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# Are more extensive procedures warranted at the time of aortic arch reoperation?†

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## Abstract

**OBJECTIVES:** To determine the early and late outcomes of patients undergoing aortic arch reoperations.

**METHODS:** The follow-up of 70 patients undergoing a second arch operation (excluding univentricular physiology) between 1979 and 2015 was reviewed. Median age at initial arch operation and second operation was 9 days (interquartile range: 5–35) and 10 months (interquartile range: 3–64), respectively. The most common indication for initial arch operation was coarctation in 79% (55/70). The most common indication for a second arch operation was arch reobstruction in 90% (63/70).

**RESULTS:** There were 2 hospital deaths (2/70, 3%) and 3 early third arch operations (3/70, 4%). Late follow-up was available in 94% (64/68) of hospital survivors. After a mean of 9 ± 7 years, there were 5 late deaths (5/64, 8%). Fifteen-year survival was 90% (95% confidence interval: 75–96). Arch reobstruction (echocardiogram gradient >25 mmHg/third operation for reobstruction) was present in 28% (18/64) and 16% (10/64) required a third arch operation. Fifteen-year freedom from arch reobstruction and third arch operation was 63% (95% confidence interval: 43–78) and 74% (95% confidence interval: 52–87), respectively. On multivariable analysis, hypoplastic arch at initial arch repair ($P = 0.03$) and interposition graft at second arch operation ($P < 0.0001$) were risk factors for third arch operation.

**CONCLUSIONS:** Patients undergoing a second arch operation have significant rates of arch reobstruction and reoperation. The high rates of arch reobstruction and third arch operation warrant more extensive procedures at the time of second arch operation, especially in patients with a hypoplastic arch. Regular long-term monitoring after arch reoperation is mandatory.

**Keywords:** Aortic arch • Coarctation of the aorta • Hypoplastic arch • Reintervention • Reobstruction • Reoperation

## INTRODUCTION

Arch reoperations complicate 7–10% of paediatric aortic arch repairs for aortic arch lesions such as coarctation of the aorta, interrupted aortic arch and hypoplastic aortic arch [1, 2]. Arch reobstruction is the most common indication for an arch reoperation [2], but other complications of arch repair may also necessitate reoperation such as aneurysm formation or bronchial compression. There is some evidence that patients undergoing a second arch operation have a considerable burden of mortality and morbidity, both in the immediate postoperative period and in long-term follow-up [3–5]. However, these studies often have small cohort sizes and short follow-up times, so little is known about the predictors of these adverse outcomes. Furthermore, there is currently no consensus in the literature on the best surgical technique at arch reoperation to achieve long-lasting successful results.

This study aims to determine the early and late outcomes of patients undergoing a second arch operation, and identify predictors of late mortality, arch reobstruction, and third arch operation.

## MATERIALS AND METHODS

### Study population

The design of the study was approved by The Royal Children's Hospital Human Research and Ethics Committee, and the need for consent was waived because of the retrospective nature of the study. Between 1979 and 2015, 70 consecutive patients with biventricular physiology (36 males; 51%) underwent a second arch operation at The Royal Children's Hospital, Melbourne.

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‡The first two authors contributed equally to this study.

**Table 1:** Patient characteristics

| Characteristics ($n = 70$) | $n$ (%) |
|---|---|
| Male | 36 (51%) |
| Median age at follow-up (years; IQR) | 13 (4–18) |
| Aortic arch lesion | |
| Coarctation | 55 (79%) |
| Interrupted aortic arch | |
| Type A | 3 (4%) |
| Type B | 9 (13%) |
| Isolated hypoplastic aortic arch | 3 (4%) |
| All hypoplastic arches | 38 (54%) |
| Associated cardiac anomalies | |
| Atrial septal defect | 44 (63%) |
| Ventricular septal defect | 41 (59%) |
| Bicuspid aortic valve | 16 (23%) |
| Left superior vena cava | 7 (10%) |
| Left ventricular outflow tract obstruction | 7 (10%) |
| Truncus arteriosus | 5 (7%) |
| Borderline small left ventricle | 5 (7%) |
| Bovine aortic arch | 3 (4%) |
| Aberrant right subclavian artery | 3 (4%) |
| Double outlet right ventricle | 3 (4%) |
| Transposition of the great arteries | 2 (3%) |
| Atrioventricular septal defect | 1 (1%) |
| Partial anomalous pulmonary venous drainage | 1 (1%) |
| Associated congenital syndromes | |
| Turner | 3 (4%) |
| Williams | 3 (4%) |
| Shone's | 2 (3%) |
| Down | 1 (1%) |
| VACTERL | 1 (1%) |

IQR: interquartile range.

