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Research Article

Heart Function and Ventricular Recovery After Percutaneous Closure of Perimembranous Ventricular Septal Defect in Children: A Cross-sectional Study

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Abstract

Background: Perimembranous ventricular septal defect (VSD) is the most common congenital heart defect. There is a trend for percutaneous VSD closure. However, little evidence is available for the effect of this method on ventricular remodeling.
Objectives: This study aimed to investigate the effect of percutaneous closure of perimembranous VSD on cardiac function and ventricular recovery.
Methods: A total of 46 pediatric patients (32 males vs. 14 females) who underwent transcatheter closure of perimembranous VSD from 2010 to 2020 were randomly included in the study. 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 the corresponding age groups.
Results: The mean duration of follow-up was 15.76 $\pm$ 12.20 months. In M-mode echocardiography, 84.6% had interventricular septum diastolic diameter Z-score $\geq$ 2; 23.8% had interventricular septum systolic diameter Z-score $\geq$ 2; 38.5% had left ventricular internal diameter in diastole Z-score $\geq$ 2; 34.6% had left ventricular internal diameter in systole Z-score $\geq$ 2; and 65.4% had left ventricular posterior wall in diastole Z-score $\geq$ 2. In the evaluation of Doppler and tissue Doppler, 36.4% of the patients had a Z-score $\geq$ 2 for E/Ea of tricuspid. Also, VSD size had a positive correlation with interventricular septal diameter in systole Z-score (P = 0.015, r = 0.537).
Conclusions: In the midterm follow-up after percutaneous perimembranous VSD closure, left ventricular dilation and hypertrophy persisted in a significant number of patients. However, early closure of the VSD, especially in patients with lower weight could affect ventricular hemodynamics and remodeling.

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

1. Background

Ventricular septal defect (VSD) is the most common congenital heart defect worldwide (1, 2). Perimembranous VSD accounts for almost 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 are closed 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).

2. Objectives

The effect of transcatheter closure of VSD on heart remodeling after percutaneous VSD closure has not yet been fully elucidated (17). Hence, the purpose of our study is to investigate the intermediate-term effect of the catheter-based approach for perimembranous VSD closure on heart function and ventricular recovery.

3. Methods

The present study was designed as a cross-sectional evaluation 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, affiliated with Shiraz University of Medical Sciences, Shiraz, Iran. Patients were selected by a computer-based random selection method from our electronic database and data were collected and recorded in questionnaire templates with the informed consent of all participants' guardians and the approval of the ethics committee of Shiraz University of Medical Sciences (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 the questionnaires. The patients under 14 years of age with perimembranous VSD and without any other congenital heart disease were enrolled in this study. Patients with a residual shunt, QP/QS more than 1.5, any periprocedural complications, any conduction abnormalities (right bundle branch block, left bundle branch block, heart block, and left ventricular dilation), and those with more than mild valvular regurgitation were excluded from the study. All patients were followed using M-mode, 2-dimensional, flow Doppler, and tissue Doppler imaging (TDI) echocardiography methods. All the echocardiography studies were performed by the same physician with at least 20 years of experience in the field of pediatric echocardiography.

3.1. Transthoracic Echocardiography Method

Echocardiography was performed using 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 curser was placed on mitral and tricuspid valve leaflets, and the inflow E and A velocity was measured. 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.

The parameters were obtained in three cycles, and the average values were used in the study. IVSDd (interventricular septum diastolic diameter), IVSDs (interventricular septum systolic diameter), LVIDd (left ventricular internal diameter in diastole), LVIDs (left ventricular internal diameter in systole), LVPWd (left ventricular posterior wall thickness in diastole), LVPWs (left ventricular posterior wall thickness in systole), LVEF, LVFS, Em (early diastolic velocity of mitral valve), Am (atrial contractility velocity of mitral), Et (early diastolic velocity of tricuspid valve), At (atrial contractility velocity of tricuspid), EaM (early diastolic velocity of lateral mitral annulus), AaM (late diastolic velocity of lateral mitral annulus), EaT (early diastolic velocity of lateral tricuspid annulus), and Aat (late diastolic velocity of lateral tricuspid annulus) were recorded. Echocardiography data were expressed as Z-scores according to previously published Z-score values in the corresponding pediatric age group (18-20).

