Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.61, No.6(2021). p.311-6; DOI: 10.14238/pi61.6.2021.311-6

Original Article

Predictors of transcatheter closure cancellation in children with ventricular septal defect

Arta Christin Yulianti, Indah Kartika Murni, Noormanto, Sasmito Nugroho

Abstract

Background Ventricle septal defect (VSD) is the most common type of congenital heart disease in children. If definitive therapy delayed, failure to thrive and developmental delays can lead to decreased quality of life. The options for VSD closure include surgical and minimally invasive procedures with transcatheterization. Although transcatheterization is considered to be the safest therapy, the risk of complications can lead to cancellation of procedure.

Objective To determine whether nutritional status, body height, VSD type and size, and type of device used were predictors of cancellation of transcatheter closure of VSD.

Methods A retrospective cohort study using medical records was performed for all children who underwent transcatheter closure of VSD at Dr. Sardjito Hospital, Yogyakarta, Central Java, between January 2017 to March 2020. Cancellation of closure was defined as complications occurring during the procedure, such as cardiac conduction problems, valve regurgitation, and device embolization. Multivariate logistic regression analysis was done to determine independent predictors of closure cancellation.

Results One hundred thirty-four children were enrolled. Independent variables that were significant predictors were doubly committed subarterial (DCSA) VSD type (OR 5.98; 95%CI 1.52 to 23.61; P=0.045), moderate VSD size (OR 15.59; 95%CI 4.67 to 52.06; P=0.001), and types of devices used: symmetric (OR 27.06; 95%CI 2.75 to 266.17; P=0.001), asymmetric (OR 16.46; 95%CI 2.15 to 210.0; P=0.001), and coil (OR 21.26; 95%CI 2.15 to 210.0; P=0.001). Taller body height was a protective factor against cancellation of the procedure (OR 0.98; 95%CI 0.96 to 1.00; P=0.008).

Conclusion Significant predictors of cancellation of transcatheter VSD closure are DCSA VSD, moderate VSD size, as well as coil, symmetric, and asymmetric devices, and increased body height. **[Paediatr Indones. 2021;61:311-6 ; DOI: 10.14238/pi61.6.2021.311-6**].

Keywords: *ventricular septal defect; transcatheterization closure; procedure cancellation; children*

Ventricular septal defect is the most common of congenital heart malformations, accounting for 20-30% of all congenital heart defects.[1] This non-cyanotic defect is marked by a ventricular shunt and affects blood flow to the lungs. Clinical manifestations depend on the size of the defect. In 2011, the *World Health Organization* (WHO) reported an incidence of congenital heart disease (CHD) to be 8 in every 1,000 births.[2] In 2017, the estimated CHD prevalence was 10-12 per 1,000 live births, and represented 1.35 million live births each year. The highest CHD birth prevalence was in Asia at 9.3 per 1,000 live births, and the lowest in Africa at 1.9 per 1,000 live births.[2] If the defect remains uncorrected, pulmonary resistance could increase, leading to malnutrition, decreased immunity, and reduced quality of life.[3]

Almost all types of VSD can be corrected. Surgery was once the first choice for VSD repair, but nowadays, catheterization closure is preferred because it is less invasive. Although CHD can be optimally managed

From the Department of Child Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/Dr. Sardjito Hospital, Yogyakarta, Central Java, Indonesia.

Corresponding author: Indah K Murni, Department of Child Health, Faculty of Medicine, Public Health and Nursing, Universitas Gadjah Mada/ Dr. Sardjito Hospital. Jl. Kesehatan no. 1 Sleman, Yogyakarta. Phone: +62816685894. Email: indah.kartika.m@ugm.ac.id.

