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ORIGINAL ARTICLE

Role of Targeted Neonatal Echocardiography in Diagnosis of Patent Ductus Arteriosus in Neonatal Intensive Care Unit

Amr I. Risha[1]*, H MSaad[1], L M. Elsayed[1], SoadShedeed[1], Wesam A. Mokhtar[1], Mohammed M. Shehab[1].

[1]*Pediatric Department, Faculty of Medicine, Zagazig University, Egypt.*

Corresponding author*:
Amr Ibrahim Risha

Email
Dr.amr@zu.edu.eg

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ABSTRACT

Background: Numerous negative outcomes are linked to the existence of patent ductus arteriosus (PDA) in neonates. There is a lack of information regarding the proper diagnosis and pathophysiologyin relation to long-term outcomes. We aimed to investigate the role of targeted neonatal echocardiography (TNE) in hemodynamically unstable neonates for diagnosis of neonatal PDA that may help in changing the management plan and improving the survival outcome

Methods: This cohort study was conducted at the Pediatric Neonatology and Cardiology Units at Pediatrics Department, Faculty of Medicine, Zagazig University on 85 neonates who were clinically suspected to have PDA. We performed TNE for all patients and cases with confirmed PDA were followed up every 3 days to assess changes in management plan till improvement or death.

Results: Out of 85 cases examined, 43 were confirmed to have patent ductus arteriosus (PDA). Therapeutic interventions were provided, and Post treatment echo revealed that PDA was closed in 34.9% of patients, 25.6% still had PDA, and39.5% died. Comparing pre- to post-echocardiographic analysis, there was statistically significant decrease in the mean of TR pressure gradient, pulmonary artery pressure, LT atrial/aortic ratio and LVESV also there was statistically significant decrease in LV output.

Conclusions: We concluded that TNE can help in diagnosis of neonatal PDA. We recommend considering TNE as an early detector of PDA to achieve better outcomes.

Keywords: PDA;TNE; NICU.

INTRODUCTION

There is a debate about the significance of a patent ductus arteriosus (PDA) and how it affects long-term cardiorespiratory health among neonatology professionals **[1,2].** Even the chronic patency of a PDA is a clinical challenge because most premature newborns whose PDAs fail to close within the first week of life or even at discharge will spontaneously close without suffering from significant cardiac morbidity **[3,4].**

Long-term patency has been linked to several negative outcomes, but it is unclear how much of these effects can be directly attributed to the hemodynamic effects of ductal patency, if at all **[5].**

The bedside use of echocardiography is known as targeted neonatal echocardiography (TNE) or functional echocardiography **[6].** It is being gradually implemented in neonatal intensive care units (NICU) to guide treatment decisions. TNE is added to the evaluation of traditional clinical parameters to individualize care based on the pathophysiology being addressed. It must be used in conjunction with clinical assessment rather than in place of a cardiologist's examination, as their goals are complimentary and distinct **[7].**

Pediatric cardiologists have traditionally conducted echocardiography, the preferred diagnostic procedure for congenital cardiac abnormalities. It is the perfect instrument for assessing hemodynamics and obtaining physiological and anatomical data in critically sick patients because it is non-invasive, easily accessible, administered at the patient's bedside, and delivers information in real time **[8].**

TNE is indicated in cases of clinically suspected PDA, particularly in very low birth weight (VLBW) neonates during the first 24 to 72 postnatal hours and beyond, also it is indicated in diagnose low systemic blood flow state, suspected persistent pulmonary hypertension in neonates. Assessment of neonates with perinatal asphyxia, abnormal cardiovascular adaptation presenting with hypotension, lactic acidosis, or oliguria during the first 24 postnatal hours and beyond in VLBW infants **[9].**

TNE is also employed in the diagnosis of pericardial effusions, the examination of newborns with sudden cardiovascular collapse, and the assessment of catheter tip location for central venous catheters **[10].**

METHODS

This cohort study was conducted at the Pediatric Neonatology and Cardiology Units at Pediatrics Department, Faculty of Medicine, ZagazigUniversity from January 2022 to May 2023 on 85 neonates with clinically suspected PDA. All neonates diagnosed with PDA and admitted to the Neonatal Unit underwent TNE if their clinical presentation met the study's inclusion criteria

Neonates born both vaginally and through cesarean section, including full-term and preterm babies, were eligible for this study if they were suspected to have PDA, as evidenced by a systolic murmur, wide pulse pressure, bounding pulses, hyperactive precordium, pulmonary edema, and increased oxygen requirements **[11]**.

