

THE TRANSIENT EFFECTS OF TRANS-CATHETER PATENT DUCTUS ARTERIOSUS CLOSURE ON LEFT VENTRICULAR SYSTOLIC FUNCTION

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ABSTRACT

Background: Patent Ductus Arteriosus (PDA) is a common congenital cardiac lesion with incidence up to 1 in 500 live births. After closure of a notable PDA, the concurrent decline in preload the left ventricular end diastolic volume (LVEDD) and step-up in the afterload may reduce systolic performance of left ventricle. This dysfunction has been reported to be temporary and improvement has been observed as early as 48 hours after procedure.

Objectives: To measure transient effects of trans-catheter Patent Ductus Arteriosus closure on left ventricular systolic function, and to present related findings and discuss implications.

Methods: A prospective study was conducted from July 2021-June 2022. The study included 102 patients of which (96/102) experienced percutaneous closure of PDA in this duration. (6/102) Patients had preexisting LV dysfunction and significant associated cardiac lesions and were not included in the study. LV function was assessed before and then one day, one month and three months after the transcatheter closure. (10/96) patients off-track follow up and were later barred from study.

Results: PDA was occluded in 86 children by transcatheter intervention. Average age of the cohort was 65 ± 58 months with 70% female patients. The mean size of the ductus was 3.67 ± 1.78 . LV systolic function remained normal in 65 patients (86%) while 21 patients (24%) suffered from a fall in systolic function of left ventricle after PDA occlusion. LVEDd, FS, and EF significantly dropped within 24 hours after occlusion of the ductus. LV- systolic dysfunction improved in almost all the patients at 3 months follow up except for 4 (4.6%) patients who had persistently poor systolic function of LV.

Conclusion: Trans-catheter closure of PDA can cause a significant but temporary decline in LV systolic function. Large PDA, LAd, higher PDA/AOd, LAd/AOd and larger LV dimensions can predict LV dysfunction in high-risk patients.

Key words: Patent ductus arteriosus, Transcatheter PDA closure, LV systolic dysfunction

How to cite this article: Talat S, Malik A, Sattar H, Kanwal A, Akbar T, Asghar H. The transient effects of trans-catheter Patent Ductus Arteriosus closure on left ventricular systolic function. *Pak Postgrad Med J* 2023;34(2):88-92

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DOI: <https://doi.org/10.51642/ppmj.v34i01.576>

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INTRODUCTION

Patent Ductus Arteriosus (PDA) is a common congenital cardiac lesion with incidence up to 1 in 500 live births¹⁻⁵. The diagnosis mainly depends on the physical examination and echocardiography.⁶ The incidence is twice in females as compared to males². Preterm babies are more likely to have patent ductus secondary to multiple factors.⁷ Preterm new-

borns with heart failure, infants with recurrent chest infections and asymptomatic adults who are diagnosed by coincidence are just a few of many possible clinical manifestations of PDA.⁸ Signs and symptoms depend mainly upon the size of the ductus, magnitude of its shunt and the pulmonary vascular resistance.^{1,2,9} PDA with hemodynamic significance can lead to chronic volume overload of Left Ventricle (LV) and may result in the development of congestive cardiac failure, rhythm disturbances, endarteritis, abnormal dilatation of the ductus and Eisenmenger's syndrome, in untreated cases.^{1-4,10,11}

PDA transcatheter occlusion was initially reported in 1967 and since then several advancements have been made to

the technique.^{12,13} Trans catheter closure is the recommended approach, as it is now widely accepted to be safe and successful, with outcomes that are equivalent to surgical closure both immediately after closure and in long term follow up.¹⁴⁻¹⁸

LV hypertrophy is caused by chronic volume overload which remodels cardiac filling and contractility of myocardium.¹ After closing a notable PDA, the preload to the LV is reduced because of cessation of blood shunting through the ductus. Furthermore, the afterload is enhanced after pulmonary circuit is excluded from LV outflow circulation.^{4,10} The concurrent decline in the end diastolic volume of LV and step-up in the afterload may affect systolic performance of left ventricle.¹⁹ However, the LV dysfunction following PDA closure has been reported to be temporary and improvement has been observed as early as 48 hours after procedure.²⁻⁴ Long term follow up, (3-6months after closure) has shown LV function returning to baseline in most patients except for a small minority.¹⁹ Parameters such as age, weight, PDA size, PDA indexed size, PDA_d/A_{od} (PDA diameter/aortic diameter), LAd/A_{od} (Left Atrium diameter/Aortic diameter), LVEDD (LV End Diastolic Diameter), LV End Diastolic Pressure (LVEDP) have been evaluated and found to be associated with post closure dysfunction of LV.

