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The Evaluation of Left Atrial to Aortic Root Diameter Ratio after PDA Closure in Children

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Abstract

Background: Ductus arteriosus (DA) is a vascular structure that makes a link between the proximal descending aorta and main pulmonary artery near the origin of the left pulmonary artery. The present study aimed to assess the changes of LA/Ao ratio after PDA closure in children.

Methods: This cross-sectional study was performed on 635 children with PDA in the Ali Asghar clinic, Zahedan, Iran, from 2003 to 2019. The participants were followed for at least one year after discharge from the hospital after intervention. PDA diagnosis was conducted in accordance with the echocardiography performed by a pediatric cardiologist using Mylab 60 and challenged 7000 made in Italy. The analyses were performed by SPSS 20.00, considering 0.05 as the significant error.

Results: As compared to the baseline measures before the interventions, the growth rates of LA/Ao ratio decreased by 24% and 10% in the first and second 6 months after the intervention. During the first 6 months after the intervention, the percentages of LA/Ao ratio reduction were 23%, 25% and 22% in small, medium and large PDA while these percentages were 7%, 13% and 16% during the second 6 months after the intervention, respectively. Regarding the intervention, the percentages were 25%, 24%, 24% and 24% in PDAs that were, respectively, closed by medication, surgery, occlusion device and VATS in the first six months after the intervention. The percentages were, respectively, 9%, 10%, 11% and 9% for the second 6 months after the intervention. The percentages were, respectively, 24%, 24% and 21% in those PDAs with residuals, no complication and PH in the first six months after the intervention. This pattern was, respectively, 8%, 9% and 16.6% for the second 6 months after the intervention.

Conclusion: It was concluded that LA/AO ratio had the highest decrease during the first six months after the intervention, so that PDAs with moderate sizes or those who had medication as intervention or those with residual complications had the highest percentages of reduction.

Key Words: Children, Closure, LA/Ao ratio, PDA.

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1- INTRODUCTION

Ductus Arteriosus (DA) is a body structure that connects the proximal aorta to the roof of the most arterial blood vessel close to the origin of the left arterial blood vessel (1). Epithelial tissue adhesion followed by replacement of the muscle fibres with connective tissue leads to the remaining ligamentum arteriosum among 2 to 3 weeks; otherwise, there is a patent or Persistent Ductus Arteriosus (PDA) (1-3). The incidence of PDA is just about 1 in 2000 in mature infants and consists 5 to 10 percent of all CHD in children (4). The incidence of PDA in preterm neonates is more, from 20–60% (5) and double in females (4). The inflated incidence of PDA within preterm infants is due to the dearth of traditional closure mechanisms because of immaturity (5). In adulthood a PDA isn't usually encountered, since it's typically discovered and treated throughout childhood (2). The mortality of untreated PDA in adults is estimated to be 1.8% per year (3). PDA normally closes unexpectedly within 24 to 48 hours after birth by the contraction of medial smooth muscle in the vessel wall, due to the increased oxygen tension and reduced prostaglandin E2 and I2 levels (2). The other types of PDA closure include surgery and occlusion devices (6).

After closure, some complications may be observed in some cases such as hemolysis, embolization, infective endocarditis, and the narrowing of adjacent vessel. In order to minimize these complications, it is vitally important to select the appropriate closure method, depending on the ductal morphology and narrowest diameter, the size of the descending aorta, along with the age and weight of the patient (7).

Recently many studies demonstrated that the LA/Ao ratio is a good predictor (8) of normality in heart chambers particularly in the left one. LA/Ao ratio can be estimated from the parasternal long axis view utilizing M-mode with the cursor opposite to the aorta at the level of the aortic valve or at the septum at the tip of the mitral valve pamphlets, respectively (9). An increase in the pulmonic blood flow from a huge left-to-right ductal shunt causes pulmonary blood flow and consequently increases pulmonary venous return (9).

This prompts expanded volume overload in the left atrial which has continuously widened, and in the event that this cycle of critical left to right shunt continues, this volume overload causes the left ventricle dilatation via preload increasing, particularly without a huge intra-atrial shunt. As Aortic valve annulus (Ao) is a generally fixed design, it doesn't get widened because of left heart over-burdening. Subsequently, a proportion of LA/Ao can be utilized as a proxy of expanded pulmonary venous return (9).