Submitted January 14, 2020. Accepted November 22, 2021.

through surgical techniques and medical management to prevent congestive heart failure, morbidity and mortality rates in CHD are still high. Through developments in the field of interventional cardiology, currently several types of CHD can be closed by cardiac catheterization.[4]

However, transcatheter closure of VSDs remains a major challenge because side effects could lead to cancellation, including complete atrioventricular block (AVB) which is the most serious complication ranging from 3 to 20%, valve impairment, especially of the tricuspid and aortic valves with incidences of 5-26%, and device embolization, which can cause the device to escape from the defect and migrate to another cardiac chamber with an incidence of 4%.[4,5] These complications cannot be completely prevented during the procedure and result in cancellation of the procedure. Therefore, it is very important to determine predictive factors for cancellation prior to the procedure.[6]

The *American Heart Association* (AHA) stated the risk of device embolization occurred because of unmatched defect and device sizes. The valve disorder risk results from the VSD being located very close to the heart valve. For example, the doubly committed subarterial (DCSA) type of VSD is very close to the aortic valve. Furthermore, impaired cardiac conduction due to the proximity of the defect to the conduction system pathway can occur especially in perimembraneous outlet (PMO) VSDs, as well as vascular damage related to the procedure.[5] The larger the defect size, the higher the risk of procedure cancellation in the transcatheterization of the VSD closure, since the attachment area of the device to the septum is smaller in larger defects. The location of the defect can also predict procedure cancellation. The PMO type of VSD is commonly associated with heart conduction disturbances, while DCSA VSD tends to occur in aortic valve disorders because of close proximity.[7]

Therefore, it is important to determine factors that can predict the cancellation of transcatheter VSD closure, in order to minimize the complications and improve the quality of cardiac transcatheterization as a therapeutic modality.

Methods

This retrospective cohort study was done using information from patients' medical records. All children aged less than 18 years who underwent transcatheter closure of VSDs in Dr Sardjito Hospital, Yogyakarta, Central Java, between January 2017 and March 2020 were included. Cancellation of VSD closure was defined as complications occurring during the procedure, such as cardiac conduction disorders, heart valve impairment (especially the tricuspid and aortic valves), and device embolization, that forced the physician to abort the procedure. Patients with more than one lesion, complex congenital heart disease, or irreversible pulmonary hypertension were excluded from this study. Patients were observed for the duration of the procedure and up to 24 hours after the procedure.

Five potential predictor factors for cancellation of transcatheter VSD closure were included as follows: nutritional status, body height, types of VSD, sizes of VSD, and types of devices used. Data analysis was performed using *SPSS version 20.0* software. The VSD was considered small if the size was less or equal to 25% of the aortic annulus diameter, medium if more than 25% but less than 75%, and large if it was greater than 75% of the aortic annulus diameter.

Baseline data and outcomes were described using mean, median, or proportions, as appropriate. Bivariate analysis by Chi-square test was used to analyze each predictor and cancellation of transcatheter VSD closure. Further, multivariable analysis was conducted to determine which predictors were independently associated with the cancellation of transcatheter VSD closure. All potential predictors with P values less than 0.25 in the bivariate analysis were included in the multivariable model. Findings were presented as odds ratios with corresponding 95% confidence intervals (CIs) and P values. This study was approved by the Medical Research Ethics Committee of the Universitas Gadjah Mada, Yogyakarta, Indonesia.

Results

During the study period, 134 children underwent transcatheter VSD closure, of whom 32 (23.8%) had their procedures cancelled during transcatheterization (**Table 1**).

A total of five predictors were analyzed to predict transcatheter closure cancellation in children with VSD. Bivariate analysis identified four predictors that were significantly associated with cancellation of the procedure including body height, type of VSD, size of VSD, and type of device (**Table 2**). Multivariable analysis revealed that type of VSD, size of VSD, and type of device were predictors that remained independently associated with procedure cancellation. The DSCA type of VSD was associated with the an almost six-fold increase in the probability of procedure cancellation. Moderate size VSD was independently

Table 1. Bivariate analysis of subject characteristics

Characteristics	Cancelled (n=32)	Continued (n=102)	P value
Male sex, n (%)	22 (68.8)	61 (59.8)	0.363
Median age (range), years	3.75 (1-17)	5.08 (1.1-17.67)	0.086
Median body weight (range), kg	12.7 (4.3-55.0)	16.0 (7.6-54.0)	0.041
Median body height (range), cm	93 (54-165)	104 (71.5-174)	0.008
Nutritional status, n (%)			0.501
Severe malnutrition	2 (6.3)	13 (12.7)	
Moderate malnutrition	11 (34.3)	38 (37.3)	
Good	19 (59.4)	51 (50.0)	
Type of VSD, n (%)			0.045
DCSA	11 (34.4)	18 (17.6)	
PMO	21 (65.6)	84 (82.4)	
Size of VSD, n (%)			0.001
Moderate	19 (59.4)	11 (10.8)	
Small	13 (40.6)	91 (89.2)	
Type of device, n (%)			0.001
Coil	10 (31.3)	15 (14.7)	
Asymmetric	9 (28.1)	22 (21.6)	
Symmetric	11 (34.4)	14 (13.7)	
ADO II	1 (3.1)	10 (9.8)	
MFO	1 (3.1)	41 (40.2)	

