EF: ejection fraction; bold values, $P < 0.05$.

52.9 ± 4.5% at 10 years, 30.3 ± 4.3% at 15 years, 7.7 ± 2.7% at 20 years and 0.0 ± 0.0% at 23 years, respectively (Fig. 1B).

A multivariate analysis indicated that the size discrepancy of the great arteries, post-ASO aortic root dilatation and post-ASO follow-up duration were independent predictors for neoAR (Table 2).

Time-related correlation for aortic regurgitation (Figs 2 and 3)

These indexed values of the ratio of the SJ diameters to Ao progressively increased over time after the ASO (the ratio of SJ/Ao vs follow-up duration after the ASO: $r = 0.203$, $P = 0.036$, Pearson) (Fig. 2). The grade of AR progressively increased over time after the ASO (AR grade vs follow-up duration after the ASO: Spearman rank correlation coefficient $r_s = 0.340$, $P = 0.001$) (Fig. 2).

The increase of the AR grade did not significantly correlate with these *Z*-values of Ao diameter (AR grade vs *Z*-value of Ao: Spearman rank correlation coefficient $r_s = 0.151$, $P = 0.87$). The increase of the AR grade significantly correlated with these *Z*-values of the AS diameter (AR grade vs *Z*-value of AS: Spearman rank correlation coefficient $r_s = 0.289$, $P = 0.001$). The increase of the AR grade significantly correlated with these *Z*-values of the SJ diameter (AR grade vs *Z*-value of SJ: Spearman rank correlation coefficient $r_s = 0.242$, $P = 0.012$) (Fig. 3).

The increase of the AR grade significantly correlated with these indexed values of the ratio of the AS diameters to Ao (AR grade vs ratio of AS/Ao: Spearman rank correlation coefficient $r_s = 0.234$, $P = 0.009$). The increase of the AR grade significantly correlated with these indexed values of the ratio of the SJ diameters to Ao (AR grade vs ratio of SJ/Ao: Spearman rank correlation coefficient $r_s = 0.216$, $P = 0.026$). However, the increase of the AR grade did not significantly correlate with these indexed values of the ratio of the SJ diameters to AS (AR grade vs the ratio of SJ/AS: Spearman rank correlation coefficient $r_s = 0.088$, $P = 0.368$) (Fig. 3).

Risk factors of pulmonary stenosis

Freedom from PS ≥36 mmHg was 98.9 ± 0.8% at 1 year, 97.5 ± 1.2% at 5 years, 94.3 ± 2.2% at 10 years, 87.2 ± 4.0% at 15 years, 69.6 ± 9.0% at 20 years and 34.8 ± 18.0% at 23 years, respectively. Freedom from PS ≥20 mmHg was 96.8 ± 1.3% at 1 year, 90.8 ± 2.3% at 5 years, 80.8 ± 3.4% at 10 years, 61.4 ± 5.1% at 15 years, 35.5 ± 7.4% at 20 years and 17.7 ± 9.6% at 23 years (log-rank $P = 0.001$) (Fig. 1C). The pressure gradients of PS significantly increased over time after the ASO (pressure gradients of PS vs follow-up duration after the ASO: $r = 0.254$, $P = 0.011$, Pearson) (Fig. 4).

Table 2: Risk factors for aortic regurgitation

Variable	Univariable			Multivariable		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Sex	1.029	0.608–1.742	0.915			
Age	1.000	0.999–1.000	0.513			
Body weight	0.982	0.894–1.078	0.698			
Diagnosis (TB vs TGA)	0.908	0.284–2.906	0.871			
Diagnosis (VSD)	1.075	0.680–1.698	0.757			
Arch anomaly	**2.543**	**1.065–6.077**	**0.036**			
LVOTO	0.682	0.320–1.452	0.320			
RVOTO	0.046	0.000–10.713	0.269			
GA relation (side-by-side)	1.078	0.337–3.448	0.899			
GA size discrepancy	**2.558**	**1.220–5.364**	**0.013**	**3.155**	**1.305–7.631**	**0.011**
Bicuspid pulmonary valve	1.665	0.848–3.270	0.139			
Usual coronary artery	0.917	0.497–1.694	0.783			
Single coronary artery	1.746	0.619–4.923	0.292			
Preoperative PR	1.388	0.696–2.769	0.352			
Staged operation	1.194	0.741–1.926	0.466			
Preoperative PA banding	1.492	0.734–3.030	0.269			
Preoperative shunt	1.469	0.670–3.218	0.337			
Preoperative arch repair	1.588	0.381–6.617	0.525			
Cardiopulmonary bypass time	**1.006**	**1.002–1.011**	**0.009**			
Aortic cross-clamp time	**1.018**	**1.009–1.027**	**0.001**			
Coronary artery transfer (trapdoor)	**3.154**	**1.946–5.112**	**0.001**			
Open sternum	3.177	0.971–10.395	0.056			
Mechanical support	**3.000**	**1.200–7.500**	**0.019**			
Hospital stay	0.992	0.979–1.005	0.215			
Follow-up duration	**1.089**	**1.068–1.110**	**0.001**	**1.086**	**1.062–1.110**	**0.001**
Reoperation	0.926	0.475–1.806	0.823			
Postoperative aortic root dilatation	**1.925**	**1.111–3.335**	**0.020**	**1.872**	**1.005–3.489**	**0.048**
Pulmonary stenosis	0.838	0.505–1.391	0.494			
Coronary event	0.567	0.077–4.163	0.577			
Postoperative left ventricular EF	1.003	0.966–1.042	0.869			