**Table 2:** Operative data

| Surgical characteristics ($n = 70$) | Initial arch operation | Second arch operation |
|---|---|---|
| Surgical era | | |
| 1970–1989 | 25 (36%) | 20 (28%) |
| 1990–1999 | 13 (18%) | 11 (16%) |
| 2000–2015 | 32 (46%) | 39 (56%) |
| Median age at operation (years; IQR) | 0.02 (0.01–0.1) | 0.9 (0.2–5) |
| Arch repair technique | | |
| Sternotomy | 28 (40%) | 40 (57%) |
| End-to-end anastomosis | 3 (11%) | 0 (0%) |
| Extended end-to-end anastomosis | 4 (14%) | 3 (7%) |
| End-to-side anastomosis | 14 (50%) | 5 (13%) |
| Patch repair | 6 (21%) | 31 (78%) |
| Extra-anatomic bypass | 1 (4%) | 0 (0%) |
| Interposition graft | 0 (0%) | 1 (2%) |
| Thoracotomy | 42 (60%) | 27 (39%) |
| End-to-end anastomosis | 12 (29%) | 3 (11%) |
| Extended end-to-end anastomosis | 5 (12%) | 2 (7%) |
| End-to-side anastomosis | 2 (5%) | 1 (4%) |
| Subclavian flap repair | 20 (48%) | 1 (4%) |
| Patch repair | 1 (2%) | 14 (52%) |
| Extra-anatomic bypass | 1 (2%) | 1 (4%) |
| Interposition graft | 0 (0%) | 4 (15%) |
| Miscellaneous arch repair | 1 (2%) | 1 (4%) |
| Thoracotomy followed by sternotomy | 0 (0%) | 3 (4%) |
| Patch repair | 0 (0%) | 2 (67%) |
| Interposition graft | 0 (0%) | 1 (33%) |
| Associated cardiac procedures | | |
| Ventricular septal defect closure | 19 (27%) | 6 (9%) |
| Atrial septal defect closure | 13 (19%) | 1 (1%) |
| Pulmonary artery banding | 10 (14%) | 1 (1%) |
| Left ventricular outflow obstruction repair | 5 (7%) | 12 (17%) |
| Truncus arteriosus repair | 4 (6%) | 0 (0%) |
| Right ventricle-pulmonary artery conduit | 3 (4%) | 1 (1%) |
| Aortic valve repair | 2 (3%) | 4 (6%) |
| Tricuspid valve repair | 1 (1%) | 0 (0%) |
| Mitral valve repair | 0 (0%) | 2 (3%) |
| Pulmonary valve repair | 0 (0%) | 1 (1%) |
| Pulmonary artery repair | 1 (1%) | 4 (6%) |
| Arterial switch procedure | 1 (1%) | 0 (0%) |
| Repositioning of retro-aortic innominate vein | 2 (3%) | 0 (0%) |
| Left subclavian artery repair | 1 (1%) | 1 (1%) |
| Atrial septectomy | 1 (1%) | 0 (0%) |
| Intraoperative data | | |
| Sternotomy | | |
| Mean time on bypass (min) | 152 ± 59 | 121 ± 63 |
| Mean cross-clamp time (min) | 78 ± 40 | 60 ± 41 |
| Mean circulatory arrest time (min) | 16 ± 22 | 11 ± 20 |
| Thoracotomy | | |
| Mean cross-clamp time (min) | 21 ± 11 | 19 ± 12 |

Values are $n$ (%) unless otherwise specified.
IQR: interquartile range.

This represents 4% (70/1621) of all patients with biventricular physiology who underwent an arch repair during the same period.

Baseline characteristics of the patients are displayed in Table 1, and the operative data for initial and second arch operations are displayed in Table 2. The arch was defined as hypoplastic if the initial preoperative echocardiogram report, the cardiologist's report or the surgical notes at the time of initial arch repair labelled it as hypoplastic. The median time to second arch operation from initial repair was 0.6 years (interquartile range: 0.1–3.3). Seventeen patients (17/70, 24%) underwent at least 1 balloon angioplasty prior to a second arch operation, and half of these patients had a hypoplastic arch (9/17, 53%) at the time of initial repair. Prior to second arch operation, the median time to balloon angioplasty from initial arch repair was 0.4 years (interquartile range: 0.3–0.9).

Indications for initial arch repair included coarctation in 55 (55/70, 79%), interrupted aortic arch in 12 (12/70, 17%) and isolated hypoplastic arch in 3 (3/70, 4%). A total of 38 patients had a hypoplastic arch (38/70, 54%) including 34 patients with coarctation (34/55, 62%) and 1 patient with interrupted aortic arch (1/12, 8%). The patient with interrupted aortic arch and arch hypoplasia had a distal interruption and significant narrowing of the transverse arch.

