RESEARCH ARTICLE

Early Versus Late Trans Catheter PDA Closure : Effect on LV Remodelling and Recovery Post Closure

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Received: 12th Sep 2024; Revised: 23rd Oct, 2024; Accepted: 15thNov, 2024; Available Online: 25th Dec, 2024

ABSTRACT

Background There is paucity of data concerning the hemodynamic effect of delayed trans-catheter patent ductus arteriosus (PDA) closure. The current study tried to address this issue

Methods This was a prospective observational study including 42 patients with mean age of 48 months and mean PDA diameter of 2.7±0.8 mm. The study group was subdivided into 2 subgroups (1st group less than and 2nd group more than 2 years of age at time of PDA closure). The 2 groups were assessed regarding the impact of PDA closure on different LV parameters measured by trans thoracic echocardiogram (2D dimensions, systolic function and 2D speckle tracking).

Results LVEF in both groups decreased significantly immediately post PDA closure **(p< 0.0001)**, but at 3 months follow up only in older group did it continue to be significantly lower than baseline values **(p< 0.002)**. In group 1, indexed LVEDV and LVESV demonstrated significant early and continuous improvement at immediate and 3 months follow up **(p<0.0001)**. Group 2 demonstrated only late improvement at 3 months follow up in indexed LVESV. GLS in both groups dropped significantly immediately post closure with significant improvement at 3 months follow up but GLS values remained significantly lower in group 2 compared to group 1 **(p< 0.006)**. In both groups, age was positively correlated with percent reduction in GLS immediately post PDA closure and was negatively correlated with percent increase in GLS from immediate to 3 months follow up (degree of recovery). PDA size was negatively correlated with percent increase in LVEF from immediate to 3 months follow up (degree of recovery)

Conclusion Trans catheter PDA closure in children 2 years old or less was associated with early reduction in LVEDV, LVESV, and greater improvement in LVEF and GLS after initial drop. It is crucial to diagnose and close hemodynamically significant PDAs as early as possible to ensure better LV reverse remodelling.

Keywords: PDA, GLS, transcatheter closure, per cent change.

How to cite this article: Alaa Mahmoud Roushdy, Tarek M AbdelRahman, Mahmoud Abozaid Mohamad, Hazem M A Farrag. Early Versus Late Trans Catheter PDA Closure : Effect on LV Remodelling and Recovery Post Closure. International Journal of Pharmaceutical Quality Assurance. 2024;15(4):2123-28. doi: 10.25258/ijpqa.15.4.4

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

The size and magnitude of the shunt have a major impact on the clinical signs and symptoms of PDA. Majority of patients with small to moderate shunts may continue without symptoms all through childhood. However long-standing shunting through PDA leads to LV volume overload and development of heart failure in adulthood. If left untreated, other serious complications can occur especially with larger shunts, like pulmonary hypertension, arrhythmias, aneurysms or infective endarteritis.[1] Transcatheter PDA closure has become the recommended treatment of choice in suitable patients. There are many studies demonstrating hemodynamic changes after TCC PDA closure, however there is rarity of data comparing the effectiveness of trans catheter PDA closure in different age groups.

MATERIALS AND METHOD

This was a prospective observational study. 46 patients with PDA who were referred for trans-catheter PDA closure in Ain Shams university hospital from December 2020 to December 2022 were included. The study group was subdivided into 2 subgroups according to age at time of closure, group 1 less than 2 years and group 2 more than 2 years old. Inclusion criteria was hemodynamically significant PDAs that are suitable for trans catheter closure. Exclusion criteria was Eisenmenger syndrome, anatomically unsuitable PDAs, PDAs associated with other CHD like AVSD, VSDs, aortic Coarctation. or silent PDAs. An informed approval was obtained from the study participants or their related guardians. The study was conducted after approval of Ethical Committee of Ain Shams University of Medical Science.

