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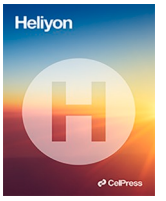

Research article

Rapid left ventricular dimension normalization following transcatheter ventricular septal defect closure in children

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ABSTRACT

Background: This study evaluated left ventricular (LV) dimension changes after transcatheter ventricular septal defect (VSD) closure in children and identified factors influencing these changes.

Methods: We retrospectively studied 124 children (mean age: 3.5 ± 3.0 years) with preoperative LV Z-scores ≥2 who underwent successful transcatheter VSD closure. LV end-diastolic diameter (LVEDD) Z-scores were assessed using echocardiography at 1, 3, 6, and 12 months post-operatively. Predictors of LV dimension normalization were identified using binary logistic regression.

Results: The mean VSD size was 5.7 ± 2.0 mm. LVEDD Z-scores significantly decreased over time, with 87.1 % of patients achieving normalization at 1 month. The most rapid change occurred in the first postoperative month (64 % decrease). Age showed an inverse association (OR 0.41, $p = 0.036$) and VSD size a positive association (OR 1.53, $p = 0.007$) with LVEDD Z-score normalization at 1 month. Device-specific complications, including conduction disturbances, occurred more frequently with non-symmetric occluders (13.0 %) than with perimembranous symmetric occluders (3.0 %) ($p = 0.077$). Although complications delayed recovery, normalization was achieved by 12 months in nearly all cases.

Conclusions: Transcatheter VSD closure results in rapid normalization of LV dimensions in children, with the most significant changes occurring in the first postoperative month. The identified associations of age and VSD size with LV dimension improvement support transcatheter VSD closure as an effective treatment for hemodynamically significant VSDs in children.

1. Introduction

Ventricular septal defects (VSDs) are the most prevalent congenital heart defects, constituting approximately 20 %–40 % of all cases [1,2]. The incidence of VSDs varies across populations and age groups, with an estimated occurrence of 2–5 per 1000 live births [3]. Historically, the prevalence of VSDs has been challenging to determine accurately due to variations in diagnostic criteria and the spontaneous closure of some defects in early childhood [4]. VSDs are characterized by the presence of a defect in the interventricular

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septum, allowing for the shunting of blood from the left ventricle (LV) to the right ventricle. This left-to-right shunting leads to LV volume overload and subsequent dilation, which, if left untreated, can result in pulmonary hypertension, ventricular dysfunction, and ultimately, heart failure [5].

The management of VSDs has evolved significantly over the past century. In the early 1950s, the first successful surgical repairs of VSDs were performed using hypothermia and inflow occlusion [6]. The introduction of cardiopulmonary bypass in the late 1950s revolutionized the field, allowing for more complex intracardiac repairs [7]. For decades, surgical repair has been the gold standard for the treatment of VSDs [8], involving open-heart surgery with significant associated risks and recovery time. However, recent advancements in interventional cardiology have led to the development of transcatheter closure techniques, which have emerged as a safe and effective alternative to surgical intervention [9,10]. The first successful transcatheter closure of a VSD was reported in 1988 [11], and since then, the technique has been refined and widely adopted. Transcatheter VSD closure has been associated with lower complication rates, reduced hospital stays, and more rapid recovery compared to traditional surgical approaches [10]. While transcatheter VSD closure has emerged as an important treatment option, it is crucial to note that this approach cannot completely replace surgical treatment. The selection of appropriate candidates for transcatheter closure requires careful consideration of specific anatomical and clinical criteria. Generally accepted indications for transcatheter VSD closure include: (1) perimembranous VSDs with a diameter $\leq$12 mm and adequate rim distances (>2 mm) from the aortic, tricuspid, and mitral valves; (2) muscular VSDs with suitable anatomy for device placement; (3) residual VSDs after surgical repair; and (4) patients with significant left-to-right shunting (Qp:Qs > 1.5:1) but without severe pulmonary hypertension. Conversely, surgical treatment remains the preferred option for patients with: large defects (>12 mm), inadequate septal rims, multiple VSDs requiring closure, associated cardiac anomalies requiring surgical correction, significant aortic valve prolapse or regurgitation, or severe pulmonary hypertension with bidirectional shunting. Understanding these indications and contraindications is essential for optimal patient selection and outcomes.