Indications for a second arch operation included arch reobstruction in 63 (63/70, 90%), bronchial compression in 5 (5/70, 7%) and aneurysm formation in 2 (2/70, 3%). Six patients (6/70, 9%) underwent an interposition graft at second arch operation for left main bronchial compression in 4 patients and aneurysm formation in 2 patients.

Details of the techniques for arch reoperation have been previously described [6, 7]. Earlier in our series, left thoracotomy was preferred with 17 of 20 (85%) second arch operations performed through a left thoracotomy before 1990. However, since 1990 we have performed the vast majority of second arch operations through a median sternotomy (40/50, 80%). For the purposes of this study, patients who underwent a left thoracotomy followed

by a median sternotomy (3/70, 4%) were considered to have had a median sternotomy.

## Outcomes

Early outcomes were defined as outcomes that occurred within 30 days after surgery or during hospital stay. Late outcomes were defined as outcomes that occurred after this period of time.

Third arch intervention was defined as either a third balloon angioplasty or arch operation. Arch reobstruction was defined as a peak gradient exceeding 25 mmHg across the repair site on transthoracic echocardiogram or requiring an arch intervention for reobstruction.

Resting hypertension for children and adolescents was defined as a systolic or diastolic blood pressure ≥95th percentile for age and height; prehypertension was defined as between the 90th and 95th percentiles or if blood pressure was greater than 120/80 mmHg [8]. In adults, resting hypertension was defined as a systolic blood pressure greater ≥140 mmHg or a diastolic blood pressure ≥90 mmHg; and prehypertension was defined as a systolic blood pressure between 120 and 139 mmHg or a diastolic blood pressure between 80 and 89 mmHg [9].

The left ventricular mass was calculated from 2D-guided M-mode measurements of the left ventricle using the recommended formula of the American Society of Echocardiography [10]. Left ventricular mass index was calculated by dividing left ventricular mass by (height in meters)$^{2.7}$ to minimize the effects of age, gender, ethnicity and body mass index [11, 12]. Left ventricular hypertrophy in children and adolescents was defined as a left ventricular mass index ≥95th percentile (38.6 g/m$^{2.7}$) for healthy children and adolescents [11]. In adults, it was defined as a left ventricular mass index ≥51 g/m$^{2.7}$ [12].

## Statistical analysis

All data were exported to and analysed using STATA version 13.1 (Stata Corporation, College Station, TX, USA). Data are summarized as counts and percentages for categorical variables and either mean ± standard deviation or median (interquartile range) for continuous variables, as appropriate. $\chi^2$ tests (or Fisher's exact test where appropriate) were performed to examine the effect of surgical approach on late arch reobstruction and third arch operation; and to assess risk factors for hypertension and left ventricular hypertrophy at last follow-up.

Kaplan–Meier curves were drawn to examine long-term mortality, arch reobstruction, third arch intervention and third arch operation. Survival data were expressed as survival percentage with a 95% confidence interval (CI). All collected patient and surgical characteristics were tested for their impact on the outcomes of late mortality, arch reobstruction, and third arch operation by univariable Cox regression analysis using the Breslow method for ties, and all factors shown to have a significant effect were then entered in a multivariable Cox regression in a stepwise fashion. A *P*-value ≤0.05 was considered statistically significant.

# RESULTS

## Early outcomes

***Early mortality.*** Two patients (2/70; 3%) died within the first 30 days of hospital stay. One patient had a cardiac arrest 6 days after second arch operation and was commenced on extracorporeal life support for low cardiac output syndrome. Extracorporeal support was withdrawn 2 days later due to poor neurological prognosis from bilateral intraventricular haemorrhage on brain imaging. The other patient underwent interposition grafting with a pulmonary branch artery homograft for relief of bronchial compression, and required a further early reoperation 6 days later for revision of the interposition graft with aortopexy due to continued bronchial compression. Despite subsequent placement of a left main bronchus metal stent that expanded beyond the bronchial wall, the patient suffered respiratory failure with massive oral haemorrhage and died.

***Early third arch intervention.*** Three patients (3/70; 4%) required early third arch operations during the early postoperative period for arch reobstruction in 2 patients and bronchial compression in 1 patient who subsequently died early. One of the patients with arch reobstruction required revision of the arch repair using a homograft pulmonary artery patch, and the other patient required an ascending-to-descending aorta extra-anatomic bypass using a Dacron graft. The patient with bronchial compression underwent revision of the interposition graft with aortopexy through thoracotomy to relieve this compression, and subsequently died early after bronchial stent placement.