Echocardiography was performed for every patient planned for trans catheter PDA closure at 3 occasions (pre closure within 48 hours before PDA closure, immediately and at 3 months following PDA closure). 2D echocardiogram was performed in supine position using Philips EPIQ 7 CVXi ultrasound machine with S8-3 or S5-1 probes. Chloral hydrate (50mg/kg) was used for younger

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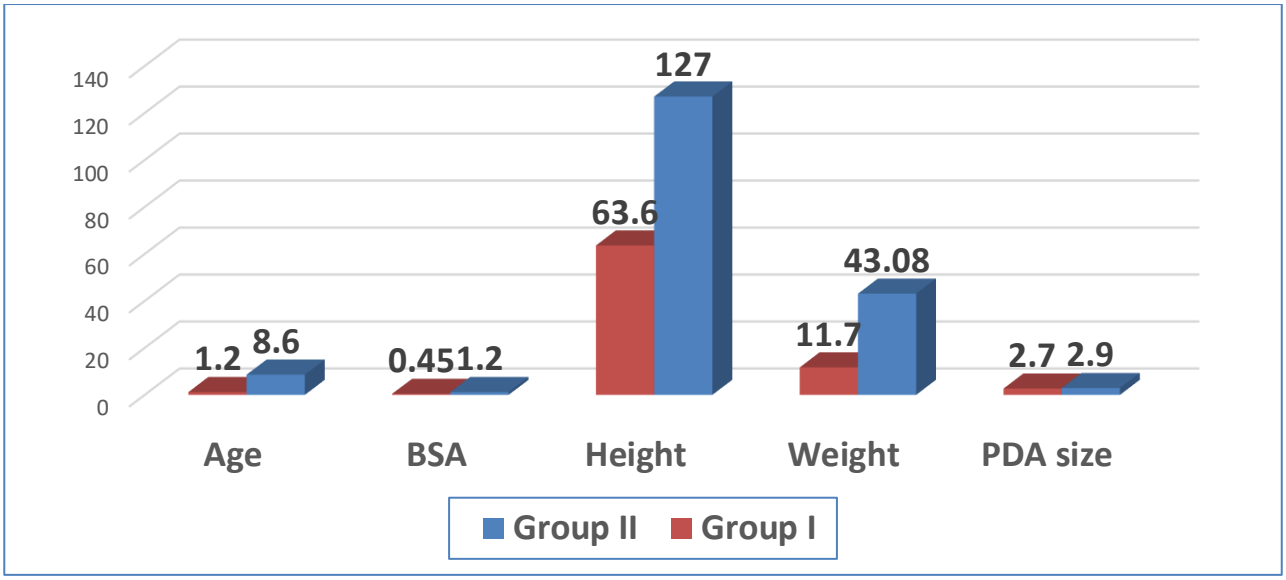

Figure 1: Baseline characteristics of the patients in both groups

patients requiring sedation. LVEF, indexed LVEDV and indexed LVESV were measured by Simpson's biplane method.[2,3] PDA assessment (size, and orientation) was done at ductal and suprasternal views.[4] After completing the conventional trans thoracic echocardiogram two-dimensional speckle tracking was done by acquiring grayscale imaging from the apical 4, 2 and long-axis views. The images were acquired at frame rate of 80–100 frames/second. For offline analysis, three subsequent cardiac cycles were recorded and digitally preserved.. Automatic tracking was carried out, and it was manually manipulated as needed to cover the whole myocardial wall.. Following visual review and when the software showed sufficient tracking, the analysis was approved. Using Q analysis software, off-line assessments of the two-dimensional global longitudinal strain have been obtained.[5,6]

Cardiac catheterization and PDA closure

Cardiac catheterization was performed under general anaesthesia. Arterial and venous access was obtained using Sildenger's technique through the femoral route. Aortogram was obtained in the lateral and RAO views to assess the PDA type and size. Accordingly, PDAs were closed by either coil or occluder device. Ten minutes after deployment, aortogram was repeated to exclude any complications before coil/device release.

