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Original Article

Time period after transcatheter PDA closure with changes in left ventricular function and nutritional status

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Abstract

Background Few studies perform follow ups on patent ductus arteriosus (PDA) patients who undergo transcatheter closure. In addition to side effects from the procedure, it is important to evaluate changes in left ventricular function (LVF) parameters and nutritional status.

Objective To compare LVF and nutritional status before and during the one-year period post-transcatheter PDA closure, and evaluate potential associated factors in post-closure PDA transcatheter patients.

Methods This retrospective cohort study was done in a single center in patients diagnosed with PDA who had undergone transcatheter closure. Data were obtained from subjects' medical records. The relationship between the post-closure PDA time span and LVF parameters [ejection fraction (EF) and fractional shortening (FS)] was analyzed by Friedman and repeated ANOVA tests; the post-closure PDA time period and nutritional status was analyzed by Friedman test. The time periods analyzed were 1, 3, 6, and 12 months post-closure. Factors potentially associated with LVF 12 months post-closure were analyzed by linear regression.

Results A total of 30 patients who had undergone transcatheter PDA closure were included. The body weight mean of at the time of transcatheter PDA closure was 13.1 kg. We found a significant relationship between time period after PDA closure and nutritional status, before and at 1, 3, 6, and at 12 months post-closure. In a comparison of pre-closure to 12 months post-closure, subjects' mean EF (66.6 *vs.* 70.9%, respectively; P<0.001) and FS (34.4 *vs.* 37.8%, respectively; P<0.001) were significantly higher. In addition, significantly more patients had normal nutritional status 12 months post-closure than before closure. Age was not related to LVF parameters (EF: r=0.212; P=0.260; FS: r=0.137; P=0.471).

Conclusion Both LVF and nutritional status significantly improve gradually over the 12 months post-closure compared to pre-closure. PDA size is not significantly associated with improved LVF parameters and nutritional status. **[Paediatr Indones. 2021;61:100-6 ; DOI: 10.14238/pi61.2.2021.100-6].**

Keywords: *left ventricle; nutritional status; patent ductus arteriosus; transcatheter closure*

Congenital heart disease (CHD) is a cardiac or great vessel abnormality within the thoracic cavity. These abnormalities appear during the development of the heart and persist at birth.[1] Congenital heart disease comprises nearly one-third of all major congenital abnormalities. Worldwide, 1.35 million babies are born with CHD annually.[2] In North America, CHD occurs in 8.1 per 1,000 live births. In Asia, CHD occurs in 9.1 per 1000 live births.[2,3] In Indonesia, CHD occurs in 8 per 1,000 live births.[4,5]

In general, CHD can be classified into cyanotic and acyanotic types.[6] Patent ductus arteriosus (PDA) is an acyanotic CHD caused by failure of the ductus to close. A meta-analysis study produces a result there are supposed to be increasing CHD patient linearly.[3]

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The PDA occurs in approximately 1 per 2,000-5,000 births or around 10-12% of all CHD. This condition is more common in girls than boys, with 2-3 to 1 ratio.[7] In addition, PDA is more common in premature infants, at 22.5% of live births. In Indonesia, 4,000 infants with PDA are born annually.[8] Large and moderate PDA usually causes heart failure and failure-to-thrive in children.[8]

Patent ductus arteriosus can be managed by several means, such as medication, surgery, and transcatheter closure. Closure of the PDA is indicated in almost all cases, except in ductal-dependent CHD with Eisenmenger syndrome. In recent years, interventional cardiology has become the standard treatment for most PDA patients above neonatal age.[9] A study in Dr. Hasan Sadikin Hospital, Bandung, West Java, Indonesia showed that transcatheter PDA closure was safe and effective in short and moderate follow up, thus it is the standard of treatment, especially in medical centers with limited ward capacity.[10]

A study conducted in Ain Shams University Hospital, Egypt, showed that after PDA transcatheter closure, systolic and diastolic function were significantly decreased, but still reversible and returned to normal 1 month after closure.[11] Other studies that assessed systolic function after transcatheter closure had similar results.[12,13]

A Yogyakarta study noted a significant increase in body weight after transcatheter PDA closure. But the increased body weight was not associated with sex, birth weight, pulmonary hypertension, heart failure, parental employment, or earnings.[14]

The aim of this study was to analyze for relationships between the time period following transcatheter PDA closure and changes in LVF parameters and nutritional status. The other aim was to analyze for potential associations between age, sex, and PDA size to LVF and nutritional status in patients who underwent transcatheter PDA closure.

