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Long-term outcomes after surgical repair of the coarctation of aorta beyond infancy period

Bebeklik dönemi sonrası yapılan aort koarktasyonunun cerrahi tamiri sonrası uzun dönem sonuçları

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ABSTRACT

Background: This study aims to evaluate the long-term results of the patients in whom coarctation of the aorta was surgically repaired beyond the infancy period.

Methods: Between January 1999 and August 2016, a total of 49 patients (28 males, 21 females; mean age 22.9 ± 11.3 years; range 3 to 56 years) who underwent surgical repair of coarctation of the aorta and followed in the outpatient clinic were included in this study. The repair procedures included patch angioplasty (51%), interposition grafting (40.8%), simple and extended end-to-end anastomosis (6.12%), and subclavian plasty (2%).

Results: The mean follow-up was 78.1 ± 33.5 months (range 2 to 144 months). Of the patients, 22 (44.9%) had recoarctation, 19 (38.7%) had hypertension, three (6.1%) had an aneurysm of the ascending aorta, five (10.2%) had aortic valve stenosis, five (10.2%) had aortic insufficiency, and two (4.08%) had coronary artery disease. There was no significant difference (p=0.787) in the recoarctation rates between the patients who initially underwent patch angioplasty and the patients who initially underwent interposition grafting. The mean age in the initial surgery was not statistically significantly different (p=0.696) between the patients with and without recoarctation. However, the mean age was significantly higher (p=0.006) in the patients with postoperative hypertension than those who did not. None of the patients had in-hospital mortality or cerebrovascular accident.

Conclusion: Even following a successful repair of coarctation of the aorta, further cardiac diseases may develop. Therefore, early diagnosis and treatment of such cardiac pathologies are of utmost importance.

Keywords: Aortic aneurysm; aortic valve disease; coarctation of the aorta; long-term.

ÖΖ

Amaç: Bu çalışmada bebeklik döneminden sonra aort koarktasyonu cerrahi olarak tamir edilen hastalarda uzun dönem sonuçlar değerlendirildi.

Çalışma planı: Ocak 1999 - Ağustos 2016 tarihleri arasında aort koarktasyonunun cerrahi tamiri yapılan ve poliklinik takibinde olan toplam 49 hasta (28 erkek, 21 kadın; ort. yaş 22.9±11.3 yıl; dağılım 3-56 yıl) bu çalışmaya alındı. Tamir işlemleri yama anjiyoplasti (%51), greft interpozisyonu (%40.8), basit ve genişletilmiş uç uça anastomoz (%6.12) ve subklavyen plastidir (%2).

Bulgular: Ortalama takip süresi 78.1 \pm 33.5 ay (dağılım 2-144 ay) idi. Hastaların 22'sinde (%44.9) rekoarktasyon, 19'unda (%38.7) hipertansiyon, üçünde (%6.1) çıkan aort anevrizması, beşinde (%10.2) aort kapak darlığı, beşinde (%10.2) aort yetmezliği ve ikisinde (%4.08) koroner arter hastalığı saptandı. İlk olarak yama anjiyoplasti yapılan hastalar ve interpozisyon greftleme yapılan hastalar arasında rekoarktasyon oranları açısından anlamlı bir fark yoktu (p=0.787). İlk ameliyat sırasında cerrahi rekoarktasyon olan ve olmayan hastalar arasında ortalama yaş açısından istatistiksel olarak anlamlı bir fark yoktu (p=0.696). Ancak ameliyat sonrası hipertansiyon gelişen hastaların, gelişmeyenlere kıyasla, ortalama yaşı anlamlı düzeyde yüksekti (p=0.006). Hiçbir hastada hastane mortalitesi ve serebrovasküler olay izlenmedi.

Sonuç: Aort koarktasyonunun başarılı tamirinin ardından dahi, başka kalp hastalıkları gelişebilir. Bu nedenle, bu tür kalp hastalıklarının erken tanı ve tedavisi önem arz eder.

Anahtar sözcükler: Aort anevrizması; aort kapak hastalığı; aort koarktasyonu; uzun dönem.

