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Mortality and Restenosis Rate of Surgical Coarctation Repair in Infancy: A Study of 191 Patients

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Key Words
Congenital heart disease · Coarctation of the aorta · Long-term follow-up · Restenosis

Abstract
Study Design: This is a retrospective cross-sectional study to analyze mortality and the rate of restenosis in the follow-up of patients after surgical repair of isolated aortic coarctation in infancy. ***Patients and Methods:*** From 1974 to 2003, 191 patients underwent surgical repair of aortic coarctation in infancy. Follow-up data of 2,432 patient-years were extracted from the clinical files of our outpatient department or from family practitioners. ***Results:*** Five patients died (total mortality 2.6%): 1 patient intraoperatively and 2 within 30 days after surgery (early mortality 1.6%). The other 2 patients died within 3 months. All deaths were contributed to patients that underwent surgery in the years up to 1981 and within the first 43 days of life. Of the surviving 186 patients, 31 had reintervention because of restenosis and another 11 patients had a noninvasive brachial-ankle systolic blood pressure gradient >20 mm Hg, suggesting current restenosis. Risk factors for death or restenosis were a hypoplastic aortic arch and a low body length at surgery. ***Conclusions:*** Nowadays, surgical repair of coarctation can be performed in infancy with minimal risk. The restenosis rate is considerably high (23%). It is mainly caused by the size of the whole aortic arch, but can also develop during later follow-up.

Introduction

Coarctation of the aorta is a common congenital lesion with a prevalence of 0.33 infants per 1,000 live births [1]. Surgical relief of stenosis was introduced more than 60 years ago. Since the advent of balloon angioplasty and stent implantation in the catheter laboratory, there has been an ongoing discussion about the optimal treatment strategy. Two randomized studies with short- and mid-term follow-up showed the advantages of surgical techniques over balloon dilatation in primary treatment [2–4]. However, comparative stent implantation data are still missing. In this discussion, surgical data are often

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cited that are outdated, are drawn from small or selected patient groups [5], or are drawn from patients with additional cardiac malformations [6–8]. These studies included approximately one third of patients with isolated coarctation, another third of patients with coarctation and ventricular septal defect and a third of patients with concomitant complex heart defects. This is most important for coarctation repair in infancy, as there is an increased risk of surgical mortality, and this risk also and mainly depends on the concomitant defects. On the other hand, it is recommended to relieve coarctation early to prevent hypertension in the long-term follow-up [9–11].

We performed a retrospective, adequately sized, cross-sectional study of all patients in our institution that underwent surgical repair of isolated aortic coarctation in the first year of life to assess long-term mortality and restenosis rate. The aim of the study was to find risk factors for death and restenosis and whether they had changed with time.

Fig. 1. Surgical methods performed in the study periods.

Patients and Methods

Study Subjects

From April 1974 to December 2003, 191 patients with isolated aortic coarctation underwent surgical repair in infancy at our institution, 79 of them within their first month of life. Patients with a ventricular septal defect or any other congenital heart defect were not included, except for a persistent arterial duct, a bicuspid aortic valve with no or only mild stenosis/regurge, or a parachute mitral valve with no or only mild stenosis. Demographic data of the patients are presented in table 1. The anatomical definition of a hypoplastic aortic arch was based on the findings of the surgeon and his/her description in the surgical report. The description of left ventricular function and hypertrophy was extracted from the preoperative angiography or echocardiography report.

All patients gave written consent to have their medical data published anonymously.

Surgical Technique

The surgical aim of coarctation repair is the complete removal of the narrowed aortic region, followed by an anastomosis leading to a stenosis-free blood flow from the ascending to the descending aorta. This was achieved in most of our patients with an end-to-end anastomosis, with or without extension into the aortic arch [12]. Several surgeons in our institutions performed the operations.

In recent years and depending on the surgeon's choice, end-to-side anastomosis [13] was performed in small infants with a hypoplastic aortic arch, 3 of them on cardiopulmonary bypass from a sternal incision. Other surgical methods, like the subclavian flap procedure [14] or subclavio-aortic anastomosis [15], were rarely performed (fig. 1).

Follow-Up

During the follow-up of up to 30 years, 5 of our 191 patients died. From the remaining 186 patients, an analysis of the hospital files was performed. For some patients, no recent data were available, and the patient and their family practitioners were contacted to obtain the data. As that could not be achieved in the case of 37 patients, the most recent available data were included into the analysis to achieve the follow-up of 2,432 postoperative patient-years (median follow-up 13 years, maximal follow-up 30 years). The focus of the data sampling was on reintervention because of restenosis and the current brachial-ankle systolic blood pressure difference. Reinterventions were defined as reoperation, balloon angioplasty or stent implantation performed because of restenosis. Current restenosis was defined as a brachial-ankle blood pressure difference of more than 20 mm Hg [16].

Statistical Analysis

Results are shown as medians (ranges), as most of the data were skewed. Data were analyzed with SPSS 14.0.1 software.

