Research Progress of Noninvasive Cardiac Output Monitor (NICO™) and Hemodynamic Monitor in Neonates

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Abstract

Objective: Hemodynamic monitoring plays a crucial way in guiding the clinical decision-making process for the management of critically ill neonates. Noninvasive hemodynamic monitoring is characterized by continuous, convenient, and accurate assessment, presenting a viable option for implementation in neonatal intensive care units (NICU). This review article summarizes the research advancements made in noninvasive hemodynamic monitoring and electronic cardiometry (EC) applications in neonates, providing valuable reference resource for studies in the field of hemodynamic monitoring. Mechanism: The clinical significance of hemodynamic monitoring in neonates is first introduced and followed by a comprehensive description of both invasive and noninvasive techniques employed in hemodynamic monitoring. Furthermore, the research progress of EC in neonates is discussed, focusing particularly on its feasibility and accuracy. Finally, the application and influencing factors of EC in diverse diseases, encompassing neonatal conditions, are presented.

Findings in Brief: Due to the risks associated with invasive cardiac output monitoring, noninvasive or minimally invasive alternative techniques are needed for hemodynamic monitoring. In recent years, noninvasive and minimally invasive techniques, such as ultrasound cardiac output monitor (USCOM) and impedance cardiography have been utilized. EC, as an impedance-based monitoring, facilitates noninvasive and real-time assessment of hemodynamic parameters. The integration of EC enables real-time and continuous monitoring of dynamic changes in cardiac and vascular functions in patients, thereby assisting in clinical evaluation and guiding the clinical decision-making. Conclusion: EC is a noninvasive, highly sensitive, and accurate monitoring technique that holds important guiding significance in clinical practice.

Keywords: noninvasive hemodynamics; electrical cardiography; NICO™

1. Clinical Significance of Hemodynamic Monitoring

During the first several days of neonatal life, hemodynamic monitoring is a great challenge due to the existence of continuous shunt and complex physiological changes, as the transition from fetal circulation to adult circulation. Currently, circulatory monitoring indicators in most neonatal wards are limited to heart rate (HR) and blood pressure assessment. Arterial blood pressure is still the most commonly used indicator for evaluating the neonatal circulation status. Blood pressure is determined by a complex interaction of circulating blood volume, venous return (preload), myocardial contractility, systemic vascular resistance (postload), and pulmonary vascular resistance (in the case of patent ductus arteriosus (PDA)). However, as reported by Groves et al. [1], total perfusion of neonates generally shows only a weak positive correlation with blood pressure, but arterial blood pressure is largely affected by systemic vascular resistance. Newborns with reduced systemic perfusion tend to have normal or elevated blood pressure in the first few hours after birth, suggesting that high systemic vascular resistance may lead to reduced blood flow.

The commonly applied indexes for evaluating systemic hemodynamics generally include blood pressure, HR, capillary filling time, urine volume, and blood lactate acid. However, studies have shown that blood pressure, capillary refill time and urine volume are not well correlated with systemic blood flow [2,3]. HR is innervated by sympathetic nerves and vagus nerves, and is also susceptible to drugs, pain, body temperature and other factors. As such, it can neither accurately reflect hemodynamic changes, nor evaluate the patient’s systemic blood flow and tissue perfusion. Yuan et al. [4] have pointed out that the severity and prognosis of shock can be assessed by dynamic monitoring of arterial blood lactic acid level. Blood lactic acid level increases with the severity of neonatal shock. Seri [5] notes that the management of critically ill premature infants with hypotension remains challenging, requiring a better understanding of the pathophysiology of neonatal shock, and improving our ability to assess cardiac output, organ blood flow, and tissue perfusion at the bedside.

The neonatal intensive care unit (NICU) primarily treats premature infants. Preterm infants may present with conditions such as neonatal respiratory distress syndrome, absence of secondary pulmonary artery catheter, bron-
chopulmonary hypoplasia, congenital heart disease, neonatal meconium inhaled syndrome, neonatal infectious diseases, neonatal low blood volume shock, and septic shock [6,7]. In addition, premature infants may also experience severe arrhythmia caused by neonatal heart failure, and multiple organ dysfunction syndrome caused by neonatal asphyxia [8]. Newborns are a special population characterized by fragile vitality. NICU real-time dynamic monitoring of neonatal hemodynamic changes is helpful for the early detection of unstable hemodynamics, and for timely adjusted strategy of treatments, thus reducing the viscera ischemia hypoxia and tissue damage [9]. It can also minimize the premature infant brain injury caused by cerebral blood supply insufficient and reduce premature neurological sequelae and disability. In order to improve the survival rate and quality of life, real-time comprehensive monitoring of children’s hemodynamic status is of vital clinical significance.

