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Research Article

Aortic Coarctation Associated with Distal Aortic Arch Hypoplasia in Neonates Can Be Effectively Repaired through Left Thoracotomy

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Objectives. Aortic coarctation in neonates remains a clinical challenge. Low weight, arch hypoplasia and ductal dependence have been identified as risk factors for recurrent coarctation. We hypothesized that a tailored surgical technique may prevent recurrence. *Methods*. Retrospective evaluation of neonates treated for coarctation through thoracotomy was done. No primary percutaneous procedure was performed and repairs through sternotomy were excluded. Aortic hypoplasia was defined as a ratio arch diameter (mm)/patient's weight (kg) < 1. Extended end-to-end anastomosis (EEEA), subclavian flap (Waldhausen) and Amato aortoplasty were performed. Mortality and recurrent obstruction requiring re-intervention were assessed. *Results*. Records of 340 consecutive patients (2003–2019) were analyzed. Preoperative median age and weight were, respectively, 10 days (1–30) and 3080 grams (1400–5180). Arch hypoplasia was documented in 31 patients (9.1%). Prostaglandin was infused in 220 (65.3%). Critical preoperative status was documented in 35 (10.8%). EEEA repair was performed in 273 (80.3%), Waldhausen was performed in 42 (12.4%), and Amato was performed in 25 (7.4%). The last two were more likely to be performed in the presence of arch hypoplasia ($p < 0.0001$). Hospital mortality occurred in 2 patients (0.6%). Thirty-six procedures (31 percutaneous/5 surgical) were performed for recurrent arch obstruction in 33 patients. Three late deaths occurred. Low-weight, hypoplastic arch, and ductal dependency did not influence the outcome. All survivors were free from residual coarctation at a mean follow-up of 3.6 ± 3.4 years postoperatively. *Conclusions*. Surgical repair remains the procedure of choice for neonatal coarctation. A tailored approach using alternative techniques seemed to offer comparable results even in presence of associated risk factors.

1. Introduction

The main challenge of aortic coarctation (CoA) repair in infancy remains to obtain durable results without morbidity. Data from literature show recurrence rate between 2% and 14%, owing to the type of CoA, surgical repair technique, and mostly age of repair [1–3].

First described by Crafoord in 1945, end-to-end anastomosis has been for long the main technique for surgical repair of CoA [4]. Patients with a moderately hypoplastic arch treated by conventional CoA repair have adequate arch growth demonstrated at long-term follow-up [5]. Extended end-to-end (or end-to-side) anastomosis (EEEA), consisting in a large incision in {Citation} the concavity of the aortic arch, permitted to enlarge indications and improve outcome [1, 6–8]. Indeed, some patients requiring a CoA repair also present with aortic arch hypoplasia. This latter has been described to be associated to a higher risk of recurrent arch obstruction [9, 10]. Waldhausen and Amato techniques of repair were introduced useful alternative techniques of arch aortoplasty, giving the possibility to treat some degree of arch hypoplasia through thoracotomy [11, 12].

There is still a controversy regarding the hypoplastic aortic arch repair approach. Studies suggest that patients

undergoing repair through sternotomy under cardiopulmonary bypass (CPB) had less recurrent arch obstruction than those undergoing repair through thoracotomy [13]. Recent trend toward increase in repair through midline sternotomy was observed, and borderline cases are more repaired using this approach. However, neonatal CPB, hypothermia, total circulatory arrest or regional cerebral perfusion and longer anesthesia exposure have also demonstrated deleterious effect on neurodevelopmental outcome [14, 15].

Neonates (<30 days of age) are particularly at risk for CoA recurrence [9, 15]. Few studies focused on this particular population, describing its specificities and identifying risk factors that influence outcome. Neonatal CoA may be difficult to repair, thus, is a surgical challenge. In this population, preoperative clinical presentation is very specific. Nowadays, prenatal suspicion of aortic arch obstruction is common, ductal-dependence results in early referral, yet subsequent cardiogenic shock can still be observed. Associated anomalies such as ventricular septal defect (VSD) and prematurity/low birth weight may amend clinical condition and impact surgical strategy. However, efficient and durable release of aortic arch obstruction remains mandatory.