To find risk factors for 'survival without reintervention or restenosis', Cox regression analyses with all available anatomic, presurgical and surgical variables were performed (table 2). Variables were entered stepwise conditional, if $p < 0.05$, and excluded if p values >0.05 in the two-sided model were achieved.

If a continuous variable proofed to be a significant risk factor, a receiver operating characteristic curve analysis was performed to define thresholds, their sensitivity and specificity.

Table 1. Surgical data of primary coarctation repair and survival

	Patients	Patients succumbed	Patients alive	p value[1]
Patients	191	5	186	
Male/female	121/70	1/4	120/66	(0.061)
Preterm, yes/no	9/182	1/4	8/178	(0.216)
Need for mechanical ventilation prior to surgery, yes/no	26/165	3/2	23/163	0.019
Patent arterial duct, yes/no	71/120	3/2	68/118	(0.362)
Bicuspid aortic arch, yes/no	95/96	2/3	93/93	(1.000)
Parachute mitral valve, yes/no	17/174	0/5	17/169	(1.000)
Hypoplastic aortic arch, yes/no	55/136	2/3	53/133	(0.627)
Left ventricular function[2] (6 missing)	69/77/39	2/2/0	67/75/39	(0.383)
Left ventricular hypertrophy[3] (3 missing)	49/68/71	2/1/1	47/67/70	(0.365)
Calendar year of surgery	1990 (1974–2003)	1976 (1976–1981)	1990 (1974–2003)	0.002
Age at surgery, days				
Median	41	9	42	0.010
Range	3–352	3–43	3–352	
Type of surgery				
Resection and end-to-end anastomosis	97	5	92	
Resection and extended end-to-end anastomosis	81	0	81	
Resection and end-to-side anastomosis	13	0	13	(0.704)
Subclavian flap	4	0	4	
Resection and subclavian to descending aorta anastomosis	1	0	1	

p values in parentheses indicate not significant results in the comparison of succumbed and alive patients.
[1] Fisher's exact test in binary variables, χ^2 test in categorical variables, or Mann-Whitney U test in ordinal/numerical variables.
[2] Left ventricular function from preoperative angiogram or echocardiogram (good/reduced/bad).
[3] Left ventricular hypertrophy from preoperative angiogram or echocardiogram (no/moderate/severe).

Table 2. Risk factors for death, reintervention because of restenosis, or current restenosis in a multivariable Cox regression model

	Odds ratio	95% CI	Wald	p value
Hypoplastic aortic arch	2.864	1.581–5.186	12.055	0.001
Body length at surgery	0.923	0.560–0.970	10.162	0.001

Variables not entered in the model ($p > 0.05$): sex, prematurity, monosomy X0, DiGeorge syndrome, patent arterial duct, bicuspid aortic valve, parachute mitral valve, and left ventricular hypertrophy; need for mechanical ventilation and use of prostaglandin E prior to surgery; age and weight at surgery, calendar year of surgery, type of surgery, need for extracorporeal circulation, suture material (absorbable vs. nonabsorbable) and technique (single stitch vs. continuous suture vs. mixed).

Results

Survival

From all 191 patients with coarctation repair in infancy, 5 died (total mortality 2.6%). One of them died at surgery, 2 within 30 days after surgery (early mortality 1.6%), both from postoperative pneumonia. Another 2 patients died in the third month after surgery, both from postoperative heart failure. All of these patients underwent surgery within the first 43 days of life and in the years up to 1981. The total mortality of those undergoing surgery in the first 43 days of life and before 1981 was 5/19 (26%). After 1981, there was no mortality, not even in the 81 patients undergoing surgery in the first 43 days of life.

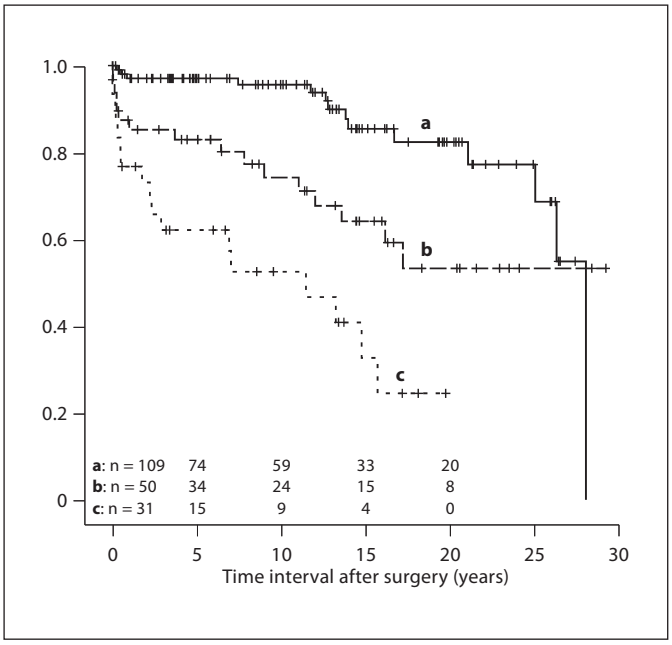

Fig. 2. Kaplan-Meier analysis for survival without restenosis after surgical coarctation repair in infancy in 3 groups (n = 191, log rank $\chi^2 = 9.268$, p = 0.002). Body length at surgery >53.5 cm (**a**); body length at surgery <53.5 cm without a hypoplastic aortic arch (**b**); body length at surgery <53.5 cm with a hypoplastic aortic arch (**c**).