Patients with age more than 28 days, lack of suspicion criteria of PDA and refusal of the family to share in this study were excluded. Selected patients were subjected to complete history taking, full clinical examination, and routine investigations as arterial blood gas and chest x ray. Targeted Neonatal Echocardiography (TNE) was performed and all TNE evaluations, which included measurements of all the different parameters were carefully integrated within the clinical context to reach a diagnosis or clinical impression, leading to the formulation of a therapeutic recommendation. Echocardiography examinations were performed using Philips EPIQ cvx echocardiography machine with S9-2 transthoracic transducer. At the time of the consultation, the active patient morbidity and the indication for TNE were noted. Neonatologists with substantial training in echocardiography carried out each scan. A neonatologist who was on site and committed to providing this service reported on each scan in real time. Assessment of systemic blood flow, PDA, and cardiac function were among the common indications for TNE.

Follow up was done for neonates proved to have PDA every 3 days to assess changes in management plan till improvement or death.

Administrative Design:

The Zagazig University Faculty of Medicine's institutional review board and research ethics committee gave their approval to this work which was completed in compliance with the Declaration of Helsinki, the World Medical Association's code of ethics for human subjects' research.

STATISTICAL ANALYSIS

Data analysis was performed usingthe statistical package for social sciences software version 25 (SPSS, IBM Corporation, Armonk, NY, USA). Quantitative data were presented as mean ± standard deviations (SD), while categorical variables were labeled with their absolute frequencies. Data were tested for normality by Shapiro test and Q-Q plot. Paired sample T-test was used to compare normally distributed quantitative data before and after the intervention. Statistically significant and highly significant levels were set at $P < 0.05$ and $P < 0.001$, respectively.

RESULTS

Out of 85 cases underwent TNE, 43/85 cases proved to have PDA 33/85 had pulmonary hypertension, and 9/85 had shock**.** Table 1 shows the basic characteristics among studied newborns with PDA. Table 2 shows that among the patients assessed, one patient (2.3%) presented with cyanosis,18(41.9%) with tachycardia and 23 patients (53.5%) with murmur, over 60% of patients (26 out of 43) required supplementary oxygen due to their condition. Additionally, more than a third of cases (14 out of 43) exhibited prolonged capillary refill time.

Nearly 28% of patients (12 out of 43) exhibited abnormal urine output, and the same percentage (12 patients) had lactic acidosis. In terms of therapeutic interventions, mechanical ventilation was provided to over 37% of patients (16 out of 43). Additionally, around 30% of patients (13 out of 43) received anti-failure therapy, and the majority (76.7% or 33 patients) received ibuprofen or paracetamol.

Post treatment echo revealed closure of PDA in 15 (34.9)patients, failure of closure in 11 (25.6%) patients and 17 (39.5%) patients died.

Table 3 shows that, there was statistically significant decrease in the mean of each of (TR pressure gradient, Pulmonary artery Pressure, LT atrial/aortic ratio, and LVESV) in post-echocardiographic analysis when compared to pre analysis, while there was no statistically significant difference in the mean of EF and FS in post-echocardiographic analysis when compared to pre-analysis. Table 4 shows statistically significant decrease in LV output in post-treatment evaluation when compared to pre-treatment evaluation. There was statistically no significant change in RV output and SVC flow and diameter in post-treatment evaluation when compared to pre-treatment evaluation.

Table (1): Basic characteristics among studied newborns with PDA (n=43)

Characteristic	Category	Study group (n=43)	
		No.	%
Gender	**Female**	20	46.5
	Male	23	53.5
Gestational age (weeks)	**Preterm =37** **Term=6**		
Mean ± SD Range	33.58±3.91 (26-41)		
Birth weight (gm) Mean ± SD Range	1936.05±781.28 (800-3300)		
Postnatal age at first scan (days) Mean ± SD Median (IQR)	2.44±0.80 (1-4)		
Number of scans per infant Mean ± SD Range	1.91±0.29 (1-2)		

Table (2): Clinical criteria and some therapeutic parameters among studied newborns with PDA (n=43)

Characteristic	Category	Study group (n=43)	
		No.	%
Cyanosis	Present	1	2.3
Tachycardia	Yes	18	41.9
Murmur	Present	23	53.5
Increased O2 requirement	Yes	26	60.5
Prolonged capillary refill time (seconds)	Yes	14	32.6
Urine output(ml/kg)	Normal	31	72.1
	Low	12	27.9
Lactic acidosis	Present	12	27.9
Mechanical ventilation	Yes	16	37.2
Receiving anti-failure	Yes	13	30.2
Receiving ibuprofen or paracetamol	Yes	33	76.7

Table (3): Comparing pre and post-echocardiographic evaluation among studied newborns with PDA

