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Original Article

Transcatheter Closure for Ventricular Septal Defect (VSD): Unveiling Key Predictors in Pediatric Interventions

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Abstract

Background: Ventricular septal defect (VSD) stands out as the most prevalent congenital heart disease (CHD) in childhood, accounting for 15-20% of all defects, and results from deficiencies, misalignment, or failures in the fusion of components in the ventricular septum during embryological heart development. This study aims to investigate the factors influencing the failure of transcatheter closure for VSD.

Methods: This retrospective cohort study was conducted at the Integrated Heart Service Center, Udayana University Hospital. The study concentrated on examining the remaining 38 cases of children with VSD and AVP.

Results: This study demonstrates that the failure of transcatheter closure for VSDs is not linked to age, AVP, VSD size, and MSA. VSD type emerges as a significant and independent predictor of procedural failure, with a notable correlation. VSDs lacking membranous septal aneurysm and aortic regurgitation carry a heightened risk of failure, with SADC-type VSDs exhibiting a 3.5 times higher failure rate than PMO-type VSDs.

Conclusion: These findings underscore the critical role of VSD type in evaluating the success or failure of transcatheter closure procedures.

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Keywords: ventricular septal defect, transcatheter closure, pediatric interventions.

Introduction

The most common congenital heart defect in infants is a ventricular septal defect (VSD), which is also the second most common congenital abnormality in adults, behind a bicuspid aortic valve. The primary cause of hemodynamic compromise in VSD is improper communication between the left and right ventricles, which results in the creation of a shunt. Large flaws can cause harmful consequences such as pulmonary arterial hypertension (PAH), ventricular dysfunction, and an increased risk of arrhythmias, even though many VSDs repair naturally.[1–3]

Among all congenital heart diseases (CHD), VSD represents the most common form in childhood, constituting 15-20% of all defects.[1,2] These defects arise from a deficiency, misalignment, or failure of fusion of components within the ventricular septum during embryological heart development.[3]

The untreated or undiagnosed VSD follows a natural course marked by various complications, including hemodynamic disruptions, congestive cardiac failure, growth impairment, obstructions in the right or left ventricular outflow tract, aortic valve prolapses (AVP), and the eventual onset of aortic regurgitation (AR). Aortic regurgitation stands out as a significant and major complication, and the likelihood of AVP and AR significantly rises when VSD is not addressed.[4] Aortic valve prolapse and AR have prevalences of 4% to 9% and 2% to 6%, respectively.[5-9] These factors contribute to an elevated mortality risk linked with unrepaired VSD. Typically, spontaneous closure of VSD tends to happen within the first year of life.[2]

VSDs were shown to be the least prevalent types of VSDs in two different studies, pm-VSD was found to be the most common. Surgery is recommended when even minimal AR or AVP is present because AR is a progressive condition.[5,6] The literature indicates that AR is more commonly associated with VSD than with posterior malalignment VSD. The mechanisms leading to AVP include insufficient structural support of the leaflets due to VSD, abnormalities in commissural suspension, the absence of opposing forces, a lack of continuity between the aortic media and annulus, and the venturi effect.6. Tohyama et al.[7] found that AVP occurred in 69% of cases with DCSA-VSD. While most literature from Western countries reports a higher incidence of AR with DCSA, data from Pakistan suggest a higher incidence of AR in cases of pm-VSD.[8,9]

The initial two years of life are deemed critical for early correction, enhancing the likelihood of complete recovery of left ventricular function. Traditionally, surgical intervention is required for patients with VSD and AVP, but it frequently comes with complications such as bleeding, wound infection, diaphragm paralysis, and chylothorax.[1] However, the evolving field of transcatheter closure is increasingly being explored as an alternative for patients with VSD and AVP, though the effectiveness and safety of this approach for perimembranous VSD with AVP remain a subject of debate.

A further study by Ghosh et al. (2018) showed that the success rate of a transcatheterization procedure depends on the selection of the device being used. ADO-I or ADO-II devices were used depending on the size of the defect when the size of the subaortic rim was adequate, that is, ≥ 3 mm. If the defect is more than 5 mm, ADO-I was selected. In the case of subaortic VSD, where AVP is mild and the size of the true VSD is small (≤ 5 mm), device closure was attempted. This approach has been proven to show a good outcome in intermediate-term follow-up studies, with a success rate of 79%.[1] However, this study does not investigate the further selection of devices depending on the defect size, resulting in an insignificant correlation.

