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Heart Function and Ventricular Recovery after Percutaneous Closure of Peri-Membranous Ventricular Septal Defect in Children: A Cross-Sectional Study

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Abstract

Background: Peri-membranous ventricular septal defect (VSD) is the most common congenital heart defect. There is a trend for percutaneous VSD closure.

Objectives: The purpose of our study is to investigate the effect of percutaneous closure of peri-membranous VSD on cardiac function and ventricular recovery.

Methods: Forty-six pediatric patients (32 males, 14 females) who underwent transcatheter closure of peri-membranous VSD from 2010 to 2020 were included randomly. Data regarding the demographic profile, angiographic records, and follow-up echocardiography were extracted from their files and recorded in questionnaire templates. The echocardiographic parameters were recorded and compared with published Z-scores for pediatric age groups.

Results: The mean duration of follow-up was 15.76±12.20 months. In M-mode echocardiography, 84.6% had IVSDd Z-score ≥2; 23.8% had IVSDs Z-score ≥2; 38.5% had LVIDd Z-score ≥2; 34.6% had LVIDs Z-score ≥2; 65.4% had LVPWd Z-score ≥2. In the evaluation of Doppler and tissue Doppler, 36.4% of the patients had a Z-score of more than two for E/Ea of tricuspid. VSD size had a positive correlation with IVSs Z-Score (p=0.015, r=0.537).

Conclusions: In the midterm follow-up after percutaneous peri-membranous VSD closure, left ventricular dilation and hypertrophy persisted in a significant number of patients. Early closure of the VSD in lower age and lower weight may also affect the remodeling and hemodynamic of ventricles.

Keywords: Ventricular Remodeling; Echocardiography; Hemodynamics; Cardiac Catheterization; Heart Septal Defects

Introduction

Ventricular septal defect (VSD) is the most common congenital heart defect worldwide [1, 2]. Peri-membranous VSDs accounts for about 70% of the cases [3]. Due to the advances in imaging and screening of infants, the detection rate of confirmed cases of VSD has risen considerably [4]. Approximately 45% of VSDs which occur in isolation close spontaneously [5]. Surgical treatment is often recommended for patients with medium and larger defects [1]. Although traditional surgical procedures have shown excellent results, they still carry risks such as complete atrioventricular block, residual shunt, post-pericardiotomy syndrome, wound infection, reoperation, aortic regurgitation, outflow tract obstruction, and even death [2, 6, 7].

Since the introduction of transcatheter VSD closure in 1988 (8), this catheter-based approach has been widely used as an alternative to open-heart surgery with acceptable mortality and morbidity as well as promising results [9-16]. Nevertheless, this technique is also associated with complications such as complete heart block, aortic insufficiency, hemolysis, and embolization of the device [1].

Few studies have evaluated the effect of transcatheter closure of VSD on heart remodeling after percutaneous VSD closure [17]. Hence, the purpose of our study is to investigate the intermediate-term effect of the catheter-based approach for peri-membranous VSD closure on heart function and ventricular recovery.

Materials and Methods

The present study was designed as a cross-sectional survey of cardiac remodeling and heart function in patients under 14 years of age who had undergone percutaneous VSD closure by occluder device from 2010 to 2020 in Namazi hospital of Shiraz University of Medical Sciences, Shiraz, Iran. Data were collected randomly from our electronic database and recorded in questionnaire templates with the informed consent of all participants' guardians and the approval of Shiraz University of Medical Sciences ethics committee (ethics code: IR.SUMS.MED.REC.1399.196). Patients' demographic profiles, including age, sex, body weight, duration of follow-up, echocardiography, and angiographic records regarding VSD size, size of the occluder device, and complications during angiography, were collected and recorded in questionnaires. The patients under 14 years of age without another congenital heart disease, with peri-membranous VSD, uncomplicated VSD closure, QP/QS more than 1.5, left ventricular dilation, and without residual VSD were enrolled in this study. The patients with a residual shunt, other associated congenital or valvular disease, heart block, or bundle branch block were excluded from the study. All patients were followed by M-mode, 2- dimensional, flow Doppler, and tissue Doppler imaging (TDI) echocardiography methods.