Statistical analysis

Data analysis was carried out by using the Statistical Package for Social Science (SPSS) version 21.0 windows software. Continuous data were expressed as mean ±SD and analysed by paired t-test and Man-Whitney test. Categorical data were expressed as frequency and percentages. Correlation was calculated using Pearson's correlation. P-value < 0.05 was considered statistically significant.

RESULTS

The study included 42 patients with mean age of 4 years and mean PDA diameter 2.7±0.8 (at pulmonic end). Comparison between the demographic characters of the 2 groups is shown in figure 1. There was no significant difference between the 2 groups regarding PDA diameter. Base line LVEF, indexed LVEDV and indexed LVESV did not show significant difference between the 2 groups. Both groups demonstrated significant drop of LVEF immediately post closure (p value = 0.0001) with near complete LVEF recovery at 3 months follow up in group 1 (P value = 0.3) , but this difference was significant in group 2 with EF measuring 65.3±3.04 at baseline compared to 60.6±2.7at follow up (p value 0.002). At 3 month follow up LVEF in group 2 was less than that in group 1 despite non-significant baseline difference. In group 1, Indexed LVEDV and indexed LVESV demonstrated significant improvement immediately post closure and at 3 months follow up compared to baseline. In group 2 indexed LVEDV and indexed LVESV did not show significant change at immediate or 3 months follow up when compared to baseline. Immediate and 3 months indexed LVEDV and LVESV were less in group 1 than group 2 (47.8±9.8 Vs 63.1±10.6, 43.1 ±8.1 Vs. 62.8±10.9 respectively for EDV, P value <0.05) and (18.3±3.4 Vs 25.1±3.7, 16.2±1.9 Vs. 23.8±2.7 respectively for ESV, P value <0.05)(Table 1).

The percent Δ in LVEDVI, LVESVI and LVEF was calculated as percentage of baseline change when immediate and 3 months follow up were compared to base line measurements. The percent Δ in LVEF demonstrated more LVEF reduction and less LVEF recovery at 3 months follow up in group 2 compared to group 1 (0.005±0.06 Vs. 0.05±0.06, p value = 0.005, 0.12±0.05 Vs 0.03±0.05, p value = 0.0001 respectively). The percent Δ in LVEDVI from baseline to immediate and 3 months follow up post closure was less in group 2 than group 1 (0.22±0.08 Vs. 0.07±0.1, 0.40±0.1 Vs. 0.02±0.1, 0.41±0.24 Vs 0.001±0.3 with P value = 0.0001). The percent Δ in LVESVI from baseline to immediate and 3 months follow up post closure was less in group 2 than group 1 (0.15±0.1 Vs. 0.04±0.1 , 0.33±0.1 Vs. 0.16±0.1 , 0.24±0.1 Vs. 0.12±0.1 with P value = 0.01 , 0.001 , 0,008 respectively) (Table 1).

Table 1: Echocardiographic parameters at baseline, 1 day, and 3 months after the procedure in the two groups

		Group 1(N = 26)			Group 2 (N=16)		
		Baseline	immediate	3 months	Baseline	immediate	3 months
LVEF		65.9±3.3*	58.2±3.3**	66.3±2.3	65.3±3.04*	58.3±3.6**	60.6±2.7¶
LVEDVI (mL/m2)		57.1±11.7*	47.8±9.8**	43.1±8.1¶	63.3±10.8	63.1±10.6§	62.8±10.9
LVESVI (mL/m2)		22.1±4*	18.3±3.4**	16.2±1.9¶	24 ±2.7	25.1±3.7§	23.8±2.7
LVGLS		-23.6±2.2*	- 15.07±3.03**	-21.03±3.1¶	-22.6±2.2*	-16.6±2.1**	-18.0±2.6¶
ΔLVGLS	**Δ 1**		0.29±0.08			0.24±0.08	
	Δ 2		0.12±0.09			0.19±0.09	
	Δ 3¥		0.35±0.2			0.06±0.12	
ΔLVEDVI	**Δ 1¥**		0.22±0.08			0.07±0.1	
	Δ 2¥		0.40±0.1			0.02±0.1	
	Δ 3¥		0.41±0.24			-0.001±0.3	
Δ LVESVI	**Δ 1¥**		0.15±0.1			0.04±0.1	
	Δ 2¥		0.33±0.1			0.16±0.1	
	Δ 3¥		0.24±0.1			0.12±0.1	
ΔLVEF	**Δ 1**		0.11±0.05			0.10±0.06	
	Δ 2¥		0.005±0.06			0.05±0.06	
	Δ 3¥		0.12±0.05			0.03±0.05	