Notes: VSD=ventricular septal defect; DCSA=doubly committed subarterial; PMO=perimembraneous outlet; ADO II = Amplatzer ductal occluder II; MFO=multifunctional occluder

Table 2. Multivariable analysis of predictors of procedure cancellation

Predictors	OR (95%CI)	Adjusted OR (95%CI)	P value
Nutritional status			
Severe malnutrition	0.49 (0.13 to 1.89)		0.260
Moderate malnutrition	0.83 (0.43 to 1.58)		0.562
Good			
Median body weight (range), kg		1.08 (0.94 to 1.24)	0.273
Median body height (range), cm		0.98 (0.96 to 1.00)	0.008
Type of VSD			
DCSA	1.89 (1.04 to 3.46)	5.98 (1.52 to 23.61)	0.045
PMO			
Size of VSD			
Moderate	5.07 (2.85 to 9.02)	15.59 (4.67 to 52.06)	0.001
Small			
Type of device			
Coil	16.80 (2.28 to 123.53)	21.26 (2.15 to 210.0)	0.001
Asymmetric	12.19 (1.63 to 91.29)	16.46 (1.66 to 163.16)	0.001
Symmetric	18.48 (2.54 to 134.69)	27.06 (2.75 to 266.17)	0.001
ADO II	3.82 (0.26 to 56.31)		0.375
MFO			

Notes: DCSA=doubly committed subarterial; PMO=perimembraneous outlet; ADO II=amplatzer ductal occluder II; MFO=multifunctional occluder

predictive of almost 16-fold higher cancellation. Types of devices used were independently associated with a 3 to 27-fold increase in the probability of cancellation.

Discussion

We explored the relationship of several factors with predicting the probability of the cancellation of transcatheter closure in 134 children with VSD in Yogyakarta, Indonesia. The type of VSD, size of VSD, type of device, and body height were independent predictors of the procedure cancellation.

We found that the nutritional status of children at the time of the procedure was not a significant predictor for cancellation. This finding was not in agreement with a previous study which stated that worse nutritional status of the child increased the risk of cancellation of transcatheter VSD closure.[8] Lower nutritional status meant lower components of body weight compared to age, weight compared to height, and height compared to age. Lower body weight also meant the child's blood vessels were more fragile and the tunica intima were thinner. In addition, lower body weight, indicated worse myocardial contractility, due to reduced basal metabolism.[8] Another study also stated that cancellation of transcatheter VSD closure was significantly associated with patient body weight below 10 kg and increased risk of aortic valve disorders. Body weight <10 kg at the time of the procedure might be related to the fragility of the blood vessels and ifficulty in attaching the device to the VSD, leading to cancellation.[8] In our study, the potential predictors chosen were nutritional status which comprised body weight based on age, height for age, and weight based on height. Previous study reported that nutritional status is considered to be related to the amount of total body fat mass, so that it reflects the level of body phospholipids, which are one of the major components in the construction of blood vessels in the body, thus reflecting the maturity of vascularization with good myocardial function so that the pressure is maintained in the heart chambers.[8] However, we found no relationship between nutritional status and cancellation of transcatheter VSD closure. This observation may have been caused by the uneven distribution of subjects for each nutritional status category, as 52.2% of all subjects had good nutritional status.