Several studies have investigated the efficacy of transcatheter VSD closure in reducing LV volume overload and improving ventricular function [12,13]. However, there is limited data regarding the time course of LV dimension normalization following the procedure, particularly in pediatric populations. Furthermore, the factors influencing these changes have not been extensively explored.

The objective of this retrospective study was to evaluate the temporal changes in LV dimensions following transcatheter VSD closure in a pediatric cohort and to identify factors associated with the normalization of LV size. Elucidating these aspects of transcatheter VSD closure can provide valuable insights into patient management and inform follow-up strategies.

2. Materials and methods

2.1. Study design and patient population

This retrospective, single-center study was conducted at our institution from January 2014 to October 2022. The study protocol was approved by the institutional review board, and the requirement for informed consent was waived due to the retrospective nature of the study.

From the total of 1061 pediatric patients who underwent transcatheter VSD closure during the study period, 124 patients were selected based on the following inclusion criteria (1) age $\leq$18 years at the time of intervention, (2) preoperative left ventricular end-diastolic diameter (LVEDD) Z-score $\geq$2, indicating significant left ventricular dilation, (3) completion of routine follow-up examinations (immediately postoperative, and at 1, 3, 6, and 12 months post-intervention), and (4) successful device deployment without immediate major complications requiring surgical intervention. Exclusion criteria: (1)Presence of additional congenital heart defects other than the VSD being treated, and (2)Patients who underwent any concomitant cardiac procedures alongside the VSD closure.

2.2. Transcatheter VSD closure procedure

All procedures were performed under general anesthesia with fluoroscopic and transesophageal echocardiographic guidance. The choice of closure device was determined by the interventional cardiologist based on the size, morphology, and location of the VSD. The closure devices used in this study included the perimembranous symmetric VSD occluder, eccentric occluder, small-waisted large-sided occluder, and Amplatzer Duct Occluder II (ADOII).

The procedure was performed using standard techniques, as previously described [11]. Briefly, the VSD was crossed from the left ventricle using a catheter and guidewire, and the closure device was deployed under fluoroscopic and echocardiographic guidance. Device position and residual shunting were assessed before final release.

2.3. Data collection and follow-up

Demographic, clinical, and procedural data were obtained from electronic medical records. Transthoracic echocardiography was performed before the intervention, immediately after the procedure, and at 1, 3, 6, and 12 months post-intervention. All echocardiographic examinations were performed using the same ultrasound system (Philips Epiq 7c) under standardized conditions. To ensure consistency, all examinations were performed with patients in the left lateral decubitus position after a 5-min rest period. For pediatric patients requiring sedation, chloral hydrate was administered according to standard protocol to maintain similar sedation levels across examinations.

LVEDD measurements were performed according to the American Society of Echocardiography guidelines. To assess measurement

reliability, all preoperative and 1-month postoperative echocardiographic images were independently analyzed by two experienced pediatric cardiologists (each with >5 years of experience in pediatric echocardiography) who were blinded to the clinical data and timing of the examination. When measurements differed by more than 5 %, a third observer reviewed the images, and consensus was reached through discussion. Z-scores were calculated based on body surface area using published normative data [14].

Pulmonary artery systolic pressure (PASP) was estimated using the modified Bernoulli equation [15]. Pulmonary hypertension was defined as a PASP >35 mmHg on echocardiography or a mean pulmonary artery pressure >20 mmHg on cardiac catheterization.

Procedural success was defined as: (1) proper device positioning confirmed by fluoroscopy and echocardiography, (2) residual shunt <2 mm on immediate post-procedure evaluation, (3) absence of new-onset severe valvular regurgitation (defined as more than moderate aortic, mitral, or tricuspid regurgitation), and (4) absence of major complications requiring immediate surgical intervention.

2.4. Statistical analysis

Continuous variables were expressed as mean ± standard deviation or median (interquartile range), as appropriate. Categorical variables were presented as frequencies and percentages. Changes in LVEDD Z-scores over time were analyzed using repeated-measures analysis of variance (ANOVA) with post hoc pairwise comparisons.

