Comparing the tissue Doppler-derived left ventricular myocardial performance index before and after recovery from respiratory distress in neonates: A prospective observational study

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ABSTRACT

Background and Objective : **Respiratory distress is the most common cause requiring neonatal intensive care unit admission. As respiratory and cardiac functions are closely interrelated, some cardiac dysfunction is expected in respiratory distress. The myocardial performance index (MPI) is an index to assess global myocardial function, easily measurable by bedside echocardiography and reliable. Here, we conducted this study to determine the change in cardiac function in neonates with respiratory distress before initiating respiratory support and after weaning from the support.**

Methodology : **The study was carried out in 92 neonates with a gestational age of more than 32 weeks who required invasive or noninvasive respiratory support. The tissue Doppler left ventricular MPI (LV MPI) was calculated before the initiation of respiratory support and after weaning from respiratory support. The data were analyzed using a paired *t*-test and a Wilcoxon signed-rank test.**

Results : **This study comprised 92 neonates with a median (interquartile range) LV MPI value of 0.56 (0.10) before initiation of respiratory support and 0.47 (0.04) after weaning from respiratory support with $P < 0.001$. The isovolumetric contraction time, isovolumetric relaxation time, and ejection time increased after weaning from respiratory support (all $P < 0.0001$). The severity of respiratory distress determined by invasive mode of ventilation and longer duration of respiratory support caused higher initial LV MPI before initiation of respiratory support compared with recovery and $P < 0.001$, suggesting subclinical ventricular dysfunction with respiratory distress in neonates.**

Conclusion : **LV MPI was higher in neonates with respiratory distress and normalized after weaning from respiratory support, which indicates that neonates requiring respiratory support may have subclinical ventricular dysfunction and should be followed up carefully.**

Keywords : Left ventricular myocardial performance index, neonate, respiratory distress

INTRODUCTION

The transitional neonatal period after birth encompasses

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rapidly evolving respiratory and circulatory changes. Prematurity adds to the autonomic and neurobehavioral dysregulation to maintain hemodynamics. The nonspecific nature of routine clinical symptoms and signs, such as hypoxemia, respiratory distress, metabolic or respiratory acidosis, and the limited diagnostic potential of chest radiographs, makes it difficult for clinicians to differentiate primary lung from cardiovascular disease.[1] Considering the biological nature of cardiac and respiratory physiology as one unit, a potential relationship between respiratory pathology and its hemodynamic effects is often overlooked, and literature supporting the same is scarce. Impairment of myocardial systolic and diastolic function accompanies intrauterine and neonatal infections, birth asphyxia, cardiac anomalies, and volume overload status. It affects preterm neonates with bronchopulmonary dysplasia, hypoxia, and intrauterine growth retardation due to prolonged respiratory pathology.[2] Apart from clinical assessment, for determining systolic and diastolic cardiac function, varying echocardiographic parameters are used such as ejection fraction, E/A ratio, E/e' ratio, pulmonary vein diastolic Doppler velocity, and tricuspid annular plane systolic excursion. In recent days, targeted neonatal echocardiography (TnECHO) has been widely used in neonatal intensive care units (NICUs). The global myocardial function has been precisely measured using the myocardial performance index (MPI) or Tei index. There are no published studies in neonates assessing the cardiac function with respiratory distress before initiating respiratory support and the change with weaning from respiratory support and complete recovery. In this study, we evaluated the hemodynamic impact of respiratory distress in neonates using left ventricular MPI (LV MPI) as a marker for global cardiac function and its changes with recovery.

METHODOLOGY

This prospective observational study was conducted in a tertiary care NICU from October 2022 to April 2024 in neonates with respiratory distress using TnECHO. The institutional ethics committee approved the study. Written informed consent was taken from the parents/guardians. All neonates with gestational age (GA) more than $32^{0/7}$ weeks admitted in the NICU requiring respiratory support (invasive/noninvasive) for various causes were enrolled in the study. Neonates with major congenital cardiac anomalies, including hemodynamically significant patent ductus arteriosus (PDA) and syndromic features, were excluded from the study.