Exercise intolerance may result from significant impairment of LV function and necessitate prolonged hospital stays and the use of afterload reducing agents.²⁰

This study aims to inquire into the alteration of LV systolic function following PDA closure, and to link if pre- procedure echocardiographic parameters could predict decline in LV function after occlusion of PDA.

METHODS

After approval of the study and Informed consent, 102 patients were registered in this study. Diagnosis of isolated PDA was confirmed on echocardiography in all patients. Of them 96 patients underwent successful percutaneous PDA closure between July 2021 and June 2022. Procedure was deferred for 6 patients with unfavorable PDA size or anatomical detail. Out of total, 10 patients off-track follow up and were later barred from study. Transthoracic 2D echocardiography and M mode were performed on OPD

basis. A three or five MHz transducer was used by a single researcher on an outpatient basis to collect data including diameters of ductus, aortic root, and LA (PDA_d, A_{od}, LAd), the ratios of PDA_d to A_{od}, and LAd to A_{od} (PDA_d/A_{od}, LAd/A_{od}), and LV dimensions; (LVEDD, LV End Systolic Diameter, LV Ejection Fraction (LVEF), Fractional Shortening (FS)). Same parameters were recorded before the procedure, and then a day, a month, and three months after the procedure. The Echocardiographic examination was completed by performing standard views to find out associated cardiac lesions. Cardiac catheterization was performed under general anesthesia in all cases. The PDA was crossed, and pigtail catheter was placed in descending thoracic aorta for angiographic assessment of ductus. PDA size was measured in angiograms taken in full lateral view. PDA was closed in all patients using appropriately sized Occlutech devices. After deploying the device, a check angiogram was performed to confirm the device position. Descending thoracic aortic and left pulmonary artery were assessed for any obstruction caused by the device. Residual shunt was also excluded before releasing the device.

RESULTS

Data was analyzed and arranged utilizing SPSS program Version 20. Frequencies were compared using the Fisher exact test to present categorical data. Continuous variables were compared using Student paired t-test and expressed as mean values ± standard deviation. Differences were detected using Pearson Chi-Square tests among groups for categorical variables. The relationship between PDA size and changes in echocardiographic parameters was verified using Pearson linear correlation and the linear regression analysis. *P*-value of <0.05 was considered significant.

Of the 86 children, 24 showed LV systolic dysfunction within 24 h of PDA closure. The parameters which showed significant drop at one day after the procedure as compared to pre-procedure values included, LVEDd, FS, and LVEF (see Table 1), whereas LAd, A_{od} and LVESd values did not change significantly. However, the values of LVEDd, FS and LVEF were not statistically significant at one-month and three- months follow up when compared with the baseline values. (Table 1).

Table 1: Comparison of echocardiography parameters (n = 86)

	Pre-Closure	1 Day Post	1 Month Post	3 Months Post
A _{od}	18.15 ± 4.74	18.81 ± 4.93	17.96 ± 3.84	17.47 ± 3.48
Lad	20.82 ± 6.05	20.87 ± 4.90	19.45 ± 4.02	18.51 ± 4.01
LAd/A _{od} ratio	1.16 ± 0.30	1.14 ± 0.30	1.10 ± 0.21	1.06 ± 0.21
LVEDd	34.59 ± 10.99	27.49 ± 9.36	34.90 ± 7.17	31.14 ± 8.31
LVESd	22.28 ± 7.56	27.42 ± 9.87	23.78 ± 6.57	19.74 ± 6.46
FS (%)	36.23 ± 7.72	26.04 ± 7.64	32.98 ± 6.22	37.81 ± 5.32
LVEF (%)	66.51 ± 9.00	51.01 ± 12.56	62.17 ± 8.72	69.26 ± 6.79

LAd, PDA_d/A_{Od}, and LAd/A_{Od} were found elevated in the subjects who later suffered from LV systolic dysfunction than those who did not suffer from dysfunction after PDA closure. (See Table 2).