***Other early complications.*** Other early complications of second arch operation occurred in 37 of the 70 patients (53%). Seven patients (7/70, 10%) had neurological complications such as left recurrent laryngeal nerve palsy, 20 patients (20/70, 29%) had pulmonary complications such as pleural effusion and atelectasis, 5 patients (5/70, 7%) had bleeding complications, while 19 patients (19/70, 27%) had other complications such as sepsis and complete heart block requiring a pacemaker.

## Late outcomes

Four of the 68 hospital survivors were lost to follow-up, leaving 64 patients followed up (94%) for a mean of 9 ± 7 years after second arch operation. The median age at last follow-up was 13 years (interquartile range: 4–18).

***Late mortality.*** There were 5 late deaths (5/64, 8%). One death was attributed to an out of hospital cardiac arrest presumably due to a life-threatening arrhythmia but no post-mortem was performed, and another death was due to *Varicella* pneumonia. The cause of death for the remaining 3 patients is unknown. These 5 late deaths occurred entirely in patients who required additional non-arch cardiac operations for associated cardiac lesions. These procedures included both atrial septal defect closure and ventricular septal defect closure in 2 patients, aortic and mitral valvotomy in 1, left ventricular outflow tract obstruction repair followed by a modified Konno-Rastan procedure in 1, and a Ross-Konno procedure followed by a mitral valve replacement in 1.

Late survival from second arch operation was 98% (95% CI: 89–100) at 5 years, 90% (95% CI: 75–96) at 10 years and 90% (95% CI: 75–96) at 15 years (Fig. 1). No significant risk factors for late mortality were determined on multivariable analysis (Table 3).

***Late arch reobstruction.*** A total of 18 patients (18/64; 28%) had arch reobstruction. Of these 18 patients, 9 patients had a third arch intervention for arch reobstruction in 7 patients,