Characteristic	Pre- evaluation Study group (n=43)	Post-evaluation Study group (n=38)	Test (t)	P value
TR pressure gradient mm Hg Mean ± SD Range	15.44±2.11 (12-19)	14.74±1.16 (12-17)	3.481	**0.001***
Pulmonaryartery pressuremm Hg Mean ± SD Range	25.44±2.11 (22-29)	24.74±1.16 (22-27)	3.481	**0.001***
TAPSE/mm Mean ± SD Range	10.36±0.37 (9.6-11)	10.28±0.26 (9.8-10.9)	1.706	0.096
LT atrial/aortic ratio Mean ± SD Range	1.31±0.26 (1-1.80)	1.15±0.13 (1-1.5)	4.332	**<0.001***
LVEDV (mm) Mean ± SD Range	14.28±1.10 (11.6-15.9)	14.21±0.71 (13-15.2)	1.240	0.223
LVESV mm Mean ± SD Range	9.53±0.81 (7.5-11.1)	9.40±0.55 (8.6-10.7)	4.676	**<0.001***
EF% Mean ± SD Range	61.32±3.6 (54-72)	61.94±2.5 (54-70)	-1.55	0.129
FS% Mean ± SD Range	31.24±2.17 (27-38)	32.62±1.38 (28-36)	-1.217	0.231

tricuspid valve regurgitation (TR), Tricuspid annular plane systolic excursion (TAPSE), LV end-diastolic (LVED), LV end-systolic (LVES) ejection fraction (EF), Fractional shortening (FS), Tricuspid regurgitation pressure gradient (TRPG)

^ p-value for paired samples T-test,

*** Statistically highly significant*

Table (4): Comparing pre- and post-echocardiographic evaluation regarding SVC flow, SVC diameter and ventricular output among studied newborns with PDA

Characteristic	Pre-evaluation Study group (n=43)	Post-evaluation Study group (n=38)	Test (t)	P value
SVC flow ml/kg/min Mean ± SD Range	103.03±9.13 (88-132)	104.02±12.58 (72-124)	0.797	0.430
SVC diameter (3.8-4.4 mm) Mean ± SD Range	4.03±0.24 (3.7-4.7)	4.05±0.16 (3.8-4.4)	1.1	0.435

Characteristic	Pre-evaluation Study group (n=43)	Post-evaluation Study group (n=38)	Test (t)	P value
LV output ml/kg/min Mean ± SD Range	238.37±31.07 (170.6-289)	224.29±28.29 (180-274)	2.701	**0.010***
RV output ml/kg/min Mean ± SD Range	257.92±36.02 (184-325.9)	281.82±27.97 (195-309)	1.38	0.176

^p-value for paired samples T-test,
** Statistically significant*

DISCUSSION

TNE strengthens the evaluation of conventional clinical parameters in an effort to deliver individualized care depending on the present pathophysiology. It must be used in conjunction with clinical evaluation rather than in place of a cardiologist's evaluation because their goals are distinct and complementary **[12]**.

When comparing pre- and post-treatment echocardiographic analysis, the mean TR pressure gradient, Pulmonary artery Pressure, LT atrial/aortic ratio, LVESV and LV output decreased in a statistically significant manner while TAPSE, LVEDV, EF and FS, SVC diameter and flow and RV output mean values did not differ statistically significantly after therapy echocardiographic analysis when compared to pre-treatment analysis.

The difference in LA/AO ratio when comparing pre- and post-treatment echocardiographic analysis may be attributed to the decrease in size or closure of PDA spontaneously or after medical treatment **[13]**.

In a study done by **Evans** and**Iyer [14]** to reevaluate the LA/AO ratio as a marker of PDA, they found that LA/AO ratio above 1.5 reflect wide PDA, while LA/AO ratio below 1.5 reflect hemodynamically insignificant PDA.

The pathophysiologic features of a PDA relay on the magnitude of the left to right shunt and the cardiac and pulmonary responses to this shunt. The immature fetal ventricles are less distensible than at term. As a result, LV distension, secondary to the left to right PDA shunt, produces higher LV end diastolic pressures at smaller ventricular volumes in preterm infants than at term**[15]**.

The increase in LV pressure increases pulmonary venous pressure, which lead to pulmonary congestion. Because the pulmonary vascular bed in the preterm newborn is already fully recruited, the increase in pulmonary blood flow from the left to right PDA shunt produces an increase in pulmonary arterial pressure [**16]**.

Alfaleh et al. [16]reported that early medical treatment is effective in closing the PDA and decreasing the risk of hemorrhagic pulmonary edema, hypotension and need for early inotropic and ventilator support.

Surgical ligation is indicated when medical therapy is unsuccessful or is contraindicated. As the post-operative period is often complicated by a post ligation cardiac syndrome (PLCS), which is characterized by hemodynamic instability and respiratory failure, so TNE facilitates early detection of infants at greatest risk for subsequent cardiorespiratory deterioration [**17**].

Our study revealed statistically significant decrease in LV output in post-treatment evaluation when compared to pre-treatment evaluation. While there was no statistically significant change in RV output.