In our institution, sternotomy approach is the reference if proximal aortic arch is hypoplastic, and/or if a significant VSD has to be closed. On the other hand, isolated CoA without hypoplasia is always repaired through thoracotomy. For borderline cases, as patients with hypoplasia localized to the distal arch and/or atypical supra-aortic trunks anatomy, we developed over the last 20 years a tailored approach, leaving a large place for alternative repairs through thoracotomy.

We reviewed this experience with CoA repair through thoracotomy in neonates in order to determine outcomes according to the surgical technique employed, and to assess the efficiency of our strategy. We hypothesized that an associated arch hypoplasia is not an absolute contraindication to repair through thoracotomy if a tailored approach is employed.

2. Materials and Methods

2.1. Patients. The study design was approved by the local Ethical Committee.

We identified all consecutive neonates (<30 days of age) who underwent CoA repair through thoracotomy, between February 2002 and October 2019.

All patients presenting with isolated aortic CoA as well as those presenting with associated VSD(s) who underwent concomitant palliation by means of pulmonary artery banding (PAB) were included. Complex-associated cardiac anomalies such as transposition of the great arteries, Taussig-Bing anomaly, and common atrioventricular septal defect were excluded.

Patient data, collected from institutional reports, included demographic data (age at repair, sex, weight), echocardiographic data (size of aortic arch, aortic vessels anatomy with left subclavian artery (LSCA) arising anomaly, associated defects such as VSD and left ventricular function), need for prostaglandin infusion and preoperative clinical status (need for inotropic support and mechanical ventilation).

A computed tomography scan was performed in the following cases: doubt about supra aortic vessel anomaly, difficulty to assess detailed aortic arch anatomy by transthoracic echocardiography, and clinical condition that may contraindicate sternotomy repair under CPB (Figure 1).

Aortic arch was analyzed in 3 segments:

(i) Proximal arch (if any), between the innominate and left carotid artery,

(ii) Distal arch, between the left carotid and LSCA,

(iii) Isthmus (if any), between the LSCA and ductus/ligamentum arteriosus.

Hypoplasia of the arch, proximal and/or distal, was defined by a diameter in (mm)/patients weight in kg < 1 [13, 16].

2.2. Surgical Procedures. All patients underwent left thoracotomy. A wide release of the arch from ascending to descending aorta was performed. Aortic arch and supra aortic vessels anatomy was assessed. If the aortic arch presented an appropriate size (>1 mm/kg), an EEEA was performed in most cases, with a large split in the concavity of the aortic arch. When aortic arch hypoplasia was suspected on pre-operative echocardiography and confirmed during surgery, techniques of repair were Amato, subclavian flap, or EEEA according to the specific arch anatomy and also surgeon's preference. Amato repair was performed in 2 sequences: side-to-side anastomosis between left common carotid artery and LSCA (leaving the descending aorta perfused through ductus arteriosus), followed by classic EEEA. Waldhausen consisted in an aortoplasty by LSCA patch (only if LSCA was considered wide enough). The choice of repair technique was based on aortic arch anatomy, size, and surgeon's experience (Figure 2 and Table 1).

2.3. Outcome. Postoperative data were intensive care unit (ICU) and hospital length-of-stay. Early outcomes were those that occurred within 30 days post-operative or during the hospital stay, while late ones occurred after this period. Surgical complications (chylothorax requiring surgery, phrenic nerve palsy, neurological event, and wound infection), residual CoA requiring reintervention, and death were documented. Follow-up duration was defined as the period between initial surgery and the last clinical record, and was complete for 95% patients. Phone correspondence with the referring pediatric cardiologist was requested if the follow-up was inferior to 1 year. Clinical status, recurrent CoA, and presence of hypertension were collected.

Recurrent CoA was defined by arm-leg blood systolic pressure gradient more than 20 mmHg, and/or echocardiographic peak gradient exceeding 25 mmHg across the repair site associated with persistent diastolic flow. Hypertension was sought at rest on outpatient (left-arm systolic or diastolic blood pressure exceeding the 95th percentile) and need for antihypertensive medication was collected.

