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Heart function and remodeling after successful stenting of coarctation of aorta in children

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Abstract

Background: There are not enough studies investigating the results of stent implantation for Coarctation of the Aorta (COA) in the pediatric age group.

Objective: This investigation evaluated the heart function and remodeling after successful COA stenting in children.

Materials and method: The study was performed from April 2017 till April 2020 on patients with COA (<18 years old) referring to Namazi, Faghihi and Kowsar hospital, tertiary centers from 2010 till 2017. Demographic data, clinical examination results and echocardiographic parameters were reported. All statistical analyses were performed with the SPSS version 22.

Results: Fourty-two children were enrolled in this study. Mean age at the time of stenting was 10.44 ± 3.93, and mean follow-up was 3.57 ± 3.40 years (1-6 years). 24 patients (77.8%) were male. Measurement of thoracic aorta diameters revealed that mean transverse arch, isthmus and distal arch diameter with its z-scores were 1.40 ± 0.43 (Z score = -1.50 ± 1.33), 1.17 ± 0.28 (Z score =-0.72 ± 1.43) and 1.21 ± 0.42 (Z score = -0.94 ± 3.46). Mean systolic blood pressure at the follow-up time was 122.5 ± 17.70 mmHg, and mean diastolic blood pressure was 81.25 ± 9.57. Significant correlation existed between IVSd value and transverse arch diameter (P=0.023, r=0.564), and also distal arch diameter (P=0.039, r=0.521). There was also a significant correlation between LVIDd and measured transverse (P=0.007, r=0.648) and distal arch diameter (P=0.034, r=0.521). Instead, the correlation between E/A value and IVSs (P=0.023) and IVSs Z score (P=0.044, r=0.480) was significant. There was a significant correlation between LVPWd parameter and Doppler measurement of the gradient at the stent site (P=0.024, r=0.621) measured at the time of follow-up.

Conclusion: Based on the results, endovascular stenting to treat CoA appears to be a safe and efficient method. LV hypertrophy and diastolic dysfunction did not regressin a significant number of patients after successful stenting.

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Background

Coarctation Of the Aorta (CoA) is usually a lesion next to the origin of ductus arteriosus or ligamentum arteriosum [1]. CoA has different clinical performances in neonates, kids and adult patients, which is the one of most common Congenital Heart Disease (CHD) with an incidence rate of 1 in 2500 live births [2]. The incidence rate may be higher in miscarried neonates. It is more commonamong male babies, with a reported male to female ratio between 1.27 to 1.74:1 [3].

Human studies have recognized genes that cause different forms of inherited or sporadic heart defects [4]. Even though most patients with CoA are sporadic, the possibility of a geneticelement is high. CHDs occurring in at least 4% of women's offspring with CoA, while there are approximately five-times increased possibility of the bicuspid aortic valve in relative of children with left-sided obstructive lesions [5].

Recognizing it very early is important because rapid deterioration might occur with the arterial duct closure, which tends to have a less favorable prognosis in ill pre-operative children [6].

CoA treatment options include surgery, balloon angioplasty, and endovascular stenting. In the last three decades, percutaneous transcatheter balloon angioplasty orstenting has become aproper substitute for open-heart surgery. Nevertheless, these procedures might result in some complications, such as aneurysm formation, dissections, and sometimes lethal rupture of the aortic. Endovascular stenting was developed two decades ago, but its application in growing children is still controversial [7].

Stenting of COA can reduce shrinkage of the stenotic segment, which reduces the frequency of aneurysms. In the mid-term follow-up, this rate is about 8%. Stenting in children similar to adults has achieved great success by reducing the stenotic part pressure gradient to < 20 mmHg or in most patients increase the stenotic part diameter ratio to the descending aorta to more than 0.8. The post-stent CoA systolic gradient of less than ten mmHg was also detected in almost 92% of patients [8,9].

Objective: Few studies have investigated stenting for CoA in the pediatric age group. Therefore, our study was designed to evaluate heart function and remodeling after CoA in pediatric patients.