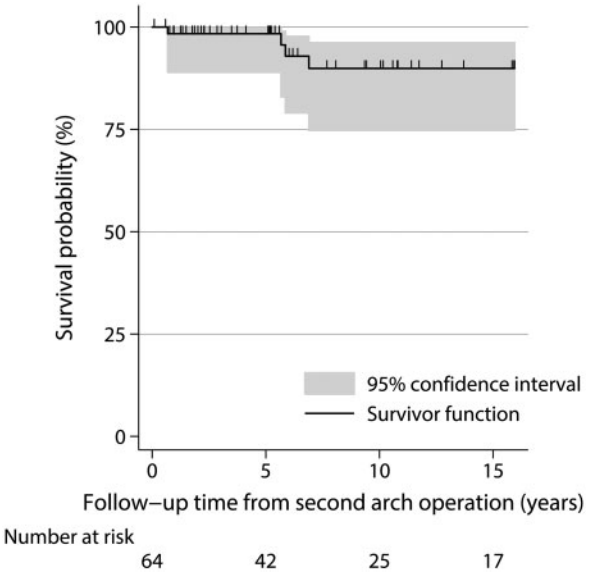


**Figure 1:** Late survival.

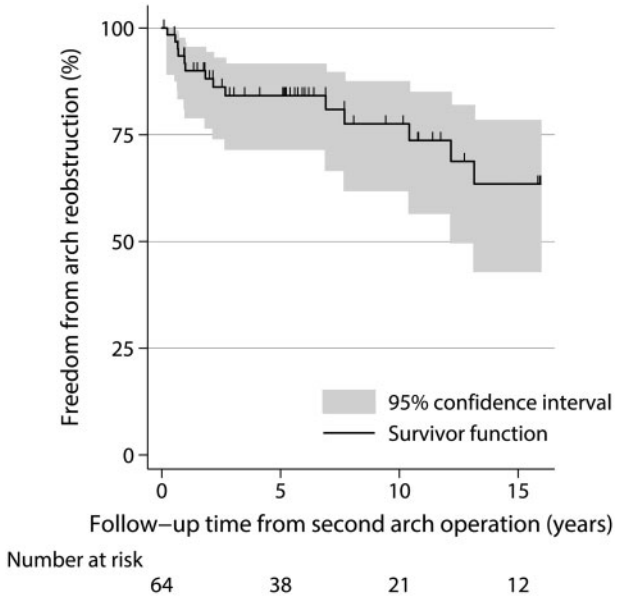


**Figure 2:** Freedom from late arch reobstruction.

**Table 3:** Univariable Cox regressions describing factors associated with late mortality

| | Univariable analysis | |
|---|---|---|
| | HR (95% CI) | *P*-value |
| Male | 2.12 (0.35–12.80) | 0.4 |
| Associated congenital syndrome[a] | | |
| Aortic arch lesion | | |
| Coarctation | 1.58 (0.14–18.43) | 0.7 |
| Interrupted aortic arch | 0.75 (0.06–9.39) | 0.8 |
| All hypoplastic arches[b] | 1.11 (0.16–7.92) | 0.9 |
| Associated cardiac anomalies | | |
| Bicuspid aortic valve | 1.72 (0.18–16.63) | 0.6 |
| Left ventricular outflow tract obstruction | 3.79 (0.39–37.09) | 0.3 |
| Initial arch repair | | |
| Surgical age (years) | 0.30 (0.01–15.56) | 0.5 |
| Sternotomy approach | 1.28 (0.19–8.57) | 0.8 |
| Second arch operation | | |
| Surgical age (years) | 1.03 (0.86–1.24) | 0.7 |
| Sternotomy approach | 4.36 (0.44–43.02) | 0.2 |
| Interposition graft[a] | | |
| Arch reobstruction | 0.42 (0.05–3.75) | 0.4 |
| Third arch intervention | 0.47 (0.05–4.97) | 0.5 |
| Late resting hypertension | 2.76 (0.24–31.08) | 0.4 |

No independent risk factors for late mortality could be determined on multivariable analysis.
CI: confidence interval; HR: hazard ratio.
[a]Unable to be calculated as all patients with the variable survived.
[b]At time of initial arch repair.

aneurysm formation in 1 patient, and revision of interposition graft in 1 patient. The remaining 9 patients had arch reobstruction on echocardiography at last follow-up.

Patients who underwent a left thoracotomy at the time of second arch operation had a higher rate of arch reobstruction than patients who underwent a median sternotomy [40% (10/25) vs 21% (8/39), $P = 0.09$]. In patients with a hypoplastic arch at the time of initial repair, the rate of arch reobstruction was higher after a left thoracotomy at the time of second arch operation than after a median sternotomy [75% (6/8) vs 24% (6/25), $P = 0.02$].

Freedom from arch reobstruction was 84% (95% CI: 72–91) at 5 years, 78% (95% CI: 62–87) at 10 years and 63% (95% CI: 43–78) at 15 years (Fig. 2). On multivariable analysis, a hypoplastic arch at initial repair [hazards ratio (HR) 3.42, $P = 0.02$, 95% CI: 1.18–9.90] and a bicuspid aortic valve (HR 3.16, $P = 0.04$, 95% CI: 1.05–9.48) were risk factors for arch reobstruction (Table 4).

***Late third arch intervention.*** Ten of the 64 followed patients (16%) required a third arch intervention, 5 of whom required a fourth arch intervention (5/64; 8%). These 10 patients (10/64; 16%) required 11 third arch operations for arch reobstruction in 8 patients, aneurysm formation in 1 patient, bronchial compression in 1, and revision of interposition graft in 1 patient. Three of those 10 patients (30%) additionally required balloon dilatation for arch reobstruction.

Patients who underwent a left thoracotomy at the time of second arch operation had a higher rate of third arch intervention than patients who underwent a median sternotomy [24% (6/25) vs 10% (4/39), $P = 0.1$].

Freedom from third arch operation and intervention was 86% (95% CI: 74–93) at 5 years, 86% (95% CI: 74–93) at 10 years and 74% (95% CI: 52–87) at 15 years (Fig. 3). On multivariable analysis, hypoplastic arch at initial repair (HR 6.01, $P = 0.03$, 95% CI: 1.18–30.70) and interposition graft at second arch operation (HR 26.26, $P < 0.0001$, 95% CI: 4.77–144.49) were risk factors for third arch operation (Table 5).

***Late hypertension.*** Resting blood pressure measurements were available in 51 of the 64 (80%) followed patients at last follow-up. Resting hypertension was present in 11 (11/51; 22%), prehypertension was present in 10 patients (10/51; 20%), and an additional 7 patients (7/51; 14%) were on an antihypertensive medication. A total of 12 patients (12/64, 19%) were on an antihypertensive medication at the time of last follow-up, 5 of whom

**Table 4:** Univariable Cox regressions and the final multivariable Cox regression model describing factors associated with arch reobstruction

| | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value |
| Male | 2.61 (0.97–6.70) | 0.06 | | |
| Associated congenital syndrome | 2.05 (0.66–6.41) | 0.2 | | |
| Aortic arch lesion | | | | |
| Coarctation | 0.90 (0.31–2.62) | 0.9 | | |
| Interrupted aortic arch | 0.48 (0.11–2.16) | 0.3 | | |
| All hypoplastic arches[a] | 4.17 (1.41–12.27) | 0.01 | 3.42 (1.18–9.90) | 0.02 |
| Associated cardiac anomalies | | | | |
| Bicuspid aortic valve | 2.60 (0.88–7.66) | 0.08 | 3.16 (1.05–9.48) | 0.04 |
| Left ventricular outflow tract obstruction | 1.26 (0.35–4.52) | 0.7 | | |
| Initial arch repair | | | | |
| Surgical age (years) | 1.10 (0.96–1.27) | 0.2 | | |
| Sternotomy approach | 0.87 (0.32–2.34) | 0.8 | | |
| Second arch operation | | | | |
| Surgical age (years) | 1.05 (0.95–1.17) | 0.3 | | |
| Sternotomy approach | 0.97 (0.37–2.55) | 1.0 | | |
| Patch repair | 1.06 (0.37–2.99) | 0.9 | | |
| Interposition graft | 1.24 (0.28–5.55) | 0.8 | | |
| Late resting hypertension | 1.35 (0.28–6.56) | 0.7 | | |

The model includes 63 patients, 17 failures, $P = 0.02$.
[a]At time of initial arch repair.

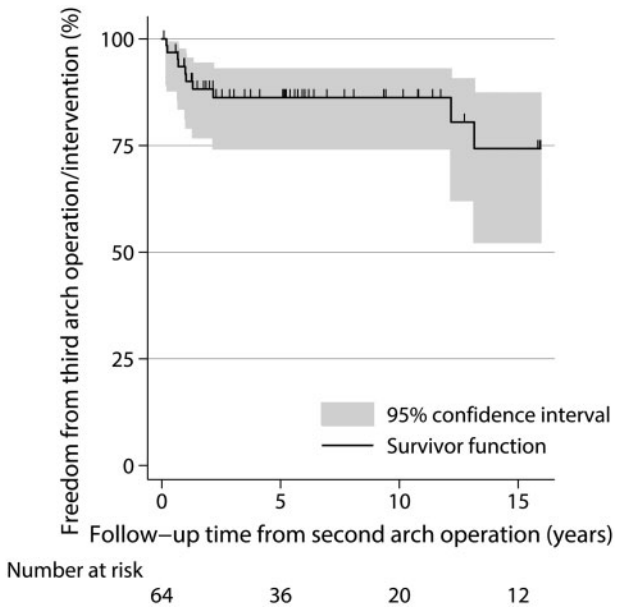


**Figure 3:** Freedom from late third arch operation or intervention.

still had resting prehypertension or hypertension. On multivariable analysis, male gender was the only risk factor identified for the development of late resting hypertension (odds ratio: 5.44, $P = 0.05$, 95% CI: 0.99–29.92).

***Late left ventricular hypertrophy.*** Twenty-five of the 64 (39%) followed patients had transthoracic echocardiographic measurements of the left ventricle at last follow-up. Left ventricular hypertrophy was present in 48% (12/25), and was not associated with resting hypertension ($P = 1.0$).

## DISCUSSION

Alarmingly, up to 75% of patients may develop hypertension after coarctation repair or interrupted aortic arch [7, 13–15], which may be associated with mortality at a young age [16]. Residual arch obstruction is the most intuitive cause for this late hypertension and necessitates prompt relief [14]. However, the optimal surgical technique for arch reobstruction is still debated and little is known about the long-term outcomes of patients undergoing aortic arch reoperations. The largest known contemporary studies investigating outcomes of patients requiring arch intervention after initial arch repair are by Brown *et al.* [2] and Mery *et al.* [3] where they reported on 108 patients and 48 patients over a median of 14.2 years and 6.3 years, respectively, but both studies included patients with complex single ventricle physiology. In our study, we examined biventricular patients undergoing arch reoperations after initial repair for coarctation, interrupted aortic arch repair, or hypoplastic arch, while the majority of similar studies have only focused on patients undergoing arch reoperations after initial coarctation repair [2, 5]. To our knowledge, our study is the largest to date investigating the outcomes of biventricular patients undergoing second arch operations with one of the longest follow-up times. Our late arch reobstruction rate of 28% was considerably higher than those reported by similar studies, which range from 0 to 14% [3, 5, 17, 18]. Consequentially, our late third arch intervention rate of 16% was also higher than the 0–13% quoted by these studies [3, 5, 17, 18]. We were able to identify a number of risk factors for a third arch intervention after second arch operation.