Data are shown as mean± SD

* P<0.05 when compared with immediate follow at same group

** P<0.05 when compared with 3 months follow up at same group

¶ P<0.05 when compared with baseline at same group or 3 months follow up of other group

§ P<0.05 when compared with immediate follow up at group 1

¥ P<0.05 with comparison between 2 groups

Δ 1: Pre-closure versus 48 h post-closure, Δ 2: Pre-closure versus 3 month post-closure, 3: 48 h post-closure versus 3 month post-closure

Baseline GLS didn't show significant difference between the 2 groups. Both groups demonstrated significant GLS decline immediately post PDA closure. Despite significant GLS recovery at 3 months follow up, these values were still significantly lower than pre-closure ones. At 3 months follow up, GLS values were greater in group 1 than 2. The percent Δ in LVGLS from immediate to 3 months follow up post closure was less in group 2 than group 1 (0.35±0.2 Vs. 0.06±0.12 P value 0.0001) (Table 1).

There was significant positive correlation between age and percent Δ of GLS from pre-closure to 3 months follow up and significant negative correlation between age and percent Δ of GLS from immediate to 3 months follow up (figure 2, 3).

There was significant negative correlation between PDA size and percent Δ of LVEF and also indexed ESD from immediate post closure to 3 months follow up i.e recovery percentage.

DISCUSSION

The current study demonstrated early LVEF decline immediately post PDA closure and spontaneous recovery at 3 months follow up with difference in recovery pattern according to the age at trans-catheter closure. Initial drop

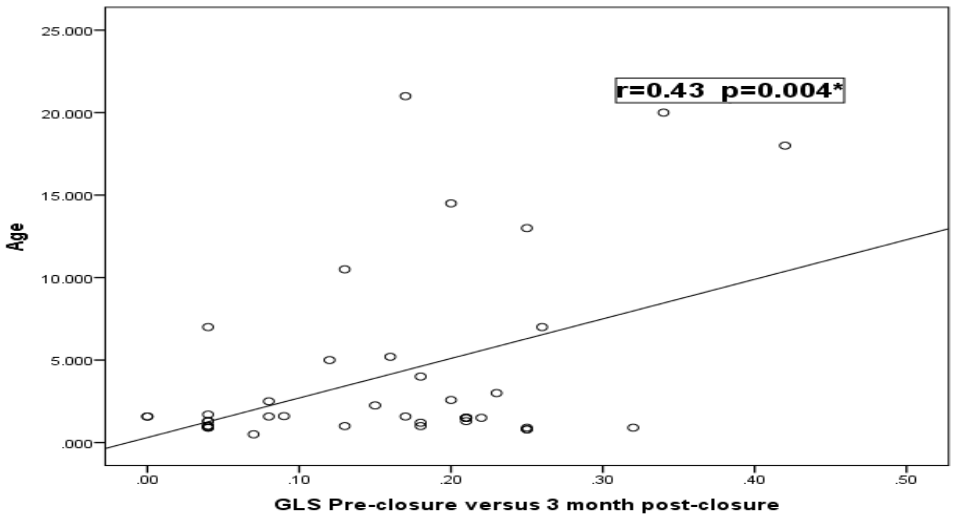

Figure 2: correlation between age and Δ of GLS from pre-closure to 3 months follow up.