Patients and methods

This study was performed from April 2017 till April 2020 in all children with CoA (<18 years old) referred to Namazi, Faghihi, and Kowsar hospital, tertiary healthcare centers affiliated to Shiraz University of Medical Sciences, from 2010 to 2017 and their data was avilable. CoA diagnosis was based on clinical signs, such as >20 mmHg blood pressure difference between upper and lower limb.

Inclusion criteria were patients diagnosed with CoA, and they were younger than 18, their catheterization data were complete and accepted the participation in this study. The Exclusion Criteria were the patients with uncompleted documents and inaccessible for follow-ups.

Interventions and outcomes

Stenting of coarctation was achieved under fluoroscopy. The stenting was done under a pediatric anesthesiologist's supervision, and sedation with performed with combination of midazolam, ketamine, fentanyl, and propofol. Baseline features included gender, age and Body Mass Index (BMI), cardiovascular medication, blood pressure, previous cardiac interventions detail, coarctation gradient, and anatomy, the result after stent implantation was obtained from the patient's chart and recorded catheterization movies.

To obtain the results of stent implantation, all patients were asked to return for follow-up examinations that included blood pressure measurements and echocardiography to determine blood pressure status, the diameter of the thoracic aorta, Left Ventricle (LV) systolic heart function, diastolic heart function during follow-up.

Echocardiography

Echocardiography was performed with a Mindray echocardiography machine using 2-4 MHz transducer. Echocardiographic studies included measuring the left ventricle's M-mode parameters, two-dimensional study of coarctation segment, Doppler peak velocities, and tissue Doppler peak velocities.

The measured M-Mode echocardiography parameters of LV contained inter-ventricular septum, posterior wall diameter, and internal diameter.

Inpulsed Doppler, velocities of mitral and tricuspid valve were measured (early peak diastolic velocity (E), peak late diastolic velocity (A), and their ratio were measured.

Tissue Doppler peak velocities were acquired in theapical four-chamber view from the lateral mitral annulus, inter-ventricular septum, and lateral tricuspid annulus. In each area, peak systolic velocity (S), early peak diastolic velocity (Ea), and late peak diastolic velocity (Aa) were documented.

EtoAratioofmitralvalvedecreasesintheearlyphaseofdiastolic dysfunction. Another parameter to define diastolic dysfunction is E to Ea ratio that increases in the state of diastolic dysfunction.

All recorded values were compared with normal Z scores from pediatric and fetal Z score calculator websites (73,74). Z score values of echocardiographic parameters higher than 2 and less than -2 were considered abnormal. The normal range of E/A value was considered 1-2 and measured E/Eam values of less than 10 were considered normal.

Statistical analysis

All statistical studies were directed with the SPSS version 22 (SPSS Inc., Chicago, IL, USA). Data were offered as the mean ± one Standard Deviation (SD). The t-test was used to evaluate the deference of mean and Chi-square test to present categorical variables. P-values less than 0.05 were considered to be statistically significant.

Results

Fourty-two patients were enrolled in this study. Patients characteristics are shown in Table 1.

Table 1: Baseline characteristics of subjects.

Title	Patients
Age (at time of implantation, year) Mean ± SD (Min – Max)	10.44 ± 3.93 3 – 17
Age (at time of follow up, year) Mean ± SD (Min – Max)	12.61 ± 3.55 5 – 18
Follow up duration (year) Mean ± SD (Min – Max)	3.57±3.40 (1-6)
Weight (Kg) Mean ± SD (Min – Max)	43 ± 35.5 22 – 85
Gender Male (N/%)	24 (77.8%)

Table 2: M-mode, doppler and tissue doppler echocardiographic parameters and Z scores (mean ± SD).