2. Research Progress of Hemodynamic Monitoring Methods

The primary index utilized in hemodynamic monitoring is cardiac output (CO), which is adapted to the metabolism of tissues and cells throughout the body. CO is an effective indicator for the evaluation of the efficiency of circulatory system. Besides, perfusion index (PI) and plethysmograph variability index (PVI) are also applied for monitoring early postnatal peripheral circulatory changes, with the advantages of convenience and noninvasiveness [10]. During circulatory disturbances, blood flow shifts from nonvital organs and tissues (skin, subcutaneous tissue, muscles, gastrointestinal tract) to vital organs (heart, brain, kidneys) [11]. Monitoring the peripheral perfusion of nonvital tissues helps in the early detection of inadequate perfusion in vital organs. The techniques of hemodynamic monitoring can be divided into two categories, depending on whether invasive or noninvasive procedures are performed. The first category is the invasive CO monitoring techniques, including traditional hot dilution method, pulmonary artery floating catheter and direct Fick law [12]. Regarded as the gold standard for CO measurement, the invasive hemodynamic monitoring approaches require a high-level technical know-how of operators due to intricate operation protocols, leading to elevated risks of complications, higher costs, and failure in an extensive application within NICU. The second category is minimally invasive and noninvasive CO measurement techniques, including the common pulse indicator continuous cardiac output (PiCCO) thermodilution technology, cardiovascular nuclear magnetic resonance imaging (MRI) technology, repeated partial respiration method, ultrasound cardiac output monitor (USCOM), and impedance cardiography [13].

2.1 Invasive Hemodynamic Monitoring

2.1.1 Thermal Dilution Method

The basic principle of thermal dilution, also known as temperature dilution, is related to temperature changes. A floating catheter is inserted into the subclavian vein, and CO and other hemodynamic indicators are calculated by tracing the area under the time-temperature curve [14].

2.1.2 Fick Equation

Nachman et al. [15] have performed studies combined with the principle proposed by Fick, and demonstrated that Fick is accurate enough to serve as a basis for clinical decision-making. This technique is routinely used in cardiac catheterization and is considered as a reference technique for CO in children. Blood oxygen concentration and other precise measurements of respiration and inhalation are also helpful to calculate CO and oxygen consumption.

2.1.3 Invasive Blood Pressure and Central Venous Pressure Monitoring

Invasive blood pressure monitoring requires the placement of an arterial indwelling needle, which is susceptible to factors such as the length of patency, hardness, and presence of gas of the pipeline. Central venous pressure monitoring needs operators with professional technical skills and provides a single monitoring index, and it fails to reflect other hemodynamic indexes. Moreover, there is noninvasive operation and its application is limited.

2.2 Noninvasive and Minimally Invasive Hemodynamic Monitoring Methods

2.2.1 PiCCO Measurement

Pulse indicator continuous cardiac output (PiCCO) is actually a combination of pulmonary temperature dilution and invasive blood pressure waveform analysis technology (Fig. 1), incorporating the analysis of arterial pressure waveform and continuous output measurement, and the accuracy is likely to be compromised in the presence of severe anatomical, functional variations, and severe rapid hemodynamic changes in the cardiovascular system. The side effects mainly include the risks of bleeding, infection, and thrombosis after catheterization. Especially for critically ill patients with hemodynamic instability, its detection accuracy may not be satisfactory with relatively high cost of consumables, making it not suitable for neonatal diseases.

2.2.2 Cardiovascular Magnetic Resonance Imaging (MRI)

CO monitoring based on the MRI technique is reported with good repeatability, reflecting CO accurately and objectively, and it can be used to evaluate myocardial blood supply and cardiac function indicators (Fig. 2). However, it is difficult to be promoted in wards because of continuous detection and expensive equipment [16].
2.2.3 Ultrasonic Doppler Monitoring Method

USCOM has been applied in clinical for over 40 years (Fig. 3), which is now commonly used as hemodynamic noninvasive monitoring means. Despite the benefit of real-time dynamic monitoring, this approach requires stringent operation expertise and skills. Ultrasonic signals are susceptible to interference, overhaul time is longer than the other factors, such as in the NICU using a wide range of standardized training is needed.