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Coarctation of the aorta (CoA) constitutes about 5 to 8% of all congenital cardiac diseases and is twice as common in males.^[1] The first successful coarctation repair, which entailed an end-to-end anastomosis, was performed by Crafoord in 1945.^[2] Since then, there has been a rapid increase in the surgical treatment of CoA with techniques such as patch plasty using synthetic materials, graft interposition, bypass grafting, and subclavian flap aortoplasty.^[1,3,4] Coarctation of the aorta, particularly without an associated lesion, is a simple condition to treat. However, several studies have demonstrated that the life expectancy following surgery is reduced, and these patients are at an increased risk of developing certain pathologies.^[5,6]

Patients with a previously repaired CoA have continued to be a risk of major complications throughout their lives including hypertension and recoarctation, leading to aortic stenosis and/or insufficiency, aneurysms of the ascending aorta, coronary artery disease, and other cardiac pathologies. Therefore, longterm follow-up of these patients is critical for early diagnosis of the cardiac pathologies.

In this study, we aimed to evaluate the long-term follow-up results of the surgical repair of CoA beyond the infancy period and to investigate the incidence of reintervention after initial coarctation operations.

PATIENTS AND METHODS

A total of 110 patients who underwent surgical repair for CoA at our institution between January 1999 and June 2011 were screened. Forty-nine patients (28 males, 21 females; mean age 22.9±11.3 years; range 3 to 56 years) who met the inclusion criteria and were followed until August 2016 in the outpatient setting were included in this study. Attempts were made to contact all patients by questionnaire. They were, then, scheduled for clinical examination. All the patients included (44.5%) were contactable and were evaluated in our outpatient clinic. The patients were assessed by clinical examination followed by blood pressure measurement, blood tests, chest X-ray, electrocardiography (ECG), and echocardiography. Those with signs of cardiac ischemia on ECG also underwent coronary angiography. Echocardiography revealed any gradient of the descending aorta, systolic and diastolic function of the left ventricle, and cardiac pathologies such as aortic and mitral valve disease, dilatation and/or aneurysms of the ascending aorta. Computed tomography (CT) was performed in the patients who had a high-pressure gradient in the descending aorta for a more accurate evaluation of the stenotic segment. All patients were evaluated for potential clinical risk factors including hypertension and they were on regular antihypertensive treatment. A residual coarctation pressure gradient was measured by the right arm and leg blood pressure during the follow-up visit. The study protocol was approved by the Türkiye Yüksek İhtisas Hospital Institutional review board. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Indications for reoperation for recoarctation included an arm/leg pressure gradient higher than 30 mmHg and presence of hypertension. Hypertension was defined as a blood pressure higher than 140/90 mmHg in adults and higher than 20% than normal pressure for their age category in children. Doppler echocardiography was used to measure gradients across the coarctation segment. If hypertension developed or there was a gradient \geq 30 mmHg across the coarctation segment, reintervention was performed.^[7-10]

We used reintervention techniques after recoarctation of the aorta including patch angioplasty with a Dacron[®] graft, interposition grafting, extended end-to-end anastomosis, and subclavian plasty.

Statistical analysis

Statistical analysis was performed using the SPSS version 15.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed in mean and \pm standard deviation (SD). Categorical variables were expressed in numbers and percentages. Demographic characteristics and perioperative variables values were compared using the independent samples t-test or Mann-Whitney U test for continuous variables and chi-square test or Fisher's exact test for categorical variables. A *p* value of <0.05 was considered statistically significant with 95% confidence interval.

RESULTS

The mean follow-up was 78.1 ± 33.5 (range 2 to 144) months. The demographic data of the patients and previous repair procedures are demonstrated in Table 1. Concomitant ligation of patent ductus arteriosus was performed in five patients (10.2%). Bicuspid aortic valve was present in 13 patients (26.53%). There were no recorded cases of intraoperative or in-hospital mortality or cerebrovascular accidents. During the early postoperative period, revisions were performed in three patients due to bleeding and in one patient due to pleural effusion. One patient had a prolonged in-hospital stay due to development of chylothorax, while another patient developed hoarseness of the voice.

Table 1. Patient characteristics (n=49)

| Characteristics | n | % | Mean±SD |
|------------------------------|----|-------|-----------|
| Age (year) | | | 22.9±11.3 |
| Gender | | | |
| Male | 28 | 57.1 | |
| Female | 21 | 42.9 | |
| Previous surgical procedures | | | |
| Patch angioplasty | 25 | 51.00 | |
| Interposition grafting | 20 | 40.8 | |
| Simple and extended | | | |
| end-to-end anastomosis | 3 | 6.12 | |
| Subclavian-plasty | 1 | 2.00 | |

SD: Standard deviation.