Title	Mean ± SD	Z-Score
IVSs (mm)	1.30 ± 0.31	1.72 ± 1.34
IVSd (mm)	1.02 ± 0.28	2 ± 1.08*
LVIDs (mm)	2.13 ± 0.48	-1.01 ± 1.94
LVIDd (mm)	4.29 ± 0.48	0.08 ± 1.07
LVPWs (mm)	1.13 ± 0.27	-0.01 ± 1.33
LVPWd (mm)	0.89 ± 0.17	2.07 ± 0.98*
EF (%)	81.19 ± 7.99	
Doppler		
Mitral Valve E	124.3 ± 20.07	1.83 ± 0.52
Mitral Valve A	72.09 ± 17.27	1.78 ± 0.81
E/A	1.78 ± 0.36	-0.36 ± 0.22
Tissue doppler		
S	9.80 ± 2.33	1.02 ± 0.21
Ea	16.81 ± 3.63	-1.06 ± 0.61
Aa	8.41 ± 1.85	1.2 ± 0.43
S	10.11 ± 2.66	0.51 ± 0.21
Ea	13.82 ± 2.51	1.35 ± 0.76
Aa	9.32 ± 3.62	1.01 ± 0.63

*Abnormal, IVSs: Inter Ventricular Septal Diameter in Systole; IVSd: Inter-Ventricular Septal Diameter In Diastole; LVIDd: Left Ventricular Diameter In Diastole; LVIDs: Left Ventricular Diameter In Systole; LVPWs: Left Ventricular Posterior Wall Diameter In Systole; LVPWd: Left Ventricular Posterior Wall Diameter Indiastole; EF: Ejection Fraction; FS: Fractional Shortening; ESV: End Systolic Volume; SV: Systolic Volume.

The treated patients' M-mode echocardiographic parameters were not different from their normal values except in interventricular septum in diastole and LV posterior wall in diastole. Values and Z- scores are shown in Table 2.

The number and percent of patients with an abnormal z score value of M mode echocardiography are shown in Table 2.

In our study population, ten patients (27.7%) had abnormal E/A values and four of them (11.1%) had E/Ea abnormal values that were indexes of diastolic dysfunction. Obtained Doppler and tissue Doppler parameters are reported in Table 2,3.

Aortic isthmus diameter z score increased significantly after stenting, which was stable during the follow-up. Aortic arch diameter just after stenting and at the time of follow-up are reported in Table 4.

Table 3: The number (percent) of patients with abnormal z score value of echocardiographic parameters.

Title	Number (%)	Title	Number (%)
IVSd Z-score	18 (50%)	LVIDd Z	0
IVSs Z-score	16 (44.4%)	LVPWs Z-score	4 (11.1%)
LVIDs Z-score	14 (38.8%)	LVPWd Z-score	20 (55.5%)

Table 4: Aortic isthmus diameter before stenting, after stenting and at follow up.

Variable	Diameter before stenting	Z score before stenting	After stenting	Z score After stenting	Diameter at follow up	Z score at follow up
Aortic isthmus diameter	149.6 ± 22.40	-2.48 ± 1.78*	138.1 ± 24.86	-0.82 ± 0.66*	1.17 ± 0.28	-0.92 ± 0.83
Gradient of coarctation	41.12 ± 23.13		5.07 ± 5.0		35.04 ± 11.43	

Table 5: The correlation between M-mode and tissue doppler echocardiographic parameters and other studied parameters.

Title		P value	Correlation
IVSd	Transverse Arch of CoA	0.023	0.564
	Distal Arch of CoA	0.039	0.521
	Diaphragm diameter of Aorta	0.002	0.532
IVSs	E/A	0.023	0.532
IVSs – Z score	DBP	0.018	0.581
	E/A	0.044	0.480
LVIDd	Transverse Arch of CoA	0.007	0.648
	Transverse Arch of CoA – Z score	0.008	0.640
	Distal Arch of CoA	0.034	0.531
LVPWd	Diaphragm diameter of Aorta	0.006	0.611
	Septum S	0.045	0.492
	gradient of CoA at follow up	0.024	0.621
Transverse Arch	Septum S	0.034	0.548
	Septum Aa	0.010	0.639
Transverse Arch Z score	Septum S	0.008	0.657
	Septum Aa	0.016	0.609
Transverse Arch	Septum S	0.034	0.548

At the time of stent implantation, 18 patients had systolic hypertension. However, after that, only 4 patients had systolic hypertension (who managed with anti-hypertensive drugs), and the mean systolic blood pressure in patients at the time of follow-up visit was 122.5 ± 17.70 mmHg (Min = 90, Max = 150) and mean diastolic blood pressure was 81.25 ± 9.57 (Min = 70, Max = 100).

