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Percutaneous Secundum Atrial Septal Defect Closure: Failure Rate and Procedural Predictors

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Background: Percutaneous atrial septal defect (ASD) closure is one of therapeutic options for patients with a suitable ASD anatomy, however in developing countries, the exact figure and procedural characteristics remain unknown. Therefore, this study was conducted to identify the failure rate and procedural predictors of the percutaneous ASD closure.
Materials and methods: A retrospective study using a database of all patients undergoing percutaneous ASD closure was conducted between March 2010 to November 2023. Patients who developed a pulmonary hypertensive crisis during the procedure were excluded. Procedural and echocardiographic parameter were measured and analyzed.
Results: A total of 112 samples were included in this study, 74.1% were female and 55.36% were pediatric patients. The failure rate was 12.5% (n=14) with diameter index was higher in the failed group. Unpaired T-test revealed that ASD size was one of the predictor failure in pediatric patients (mean diameter: 24.7±6.46 mm *vs.* 16.36±5.94 mm, *p*=0.001). There were no statistically significant variations in rim diameters, while compared with all patients with appropriate rims (rim ≥7mm), the failure rate was higher in patients with two rims measuring between 5.9 and 6.9 mm and rims less than 5 mm. Two patients presented with device embolization and required surgical device removal.
Conclusion: The failure rate of percutaneous ASD closure was 12.5%. A larger ASD increases the risk of failure of percutaneous closure in pediatric patients. Furthermore, patient with 5-6.9 mm on two or more rims as well as those with rim less than 5 mm, have a higher failure rate.

Keywords: *secundum atrial septal defect, percutaneous closure, failure rate*

Introduction

Atrial septal defect (ASD) is an interatrial septum (IAS) defect in the heart. There are four types of ASD based on the location of the defect, namely defects in the ostium secundum, ostium primum, sinus venosus and coronary sinus. Ostium secundum defects are the most prevalent defects in ASD with an incidence of 144/100,000 live births.[1,2] Spontaneous closure of ASD can occur in the first year of life, especially if a defect measuring <5 mm is found, while defects >1 cm generally require defect closure.[3-5] Defect closure with a surgical procedure is one of therapeutic options, Nonetheless, over the last 40 years, percutaneous defect closure has become an alternative.[4,5] Percutaneous defect closure should not be performed in ASD patients except for septum secundum defects. This procedure is

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indicated for children with hemodynamically significant in suitable ASD anatomy or defect with right to left shunt with embolism-related symptoms or small secundum ASD with risk of thromboemboly and patient weighing more than 15 kg. The failure rate of percutaneous ASD closure in South Korea reached 1.96%, while in developing countries it is still unclear.[8]

Considerations for ASD closure in hemodynamically significant children can be done when the ASD size and anatomical procedure criteria are appropriate. In children, large-sized ASD has the potential to predict the procedural failure (odds ratio (OR)=1.828, p=0.012) and challenging cases (odds ratio 1.371, p<0.001).[8] In children weighing <10 kg, defect size as large as three times the weight in kg can be closed, and device as large as 28 mm can be used provided the surrounding rims are adequate.[9] Nonetheless, in developing countries, these procedural characteristics and predictor of procedural failure are still unknown. Therefore, this study was conducted to determine the failure rate and procedural characteristics which can influence the outcome of percutaneous ASD closure.

Materials and methods

Study Design and Data Collection

A retrospective study was performed to evaluate the failure rate and procedural characteristics of percutaneous secundum ASD closure. This study used a database of all patients with secundum ASD who underwent percutaneous ASD closure at Prof. Dr. I.G.N.G. Ngoerah Hospital, Denpasar, Bali between March 2010 to November 2023. Individuals who experienced a pulmonary hypertension crisis during the procedure were excluded. This study has been approved by the Ethics Committee of Faculty of Medicine, Udayana University with ethical clearance number 668/UN14.2.2.VII.14/LT/2023.