Table 2: Pre-closure echocardiography parameters in patients with and without post-closure LV systolic dysfunction.

Parameters	Without LV dysfunction (n=62)	LV dysfunction (n=24)
A _{od}	17.58 ± 4.11	19.91 ± 6.11
L _{ad}	20.23 ± 5.21	22.61 ± 8.02
PDA _d	3.56±1.84	3.83± 1.8
LAd/A _{Od}	1.16 ± 0.29	1.18 ± 0.31
PDA _d /A _{Od}	0.21 ± 0.08	0.33 ± 0.09
LVED _d	33.69 ± 11.00	37.35 ± 10.81
LVES _d	20.64 ± 6.94	27.26 ± 7.33
EF	69.57 ± 8.28	57.16 ± 1.50

Clinical characteristics of the cohort (n=86):

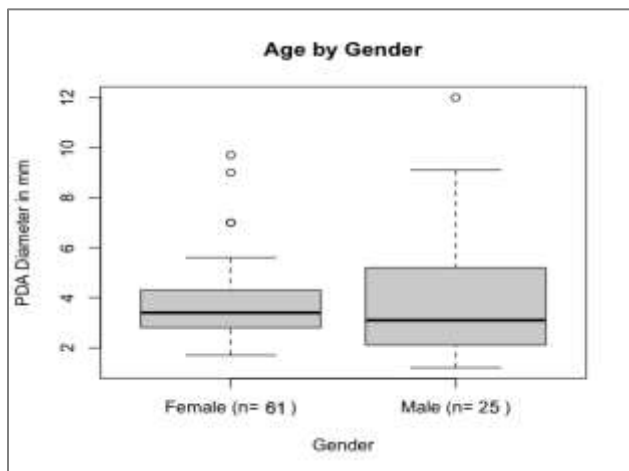


Figure. 1

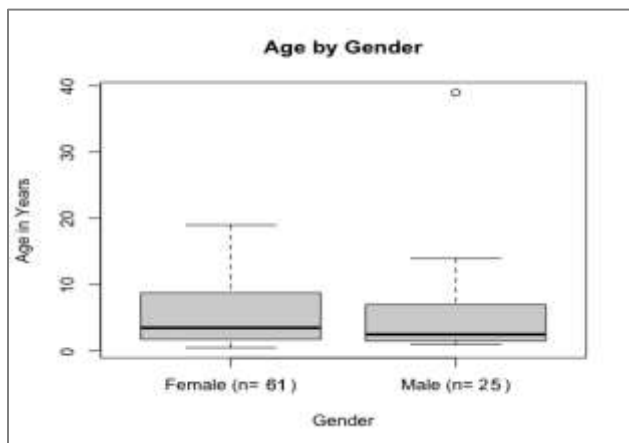


Figure. 2

Fig. 1 & 2 describe clinical features of patients. The cohort included 25(21.5%) boys and 61 (70.9%) girls with the

median age of 5.4 ± 4.8 years. Mean weight was 19.2 ± 12.3. the measurement of PDA from pulmonic end was 3.67 ± 1.78.

Stepwise multiple linear regression analysis was conducted to identify the echocardiographic predictors of post-closure LV systolic dysfunction. PDA_d ($r = -0.48, P < 0.01$), PDA_d/A_{Od} ($r = -0.50, P < 0.01$), and LAd ($r = -0.55, P < 0.05$), LVED_d ($r = -0.50, P < 0.01$) negatively correlated with post-closure LVEF on univariate linear regression analysis, and LVEF ($r = 0.66, P < 0.01$) was observed to have positive correlation with post-closure LVEF (see table 4 below)

Table 3: Multiple linear regression analysis for post-closure LV dysfunction.