The baseline data such as perinatal risk factors, Apgar score, mode of delivery, GA, birth weight, vital parameters, capillary blood gas values before initiation of respiratory support, clinical history, day of life at the initiation of respiratory support, and physical findings such as respiratory distress score (Downes score for term neonates and Silverman-Anderson score for preterm neonates), type, and duration of respiratory support requirement were noted in a predefined pro forma. The required mode of respiratory support, invasive or noninvasive ventilation, was started based on clinical parameters, radiological assessment, and diagnosis. Tissue Doppler imaging to measure LV MPI was performed before initiating sustained respiratory support and after recovery from respiratory support. "After recovery" is defined as weaning the neonate from respiratory support to room air, normalizing the respiratory distress score, and having no tachypnea.

A transthoracic echocardiography examination was performed by a single trained neonatologist with a Philips CX-50 Ultrasound machine using a footprint probe (S12-4) with a 4–12-Hertz frequency. After capturing the two-dimensional image in a four-chamber apical view, tissue Doppler was measured at the junction of the interventricular septum and medial aspect of the mitral valve and derived isovolumetric contraction time (IVCT), isovolumetric relaxation time (IVRT), and ejection time (ET) and calculated MPI. MPI is defined as the sum of IVCT and IVRT divided by ET [Figure 1]. Each time, the MPI was calculated three times, and the mean of the three values was taken for the final calculation to minimize the intraobserver variation. The results were validated by a senior neonatal consultant trained in functional echocardiography. Interobserver correlation coefficient (ICC) for MPI before initiation of support values was found to be 0.983 (95% confidence interval [95% CI] [0.974, 0.989]) and after values was 0.959 (95% CI [0.939, 0.973]). A two-tailed hypothesis test was performed to assess the statistical significance of the ICC, and the *P* value was < 0.0001. Echocardiography was performed in a thermoneutral environment, with

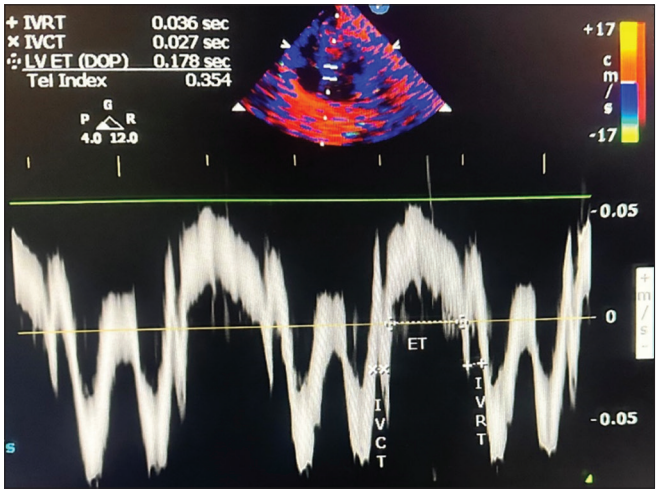

Figure 1: Tissue Doppler imaging demonstrating components of myocardial performance index. IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, LV ET: Left ventricular ejection time, ET: Ejection time, DOP: Doppler

Table 1: Demographic Profile of neonates (total number *n*=92)

Variable	Number (%)	
SEX		
Male	55 (59.7%)	
Female	37 (40.2%)	
Mode of Delivery	44 (47.8%)	
NVD	48 (52.1%)	
LSCS		
BW (kilograms) mean±SD	2.635±0.695	
Inotropes		
Yes	8 (8.7%)	
No	84 (91.3%)	
		MAP (mmhg) Mean±SD
Gestational age in weeks		
32-33$^{6/7}$	19 (20.6%)	38±6
34$^{0/7}$-36$^{6/7}$	38 (41.3%)	47±4
≥37$^{0/7}$	35 (38%)	48±6
Type of Support		
CPAP	48 (52.1%)	
HFNC	24 (26.0%)	
NIPPV	4 (4.3%)	
SIMV	16 (17.3%)	
Day of Life at initiation of Respiratory support		
<3	71 (77.2%)	
3-14	7 (7.6%)	
>14	14 (15.2%)	
Duration of respiratory support		
<3 days	48 (52.2%)	
3-7 days	28 (30.4%)	
7-14 days	13 (14.1%)	
>14 days	3 (3.3%)	
Heart rate in BPM mean±SD	148±20	
Disease		
Cardiac	3 (3.2%)	
Central nervous ystem	3 (3.2%)	
Miscellaneous	5 (5.4%)	
Respiratory	76 (82.6%)	
Sepsis	5 (5.4%)	