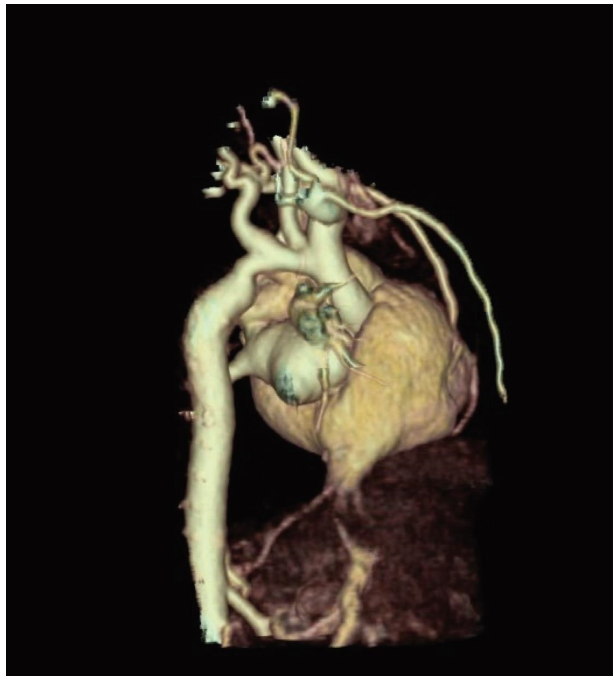
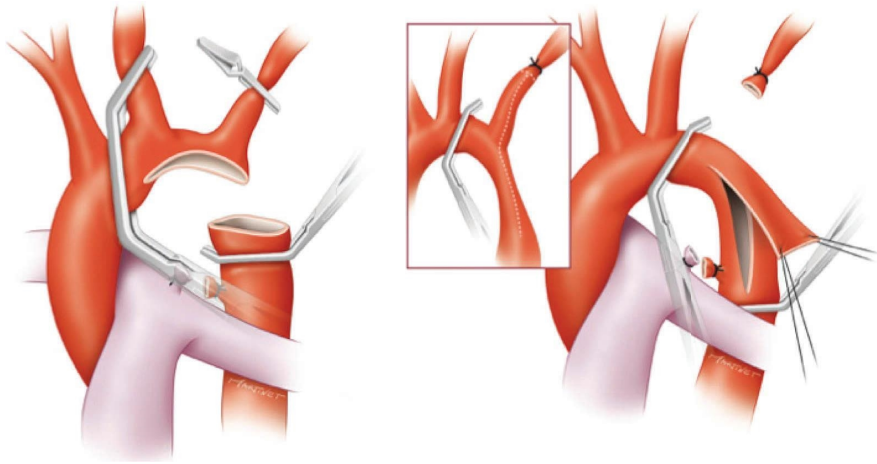
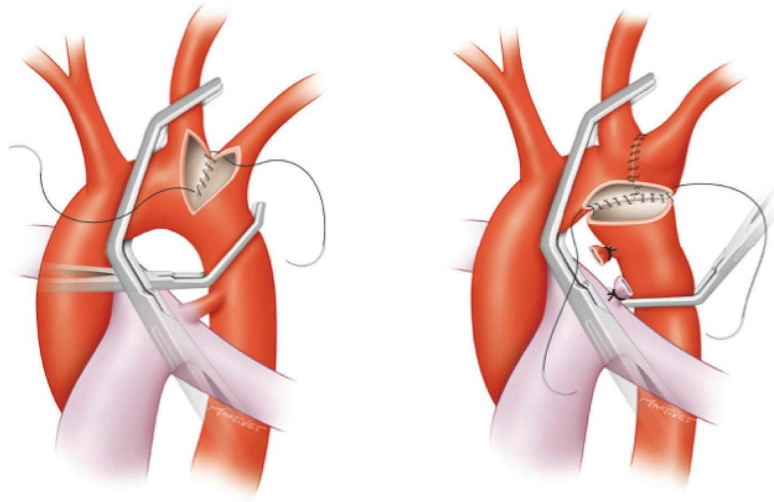


Figure 1: CT-scan preoperative view of an aortic coarctation with arch hypoplasia in a 4 day-old boy. Transverse arch is absent, and distal arch is hypoplastic. A Waldhausen repair was performed in this case.



(a) (b)

Figure 2: Continued.



(c) (d)

Figure 2: Surgical techniques. Extended end-to-end anastomosis (a), Waldhausen technique (b), and Amato technique including side-to-side anastomosis between left carotid artery (c) followed by an end-to-end anastomosis (d).