In Bali, there is currently a lack of data on risk factors for the failure of transcatheter VSD closure. Many VSDs in the region remain uncorrected or are diagnosed later in life, making it particularly intriguing to examine the characteristics of the disease and the outcomes of transcatheter closure in VSD patients. Acquiring such data is crucial for understanding the effectiveness of this procedure and establishing a baseline for early intervention in VSD cases, with the ultimate aim of reducing the incidence of procedure failures.

Methodology

This retrospective cohort study, was conducted at the Integrated Heart Service Center, Udayana University/ Prof. Dr. I G.N.G. Ngoerah Hospital from July 2009 to June 2022, explored the outcomes of transcatheter closure in patients with VSDs and AVP involvement. Inclusion criteria involved patients meeting these conditions within the specified timeframe, excluding cases with incomplete data. Data, including identity, age, gender, VSD size, type, device used, and outcomes, were extracted from the VSDs register. Consecutive sampling was employed, encompassing eligible patients meeting the criteria.

This study used instruments to collect data on variables including identity, age, gender, diagnosis, VSD characteristics, aortic regurgitation, device, and procedural outcomes. Data was obtained from the catheterization lab registry at Pelayanan Jantung Terpadu (PJT) in Prof Ngoerah Hospital. Consecutive sampling, based on inclusion/exclusion criteria, was employed until reaching the required sample size. Data collection involved recording details for statistical analysis using IBM SPSS 27. Descriptive analysis presented variable summaries, and Chi-square tests assessed relationships, with significance at $p \le 0.05$. Ethical approval was granted by the Research Ethics Commission of the Faculty of Medicine, Universitas Udayana/Prof. DR. I G.N.G. Ngoerah Hospital (Letter: 1706/UN14.2.2.VII.14/LT/2023), and a research permit was obtained (Letter: DP.04.03/XIV.2.2.2/37294/2023)

Results

In the initial phase of the study, 428 children who had been diagnosed with VSD were considered. Among them, 146 were excluded from the study as they had undergone only angiography, and not transcatheter VSD closure. The primary focus of the investigation was then directed towards 282 cases of VSD, encompassing both those with and without aortic valve prolapse, that underwent transcatheter VSD closure. Within this subset, 244 cases without aortic valve prolapse were further excluded from the analysis. Consequently, the study concentrated on examining the remaining 38 cases of VSD with aortic valve prolapse. The visual representation of this study's progression is outlined in **Figure 1**, providing a flowchart that illustrates the selection and exclusion criteria.

From our study population of 38 participants, a greater proportion of patients who achieved success in the transcatheter VSD closure procedure were observed among those aged < 5 years compared to those aged > 5 years, with a higher prevalence among female patients. AVP with AR was identified in 25 patients (65.72%), with the most successful closures occurring in VSD cases without aortic regurgitation (84.6%). The highest success rate was found in small-sized VSDs (81.8%), followed by moderate-sized VSDs (73.3%), while large-sized VSDs had the lowest success rate. Perimembranous VSD (Pm-VSD) was the predominant type (60.5%) in our study. MFO was utilized in 24 patients, with the ADO-II group showing the highest

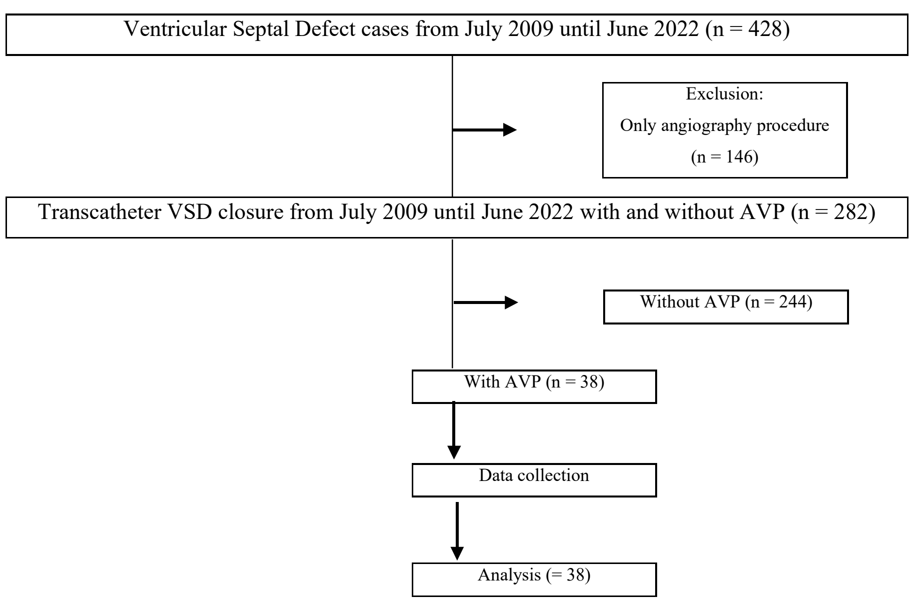

Figure 1. Research flow.

