Surgical repair of coarctation of aorta in neonates and infants: a 10 years experience

Yenidoğan ve infantlarda aort koarktasyonunun cerrahi onarımı: 10 yıllık deneyim

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Background: This study reviews the experience of a single center with surgery for coarctation of aorta (CoA) in neonates and infants over 10 years.

Methods: Thirty five neonates and 56 infants, a total of 91 patients (mean age 3 months, min. 8 days - max. 11 months) who were operated for CoA in our clinic between June 1996 and June 2006, were retrospectively included in the study. The present cohort is similar to recent series in the literature, where neonates and infants predominate and severe cardiovascular morbidity is frequent. End-to-end anastomosis was the most used technique (74.7%) in both neonates and infants.

Results: Postoperative systemic hypertension was seen with a higher incidence in infants. None of the patients, except the ones with significant gradient at the repaired segment and who had reintervention, required antihypertensive medication six months after surgery. During a mean follow-up period of 44 months (range, 23 to 118 months), 13 patients (12.1%) demonstrated recoarctation. 3.3% of the patients were treated for recoarctation by surgery and 7.7% of the patients had endovascular intervention. Mortality in both the early and late postoperative periods was 2.2%. Overall mortality over the whole duration of follow-up was 4.4%. The probability of avoiding death, reintervention for CoA, and cardiovascular complications in the entire study population was 93.4%, 90.1% and 83.5% 1, 5 and 10 years after surgery, respectively. During follow-up complications occurred almost equally in both groups.

Conclusion: Although surgical repair for CoA seems to be the gold standard, it is still associated with mortality and morbidity and there is still a need for reintervention. These patients therefore need careful and close follow-up which is as important as timing and technique of surgery.

Key words: Aortic coarctation; mortality, morbidity; surgical technique.

Amaç: Bu çalışmada tek merkezde 10 yıl boyunca yenidoğan ve infant grubunda gerçekleştirmiş olduğumuz aort koarktasyonu (AK) cerrahisi ile ilgili deneyimlerimiz sunuldu.

Çalışma planı: Haziran 1996 - Haziran 2006 tarihleri arasında kliniğimizde ameliyat edilmiş 35 yenidoğan ve 56 infanttan oluşan toplam 91 hasta (ort. yaş 3 ay; min. 8 gün - maks. 11 ay) geriye dönük olarak çalışmaya dahil edildi. Çalışmamızın kohortu, literatürdeki son zamanlarda yapılmış yenidoğan ve infantların ağırlıkta olduğu ve sık olarak karşılaşılan kardiyovasküler komplikasyonlarla benzerlikler göstermekte idi. Uç-uca anastomoz tekniği her iki grupta da en sık (%74.7) kullanılan teknik oldu.

Bulgular: İnfantlarda ameliyat sonrası tedavi gerektiren sistemik hipertansiyona daha sık rastlanırken, tamir yapılan segmentte ciddi gradient olan ve tekrar girişim uygulanan bir hasta dışında, altı ay sonunda hiçbir hastanın antihipertansif medikasyon ihtiyacı olmadı. Ortalama 44 aylık takip süresinde (dağılım, 23-118 ay) 13 hastada (%12.1) ciddi rekoarktasyon ile karşılaşıldı. Hastaların %3.3'ünde ikinci bir koarktasyon girişimi, %7.7'sinde ise endovasküler girişim gerekti. Ameliyat sonrası erken ve geç dönem mortalite %2.2 oldu. Takip süresince genel mortalite ise %4.4 olarak hesaplandı. Çalışmaya alınan hastalarda, sağkalım ve AK nedeniyle ikinci bir girişim gereksiniminin olmaması ve kardiyovasküler komplikasyonların gelişmemesi olasılıkları ameliyat sonrası 1, 5 ve 10 yıl için sırasıyla %93.4, %90.1 ve %83.5 oldu. Takip süresince komplikasyonlarla her iki grupta da eşit olarak karşılaşıldı.