The type of VSD was a significant predictor for cancellation of transcatheterization, with an almost 6-fold higher incidence of cancellation in the DCSA VSD type than the PMO type. Furthermore, the DCSA VSD whose procedure was cancelled were mostly dominated by aortic valve disorders (8 subjects; 61.5%). Similarly, previous studies reported that in DCSA VSD patients, cancellation was caused by aortic valve disorders resulting in aortic regurgitation to aortic prolapse. The incidence of cancellation due to heart conduction disturbances was smaller than that of the VSD PMO type.[9,10] Another study revealed that aortic valve disorders occur in 5-8% of the PMO-type VSD and 30% of the DCSA type, 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 cancellation of the procedure.[11]

The type of device was also a significant predictor of VSD transcatheter closure cancellation. Coil, symmetric, and asymmetric devices had a high risk of procedure cancellation. Similarly, several case reports and previous studies demonstrated that coil devices quite often led to procedure cancellation in transcatheter and percutaneous VSD closure. Tricuspid valve disorders are the most common complication during the procedure, especially in PMO VSD cases, because of direct mechanical compression of the device against the tricuspid valve. Complications after the procedure include the occurrence of tricuspid valve disorders and arrhythmias in the form of complete atrioventricular block and PR wave interval prolongation, which improves with corticosteroid therapy.[11-14] The anatomical position of the PMO VSD, which is very posterior and close to the tricuspid valve, as well as the suboptimal configuration of the device, are the most likely causes. Furthermore, the incidence of arrhythmias after the procedure is related to the inflammatory process that occurs due to the shape of the device not matching the VSD anatomy, resulting in friction which causes edema and disrupts the cardiac conduction system.[15] In the PMO VSD, the incidence

of tricuspid valve disorders is quite high with the use of asymmetric devices, especially in PMO VSD with aneurysms.[16] This observation was in agreement with our study; among children with PMO VSDs who used asymmetrical devices, cancellation occurred in 1 of 3 children. In DCSA VSDs, the use of symmetrical devices increased the risk of procedure cancellation because the DCSA VSD has a very short muscular rim (<2mm), so that aortic valve disorders are very frequent.[17] Hence, of the 6 DCSA VSD using the symmetrical device, 4 subjects had their procedures cancelled. The main causes of cancellation were aortic valve disorders.

We found that every 1 cm increase in height reduced the risk of procedure cancellation by 0.98 times. Thus, height was a protective factor against cancellation of transcatheter VSD closure. Previous studies found that lower height meant smaller body surface area, possibly resulting in lower vascular thickness, which can lead to an increased risk of vascular disorders and complications of cardiac catheterization.[18,19] However, previous studies did not directly investigate the relationship of patient height specifically to transcatheter VSD closure, but only to extensive cardiac catheterization.

These findings strengthen the need for careful consideration in choosing the type of device most appropriate to the VSD anatomy. Such consideration could reduce the incidence of cancellation of transcatheter VSD closure in pediatric patients.

This study was limited by its retrospective design, as we used secondary data from medical records, which enabled us to analyze only the available predictors. Furthermore, this study was conducted in a single referral hospital in Yogyakarta, Indonesia, which may limit the generalizability of this study. In conclusion, DCSA VSD type, moderate size VSD, device type (coil, symmetrical, and asymmetrical), and height are independent predictors of cancellation of transcatheter closure in pediatric patients with VSD.

Conflict of interest

None declared.

Funding Acknowledgment

The authors received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors.