NVD: normal vaginal delivery, LSCS: lower segment caesarian section, CPAP: continuous positive airway pressure, HFNC: high flow nasal cannula SIMV: synchronized intermittent mandatory ventilation, MAP: mean arterial pressure NIPPV: noninvasive intermittent positive pressure ventilation

Table 2: Median values comparing before initiation and after stopping of respiratory support

Variable	Before the initiation of respiratory support, median (IQR)	After weaning from respiratory support, median (IQR)	*P*
IVCT	0.052 (0.012)	0.044 (0.004)	<0.0001
IVRT	0.051 (0.010)	0.047 (0.006)	<0.0001
ET	0.188 (0.012)	0.192 (0.011)	<0.0001
MPI	0.56 (0.10)	0.47 (0.05)	<0.0001

IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, ET: Ejection time, MPI: Myocardial performance index, IQR: Interquartile range

the neonate lying quiet without sedation and taking all aseptic precautions. Repeat measurement of MPI through the tissue Doppler method was done within 24 h of recovery.

Statistical analysis

Based on the published literature for LV MPI in neonates as per various studies[3-5] and the Feigenbaum textbook of echocardiography,[6] the normal range of MPI was taken as 0.39 ± 0.05, and values more than 0.45 were considered to be abnormal. Based on the study by Bokiniec *et al.*, the LV MPI value before and after PDA closure was 0.37 ± 0.1 and 0.35 ± 0.09.[7] To estimate a minimum difference of 0.02 between before and after respiratory support, the sample size calculated was 81 with 90% power and 5% level of significance. Collected data were entered into a Microsoft Excel worksheet and analyzed using R software (version 4.3.2) Foundation of statistical computing, Vienna, Austria. A prospective pre–post study design was used in the current study. The Shapiro–Wilk test was used to test whether the continuous variables in the data followed a normal distribution. All the normally distributed (continuous) variables were described with mean and standard deviation. The continuous variables that did not follow normal distribution were expressed with the median and interquartile range (IQR). The paired *t*-test was used when normality assumptions were satisfied; otherwise, the Wilcoxon signed-rank test was used. The categorical variables were summarized using frequencies and percentages. The level of significance for all the statistical tests was set as 5%.