Table 1: Choice for surgical strategy, owing to arch anatomy.

Proximal arch	Distal arch	Isthmus	Technique of repair
No hypoplasia	No hypoplasia	Long/short	EEEA
No hypoplasia	Hypoplasia	Short	EEEA
No hypoplasia	Hypoplasia	Long	Amato or EEEA
Hypoplasia	Hypoplasia	Long/short	Waldhausen
Absent	No hypoplasia	Long/short	EEEA
Absent	Hypoplasia	Long/short	Waldhausen

EEEA: Extended end-to-end anastomosis.

2.4. Statistical Analysis. Continuous variables are expressed as mean ± Standard deviation (SD) or median (minimum-maximum), as appropriate. Normality of the distribution was tested with the Shapiro–Wilk test. Risk factors for recurrent arch CoA after surgical repair were tested using Fine and Grey univariable analysis, with reintervention as the primary outcome and death as competing risk. Freedom from reintervention was defined as the time between initial arch repair and reintervention for recurrent arch obstruction. Kaplan–Meier curves were used to analyze long-term survival and aortic arch reintervention. Survival data were exposed as percentage with 95% confidence interval (CI).

For all analyses, a threshold of $p = 0.05$ was chosen for statistical significance. Statistical analyses were performed using Stata® software, version 11.2 (StataCorp, College Station, TX, USA).

3. Results

3.1. Patient Population. Records of 340 consecutive neonates with CoA repair through thoracotomy were reviewed. Diagnosis was made during pregnancy in 137 patients (40.3%). Median age at surgery was 10 days (1–30), and median weight was 3080 grams (1140–5180). Patient's characteristics are displayed in Table 2.

Table 2: Patient characteristics ($n = 340$).

	All ($n = 340$)
Age at operation, days, median (min-max)	10 days (1–30)
Weight at operation, grams, median (min-max)	3080 (1140–5180)
Hypoplastic distal arch, *n* (%)	31 (9.1%)
Left ventricle function	
Good	262
Altered	78
Associated anomalies	
Ventricular septal defect, *n* (%)	125 (36.8%)
Bicuspid aortic valve, *n* (%)	205 (60%)
Preoperative state	
Cardiogenic shock, *n* (%)	51 (15%)
Prostaglandin infusion, *n* (%)	221 (65%)
Inotropic support, *n* (%)	37 (10.8%)
Mechanical ventilation, *n* (%)	35 (10.3%)

Before surgery, 51 patients (15%) required a critical preoperative care, among which 35 (10.3%) were under mechanical ventilation, and 37 (10.8%) had inotropic support.

Other cardiac anomalies were VSD in 125 patients (36.8%) and bicuspid aortic valve in 205 (60%).

Prostaglandin was infused in 221 patients (65%), identifying ductal-dependency in 2/3 of the study cohort. In 31 patients (9.1%), an associated hypoplastic aortic arch was documented.

3.2. Surgical Procedure. Operative data are presented in Table 3.

The arch was repaired by EEEA in 273 patients (80.3%), Waldhausen technique in 42 (12.4%), and Amato technique in 25 (7.5%). When arch hypoplasia was present, Waldhausen and Amato techniques were more likely to be performed for repair ($p < 0.0001$).

Concomitant PAB was performed in 72 patients (21.2%). Indications for associated PAB included multiple VSD ($n = 18$), large muscular VSD ($n = 19$), and muscular VSD(s) judged as a potential candidate for spontaneous closure ($n = 28$).

3.3. Early Outcomes. The median delay of extubation was 23 hours (1–240) and hospital length of stay was 7 days (3–30).

Two patients (0.6%) died in the immediate postoperative period. One death occurred because of multiple organ failure in a patient with associated VSD and inefficient PAB, and the second death occurred following conversion to a Norwood palliation in a patient presenting with Shone's complex and borderline left ventricle. Four patients (1.1%) required iterative surgery for complication: 1 for chylothorax, and 2 for phrenic nerve paraplegia. Glue application and mediastinal pleura were performed in the first case, and diaphragmatic plication in the last two. One transient paraplegia was reported, and 1 neurological stroke (anoxo-ischemic encephalopathy after cardiac arrest) (Table 4).