### Arch hypoplasia

We demonstrated arch hypoplasia to be an independent risk factor for arch reobstruction and third arch operation. More than half of

**Table 5:** Univariable Cox regressions and the final multivariable Cox regression model describing factors associated with third arch operation

| | Univariable analysis | | Multivariable analysis | |
|---|---|---|---|---|
| | HR (95% CI) | *P*-value | HR (95% CI) | *P*-value |
| Male | 2.95 (0.76–11.50) | 0.1 | | |
| Associated congenital syndrome | [a] | | | |
| Aortic arch lesion | | | | |
| Coarctation | 0.59 (0.15–2.27) | 0.4 | | |
| Interrupted aortic arch | 1.38 (0.29–6.56) | 0.7 | | |
| All hypoplastic arches[b] | 2.72 (0.70–10.57) | 0.1 | 6.01 (1.18–30.70) | 0.03 |
| Associated cardiac anomalies | | | | |
| Bicuspid aortic valve | 1.23 (0.25–5.96) | 0.8 | | |
| Left ventricular outflow tract obstruction | 0.93 (0.12–7.49) | 0.9 | | |
| Initial arch repair | | | | |
| Surgical age (years) | 0.99 (0.77–1.29) | 1.0 | | |
| Sternotomy approach | 1.29 (0.36–4.62) | 0.7 | | |
| Second arch operation | | | | |
| Surgical age (years) | 0.97 (0.83–1.14) | 0.7 | | |
| Sternotomy approach | 0.55 (0.15–1.98) | 0.4 | | |
| Patch repair | 0.63 (0.18–2.24) | 0.5 | | |
| Interposition graft | 11.01 (2.71–44.69) | 0.001 | 26.26 (4.77–144.49) | <0.0001 |
| Late resting hypertension | 0.90 (0.10–7.77) | 0.9 | | |

The model includes 64 patients, 10 failures, $P = 0.001$.

CI: confidence interval; HR: hazard ratio.

[a]Unable to be calculated as all patients with an associated congenital syndrome did not have a third arch operation.

[b]At time of initial arch repair.

patients had arch hypoplasia in this study, a proportion higher than previously reported [4, 5], and this may have contributed to our high rate of late arch reobstruction and third arch intervention. It should be noted that arch hypoplasia is a concept that is still poorly defined [19]. Similarly to others [2, 4], we demonstrated higher rates of arch reobstruction after balloon angioplasty compared with surgical intervention, especially in the presence of a hypoplastic arch [4]. A quarter of patients who had at least 1 balloon angioplasty after their initial arch operation subsequently had a second arch operation, with over half of these patients also having a hypoplastic arch before their initial arch operation. We have previously demonstrated that the proximal segment of a hypoplastic transverse arch does not always grow reliably after initial coarctation repair [20]. We believe that patients with a hypoplastic arch who develop an arch reobstruction should be preferentially treated with a surgical reoperation instead of balloon angioplasty.

## Surgical technique

As expected, the use of interposition grafts at second arch operation was associated with late third arch interventions. Interposition grafts were mainly used at second arch operation in patients with left main bronchus stenosis. This is a simple and effective technique to augment the space below the concavity of the arch. Apart from this indication, we believe that interposition grafts should not be used for arch reoperations for reobstruction in young children.

Patients who had an arch reoperation via a left thoracotomy had a higher rate of arch reobstruction than patients who had a median sternotomy, even if this difference did not reach statistical significance. Our work demonstrated that more than a quarter of patients undergoing a second arch operation still needed a third arch operation by 15 years of follow-up. We identified a hypoplastic arch and reoperations using a thoracotomy approach as risk factors for these third operations. We therefore believe that more extensive arch procedures may be necessary if we want to adequately relieve arch obstruction and avoid the risk of subsequent reoperations. Similar to others [3], we are now advocating for more extensive procedures at arch reoperation via a median sternotomy with our preference being a patch aortoplasty. Previously, we performed extra-anatomic bypass in patients who have reached adult size, but we are now cautious with this operation because we have demonstrated the risks of prolonged effusion drainage and mediastinitis associated with this approach [21]. We believe that the high-attrition rate associated with late hypertension [16] justifies the risks associated with more extensive surgery.

## Limitations

Due to the historical nature of this series spanning over 36 years, the results presented may not accurately reflect current practice, and we were unable to access preoperative echocardiogram or catheter data in all patients to objectively examine for arch hypoplasia. The patients were not randomly assigned to the various surgical procedures, and therefore the design of the study may not have allowed us to compare adequately all techniques employed.

The diagnosis of arch obstruction using transthoracic echocardiography can be subjected to criticism because of the difficulty in acquiring adequate visualization of the descending aorta.

# CONCLUSIONS

Patients undergoing a second arch operation have significant rates of arch reobstruction and reoperation. The high rates of

arch reobstruction and third arch operation warrant more extensive procedures at the time of second arch operation, especially in patients with a hypoplastic arch. Regular long-term monitoring after arch reoperation is mandatory.

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**Conflict of interest:** Christian Brizard is a consultant for Allied Health Care Group. Yves d'Udekem is a consultant for Actelion and MSD.