Sonuç: Her ne kadar AK tedavisi için cerrahi girişim altın standart olsa da, halen AK cerrahisi sonrası morbidite ve mortalite ile karşılaşılır ve tekrar girişim gerekebilir. Bu nedenle, bu hasta grubunda çalışmamızdaki hasta grubunda olduğu gibi yakın takip, cerrahinin zamanlaması ve tekniği kadar önemlidir.

Anahtar sözcükler: Aort koarktasyonu; mortalite, morbidite; cerrahi teknik.

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Coarctation of aorta (CoA) is an important treatable cause of secondary hypertension. Untreated CoA is associated with premature mortality and morbidity.[1] Its prevalence varies from 5% to 8% of all congenital heart defects. In the early years, repair for CoA was considered curative and no systematic follow-up was done.[2] Later, it became clear that CoA, even after successful repair, is associated with an increased risk of later development of recoarctation (reCoA), systemic hypertension, cerebrovascular disease, premature atherosclerosis and formation of aortic aneurysms.[1,3] Several reports have documented both the efficacy and the safety of the procedure of interventional cardiology.[4,5] However, there is very little data available on the long-term follow-up of pediatric patients treated with angioplasty techniques.[4,5] Before the introduction of interventional angioplasty, surgery was the treatment of choice for native aortic coarctation as well as for recoarctation in children.[6-8] Therefore, we decided to perform this retrospective study in order to identify pediatric patients under one year of age who underwent surgery for CoA over a period of 10 years at the Başkent University Hospital, and to assess surgical and late mortality and morbidity in this cohort, thereby also identifying survivors who could be targeted for systematic clinical follow-up in order to prevent long-term complications, especially postoperative systemic hypertension. We wanted to further examine the role of possible risk factors for surgical and late mortality.

PATIENTS AND METHODS

We identified 91 patients who were operated for CoA at the Başkent University Hospital. Criteria for inclusion in the study were: *(i)* the presence of aortic coarctation, either isolated or associated with other congenital heart defect; *(ii)* surgery performed between 1996 and 2006, in patients under one year of age. The sources of clinical data were: *(i)* hospital documents; *(ii)* direct contact with the patients or their families; *(iii)* direct contact with the referring cardiologist or pediatric cardiologist. For each patient the following data were recorded: *(i)* date of surgery; *(ii)* age and weight at surgery; *(iii)* associated lesions; *(iv)* type of surgical technique; *(v)* early and late surgical results in terms of: (a) deaths; (b) need for re-operation because of development of recoarctation; (c) residual/recurrent pressure gradient; (d) systemic hypertension, requiring medical treatment; (e) any kind of reintervention for re-CoA; (f) operative complications. Since the presentation of this disease is completely different in different age groups and cases of combined surgery (CoA combined with open heart corrections), patients older than one year and cases of combined surgery were excluded from this study.

The demographic data was as follows: 35 neonates (<1 month of age) and 56 infants (1 month-1 year), with a mean age of three months, ranging from eight days to eleven months.

Blood pressure was measured with the oscillometric method using an appropriate-sized cuff and with the patient supine and quiet. The right arm systolic pressure was used to assess the presence of arterial hypertension. Right arm and right leg pressures were compared to assess the pressure gradient across the site of operation.

Hypertension was defined as the condition requiring the use of antihypertensive drugs. Patients, who had filled at least one prescription for antihypertensive drugs, including beta-blockers, diuretics, calcium antagonists, angiotensin II antagonists or anjiotensin converting enzim (ACE) inhibitors, during their follow-up were classified as hypertensive. Recoarctation was defined as a systolic blood pressure gradient of greater than 20 mmHg between the right arm and right leg. Echocardiographic pressure gradients were derived from the velocity in the descending aorta using a continuous Doppler with the transducer positioned in the suprasternal notch. The presence of a blood pressure gradient greater than 30 mmHg with arterial hypertension was considered an indication for reintervention.