Table 2. Adverse cardiac events and repeat cardiac procedures (n=49)

| | n | % |
|----------------------------------|----|------|
| Outcomes; adverse cardiac events | | |
| Recoarctation | 22 | 44.9 |
| Hypertension | 19 | 38.7 |
| Ascending aortic aneurysm | 3 | 6.1 |
| Aortic valve stenosis | 5 | 10.2 |
| Aortic valve insufficiency | 5 | 10.2 |
| Coronary artery disease | 2 | 4.08 |
| Repeat cardiac procedures | | |
| Recoarctation | 3 | 6.1 |
| Aortic valve replacement | 2 | 4.08 |
| Ascending aorta replacement | 2 | 4.08 |
| Bentall procedure | 1 | 2.04 |

The long-term follow-up of the patients with adverse cardiac events and re-do cardiac procedures are shown in Table 2. Of the patients, 22 (44.9%) had recoarctation and three (6.12%) underwent reoperation, while two (4.08%) underwent aortic valve replacement, two (4.08%) underwent supra-coronary graft replacement due to an aortic aneurysm, and one (2.04%) underwent the modified Bentall procedure. The most common adverse cardiac event was recoarctation. Types of previous surgical procedures and recoarctation are

shown in Table 3. There was no statistically significant difference in the incidence of recoarctation rates according to the type of surgery (p=0.787).

During long-term follow-up, there was no evidence of cerebrovascular accidents. However, there was (2.04%) mortality in one patient occurring 11 years postoperatively. There was no significant difference in the recoarctation rates between the patients who initially underwent patch angioplasty (recoarctation was seen in 44%) and the patients who initially underwent interposition grafting (recoarctation was seen in 40%) (p=0.787). The mean age at initial surgery of the patients with and without recoarctation was 20.5±11.5 years and 22.8±10.9 years, respectively, indicating no statistically significant difference (p=0.696).

A total of 61.5% of the patients with a bicuspid aortic valve previously had also aortic stenosis or aortic insufficiency on long-term follow-up. In contrast, aortic stenosis or aortic insufficiency in the absence of a bicuspid aortic valve was seen in only 22.2% of the patients (p=0.010, OR 5.6, 95% CI 1.4-21.9). The mean age of the patients at the time of surgery with postoperative hypertension was 27.7 ± 9.9 years. This was significantly higher (vs 18.9±10.6 years) than those who did not (p=0.006).

Of all patients, 22 had recoarctation of whom only three (6.12%) underwent repeat surgery. The first patient was a 48-year-old male who underwent aortoplasty. He had a peak gradient of 45 mmHg and presented with resistant hypertension and underwent a graft interposition 10 years after the initial operation. The second patient was a nine-year-old male who underwent end-to-end anastomosis. He presented with dyspnea and had a peak gradient of 35 mmHg and underwent aortic patch plasty nine years after the initial operation (end-to-end anastomosis). The third patient was a 19-year-old male with a peak gradient of 40 mmHg and presented with dyspnea and resistant hypertension. He had a residual gradient of 20 mmHg after the initial operation (end-to-end anastomosis) and he underwent aortic patch plasty four years later.

Table 3. Type of previous surgical procedures and recoarctation (n=49)

| | Recoarctation | | Reoperation | |
|---------------------------------------|---------------|------|-------------|---|
| | n | % | n | % |
| Type of previous surgical procedures | | | | |
| Patch angioplasty (n=25) | 11 | 44 | 2 | 8 |
| Interposition grafting (n=20) | 8 | 40 | 1 | 5 |
| Extended end-to-end anastomosis (n=3) | 2 | 66.6 | - | |
| Subclavian-plasty (n=1) | 1 | 100 | | |



Figure 1. Freedom from recoarctation rates after coarctation repair.

The remaining 19 patients who had a peak gradient of ≥ 20 mmHg were asymptomatic and, hence, are still under follow-up annually. Figure 1 shows the freedom from recoarctation rates of the patients after CoA repair. The rates of freedom from recoarctation were 93%, 84%, 74%, and 39% at three, five, seven, and 10 years, respectively. In the patch angioplasty group, the rates of freedom from recoarctation were 92%, 79%, and 74% at three, five, and seven years, respectively. In the interposition grafting group, the rates of freedom from recoarctation were 94% and 81% at three and seven years, respectively. There was no significant difference in the freedom from recoarctation rates according to the type of surgery (p=0.928) (Figure 2). The rates of freedom from reintervention after CoA repair are shown in Figure 3. The rates from freedom from intervention were 95% and 91% at five and seven years, respectively.