Binary logistic regression analysis was performed to identify predictors of LVEDD Z-score normalization (Z-score <2) at 1 month post-intervention. A p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA).

3. Results

3.1. Patient characteristics

A total of 1061 pediatric patients underwent transcatheter VSD closure at our institution during the study period. After excluding patients with incomplete follow-up data (n = 578), those with preoperative LVEDD Z-score <2 (n = 342), and those with unsuccessful device deployment or immediate major complications requiring surgical intervention (n = 17), 124 patients (51.6 % female) who met all inclusion criteria were included in the final analysis. The mean age at intervention was 3.5 ± 3.0 years. The majority of patients (97.6 %) had perimembranous VSDs, with one case of muscular VSD and two cases of subpulmonic VSD. The mean VSD size, as measured by transthoracic echocardiography, was 5.7 ± 2.0 mm. The mean LV side diameter of VSD was 7.83 ± 2.85 mm, The mean number of exits from the RV side was 2.07 ± 1.02. Ventricular septal aneurysm (VSA) was present in 99 (79.8 %) out of the 124 patients. Preoperative pulmonary hypertension was present in 33 patients (26.6 %) based on cardiac catheterization data [Table 1].

3.2. Procedural outcomes

Transcatheter VSD closure met our defined success criteria in all 124 included patients. The most commonly used closure device was the perimembranous symmetric VSD occluder (82.8 %), followed by the small-waisted large-sided occluder (8.2 %), eccentric occluder (8.2 %), and ADOII (2.5 %). The mean device diameter was 8.0 ± 2.3 mm [Table 1].

Immediate post-procedure echocardiographic evaluation showed mild residual shunting (color Doppler jet width <2 mm) in 27 patients (21.8 %). No patient developed severe valvular regurgitation (more than moderate) of any valve immediately post-procedure. Mild aortic valve regurgitation was observed in 2 patients (1.6 %), and moderate tricuspid valve regurgitation was noted in 1 patient (0.8 %). At the 12-month follow-up, 13 patients (10.5 %) had persistent mild residual shunting (mean shunt diameter 1.6 ± 0.7 mm),

Table 1
Patient characteristics and procedural data (n = 124).

Characteristic	Value
Age at intervention, years (mean ± SD)	3.5 ± 3.0
Female, n (%)	64 (51.6 %)
VSD type, n (%)	
Perimembranous	121 (97.6 %)
Muscular	1 (0.8 %)
Subpulmonic	2 (1.6 %)
VSD size, mm (mean ± SD)	5.7 ± 2.0
LV side diameter, mm (mean ± SD)	7.83 ± 2.85
Number of exits from RV side (mean ± SD)	2.07 ± 1.02
Presence of VSA, n (% of total)	99 (79.8 %)
Preoperative pulmonary hypertension, n (%)	33 (26.6 %)
Device type, n (%)	
Perimembranous symmetric occluder	101 (82.8 %)
Small-waisted large-sided occluder	10 (8.2 %)
Eccentric occluder	10 (8.2 %)
ADOII	3 (2.5 %)
Device diameter, mm (mean ± SD)	8.0 ± 2.3

with no progression in the severity of valvular regurgitation observed during follow-up.

3.3. Changes in left ventricular dimensions

The mean preoperative LVEDD Z-score was 2.98 ± 0.90. Following transcatheter VSD closure, a significant decrease in LVEDD Z-scores was observed over time ($p < 0.001$, repeated-measures ANOVA). The most rapid change occurred within the first postoperative month, with a 64 % decrease in the mean LVEDD Z-score from 2.98 ± 0.90 to 1.07 ± 1.05. At 1 month post-intervention, 108 patients (87.1 %) had normalized LVEDD Z-scores (<2).

The proportion of patients with normalized LVEDD Z-scores continued to increase throughout the follow-up period, reaching 92.7 %, 98.4 %, and 99.2 % at 3, 6, and 12 months, respectively. The mean LVEDD Z-scores were 0.71 ± 0.99, 0.65 ± 0.75, and 0.67 ± 0.79 at 3, 6, and 12 months post-intervention, respectively [Fig. 1].