In accordance with our results, **Jain et al. [18]** did an observational investigation of 62 preterm newborns for a prospective physiologic study who previously had serial targeted neonatal echocardiography before and after PDA ligation.

Knight [19] in his study supported this finding and demonstrated that both left, and right ventricular outputs can be low in the first 36 h of life in sick preterm infants. They tend to increase over the first 4 days. In addition, LVO increases further because of left to right ductal shunting over this time. As pulmonary vascular resistance falls with increasing age, the left to right shunt and LVO increase so that babies with a hemodynamically significant PDA have an abnormally high LVO.

Our study also detected no statistically significant change in SVC diameter and SVC flow in post-treatment evaluations when compared to pre-treatment evaluations.

Consistent with our results, **Bischoff et al. [20]** performed a retrospective cohort study of preterm infants (< 30 weeks, < 21 days of life) who underwent comprehensive TNE. Patients were categorized as follows: (i) Hemodynamically significant left-to-right shunt; (ii): Bidirectional shunt; (iii) No PDA or insignificant shunt. Their results revealed that SVC dimensions and flow measurements were not different between the groups.

Contrary to us**, El-Khuffash et al. [21]** found statistically significant differences in all echocardiographic parameters in a retrospective study of 199 neonates who undergone TNE in a single center over a period of 4 years. TNE was associated with a change in clinical management in 41% of cases. This variation in results may be attributed to different sample size included in the two studies and different neonatal age at which echocardiography was done.

In a retrospective review by **Harabor**and **Soraisham[22]** of 303 consecutive TNE examinations performed on 129 neonates in a single NICU. Approximately half of TNE changed clinical care within the first week of life and 22% after the first week of life with presence of statistically significant differences in all echocardiographic parameters.

Regarding **O'Rourke et al**. **[23]** the prospective evaluation of clinical practice changed from introducing serial TNE in management of PDA in 192 infants compared with historical controls. Post clinical changes were associated with earlier identification and mangment of PDA as well as decrease in the incidence of severe intraventricular hemorrhage and ventilator days.

The explanation of TNE importance in PDA cases came from the fact that Persistent ductal patency, while necessary for the healthy fetal circulation, can have serious negative consequences in premature or sick-term newborns **[24]**.

Another explanation of TNE importance in PDA cases was cleared by **Szymankiewicz et al. [25]** as they demonstrated that the clinical impact is dependent on the magnitude of the shunt, comorbid conditions and the ability of the neonate to initiate compensatory mechanisms.

Reduced systemic perfusion is a result of an insufficient stroke volume response coupled with the "steal" of blood from the systemic circulation. Significant diastolic shunting with retrograde diastolic abdominal aortic flow is caused by a big ductus, which affects intestinal and renal perfusion. Increased LV diastolic pressures already have an impact on coronary perfusion; low diastolic aortic pressure can exacerbate this **[26]**.

Furthermore, **Lee et al. [27]** aimed at assessing a neonatologist's accuracy in diagnosing PDA using a portable ultrasound machine after limited training in 24 infants. Specificity and sensitivity, compared with scheduled echocardiograms interpreted by a pediatric cardiologist, were 69% and 88%, respectively. Statistically significant differences in all echocardiographic parameters were detected.

In the same line with us, **Mcnamara**and **Sehgal [28]** found that it is possible to evaluate the hemodynamic importance of PDA by integrating various echocardiographic parameters when comparing pre- and post-treatment evaluations. These parameters include the following: Ductal size, Transductal flow, Left-heart size, Mitral inflow and Ductal "steal".

In the same direction, **Mertens et al. [29]** cleared that Acute alterations in pre-load and after-load produce hemodynamic instability in certain preterm newborns shortly after ductus ligation. Determining the underlying mechanism can be aided by TNE.

El-Khuffash et al. [21] determined variations in clinical judgments over time related to TNE consultations. Of these, 20% of cases included avoiding a planned intervention and 40% involved a change in management. A PDA was the most prevalent ailment linked to a change in management. One of the modifications was to stop providing medical care when it was determined that the shunt capacity was low.

Regarding the assessment of PDA, the transductal pulse Doppler and ductal diameter were the most frequent measurements to determine the hemodynamic significance of PDA. Current guidelines by the American society of echocardiography (ASE) recommend a comprehensive protocol which includes evaluation of the magnitude of the transductal shunt by characterizing its effect on myocardial performance, systemic and/or end organ perfusion (e.g., abdominal aortic flow) and cardiac volume overload (e.g., LVO and LA/AO ratio) [**29**].

CONCLUSION

We concluded that targeted neonatal echocardiography's (TNE) use and role in the NICU are evolving, and it can significantly aid in the identification and better management of PDA in neonates.

Conflict of interests: -The authors declare that they have no conflict of interests

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