Methods

This was a retrospective cohort study to assess for relationships between post-transcatheter PDA closure time period and changes in LVF parameters and nutritional status. The study was conducted in Haji Adam Malik Hospital, Medan, North Sumatera, from February to September 2019. Subjects were Pediatric Cardiology Division patients aged 3 months to 18 years who had undergone transcatheter PDA closure and periodic monitoring for the first year after PDA closure. Subjects were included by consecutive sampling, until the minimum required sample size of 17 patients, determined by paired numerical variable formula, was fulfilled. Data were collected from medical records. Patients who died before one year of monitoring post-transcatheter closure, and those with incomplete data on LVF parameters or nutritional status were excluded.

Age was defined as chronological age at the time the patient underwent transcatheter PDA closure. Nutritional status and left ventricular function were noted before transcatheter closure, and 1, 3, 6, and 12 months after transcatheter closure. Left ventricular parameters included ejection fraction (EF) and fractional shortening (FS), measured using *Phillips Affinity 50 E Echocardiography* operated by a pediatric cardiologist. Nutritional status was measured by the *2006 WHO* weight for length/height curves for children under 5 years, or the *2000 CDC* curve for children more than 5 years of age.15 Nutritional status was categorized into normal, mild malnutrition, and severe malnutrition. PDA size in mm was assessed by angiographic examination in the cardiac catheterization lab, and categorized as very small, small, moderate, or large PDA.

There was potential bias in this study since many patients were excluded due to incomplete medical record data. However, the minimum required sample size from the paired numeric variable formula was fulfilled. Univariate analysis was done to assess the distribution of demographic characteristics. To assess for relationships between variables, we used ANOVA, Friedman, and Pearson's correlation tests, as appropriate. Statistically significant results by bivariate analysis were further analyzed by multivariate test (linear regression and logistic regression test). This study was approved by the Universitas Sumatera Utara Medical Research Ethics Committee.

Results

During the study period, 90 patients had undergone

transcatheter PDA closure, of whom 30 were included in this study. As shown in **Table 1**, subjects' mean age at closure was 53.3 months. The majority of subjects were female (19/30). Equal numbers of patients had mild and severe malnutrition, 12 patients each, while 6 subjects had normal nutritional status. Subjects' mean PDA size was 4.15 mm. The most common diagnosis was moderate PDA (14 cases); small and large PDAs numbered 8 patients each.

Table 1. Characteristics of study subjects

Characteristics	(N = 30)
Mean age (SD), months	53.3 (48.89)
Sex, n	
Male	11
Female	19
Nutritional status, n	
Normal	6
Mild malnutrition	12
Severe malnutrition	12
PDA size, n	
Small	8
Moderate	14
Large	8
Mean PDA size (SD), mm	4.15 (1.56)

Before assessing for a relationship between the time period post-PDA closure and ventricular function, a data normality test was performed. Shapiro-Wilk test revealed that the EF data were not normally distributed ($P < 0.05$), so Friedman test was performed. However, FS data were normally distributed, so repeated ANOVA test was used for analysis. Both EF and FS were significantly different from before transcatheter PDA closure compared to 1, 3, 6, and 12 months after closure, as shown in **Table 2**. Friedman test was performed to assess relationship between time period post-PDA closure with LVF parameters. Collective nutritional status significantly improved from before PDA closure compared to 1, 3, 6, 12-month post-transcatheter PDA closure ($P<0.001$) (**Table 3**). Bivariate analysis of LVF parameters and independent variables revealed that age, sex, and PDA size were not associated with pre-operative EF and FS ($P>0.05$ for all) (**Table 4**). Results with $P < 0.25$ met the requirements for a multivariate test.