3.4. Impact of occluder size on left ventricular recovery

To evaluate the influence of occluder size on LV recovery, patients were stratified into three groups based on device diameter: small (≤6 mm, n = 33), medium (6–8 mm, n = 47), and large (>8 mm, n = 44). At 1-month follow-up, the proportion of patients achieving LVEDD Z-score normalization was 93.9 %, 91.5 %, and 75.0 % in the small, medium, and large occluder groups, respectively ($p = 0.01$). However, by 6-month follow-up, these differences were no longer statistically significant (100.0 %, 100.0 %, and 95.5 % respectively, $p = 0.16$).

3.5. Complications and their impact on ventricular recovery

Analysis of device-specific complications showed that conduction disturbances tended to occur more frequently with other device types (3/23, 13.0 %) compared to perimembranous symmetric VSD occluders (3/101, 3.0 %), although this difference was not statistically significant ($p = 0.077$). The case of complete atrioventricular block occurred with a 10 mm eccentric occluder, while the four cases of left bundle branch block were associated with devices ranging from 5 to 12 mm (three perimembranous symmetric and one small-waisted large-sided occluder). Hemolysis was exclusively observed in patients with residual shunting. One case of ventricular tachycardia occurred in a patient with an 8 mm perimembranous symmetric occluder.

Patients who experienced complications (n = 14) demonstrated delayed left ventricular recovery compared to those without

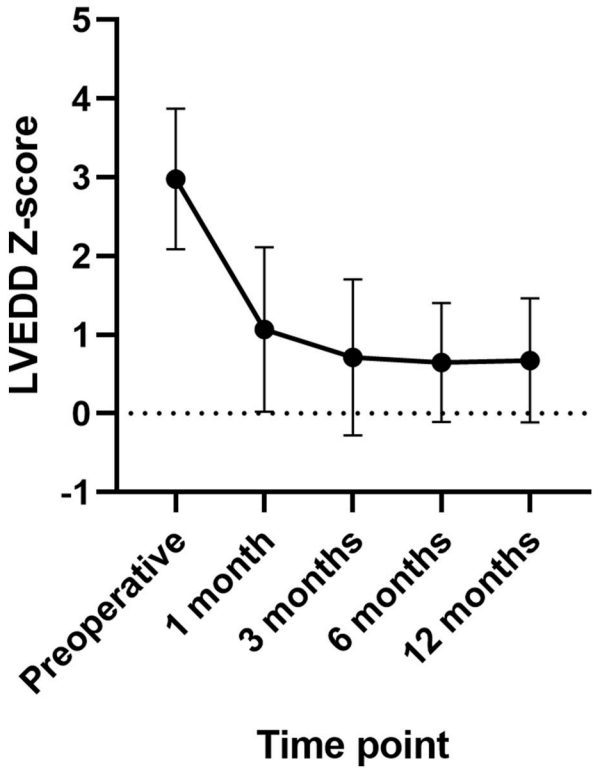

Fig. 1. Changes in left ventricular end-diastolic diameter (LVEDD) Z-scores over time following transcatheter ventricular septal defect (VSD) closure.

complications (n = 110). The rate of LVEDD Z-score normalization at one month was significantly lower in patients with complications (9/14) compared to those without complications (99/110) (p = 0.019). At the 12-month follow-up, LVEDD Z-scores had normalized in all but one patient from the complications group, suggesting that while complications may temporarily delay LV recovery, they generally do not prevent ultimate normalization in the majority of cases.

3.6. Predictors of left ventricular dimension normalization

In the univariate binary logistic regression analysis, younger age at intervention (OR 0.41, 95 % CI 0.18–0.94, p = 0.036) and smaller VSD size (OR 1.53, 95 % CI 1.12–2.08, p = 0.007) were significantly associated with LVEDD Z-score normalization at 1 month post-intervention [Table 2]. These variables remained the only significant predictors in the multivariate analysis. Gender, preoperative LVEDD Z-score, presence of pulmonary hypertension, and residual shunting were not significantly associated with LVEDD Z-score normalization at 1 month in either the univariate or multivariate analyses.