success. Complications were observed in 13 patients. Univariate analysis was conducted to describe each variable, including both independent and dependent variables, by presenting the frequency distribution of the samples. Among the samples with Membranous Septal Aneurysm (MSA), 12 VSD cases were identified, and of the total samples, 18 patients without MSA (69.2%) and 10 patients with MSA were successfully closed. The characteristics of the subjects and their outcomes are detailed in **Table 1.**

Table 2 reveals that there is no observed correlation between the failure of transcatheter VSD closure and age, the presence of aortic regurgitation, VSD size, or the presence of membranous septal aneurysm. The risk of failure in VSD with aortic regurgitation is twice as high (with a confidence interval of 0.514–8.410) compared to patients without aortic regurgitation. Similarly, the risk of failure in VSD without a membranous septal aneurysm is 1.8 times greater (with a confidence interval of 0.460–7.415) compared to patients with membranous septal aneurysm. Bivariate analysis using the chi-square test indicates a significant relationship between VSD

Table 1. Characteristics Patient and Its Outcome Results.

Variabel	Failed		Success	
	n	%	n	%
Age groups, n (%)				
≥ 5 years	4	26.7	11	73.3
< 5 years	6	26.1	17	73.9
Sex, n (%)				
Male	5	31.3	11	68.8
Female	5	22.7	17	77.3
VSD Size				
Small	2	18.2	9	81.8
Moderate	4	26.7	11	73.3
Large	4	33.3	8	66.7
VSD Type				
SADC	7	46.7	8	53.3
PMO	3	13.0	20	87.0
AVP				
With AR	8	32.0	17	68.0
Without AR	2	15.4	11	84.6
Device				
NIT	1	33.3	2	66.7
MFO	7	29.1	17	70.8
ADO-II	2	18.2	9	81.8
Complication				
Minor Complication	3	23.1	10	76.9
No Complication	7	28.0	18	72.0
MSA				
No MSA	8	30.8	18	69.2
MSA	2	16.7	10	83.3

Abbreviations: AR, aortic regurgitation; VSD, ventricular septal defect; SADC, sub arterial doubly committed; AVP, aortic valve prolapse; PMO: Peri membranous Outlet; MSA, Membranous Septal Aneurysm

Table 2. Risk Factors of transcatheter failure in VSD patients.

Variabel	Failed (n=10)		Success (n=28)		RR	95% CI	P value
	n	%	n	%			
Age groups, n (%)							
≥ 5 years	4	26.7	11	73.3	1.022	0.345 – 3.026	1.000
< 5 years	6	26.1	17	73.9			
AVP							
With AR	8	32.0	17	68.0	2.080	0.514 – 8.410	0.441
Without AR	2	15.4	11	84.6			
VSD size							
Small	2	18.2	9	81.8	2.250	0.321 –15.756	0.706
Moderate	4	26.7	11	73.3	1.375	0.262 – 7.220	
Large	4	33.3	8	66.7			
VSD Type							
SADC	7	46.7	8	53.3	3.578	1.093 –11.711	0.030
PMO	3	13.0	20	87.0			
MSA							
No MSA	8	30.8	18	69.2	1.846	0.460 – 7.415	0.453
MSA	2	16.7	10	83.3			

Abbreviations: AR, aortic regurgitation; VSD, ventricular septal defect; SADC, Sub Arterial Doubly committed; AVP, Aortic Valve Prolapse; PMO: Peri membranous Outlet; MSA, Membranous Septal Aneurysm

type and the outcome of transcatheter VSD closure, with a p-value of 0.005 ($p < 0.05$). The failure rate in transcatheter closure for SADC-type VSD is 3.5 times higher (CI 1.093–11.711; p = 0.030) compared to PMO-type VSD, with a higher success rate of closure in PMO-type VSD (n = 20, 87.0%) compared to SADC-type VSD (n = 8, 53.3%).

