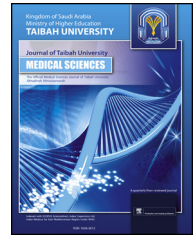




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Original Article

Electrical cardiometry for early detection of hemodynamically significant patent ductus arteriosus in preterm infants



Rania A. El-Farrash, MD, Adham M. El-Tahry, MD, Mariam N. Farag, MSc and Dina M. Shinkar, MD*

Pediatrics Departments, Faculty of Medicine, Ain Shams University, Cairo, Egypt

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المخلص

أهداف البحث: تحديد ما إذا كان من الممكن الاستفادة من معايير الديناميكية الدموية المقاسة مبكراً باستخدام قياس قوة القلب الكهربائي للتنبؤ بالقناة الشريانية السالكة ذات الأهمية الديناميكية الدموية عند الأطفال الخدج.

طرق البحث: أجريت هذه الدراسة على 75 من الأطفال الخدج بعمر حملي 35 أسبوعاً أو أقل، منومين في وحدة العناية المركزة لحديثي الولادة. تم تأكيد تشخيص القناة الشريانية السالكة عن طريق تخطيط صدى القلب. منذ الولادة، تمت مراقبة جميع الأطفال الخدج باستمرار لتقييم حالتهم الديناميكية الدموية. وشمل ذلك قياس تشبع الأكسجين ومتوسط ضغط الدم الشرياني ومعدل ضربات القلب ومخرجات البول. تم توصيل جميع الأطفال بجهاز قياس قوة القلب الكهربائي عند التنويم وبعد 12 ساعة. تم إجراء تخطيط صدى القلب ثنائي الأبعاد عبر الصدر بعد 24 ساعة من الولادة.

النتائج: أظهر الأطفال حديثي الولادة المصابون بالقناة الشريانية السالكة ذات الأهمية الديناميكية الدموية انخفاضاً كبيراً في العمر الحملي، والوزن عند الولادة، ودرجة أبعاد مقارنة بأولئك الذين يعانون من القناة الشريانية السالكة غير المهمة. بالإضافة إلى ذلك، أظهر أولئك الأطفال انخفاضاً ملحوظاً في النتاج القلبي وحجم النفخة المسجل بجهاز قياس قوة القلب الكهربائي عند التنويم وبعد 12 ساعة. كذلك ازداد النتاج القلبي وحجم النفخة بشكل ملحوظ وانخفض السائل الصدري بشكل ملحوظ بعد 12 ساعة مقارنةً بوقت التنويم. كشف تخطيط صدى القلب عن قيم مرتفعة بشكل ملحوظ لنسبة الأذين الأيسر إلى جذر الأبهري، وتدفق الوريد الأجوف العلوي، والنتاج البطيني الأيمن والأيسر عند الأطفال حديثي الولادة المصابون بالقناة الشريانية السالكة ذات الأهمية الديناميكية الدموية. تم تحليل منحني خصائص فعل المستقبلات لفحص القدرة التنبؤية لمعاملات تخطيط القلب

للتنبؤ بالقناة الشريانية السالكة ذات الأهمية الديناميكية الدموية عند عمر 12 ساعة. كانت المساحة تحت المنحني للنتاج القلبي 0.751، وكانت نقطة القطع 0.53 لتر / دقيقة مع حساسية 63.64 ونوعية تشخيصية 78.57، وقيمة تنبؤية إيجابية 70.0 وقيمة تنبؤية سلبية 73.3.

الاستنتاجات: يمكن أن يكون قياس قوة القلب الكهربائي مفيداً للكشف المبكر ومراقبة التغيرات الديناميكية الدموية عند الأطفال حديثي الولادة المعرضين للخطر.

الكلمات المفتاحية: تخطيط صدى القلب؛ القناة الشريانية السالكة ذات الأهمية الديناميكية الدموية؛ قياس قوة القلب الكهربائي؛ الخدج

Abstract

Objective: To determine whether early hemodynamic parameters measured using electrical cardiometry (EC) can be utilized for predicting hemodynamically significant patent ductus arteriosus (HS-PDA) in preterm neonates.