Transthoracic echocardiography method

Echocardiography was performed with Samsung HS70 (Samsung Electronics Co., Ltd. / Samsung Medison Co., Ltd.) with 2-4 and 3-7 MHz probe, on apical four chambers, subcostal, long axis, and short axis views. In the parasternal long axis view, left ventricular dimensions in systole and diastole, interventricular septal thickness and ejection fraction were recorded. In four chambers view, the cursor was placed on mitral and tricuspid valve leaflets, and the inflow E and A velocity was measured. Furthermore, in four chambers view, TDI was obtained as the cursor was placed 1 cm apical to the mitral and tricuspid annuli, and pulse wave Doppler velocity was in the -20 to +20 cm/sec. An experienced pediatric cardiologist performed all echocardiograms, and the parameters were obtained in three cycles, and the average values were used in the study. The following parameters were obtained: interventricular septum diastolic diameter (IVSDd), interventricular septum systolic diameter (IVSDs), left ventricular internal diameter in diastole (LVIDd), left ventricular internal diameter in systole (LVIDs), left ventricular posterior wall in diastole (LVPWd), left ventricular posterior wall in systole (LVPWs), left ventricular ejection fraction (EF), left ventricular fractional shortening (FS), early diastolic velocity of mitral valve (Em), atrial contractility velocity of mitral (Am), early diastolic velocity of tricuspid valve (Et), atrial contractility velocity of tricuspid (At), early diastolic velocity of lateral mitral annulus (EaM), late diastolic velocity of lateral mitral annulus (AaM), early diastolic velocity of lateral tricuspid annulus (EaT), late diastolic velocity of lateral tricuspid annulus (Aat). According to published Z-Score values in the pediatric age group, echocardiography data were determined and expressed as Z-Scores [18-20].

Statistical analysis

Descriptive data were presented as means and standard deviations (SD), frequencies, and percentages. Normal distribution of data was obtained by Kolmogorov-Smirnov, and differences in continuous variables were compared using an independent t-test. Pearson correlation was used to analyze univariate associations between continuous variables. The Mann-Whitney U test was used for nonparametric variables. All analyses were done using SPSS for Windows (version 22). P-value less than 0.05 was taken as statistical significance.

Results

Totally, 46 patients (32 males (69.6%) and 14 females (30.4%)) with a mean age of 4.77±2.69 years and mean weight of 16.27±6.05 Kg were randomly selected and enrolled in the study. The demographic and clinical characteristics of the participants are as shown in (Table 1).

Table 1: Demographic and clinical characteristics of patients

Variables	**Mean±standard deviation**	**Range**
The patients' age at the time of catheterization (Years)	4.77±2.69	1.40-13.90
The patients' weight at the time of catheterization (Kg)	16.27±6.05	9.00-40.00
The patients' body surface area at the time of catheterization (m^2)	0.69±0.21	0.43-1.28
Size of the VSDs (Millimeters)	6.73±2.37	4.00-14.00
Size of the occluder device (Millimeters)	8.52±2.32	6.00-16.00
Duration of follow-up (Months)	15.76±12.20	2.00-48.00

32.4% of patients were younger than three years of age, 62.2% of patients aged less than five years of age, while only 2.7% were older than ten years of age. 88.9% of patients weighed less than 20Kg (Figure 1) (Table 2).

In M-mode echocardiography, 84.6% had IVSDd Z-score ≥2; 23.8% had IVSDs Z-score ≥2; 38.5% had LVIDd Z-score ≥2; 34.6% had LVIDs Z-score ≥2; 65.4% had LVPWd Z-score ≥2; Table 2 demonstrates the characteristics of M-mode echocardiography of left ventricle.

Table 2: M-mode echocardiographic data of left ventricle

Variables	**Mean ± SD**	**The percentage of patients with Z- score≥ 2**	**The percentage of the patients with Z- score≤ -2**
IVSd Z- Score (cm)	3.59 ± 2.48	84.6	0
IVSs Z- Score (cm)	1.44±1.07	23.8	0
LVIDd Z- Score (cm)	1.72 ± 1.20	38.5	0
LVIDs Z- Score (cm)	1.27 ± 1.39	34.6	0
LVPWd Z- Score (cm)	2.42 ± 1.59	65.4	0
LVPWs Z- Score (cm)	-0.57±1.08	0	9.5
EF%	68.78 ± 9.69	-	-
FS%	38.56 ± 7.72	-	-