Furthermore, none of the patients had paraplegia or spinalis anterior syndrome after surgery.

Reintervention/Restenosis

In 31 patients (17% of the 186 patients alive), reinterventions had been performed because of restenosis with an invasive blood pressure gradient of >20 mm Hg across the stenosis. Another 11 patients (6% of the 186 patients alive) had a current brachial-ankle systolic blood pressure difference of >20 mm Hg, suggesting restenosis at late follow-up.

In the multivariable analysis, independent risk factors for 'death, reintervention because of restenosis, or current restenosis' were a hypoplastic aortic arch and a low body length at surgery (table 2). In contrast to survival, this was not dependent on the calendar year of surgery.

Receiver operating characteristic curve analysis revealed only a fairly week threshold for a length at surgery of 53.5 cm (specificity 70%, sensitivity 66%), with a rate of death/reintervention/restenosis of 41% if smaller than 53.5 cm at surgery and only 13% if longer.

A Kaplan-Meier plot for survival without reintervention or restenosis is shown in figure 2 and clearly depicts that restenosis occurrence is not confined to the early postoperative follow-up.

Discussion

Survival

This study with 2,432 patient-years of follow-up showed that nowadays coarctation repair can be performed in infancy with a very low risk. Mortality was confined to infants <43 days of age that underwent surgery till 1981. This is explained by the introduction of prostaglandin E to (re-)open the arterial duct and to relieve the stenosis caused by ductal tissue spread into the aortic wall [17, 18]. Before the prostaglandin era, patients often entered the theatre as an emergency in a poor clinical condition. This good survival is in accordance with other smaller sized studies [19, 20] reporting almost no perioperative deaths in infants undergoing surgery for coarctation nowadays.

Restenosis/Reintervention

Restenosis after surgical coarctation repair in infancy is still a matter of concern. In our complete cross-sectional study group, there was a considerable high restenosis rate of 23%. This rate was statistically related to a hypoplastic aortic arch and a low body length. Both factors can be summarized to a very small aortic arch, not only confined to the coarctation site. Several recent studies [5–7, 19] reported less restenosis rates of 4–14%, but the median follow-ups of about 4 years in each study were substantially shorter than that of our study. Additionally, a closer look at our Kaplan-Meier curve outlines that there was a substantial occurrence of restenosis also late after surgery.

Age and body weight at surgery, which correlated with body length and were also significant in a preliminary bivariate analysis, were outperformed in the multiple regression analysis by body length and not entered in the final model. Therefore, it can be assumed that age and weight are important risk factors because of the size of the aortic arch. This is in accordance with the study of McElhinney et al. [21] who measured the size of the aortic arch segments by echocardiography and came to the conclusion that the size of the transverse aortic arch is the most important risk factor for restenosis after coarctation repair in early infancy.

Astonishingly, our restenosis rate was independent from the calendar year of surgery. Therefore, the improvements in new surgical techniques and in perioperative management might be helpful to some selected patients. However, no significant improvement regarding the rate of restenosis could be found in our study for the whole group of coarctation patients.

Concerning the type of surgery, which also failed to be an outcome criterion in our analysis, it has to be mentioned that this study was a retrospective study and the type of surgery performed was up to the surgeon's choice of the best treatment for the anatomical situation given. Therefore, the most hypoplastic aortic arches and the smallest infants were more likely to be repaired with an extended end-to-end or, in recent years, an end-to-side anastomosis. Other studies report a favorable outcome after end-to-side anastomosis [22].

Data of surgical repair have to compete with data of balloon angioplasty. The 2 randomized studies [2–4] directly comparing these treatments and reporting a higher incidence of femoral artery stenosis, aneurysm formation [3] and restenosis [4] did not include infants. However, it has to be expected that balloon dilatation in infancy will even produce more of the reported residuals than in older children, as contractile ductal tissue is not removed. At least for femoral artery stenosis and aneurysm formation, this should not be expected in surgical repair. Concerning restenosis, balloon angioplasty in infancy is even considered a palliative treatment, as the restenosis rate is reported to be 50% in the short-term follow-up of infants <3 months [23].

The major limitation to our study is the cross-sectional and retrospective approach. Therefore, data are only available for when restenosis was detected and not when it occurred. This time interval between occurrence and detection might be considerable, as the study design did not assure close regular follow-ups in all patients.

In conclusion, coarctation repair can still be a challenge in small infants, if a complex aortic arch reconstruction is necessary. Nevertheless, various other studies [10, 24] showed that coarctation repair should not be postponed to a later age, as prestenotic hypertension can enhance the preexisting congenital aortic wall degeneration [25] and increase arterial hypertension in the long-term follow-up. Regular, maybe life-long, surveillance is necessary in these patients to exclude hypertension and late restenosis.

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