Variable degrees of mitral valve insufficiency are often seen in infants with persistent large PDA and significant left heart dilatation. This occurs due to left atrial dilatation resulting in stretching of mitral valve and left ventricular volume overloading. The mitral valve regurgitation usually improves significantly with normalization of left atrial size and resolves completely within weeks after PDA closure (10-12).

Many studies found that LVEDd, LA/Ao ratio, EF and FS decreased after the intervention of PDA compared to pre intervention (13, 14).

Among these parameters, LA/Ao ratio was highlighted such that Abdel-Bary found a significant decrease in LA/Ao ratio in different times after PDA closure. In a recent study Noori et al., (1) found that LA/Ao ratio decreased after closure by all types of PDA treatment with the highest decrease due to occluder devices. The present study aimed to assess the changes of LA/Ao ratio after PDA closure in children.

2- METHODOLOGY

This cross-sectional study was conducted on CHD children in the pediatric cardiac center of Ali Asghar hospital, Zahedan University of Medical Sciences, Zahedan, Sistan and Baluchestan province, Iran from 2003 to 2019.

2-1. Study design

For every CHD child who referred to the cardiac center, a medical profile was made under the supervision of a cardiologist (first author). For the present study, the patients from 2003 to 2019 were considered because the project is continuing. Complete medical and clinical features were recorded at admission. To diagnose the type of CHD, physical examination, electrocardiography and chest radiography were applied and echocardiography performed for confirmation. Echocardiography was carried out using 2D with facilities for color, Doppler and M-mode. The patients with isolated PDA accounted for about 11.8% (635) of 3950 CHD. PDA diagnosis was conducted in accordance with the echocardiography performed by a pediatric cardiologist using Mylab 60 and challenged 7000 made in Italy.

2-2. PDA closure

Video-Assisted Thoracoscopic Surgery (VATS) and occluder device closure were performed in centers out of the province of Sistan and Baluchestan, due to the lack of enough facilities; but the surgery and medical treatments were performed in our centers. VATS technique included "an electrocautery hook, titanium clips (Ligaclip LT 400; Ethicon Endo Surgery, Cincinnati, Ohio), a clip applier, lung retractor, trocar, suction device, and a videoscope (Karl StorzEndoskope GmbH, Tuttlingen, Germany)"(1, 15). Amplatzer Ductal Occluder II (ADO) is a "self-expanding Nitinol device with a central waist and two symmetrical retention discs. The central waist is designed to fill the defect and the two retention discs are designed to be deployed on the aortic and pulmonary side defect. It is like a multifold and multi segmented design creating 6 potential planes of occlusion with no central fabric (16). Surgical interruption of PDA using a left posterolateral thoracotomy was the only available technique until 1971 when Porstmann and colleagues applied it for the first time (15). Prostaglandin inhibitors (NSAIDs) are used to treat PDA in term neonates; and are identified as the medical treatment for PDA. Many studies revealed that oral ibuprofen is the best drug for this treatment (1). Medical therapy is a good method and initial treatment in PDA closure. Indomethacin and ibuprofen are among the most beneficial medicines because of low side effects (17). So in the present study, patients aged less than 28 days were treated with oral ibuprofen in the medical approach in two courses for every 3 days. The patients were discharged from the hospital after taking their telephone numbers and full addresses. Within the one-year follow-up they were asked to refer to the heart clinic for echocardiography after one, three, six months and after one year. For data analysis, we considered the data recorded in the 6th and 12th months after intervention.

2-3. LA/Ao ratio measurements

LA/Ao ratio is measured in the parasternal long axis view in M-Mode by echocardiography. This ratio correlates significantly with increased pulmonary flow attributable to excessive trans ductal flow; optimal threshold ratio > 1.5 is associated with a significant PDA in premature neonates. In the present study, the LA/Ao ratio was measured in the parasternal long-axis view before the intervention, as well as, 6 and 12 months after it. For the analysis and measuring the changes in this ratio, the amounts of changes were evaluated between pre and 6

months after intervention, between pre and 12 months after intervention and between 6 and 12 months after intervention.

2.4- Criteria

Informed consent was obtained from all participants or their parents after the study approval. The study project was approved by the Ethics Committee (code: 9356) of Zahedan University of Medical Sciences, Zahedan, Iran.