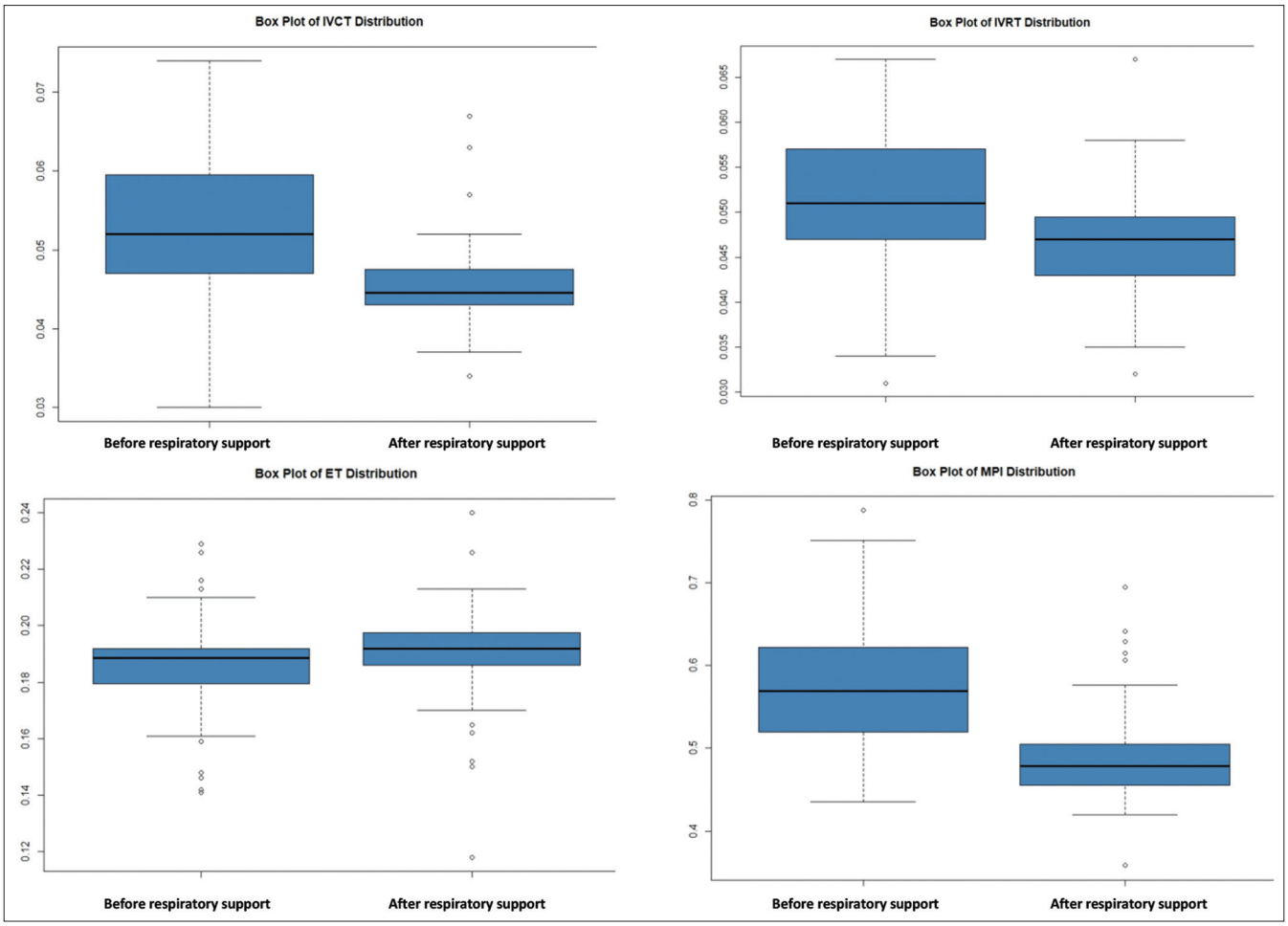

Figure 2: Boxplot showing isovolumetric contraction time, isovolumetric relaxation time, ejection time, and myocardial performance index before initiation and after weaning from respiratory support. IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, ET: Ejection time, MPI: Myocardial performance index

RESULTS

The baseline demographic parameters are given in Table 1. Our study cohort comprised 92 neonates, where 60% were male and 40% were female, with a mean birth weight of 2635 ± 695 g. Forty percent of cases were late preterm, 38% were term, and 20.6% were moderate preterm. The most prevalent diagnosis was transient tachypnea of newborns (30 cases). Fifty-two percent of neonates required continuous positive airway pressure support with a duration of less than 3 days (48%). The median age at initiation of respiratory support was 1 day (IQR: 2 days). Most cases were of primary respiratory pathology requiring respiratory support (82.6%). There were two cases of primary persistent hypertension of newborns (PPHN), one multifocal atrial tachycardia with cardiogenic shock, and three cases of neonatal seizure requiring respiratory support. Among all the instances, only six babies required inotropic support.

As described [Table 2 and Figure 2], it was observed that the LV MPI was higher before initiating respiratory support with a median (IQR) value of 0.56 (0.10). The LV MPI decreased to 0.47 (0.04) after weaning from respiratory support, and the difference was statistically significant ($P < 0.0001$). There was a decrease in IVCT from 0.520 (0.01) to 0.044 (0.004) and IVRT from 0.051 (0.01) to 0.047 (0.006) before initiation of respiratory support when compared to after weaning from support, respectively. ET increased after weaning from respiratory support, rising from 0.188 (0.012) to 0.192 (0.011). The variations in IVCT, IVRT, and ET were statistically significant.

This study revealed statistically significant increased LV MPI with respiratory distress, independent of the mode of delivery, gender, GA, and weight category [Tables 3-5]. Furthermore, when individual parameters were taken into consideration, IVCT and IVRT were high, while ET was lower with respiratory distress across all GAs. The IVCT and IVRT decreased with recovery in all the neonates, while the increase in ET was significant only in late preterm and term neonates. Additionally, statistically significant decreases in IVCT and IVRT were observed in infants with low and normal birth weights.