3.2. 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 the analysis was performed using SPSS for Windows (version 22). P-value less than 0.05 was considered as statistical significance.

4. Results

In this study, a total of 46 patients (32 males; 69.6%) with a mean age of 4.77 ± 2.69 years and mean weight of 16.27 ± 6.05 kg were randomly selected. The demographic and clinical characteristics of the participants are shown in (Table 1). As can be seen, 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 (Figure 1).

In M-mode echocardiography, 84.6% had IVSDd Z-score $\geq$ 2; 23.8% had IVSDs Z-score $\geq$ 2; 38.5% had LVIDd Z-score $\geq$ 2; 34.6% had LVIDs Z-score $\geq$ 2; and 65.4% had LVPWd Z-score $\geq$ 2. Table 2 demonstrates the characteristics of M-mode, inflow Doppler, and tissue doppler echocardiography. In the evaluation of Doppler and tissue Doppler, 36.4% of the patients had Z-score $\geq$ 2 for E/Ea of tricuspid valve. Other parameters were within normal limits (Table 2).

Table 1. Demographic and Clinical Characteristics of Patients

Variables	Mean ± Standard Deviation	Range
The patients' age at the time of catheterization (y)	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 (mm)	6.73 ± 2.37	4.00 - 14.00
Size of the occluder device (mm)	8.52 ± 2.32	6.00 - 16.00
Duration of follow-up (mon)	15.76 ± 12.20	2.00 - 48.00

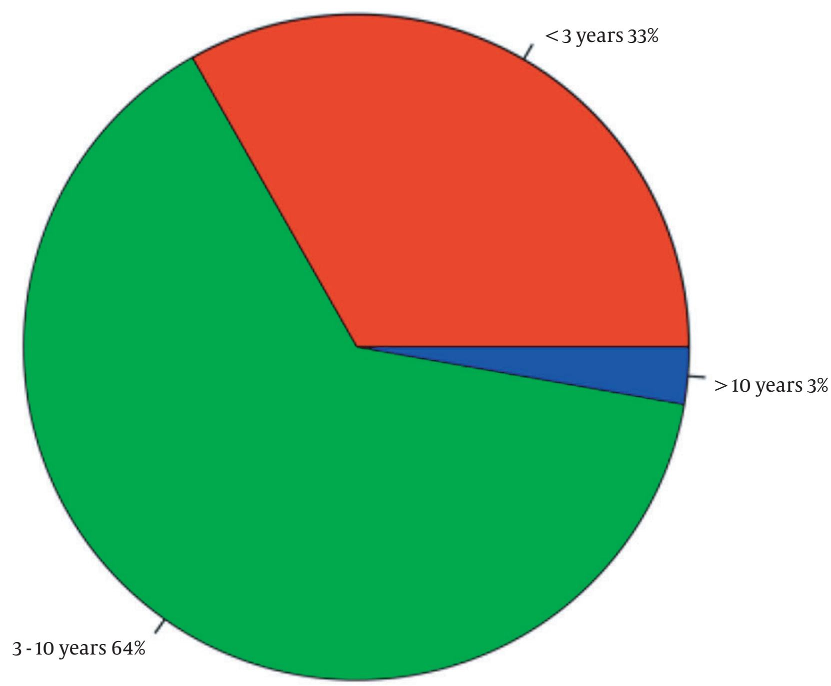

Figure 1. Distribution of the study population according to their age

Echocardiographic data were compared between the patients whose VSD was closed before and after three years of age. Z-scores of EaT and ET/EaT Z-score were significantly higher in patients older than three years of age than those who aged less than three years (P = 0.031). The comparison of variables is shown in Table 3.

Patients were divided into two groups regarding their weight with a cut-off point of 15 kg. Z-scores for LVPWs, LVEF, LVFS, EM/AM, and ET/AT were higher in patients less than 15 kg at the time of VSD closure (P = 0.008, P = 0.037, P = 0.043, P = 0.036, and P = 0.018, respectively). However, AT Z-score was lower in them compared to patients weighing more than 15 kg (P = 0.045). Mean ± SDs and P-values are as shown in Table 3.