2.2.4 Bioimpedance Method

In 1966, Kubicek et al. [17] proposed the bioimpedance method to measure CO. Through a large number of studies, the correlation between bioimpedance method and thermal dilution method is as high as 0.87–0.91. In the 1990s, the US food and drug administration (FDA) approved the noninvasive cardiac output monitor (NICO™) product to enter the clinic, a product which is based on electrical cardiography (ECG) measurement.

At present, this noninvasive CO chest impedance method is mainly used to detect blood flow in newborns by ECG measurement and biological resistance (BR). Its basic principle is that the artery blood flow volume change as the main measurement, with each heart beat caused artery blood flow changes caused by the change of blood volume and blood flow velocity makes the impedance of the conductive information transmission along the aorta or the corresponding change in resistance, calculated as per stroke volume (SV), CO, and hemodynamic indicators.

Bernstein and Osypka [18] developed and described the technical background of EC, a new model for interpreting chest bioimpedance. The NICO™ device (Fig. 4), a type of EC made by Olympus, incorporates four electrodes: two external electrodes (on the head and thigh) and two internal electrodes (on the neck and chest). The two external electrodes apply alternating current. During diastole and prior to aortic valve opening, red blood cells are randomly distributed in the aorta, resulting in an increased resistance to the current. During systole, when blood is ejected into the main arteries, red blood cells align with one another, causing changes in electrical conductivity; peak aortic flow acceleration, left ventricular (LV) prejection and ejection time (ET) are calculated to estimate stroke volume, while HR measurements from electrocardiograms are used to estimate CO.

3. Application Progress of Electronic Cardiometry (EC)

3.1 Feasibility of EC in Early Neonates

Electronic cardiometry (EC), using internal calibration, is a method for measuring SV and CO that considers the weight and length of newborns. In recent years, research efforts have been focused on examining the correlation, accuracy and precision of ultrasonic monitoring methods, bioimpedance methods, and nuclear magnetic resonance methods. Katheria et al. [19] have studied the feasibility of using EC in the first 5 minutes after delivery in 20 full-term babies with complete umbilical cord and have recorded the measurement results used for trend monitoring. Freidl et al. [20] have also used EC in the delivery room to monitor the first 15 minutes of the life of full-term infants. Studies show that EC can provide fast and accurate bedside monitoring.

3.2 Accuracy Test of EC

Torigoe et al. [21] have applied EC in 28 infants with very low birth weight (VLBW) and low birth weight (LBW), implying that PDA and ventilator’s influence on this method. Grollmuss et al. [22] compared SV and HR of 228 premature infants with transthoracic echocardiography (TTE) (134 LBW, 94 VLBW) and EC (134 LBW, 94 VLBW) by Bland-Altman diagram. The accuracy of the method was expressed by calculating coefficient of variation (CV). This study evaluated whether EC and TTE were interchangeable, even in LBW and VLBW infants, suggesting that EC was also suitable for LBW/VLBW infants, and it was a safe and easy method to perform. Song et al. [23] evaluate the practicability of EC monitoring by comparing the results of CO and system blood flow, measured by EC and echocardiography (ECHO). Through prospective observation, 40 premature infants received 108 pairs of EC and ECHO measurements, and analyzed the correlation between EC, left ventricular opacification (LVO), and right ventricular opacification (RVO), indicating that EC is expected to become the trend of CO monitoring for premature infants. EC is considered as a noninvasive method for continuous measurement of CO. Blohm et al. [24] showed that EC is comparable to the aortic flow-based TTE method for pediatric patients. Boet et al. [25,26] showed that EC method is feasible, reproducible, fast, and it is a useful tool.
for continuous monitoring, and hemodynamic evaluation of neonates. EC is particularly meaningful for the clinical treatment of premature infants.