3.7. Subgroup analysis

A subgroup analysis was performed to compare the outcomes of patients with and without preoperative pulmonary hypertension. There were no significant differences in the rates of procedural success, residual shunting, or complications between the two groups (all p > 0.05). The mean LVEDD Z-scores at each follow-up point were also similar between patients with and without preoperative pulmonary hypertension (all p > 0.05).

In summary, transcatheter VSD closure was associated with a rapid and sustained reduction in left ventricular dimensions, with younger age and smaller VSD size being significant predictors of LVEDD Z-score normalization at 1 month post-intervention. The procedure was successful in all patients, with a low incidence of complications. Preoperative pulmonary hypertension did not significantly influence the outcomes of transcatheter VSD closure in this cohort.

4. Discussion

This retrospective study demonstrates the efficacy and safety of transcatheter VSD closure in a pediatric population, focusing on the temporal changes in left ventricular dimensions following the procedure. Our results show that transcatheter VSD closure is associated with a rapid and sustained reduction in LVEDD Z-scores, with the most significant improvement occurring within the first post-operative month. Notably, 87.1 % of patients achieved normal LVEDD Z-scores within just one month post-intervention, highlighting the procedure's swift impact on cardiac remodeling. Furthermore, we identified younger age and smaller VSD size as significant predictors of greater LVEDD Z-score improvement, providing valuable insights for patient selection and management. These findings are consistent with previous studies that have reported a significant decrease in left ventricular volumes and dimensions following transcatheter VSD closure [12,16], but our study uniquely quantifies the rapidity and extent of this improvement in a pediatric cohort.

The rapid normalization of left ventricular dimensions observed in our study can be attributed to the immediate elimination of left-to-right shunting and the resulting reduction in left ventricular volume overload [17]. This is supported by our finding that smaller VSD size was a significant predictor of LVEDD Z-score normalization at 1 month post-intervention, as smaller defects are associated with a lesser degree of shunting and volume overload.

Our study also identified younger age at intervention as a significant predictor of LVEDD Z-score normalization at 1 month. This finding is in agreement with previous studies that have reported better outcomes and more rapid recovery in younger patients undergoing transcatheter VSD closure. Pacileo et al. found that age <2 years was a significant predictor of normalization of left ventricular dimensions after intervention [18]. The more rapid improvement in younger patients may be due to the greater capacity for ventricular remodeling and adaptation in younger hearts.

The success rate of transcatheter VSD closure in our cohort was 100 %, which is comparable to the success rates reported in other studies, ranging from 94 % to 100 % [19,20]. A comprehensive meta-analysis by Yang et al. (2014) reported a pooled success rate of 96.6 % (95 % CI: 95.7–97.5 %) across 37 studies involving 4406 patients [9]. The incidence of complications in our study was low and consistent with previous reports [21,22]. The most common complications were conduction abnormalities, which have been well-described in the literature [23,24].

Interestingly, our study found no significant differences in outcomes between patients with and without preoperative pulmonary hypertension. This finding contrasts with some previous studies that have reported higher complication rates and less favorable

Table 2
Logistic regression analysis of factors associated with left ventricular cavity normalization after interventional VSD closure.

Variable	B	SE	Wald	df	p-value	Exp(B)
Age	−0.886	0.423	4.394	1	0.036	0.412
Gender	−0.440	0.610	0.520	1	0.471	0.644
Defect size	0.423	0.157	7.303	1	0.007	1.527
Preoperative LV z-score	0.137	0.307	0.199	1	0.655	1.147
Pulmonary hypertension	−1.044	0.732	2.034	1	0.154	0.352
Postoperative residual shunt	0.271	0.747	0.131	1	0.717	1.311
Constant	−1.902	1.851	1.055	1	0.304	0.149

outcomes in patients with pulmonary hypertension [10]. However, our results suggest that with careful patient selection and appropriate management, transcatheter VSD closure can be safely and effectively performed in patients with preoperative pulmonary hypertension. These findings are supported by a study by Al-Kashkari et al., which reported similar success rates and complication rates in patients with and without pulmonary hypertension [25].