HR: hazard ratio; CI: confidence interval; TB: Taussig–Bing; TGA: transposition of the great arteries; VSD: ventricular septal defect; LVOTO: left ventricular outflow tract obstruction; RVOTO: right ventricular outflow tract obstruction; GA: great artery; PR: pulmonary regurgitation; PA: pulmonary artery; EF: ejection fraction; bold values, $P < 0.05$.

A multivariate analysis indicated that the diagnosis of Taussig–Bing and arch anomalies were independent predictors for PS (Table 3).

Coronary evaluation

In 95 (43.2%) patients, coronary artery evaluation was performed with angiography, computed tomography or myocardial single-photon emission computed tomography at a median of 121.3 months (5.9–268.9 months) after the ASO. Among them, 90 (94.7%) patients had normal coronary morphology or perfusion, three patients underwent reoperation of coronary ostial angioplasty for coronary ostial stenosis in two patients and coronary artery translocation for coronary compression by main PA in one and two patients had reversible perfusion defects at various regions, which were clinically not significant.

Freedom from coronary events was 98.9 ± 1.1% at 1 year, 97.7 ± 1.6% at 5 years, 94.0 ± 3.0% at 10 years, 88.1 ± 6.4% at 15 years, 88.1 ± 6.4% at 20 years and 88.1 ± 6.4% at 22 years, respectively. All events-free late survival including coronary events were 87.6 ± 2.3% at 1 year, 75.7 ± 3.2% at 5 years, 54.8 ± 4.0% at 10 years, 31.6 ± 4.1% at 15 years, 11.8 ± 3.7% at 20 years and 11.8 ± 3.7% at 23 years, respectively (Fig. 1D).

Risk factors of coronary events

A multivariate analysis indicated that the single coronary artery was independent predictors for coronary events (Table 4).

DISCUSSION

Reoperation

All reported series show that the need for reoperation after the ASO is between 5 and 10% [1, 2, 4, 8]. The indications for reoperation are obstruction of the neopulmonary outflow tract, development of obstructions of the reimplanted coronary arteries, dysfunction of the neoaortic valve and progressive left ventricular dysfunction. The more frequent indications for reoperation are coronary lesions and right ventricular outflow tract obstructions. The risk of reoperation is reported to be usually increased in the complex TGA; particularly for patients with associated aortic arch obstruction (with or without VSD) [9]. Reoperations can be carried out with a very low operative risk. The survival and functional outcome are not affected by the need for reoperation [4]. However, Mavroudis *et al.* [10] reported that 27 late