Anatomical Variable and Pulmonary Artery Resistance Index Measurements

During cardiac catheterization, anatomical defect, diameters of rims and pulmonary arterial resistance index (PARI) were identified. The variables were defined as follows: the diameter of the ASD was the widest size of the ostium secundum interatrial septal defect, measured by transthoracic echocardiogram (TTE) and transesophageal echocardiogram (TEE). The rim was the edge of the ASD defect, classified based on the location of the septal rim relative to the ASD defect, namely anterior, posterior, superior vena cava (SVC), inferior vena cava (IVC) and mitral rim.

PARI was defined as the absolute value of pulmonary artery resistance against the patient's body surface area (BSA) which represented the effect of body size on blood flow. Pulmonary hypertension was established when pulmonary artery pressure exceeded 25 mmHg, as measured during cardiac catheterization. Correctability was defined as a decline in the pulmonary arterial resistance index of more than 20% and final values of less than 6 WU/m^2, during acute vasoreactivity test with 100% oxygen.[5] These values were the basis for classifying pulmonary hypertension associated with congenital heart disease into correctable or non-correctable.[15,16] The successful outcome was complete closure of the secundum ASD with appropriate placement of the Amplatzer® septal occluder (ASO) device (Abbott medical, Chicago, IL, USA) and without any intra-procedural complications.

Statistical Analysis

Data were analyzed using SPSS for Windows version 23.0 (IBM Corporation, Armonk, NY, USA). Data on a numerical scale with a normal distribution were presented in mean±standard deviation (SD), while data on a categorical scale were presented in frequency and percentage distributions. The distribution test was performed using the Kolmogorov-Smirnov test, and it was considered normally distributed if p>0.05. Bivariate analysis was done using unpaired T-test to analyze independent variable data with a numerical scale and a normal distribution, and the Mann-Whitney test was used to analyze data with a non-normal distribution, while Fisher exact test was used to analyze categorical data. Results were presented as relative risk (RR) and 95% confidence interval (CI). The p<0.05 was considered significant.

Results

There were 112 subjects in the research sample with 74.1% were female and 55.36% were pediatric and adolescent patients. Table 1 and Table 2 showed the subjects' initial characteristics. The subjects were divided into three groups: children (aged 1–12 years 11 months), adolescents (aged 13–18 years), and adults (aged > 18 years).

Percutaneous closure of secundum ASD was successfully performed on children and adolescents with

Table 1. Clinical and laboratory characteristics of the study sample (n=112).

Variable	Failed to Close ASD (n=14)	Successful ASD Closure (n=98)
Gender, n (%)		
Female	11 (78.57)	72 (73.47)
Male	3 (21.43)	26 (26.53)
Age group, n (%)		
Child	6 (42.86)	45 (45.92)
Adolescent	4 (28.57)	7 (7.14)
Adult	4 (28.57)	46 (46.94)
Body weight (kg), mean±SD		
Child	21.75±7.22	18.74±10.3
Adolescent	41.75±8.26	44±10.55
Adult	47.75±8.58	54.34±10.73
Nutritional status, n (%)		
Well-nourished	9 (64.29)	55 (56.12)
Wasted	2 (14.29)	16 (16.33)
Severely wasted	2 (14.29)	3 (3.1)
Overweight	1 (7.14)	5 (5.1)
Obesity	0	19 (19.39)
BSA (m^2), median (interquartile range)	1.24 (0.44-1.67)	1.28 (0.36-1.91)
Diameter index, ASD/ BSA (mm/m^2)		
Children, mean±SD	32.62±15.52	23.8±7.71
Adolescent, median (range)	22.12 (11.79-25.97)	15.59 (14.41-25.62)
Other congenital abnormalities, n (%)		
Valvar pulmonary valve stenosis	0	5 (5)
Mitral valve prolapse	2 (16.67)	0
Down syndrome	0	3 (3)
Spina bifida	0	1 (1)
Hemoglobin levels (mg/dL), mean±SD	13.47±1.51	13.17±1.6