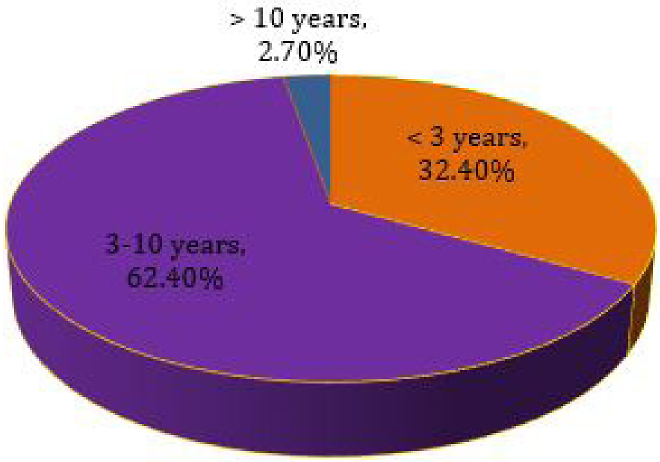

Figure 1: Distribution of the population of study according to their age

In the evaluation of Doppler and tissue Doppler, 36.4% of the patients had Z-score of E/Ea for tricuspid more than two. Other parameters were within normal limit and as shown in Table 3.

Table 3: Inflow Doppler and tissue Doppler data of the tricuspid and mitral valves

	Mean ± SD	The percentage of patients with Z-score≥ 2	The percentage of patients with Z-score≤ -2
ET Z- Score	0.38±1.14	6.9	3.4
AT Z- Score	0.83±1.14	17.9	0
ET/AT Z- Score	-0.37±0.93	0	3.6
EM Z- Score	-0.60±0.80	0	9.1
AM Z- Score	0.09±1.04	6.1	0
EM/AM Z- Score	-0.50±0.77	0	0
EaT Z-Score	-0.78±1.11	3.8	3.8
AaT Z-Score	0.60±1.22	11.5	0
EaM Z-Score	-0.87±1.10	0	17.1
AaM Z-Score	0.63±1.17	7.1	0
ET/EaT Z-Score	1.31±1.43	36.4	0
EM/EaM Z-Score	0.33±0.89	9.1	0

The echocardiographic data were compared between the patients whose VSD was closed before and after three years of age. Z score of EaT and ET/EaT Z-Score was significantly higher in patients more than three years of age than those aged less than three years old (p=0.031). Comparison of the variables are shown in Table 4.

Patients were divided into two groups regarding their weight with cut-off points of 15 Kg. Z-Scores for LVPWs, LVEF, LVFS, EM/AM, and ET/AT were higher in patients less than 15Kg at the time of VSD closure. However, AT Z-Score was lower in them comparing to patients more than 15 Kg (p=0.045). Mean ± SDs and p values are as shown in Table 5.

Table 4: Comparison of the variables in follow-up according to the age of the patients at the time of intervention

Variable	Group		
	Age ≤3 year (12 patients)	Age >3 year (34 patients)	P-value
	Mean± SD	Mean± SD	
IVSd Z-Score	3.80±1.54	3.50±2.84	0.129
IVSs Z-Score	1.88±0.83	1.27±1.13	0.267
LVIDd Z-Score	2.28±1.32	1.47±1.09	0.196
LVIDs Z-Score	0.85±1.72	1.45±1.23	0.429
LVPWd Z-Score	2.45±1.62	2.41±1.62	0.892
LVPWs Z-Score	-0.02±0.33	-0.80±1.21	0.112
LVEF	73.47±9.28	67.03±9.38	0.055
LVFS	42.23±8.00	37.18±7.27	0.067
EM Z-Score	-0.41±0.94	-0.69±0.74	0.585
AM Z-Score	-0.18±1.02	0.22±1.04	0.281
EM/AM Z-Score	-0.18±0.80	-0.65±0.73	0.166
ET Z-Score	0.09±1.04	0.55±1.20	0.387
AT Z-Score	0.59±0.80	0.98±1.31	0.458
ET/AT Z-Score	-0.47±0.73	-0.31±1.06	1.000
EaM Z-Score	-0.81±1.25	-0.91±1.04	0.461
EM/EaM Z-Score	0.45±1.09	0.27±0.80	0.611
EaT Z-Score	-0.95±0.21	-1.14±0.53	0.031
ET/EaT Z-Score	0.60±0.77	1.81±1.59	0.051
AaM Z-Score	1.04±1.45	0.42±0.97	0.327
AaT Z-Score	0.60±1.84	0.60±0.69	0.220

Table 5: Comparison of the variables in the patient below 15 Kg and more than 15 Kg