Patients were operated on by five different surgeons. Moderate body surface hypothermia (31° to 33 °C) was induced and a left lateral thoracotomy in the fourth intercostal space was performed in all patients. The descending aorta, as well as the left subclavian and carotid arteries, were exposed and mobilized. The ductus arteriosus was transected. During resection of the stenotic segment of the aorta, care was taken to excise all ductal tissue. Resection of the stenotic segment of the aorta and simple end-to-end anastomosis were performed in all children in the absence of proximal or distal hypoplastic aortic arch. In small children, particularly in the presence of hypoplastic aortic arch, our policy was to consider resection and end-to-end anastomosis enlarged to the aortic arch (extended end-to-end) as the first-line technique of surgery. The subclavian flap was taken into consideration only in the presence of hypoplasia of the distal aortic arch.

Statistical analyses

Descriptive tables of the main study variables were made for the entire study population. Follow-up began on the date of surgical repair for CoA and ended on the date of death or end of follow-up or December, 2007 whichever came first. Values are presented as mean ± 1 standard deviation. Mean values of independent samples were compared using the unpaired T-test. Differences in proportions were analyzed based on contingency tables

using the Chi square test. A *p* value less than 0.05 was considered statistically significant. Kaplan-Meier survival curves were constructed to analyze mortality. Mortality was divided into early (≤30 days after repair) and late mortality. Kaplan-Meier curves using a combined end point of death, reintervention and operative complications were also constructed describing freedom from morbidity, mortality and reintervention. We included age, gender, weight, surgical technique, cross clamp time, associated lesions, preoperative pressure gradient at the coarctation segment, postoperative blood pressure as possible predictors of mortality in a multivariate analysis.

RESULTS

Mean age at surgery was three months (min 8 days-max 11 months). Maximum follow-up was 10 years with a mean follow-up of 44 months. 38.5% of the patients were neonates and 61.5% were infants. Mean ages were 14 days for the neonatal age group and five months for the infantile age group. For the neonates, the mean weight at operation was 3.1±0.6 kg (range, 2.7 to 4.2 kg) and for the infants, the mean weight was 7±1.2 kg (range, 3.4 to 9.7 kg). Baseline data was showed in Table 1. Coarctation of aorta is said to be much more frequent in male population than female.[7,8] In our study, 62.6% were males.

Since the patients were all in neonatal and infantile age groups and our clinic is one of the referral hospitals for congenital heart surgery, many of the patients were not only cases of simple aortic coarctation, they usually had comorbidities (Table 2).

Surgical techniques for each age group are listed in Table 3. 74.7% of the patients had undergone end-to-end anastomosis, 15.4% had undergone extended end-to-end anastomosis and 9.9% had undergone subclavian flap repair. End-to-end anastomosis was the technique of choice in both neonates (74.3%) and infants (75%). The mean aortic cross-clamp time was 19±7 minutes (range, 11 to 29 minutes) in the neonates and 14±4 minutes (range, 10 to 23 minutes) in the infants (p=0.02).

The mean postoperative blood pressure gradient (at hospital discharge) was 9±6 mmHg in the neonates and 8±4 mmHg in the infants (p>0.05). Transient postoperative hypertension was seen in two neonates (5.7%), necessitating intravenous (i.v.) drug treatment for the first day. In 22 infants (39.3%), transient postoperative hypertension occurred, requiring drug therapy (between 1 day and 6 months) in all (p<0.01). Only the patients with significant gradient at the repaired segment and who had undergone reintervention required antihypertensive medication six months after surgery.

Since the patients were all under one year of age with some associated cardiac anomalies, a number of complications occurred in the study population during follow-up (Table 4).

Overall mortality in the whole duration of follow-up was 4.4%. Mortality in both the early (before 1 month) and late (after 1 month) postoperative periods were 2.2%. Neither early nor late mortality was seen in patients with simple coarctation. Early and late mortalities were seen equally in all age groups with one for each age group, for a total of four. The survival for 1, 5 and 10 years was 97.8%, 96.7% and 95.6% respectively.