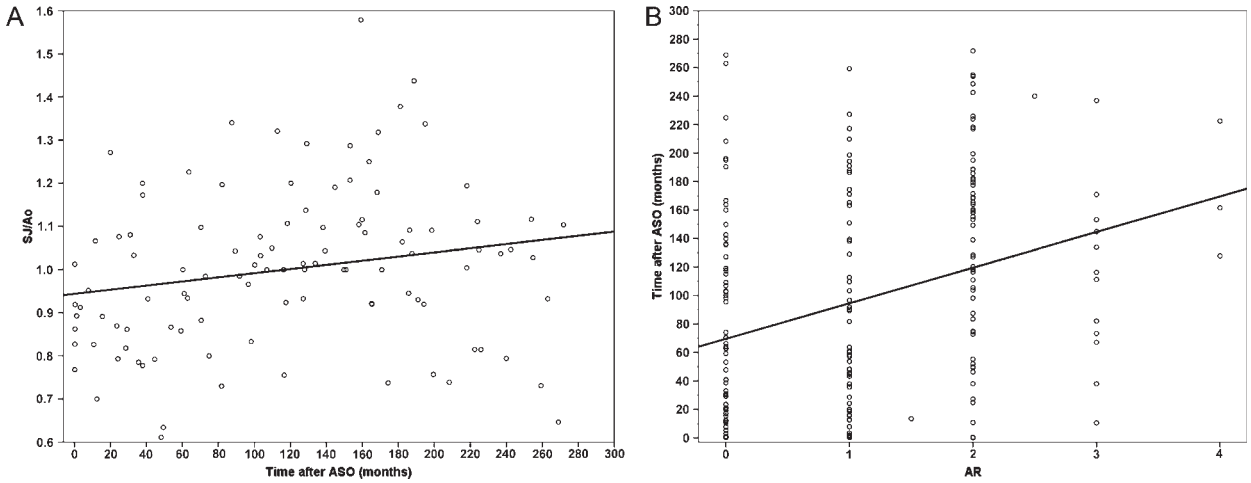

Figure 2: Time-related correlation for aortic root dilatation and AR after the ASO. (**A**) Box plot showing the ratio of SJ/Ao over time after the ASO (Pearson correlation coefficient, $r = 0.203$; $P = 0.036$). Aortic sinotubular junction diameter was indexed using ratio to aortic annulus. (**B**) Box plot showing the development of AR over time after the ASO (Spearman rank correlation coefficient, $r_s = 0.340$; $P = 0.001$). AR: aortic regurgitation; ASO: arterial switch operation; SJ: sinotubular junction: Ao: aortic annulus.

reoperations on 23 patients were performed after the ASO, and four patients died.

In this series, reoperations were required in 10.9% of the survivors with a median follow-up of 103.2 months. Reoperation is the main consequence of PS, done for this indication in 4.6% of the survivors, representing 25.6% of the reoperations after the ASO. Most of the described risk factors (Taussig–Bing anomaly, arch anomaly, side-by-side position of the great arteries, staged aortic arch repair before the ASO, PA reconstruction with non-pantaloon patch, CPB time and ACC time) that were significantly associated with reoperation in this series are closely related to PS. Although neoaortic root dilatation and minimal AR are common, reoperation for severe neoaortic valve dysfunction is, to date, very rarely necessary in accordance with other reports [4]. In this series, no patient died following reoperation after the ASO. The functional outcome as well as survival are not affected by the need for reoperation ($P = 0.781$), but reoperations were significantly related with postoperative left ventricular dysfunction (hazard ratio = 0.935; $P = 0.017$).

Aortic regurgitation

In this series, freedom from neoAR of Grades IV, III and II at 23 years was 90.2 ± 6.6%, 70.9 ± 9.6% and 20.3 ± 5.5%, respectively. The risk factors for neoAR development are reported to be cardiac anatomy, surgical methods or demographic factors, for example, heart defects associated with TGA (like VSD, aortic arch anomaly and Taussig–Bing anomaly), coronary artery anomaly, primary pulmonary regurgitation, bicuspid native pulmonary valve, arterial size discrepancy, coronary artery transplantation method, ACC time and patient age and weight at operation [1, 6, 11–13].

The association of a pulmonary to the aortic root size discrepancy is identified as the most important promoter of neoaortic valve dysfunction. The size mismatch makes the neoaortic reconstruction difficult and causes turbulence to the neoaortic valve, which may result in the development of neoAR and its progression [12, 13]. The destabilization of the junction between the enlarged native pulmonary root and the relatively small arterial trunk might also subsequently facilitate the insidious and probably mutual morphological and functional deterioration of the neoaortic root with the factor time acting as the ultimate determinant [5, 13].

Aortic root dilatation and its diameters have been reported to be a subject of many investigations as a potential anatomic correlate of neoAR incidence and progression [6, 11, 14]. The presence of neoAR also appears to accelerate the root size increase, probably based on the time-depending and reciprocal stress effects between leaflet function and root adaptation to the late neoaortic root remodelling [5]. The progressive neoaortic root dilatation over time was related to the mechanical incapability of the native pulmonary root to sustain a systemic pressure stress [12, 13], and structural abnormalities based on the histological differences between native aortic and pulmonary valves related to elastin and collagen fibres content [15, 16]. In our study population, we observed that AR and the ratio of SJ/Ao increases with time after the ASO [13]. The factor 'time' also appears to be the main determinant of the functional and anatomical fate of the neoaorta at the long-term follow-up [5]. We found a significant correlation between the *Z*-value of root dimensions (SJ and AS) and AR occurrence, and between the aortic root ratio (SJ/Ao, AS/Ao, not SJ/AS) and AR occurrence. Our results showed that aortic root diameters (SJ > AS > Ao) are important as the predictors of valve incompetence. These data clarify whether progressive dilatation of the neoaortic root may cause a failure of the leaflet coaptation [17]. This piece of evidence led us to speculate that the onset of AR over time may be induced by a complex rearrangement of the AS and SJ geometry, and the gradual increases we found in the SJ/Ao ratio seem to support this hypothesis [6]. The surgical preservation of the normal AS and SJ geometry is recommended to reduce the occurrence of AR.