Variable	Group		p-value
	Weight ≤15 Kg (13 patients)	Weight >15 Kg (33 patients)	
	Mean± SD	Mean± SD	
IVSd Z-Score	3.55±1.54	3.63±3.14	0.297
IVSs Z-Score	1.67±0.71	1.24±1.32	0.314
LVIDd Z-Score	2.09±1.23	1.41±1.14	0.193
LVIDs Z-Score	0.86±1.77	1.62±0.88	0.432
LVPWd Z-Score	2.45±1.33	2.40±1.84	0.899
LVPWs Z-Score	-0.04±1.12	-1.06±0.84	0.008
LVEF	73.63±9.92	66.96±9.10	0.037
LVFS	42.47±8.56	37.09±6.97	0.043
EM Z-Score	-0.50±0.65	-0.65±0.89	0.927
AM Z-Score	-0.39±0.75	0.37±1.09	0.089
EM/AM Z-Score	-0.08±0.82	-0.73±0.65	0.036
ET Z-Score	0.41±0.96	0.36±1.26	0.946
AT Z-Score	0.87±0.72	1.14±1.22	0.045
ET/AT Z-Score	0.58±0.23	-0.63±0.95	0.018
EaM Z-Score	-0.88±0.93	-0.87±1.19	0.400
EM/EaM Z-Score	0.36±0.98	0.31±0.86	0.868
EaT Z-Score	-0.28±1.70	-1.05±0.52	0.220
ET/EaT Z-Score	0.97±1.41	1.47±1.46	0.490
AaM Z-Score	0.82±1.59	0.54±0.91	0.745
AaT Z-Score	0.60±1.36	0.60±1.19	0.634

Patients were divided into two groups regarding their VSD size with a cut-off point of 10 mm. IVSs Z-Score was lower in patients with a VSD size of less than 10 mm than those with a VSD size of more than 10 mm (p=0.038). AaM Z-Score was lower in patients with VSD size of less than 10 mm compared to those with VSD size of more than 10mm (p=0.030). Mean ± SD and p values are as demonstrated in Table 6.

There was a positive correlation between the patients' age and AT Z-Score (p=0.014, r=0.458). Moreover, the patients' weight had positive correlation with ET Z-Score (p=0.038, r=0.426) and AT Z-Score (p=0.001, r=0.631). VSD size of the patients had a positive correlation with IVSs Z-Score (p=0.015, r=0.537) while it was negatively correlated with EM Z-Score (p=0.015, r=-0.470) and ET/EaT Z-Score (p=0.029, r=-0.499). Table 7 shows the correlation between Age, Weight, VSD size, and other variables.

Table 6: Comparison of the variables between the patients with VSD less than 10 mm and more than 10mm

Variable	Group		p-value
	VSD ≤10 mm (9 patients)	VSD >10 mm (37 patients)	
	Mean± SD	Mean± SD	
IVSd Z-Score	3.32±2.15	4.33±3.31	0.395
IVSs Z-Score	1.28±0.99	2.99±0.16	0.038
LVIDd Z-Score	1.81±1.18	1.50±1.34	0.866
LVIDs Z-Score	1.20±1.52	1.46±1.04	0.910
LVPWd Z-Score	2.41±1.36	2.45±2.23	0.735
LVPWs Z-Score	-0.48±1.10	-1.46±0.15	0.190
LVEF	69.40±9.99	67.81±9.40	0.673
LVFS	39.07±8.10	37.74±7.25	0.736
EM Z-Score	-0.56±0.74	-0.73±1.03	0.726
AM Z-Score	0.00±0.93	0.39±1.35	0.420
EM/AM Z-Score	-0.46±0.51	-0.61±1.35	0.290
ET Z-Score	0.54±1.17	-0.22±0.88	0.158
AT Z-Score	0.78±1.16	0.99±1.16	0.566
ET/AT Z-Score	-0.26±0.86	-0.78±1.14	0.460
EaM Z-Score	-0.87±1.18	-0.88±.084	0.802
EM/EaM Z-Score	0.33±0.91	0.33±0.91	1.000
EaT Z-Score	-0.96±0.67	0.15±2.41	0.607
ET/EaT Z-Score	1.43±1.40	0.58±1.69	0.523
AaM Z-Score	0.38±0.98	1.51±1.40	0.030
AaT Z-Score	0.47±1.08	1.30±1.90	0.429

Discussion

Peri-membranous VSD is the most frequent subtype of congenital heart disease (CHD) [21]. Transcatheter closure of VSD has been preferred in several countries due to imposing less invasion and showing promising outcomes [22].

In the present study, we compared the patient's echocardiographic variables with published Z-Scores reported according to body surface area.