2.5- Statistical analysis

The data were analyzed using SPSS version 20 software (IBM Corp., Armonk, NY, USA). Descriptive statistics for categorized variables are presented as percentages and frequency; and were compared with Pearson Chi‑square test considering $p < 0.05$ as the level of significance

3- RESULTS

The results of the normality test showed that all numerical data were free of distribution so that all analytical tests were performed using Non-parametric tests. In the present study the gender distribution was 244(38.4%) and 391(61.6%) for boys and girls, respectively. The mean age of the children with PDA was 29.03±41.96 at diagnosis ranging from 0.03 to 255.50 months. Similar trends were observed for age at intervention such that the results showed a mean of 36.65±42.59 and a variation range of 0.10 to 267.67.

Among 635 PDA children, death rates were 5 (0.79%) and 4 (0.63%) before and after the intervention, respectively. Decreasing growth rates of LA/Ao ratio were 24% and 10% in the first and second 6 months after the intervention. **Tables 1, 2, 3** demonstrate the details of AL/Ao decrease based on PDA size, intervention, and complications.

LA/Ao ratio decreased 24% of the primary level during the 6 months after intervention. This decrease was observed in small, medium and large sizes of PDA, such that PDA with small size had a decrease of 23%, PDA with medium size had a decrease of 25%, and PDA with large size had a decrease of 22%. LA/Ao ratio decrease was significant between pairs of small–medium ($p=0.036$) and medium-large ($p=0.003$). The LA/Ao ratio decreasing rate during the second 6 months after the intervention showed that small, medium and large PDA had a negative growth of 6.5%, 13%, and 16%, respectively.

In this period, LA/Ao ratio decrease was significant between the groups of small–medium ($p<0.001$), small–large ($p<0.001$), and medium- large ($p=0.024$) (**Table 1**).

Table 2 showed in PDA closed by medical treatment, LA/Ao ratio had 25% decreases during the first 6 months after medical treatment (ibuprofen or paracetamol). During the second 6 months after the intervention, this growth rate was 9%. For PDA closed by surgery, the LA/Ao ratio decreasing rates were 24% and 10% during the first 6 months after intervention and for PDA closed by occluder device, the LA/Ao ratio decreasing rates were 24% and 11%. PDA closed by VATS, the LA/Ao ratio decreasing rates were 24% and 9%. The analysis showed no significant difference in the decreasing growth of LA/Ao ratio between paired types of intervention in the first and second 6 months after the intervention.

Table 3 shows that PDA with residuals had a decrease of 24% during the first 6 months after the intervention, while this trend was 21% and 24% for those with PH and free of complications. Decreasing rate of LA/Ao ratio was significant between PDA with PH complication and PDA free of complication ($p=0.006$). During the second 6 months after the intervention PDA with residuals, free of complication and PH had a decrease of 8%, 9% and 17% in LA/Ao ratio with a significant

difference between PH-residuals (p=0.037) and PH- free of complication (p<0.001).

4- DISCUSSION

PDA is one of the most common heart defects in infants, which is more observed in girls than in boys with female-to-male ratio of 1.7:1(18). The consequences of a significant left-to-right shunting through the PDA may present hemodynamic and respiratory importance (19). Spontaneous closure of the PDA in normal birth weight neonates occurs in 3 days, but it may persist longer in premature babies (20). Current options for PDA closure are pharmacologic and nonpharmacologic methods. Non-pharmacologic closure of a PDA includes open division or ligation via left thoracotomy or sternotomy, transcatheter device occlusion, and ligation via video-assisted thoracoscopic surgery (VATS) (15, 20). It is important to stress short- and long-term benefits of PDA closure demonstrated by numerous studies, since delays in the treatment of PDA may lead to severe consequences for the neonate (17, 21, 22).