Low rate of morbidity and mortality prevented us from evaluating potential risk factors as the presence of hypoplasia and repair technique by multivariate analysis.

Postoperative residual CoA occured in 1 patient with extreme arch hypoplasia, who was repaired using midline sternotomy 24 hours after the initial repair.

3.4. Late Outcomes. Three patients died during follow-up:

(1) A baby with a Shone's complex (with mitral stenosis and pulmonary hypertension),

(2) A 1100 grams baby with associated PAB who died 4 months after repair because of severe LV failure,

(3) A patient died 1 year after CoA repair and PAB, secondary to multiorgan failure following VSD closure.

3.4.1. Recurrent Arch Obstruction. Thirty-three patients (9.7%) presented with recurrent arch obstruction requiring a reintervention after a median follow-up of 3.3 years (0.6–5). Reintervention occurred within a median delay of 112 days (26–3070) after CoA repair. All the procedures except one were performed during the first year after primary repair.

Reintervention consisted of balloon dilatation in 28 patients (85%), balloon dilatation followed by surgery in 3 (9%), and surgery first in 2 (6%).

Freedom from reintervention for recurrent arch obstruction was 87% (CI: 81.7–90.5) and 84% (CI: 77–92.8) at 5 and 10 years (Figure 3).

Low weight at surgery, prostaglandin infusion and distal arch hypoplasia were not associated with recurrent arch obstruction in univariate analysis (Table 5).

Rates of aortic arch reintervention were similar in the different surgery technique groups.

3.4.2. Ventricular Function and VSD. Ventricular function was normal in all patients at last follow-up.

Among the 125 patients with a VSD, PAB was performed in 72 patients (57.6%). The VSD became hemodynamically restrictive or closed spontaneously in 39 patients (54%) and 33 (46%) required surgical VSD closure.

3.4.3. Hypertension. At last follow-up, 10 patients (3%) were reported to present hypertension, among them 3 were under antihypertensive medication.

4. Discussion

The objective of CoA repair in neonates is dual: cure a life-threatening situation and prevent long-term subsequent complications. Controversies remain on the best technique for CoA repair, depending on associated arch hypoplasia, age of the patient, and associated lesions. Thoracotomy approach has long been the reference, and several studies showed relative arch growth after CoA repair whenever relative hypoplasia is associated [5, 6, 17]. However, some authors have reported poor outcomes, especially in case of transverse arch hypoplasia, thus arguing for more systematic extensive surgery through sternotomy [13]. Beside this, several studies have focused on long-term outcomes, demonstrating worrisome re-obstruction rates, with rate of late hypertension between 20-40% [13, 16] and associated mortality, until 20% at 30 years [18, 19].

Actually, most studies include heterogeneous population from neonate to adult, and thus conclusions may be difficult to be drawn.

This study reports a homogeneous population of neonate presenting with CoA for whom thoracotomy approach for repair was preferred. Evidence of aortic arch hypoplasia was identified in 9.1% of the cohort. Associated lesions requiring PAB concerned 21.2%.

The study cohort included 51 patients (15%) presenting with cardiogenic shock, including 37 (10.8%) with inotropic support and/or 35 (10.3%) under mechanical ventilation.

4.1. Hypoplasia. Definition of hypoplasia continues to raise questions. Indeed, the exact arch size under which the patient is at risk for recurrent arch obstruction and long-term

Table 3: Operative data ($n = 340$).

	Coarctation without hypoplasia $n = 309$ (90.9%)	Coarctation with hypoplasia $n = 31$ (9.1%)	p
Surgical repair			<0.001
EEEA or EESA, n (%)	260 (84.1%)	13 (42%)	
Amato, n (%)	17 (5.5%)	8 (26%)	
Waldhausen, n (%)	32 (10%)	10 (32%)	

EEEA: extended end-to-end anastomosis. EESA: extended end-to-side anastomosis.

Table 4: Outcomes ($n = 340$).