Patients were divided into two groups regarding their VSD size with a cut-off point of 10 mm. IVSDs 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 10 mm (P = 0.030). Mean ± SD and P-values are demonstrated in Table 3.

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 IVSDs Z-score (P = 0.015, r = 0.537), while it was negatively correlated

Table 2. M-mode, Inflow Doppler, and Tissue Doppler Echocardiography Data of the Tricuspid and Mitral Valves

Variables	Mean ± SD	The Percentage of Patients with Z- Score ≥ 2	The Percentage of the Patients with Z- Score ≤ -2
M-mode echocardiographic data of left ventricle			
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	-	-
Doppler and tissue Doppler data of the tricuspid and mitral valves			
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

Abbreviations: EF, ejection fraction; FS, fractional shortening.

with EM Z-Score (P = 0.015, r = -0.470) and ET/EaT Z-score (P = 0.029, r = -0.499).

5. Discussion

Perimembranous 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 patients' echocardiographic variables with published Z-scores reported according to body surface area. A significant number of patients had an abnormally high interventricular and posterior wall thickness, 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 interventricular septum thickness decreased three months after surgery, and the changes were more significant in the younger age group (23). Cordell et al. studied post-surgical VSD closure LV function and LV mass in the first two years of life, and suggested 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).

In our study, left ventricular dilation was observed in about one-third of the patients. In contrast, Zheng et al. evaluated 30 patients following transcatheter closure of VSD and reported that left ventricular end-diastolic diameter and left ventricular end-diastolic volume both started to decrease three days after the intervention, and this trend continued for six months (17). Abdelrazek Ali et al.

Table 3. Comparison of the Variables in the Follow-up Phase in Groups with Different Age, Weight, and VSD Size [a]

