Balloon Angioplasty for Native Coarctation of the Aorta in Children: Immediate Outcome and Follow-up for Heart Function

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ABSTRACT

Background: The effect of balloon angioplasty in treatment of coarctation of the aorta (COA) in pediatric patients is very important.

Objectives: This study aimed to assess the efficacy and safety of balloon angioplasty for coarctation of the aorta (CoA) and its effects on heart function in children above 3 months of age.

Patients and Methods: In this retrospective study, we reviewed the immediate outcomes of 100 consecutive pediatric patients above 3 months of age with native CoA who were treated by balloon angioplasty at a tertiary pediatric heart center from June 2002 to August 2012. The patients were followed by echocardiography. Statistical analyses were performed by descriptive statistics using the SPSS statistical software, version 20 and the significance level was set at 0.05.

Results: The patients’ ages ranged from 4 months to 15 years, with the mean of 51.56 ± 42.22 months. Additionally, their body weight ranged from 4 to 63 kg (mean: 15.44 ± 10.62 kg) at the time of CoA repair. Technical success of balloon dilation was achieved in 91/95 patients (95.7%). Besides, systolic gradient significantly reduced from 48.29 ± 21.62 mmHg (range 7 - 82 mmHg) to 13.21 ± 9.96 mmHg (range 0 - 34 mmHg) (P < 0.0001). The mean follow-up period was 2.21 ± 0.94 years. Recoarctation and cardiac dysfunction occurred only in 4 patients. Z-scores of the Left Ventricular (LV) end diastolic and systolic dimensions were more than 2 standard deviations in 15 (17.1%) and 22 (25%) patients, respectively. In addition, there were 16 children (18.8%) with abnormal E/A ratios and 6 ones (6.8%) with E/Ea > 15.

Conclusions: Percutaneous balloon angioplasty was a safe and effective treatment option for native CoA in the children above 3 months old. However, impairment of LV diastolic function should be mentioned as an important issue in long-term follow-up.

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1. Background

Native Coarctation of the Aorta (CoA) is the fifth most common congenital heart defect, accounting for 6 - 8% of all congenital heart diseases with an estimated incidence of 1 in 2,500 births (1). Open surgical repair was described by Crafoord and Nylin in 1945 (1). It was the only choice for CoA for over 4 decades until percutaneous Balloon Angioplasty (BA) was first introduced in 1982 as a less invasive procedure for treatment of native CoA (2). Since then, it was applied in many centers and a large number of studies have reported its success in treating native and recurrent coarctation (3-9). Despite more than 30 years of experience, the results of both approaches have been associated with several complications, such as aortic rupture, aneurysm formation, and recoarctation (10). Moreover, due
to limited follow-up for both surgical and transcatheter approaches, there are differences regarding the superiority of one treatment option over the other (11, 12). Although several studies have compared the outcomes of surgical and transcatheter approaches, their results have been inconsistent due to the small number of patients. Recently, the results of a meta-analysis of 9 studies comparing the outcomes of surgery versus BA approach for CoA showed that BA was comparable to surgery when considering the immediate results, but it did not provide better mid- and long-term outcomes and even increased the incidence of aneurysm formation (13). On the other hand, tendency to myocardial remodeling has been observed in children with a successful intervention for CoA. Left Ventricular (LV) impairment was also common in these patients (14-16).

2. Objectives
The present study aims to evaluate the outcome and heart function after BA of native coarctation in children.

3. Patients and Methods
From June 2002 to August 2012, 100 pediatric patients older than 3 months with native CoA were treated by BA at our tertiary pediatric heart center and they were all included in this study. CoA was diagnosed based on a combination of clinical signs (arm-leg blood pressure gradient > 20 mmHg, weakness pulses in lower extremities) and Doppler echocardiographic findings of typical coarctation flow patterns in the isthmus and the descending aorta.