Table-1: LA/Ao ratio decreasing rates at two points of time based on PDA size

LA/Ao ratio decreasing rate from baseline to 6 months after the intervention					
PDA Size	N	Mean	SD	MIN	MAX
Small	296	0.2339	0.09511	0.01	0.42
Medium	262	0.2515	0.09333	0.00	0.42
Large	73	0.2148	0.08941	0.03	0.38
Total	631	0.239	0.09435	0.00	0.42
	PDA size	PDA Size	Mann-Whitney U	P value	
	Small	Medium	34788	0.036	
		Large	9554	0.126	
	Medium	Large	7401	0.003	
LA/Ao ratio decreasing rate from 6 months to 12 months after the intervention					
PDA Size	N	Mean	SD	MIN	MAX
Small	296	0.0652	0.07915	0.00	0.31
Medium	262	0.1290	0.10002	0.00	0.41
Large	73	0.1622	0.10721	0.00	0.38
Total	631	0.1029	0.09874	0.00	0.41
	PDA size	PDA Size	Mann-Whitney U	P value	
	Small	Medium	23658	<0.001	
		Large	4974	<0.001	
	Medium	Large	7908	0.024	
LA/Ao ratio decreasing rate from baseline to 12 months after the intervention					
PDA Size	N	Mean	SD	MIN	MAX
Small	296	0.2884	0.07394	0.07	0.42
Medium	262	0.3540	0.06714	0.18	0.49
Large	73	0.3462	0.08556	0.17	0.51
Total	631	0.3223	0.07930	0.07	0.51
	PDA size	PDA Size	Mann-Whitney U	P value	
	Small	Medium	20223	<0.001	
		Large	6937	<0.001	
	Medium	Large	8895	0.361	

Table-2: LA/Ao ratio decreasing rates at two points of time based on the Intervention

LA/Ao ratio decreasing rate from baseline to 6 months after the intervention					
Intervention	N	Mean	SD	MIN	MAX
Medication	62	0.25	0.09	0.02	0.42
Surgery	243	0.24	0.09	0.02	0.41
Device occluded	275	0.24	0.1	0	0.42
Not Closed	1	0.16	-	0.16	0.16
VATS	50	0.24	0.07546	0.06	0.38
Total	631	0.24	0.09435	0	0.42
	Intervention	Intervention	Mann-Whitney U	P value	
	Medication	Surgery	6847	0.268	
		Device occluded	7751	0.264	
		VATS	1450	0.558	
	Surgery	Device occluded	33285	0.94	
		VATS	5901	0.75	
	Device occluded	VATS	6696	0.77	
LA/Ao ratio decreasing rate from 6 months to 12 months after the intervention					
Intervention	N	Mean	SD	MIN	MAX
Medication	62	0.0879	0.09421	-0.08	0.34
Surgery	243	0.1039	0.10076	0	0.36
Device occlude	275	0.1071	0.09978	-0.01	0.41
Not Closed	1	0.21	-	0.21	0.21
VATS	50	0.0916	0.08809	0	0.31
Total	631	0.1029	0.09874	-0.08	0.41
	Intervention	Intervention	Mann-Whitney U	P value	
	Medication	Surgery	6843	0.266	
		Device occluded	7515	0.145	
		VATS	1442	0.527	
	Surgery	Device occluded	32613	0.638	
		VATS	5961	0.834	
	Device occluded	VATS	6500	0.54	
LA/Ao ratio decreasing rate from baseline to 12 months after the intervention					
Intervention	N	Mean	SD	MIN	MAX
Medication	62	0.3243	0.07595	0.15	0.48
Surgery	243	0.3221	0.08218	0.08	0.5
Device occlude	275	0.3233	0.07841	0.07	0.51
Not Closed	1	0.33	-	0.33	0.33
VATS	50	0.3156	0.07664	0.15	0.48
Total	631	0.3223	0.0793	0.07	0.51
	Intervention	Intervention	Mann-Whitney U	P value	
	Medication	Surgery	7408	0.84	
		Device occluded	8397	0.853	
		VATS	1406	0.399	
	Surgery	Device occluded	33232	0.915	
		VATS	5645	0.431	
	Device Occluded	VATS	6314	0.359	

Table-3: LA/Ao ratio decreasing rates at three points of time based on complication