Simple logistic regression analysis revealed no significant association between nutritional status and PDA size (**Table 5**).

Table 2. Analysis of time period post-transcatheter PDA closure and LVF parameters

Left ventricular function		P value
Mean ejection fraction (SD), %		<0.001[a]
EF before closure	66.6 (6.01)	
EF 1 month after closure	63.0 (5.63)	
EF 3 month after closure	65.5 (4.62)	
EF 6 month after closure	68.2 (4.59)	
EF 12 month after closure	70.9 (4.20)	
Mean fractional shortening (SD), %		<0.001[b]
FS before closure	34.4 (3.92)	
FS 1 month after closure	31.8 (3.48)	
FS 3 month after closure	33.9 (2.97)	
FS 6 month after closure	35.7 (2.85)	
FS 12 month after closure	37.8 (2.91)	

[a]Friedman test; [b]Repeated ANOVA test

Table 4. Bivariate analysis of LVF parameters and three variables (age, sex, and PDA size) with pre-operative EF and FS

Variables		P value
Mean age (SD), months	53.3 (48.89)	0.260
Mean EF (SD)		0.402
Male	65.6 (5.18)	
Female	67.2 (6.51)	
Mean EF (SD)		0.524
Small PDA	67.1 (5.34)	
Moderate PDA	66.2 (6.76)	
Large PDA	66.7 (6.51)	
Mean age (SD), months	53.3 (48.89)	0.471
Mean FS (SD)		0.596
Male	32.9 (3.71)	
Female	35.4 (3.83)	
Mean FS (SD)		0.186
Small PDA	34.6 (3.00)	
Moderate PDA	35.4 (4.29)	
Large PDA	32.8 (4.27)	

Table 3. Analysis of time period post-transcatheter PDA closure and nutritional status

Nutritional status	Before closure	After closure				P value
		1 month	3 months	6 months	12 months	
Normal nutrition, n	6	8	14	19	25	<0.001
Mild malnutrition, n	12	15	13	10	5	
Severe malnutrition, n	12	7	3	1	0	

Note: Friedman test

Table 5. Simple logistic regression analysis of nutritional status with PDA size

Variables			P value
Nutrtitional status	PDA size, n		0.766
	Small	8	
	Moderate	14	
	Large	8	

Discussion

Transcatheter PDA closure at Haji Adam Malik Hospital was initiated in 2009. During the study period, 90 patients underwent transcatheter PDA closure. Prior to 2009, ligation surgery was the main treatment choice, but non-surgical intervention by transcatheter is now an option.[16,17] Ligation operations at Haji Adam Malik Hospital are currently limited to patients who cannot undergo transcatheter closure.

Patent ductus arteriosus is the third most common type of CHD.[3,18] At Dr. Sardjito Hospital, Yogyakarta, PDA constituted 16.1% of all registered CHDs.[19] The most common CHD is thought to be ventricular septal defect (VSD), but this is contrary to a Saudi Arabian study showing that PDA was more common than other CHDs based on echocardiographic examination results.[20] Diagnosis of PDA may be suspected in cases with clinical presence of continuous cardiac murmur or wide pulse pressure, and can be confirmed by echocardiography and cardiac catheterization.[21-23]

The mean age of our subjects, diagnosed with PDA and who had undergone transcatheter PDA closure, was 53.3 months. This age is quite advanced, and may have been due to delayed PDA diagnosis. A Pakistani study found that 85.1% of patients had a late CHD diagnosis. Most such cases (37.2%) were due to delayed first consultation, while 22.5% were due to late diagnosis by doctors, 13.3% due to delayed referral, 13% due to social factors, 12.3% due to financial factors, and 1.7% due to religious sensitivities.[24]

A previous study noted that transcatheter PDA closure in children under 1 year was safe and effective. They also predicted a reduction in complications from transcatheter PDA closure due to the improved occluder design.[25] Another Egyptian study found that transcatheter PDA closure in children weighing 10 kg or less was effective and safe in medium-term monitoring.[26] We found that the mean weight of subjects at the time of transcatheter PDA closure was 13.1 kg, while their mean age was 4.4 years.