During a mean follow-up period of 44 months (range, 23 to 118 months), 13 patients (12.1% of the whole population) demonstrated recoarctation according

Table 1. Preoperative data in the study population

	Number of patients (%)
Neonates	35/91 (38.5)
Infants	56/91 (61.5)
Gender (male/female)	57/34 (62.6/37.4)
Age (mean) neonates	14 days
Age (mean) infants	5 months
Weight (mean) neonates	3.1±0.6 kg
Weight (mean) infants	7±1.2 kg

Table 2. Distribution of malformations, associated anomalies (cardiac/non-cardiac) and specific conditions

Malformations and specific conditions	Number of patients
Patent ductus arteriosus	51
Bicuspid aortic valve (without stenosis)	50
Atrial septal defect / patent foramen ovale	39
Aortic arch hypoplasia (varying degrees)	29
Ventricular septal defect	11
Aortic stenosis	5
Mitral valve dysfunction	4
Vascular ring	3
Pulmonary stenosis	3
Atrioventricular septal defect	2
Double outlet right ventricle	2
Shone complex	2
Noonan syndrome	1
Turner syndrome	1
Williams syndrome	1
Pulmonary hypertension	2
Prematurity	3
Bronchopulmonary dysplasia	2
Duodenal atresia	1
Diaphragmatic hernia	1

Table 3. Surgical techniques in different age groups

	E-to-E	Ext. E-to-E	Subclavian flap	*Total*
Neonates	26	7	2	35
Infants	42	7	7	56
Total	68	14	9	91

E-to-E: End-to-end; Ext. E-to-E: Extended end-to-end.

to the definition used. Of these 13 patients, eight had primary operation as neonates, which was a 22.9% incidence of recoarctation in that group. Only five of the patients with recoarctation had operation during infancy (all at the first 6 months of life), resulting in an 8.9% incidence of restenosis in that age group. In all 13 cases, recoarctation developed within the first year after the initial repair. Of the 13 patients with restenosis, 10 (11% of the whole study population) needed reintervention between six months to two years after the initial repair. Seven (4 neonates) had successful balloon dilatation of their recoarctation and three (2 neonates) had a successful reoperation. None of the 10 patients had signs of recurrence of stenosis at the last follow-up visit. In the other three patients (2 neonates), only mild recoarctation developed (gradients of 22.24 and 27 mmHg, respectively); and this did not require treatment. None of the children operated on between six and 12 months of age showed signs of recoarctation during the entire follow-up period. Of the 91 total patients, only 7.7% had interventions for recoarctation. 3.3% patients were treated for re-CoA by surgery (Table 5, 6). The probability of avoiding death, reintervention for CoA and cardiovascular complications in the entire study population was 93.4%, 90.1% and 83.5% 1, 5 and 10 years after surgery, respectively. Recurrent or residual coarctation treated with surgical repair and endovascular intervention was seen with a statistically significant greater incidence in the neonatal age group ($p<0.05$; Table 5, 6). In our study, extended end-to-end anastomosis was associated with the lowest incidence of recoarctation requiring intervention ($p>0.05$) among all the surgical techniques, but the difference was not statistically significant (Table 6).

Table 5. Incidence of reoperation for recoarctation

	Sayı	Yüzde
With regard to the age of patient at the time of first operation		
Neonates	2/35	5.7
Infants	1/56	1.8
Total	3/91	3.3
With regard to the surgical technique		
End-to-end anastomosis	2/68	2.9
Extended end-to-end anastomosis	1/14	7.1
Subclavian flap	–/9	
Total	3/91	3.3

Table 4. Complications after surgery in the early postoperative period

	Neonates	Infants	*Total*
CVA mi*	1	1	2
CVA mj**	1	–	1
Pneumonia	2	3	5
Pneumothorax	1	–	1
Sepsis	2	1	3
Chylothorax	-	1	1
D. Paralysis***	1	1	2

*: Minor cerebrovascular accident; **: Major cerebrovascular accident; ***: Diaphragm paralysis.