LA/Ao ratio decreasing rate from baseline to 6 months after intervention					
Complication	N	Mean	SD	MIN	MAX
Residuals	8	0.243	0.06981	0.18	0.36
No complication	550	0.2427	0.09486	0	0.42
PH	73	0.2106	0.08882	0.03	0.38
Total	631	0.239	0.09435	0	0.42
	Complication	complication	Mann-Whitney U	P value	
	Residuals	No complication	2097.00	0.820	
		PH	248.00	0.486	
	No complication	PH	16094.00	0.006	
LA/Ao ratio decreasing rate from 6 months to 12 months after the intervention					
Complication	N	Mean	SD	MIN	MAX
Residuals	8	0.0789	0.06844	0.01	0.21
No complication	550	0.0949	0.09497	-0.08-	0.41
PH	73	0.166	0.10723	0.00	0.38
Total	631	0.1029	0.09874	-.08-	0.41
	Complication	complication	Mann-Whitney U	P value	
	Residuals	No complication	2156.00	0.923	
		PH	160.00	0.037	
	No complication	PH	12346.00	<0.001	
LA/Ao ratio decreasing rate from baseline to 12 months after the intervention					
Complication	N	Mean	SD	MIN	MAX
Residuals	8	0.304	0.0727	0.19	0.38
No complication	550	0.3195	0.07815	0.07	0.49
PH	73	0.3457	0.0854	0.17	0.51
Total	631	0.3223	0.0793	0.07	0.51
	Complication	complication	Mann-Whitney U	P value	
	Residuals	No complication	1780.00	0.627	
		PH	219.00	0.248	
	No complication	PH	17077.00	0.038	

According to the results of the current study, the decreasing rates of LA/Ao ratio were 24% and 10% in the first and second 6 months after intervention. Before the intervention and 6 months after it, the reduction rates of LA/Ao ratio were 23%, 25% and 22% in small, medium and large PDA while these decrease rates were 7%, 13% and 16%, respectively, in the time duration of 6 to 12 months after the intervention. In regards to types of intervention, the reduction rates of LA/Ao ratio were 25%, 24%, 24% and 24% in those children whose PDAs were closed by Medication, Surgery, occlusion Device and VATS in the first six months after the intervention. This pattern was 9%, 10%, 11% and 9% for the second 6 months after the intervention. The reduction rates of LA/Ao ratio were 24%, 24% and 21% in

those children with residuals, no complication and PH in the first six months after the intervention. This pattern was 8%, 9% and 16.6% for the second 6 months after the intervention.

Halliday et al. (23) conducted a study to find echocardiographic outcomes in large PDA in low birth weight infants before and after the treatment with indomethacin. They classified the infants in two groups; those who respond and those who do not respond to indomethacin. LA/Ao ratio decreased in infants who responded to the medication after treatment with tensity reduction of the murmur, decreased pulses and precordial activity as well, and they experienced less needs for ventilator support and finally their PDAs were closed within 3 days. The two groups of children were similar based on gestational ages, birthweights, sexes, and age at the onset of the treatment. In the present study 62 PDA children went under medical intervention (Ibuprofen or paracetamol). These children took medication in three days, each day one-time Ibuprofen and four times paracetamol. At the end of the first course, the echocardiography was performed and if open DA was observed, the second dose was run. After the end of the second course, if the PDA remained open, the child was referred to Non-pharmacological treatment. The changes of LA/Ao ratio included a 25% decrease within 6 months after the intervention. From 6 months to 12 months after the intervention, this growth rate was 9%. The difference between our results and those of Halliday et al. (23) can be attributed to the population in the study and type of medication. We used the term neonates with medication of paracetamol.

Afifi et al. (13) led a study on children with PDA aged from 6 to 108 months whose PDAs were closed by occluders. They found that the LA/Ao ratio decreased from 1.36 to 1.25 within one week after closure, and further decrease to 1.13 was achieved till the third month after successful closure. In this study, complete PDA occlusion was detected in 61.54% within 10 minutes post deployment. About 96.15% were closed completely after 3 months; and all patients were discharged safely from hospital after 24 hours. The present study found that for those 275 children, whose PDAs were closed by **occlusion devices**, the LA/Ao ratio decreased 24% and 11% in the time points within 6 months after intervention, and from the 6^{th} to the 12th month after the intervention. Aortic obstruction is a concerning complication of **occluder device** PDA closure. In most patients, obstructions were clinically insignificant (24).

Rarely, significant obstructions were observed in smaller infants with larger PDA, and a device removal was necessary in these patients (25). Albeit the reports mentioned above (24, 25), in the present study no significant aortic obstruction was observed after device occluded PDA closure.

Hamabe et al., (26) conducted an animal model study to evaluate LA/Ao ratio changes after PDA closure by surgery. Pre-surgical examination indicated an increase in LA/Ao ratio. Surgical ligation of the PDA caused a significant decrease in LA/Ao ratio to the reference range.