Baseline characteristics of the patients, including age, gender, weight, blood pressure, heart rate, and previous cardiac interventions, were extracted from their medical records. In order to obtain the results of BA, peak systolic pressure gradient across the coarctation site was measured after balloon dilation as the initial success. At follow-up, all the patients were reevaluated by 2-dimensional, M-mode, Doppler, and tissue Doppler echocardiography to determine systolic and diastolic function. In addition, blood pressure gradients between upper and lower extremities exceeding 20 mmHg were considered to be recoarctation of aorta.

Echocardiography was performed with a GE vivid 3 system (GE Vingmed, Horten, Norway) using a 2 - 7 Mhz transducer. All echocardiographic measurements were taken by one pediatric cardiologist. Indeed, several parameters of cardiac function were assessed to raise intra-observer reliability. Echocardiographic studies included 2-dimensional, M-mode, Doppler, and tissue Doppler echocardiography. M-mode echocardiography consisted of measurement of inter-ventricular septum and left ventricular posterior wall diameter in systole and diastole. Ejection fraction and fractional shortening were also measured in the long-axis view. Additionally, early diastolic inflow velocity (E), velocity during active atrial contraction (A), and E to A wave (E/A) ratio were measured by pulsed wave Doppler at leaflets mitral (M) tips. Pulsed wave tissue Doppler velocities were obtained at the cardiac base in the apical four-chamber orientation from two locations: the lateral mitral annulus and the inter-ventricular septum. Therefore, peak systolic annular velocity (S), peak early diastolic annular velocity (Ea), and peak late diastolic annular velocity (Aa) were obtained. All values were compared to normal values from pediatric and fetal Z score calculator website (17, 18).

Initial success and LV function were considered to be immediate and long-term outcomes, respectively. The initial success of balloon dilation was defined as a peak systolic pressure gradient across the coarctation site of less than 20 mmHg.

Balloon dilation was performed after written informed consents were obtained from the patients’ parents. Catheterization and angioplasty were carried out under fluoroscopy guidance in the cardiac catheterization laboratory. The procedure was performed under sedation with midazolam and propofol. Retrograde femoral arterial approach was used in all patients. In doing so, the balloon was inflated at the site of aortic stenosis 2 - 3 times under the pressure stated by the manufacturer, and radial arterial pressure was monitored during the procedure. Moreover, the technique and equipment of the procedures were similar over the 10-year period.

3.1. Statistical Analysis
The study data were analyzed using the SPSS statistical software, version 20 (SPSS Inc., Chicago, IL, USA). The values were expressed as mean ± Standard Deviation (SD) for quantitative variables and percentages for categorical ones.

4. Results
4.1. Demographics
Out of the 100 patients selected for the study, five were excluded due to missed follow-up and finally, 95 patients were included in the study. Among the participants, 56 were male and 39 were female. Besides, the patients’ age ranged from 4 months to 15 years with the mean of 51.56 ± 42.22 months. Their body weight also ranged from 4 to 63 kg (mean: 15.44 ± 10.62 kg) at the time of CoA repair.

4.2. Immediate Outcomes
The mean value of the peak-to-peak systolic ascending to descending aorta pressure gradient significantly reduced from 48.29 ± 21.62 mmHg (range: 7 - 82 mmHg) to 13.21 ± 9.96 mmHg (range: 0 - 34 mmHg) (P < 0.0001). Technical success of balloon dilation was achieved in 91.95 patients (95.7%). In 4 patients, however, the immediate success was not achieved due to persisting coarctation membrane. Therefore, they underwent a second BA after 2 - 3 months and all procedures were successful at this time.

4.3. Follow-up
The mean follow-up period was 2.21 ± 0.94 years. Recoarctation and cardiac dysfunction did not occur in any of the patients and only 4 patients did not require second percutaneous balloon dilation during the follow-up period. Additionally, two patients developed aneurysmal formation at the site of BA. Arterial damage with complete occlusion of the left femoral artery and collateral formation also occurred in one patient. Moreover, no mortality was encountered in the patients under investigation.