## REFERENCES

[1] Rakhra SS, Lee M, Iyengar AJ, Wheaton GR, Grigg L, Konstantinov IE *et al*. Poor outcomes after surgery for coarctation repair with hypoplastic arch warrants more extensive initial surgery and close long-term follow-up. Interact CardioVasc Thorac Surg 2013;16:31–6.

[2] Brown JW, Ruzmetov M, Hoyer MH, Rodefeld MD, Turrentine MW. Recurrent coarctation: is surgical repair of recurrent coarctation of the aorta safe and effective? Ann Thorac Surg 2009;88:1923–30.

[3] Mery CM, Khan MS, Guzman-Pruneda FA, Verm R, Umakanthan R, Watrin CH *et al*. Contemporary results of surgical repair of recurrent aortic arch obstruction. Ann Thorac Surg 2014;98:133–40.

[4] Zoghbi J, Serraf A, Mohammadi S, Belli E, Lacour Gayet F, Aupecle B *et al*. Is surgical intervention still indicated in recurrent aortic arch obstruction? J Thorac Cardiovasc Surg 2004;127:203–12.

[5] Dodge-Khatami A, Backer CL, Mavroudis C. Risk factors for recoarctation and results of reoperation: a 40-year review. J Card Surg 2000;15:369–77.

[6] Karl TR, Sano S, Brawn W, Mee RB. Repair of hypoplastic or interrupted aortic arch via sternotomy. J Thorac Cardiovasc Surg 1992;104:688–95.

[7] Hussein A, Iyengar AJ, Jones B, Donath SM, Konstantinov IE, Grigg LE *et al*. Twenty-three years of single-stage end-to-side anastomosis repair of interrupted aortic arches. J Thorac Cardiovasc Surg 2010;139:942.

[8] National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114:555–76.

[9] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr *et al*. The Seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. JAMA 2003;289:2560–72.

[10] Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA *et al*. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr 2005;18:1440–63.

[11] Daniels SR, Kimball TR, Morrison JA, Khoury P, Meyer RA. Indexing left ventricular mass to account for differences in body size in children and adolescents without cardiovascular disease. Am J Cardiol 1995;76:699–701.

[12] de Simone G, Daniels SR, Devereux RB, Meyer RA, Roman MJ, de Divitiis O *et al*. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. J Am Coll Cardiol 1992;20:1251–60.

[13] Lee MG, Allen SL, Kawasaki R, Kotevski A, Koleff J, Kowalski R *et al*. High prevalence of hypertension and end-organ damage late after coarctation repair in normal arches. Ann Thorac Surg 2015;100:647–53.

[14] Lee MG, Kowalski R, Galati JC, Cheung MM, Jones B, Koleff J *et al*. Twenty-four-hour ambulatory blood pressure monitoring detects a high prevalence of hypertension late after coarctation repair in patients with hypoplastic arches. J Thorac Cardiovasc Surg 2012;144:1110–16.

[15] Hager A, Kanz S, Kaemmerer H, Schreiber C, Hess J. Coarctation Long-term Assessment (COALA): significance of arterial hypertension in a cohort of 404 patients up to 27 years after surgical repair of isolated coarctation of the aorta, even in the absence of restenosis and prosthetic material. J Thorac Cardiovasc Surg 2007;134:738–45.

[16] Brown ML, Burkhart HM, Connolly HM, Dearani JA, Cetta F, Li Z *et al*. Coarctation of the aorta: lifelong surveillance is mandatory following surgical repair. J Am Coll Cardiol 2013;62:1020–5.

[17] DiBardino DJ, Heinle JS, Kung GC, Leonard GT Jr, McKenzie ED, Su JT *et al*. Anatomic reconstruction for recurrent aortic obstruction in infants and children. Ann Thorac Surg 2004;78:926–32; discussion 26–932.

[18] Kadner A, Dave H, Bettex D, Valsangiacomo-Buechel E, Turina MI, Pretre R. Anatomic reconstruction of recurrent aortic arch obstruction in children. Eur J Cardiothorac Surg 2004;26:60–65.

[19] Lee MG, D'Udekem Y. Coarctation of the aorta can no longer be considered a benign condition. Heart Lung Circ 2014;23:297–8.

[20] Liu JYJ, Kowalski R, Jones B, Konstantinov IE, Cheung MMH, Donath S *et al*. Moderately hypoplastic arches: do they reliably grow into adulthood after conventional coarctation repair? Interact CardioVasc Thorac Surg 2010;10:582–6.

[21] Brink J, Lee MG, Konstantinov IE, Cheung MM, Goh TH, Bennett M *et al*. Complications of extra-anatomic aortic bypass for complex coarctation and aortic arch hypoplasia. Ann Thorac Surg 2013;95:676–81.