Abdel-Bary et al. (14) considered 50 children whose isolated PDAs were closed by surgical ligation. After closure, the children were followed for six months. LA/Ao ratio measured in the first day, as well as the first and sixth months after intervention. They found a significant decrease in LA/Ao ratio compared to baseline values in the all-time LA/Ao ratio measurements.

In the study by Braulio et al. (27), 47.8% of the preterm neonates with PDA required surgical closure. They indicated that a LA/Ao ratio > 1.5 represented good predictors of the need for surgery. In the

present study, 247 PDA were closed by surgery such that 44.5% had LA/Ao ratio> 1.5. They confirmed that high ductal shunting is a relevant prognostic marker for surgical closure. In the present study, the patients whose PDA were closed by surgery consisted of 243 children. The LA/Ao ratio decreased to 24%, 10% and 32% in the first six months, in the second six months and in the first twelve months after the intervention.

Noori et al. (1), in a recent study considered four different PDA closures of VATS, Amplatzer, medication, and surgery. They concluded that the LA/Ao ratio had the highest decrease in Amplatzer followed by surgery in the times pointed from 1 month to 1 year after intervention. In this period, those who were treated by medication had the lowest decrease in LA/Ao ratio. They also found that the LA/Ao ratio decreased to about normal range one year after the intervention. In the present study, for those 50 children whose PDAs were closed by VATS, the LA/Ao ratio trends were 24% and 9% in the time points within 6 months after the intervention and the period between 6 to12 months after the intervention.

McNamara et al (28) conducted a study to find the association between PDA ligation and impaired left ventricular systolic performance in premature infants weighing less than 1000g. The authors reported that the LA/Ao ratio decreased from 1.7 at bassline to 1.3 at 24 hours after ligation.

According to Chiruvolu et al. (22), high left-to-right shunting is very aggressive to preterm neonates because it induces pulmonary hypertension, pulmonary congestion and enlargement of heart chambers. A hemodynamically significant degree of ductal shunting may be a decisive factor in the choice of a surgical approach. LA/Ao ratio>1.5 along with high ductal shunting are statistically significant indicators of the need for surgical closure of PDA in low birth weight preterm neonates during the first week of life. The probability of surgical intervention when any of these factors are present is greater than 60%. Moreover, when the LA/Ao ratio>1.5 is associated with the occurrence of shock, the probability of surgical closure increases to 78.4% (27).

The present study revealed that the decreases of LA/Ao ratio in different interval times were not significant between the types of intervention. The contradiction between the current study results and the above mentioned studies probably would be due to the type of subjects with low and very low birth weight.

Stankowski et al. (29) reported an age limitation for VATS used for PDA closure. They found that this technique is suitable for children with PDA. The present study demonstrated that LA/Ao ratio decreased significantly in different time points after the intervention based on the PDA size and their observed LA/Ao ratios were associated with the size. Similar trends occurred for the relationship between LA/Ao ratio and PDA complication after the intervention. It was found that those PDAs with PH complication had significantly lower LA/Ao ratio decrease within 6 months after the intervention, while the decrease amount was significantly higher in the second 6 months after the intervention. Six months after the intervention, about 25.2% of the patients had LA/Ao ratio>1.2 (reference range) and this percentage decreased to 4.4% after 12 months. It seems that PDA children who have PH need more time to be followed up.

5- STUDY LIMITATION

The main Limitation of the present study was related to the lack of cooperation by some parents in the follow-up.

6- CONCLUSION

Findings of the study revealed that the LA/Ao ratio, as an indicator of PDA improving, had the highest decrease in the first six months after the intervention; and it changed with some factors. Those PDAs with moderate size had the highest decrease during the first six months after the intervention. In the second six months after the intervention, the large PDAs had the most decreasing rate. The highest rates of PDA decrease based on the intervention, at the first six months, were attributed to those who had medication as intervention, while at the second six months after the intervention, those PDAs with occlusion devices demonstrated higher decrease rates. And the decrease based on the complication found to enjoy the highest rates at the first six months for PDAs with residuals. And the PDAs with complication of PH after the intervention had the highest rate of decrease during the second six months.

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8- CONFLICT OF INTERESTS: None

9- AUTHOR CONTRIBUTIONS

Main concept and design; Noori and Yaghuobi; Data Collection; Noori and Yaghoubi; Review of literature; Noori, Teimouri and Yaghoubi; Analysing the data; Teimouri; Writing the manuscript; Noori and Teimouri.

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