Table 3: Isovolumetric contraction time, isovolumetric relaxation time values before initiation and after weaning from respiratory support in median (interquartile range)

Variables	Results comparing IVCT before initiation and after weaning from respiratory support			Results comparing IVRT before initiation and after weaning from respiratory support		
	IVCT - before the initiation of respiratory support	IVCT - after weaning from respiratory support	*P*	IVRT - before initiation of respiratory support	IVRT - after weaning from respiratory support	*P*
Mode of ventilation						
CPAP	0.050 (0.009)	0.044 (0.004)	<0.0001*	0.049 (0.007)	0.046 (0.007)	0.001*
HFNC	0.051 (0.004)	0.045 (0.003)	0.0003*	0.051 (0.008)	0.046 (0.005)	0.0001*
SIMV	0.064 (0.004)	0.044 (0.004)	0.0005*	0.057 (0.011)	0.047 (0.008)	0.001*
NIPPV	0.058 (0.004)	0.047 (0.003)	0.09	0.058 (0.007)	0.051 (0.003)	0.375
Inotropic support						
Yes	0.062 (0.005)	0.043 (0.002)	0.01*	0.065 (0.007)	0.047 (0.006)	0.01*
No	0.051 (0.010)	0.045 (0.005)	<0.0001*	0.051 (0.010)	0.047 (0.006)	<0.0001*
Duration of support (days)						
<3	0.049 (0.009)	0.044 (0.004)	<0.0001*	0.051 (0.009)	0.046 (0.006)	<0.0001*
3–7	0.054 (0.010)	0.046 (0.004)	<0.0001*	0.052 (0.012)	0.047 (0.008)	0.004*
July-14	0.061 (0.013)	0.047 (0.004)	0.004*	0.056 (0.016)	0.047 (0.005)	0.02*
>14	0.054 (0.006)	0.043 (0.045)	0.25	0.051 (0.006)	0.052 (0.003)	0.5

*P<0.05 is considered significant, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, CPAP: Continuous positive airway pressure, HFNC: High flow nasal cannula, SIMV: Synchronized intermittent mandatory ventilation, NIPPV: Noninvasive intermittent positive pressure ventilation

Table 4: Ejection time and myocardial performance index values before initiation and after weaning from respiratory support in median (interquartile range)

Variables	Results comparing ET before initiation and after weaning from respiratory support			Results comparing MPI before initiation and after weaning from respiratory support		
	ET - before initiation of respiratory support	ET - after weaning from respiratory support	*P* Value	MPI - before initiation of respiratory support	MPI - after weaning from respiratory support	*P* Value
Mode of ventilation						
CPAP	0.186 (0.014)	0.192 (0.011)	0.0009*	0.53 (0.08)	0.47 (0.06)	<0.0001*
HFNC	0.189 (0.010)	0.192 (0.009)	0.02*	0.55 (0.05)	0.48 (0.03)	<0.0001*
SIMV	0.190 (0.013)	0.190 (0.010)	0.33	0.63 (0.03)	0.48 (0.05)	0.0003*
NIPPV	0.190 (0.009)	0.203 (0.012)	0.18	0.61 (0.01)	0.50 (0.02)	0.125
Inotropic support						
Yes	0.190 (0.015)	0.193 (0.012)	1	0.64 (0.05)	0.47 (0.03)	0.007*
No	0.188 (0.013)	0.192 (0.012)	<0.0001*	0.56 (0.09)	0.47 (0.04)	<0.0001*
Duration of support (days)						
<3	0.186 (0.012)	0.191 (0.015)	0.001*	0.54 (0.07)	0.47 (0.04)	<0.0001*
3–7	0.188 (0.012)	0.192 (0.007)	0.004*	0.58 (0.07)	0.47 (0.04)	<0.0001*
July-14	0.19 (0.013)	0.192 (0.004)	0.5	0.60 (0.07)	0.48 (0.04)	0.0002*
>14	0.192 (0.015)	0.202 (0.012)	0.5	0.59 (0.08)	0.48 (0.06)	0.25

*P<0.05 is considered significant, ET: Ejection time, MPI: Myocardial performance index ,CPAP: continuous positive airway pressure, HFNC: high flow nasal cannula SIMV: synchronized intermittent mandatory ventilation , NIPPV: noninvasive intermittent positive pressure ventilation

ET increased significantly only in infants with birth weight >2.5 kg before initiation and after weaning from respiratory support.