	All ($n = 340$)
Early death, n (%)	2 (0.6%)
Residual coarctation, n (%)	1 (0.3%)
Early morbidity, n (%)	
Chylothorax requiring surgery	1 (0.3%)
Paraplegia	1 (0.3%)
Phrenic paresia	2 (0.6%)
Stroke	1 (0.3%)
Late outcomes, n (%)	
Death	3 (0.9%)
Recurrent arch obstruction	33 (9.7%)
Hypertension	10 (3%)

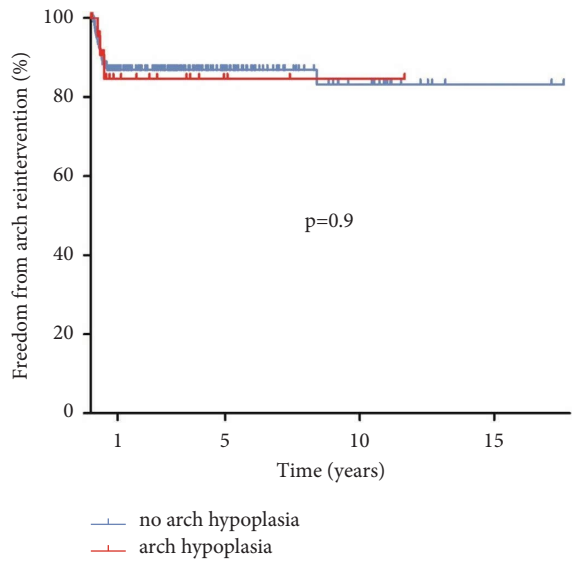


Figure 3: Freedom from recurrent arch obstruction with or without aortic arch hypoplasia.

hypertension is unknown. Many definitions have been proposed since Moulaert, who used the ratio between arch segments and ascending aorta [20]. Some authors use the ratio between innominate artery or carotid artery and arch, when some authors argue for the use of z-score [1, 13, 21]. In our center, we define hypoplasia if arch size in millimeters is <weight in kilograms, as reported in other studies [22]. Above this ratio, the word hypoplasia can be stated as "moderate" or "relative." Arch hypoplasia was always considered as a risk factor for recurrent aortic arch obstruction in neonates [9, 10].

4.2. Decision-Making. The gold standard for neonatal isolated CoA is repair through thoracotomy approach. Even if described and defended by some authors, balloon dilatation and/or stent implantation was not considered as a therapeutical option. The interventional percutaneous procedures were considered only in case of recurrent arch obstruction.

In the presence of associated VSD, primary one stage anatomical repair using sternotomy is considered. There is a cutpoint for isolated CoA, which is related to the degree of arch hypoplasia in which median sternotomy approach can be considered. The threshold for this choice varies among surgical teams. The thoracotomy repair advantage is not only the ability to effectively address distal arch hypoplasia without heterologous tissues, but also to avoid the use of neonatal hypothermic CPB run with selective cerebral perfusion (or deep hypothermic circulatory arrest) and its potential adverse neurodevelopmental consequences [14, 23]. In our center, the EEEA technique was the procedure of choice whenever possible. However, the Amato technique was considered in presence of significant distal aortic arch hypoplasia, and the Waldhausen technique was more likely to be employed in globally small aortic arch, hypotrophic babies and/or in unstable hemodynamical condition. In our reported experience including 340 consecutive neonates with aortic CoA operated on through thoracotomy, no difference regarding recurrence of arch of obstruction between patients with versus without arch hypoplasia was observed. Use of Waldhausen or Amato techniques may reduce the risk of recurrence in the presence of distal arch hypoplasia.

4.3. Early Results. Hospital mortality was 0.6%. The first death occurred in a patient with borderline left ventricle for whom biventricular pathway was undertaken, who remained in left ventricular insufficiency: a switch to univentricular repair by means of Norwood procedure was undertaken day 2 postoperatively with subsequent mortality. The second death was a 2000 g premature: initial palliation with associated PAB was performed but he remained in lung overflow, VSD closure was also performed but multiorgan failure occurred in the few days after sternotomy. Postoperative morbidity is quite low; only 3 patients were reoperated for post-operative complication. To be noted, phrenic nerve paresia or vocal cord paresia may be difficult to assess in a retrospective study.

Table 5: Univariate analysis.