Variables	Comparison Group			Comparison Group			Comparison Group		
	Age ≤ 3 Years (12 Patients)	Age > 3 Years (34 Patients)	P-Value	Weight ≤ 15 kg (13 Patients)	Weight > 15 kg (33 Patients)	P-Value	VSD ≤ 10 mm (9 Patients)	VSD > 10 mm (37 Patients)	P-Value
IVSd Z-score	3.80 ± 1.54	3.50 ± 2.84	0.129	3.55 ± 1.54	3.63 ± 3.14	0.297	3.32 ± 2.15	4.33 ± 3.31	0.395
IVSs Z-score	1.88 ± 0.83	1.27 ± 1.13	0.267	1.67 ± 0.71	1.24 ± 1.32	0.314	1.28 ± 0.99	2.99 ± 0.16	0.038
LVIDd Z-score	2.28 ± 1.32	1.47 ± 1.09	0.196	2.09 ± 1.23	1.41 ± 1.14	0.193	1.81 ± 1.18	1.50 ± 1.34	0.866
LVIDs Z-score	0.85 ± 1.72	1.45 ± 1.23	0.429	0.86 ± 1.77	1.62 ± 0.88	0.432	1.20 ± 1.52	1.46 ± 1.04	0.910
LVPWd Z-score	2.45 ± 1.62	2.41 ± 1.62	0.892	2.45 ± 1.33	2.40 ± 1.84	0.899	2.41 ± 1.36	2.45 ± 2.23	0.735
LVPWs Z-score	-0.02 ± 0.33	-0.80 ± 1.21	0.112	-0.04 ± 1.12	-1.06 ± 0.84	0.008	-0.48 ± 1.10	-1.46 ± 0.15	0.190
LVEF	73.47 ± 9.28	67.03 ± 9.38	0.055	73.63 ± 9.92	66.96 ± 9.10	0.037	69.40 ± 9.99	67.81 ± 9.40	0.673
LVFS	42.23 ± 8.00	37.18 ± 7.27	0.067	42.47 ± 8.56	37.09 ± 6.97	0.043	39.07 ± 8.10	37.74 ± 7.25	0.736
EM Z-score	-0.41 ± 0.94	-0.69 ± 0.74	0.585	-0.50 ± 0.65	-0.65 ± 0.89	0.927	-0.56 ± 0.74	-0.73 ± 1.03	0.726
AM Z-score	-0.18 ± 1.02	0.22 ± 1.04	0.281	-0.39 ± 0.75	0.37 ± 1.09	0.089	0.00 ± 0.93	0.39 ± 1.35	0.420
EM/AM Z-score	-0.18 ± 0.80	-0.65 ± 0.73	0.166	-0.08 ± 0.82	-0.73 ± 0.65	0.036	-0.46 ± 0.51	-0.61 ± 1.35	0.290
ET Z-score	0.09 ± 1.04	0.55 ± 1.20	0.387	0.41 ± 0.96	0.36 ± 1.26	0.946	0.54 ± 1.17	-0.22 ± 0.88	0.158
AT Z-score	0.59 ± 0.80	0.98 ± 1.31	0.458	0.87 ± 0.72	1.14 ± 1.22	0.045	0.78 ± 1.16	0.99 ± 1.16	0.566
ET/AT Z-score	-0.47 ± 0.73	-0.31 ± 1.06	1.000	0.58 ± 0.23	-0.63 ± 0.95	0.018	-0.26 ± 0.86	-0.78 ± 1.14	0.460
EaM Z-score	-0.81 ± 1.25	-0.91 ± 1.04	0.461	-0.88 ± 0.93	-0.87 ± 1.19	0.400	-0.87 ± 1.18	-0.88 ± .084	0.802
EM/EaM Z-score	0.45 ± 1.09	0.27 ± 0.80	0.611	0.36 ± 0.98	0.31 ± 0.86	0.868	0.33 ± 0.91	0.33 ± 0.91	1.000
EaT Z-score	-0.95 ± 0.21	-1.14 ± 0.53	0.031	-0.28 ± 1.70	-1.05 ± 0.52	0.220	-0.96 ± 0.67	0.15 ± 2.41	0.607
ET/EaT Z-score	0.60 ± 0.77	1.81 ± 1.59	0.051	0.97 ± 1.41	1.47 ± 1.46	0.490	1.43 ± 1.40	0.58 ± 1.69	0.523
AaM Z-score	1.04 ± 1.45	0.42 ± 0.97	0.327	0.82 ± 1.59	0.54 ± 0.91	0.745	0.38 ± 0.98	1.51 ± 1.40	0.030
AaT Z-score	0.60 ± 1.84	0.60 ± 0.69	0.220	0.60 ± 1.36	0.60 ± 1.19	0.634	0.47 ± 1.08	1.30 ± 1.90	0.429

[a] Values are expressed as mean ± SD.

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, we witnessed that 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 perimembranous VSD closure showed long-term survival in the patients with perimembranous VSD closure, 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 needed 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 patients' future.

This study had some limitations. Some data were extracted retrospectively, which led to missing values and deacreased statistical power. A prospective study with a larger sample size and longer follow-up duration would provide more robust evidence about ventricular remodeling after percutaneous intervention, as well as determining the diagnostic and prognostic significance of Doppler and tissue Doppler parameters.

5.1. Conclusions

According to the results of this study, in the midterm follow-up after percutaneous closure of perimembranous

VSD, left ventricular dilation and hypertrophy persisted in a significant number of patients. Early closure of VSD at lower ages and in patients with lower weights can affect the remodeling and hemodynamics of ventricles.

Footnotes

Authors' Contribution: AA, HA, and MRE designed the study; AA, MA, and NM contributed to the data acquisition; HA and HM analyzed the data; AA, HA, and GA interpreted the data analysis; AA, HA, MRE, MA, and AN wrote the manuscript. All authors have read and approved the submitted draft and have agreed both to be personally accountable for their own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which they were not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

Conflict of Interests: The authors declare that they have no conflict of interests.

Ethical Approval: All methods of this study were carried out in accordance with the Declaration of Helsinki and the data were collected with the informed consent of all participants' guardians and the approval of Shiraz University of Medical Sciences ethics committee (code: IR.SUMS.MED.REC.1399.196). ethics.research.ac.ir/EthicsProposalViewEn.php?id=140242

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Informed Consent: As the study was retrospective, it did not need informed consent.

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