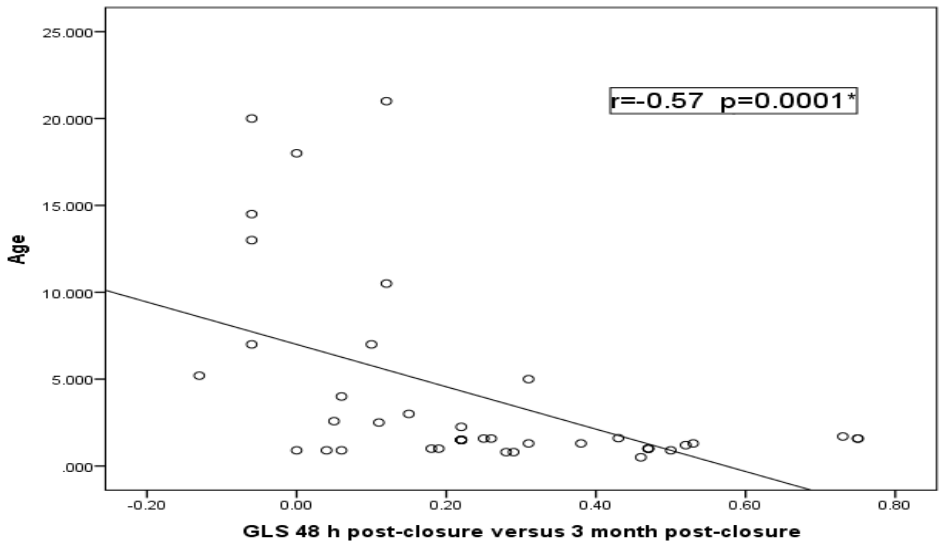

Figure 3: correlation between age and Δ of GLS from post-closure to 3 months follow up.

in LVEF immediately post closure followed by complete recovery at 3 months follow up was in agreement with El-Khuash AF et al, and Zhang C-J et al.[5,7] This decline in EF could be explained by the simultaneous decrease in preload and increase in afterload following PDA closure i.e preload-after load mismatch.[9] Non-significant immediate decline of LVEF after PDA closure with complete recovery at 1 month follow up was reported in Ezzeldin, DA et al study which could be explained by the fact that most of their study patients had small sized PDA.[8] Our study demonstrated that indexed LV volumes decreased significantly in group 1 compared to group 2 at any follow up despite non-significant difference between same parameters at pre-closure state. As regard percent change of LVEDVI, LVESVI from baseline, there was significant reduction in percent change in group one compared to group 2 when immediate and 3 months follow up were compared to baseline. Percent change of GLS and LVEF showed significant greater increase from immediate to 3 months follow up in group 1 than group 2.

Yasuhara J et al., 2020 demonstrated that trans catheter PDA closure is not associated with improvement in LV size and function in adults as compared with children. At 6 months follow up, LVEDVI, LVESVI and LVEF values were lower in children group than adult group.[10] In the current study we proved that this difference exist even within the pediatric age groups and not only between children and adults.Poor improvement in LVEDVI and LVESVI may be explained by long standing LV volume overload and consecutively more LV remodelling and structural changes in myocardium.[11,12]

In the current study, LVGLS demonstrated early decline in pattern similar to LVEF in both groups but LVGLS recovery was better in group 1 compared to group 2. Although GLS values showed notable improvement three months after

procedure, they were still significantly lower than baseline values .In agreement with our results, El-khuffash et al 2012 and El-shedody SA et al., 2017 demonstrated significant decrease in GLS immediately post PDA closure with significant rise at follow up , but values were still lower than pre-closure measurements.[5,13] It is generally known that larger ventricles have lower strain to generate the required output even without impaired contractility.