M-mode echocardiographic parameters of the treated CoA patients were represented with absolute values and Z scores
(Table 1). Accordingly, Z scores of the LV end diastolic and systolic dimensions were more than 2 standard deviations in 15 (17.1%) and 22 (25%) patients, respectively. Additionally, Z scores of the LV posterior wall thickness in systole and diastole were more than two standard deviations in 48 (54.5%) and 21 (23.8%) patients, respectively. In addition, Z scores of interventricular septal thickness in diastole and systole were more than 2 standard deviations in 36 (40.9%) and 30 (34.1%) patients, respectively.

Doppler echocardiography of mitral valve showed that mitral E wave velocity, mitral A wave velocity, and E/A ratio were 127.15 ± 28.43, 91.28 ± 34.39, and 1.52 ± 0.49, respectively (Table 2). The absolute and Z score values of tissue Doppler velocities of lower septal and lateral mitral valve annular have also been presented in Table 2. As the table depicts, there were 16 children (18.8%) with abnormal E/A ratios among whom, 7 patients (7.9%) had E/A ratio < 1 and 9 ones (10.9%) had E/A ratio > 2. Furthermore, there were 6 children (6.8%) with E/Ea > 15.

5. Discussion

The challenge continues for the ideal treatment option in children with CoA. The results of the previous experiences during the past 30 years have indicated that recoarctation, as a complication, has been associated with both coarctation repair procedures (surgical and BA). Therefore, making decision about the superiority of one procedure over the other is quite difficult (19). Wong et al. (12) reviewed the articles published from 1984 to 2005 to compare the outcomes of the two treatment options in patients with native CoA. The results demonstrated that the risk of recoarctation and aneurysmal formation was lower in BA than in surgery and, consequently, BA was preferred over surgery as the initial intervention for native CoA in children more than 3 months of age. Therefore, BA of native coarctation appears to be gaining more acceptance in older children. On the other hand, this treatment option has not been well established in neonates and young infants because of the higher incidence of recoarctation and aneurysm formation in comparison to surgery (20-22). After 20 years of experience with percutaneous intervention for CoA at our center, we still believe that percutaneous intervention provides a complementary alternative to surgery and both surgery and cardiology teams should work together to find the best possible management for each patient regarding one’s age and clinical conditions.

In the current study, the initial success rate of BA was 95.7% and only 4/95 patients required second percutaneous BA due to failure in dilatation at the first time. This was concordant with other studies in which, the early success rate ranged from 88% to 100% (7, 23). On the other hand, recoarctation occurred in 4% of the cases requiring second percutaneous BA for recoarctation during the follow-up period. This is in contrast to the results of most studies, which reported the rate of recoarctation to range from 7% to 30% in children aged above 3 months (3, 24, 25). This variation may depend on specific aspects of angioplasty technique, including balloon diameter and the high incidence of recoarctation reported in patients below 3 months old. Undoubtedly, our finding is difficult to interpret and could probably result

<table>
<thead>
<tr>
<th>Table 1. Left Ventricular M-Mode-Derived Measurements</th>
<th>Absolute Value</th>
<th>Z Score</th>
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<tbody>
<tr>
<td>LV end-diastolic dimension</td>
<td>2.64 ± 0.91</td>
<td>0.14 ± 1.95</td>
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<tr>
<td>LV end-systolic dimension</td>
<td>1.81 ± 0.59</td>
<td>-0.72 ± 1.98</td>
</tr>
<tr>
<td>Interventricular septal thickness in diastole</td>
<td>0.72 ± 0.21</td>
<td>1.68 ± 1.34</td>
</tr>
<tr>
<td>Interventricular septal thickness in systole</td>
<td>0.93 ± 0.31</td>
<td>1.43 ± 1.88</td>
</tr>
<tr>
<td>Posterior wall thickness in diastole</td>
<td>0.63 ± 0.18</td>
<td>1.98 ± 1.26</td>
</tr>
<tr>
<td>Posterior wall thickness in systole</td>
<td>0.77 ± 0.21</td>
<td>-0.52 ± 1.7</td>
</tr>
<tr>
<td>Shortening fraction (%)</td>
<td>35.45 ± 23.13</td>
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<tr>
<td>Ejection fraction (%)</td>
<td>74.63 ± 12.23</td>
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Abbreviations: LV, left ventricular