DISCUSSION

Surgery has long been considered the treatment of choice for aortic coarctation in children.[7,8] Within the last decade, promising results have been reported with the interventional angioplasty techniques for the native aortic coarctation and the recoarctation, in children.[5,6] Primary balloon dilation of coarctation has been successful in relieving the stenosis, but recent observations showed a higher rate of restenosis after balloon dilatation than after operative treatment in neonates.[9] and in infants.[10] Our retrospective study has focused on the main problems after surgery for aortic coarctation in neonates and infants reported in the literature: mortality, residual/recurrent coarctation requiring for further treatment, residual/recurrent systemic hypertension and its treatment.[7,8]

Since the patients were all under one year of age, and our clinic is one of the referral hospitals for congenital heart surgery in our country, many of the patients did not present with simple aortic coarctation, but had comorbidities. In patients with Ventricular septal defect (VSD), initial coarctation repair is ideal when the VSD is likely to close, a band is not required, and arch hypoplasia is not present. Large size defects, defined as those with diameter greater than 50% of the aortic valve annulus, and types other than muscular such as

Table 6. Incidence of reintervention (angioplasty ± surgery) for recoarctation

	Sayı	Yüzde
With regard to the age of patient at the time of first operation		
Neonates	6/35	17.1
Infants	4/56	7.1
Total	10/91	11
With regard to the surgical technique		
End-to-end anastomosis	1/68	11.8
Extended end-to-end anastomosis	1/14	7.1
Subclavian flap	1/9	11.1
Total	10/91	11

perimembranous, inlet, outlet, and malaligned are less likely to close. In our clinic, we prefer to repair associated anomalies in patients with VSD with one stage or one stage-two incisions techniques when it is obvious to avoid disadvantages of the two stage approach. However, the presentation of this disease and results of surgery are completely different from cases of combined surgery (CoA combined with open heart corrections), and these patients were excluded from this study.

As for operative therapy, especially in neonates and infants, there is an ongoing debate about the most appropriate operative technique and the optimal timing for operation to achieve the lowest rates of late postoperative hypertension, consequent cardiovascular morbidity, mortality and recoarctation. It has been shown that early repair positively affects the incidence of late postoperative hypertension.[11] The classical technique of resection and end-to-end anastomosis has been proved to be feasible in almost all cases, with the advantage of avoiding foreign material other than sutures. In the small child, particularly in the presence of hypoplastic aortic arch, our current policy is to consider resection and end-to-end anastomosis enlarged to the aortic arch as the first technique of choice. We identified 35 neonates (38.5%) who were operated for CoA and of these 35 neonates, 26 (74.3%) were operated with end-to-end anastomosis technique. For seven (20%) of the patients, extended end-to-end anastomosis was preferred. The subclavian flap was taken into consideration only in the presence of hypoplasia of the distal aortic arch in two patients. The technique of patch aortoplasty was completely abandoned because of aneurysm formation associated with the presence of a synthetic patch and increased restenosis rates.[12]

It is frequent, in our experience as well as in the literature[6-8] to observe paradoxical systemic hypertension shortly after surgery particularly in infants. We found a higher incidence (39.3%) of infants requiring medical treatment to control systemic hypertension in the early postoperative period than the neonates (5.7%). Hypertension was characterized by two components: an early component with predominantly systolic hypertension that usually resolved within 48 hours and a late component of systolic and/or diastolic hypertension that generally persisted beyond the second postoperative day. When hypertension persists beyond the second postoperative day, there is an increased risk of postcoarctectomy syndrome, characterized by abdominal pain and associated mesenteric arteritis.[13] In our clinic, antihypertensive treatments of choice are i.v. infusions of sodium nitroprusside and/or gliserol trinitrate and peroral ACE inhibitor captopril and/or β-blocker propranolol. There is a good rationale for β-blockers to reduce wall shear stress. However, ACE inhibitors are more effective in isolated systolic hypertension and better tolerated in the younger population. Captopril has demonstrated successful control of hypertension, even after other agents have failed. In our clinic we use both captopril and propranolol 1-3 mg/kg/day in divided doses. Early surgical treatment of aortic coarctation reduces the likelihood of early as well as late postoperative hypertension. In our clinic, we noticed a higher incidence of high blood pressure in patients older than one year who were operated for CoA, but these patients were not included in this study.