DISCUSSION

In the present study, we investigated the cardiovascular morbidity of a group of patients undergoing surgical repair for CoA who were followed postoperatively for a maximum of 144 months.

One of the major complications following CoA surgery is recoarctation with an incidence of 5 to 20%. However, the rate up to 60% has been also reported in the literature.^[9] The main criterion for recoarctation is a gradient difference ≥ 20 mmHg between the proximal and the distal site of the anastomosis.^[10] Some authors support the idea that a peak gradient of ≥ 35 mmHg as assessed by echocardiography is recoarctation.^[9] Recoarctation was found to be predominantly related to repair during infancy and is uncommon in adult patients.^[11] Despite other^[10,12] studies, Presbitero et al.^[6] reported higher rates in older patients. However, we found no significant difference in the mean age at the time of surgery. This may be due to the low number of



Figure 2. Freedom from recoarctation according to the type of surgery.



Figure 3. Freedom from reintervention of after coarctation repair.

patients (n=6) less than 10 years old. Our recoarctation rate was found to be 44.9% (n=22) based on an echocardiographic gradient of 20 mmHg; however, the rate was 16.3% (n=8) according to a gradient \geq 35 mmHg.

Recurrent coarctation has been reported after every type of CoA repair.^[13] The highest rate of recoarctation was seen in the patients who had patch plasty in our series. This was followed by the patients with graft interposition. The time lapse between the initial surgery and recoarctation remains undetermined; however, there was no significant difference in the time lapse between those who initially underwent patch plasty and those who underwent interposition grafting. Residual coarctation rather than coarctation may be the case in many patients, particularly within the first postoperative year.^[14,15] Recoarctation is also associated both with hypertension and increased mortality rates.^[6] The patch plasty technique has been widely used in many centers, including our hospital. However, the appearance of reports on late aneurysm formation following patch aortoplasty limited its application.^[16] Fortunately, none of our patients who underwent patch aortoplasty developed an aneurysm.

In any age group, recurrence of hypertension is common, even after a successful surgical repair of the CoA which eventually leads to occurrence of postoperative cerebrovascular diseases, heart failure, aortic ruptures, and acceleration of coronary artery disease progression.^[17] In our study, 19 patients (38.7%) presented with recurrent hypertension. The cause of late hypertension is related to abnormal baroreceptor functions and neuroendocrine activation,^[18] and the prevalence depends on age at the time of repair.^[12] Our study revealed that the mean age at the initial surgery of the patients who developed postoperative hypertension was higher than those who did not.

In a study Stewart et al.^[11] showed that 23% of the survivors had an evidence of coronary heart disease, whereas two patients (4.08%) with hypertension in our study had coronary artery disease. These patients had no significant coronary artery stenosis. In addition, data from the Cohen's study^[19] indicated that deaths due to coronary artery disease were related to the duration of preoperative hypertension and its recurrence following surgery.

Diseases of the aortic valve and the aorta itself before and after the coarctation repair play also a key role in predicting postoperative disease progression. It has been shown that bicuspid aortic valve with coexisting CoA may be present in up to 80% of the cases.^[20] The valve may function normally or may advance to stenosis or regurgitation with progressive calcification. In addition, patients with bicuspid aortic valves have a 9-18-fold higher incidence of developing an aortic aneurysm due to accelerated degeneration of the aortic media.^[21,22] This indicates that a bicuspid aortic valve is a continuous pathological process.^[23] Dilatation, aneurysm, and dissection may develop in patients due to loss of the structural support of the aortic wall.^[23,24] According to our study, the association of aortic stenosis or aortic insufficiency with presence of a bicuspid aorta was higher than in those with a tricuspid aortic valve. The imaging of the repaired CoA should be performed at least every five years,^[7] or sooner based on original anatomy and symptoms, to assess the coarctation repair site for complications such as aortic aneurysm. Therefore, we recommend annula follow-up using CT for patients with a bicuspid aortic valve.