The findings reveal that the type of VSD emerged as a distinct factor predicting the failure of the procedure. In other words, regardless of other variables considered, the specific category or type of VSD was identified as a key independent factor influencing the likelihood of the transcatheter closure procedure ending in failure. This underscores the significance of VSD type in determining procedural outcomes, indicating that certain characteristics associated with different VSD types have a notable impact on the success or failure of the transcatheter closure. The independence of this predictor suggests that its influence is not contingent on other factors examined in the analysis, emphasizing the importance of considering VSD type when assessing the potential success of the procedure.

Discussion

Transcatheter closure of specific types of VSD has been widely performed, especially in developing countries, with encouraging follow-up results. Nevertheless, adverse outcomes and failure of closure may occur, which requires sufficient attention. Failure of closure in this study is defined as several conditions that cause the defect fail to close such as worsening aortic regurgitation, AV Block condition, emboli of the device and significant residual flow. This study explored the relationship between several factors in predicting the probability of transcatheter closure failure in 38 children with VSD in Bali, Indonesia.

Correlation Between Age and Transcatheter VSD Closure

The age of the patient was not found to significantly increase the risk of failure of the procedure in this study. This was in line with results from a meta-analysis done by Huang et al. (2020) and Zhi-Nuan Hong et al. (2019), where it was found that mean age indicated no significant correlation with the success rate.[10,2] The insignificant correlation between age and the success rate of the procedure might be influenced by the homogeneity and small sample size in our study.

Correlation Between AVP and Transcatheter VSD Closure

Aortic valve lesions are common in the natural history of outlet VSDs. Previous studies identified the "venturi effect" as the predominant cause of this phenomenon. Due to the proximity of the aortic valve leaflets to the defect, a pressure gradient was formed from the valve to the defect, pulling the aortic valve cusps toward the shunting. Aortic regurgitation implies aortic valve incompetence, with a risk of developing left ventricular dysfunction, heart failure, and even death. Aortic regurgitation is one of the major considerations in the transcatheter closure of VSD. Surgery performed because of aortic regurgitation that occurred during or after the transcatheter procedure has been reported.[11]

In our study, the manifestation of aortic regurgitation increased the risk of failure by twofold compared to cases without aortic regurgitation. The result of this study is in line with another study done by Yang et al. (2021), where it was found that new onset or worsening aortic regurgitation was the primary cause for unplanned surgery after transcatheter closure of VSD in children, indicating its high influence on the failure of closure.[11] Similarly, another study done by Li et al. (2023) found that the presence of aortic regurgitation significantly increases the risk of procedure failure.[12] The possible cause of aortic regurgitation is the edema to damage of the aortic valve caused by the guidewire, delivery sheath, or occluder, especially in patients with intracristal VSD or primary aortic valve prolapse.

Aortic valve prolapse has been intimately linked to the occurrence or worsening of aortic regurgitation. This is because the distal part of the delivery sheath is difficult to press into the left ventricle, and the process of repeatedly pressing the distal part of the delivery sheath into the left ventricle and establishing an arteriovenous track would increase the risk of aortic valve injury. Furthermore, if the distal part of the delivery sheath fails to press into the left ventricle, the left disc of the occluder will be released in the ascending aorta, thereby increasing the possibility of aortic valve damage. Most importantly, significant aortic regurgitation after device implantation may be related to the failure to accurately estimate the size and location of the defect due to prolapse of the aortic valve into the defect site. [11] Further study and follow-up are needed to evaluate the progression of AR after the closure.

Correlation Between VSD Size and Transcatheter VSD Closure

VSD size has also been found to increase the risk of closure failure in our study, with the highest chance of failure occurring in the large defect (33.3%), followed by the moderate and small defect (18.2%). A study done by Huang et al. (2020) showed that mean VSD size does not correlate with success rate. This is in line with our study, as the risk of failure with small defects was not found to be significant. This might be caused by the absence of uniform patient inclusion criteria. A previous study hypothesized that there should be a clear definition of whether patients with VSD sizes between 5 mm and 10 mm or patients with mild aortic valve prolapse (AVP) could undergo the procedure. Most studies recommended that the VSD size should be less than 10 mm.[10]

However, Cao et al. recommended that the VSD size should be less than 5 mm. They found that in cases with a VSD size > 5 mm, the effective contact area of the occluder became small, and, in cases with a VSD size < 5 mm, there was a relatively small opening in the superior margin. Thus, in cases with a VSD size < 5 mm, the device rarely affects the pulmonary valve and is less likely to be displaced from the original position.[13] This highlights the importance of setting the parameter of defect size to further annotate the significant influence on the success rate of the procedure.