a mean of 18.74 kg and 44 kg respectively and a BSA of 1.28 (0.36-1.91) m^2. During the procedure, balloon sizing was carried out in 67 patients (59.82%) with rim deficiency cases were found in 13 patients (11.6%) and most patients with low pulmonary artery resistance with 7 patients (6.25%) with high pulmonary artery resistance. Of the 112 subjects, 24 (21.43%) had not succeeded in closing the defect percutaneously during the initial attempt, while on the second attempt, 14 subjects(12.5%) had failed to close the defect.

In children, the maximum ASD value that can be successfully treated is 22.3 mm (TTE) and 22.12 mm (TEE); in adults, the maximum value is 33.24 mm (TTE) and 32.54 mm (TEE). Table 3 showed the median value of each rim's size, while Table 4 presented the classification of ASD rim sizes rim and outcome.

Discussion

ASD accounts for 35% of all congenital heart defects in children.[1,2] The most common defect in ASD is ostium secundum defect, which is one of the defects that can be closed percutaneously. Percutaneous/transcatheter ASD closure has been performed with a total of 112 patients

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Table 2. Procedural characteristics of the study sample (n=112).

Variable	Failed to Close ASD (n=14)	Successful ASD Closure (n=98)
Rim deficiency (size <5 mm), n (%)		
Anterior rim	0 (0)	2 (2.04)
Posterior rim	1 (7.14)	5 (5.1)
SVC rim*	2 (14.29)	2 (2.04)
IVC rim**	0 (0)	0 (0)
Mitral rim*	1 (7.14)	0 (0)
During percutaneous closure of a secundum ASD		
Use of sizing balloons, n (%)	5 (35.71)	62 (63.27)
Tool size	(9-12F)	(7-12F)
PARI Classification, n (%)		
Low resistance (0-3.99)	11 (78.57)	75 (76.53)
Medium resistance (4-8)	2 (14.29)	17 (17.35)
High resistance (≥8.1)	1 (7.14)	6 (6.12)
Complications, n (%)		
Arrhythmia	4 (28.57)	12 (12.24)
Emboli on site (ASO migration)	7 (50)	2 (2.04)
Thrombus		
- Left atrial thrombus	1 (7.14)	1 (1.02)
- IAS thrombus	1 (7.14)	0 (0)
Bleeding	2 (14.29)	1 (1.02)
Cardiac tamponade	0 (0)	1 (1.02)

*data on 38 subjects (TEE); **data on 33 subjects (TEE).

(children and adults) and 14 patients (12.5%) who did not succeed in percutaneous defect closure, 4 adult patients (8%) and 10 pediatric patients (16.13%).

Asymptomatic patients older than 2 years of age with a large left-to-right shunt (enlarged right atrium and ventricle and/or Qp/Qs >1.5) as well as small secundum ASDs with a risk of thromboembolic events are candidates for elective closure of a secundum ASD. At Prof. Dr. I G.N.G. Ngoerah Hospital, Bali, the anatomical criteria for percutaneous closure of secundum ASD defects are as follows: mitral valve rim size >5 mm, no multiple rim deficiencies in three plane measurements (except retro-aortic rim), and no posterior and/or IVC rim deficiencies. Patients whose secundum ASD cannot be closed percutaneously will be considered for surgical intervention. Cardiac defect was closed during cardiac catheterization. Before the closure procedure, cardiac catheterization can yield data about angiographic images, using fluoroscopic imaging during contrast injection, pressure measurements, blood oxygen saturation, estimated cardiac output and pulmonary vascular resistance.[10-12] Untreated atrial septal defect will result in pulmonary hypertension, systemic embolism, right heart failure, arrhythmia, and premature death due to right ventricular chamber overload.[10,13]

In procedures to close secundum ASDs with floppy rims, large defects, or multiple defects, sizing balloons are used.[17] Atrial septal defect size and rim size (anterior, posterior, SVC, and IVC) are specific characteristics and predictors of failure of the percutaneous secundum ASD closure procedure that are assessed. Bivariate analysis revealed that, there was no significant correlation between the rim sizes (anterior, posterior, SVC, and IVC) of pediatric and adult patients with the procedural outcomes (p>0.05).