	Univariate analysis (3 month) LV dysfunction – P	Multivariate analysis (3 month) LV dysfunction – P
A _{Od}	0.178	
L _{ad}	0.001	
PDA _d	0.003	
LAd/A _{Od}	0.111	0.001
PDA _d /A _{Od}	0.001	0.001
LVED _d	0.002	
LVES _d	0.080	
LVEF	0.002	0.001

Pre-closure LVEF ($\beta = 0.443, P < 0.01$), PDA_d/A_{Od} ($\beta = -0.216, P < 0.01$), and LAd/A_{Od} ($\beta = -0.211, P < 0.01$) were statistically significant factors for the prediction of the deterioration in post-closure LV performance on multivariate regression analyses.

DISCUSSION

The study documented a notable decline in LVED_d, LVEF and LVFS immediately post- PDA occlusion, which was observed to have improved markedly after one month and coming back completely to normal within three months in 95% patients. This was in concurrence with the outcome of previous studies.^{1,4,10,12,14,15,20-22}

Frank-Starling’s Law describes that an increase in end-diastolic volume enhances the stretching of the LV muscle fibers and increases contractility. This overcomes left-to-right shunt and maintains systemic circulation through augmented systolic performance.^{13,14,21,22} The abrupt fall in LV preload occurs after PDA closure which reduces stretching of myocardial fibers leading to decline in FS. Moreover, elimination of pulmonary blood flow from left ventricular outflow circulation after closure of ductus enhances the afterload. This results in LV systolic dysfunction secondary to the coincident fall in preload and increment in afterload of left ventricle.^{19,21}

LV systolic dysfunction was defined as EF<50% and/or a fall in LVEF of ≥10% from baseline in this study, in line with previous studies.^{1,14,23} This study documents that 24.6% patients in the cohort suffered from significant reduction in LV

function which was significantly less than the study done by Hussain et al¹² but comparable to the studies done by Gupta et al. and Kiran et al. (22%) on Indian population.^{1,19} However, it was higher than what was observed in studies done on Korean and Finnish population.^{3,10}

In contrast to LVEDD, LVESD did not decline significantly. This explains the effect of reduced preload on diastolic dimensions, while systolic dimensions of LV remain unchanged. These observations have previously been documented.^{4,14,20,24}

Jeong et al. has documented a decrease in FS and EF of 11.1% in adult patients after PDA closure which did not improve on follow-up.²³ They concluded that long term exposure to chronic volume overload could lead to irreversible structural changes.

Galal et al. documented large sized PDAs to be associated with significant immediate deterioration of LV systolic function²⁰. Agha et al. also proved PDA to be a predicting factor for post-closure LV dysfunction²¹. Indexed PDA size was taken into consideration by Kiran et al who could elicit a strong association of large, indexed PDA size with post closure LV dysfunction.¹⁶ This also explains the higher percentage of LV dysfunction observed by Hussain et al. in patients with less z scores of weights.¹² PDA diameter was found to be a predictor of LV dysfunction in present study.

Miou et al. found PDA/AoD to be a better predictor of post-closure LV systolic dysfunction instead of PDA alone.¹⁰ Furthermore, LAd/AoD ratio has also been found to foretell the post-closure LV dysfunction in the study done by Miao et al and Iyer et al.^{10,25} PDA/AoD and LAd/AoD are proven to be statistically significant in predicting LV dysfunction in current study demonstrating the effect of a notably large left to right shunt causing enlargement of the left heart.

CONCLUSION

Significant but transient deterioration in LV systolic function can result immediately after PDA closure. PDA, LAd, PDA/AoD, LAd/AoD, LVEDD and EF may predict reduction in the LV systolic function immediately after PDA closure. This data may also help in the judicious allocation of resources and guide on frequency of monitoring after PDA device closure.

Ethical Approval: Submitted

Conflict of Interest: Authors declare no conflict of interest.

Funding Source: None

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AUTHOR'S CONTRIBUTIONS

ST: Conceived, planning, manuscript writing, data collection, data analysis

AMS, HS: Revision of scientific content of manuscript

AK: Critical revision

TA: Revision of manuscript

HA: Data compilation