EC was once applied to monitor stroke and CO in 79 premature infants with hemodynamic stability (mean gestational age (GA): 31 ± 3.2 weeks), and the results were well correlated with echocardiographic monitoring results. Basic hemodynamic monitoring can be performed by ECG measurements, and ultrasound during both pediatric and neonatal transport. These two techniques demonstrate considerable reliability, and the accuracy of the results were not affected by transfer processes. Noori et al. [27] conducted 115 pairs of measurements in 20 premature infants with or without PDA, with no difference in accuracy and deviation of the measurement results. The study shows that EC is in good consistency with echocardiography monitoring results. The results of LVO (EC) and LVO (Echocardiography, (ECHO)) were similar (534 ± 105 vs 538 ± 105 mL/min, p = 0.7). The EC offset was –4 mL/min and the precision was 234 mL/min. The true accuracy of EC is shown to be similar to that of ECHO (31.6% and 30%, respectively). Grollmuss et al. [28] have found that EC and Doppler TTE have good consistency in estimating SV, and they are interchangeable. EC offers the advantage of being user-friendly, allowing to continuous measurements.

CO, a product of SV and HR, is particularly important for ensuring organ perfusion, especially in the NICU. Due to the risk of complications associated with invasive CO monitoring, noninvasive alternatives are required. Ren Xinrui et al. [29] selected 17 children with congenital heart disease using EC and TTE to examine SV, stroke volume variation (SVV) and distensibility index of the inferior vena cava (dIVC), and found that EC had good consistency with TTE monitoring results. Critchley et al. [30] conclude that when bias and accurate statistics are used, CO bias, consistent limit, and percentage error standards are proposed, acceptance of new technology should rely on a consistent limit of ±30%. Sanders et al. [31] have found through meta-analysis that ECG cannot replace thermodilution and TTE to measure absolute CO. However, Suehiro et al. [32] conducted a series of prospective observational meta-analysis of more than 300 premature infants and more than 100 full-term infants, and they found that ECG measurement had a minimal deviation (–0.03 L min⁻¹) and a smallest percentage error (23.6%). The EC method is considered to be the most accurate and precise technique for monitoring CO in children compared to noninvasive and invasive techniques. Most premature infants require respiratory support that includes both noninvasive and invasive ventilation techniques. The hemodynamic monitoring indexes of premature infants will be affected during high-frequency oscil-
lation and PDA occurrence [21]. Hsu et al. [33] reported that a total of 280 neonates are studied and the results indicate that CO is positively correlated with gestational age, body weight and body surface area ($r = 0.681, 0.822, 0.830$; all $p < 0.001$). The hemodynamic index of EC is significantly different in neonates with different maturity.

4. Research Progress in the EC Application

4.1 Application of EC in Postoperative Monitoring of Patients with Congenital Heart Disease

Huang et al. [34] reported that the use of EC to guide the intraoperative treatment of target fluid in patients undergoing surgery for congenital heart disease significantly reduce the dose of artificial colloid during surgery, and the tissue perfusion and oxygen supply are sufficient, thus reducing the postoperative tracheal catheter removal time.

4.2 Application of EC in Monitoring Patients with Septic Shock

Chen Bailang et al. [35] report that EC is used to monitor fluid management and treatment for early resuscitation of patients with septic shock, so as to guide fluid resuscitation and accurate fluid replenishing, which is conducive to disease recovery and reduced complications caused by blind fluid replenishing.

4.3 Application of EC in Neonatal Congenital Heart Disease Monitoring

Yuan et al. [36] used EC to monitor newborn children with congenital heart disease, and they found that the differences in cardiac index (CI), left ventricular ejection fraction (LVEF), N-terminal pro-brain natriuretic peptide (NT-probNP) and pulmonary arterial pressure (PAP) among groups with heart failure were statistically significant. CI to some extent reflects the degree of heart failure and holds significant clinical applicability in assessing heart failure in newborns with congenital heart disease.

4.4 Application of EC in the Monitoring of Neonatal Sepsis

Zhang et al. [37] have indicated that patients with sepsis used EC to dynamically and continuously monitor the changes of CI, integrated cardiopulmonary operating network (ICON) and other indicators of cardiac function, so as to evaluate the changes of patients’ early cardiac function and guide clinical decision-making. Liu et al. [38] report 62 cases of neonatal meconium aspiration syndrome with pulmonary hypertension who are treated with mechanical ventilation using electronic cardiac hemodynamics measure-
ment, implying that electronic cardiac measurement is a noninvasive, a highly sensitive, and a highly accurate monitoring tool.