We speculate that there are potential interrelations between coronary reimplantation techniques and aortic root morphology. For this reason, the punch technique is recommended for repair in all but the most complicated coronary pattern [6]. Evolution of AR underlines the need for close long-term monitoring and further studies to clarify the risk factors and possibly to modify the surgical technique in some patients with complex coronary anatomy.

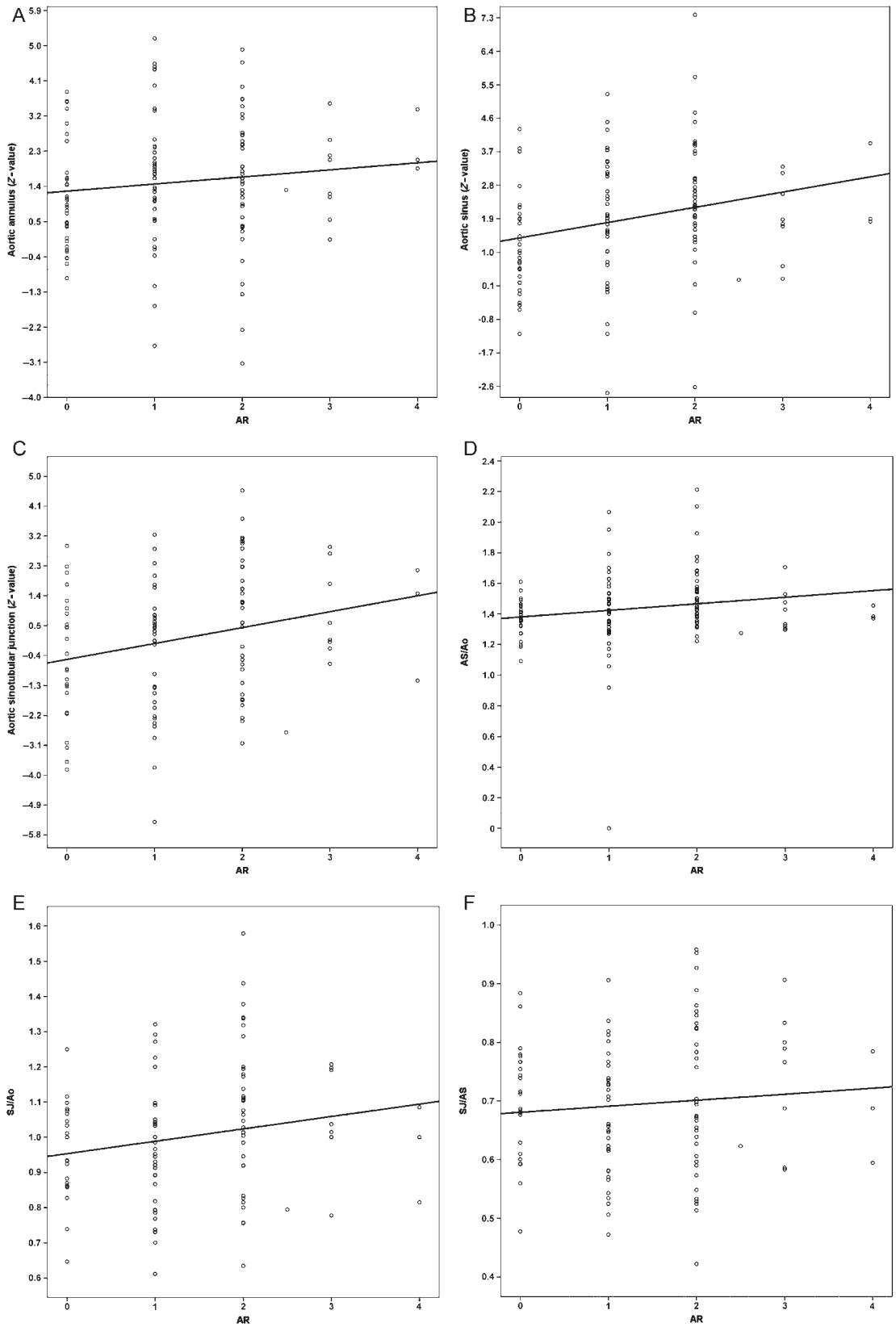

Figure 3: The relationship between degree of aortic root dilatation and degree of AR using the Spearman rank correlation coefficient. (**A**) The relationship between aortic annulus *Z*-value and degree of AR ($r_s = 0.151$, $P = 0.87$). (**B**) The relationship between AS *Z*-value and degree of AR ($r_s = 0.289$, $P = 0.001$). (**C**) The relationship between aortic sinotubular junction *Z*-value and degree of AR ($r_s = 0.242$, $P = 0.012$). (**D**) The relationship between the ratio of AS/Ao and degree of AR ($r_s = 0.234$, $P = 0.009$). Aortic sinus diameter was indexed using the ratio to aortic annulus. (**E**) The relationship between the ratio of SJ/Ao and degree of AR ($r_s = 0.216$, $P = 0.026$). The aortic sinotubular junction diameter was indexed using the ratio to aortic annulus. (**F**) The relationship between the ratio of SJ/AS and degree of AR ($r_s = 0.088$, $P = 0.368$). The aortic sinotubular junction diameter was indexed using the ratio to AS. AR: aortic regurgitation; AS: aortic sinus; Ao: aortic annulus; SJ: sinotubular junction.

Pulmonary stenosis

PS is related either to the inadequate growth of the pulmonary anastomotic site or to the inadequate growth of the whole new right ventricular outflow tract in patients with associated aortic arch obstruction [4]. Nakanishi *et al.