Tabel 3. Echocardiography characteristics of the study sample.

Variable	Outcome		*p*-value	CI 95%
	Failed to Close ASD	Successful ASD Closure		
ASD size (mm), TTE				
Children	24.7±6.46	16.36±5.94	**0.001**	4.18–12.5
Adult	29.39±6.07	25.98±7.26	0.369	(-10.9)–4.15
ASD size (mm), TEE				
Children*	31.38±8.07	15.77±6.35	**0.001**	8.04–23.19
Adult**	32.06±1.99	24.43±8.11	0.12	(-17.4)–2.12
Anterior rim (mm)				
Children	8.81±2.7	9.79±3.13	0.391	(-1.39)–3.34
Adult	13.15±4.33	12.55±3.38	0.722	(-4.74)- 3.54
Posterior rim (mm)				
Children	8.1±4.03	9.1±3.01	0.282	(-1.33)–3.33
Adult	9.92±4.2	11.3±5.34	0.664	(- 5)–7.06
SVC rim (mm)†				
Children	7.44±4.8	7.22±1.38	0.907	(-4.49)–4.04
Adult	11.06±6.17	9.99±5.82	0.765	(-8.4)–6.24
IVC Rim (mm) ††				
Children	7.9±1.89	9.93±3.13	0.444	(-4.26)–8.32
Adult	7.45±3.46	11.87±4.49	0.191	(-2.36)–11.19
Mitral rim (mm) †				
Children	6.93±2.22	7.37±2.13	0.753	(-2.48)–3.36
Adult	9.5±4.78	9.36±2.36	0.935	(-3.69)–3.4

*data on 23 pediatric subjects; **data on 31 adult subjects; †data on 38 subjects; ††data on 33 subjects. Unpaired t-test was used.

Meanwhile, pediatric patients who had successful and unsuccessful outcomes had considerably different ASD defect sizes. The average size of ASD defects was 24.7±6.46 mm in children who had failed outcomes and 16.36±5.94 mm in children who had successful outcomes, with a p=0.001. Similarly, a significant difference in the size of the

Table 4. Classification of ASD rim sizes rim and outcome.

	n	Failed to Close ASD [n (%)]	*p*-value	RR	CI 95%
Adequate all rims (≥7 mm)	16	2 (12.5)			
Rim 5-6.9 mm					
One rim*	24	3 (12.5)	0.639	1.14	0.17–7.67
Two rims*	8	2 (25)	0.359	2.67	0.3–23.43
Three rims	3	0	-	-	-
Rim <5 mm					
One rim*	9	2 (22.22)	0.407	2.29	0.27–19.67
Two rims*	2	1 (50)	0.284	8	0.35–184.36
Three rims	0	0	-	-	-

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ASD defect was found using TEE between pediatric patients with successful and failed outcomes, with a p=0.001. Meanwhile, the size of the ASD defect in adult patients did not differ significantly between failed and successful group. This is consistent with a study in Korea, which found that in pediatric patients <6 years old, ASD size was a predictor of failure of percutaneous ASD closure procedures (OR=1.828, 95% CI: 1.139-2.934, p=0.012) as well as a predictor of difficult cases (OR=1.371, 95% CI: 1.180-1.593, p=0.001), with the area under the curve (AUC) value of atrial septal defect and predictor of procedure failure being 0.952 (95% CI: 0.906–0.999; p=0.001).[8]