In our study, more females than males had PDA, consistent with a study reporting a female-to-male ratio of 2-3:1.[7] However, other studies in Iraq and Colombia found no significant differences in PDA incidence between males and females.[27,28]

Most studies followed up on success rate, side effects, or complications of the procedure.[8,29,30] In addition to monitoring for complications, some studies also assessed changes in LVF parameters and body weight, but most monitoring was not done for a full year after closure.[11,14,31,32] We monitored both LVF parameters and nutritional status, according to the WHO or CDC growth charts depending on patient age.[15]

A Nigeria study reported that 92% of CHD patients had malnutrition and 90% of those had severe malnutrition.[33] Malnutrition in PDA may induce failure to thrive, as well as developmental and cognitive disorders.[34] In Yogyakarta, malnutrition was noted in 76.7% of patients diagnosed with PDA.[14] Similarly, 80% of our patients had malnutrition, including 40% with severe malnutrition prior to transcatheterization. An Egyptian study concluded that malnutrition in PDA patient significantly correlated with low hemoglobin level, low oxygen saturation, pulmonary hypertension, heart failure, and history of poor nutritional intake.[37] Our subjects had been diagnosed with PDA without any secondary diagnoses, to as we aimed to minimize the bias that might occur. However, we did not analyze hemoglobin level and arterial oxygen saturation.

Our study subjects' mean PDA size was moderate, at 4.15 mm. Larger PDAs typically lead to more rapid development of complications.[35] A 2019 Yogyakarta study found that moderate PDAs had a 7.6 times greater risk of congestive heart failure than small PDAs. In cases with large PDAs, the risk of developing congestive heart failure was 21.1 times compared to small PDAs.[36]

We found a significant relationship between the time span post-transcatheter PDA closure and LVF parameter changes, consistent with previous studies which showed a significant change in EF after transcatheter closure of PDA.[11,31] Sudden

drop in left ventricle preload after PDA closure made systolic performance decreased. After one month, there is improvement in myocardial function, so the LVF parameters improved.[11] A 2019 study from China assessed LVF parameters [EF, FS, and left atrium diameter/aortic diameter (LAd/AOd) ratio], before and after transcatheter closure. They found a significant decrease of left ventricle function parameters after transcatheter closure, and 3 months after closure.[38]

Unmanaged PDA or other CHDs may an increase the risk of malnutrition. Age was associated with the incidence of malnutrition in unmanaged PDA.[37] We did not assess for such a relationship between age and nutritional status at the time of PDA diagnosis.

A study in Iran compared CHD in both cyanotic and acyanotic types, with or without pulmonary hypertension, for body weight and body height also found significant differences. Patients with cyanotic or acyanotic CHD without pulmonary hypertension had higher body weight and body height rates compared to CHD with pulmonary hypertension.[34]

We found a significant relationship between time period after PDA closure and nutritional status, before and 1, 3, 6, and 12 months post-closure. A Yogyakarta study also showed that body weight significantly increased after transcatheter PDA closure. While weight monitoring was carried out at the same time points as our study,[14] we determined nutritional status by body weight based on body height.

The PDA size variable was eligible for multivariate analysis with FS, but other variables (age and gender) did not meet the significance requirements. No independent variables (age, sex, and PDA size) were eligible for multivariate analysis with EF. Because only one variable qualified for the multivariate test, we did not perform the analysis.

The strength of our study was that this study assessed the relationship between the time span after transcatheter PDA closure and changes in LVF parameters and nutritional status, before and 1, 3, 6 and 12 months after transcatheter closure. Other studies usually only assessed changes in LVF parameters or nutritional status, not both.[11,14,32] The weakness of our study was the small sample size, due to the large number of patients excluded due to patient non-compliance to clinic visits for evaluation of LVF parameters, as well as incomplete medical record nutritional status data. As such, further study is needed with a larger sample size, and assessment of other possible confounding variables to better elucidate relationships between variables.

Conflict of Interest

None declared.

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