* [18] observed a small annulus or even growth failure of the neopulmonary annulus after the ASO in 18% of their series. The reported incidence of PS varies from 7 to 50% [19]. In this series, freedom from PS ≥36 mmHg is 34.8 ± 18.0% at 23 years and freedom from PS ≥20 mmHg is 17.7 ± 9.6% at 23 years. Our analysis revealed that the risk factors for PS are Taussig–Bing anomaly, arch anomaly, unusual coronary pattern and side-by-side position of the great arteries in univariate analysis, and Taussig–Bing anomaly and arch anomaly in multivariate analysis. This anatomical feature may predispose to the possible changes of pulmonary root geometry resulting in PS over time after the ASO.

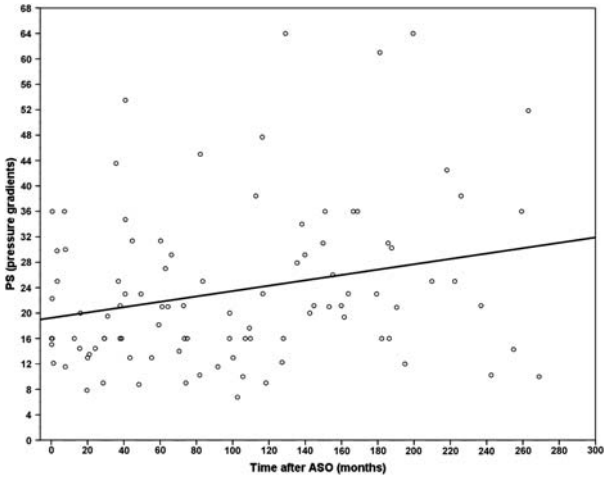

Figure 4: Box plot showing the development of PS over time after the ASO using the Pearson correlation coefficient ($r = 0.254$, $P = 0.011$, $R^2 = 0.065$). PS: pulmonary stenosis; ASO: arterial switch operation.

PS was reported to often complicate the postoperative course of Taussig–Bing hearts and to be the main indication for reoperation [20]. The subaortic stenosis by the conal malalignment has also played a major role in the occurrence of PS after the ASO. In Taussig–Bing anomaly and aortic arch anomaly, the small size of the original aortic valve annulus before the ASO corresponds to the small size of the neopulmonary annulus after the ASO. Nogi *et al.* [19] demonstrated that the neopulmonary valve size remains currently small if the native aortic valve was small, and might be susceptible to the growth retardation. The small size and the growth retardation of the neopulmonary annulus eventually lead to PS. In a multi-institutional study, Williams *et al.* [21] reported that PS was associated with the aorta and pulmonary trunk positioned side-to-side, and coexisting coarctation in accordance with our study. The PA reconstruction with a one pantaloon-shaped patch as well as Taussig–Bing