4.5 Application of EC in Mild Hypothermia in Hypoxic Ischemic Encephalopathy (HIE)

Wu et al. [39] used EC and ECHO to detect the change of CO in 20 children with moderate and severe HIE during rewarming. CO measured by EC and ECHO during rewarming increased from 153 ± 43 mL/kg/min to 197 ± 42 mL/kg/min and 149 ± 35 mL/kg/min to 179 ± 34 mL/kg/min, respectively. It is found that the CO change during mild hypothermia is not related to stroke output, which remained unchanged, but is related however to the obvious change of cardiac rate during mild hypothermia. Studies show that the increase of the central rate leads to CO increase in neonates with HIE during the whole rewarming process of mild hypothermia treatment. During the rewarming period, systemic vascular resistance and mean arterial blood pressure decreased, but did not reach the gestational age threshold of intervention. Further studies are necessary to investigate whether the significant effect of mild hypothermia on HR and CO is a response to the reduction of basal metabolic rate, or the initiation of a self-protection mechanism. Noninvasive CO monitoring during mild hypothermia is feasible.

4.6 Application of EC in Neonates with Respiratory Distress Syndrome

Neonatal Acute Respiratory Distress Syndrome (NARDS) is a common respiratory system disorder in neonatal care units, often leading to critical conditions. It typically occurs shortly after birth (<24 hours) or during birth. The most severe cases occur within 48 hours after delivery, characterized by progressive respiratory distress, cyanosis, and even respiratory failure. Chest digital radiography (DR) examination is recommended for a comprehensive diagnosis, looking for indicators such as reduced lung translucency or “white lung”. Severe cases of NARDS often require the use of surfactant replacement therapy and mechanical ventilation. The use of EC to monitor hemodynamic changes in NARDS can timely detect unstable blood flow during the disease process, facilitating clinical decision-making. Paviotti et al. [40] include 96 neonates with gestational age of 37.9 ± 2.6 weeks in the study. Thoracic fluid content (TFC) is recorded within 3 h after birth (TFC1) and 24 h after birth (TFC2) by the bioimpedance method. It is found that TFC measured by electrical bioimpedance is independently associated with respiratory distress at birth and 24 h after birth in late preterm and term neonates.

4.7 Application of EC in Neonates with Sepsis

Bohanon et al. [41] have found that HR variability analysis is more sensitive than routine vital signs in the diagnosis of neonatal sepsis, being the largest preventable decrease of neonatal death in the world. Heart rate (HR) variability (HRV) analysis and noninvasive CO shown in many patients with sepsis are a useful auxiliary recognition, unconventional vital signs than traditional vital signs (HRV and CO) and mean arterial pressure are more sensitive to the confirmation of VLBW neonates with sepsis, which helps early recognition of sepsis.

4.8 Application of EC in Neonates with Pulmonary Catheter

The survey of Katheria et al. [42] show that an increase in LV output and a decrease in average blood pressure, indicating the necessary management of clinically significant PDA. Rodriguez et al. [43] used EC to detect hemodynamic changes in neonates undergoing surgical ligatation or drug closure of PDA, and found that CI, stroke volume index (SVI), and ICON decreased in children with closed ductus arteriosus.

4.9 Application of EC in Perinatal Asphyxia Patients

Eriksen et al. [44] have found that normal neonatal CO is stable within 0.5–6 hours after birth, and infants with perinatal asphyxia have lower CO before and during treatment. The lower rate of lactic acid loss is found to be less likely to be related to CO but more likely to be an indicator of organ damage due to asphyxia.

5. Influencing factors of EC

5.1 Postural Factors

Literature reported that three small cohort studies compared the effect of infant position on CO and the presence of differences between prone, left decubitus, and supine positions [45,46]. Ma et al. [45] found that neonatal EC detection in different positions resulted in reduced CO and stroke output in prone position compared with supine position. Wu et al. [46] used EC (Electrocardiogram) and ECHO (Echocardiography) techniques to confirm that in healthy full-term infants, the decrease in cardiac output (CO) in the prone position is due to a reduction in stroke volume (SV) rather than heart rate (HR) decrease. The cardiac output recovers when in the supine position. These results investigate the changes in systemic and cerebral hemodynamics between supine and prone sleep in healthy term infants, which may have important implications for clinical use, especially as many premature babies tend to be prone to feeding. Paviotti et al. [47] used the EC technique to compare left and supine positions, indicating that SV and CO were reduced.