Patients remained normotensive and only two in the neonatal age group (5.7%) needed i.v. or oral antihypertensive medication in the early postoperative period. Only the neonates with a significant gradient at the repaired segment which required surgical and/or percutaneous reintervention, needed antihypertensive medication six months after operation.

Restenosis remains to be an important complication to watch out for. While restenosis has been treated surgically, experience is growing in the use of endovascular interventions to treat restenosis. This may be the treatment approach of choice. In our study population of 91 patients, 11% had reinterventions for recoarctation. 3.3% of the patients were treated for re-CoA by surgery. In many surgical reports, residual/recurrent coarctation is generally absent in older children[2,4,7,8] and, as in our experience, is more frequent in two categories: neonates and patients with associated hypoplasia of the aortic arch. In this cohort of patients, recoarctation was seen with relatively higher incidence than in the neonatal age group (5.7% of the neonates required surgery and 17% of the neonates required some kind of intervention) achieving statistical significance ($p<0.05$; Table 5, 6). The need for reintervention with regard to the surgical technique was relatively less in the extended end-to-end group (7.1%) but did not achieve statistical significance ($p>0.05$; Table 5, 6).

The combination of a bicuspid aortic valve and coarctation appears to predispose patients to aortopathy and deserves special mention. Sixty-three percent of patients reported aortic valve disease and 28% of patients noted aortic arch dilatation in a recent study.[14] We actively searched for evidence of aortic valve dysfunction with regular echocardiograms. 60.4% of this study population had confirmed bicuspid valves (with/without stenosis). Three of them had undergone aortic valve surgery. Six of our patients are now being monitored for aortic root dilatation and significant aortic valve gradients.

• Overall mortality over the whole duration of follow-up was 4.4%. Mortality in both the early and late

postoperative periods was 2.2%. As seen in literature,[1-8] hospital deaths and complications occurred mainly in neonates and infants with complex associated lesions indicating that, surgery performed in infants and neonates with simple CoA has low risk.

Limits of the study

This study was the retrospective evaluation of 10 years of experience from five different surgeons in our clinic. We did not have the control on the type of surgical technique and the suture materials preferred, as well as on the timing and indication of surgical approach. Moreover, since various techniques have been utilized in each age group, the numbers were not large enough to justify different variables: suture materials, blood pressure at the last follow-up, etc. To better study the effect of patient age at the time of repair on the operative technique used, we should have excluded patients if they had associated congenital cardiovascular malformations. However, most of our patients in this cohort had associated malformations.

In conclusion the present cohort of patients who underwent surgery for CoA is not very different from recent series where neonates and infants predominate and cardiovascular morbidity is frequent. The long-term results in many favorable surgical reports, confirm that surgery has to be considered the gold standard for the treatment of aortic coarctation. The interventional angioplasty techniques, apparently so appealing because they avoid an invasive operation, have yet to provide long-term outcome at least similar to the results obtained with surgery. Although surgery is the gold standard, it is not a totally curative treatment for CoA.

It is now clear that repaired CoA is not a benign condition. Coarctation of aorta after surgical repair is associated with excess long-term mortality and morbidity compared with sex and age matched reference groups, due to ischemic heart disease, aneurysms of aorta, recoarctation, hypertension, premature atherosclerosis, valve abnormalities and other associated cardiac malformations. It was shown that high numbers of patients were lost in the long-term follow-up and a high frequency of patients were inadequately treated or had under-diagnosed complications. Careful follow-up should be carried out and would probably identify many patients in whom medical, surgical or catheter intervention would improve the long-term outcome.

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