A further study by Ghosh et al. (2018) showed that the success rate of a transcatheterization procedure depends on the selection of the device being used. ADO-I or ADO-II devices were used depending on the size of the defect when the size of the subaortic rim was adequate, that is, ≥ 3 mm. If the defect is more than 5 mm, ADO-I was selected. In the case of subaortic VSD, where AVP is mild and the size of the true VSD is small (≤ 5 mm), device closure was attempted. This approach has been proven to show a good outcome in intermediate-term follow-up studies, with a success rate of 79%.[1] However, this study does not investigate the further selection of devices depending on the defect size, resulting in an insignificant correlation.

Correlation Between VSD Type and Transcatheter VSD Closure

The type of VSD was a significant predictor of transcatheterization procedure failure, with an almost 4-fold higher incidence of failure in the DCSA VSD type than the PMO type. A higher success outcome of closure was found in PMO-type VSD (87.0%) compared to DCSA-type VSD (53.3%). This study was in line with the study by Diandong et al. (2003), which showed a procedural success rate of 96.3% and 84.6% in the PMO VSD and DCSA groups, respectively (P = 0.002). Similarly, a previous study done by Yulianti et al. (2016) reported that in DCSA VSD patients, failure was caused by aortic valve disorders resulting in aortic regurgitation and aortic prolapse.

The incidence of cancellation due to heart conduction disturbances was smaller than that of the VSD PMO type. The study reported by C. Zhao Yang, C. Hua, M. Yuan Ji, et al. showed a lower success rate of transcatheter closure of DCSA-VSD around 66%.28 Another study revealed that aortic valve disorders occur in 5-8% of the PMO-type VSD and 30% of the DCSA-type VSD because the DCSA VSD is located just below the aortic valve. In the case of DCSA VSD, the aortic valve disorder occurs initially in the diastolic phase due to the venturi effect produced by the left-to-right shunt, then prolapse can occur during the systolic phase because the damaged aortic valve is no longer able to withstand high aortic pressure. In the case of DCSA VSD, aortic prolapse also occurs due to the deficiency of the support structure in the subaortic area, such that this event happens quickly, leading to the failure of the procedure.[14]

Correlation Between MSA and Transcatheter VSD Closure

The absence of MSA has been found to increase the risk of failure of closure as high by almost twofold. This result was in line with a study done by Shedoudy et al. (2019), where it was found that the success rate of VSD closure in patients with a membranous septal aneurysm was as high as 98.75% in 79 patients.[15] Another study done by Zhao et al. (2017) also found a successful transcatheter closure of multiple membranous ventricular septal defects with giant aneurysms using double occluders in four patients.[16] Previous case reports done by Bakr et al. (2020) on a five-year-old boy with MSA also resulted in a successful closure.[17]

An aneurysm of the membranous ventricular septum is a tissue dilatation of this portion, and since it is weak, it bulges to the right ventricle (RV) as a consequence of left ventricle pressure. The most widely accepted theory regarding the etiology of a membranous septum aneurysm is that it forms during spontaneous closure or diminution in the size of a VSD. According to a previous study, the possibility of MSA causing an obstruction is rare.[17] It was also noted that the presence of MSA can provide sufficient space to hold two devices while avoiding aortic valve interference. Thus, another venous access and another A-V loop could be created via the residual defect.[16] This might contribute to a higher chance of successful closure in patients with membranous septal aneurysms.

Study Limitation

Our study faced limitations due to its retrospective design, relying on secondary data from medical records, which restricted our analysis to available predictors. Moreover, the research was conducted solely in a single referral hospital, potentially limiting the generalizability of our findings. The sample size was relatively small, with only 38 results, possibly leading to insufficient data distribution and insignificant correlations between some analyzed factors. Additionally, the absence of multivariate analysis was due to the small number of participants, hindering a comprehensive exploration of how different factors collectively influence the success or failure of the transcatheter VSD closure procedure. To address these limitations and enhance future studies, it is recommended to include a larger and more diverse sample and to conduct multivariate analysis for a more accurate understanding of the combined impact of various factors on VSD closure outcomes..

Conclusion

This study reveals that the failure of transcatheter closure for VSDs is not associated with age, aortic regurgitation, VSD size, or the presence of MSA. However, VSD type is identified as a significant independent predictor of procedure failure, showing a substantial correlation. Specifically, VSDs without membranous septal aneurysm and aortic regurgitation exhibit a higher risk of failure. Notably, SADC-type VSDs have a 3.5 times higher failure rate compared to PMO-type VSDs. These findings emphasize the importance of considering VSD type when assessing the success or failure of transcatheter closure procedures.

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