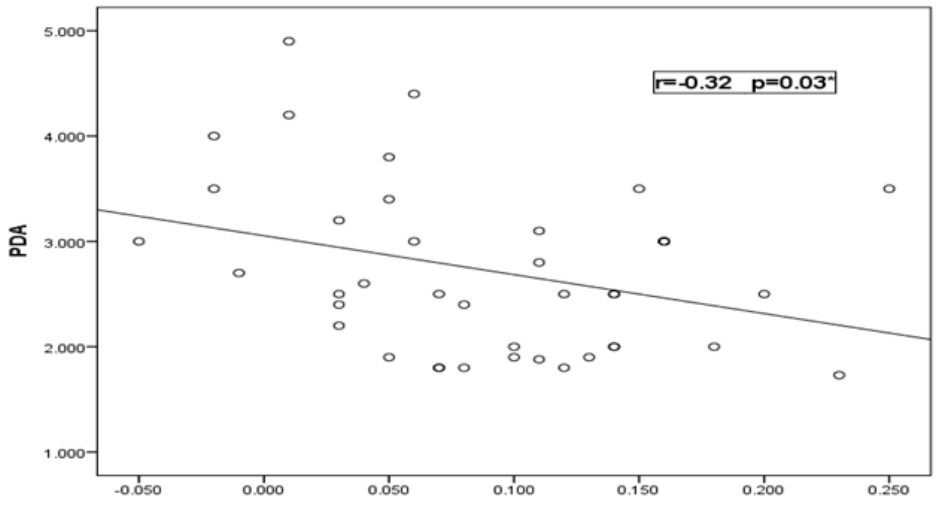

Figure 4: correlation between PDA and Δ of LVEF from immediate post closure to 3 months follow up.

Additionally, strain measurements are directly influenced by loading conditions, with preload positively impacting strain and afterload associated with its reduction.[14] Thus, highest strain values were noted at baseline and early post closure decline was in parallel to LV systolic dysfunction due to elimination of increased preload and increased after load.[5,15]

Percent change of GLS showed significant greater increase from immediate to 3 months follow up in group 1 than group 2. Extended exposure to left ventricular volume overload may result in myocardial structural changes that cannot be reversed, which could compromise myocardial recovery following loading condition reduction.[12] Pre-closure GLS, PDA size and age were shown to be predictors of post-closure myocardial dysfunction.[9,16] Our study demonstrated significant negative correlation between PDA size and changes in LVEF and indexed ESD from immediate post closure to 3 months follow up. This can be explained by extensive LV remodelling that occurs with large PDAs leading to irreversible LV structural changes that affect recovery. Amoogzar H et al., 2015 demonstrated there is a negative correlation between the PDA size and changes in EF and LV dimensions post PDA closure.[17] Hou M et al.,2019 proved that PDAd/AOd ratio is a predictor of post-closure LV systolic dysfunction i.e. The greater the ratio value, the higher the probability of LV dysfunction following closure.[2]

In the current study there was significant positive correlation between age and percent Δ of GLS from pre-closure to 3 months follow up and significant negative correlation between age and percent Δ of GLS from immediate to 3 months follow up. Kumar Sharma et al.,2021 reported that patients with delayed PDA closure (closure after 2nd year of life) had a higher incidence of LV dysfunction in adults and adolescents.[18] It is explained that, in particular, with greater LV afterload brought on by PDA ligation, late surgical PDA closure results in a longer left to right shunt and, thus, higher LV overload and dysfunction.[12]

Limitations, Recommendations

This was an assessment of the age at time of PDA closure on the immediate and short term effect on different LV parameters. Larger sample size with longer follow up period is recommended.

CONCLUSION

Trans catheter PDA closure in children 2 years old or less is associated with early reduction in LVEDV, LVESV, and greater improvement in LVEF and GLS after initial drop. It is crucial to diagnose and close significant PDAs as early as possible to ensure better LV reverse remodelling.

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