<table>
<thead>
<tr>
<th>Table 2. Longitudinal Systolic and Diastolic Functions</th>
<th>Absolute Value</th>
<th>Z score</th>
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<tr>
<td>Mitral valve Doppler</td>
<td></td>
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<tr>
<td>E (cm/s)</td>
<td>127.15 ± 28.43</td>
<td></td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>91.28 ± 34.39</td>
<td></td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.52 ± 0.49</td>
<td></td>
</tr>
<tr>
<td>Tissue Doppler, septal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sa (cm/s)</td>
<td>8.51 ± 2.1</td>
<td>1.05 ± 1.47</td>
</tr>
<tr>
<td>Ea (cm/s)</td>
<td>11.58 ± 3.34</td>
<td>-0.01 ± 1.56</td>
</tr>
<tr>
<td>Aa (cm/s)</td>
<td>8.76 ± 1.93</td>
<td>1.95 ± 1.41</td>
</tr>
<tr>
<td>E/Ea</td>
<td>11.65 ± 3.84</td>
<td></td>
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<tr>
<td>Tissue Doppler, lateral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sa (cm/s)</td>
<td>8.69 ± 2.26</td>
<td>1.27 ± 1.24</td>
</tr>
<tr>
<td>Ea (cm/s)</td>
<td>13.51 ± 4.07</td>
<td>-0.35 ± 0.4</td>
</tr>
<tr>
<td>Aa (cm/s)</td>
<td>8.72 ± 2.11</td>
<td>0.51 ± 1.5</td>
</tr>
<tr>
<td>E/Ea</td>
<td>10.16 ± 3.77</td>
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from intermediate follow-up. Hence, we need to increase the duration of the follow-up period.

Similar to the results of BA found in the previous studies, the findings of the present study revealed a significant reduction in peak systolic pressure gradient across the coarctation site immediately after balloon dilation (2-5, 7-10). Reduction of the residual gradient can be certainly expected when growth occurs and flow increases relatively after CoA repair procedures (26). However, the results of a review article including 9 studies with 623 patients demonstrated no significant difference between the two CoA repair procedures (surgery or BA) concerning the post-intervention gradient (13). In our study, the pressure gradient reduced by about 35 mmHg, which was more pronounced compared to the previous experiences.

Review of the literature showed that LV diastolic function was significantly impaired even in children with a successful CoA repair compared to healthy controls, which might be due to the persistently elevating aortic stiffness (27). Generally, vascular stiffening is associated with aging, hypertension, and a variety of systemic disorders. In this context, multifold mechanisms, including atherosclerosis, vascular smooth muscle cell stiffening, congenital or acquired changes in extracellular matrix, endothelial dysfunction, and inflammation have been described (28-30). It seems that primarily abnormal aortic wall structure also plays a role in increasing aortic stiffness in children with repaired CoA, bicuspid aortic valves, or Marfan syndrome (31, 32). Indeed, chronic inflammation and endothelial dysfunction should be mentioned as other causes of increase in aortic stiffness in patients with repaired CoA.

In accordance with a previous study, the echocardiographic findings of our study demonstrated that LV diastolic function was impaired in about 50% of the children with repaired CoA (27). However, we did not measure the parameters of aortic stiffness in echocardiography, which is one of the limitations of our study. Further limitations are lack of a long-term follow-up and the relatively small sample size. In conclusion, percutaneous BA was a safe and effective treatment option for native CoA in the children above 3 months of age depending on their clinical conditions. However, impairment of LV diastolic function should be mentioned as an important issue in long-term follow-up in children with repaired CoA.

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Authors’ Contribution

Study design: Amoozgar, Bahmanpour; Drafting: Amoozgar, Edraki; Analysis: Farhadi, Edraki, Bahmanpour; Supervision: Borzoei, Ajami, Mohammadi, Cheriki.

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