In cases of primary respiratory etiology, LV MPI reduction postweaning from respiratory support was significant ($P < 0.0001$), along with significant alterations in IVCT, IVRT, and ET in similar trends with overall results. Conversely, although there was a decrease in LV MPI values in other disease categories, the reduction was not statistically significant. Statistically significant changes in MPI and respective parameters were observed across all ventilation modes except for noninvasive positive pressure ventilation (NIPPV) ($P < 0.0001$). The increase in ET with recovery was only significant in noninvasive modes. Notably, the NIPPV mode exhibited an overall LV MPI decrease, albeit not statistically significant ($P = 0.125$). Statistically significant changes in LV MPI were evident with respiratory support durations under 14 days ($P < 0.0001$). Conversely, no significant MPI changes were observed for support durations exceeding 14 days ($P > 0.25$). Similar trends were noted for IVCT and IVRT, with significant changes observed with shorter durations of support (<14 days). The increase in ET was significant when the duration of support was <7 days.

DISCUSSION

MPI is a simple Doppler-derived index that can be calculated

Table 5: Change in myocardial performance index before initiation and after weaning from respiratory support in median (interquartile range)

Variables	Results comparing MPI before initiation and after weaning from respiratory support		
	MPI - before initiation of respiratory support	MPI - after weaning from respiratory support	*P*
Sex			
Male	0.56 (0.10)	0.47 (0.04)	<0.0001*
Female	0.57 (0.07)	0.48 (0.06)	<0.0001*
GA (weeks)			
32–34	0.59 (0.09)	0.49 (0.07)	<0.0001*
34–37	0.56 (0.10)	0.47 (0.04)	<0.0001*
>37	0.56 (0.08)	0.48 (0.04)	<0.0001*
Mode of delivery			
NVD	0.56 (0.11)	0.47 (0.04)	<0.0001*
LSCS	0.57 (0.08)	0.47 (0.05)	<0.0001*
BW (kg)			
≤1.5	0.62 (0.04)	0.51 (0.07)	0.03*
1.5–2.5	0.57 (0.07)	0.47 (0.04)	<0.0001*
>2.5	0.58 (0.09)	0.48 (0.04)	0.0001*
Birth centile in percentile			
<10	0.58 (0.06)	0.49 (0.06)	<0.0001*
11–90	0.55 (0.09)	0.47 (0.05)	<0.0001*
>90	0.58 (0.09)	0.47 (0.05)	0.007*

*P<0.05 is considered significant, MPI: Myocardial performance index, BW: Birth weight, GA: Gestational age, NVD: Normal vaginal delivery, LSCS: Lower segment caesarian section

by neonatologists performing echocardiography. The elevated pulmonary pressure in the immediate neonatal period causes high right ventricular (RV) MPI values, and there is a sudden dramatic drop in MPI during the initial 12–24 h and a further drop in the next 36 h, stabilizing by 72 h of life. However, the LV MPI does not show much variation with age as it mainly depends on systemic circulation.[7-9] As reported by Tei *et al*., these LV MPI normal values can be applied to the entire spectrum of the pediatric population with no clinically significant effects on age, heart rate, and body surface area. Although there were some slight statistical differences between LV MPI results because of the effect of body surface area, this difference of approximately 0.02 is so small that it seems negligible in the clinical setting.[10] The LV MPI values do not change significantly with physiological PDA closure, as shown in studies by Bockinec *et al*.[7] Hence, we have taken LV MPI to determine the change associated with respiratory distress.

Respiratory conditions, including respiratory distress syndrome (RDS) and meconium aspiration syndrome, cause pulmonary arterial hypertension and right to left shunting through ductus arteriosus, leading to ventricular dysfunction. The resultant acidosis causes myocardial dysfunction and increased MPI. The hyperinflated lungs directly compress the heart, reduce cardiac compliance, and lessen ventricular filling and end-diastolic volumes, causing the IVCT and IVRT to increase and ET to decrease, as reported in our study. As reported by various studies, the normal LV MPI was 0.39 ± 0.07. In our study, the LV MPI decreased to a normal value after weaning from respiratory support. Similar results were noted in a study done by Khattab where the MPI was 0.49 ± 0.02, 0.47 ± 0.014, and 0.35 ± 0.02 in neonates with respiratory distress in perinatal asphyxia and normal neonates, respectively, and the difference was statistically significant.[11]