The rim size (anterior, posterior, SVC, IVC) did not differ significantly between the two groups of patients; however, it could be influenced by discharge of patients with presence of posterior rim deficiency (rim size <5 mm) and/or IVC rim deficiency (rim size <5 mm). Moreover, we compared the failure rate between groups with all adequate rims, rims 5-6.9 mm (one/two/three rims) and rims <5mm (one/two/three rims), with the result showed on Table 4. Patients with 5-6.9 mm rims on two rims had a failure rate of up to 25% with an insignificant p-value (p=0.359), while patients with 5-6.9 mm rims on one rim had the same failure rate as the all adequate rims group, namely 12.5%. Meanwhile, patients with rims <5 mm on one rim had a failure rate of up to 22.5% with an insignificant p-value (p=0.407) and patients with rims <5mm on two rims had a failure rate of up to 50% with an insignificant p-value (p=0.284). According to a study in Korea, ASD size, as well as a combination of SVC-posteroinferior rims deficiency and IVC-retroaortic rim deficiency, were predictor factors for failure to close ASD percutaneously, but multivariate analysis revealed that only the ASD size variable was significant as a predictor of percutaneous ASD closure failure.[8]

The most common cause of acute post-procedure complications during the hospital stay was arrhythmia, which affected 21 patients (21.65%), other complications included bleeding in 3 patients (3.1%), ASO device embolism in 2 patients (2.1%), anterior mitral leaflet prolapse in 2 patients (2.1%), thrombus in the left atrium in 2 patients (2.1%), thrombus in the IAS in 1 patient (1%) and cardiac tamponade in 1 patient (1%). Ventricular tachycardia, ventricular extrasystole (VES) are the most common arrhytmias which can be found, followed by supraventricular tachycardia (SVT), inferior ischemia, premature atrial contraction (PAC), bradycardia, and atrial fibrillation. Two patients experienced ASO device embolism in the right ventricle; percutaneous closure was performed on one of them, while surgical ASD closure was performed on the other. In our center, there were no major complications with percutaneous ASD closure. In line with a study in Turkey revealed that majority of patients had successful percutaneous closure of ASDs with a low complication rate.[10,15]

Increased mitral regurgitation (MR) turbulence in some patients may be caused by the ASO device occluding the left-to-right shunt, limiting mitral valve movement, and AML prolapse. A cohort study conducted in New Zealand revealed that following percutaneous ASD closure, 9% of patients in both of pediatric and adult groups progressed to mitral valve regurgitation.[16] This phenomenon could be caused by left ventricular decompensation as a result of increased inflow following ASD closure. Meanwhile, a study in Korea discovered that approximately 1% of patients also had progression of mitral valve regurgitation and the incidence of new mitral valve regurgitation was much lower in children than in adults.[8] As a result, regular follow-up echocardiography is advised.

Patients with 5-6.9 mm rims on two rims had a failure rate of up to 25% also patients with rim <5 mm, either one or two rims had a higher failure rate, reaching 22.5% and 50% compared to patients with all adequate rims (≥7 mm). Percutaneous closure may be considered to be postponed in these groups because of the significant failure rate. Due to the lack of a three-dimensional transesophageal echocardiography (3D TEE) tool in our centre, it was not possible to evaluate the morphology of the atrial septal defect in this study. Future studies are expected to evaluate defect morphology to assess additional procedural parameters that influence the outcomes.

Conclusion

The size of the atrial septal defect is a significant predictor of failure in pediatric patients but not in adult patients. The size of the rim has no significant difference toward the outcome of the patient, meanwhile, group of patients with 5-6.9 mm on two rims or more also patients with rim <5 mm had a significant failure rate. Due to the higher failure rate in these groups, evaluation of defect morphology is required.

Authors Contribution

EY, EG and VK were involved in concepting and planning the research. EY, EG and VK performed the data acquisition/collection, EY calculated the data and performed the analysis. EY drafted the manuscript and designed the figures, EG and VK aided in interpreting the results. All authors took parts in giving critical revision of the manuscript.

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