All M-Mode echocardiographic values had a statistically significant correlation with aortic diameters and Doppler and tissue doppler parameters. These correlations are shown in Table 5.

Aortic arch diameters had a significant correlation with tissue Doppler parameters. The results are shown in table 5.

Discussion

If not treated, CoA might result in complications and mortality. The mean age of patients'life expectancy is 34 years [10]. CoAstenting is an alternative to surgery [9]. For the treatment of native and recurrent CoA, endovascular stenting seems to bean efficient method with lower complications than surgery. Some patients might demand further redilation in the upcoming follow-ups [11,12]. In Carr JA et al. study, they had performed a review to compare endovascular therapy results (stenting and angioplasty) with heart surgery in the repair of adults with CoA, and they showed that morbidity during primary stenting had a lower risk of complication, and balloon angioplasty had statistically significantly higher risk [13]. The most common re-interventions were repeated angioplasties for the recurrent of COA, due to migrations of the stent or dissections of the aortic wall, and referral to the operating room for repair of the iatrogenic aneurysm. There was a higher risk of repeating the intervention after percutaneous angioplasty and stenting in comparison with the invasive operation [14]. Hence, they concluded that both therapies relieve hypertension with similar effectiveness; however, there are no studies on the long-term effect of CoA stenting.

At the time of stenting, the mean age of patients was 10.44 ± 3.93 which shows delayed diagnosis of CoA in our study. In Yıldırım Iet al., study [15], the mean age at diagnosis was12 ± 4.6 years. However, in Correia AS et al., study the mean age of CoA diagnosis in hypertensive and non-hypertensive patients was 6.2 ± 6.9 and 6.9 ± 8.2 years, respectively [16]. Considering the time of intervention and CoA diagnosis in several studies in comparison to ours, their results were in line with ours. In our study, 14 patients (77.8%) were male, male dominancy was similarly reported in other studies (77,78). 70.3 % (N=576) patients were male in Brown ML et al., [17] study, and also in Tong F et al., [18] study 75.7% (N=81) patients were male.

M-mode echocardiographic measurements showed LVPWd diameter in 55.5%, IVSd in 50% patients, IVSs in 44.4%, and LVIDs in 38.8% patients were thicker than normal. These values show that LV hypertrophy had not regressed in significant number of patients despite successful stenting,and was not related to blood pressure, age and time after stenting [19].

In Doppler echocardiography five patients (27.7%) had abnormal E/A values, and two of them (11.1%) had E/Ea abnormal values. A study by Yat Yin Lam et al. in adult patients before and 14 months after stenting showed no significant difference in LV ejection fraction and conventional Doppler measurements. N However, LV function upgraded at follow-up [19]. Another study showed that left ventricle thickening persisted, and long axis function and dilation of left atrium persist after the intervention [20].

The aortic arch evaluation revealed that mean transverse arch, isthmus, and distal arch mean Z-score of these parameters were less than normal for body surface area.

Blood pressure monitoring revealed that nine patients had systolic hypertension at the time of stenting. However, after stenting, only two patients had systolic hypertension, and the mean systolic blood pressure in patients at the time of follow-up visit was 122.5 ± 17.70 mmHg (Min = 90, Max = 150) and mean diastolic blood pressure was 81.25 ± 9.57 (Min=70, Max=100). Consequently, in our study population, significant decrease in systolic blood pressure was observed. As in Bentham et al., study [21] improvement in lifelong systemic BP control after transcatheter stent placement was evaluated. They found that after stenting there was a significant improvement in systolic BP in midterm follow-ups. Hence, they concluded that transcatheter stenting to manage CoA was accompanying by reduced systolic BP. Few patients remained significantly hypertensive, but the best strategy to manage this group is still unclear.