Positive pressure ventilation (PPV) further complicates the matter by causing a reduction in RV afterload, decreased left ventricular preload, stroke volume, and cardiac output in compliant lungs. There is decreased ventricular filling and end-diastolic volumes, thus increasing the IVCT and IVRT.[1,12,13] However, in surfactant deficiency or lung consolidation where the lung is poorly compliant, the effect on venous return is minimal with PPV. Understanding these possible adverse effects of respiratory support on pulmonary and systemic hemodynamics is crucial for devising the most appropriate ventilatory and weaning strategies. Our study focused only on the entry and exit point in neonates before and after respiratory support, where the respiratory score was primarily used, and MPI was measured to determine whether any changes could be appreciated.

In cases with cardiac etiology, the median MPI value decreased after weaning from respiratory support (0.60–0.50) but remained above the normal value, which can be attributed to PPHN. Various earlier studies show higher RV MPI and correlation with PPHN. Tei *et al*. reported an RV MPI of 0.93 ± 0.34 in PPHN cases versus 0.28 ± 0.04 in normal control, $P < 0.001$.[14] A study done by Dai *et al*. in 75 neonates with PPHN showed a significant increase in RV function and index compared to the control group.[15] In cases of sepsis, we did not find a significant change in the MPI value, which could be because the number of cases was much less, but a study done by Abdel-Hady *et al*.[16] suggested that the MPI value was significantly higher in septic neonates compared to nonseptic neonates.

Neonates requiring invasive ventilation and longer duration of respiratory support (>7 days) had a higher MPI value as compared to neonates requiring noninvasive ventilation and shorter duration (<7 days) of ventilation, suggesting that the initial cardiac dysfunction was proportionate to the respiratory compromise. In preterm neonates, the myocardium has more water and less contractile mass, leading to diminished compliance and less force generated per sarcomere compared to term neonates; this may be the cause of the slightly higher MPI observed in moderate preterm infants. Studies done by Bokiniec *et al.* have reported similar LV MPI values in preterm neonates at 40 weeks of postconceptional age (0.37) and in term neonates after PDA closure (0.39) and on the 28th day of life (0.37).[7] Similarly, in a study by Hirose *et al.*,[6] MPI was similar in preterm neonates at 40 weeks of postconceptional age and term neonates measured on the 28th day of life (0.44 vs. 0.43, respectively), suggesting that the MPI values are independent of chronological age.

However, this study has a few limitations. We have not measured other echocardiographic parameters such as ejection fraction, tricuspid and mitral annular plane systolic excursion, or inferior vena cava status in cases of hypotension. We understand that MPI is load-dependent but did not attempt to compare heart rate and blood pressure with MPI directly. Changes in MPI with various modes of ventilator support are a point to be looked into in future research.

MPI can easily be obtained as a noninvasive technique by neonatologists. Its diagnostic value as part of a functional echocardiogram is significant, offering insights into the global myocardial function of neonates and enabling critical monitoring of their health status. Future research in determining MPI cutoff values as single point indicators for further intervention, such as initiation or titration of inotropes or inodilators in neonatal shock or PPHN, adjunct to RDS clinical scoring system or before extubation to curtail the extubation failure rates are needed and will add utmost value to functional echocardiography.

CONCLUSIONS

Our study underscores the utility of the MPI as a valuable tool in assessing global cardiac function in neonates with respiratory distress. We observed higher LV MPI values in neonates requiring respiratory support, indicative of potential subclinical ventricular dysfunction. Importantly, these LV MPI values normalized following weaning from respiratory support, suggesting the resolution of cardiac compromise. As a simple Doppler-derived index, the MPI provides a comprehensive evaluation of both systolic and diastolic function and can be adjunctive to clinical severity score and further management.

What this study adds:

- The myocardial performance index (MPI) can be used as an adjunct to the respiratory distress score in neonates needing respiratory support as it was shown in our study that the MPI was higher in neonates with respiratory distress before initiating the support and normalized at recovery.

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Conflicts of interest

There are no conflicts of interest.

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