In this study, a significant number of patients had an inter-ventricular and posterior wall thickness more than normal, and the size of VSD had a positive correlation with septal thickness. Aminullah et al. studied 24 patients with mean age of 12.60±12.09 years who had undergone surgical closure of VSD. They found that left ventricular posterior wall thickness and inter-ventricular septum thickness decreased three months after surgery, and the changes were more significant in the younger age group [23]. Cordell et al. suggested in a study of post-surgical VSD closure LV function and LV mass in the first two years of life that when early surgical closure of VSD is necessary, promising results in terms of postoperative left ventricular size and function can be expected. They demonstrated that LV mass was mildly elevated at the preoperative assessment, which was decreased significantly following surgical repair [24].

Table 7: Correlation of the echocardiographic variables with age, weight, and VSD size

Variable		Age	Weight	VSD size
IVSd Z-Score	P value	0.815	0.801	0.354
	R	0.048	-0.052	-0.219
IVSs Z-Score	P value	0.562	0.435	**0.015**
	R	-0.134	-0.180	0.537
LVIDd Z-Score	P value	0.427	0.322	0.440
	R	-0.163	-0.202	0.183
LVIDs Z-Score	P value	0.637	0.747	0.605
	R	0.097	-0.066	0.123
LVPWd Z-Score	P value	0.184	0.572	0.703
	R	-0.269	-0.116	-0.091
LVPWs Z-Score	P value	0.194	0.453	0.828
	R	-0.295	-0.173	-0.052
LVEF	P value	0.528	0.553	0.790
	R	-0.110	-0.122	0.053
EM Z-Score	P value	0.562	0.202	**0.015**
	R	-0.105	0.259	-0.470
AM Z-Score	P value	0.521	0.213	0.166
	R	0.116	0.253	-0.280
ET Z-Score	P value	0.115	0.038	0.206
	R	0.299	0.426	-0.268
AT Z-Score	P value	0.014	0.001	0.400
	R	0.458	0.631	-0.184
EaM Z-Score	P value	0.672	0.075	0.164
	R	-0.074	0.356	-0.270
AaM Z-Score	P value	0.277	0.939	0.615
	R	-0.189	0.016	-0.099
EaT Z-Score	P value	0.298	0.821	0.251
	R	-0.212	-0.054	0.255
AaT Z-Score	P value	0.963	0.176	0.702
	R	0.010	0.315	-0.086
EM/AM Z-Score	P value	0.337	0.622	0.737
	R	-0.173	-0.102	-0.069
EM/EaM Z-Score	P value	0.748	0.477	0.980
	R	-0.058	-0.146	0.005
ET/AT Z-Score	P value	0.511	0.372	0.919
	R	-0.129	-0.195	-0.022
ET/EaT Z-Score	P value	0.085	0.072	0.029
	R	0.376	0.435	-0.499

Left ventricular dilation was seen in about one-third of the patients. Zheng et al. in a study of 30 patients following transcatheter closure of VSD, reported that left ventricular end-diastolic diameter and left ventricular end-diastolic volume both started to decrease as soon as three days following the intervention, this trend continued for six months (17). Yasmin Abdelrazek et al. evaluated left ventricular systolic function after VSD closure using speckle tracking, which showed decreased LV volume overload with improved contractility [25].

In the evaluation of Doppler and tissue Doppler, one-third of the patients had Z-score of E/Ea of tricuspid more than normal, showing persistence of right-sided diastolic abnormality. In a study conducted by Klitsie et al. after one year of surgical VSD closure, LV systolic function became normal. In contrast, RV systolic function remained impaired up to 20 months after surgery [26].

Long-term evaluation of the patients after surgical peri-membranous VSD closure showed long-term survival in the patients with peri-membranous VSD closure seems to be fair, but not without any event. Some patients established significant aortic regurgitation or left ventricular outflow obstruction regardless of VSD repair. Some subjects without any predisposing factor developed atrial arrhythmia who need pacemaker implantation [27].

In the present study, the patients' age correlated positively with AT Z-Score, and their weight correlated positively with ET Z-Score and AT Z-Score, and negatively with EM-Z Score and ET/EaT Z-Score. More studies are needed to evaluate the significance of these parameters in the future of the patients.

Limitation of the study

Some data was extracted retrospectively, which led to missing values and a lower statistical power. A more extended study is recommended for determining the significance of Doppler and tissue Doppler parameters.

Conclusion

In the midterm follow-up after percutaneous closure of peri-membranous VSD, left ventricular dilation and hypertrophy persisted in a significant number of patients. Early closure of VSD in lower age and lower weight can also affect the remodeling and hemodynamic of ventricles.

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