The long-term follow-up data in our study demonstrate the durability of the results, with no significant changes in LVEDD Z-scores or new complications observed beyond 1 year post-intervention. These findings are in line with previous studies that have reported sustained benefits and low rates of long-term complications following transcatheter VSD closure [26]. In a study by Ghaderian et al. the authors reported a 96.4 % complete closure rate and no significant complications at a median follow-up of 3.3 years [27].

Our study has several limitations that should be considered. First, the retrospective nature of the study and the single-center design may limit the generalizability of the results. More importantly, the lack of a surgical comparison group prevents us from drawing direct comparisons between transcatheter and surgical approaches regarding the speed and extent of LV dimension normalization. While our findings demonstrate rapid improvement in LV dimensions following transcatheter closure, future prospective studies comparing transcatheter versus surgical approaches are needed to determine whether one approach offers advantages in terms of LV remodeling. Such studies should consider not only the speed of LV normalization but also factors such as the impact of cardiopulmonary bypass, duration of hospital stay, recovery time, and long-term outcomes. Additionally, cost-effectiveness analyses comparing both approaches would provide valuable information for clinical decision-making. Future prospective, multi-center studies with longer follow-up periods are needed to further validate our findings and compare the outcomes of transcatheter and surgical VSD closure.

Our study provides further evidence supporting the use of transcatheter VSD closure as an effective and safe treatment option for pediatric patients with hemodynamically significant VSDs. The rapid normalization of left ventricular dimensions, low complication rates, and durability of the results highlight the advantages of this minimally invasive approach. Younger age and smaller VSD size were identified as predictors of more rapid left ventricular dimension normalization, which may help guide patient selection and follow-up strategies. The favorable outcomes observed in patients with preoperative pulmonary hypertension suggest that this subgroup may also benefit from transcatheter VSD closure, although careful patient selection and management remain crucial.

The rapid improvement in left ventricular dimensions following transcatheter VSD closure has important clinical implications. The prompt reduction in left ventricular volume overload may help prevent the development of adverse outcomes, such as ventricular dysfunction and arrhythmias [28]. Furthermore, the normalization of left ventricular size may allow for earlier discontinuation of medical therapy, such as diuretics and angiotensin-converting enzyme inhibitors, which are often prescribed to manage the hemodynamic consequences of VSD [29].

The low incidence of complications and the absence of significant differences in outcomes between patients with and without preoperative pulmonary hypertension in our study support the safety and efficacy of transcatheter VSD closure in a broad range of pediatric patients. These findings are particularly relevant given the increasing trend towards the use of transcatheter interventions in the management of congenital heart defects [30].

However, it is important to acknowledge that transcatheter VSD closure is a technically challenging procedure that requires a high level of expertise and a comprehensive understanding of the anatomy and hemodynamics of VSD [31]. The success of the procedure depends on careful patient selection, accurate device sizing, and optimal device positioning [32]. Therefore, it is essential that transcatheter VSD closure be performed by experienced operators in centers with adequate resources and support services.

In summary, our study demonstrates that transcatheter VSD closure is associated with a rapid and sustained improvement in left ventricular dimensions in pediatric patients, with younger age and smaller VSD size being predictors of more rapid normalization. The procedure is safe and effective, with favorable outcomes observed even in patients with preoperative pulmonary hypertension. These findings support the continued use and expansion of transcatheter VSD closure as a viable alternative to surgical intervention in appropriately selected patients. Future research should focus on long-term outcomes, cost-effectiveness, and the development of novel devices and techniques to further optimize the results of this promising approach.

CRediT authorship contribution statement

Hui Yuan: Writing – original draft. **Wenjing Zhu:** Data curation. **Jianli Lv:** Writing – review & editing.

Disclosures

The authors have no conflicts of interest to declare.

Ethical approval

This study was a retrospective analysis of clinical data. The Institutional Review Board (IRB) of Shandong Provincial Hospital Affiliated to Shandong First Medical University waived the requirement for ethical approval and informed consent due to the retrospective nature of the study and the use of anonymized patient data.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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