Table 3: Risk factors for pulmonary stenosis

Variable	Univariable			Multivariable		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Sex	0.727	0.363–1.453	0.367			
Age	0.999	0.997–1.000	0.162			
Body weight	0.907	0.778–1.058	0.214			
Diagnosis (TB vs TGA)	**3.921**	**1.884–8.160**	**0.001**	**2.815**	**1.290–6.146**	**0.009**
Diagnosis (VSD)	1.415	0.824–2.431	0.208			
Arch anomaly	**5.775**	**2.733–12.205**	**0.001**	**4.581**	**2.073–10.125**	**0.001**
RVOTO	2.183	0.780–6.114	0.137			
GA relation (side-by-side)	**3.972**	**1.847–8.544**	**0.001**			
GA size discrepancy	0.985	0.378–2.566	0.975			
Usual coronary artery	**0.536**	**0.289–0.991**	**0.047**			
Single coronary artery	1.423	0.433–4.682	0.561			
Preoperative PR	1.505	0.750–3.020	0.250			
Staged operation	0.813	0.474–1.395	0.452			
Preoperative PA banding	1.843	0.859–3.956	0.116			
Preoperative shunt	0.844	0.262–2.716	0.776			
Preoperative arch repair	**6.850**	**2.786–16.841**	**0.001**			
Cardiopulmonary bypass time	**1.012**	**1.008–1.016**	**0.001**			
Aortic cross-clamp time	**1.033**	**1.025–1.042**	**0.001**			
Lecompte manoeuvre	0.242	0.033–1.790	0.165			
PA reconstruction (pantaloon)	1.392	0.756–2.563	0.289			
Open sternum	1.215	0.165–8.957	0.848			
Mechanical support	0.047	0.000–89.508	0.428			
Hospital stay	0.997	0.983–1.011	0.667			
Follow-up duration	**1.107**	**1.079–1.136**	**0.001**			
Reoperation	**2.311**	**1.268–4.210**	**0.006**			
Postoperative aortic root dilatation	0.925	0.494–1.735	0.808			
Postoperative left ventricular EF	1.021	0.979–1.065	0.330			
Coronary event	0.046	0.000–97.836	0.431			

HR: hazard ratio; CI: confidence interval; TB: Taussig–Bing; TGA: transposition of the great arteries; VSD: ventricular septal defect; RVOTO: right ventricular outflow tract obstruction; GA: great artery; PR: pulmonary regurgitation; PA: pulmonary artery; EF: ejection fraction; bold values, $P < 0.05$.

Table 4: Risk factors for coronary events

Variable	Univariable			Multivariable		
	HR	95% CI	*P*-value	HR	95% CI	*P*-value
Sex	0.908	0.100–8.280	0.932			
Age	0.992	0.968–1.016	0.503			
Body weight	0.792	0.346–1.811	0.580			
Diagnosis (VSD)	0.303	0.034–2.729	0.287			
GA size discrepancy	0.113	0.003–3.849	0.226			
Unusual coronary artery	5.435	0.880–33.333	0.068			
Single coronary artery	**11.315**	**1.574–81.353**	**0.016**	**11.248**	**1.564–80.914**	**0.016**
Staged operation	0.422	0.070–2.541	0.346			
Cardiopulmonary bypass time	0.924	0.847–1.008	0.075			
Aortic cross-clamp time	0.969	0.914–1.028	0.296			
Coronary artery transfer (trapdoor)	5.789	0.504–66.446	0.158			
PA reconstruction (pantaloon)	0.434	0.071–2.636	0.364			
Hospital stay	1.012	0.988–1.037	0.325			
Reoperation	**8.797**	**1.393–55.560**	**0.021**			
Postoperative aortic root dilatation	0.407	0.042–3.966	0.439			
Postoperative aortic regurgitation	0.199	0.021–1.882	0.159			
Postoperative pulmonary stenosis	0.025	0.000–56.172	0.349			
Postoperative left ventricular EF	0.967	0.818–1.145	0.699			

HR: hazard ratio; CI: confidence interval; VSD: ventricular septal defect; GA: great artery; PA: pulmonary artery; EF: ejection fraction; bold values, $P < 0.05$.

anomaly and a smaller aortic valve Z-value were demonstrated to be risk factors for PS [22]. But, in our series, the PA reconstruction technique with a one pantaloon patch is not a risk factor for PS. The flattening and transformation of the main PA with somatic growth occur around the circumference of the suture line, and the development of fibrous tissue around that region may also lead to PS, although the mechanism of the PS progress has not yet been clarified [2].

Coronary events

Early coronary lesions are more frequent in patients with unusual coronary patterns [3, 23] and various technical factors have been incriminated (inadequate coronary transfer, excessive use of fibrin glue and abnormal early fibrosis) [4]. In late coronary lesions, reimplantation of the coronary arteries may produce subtle flow abnormalities, which, in turn, alter shear stress and induce progressive intimal thickening [4]. The risk of a clinically silent late coronary artery obstruction of the reimplanted coronary arteries warrants a prolonged regular follow-up protocol involving invasive angiographic assessment [24], because it has been clearly established that most patients with coronary lesions did not show any clinical, electrocardiographic or echocardiographic evidence of myocardial ischaemia [25]. A complex native coronary artery anatomy was associated with the occurrence of late coronary stenosis, while the reimplantation technique had little-to-no impact on coronary prognosis [23, 24]. Patients with complex coronary anatomy were more likely to have coronary artery reintervention [23]. In this series, freedom from coronary events was 88.1 ± 6.4% at 22 years. A multivariate analysis indicated that the single coronary artery was an independent predictor for coronary events. An unusual coronary artery ($P = 0.068$; hazard ratio = 5.435) tended to be a risk factor for coronary events in an univariate analysis, although it did not reach statistical significance, while the trap-door technique of coronary artery transfer was not a risk factor for coronary events ($P = 0.158$). A longer follow-up is required to evaluate the coronary events after the ASO, particularly in an unusual coronary anatomy such as a single coronary artery.