5.2 Invasive Mechanical Ventilation

Invasive mechanical ventilation is reported to affect hemodynamics by changing intrathoracic pressure and venous return volume. Studies are reported that positive end-expiratory pressure (PEEP) have little influence on hemodynamics in the range of 1–10 cm, and high-frequency ventilation affects hemodynamics changes.
5.3 Blood Flow Significantly Affects PDA

Hsu et al. [48] report that PDA may affect EC measurement of CO in 79 premature infants with pulmonary PDA by comparing EC measurement with transthoracic echocardiography. Artery catheter refers to the fetal period significantly connected to the pulmonary artery; the aorta artery catheter function closes shortly after childbirth. However, for various reasons, it leads to the increase of pulmonary vascular resistance, ductus delay shut down and continue to exist. A large number of aorta shunt blood flow to the pulmonary artery, resulting in a large amount of blood flow from left to right shunt, and circulatory blood volume reduction. Increased blood flow in the pulmonary circulatory system leads to abnormal hemodynamic indicators.

5.4 Severe Anemia

The principle of ECG electromechanical measurement is based on the electrical conductivity of blood, and the content of red blood cells in the catheter affects the conduction of electrical signals. In the early stage, our research group conducted a study on two groups of premature infants with gestational age of 32–33 weeks, measured CO at 0.28 L/min in the non-transfusion group and 0.17 L/min in the transfusion group. This indicates that measurements of CO in children with anemia requiring transfusion are lower than those in the non-transfusion group.

5.5 Mild Hypothermia Treatment

A number of studies reported that CO decreases in all infants during mild hypothermia treatment, and the reason after analysis mainly lies in the reduction of HR and the constant output per wave [49,50]. Study has found that lactic acid clearance rate has nothing to do with CO in HIE children [51].

5.6 Caffeine Treatment

Walther et al. [52] found that left ventricular output and stroke output of preterm infants significantly increased from day 1 to day 7 after caffeine treatment. Caffeine increased left ventricular output of preterm infants through the combination of positive inotropic and chronotropic effects, and such inotropic effects were accompanied by pressure-boosting effects.

6. Conclusion

In summary, EC is an impedance-based monitoring method that provides a noninvasive, real-time assessment of hemodynamics. Despite the newborn’s reference has not yet been determined, the birth weight of different gestational age segment, the volatile CO range, how the children’s diseases and other complicated factors affect hemodynamic indexes, the noninvasive hemodynamic monitoring is widely used in the common severe neonatal diseases, and the clinical guidance is of great significance. The use of noninvasive cardiac displacement meter electronic heart monitoring method can be real-time, continuous understanding of patients’ heart and vascular function changes, allowing to perform the clinical evaluation of diseases, guiding clinical decision-making, improving the success rate of rescue, and reducing the death rate, which is worthy of clinical application.

Abbreviations

NICO, Noninvasive Cardiac Output Monitor; NICU, Neonatal Intensive Care Units; EC, Electronic Cardiometry; USCOM, Ultrasound Cardiac Output Monitor; HR, Heart Rate; PDA, Patent Ductus Arteriosus; CO, Cardiac Output; PI, Perfusion Index; PVI, Plethysmograph Variability Index; PiCCO, Pulse indicator Continuous Cardiac Output; MRI, Magnetic Resonance Imaging; FDA, Food and Drug Administration; ECG, Electrical Cardiography; BR, Biological Resistance; SV, Stroke Volume; LV, Left Ventricular; ET, Ejection Time; VLBW, Very Low Birth Weight; LBW, Low Birth Weight; TTE, Transthoracic Echocardiography; CV, Coefficient of Variation; ECHO, Echocardiography; LVO, Left Ventricular Opacification; RVO, Right Ventricular Opacification; GA, Gestational Age; SVV, Stroke Volume Variation; dIVC, distensibility Index of The Inferior Vena Cava; CI, Cardiac Index; LVEF, Left Ventricular Ejection Fraction; NT-probNP, N-Terminal pro-brain Natriuretic Peptide; PAP, Pulmonary Arterial Pressure; ICON, Integrated Cardiopulmonary Operating Network; NARDS, Neonatal Acute Respiratory Distress Syndrome; DR, Chest Digital Radiography; TFC, Thoracic Fluid Content; HRV, HR Variability; PEEP, Positive End-Expiratory Pressure.

Author Contributions

FL and WD designed the research study. FL and WD performed the research. FL and WD wrote the manuscript. Both authors read and approved the final manuscript. Both authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

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