The presence of cerebrovascular accidents may result from recurrent hypertension and its prolonged duration. Pre-existing Berry aneurysms and wall defects in the circle of Willis may also play an important role. None of our patients had cerebrovascular complications. This may be due to strict blood pressure control following CoA repair. In addition, all patients were informed that their life-long blood pressure control was critical and routine check-up was strictly applied.

Bearing in mind the aforementioned issues, the reduction in the long-term survival of these patients is obvious. Brown et al.^[25] reported the actuarial survival of the patients undergoing surgical repair of CoA as 93.3%, 86.4% and 73.5% at 10, 20, and 30 years, respectively. Therefore, all the patients should be well-informed about the necessary postoperative follow-up procedures.

With many controversial options, deciding on the optimal treatment strategy for CoA can be complicated, and it varies in different age groups. Studies with CoA are usually in newborns and infant patients. Our study in which the majority of the patients were in the adolescent and adult age groups, therefore, is different from the classical CoA studies by age. We believe that this study put forth valuable information due to the age of our population.

Surgical treatment was the only treatment option for CoA until 1982, when the use of balloon angioplasty was described by Lock et al.^[26] Several studies since then have shown balloon angioplasty to be a relatively effective acute intervention for native coarctation with rates of recoarctation ranging from 8 to $32\%^{[27-29]}$

and aortic aneurysm 24%.^[29] In contrast to native coarctation, balloon angioplasty is often the preferred procedure for recurrent coarctation in children.^[8] In the older children, adolescent, or adult presenting with a simple, juxta-ductal, native coarctation, stent placement is considered a reasonable approach, offering a less invasive alternative to surgical intervention and favorable long-term outcomes.^[7,8] For recurrent coarctation in younger children, it is reasonable to consider initial balloon angioplasty, as aneurysm formation is less of a long-term concern than with native coarctation.^[8] Balloon angioplasty is variably successful, and surgical reintervention may be required, when there is incomplete relief of obstruction.^[29] In rare cases with aneurysm development at the initial presentation of CoA, surgical intervention may deem necessary without seeking for percutaneous treatment options.^[30] Stent placement can be also considered for recoarctation in older children and adolescents.^[8] In brief, Surgical intervention continues to be an option in all age groups for the treatment of recoarctation.

Furthermore, the long-term prognosis and possible morbidity of these patients following surgical repair of CoA underlines the necessity for effective long-term follow-up. Recommendations include strict control of blood pressure using ECG, chest radiography, echocardiography, and CT or magnetic resonance imaging (MRI), when necessary. Electrocardiography is useful in detecting ischemia and left ventricular hypertrophy.^[14] However, ECG results are normal in 25 to 48% of cases following surgery.^[6] Chest radiography may also demonstrate cardiomegaly in approximately 20% of cases, mostly in those with hypertension or aortic valve disease.^[11,14,31,32] Echocardiography may provide useful information about the valvular valvar diseases, ejection fraction, wall motion abnormalities, ventricular hypertrophy, other associated congenital lesions, and the diameter of the ascending aorta. A more important application of echocardiography is for the evaluation of gradient following surgery. In particular, patients who are at a high risk of recoarctation should undergo regular echocardiographic evaluation. For patients requiring further assessment, CT/MRI or catheterization can be performed. All patients should be recommended for endocarditis prophylaxis.^[20]

Nonetheless, there are some limitations to this study. Although 110 patients underwent surgical repair for CoA, only 49 patients (44.5%) were contactable and underwent follow-up in the outpatient setting. The rest of the patients, who were suspected to be symptom-free, did not attend regular postoperative examinations and failed to update their contact information; therefore,

they were unable to be contacted. In addition, the longest follow-up period is no longer than 144 months in our clinic. The patients who underwent surgery from January 2011 to date were excluded from the study, since the follow-up period would be too short for a complete evaluation. Furthermore, the patient population was heterogeneous, including children from the age of three to adults aged 56 years.

In conclusion, our study results showed no significant difference in the rates of freedom from recoarctation according to the type of surgery. Any technique can be selected for the repair of coarctation of the aorta; however, further studies are needed in larger patient series. Based on our study results, even following a successful repair of coarctation of the aorta, recoarctation and further cardiac diseases such as aortic aneurysms, aortic valve diseases, and ischemic heart disease may develop in these patients. Long-term survival of these patients is also reduced in these patients, and some require re-do surgery. The impaired long-term prognosis and high morbidity rates, despite a successful surgical repair, highlight the importance of long-term follow-up in this patient population.

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