The survival and functional outcomes of early survivors after the ASO were excellent in the long-term. This study also provides grounds for increased awareness of common complications over time closely related to the long-term functional outcomes of ASO. Since the factor 'time' appears to be the principal determinant of late neoaortic valve dysfunction associated with root dilatation and coronary events as well as PS, strict serial surveillance for AR and PS including coronary events after the ASO will actually better define the long-term clinical significance of this issue particularly in the high-risk anatomies such as the Taussig–Bing anomaly, arch anomaly, side-by-side position of the great arteries, size discrepancy of the great arteries and unusual coronary artery.

Conflict of interest: none declared.

REFERENCES

[1] Prêtre R, Tamisier D, Bonhoeffer P, Mauriat P, Pouard P, Sidi D *et al*. Results of the arterial switch operation in neonates with transposed great arteries. Lancet 2001;9:1826–30.
[2] Crucean A, Bonacchi M, Bernabei M, Murzi B, Luisi SV, Vanini V. Early and long term outcome of the arterial switch operation for transposition of the great arteries: predictors and functional evaluation. Eur J Cardiothorac Surg 2002;22:864–73.
[3] Tamisier D, Ouaknine O, Pouard P, Mauriat P, Lefebvre D, Sidi D *et al*. Neonatal arterial switch operation: coronary artery patterns and coronary events. Eur J Cardiothorac Surg 1997;11:810–7.
[4] Angeli E, Raisky O, Bonnet D, Sidi D, Vouhé PR. Late reoperations after neonatal arterial switch operation for transposition of the great arteries. Eur J Cardiothorac Surg 2008;34:32–6.
[5] Bové T, De Meulder F, Vandenplas G, De Groote K, Panzer J, Suys B *et al*. Midterm assessment of the reconstructed arteries after the arterial switch operation. Ann Thorac Surg 2008;85:823–30.
[6] Formigari R, Toscano A, Giardini A, Gargiulo G, Di Donato R, Picchio FM *et al*. Prevalence and predictors of neoaortic regurgitation after arterial