References

1. Djer MM, Madiyono B. Tatalaksana Penyakit Jantung Bawaan. Sari Pediatr. 2000;2:155-62. DOI: 10.14238/sp2.3.2000.155-62.
2. Musa NL, Hjortdal V, Zheleva B, Murni IK, Sano S, Schwartz S, *et al.* The global burden of paediatric heart disease. Cardiology in the young. 2017. 2017;27:S3-S8. DOI: 10.1017/S1047951117002530.
3. Sari NK, Soetadji A, Kosim MS. Hubungan antara Besarnya Defek Septum Ventrikel dengan Fungsi Paru. Sari Pediatr. 2016;16:189-94. DOI: 10.14238/sp16.3.2014.189-94.
4. Carminati M, Butera G, Chessa M, De Giovanni J, Fisher G, Gewillig M, *et al.* Transcatheter closure of congenital ventricular septal defects: Results of the European Registry. Eur Heart J. 2007;28:2361-8. DOI: 0.1016/j.amjcard.2005.09.068.
5. Feltes TF, Bacha E, Beekman RH, Cheatham JP, Feinstein JA, Gomes AS, *et al.* Indications for cardiac catheterization and intervention in pediatric cardiac disease: A scientific statement from the American Heart Association. Circulation. 2011;123:2607-52. DOI: 10.1161/CIR.0b013e31821b1f10.
6. Zhao LJ, Han B, Zhang JJ, Yi YC, Jiang DD, Lyu JL. Postprocedural outcomes and risk factors for arrhythmias following transcatheter closure of congenital perimembranous ventricular septal defect: A single-center retrospective study. Chin Med J (Engl). 2017; 130:516-21. DOI: 10.4103/0366-6999.200551 .
7. Mandal KD, Su D, Pang Y. Long-term outcome of transcatheter device closure of perimembranous ventricular septal defects. Front Pediatr. 2018; 6:128. DOI:10.3389/fped.2018.00128.
8. Radman M, Mack R, Barnoya J, Castañeda A, Rosales M, Azakie A, *et al.* The effect of preoperative nutritional status on postoperative outcomes in children undergoing surgery for congenital heart defects in San Francisco (UCSF) and Guatemala City (UNICAR). J Thorac Cardiovasc Surg. 2014; 147:442-50. DOI: 10.1016/j.jtcvs.2013.03.023.
9. Huang JS, Sun KP, Huang ST, Chen Q, Chen LW, Kuo YR. A meta-analysis of perventricular device closure of doubly committed subarterial ventricular septal defects.

J Cardiothorac Surg. 2020; 15:28. DOI: 10.1186/s13019-020-1062-0.

10. Huang Y, Yan X, Lu L, Fang J, Sun X, Zhong L, *et al.* Transcatheter closure of doubly committed subarterial ventricular septal defects with the Amplatzer ductal occluder: Initial experience. Cardiol Young. 2019;29:570-5. DOI: 10.1017/S104795111900009X.
11. Ghosh S, Sridhar A, Solomon N, Sivaprakasham M. Transcatheter closure of ventricular septal defect in aortic valve prolapse and aortic regurgitation. Indian Heart J. 2018;70:528-32. DOI: 10.1016/j.ihj.2017.11.023.
12. Zhao J, Li J, Wei X, Zhao B, Sun W. Tricuspid valve detachment in closure of congenital ventricular septal defect. Texas Hear Inst J. 2003;30:38-41.
13. Andersen H, de Leval MR, Tsang VT, Elliott MJ, Anderson RH, Cook AC. Is Complete Heart Block After Surgical Closure of Ventricular Septum Defects Still an Issue? Ann Thorac Surg. 2006;82:948-56. DOI: 10.1016/j.athoracsur.2006.04.030.
14. Liu J, Wang Z, Gao L, Tan HL, Zheng Q, Zhang ML. A large institutional study on outcomes and complications after transcatheter closure of a perimembranous-type ventricular septal defect in 890 cases. Acta Cardiol Sin. 2013;29:271-6. PMID: 27122716.
15. Sanz AP, Álvarez-Fuente M, Centella T, del Cerro MJ. Early complete atrioventricular block after percutaneous closure of a perimembranous ventricular septal defect with a Nit-Occlud (®) Lê VSD coil. Prog Pediatr Cardiol. 2018;49. DOI: 10.1016/j.ppedcard.2018.02.009.
16. Li P, Zhao XX, Zheng X, Qin YW. Arrhythmias after transcatheter closure of perimembranous ventricular septal defects with a modified double-disk occluder: Early and long-term results. Heart Vessels. 2012;27:405-10. DOI: 10.1007/s00380-011-0155-z.
17. Gu M, You X, Zhao X, Zheng X, Qin YW. Transcatheter device closure of intracristal ventricular septal defects. Am J Cardiol. 2011;107:110-3. DOI: 10.1016/j.amjcard.2010.08.053.
18. Roushdy AM, Abdelmonem N, El Fiky AA. Factors affecting vascular access complications in children undergoing congenital cardiac catheterization. Cardiol Young. 2012;22:136-44. DOI: 10.1017/S1047951111000989.
19. Roushdy AM, Abdelmonem N, El Fiky AA. Factors affecting vascular access complications in children undergoing congenital cardiac catheterization. Cardiol Young. 2012;22:136-44. DOI: 10.1017/S1047951111000989.