	Recurrent CoA ($n = 33$)	No recurrent CoA ($n = 305$)	p
Weight	2927.5 [1400–4000]	3100 [1140–5180)	0.170
Age at surgery	12 [4–29)	10 [1–30]	0.62
Prostaglandin infusion	19 (57%)	201 (65%)	0.330
Cardiogenic shock	5 (15%)	46 (15.1%)	0.540
Aortic arch hypoplasia	3 (9%)	28 (9.1%)	0.890
Bicuspid aortic valve	18 (54%)	186 (60.9%)	
Technique of repair			0.890
EEEA or EESA	26 (79%)	247 (80.9%)	
Amato	3 (9%)	22 (7.2%)	
Waldhausen	4 (12%)	38 (12.4%)	
VSD	10 (30%)	115 (38%)	0.140
PA banding	3 (9%)	69 (22%)	**0.042**

EEEA: extended end-to-end anastomosis. EESA: extended end-to-side anastomosis. VSD: ventricular septal defect. PA: pulmonary artery. CoA: coarctation. The bold values indicate statistically significant p values.

4.4. Recurrent Arch Obstruction and Hypertension. Recurrent CoA was observed in 33 patients. Thirty-one were treated using balloon dilatation (28 succeeded and secondary surgery was required for 3) and 2 patients were operated at first. Procedures for recurrent arch obstruction are safe nowadays, and no procedural complications were deplored.

We report a 9.7% recurrent arch obstruction rate in neonates, which is coherent with other studies. Sakurai et al. reported 13% of CoA recurrence in patients operated using thoracotomy and Ijsselhof et al. reported a 10.3% recurrent arch obstruction rate at 3 years in a neonate subgroup [22, 24]. Neonatal CoA, often Ductus Arteriousus dependent, is more at risk than infant beyond that period. The recurrence rate in adult CoA is very low, but this is a very different population.

In our study, neither weight nor age nor prostaglandines infusion were associated with recurrent arch obstruction. The repair technique was not associated with recurrent arch obstruction either, even if Amato and Waldhausen were the procedures of choice in these cases. It seems that the cut-point we choose (1 mm/kg body weight) is associated with favorable ouctomes.

We observed a low rate of hypertension during follow-up, with only 3 patients under antihypertensive medication. Among series, it is reported between 2% and 59% after CoA repair [1, 13, 18, 25], but in populations of heterogeneous ages. This low rate may be explained by an information bias, but also to a true low incidence of late hypertension in the neonate. Indeed, there seems to be a positive link between age at surgery and risk of hypertension, thus very young patients might be at very low risk of developing hypertension [18]. Lee et al. showed that late hypertension was strongly associated to re CoA. In their observational series, hypertensive prevalence was 59% and late arch reobstruction was present in 23% at 22 year after surgery. Patients with early post-operative hypertension and/or early reobstruction were at high risk of developing late hypertension [25].

4.5. Limitations. The median follow-up in this retrospective study is quite low, but it reflects a contemporary approach. As a tertiary medical center, we often operate on patients referred from distant cities, and long-term follow-up is sometimes lacking. However, the great majority of recurrent arch obstruction occurs in the first-year post repair, we also may have the ability to detect most of them during the follow-up.

CoA repair in neonates remains controversial and further progress is still mandatory to optimize their outcome. On the one hand, studies shown higher rates of recurrent arch obstruction in neonates; on the other hand, these patients seemed to be at lesser risk for long-term hypertension. A tailored repair could help to decrease this risk.

5. Conclusion

This study is unique as it reports a homogeneous cohort of neonates operated for coarctation by thoracotomy. More long-term follow-up will give precious data about survival and late complications in this particular population. Thoracotomy approach should always be considered, even if aortic arch is hypoplastic and in particular aortic arch anatomies. Amato and Waldhausen techniques of repair achieve efficient arch enlargement with low rate of morbidity and mortality, compared to that obtained by EEEA without arch hypoplasia [26]. Interestingly, hypertension incidence has been found lower than expected in this neonate cohort. Long term follow-up is mandatory to determine if these findings are durable.

Abbreviations

CPB: Cardiopulmonary bypass
CoA: Aortic coarctation
EEEA: Extended end-to-end anastomosis
EESA: Extended end-to-side anastomosis
LSCA: Left subclavian artery
PAB: Pulmonary artery banding
VSD: Ventricular septal defect.

Data Availability

The data used to support the findings of this study are available on reasonable request to the corresponding author.

Disclosure

This manuscript has been presented at the 35th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Barcelona, 13–16 october 2021.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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