switch operation for transposition of the great arteries. J Thorac Cardiovasc Surg 2003;126:1753–9.
[7] Tani LY, Minich LL, Day RW, Orsmond GS, Shaddy RE. Doppler evaluation of aortic regurgitation in children. Am J Cardiol 1997;80:927–31.
[8] Chiu IS, Huang SC, Chen YS, Chang CI, Lee ML, Chen SJ *et al*. Restoring the spiral flow of nature in transposed great arteries. Eur J Cardiothorac Surg 2010;37:1239–45.
[9] Huber C, Mimic B, Oswal N, Sullivan I, Kostolny M, Elliott M *et al*. Outcomes and re-interventions after one-stage repair of transposition of great arteries and aortic arch obstruction. Eur J Cardiothorac Surg 2011; 39:213–21.
[10] Mavroudis C, Stewart RD, Backer CL, Rudra H, Vargo P, Jacobs ML. Reoperative techniques for complications after arterial switch. Ann Thorac Surg 2011;92:1747–55.
[11] Schwartz ML, Gauvreau K, del Nido P, Mayer JE, Colan SD. Long-term predictors of aortic root dilation and aortic regurgitation after arterial switch operation. Circulation 2004;110(Suppl II):II128–32.
[12] Hwang HY, Kim WH, Kwak JG, Lee JR, Kim YJ, Rho JR *et al*. Mid-term follow-up of neoaortic regurgitation after the arterial switch operation for transposition of the great arteries. Eur J Cardiothorac Surg 2006; 29:162–7.
[13] Losay J, Touchot A, Capderou A, Piot J-D, Belli E, Planche C *et al*. Aortic valve regurgitation after arterial switch operation for transposition of the great arteries: incidence, risk factors, and outcome. J Am Coll Cardiol 2006;47:2057–62.
[14] Bottio T, Thiene G, Tarzia V, Rizzoli G, Gerosa G. Arterial switch operation, aortic root dilation, and long-term aortic valve competence. Ann Thorac Surg 2008;86:2025–6.
[15] Niwa K, Perloff JK, Bhuta SM, Laks H, Drinkwater DC, Child JS *et al*. Structural abnormalities of great arterial walls in congenital heart disease: light and electron microscopic analyses. Circulation 2001;103: 393–400.
[16] Lalezari S, Hazekamp MG, Bartelings MM, Schoof PH, Gittenberger-de Groot AC. Pulmonary artery remodeling in transposition of the great arteries: relevance for neo-aortic root dilatation. J Thorac Cardiovasc Surg 2003;126:1053–60.
[17] Marino BS, Wernovsky G, McElhinney DB, Jawad A, Kreb DL, Mantel SF *et al*. Neo-aortic valvar function after the arterial switch. Cardiol Young 2006;16:481–9.
[18] Nakanishi T, Momoi N, Satoh M, Yamada M, Terada M, Nakazawa M *et al*. Growth of the neopulmonary valve annulus after the arterial switch operation in transposition of the great arteries. Circulation 1996;94 (Suppl 2):27–31.
[19] Nogi S, McBrindle BW, Boutin C, Williams WG, Freedom RM, Benson LN. Fate of the neo-pulmonary valve after the arterial switch operation in neonates. J Thorac Cardiovasc Surg 1998;115:557–62.
[20] Wetter J, Sinzobahamvya N, Blaschczok HC, Cho MY, Brecher AM, Grävinghoff LM *et al*. Results of arterial switch operation for primary total correction of the Taussig–Bing anomaly. Ann Thorac Surg 2004; 77:41–7.
[21] Williams WG, Quaegebeur JM, Kirklin JW, Blackstone EH. The Congenital Heart Surgeons Society. Outflow obstruction after the arterial switch operation: a multi-institutional study. J Thorac Cardiovasc Surg 1997;114: 975–90.
[22] Hirata Y, Chen JM, Quaegebeur JM, Mosca RS. Should we address the neopulmonic valve? Significance of right-sided obstruction after surgery for transposition of the great arteries and coarctation. Ann Thorac Surg 2008;86:1293–8.
[23] Metton O, Calvaruso D, Gaudin R, Mussa S, Raisky O, Bonnet D *et al*. Intramural coronary arteries and outcome of neonatal arterial switch operation. Eur J Cardiothorac Surg 2010;37:1246–53.
[24] Angeli E, Formigari R, Napoleone CP, Oppido G, Ragni L, Picchio FM *et al*. Long-term coronary artery outcome after arterial switch operation for transposition of the great arteries. Eur J Cardiothorac Surg 2010;38:714–20.
[25] Bonhoeffer P, Bonnet D, Piéchaud JF, Stümper O, Aggoun Y, Villain E *et al*. Coronary artery obstruction after the arterial switch operation for transposition of the great arteries in newborns. J Am Coll Cardiol 1997; 29:202–6.

European Journal of Cardio-Thoracic Surgery 43 (2013) 334–335
doi:10.1093/ejcts/ezs272 Advance Access publication 7 May 2012

EDITORIAL COMMENT

Arterial switch operation: is the glass half full or half empty?

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Keywords: Transposition of the great arteries • Arterial switch operation

Dr Lim *et al.* [1] report their experience with the arterial switch operation (ASO). Between 1987 and 2011, 258 patients underwent ASO; the late results were evaluated in 220 operative survivors after a mean follow-up of 8.5 years.

The results can be looked at in two different ways.

On the one hand, the outcome is satisfactory. Late mortality was low, achieving a 97% probability of survival at 20 years (excluding operative mortality). Freedom from reoperation was 82% at 20 years; the main indications for reoperation were pulmonary stenosis (10 patients), aortic regurgitation (four patients) and coronary artery lesions (three patients). At the last follow-up, 96% of patients were free of symptoms.

On the other hand, several concerns arise. The early mortality rate was not negligible (14.7%); the actual late survival was, therefore, far from optimal. Coronary lesions were detected in five patients, but only 95 (43%) patients actually underwent coronary evaluation. At 20 years, the freedom from more than moderate aortic regurgitation was 71% and the freedom from significant pulmonary stenosis was 35%. The incidence of both aortic regurgitation and pulmonary stenosis increased linearly with the length of the follow-up.

These results raise two further comments:

1. The results of the present study should be taken with caution.

The study group is relatively small for a common surgical procedure (258 patients during a 23-year study period). This represents a mean of 11 operations/year and <4 patients/year for each attending surgeon. ASO is a procedure in which both experience and volume of practice play a major role [2]. This factor alone may account for the relatively high early mortality