In a study by Melissa G. Y. Lee et al., the prevalence of hypertension late after coarctation repair was determined, and the possibility for end-organ injury related to systemic hypertension after coarctation repair was evaluated. In their study, after a follow-up of 24 years, 27% were suffering from resting hypertension. On 24-hours BP monitoring, 61% and 21% suffered hypertension and borderline hypertension, respectively. They concluded that there was a significant percentage of hypertension after coarctation repair. The presence of retinal imaging defects, as well as left ventricular hypertrophy, showed the presence of end-organ damage [22].

Tissue Doppler echocardiographic parameters such as septum S, Aa and Ea values significantly correlated with arch diameters. Septum S wave and Aavalue velocity had a significant correlation with the transverse arch diameter and their Z score.

The correlation between E/A value and IVSs and IVSs z score was significant. IVSs z score had a significant correlation with diastolic blood pressure. Evaluation of flow gradient revealed a statistically significant correlation between LVPWd parameter and gradient of CoA measured during the follow-up.

In Melissa G. Y. Lee et al., study [22], recoarctation (peak echocardiography gradient > 25 mmHg) was present in 15%, and only 15% had hypertension during 24-hours post CoA repair. Hypertrophy of left ventricle in echocardiography was present in 63% who had hypertension in 24 hours BP monitoring in comparison with only 42% with normal 24-hours BP monitoring (p = 0.06).

During the study period, there was no complication or reintervention reported. In Tzifa et al. Study, the peak systolic gradient of the CoA decreased from 36 mmHg to 4 mmHg after stenting, and the stenotic width augmented from 6.4 mm to 17.1 mm [23]. In another study to investigate stenting for native Coa or the children and adults with recurrent CoA, Erdem A et al., [24] showed that stenting was effective in decreasing coarctation gradient without significant complication and can increase the diameter of the stenotic segment.

In Meadows et al.'s [25] study, the intermediate outcomes in a multicenter study for Coarctation Of the Aorta Stent Trial (COAST) were evaluated. In that study, a total of 105 patients underwent stent implantation; 104 of them were successful. No procedural death nor any major complications or surgical operation was reported. All patients had a reduction in blood pressure difference in extremities with a sustained decrease within the next 24 months. Hypertension rate and consuming medication was reduced and stayed unchanged up to 24 months. Six aneurysmal dilations were detected, which 5 of them were successfully resolved with covered stenting, and 1 improved without intervention. Nine re-interventions was needed in the first 2 years for redilation of the stent or treatment of aneurysms, and 10 additional re-interventions occurred after 2 years. Based on their results, the Cheatham-Platinum stent seems to be harmless, and linked with continuous relief of stenosis. Re-intervention is very usual, which mostly related to aortic wall injury and anurysem formation or need for re-expansion of stent with increasing age.

Limitations

A limitation of this study was the small sample size, hence it is recommended that further investigations be performed in multicenter setting with larger sample size and longer follow-ups.

Conclusion

Based on our results, endovascular stenting to treat CoA appears to be a safe and efficient way to treat COA. LVH and diastolic dysfunction did not regress in significant number of patients, after successful stenting.

Declarations

Authors' contribution: H.A. Study concept and design, analysis and interpretation of data H.R. Data collecting, Drafting of the manuscript, analysis and interpretation of data M.R.E. Drafting of the manuscript, Analysis and interpretation of data N.M Drafting of the manuscript, analysis and interpretation of data H.M Drafting of the manuscript, analysis and interpretation of data M.B. Drafting of the manuscript, analysis and interpretation of data G.A Drafting of the manuscript, analysis and interpretation of data E.D Drafting of the manuscript, Data collecting P.MD rafting of the manuscript, Data collecting.

Ethical approval code: After explaining the study objectives, informed consent was obtained from each patient or their parents/guardian. In accordance with the local ethical standards of Shiraz University of Medical Sciences research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards, all procedures were performed. Ethic code 92-01-01-6282.

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