Study design: This study involved 75 preterm neonates with gestational age (GA) ≤ 35 weeks who were admitted to a neonatal intensive care unit. Diagnosis of PDA was confirmed by echocardiography. All preterm neonates were continuously monitored since birth to assess their hemodynamic condition by measuring their oxygen saturation, mean arterial blood pressure, heart rate, and urinary output. All preterm neonates were connected to the EC on admission and after 12 h. Transthoracic two-dimensional echocardiography was performed 24 h after birth.

Results: GA, birth weight, and Apgar score were substantially lower in neonates with HS-PDA than those with hemodynamically nonsignificant PDA. In addition, the cardiac output (CO) and stroke volume (SV) recorded

* Corresponding address: Department of Pediatrics, Faculty of Medicine, Ain Shams University, Abbassya Square 11566, Cairo, Egypt.

E-mail: dinashinkar@med.asu.edu.eg (D.M. Shinkar)

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by EC were significantly lower on admission and at 12 h ($p < 0.01$). CO and SV were significantly higher at 12 h compared with admission. Furthermore, echocardiography showed that the values of the left atrium to aortic root ratio, superior vena cava flow, right ventricular output, and left ventricular output were significantly elevated in neonates with HS-PDA than hemodynamically nonsignificant PDA. The receiver operator characteristic curve was analyzed to examine the capacity of the electrocardiometry parameters to predict HS-PDA. The area under the curve for CO was 0.751 and the cut-off point was ≤ 0.53 L/min, with sensitivity of 63.64 %, specificity of 78.57 %, positive predictive value of 70.0 %, and negative predictive value of 73.3 %.

Conclusion: EC could be beneficial for the early detection and monitoring of hemodynamic changes in high-risk neonates.

Keywords: Echocardiography; Electrical cardiometry; HS- PDA; Preterm

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Introduction

Targeted early intervention for patent ductus arteriosus (PDA) in preterm infants continues to be a significant issue. Preterm infants have a higher risk of developing morbidities such as bronchopulmonary dysplasia, intraventricular hemorrhage (IVH), and necrotizing enterocolitis (NEC), but clinicians remain uncertain regarding whether or not to manage PDA.¹

Currently, a less severe approach is advised to the surgical and pharmacological treatment of PDA.² Consequently, the identification of hemodynamically significant PDA (HS-PDA) is even more crucial.

PDA management in preterm neonates is controversial due to the lack of agreement concerning the precise definition of HS-PDA.³ Numerous previous trials lacked treatment criteria.⁴ Some focused on very early treatment (the initial 48 h), with varying definitions for treatment criteria.⁵ There is evidence that PDA treatment may mitigate severe morbidities such as IVH, but the elevated rate of PDA spontaneous closure makes it complex.

Noninvasive techniques have also been investigated for the diagnosis of PDA in premature infants, such as electrical cardiometry (EC) and near-infrared spectroscopy.⁶ In particular, EC is utilized to determine changes in conductivity to quantify the cardiac output (CO), stroke volume (SV), and other hemodynamic parameters.⁷ Specific investigations have started to utilize EC for assessing CO and SV in hemodynamically stable preterm infants in a manner comparable to echocardiography.⁸ It has been suggested that EC is a secure, simple, and precise method for measuring the hemodynamics of infants and children,⁹ and its efficacy has been demonstrated in animal models¹⁰

as well as adult patients.¹¹ A positive correlation was observed between EC and pulmonary artery catheter thermodilution in children undergoing catheterization.¹² It has been demonstrated that EC measurements of CO in infants with congenital heart disease are comparable to those obtained using transesophageal Doppler and direct oxygen Fick methods.¹³

Numerous studies have also shown that the accuracy of EC for determining neonatal CO is equivalent to that of transthoracic echocardiogram,¹⁴ even in very low birth weight preterm infants.¹⁵

In the present study, we aimed to determine whether early hemodynamic parameters evaluated utilizing EC can predict HS-PDA in preterm neonates.

Materials and Methods

Study population

This prospective cohort study was conducted based on 75 preterm neonates with gestational age (GA) ≤ 35 weeks who were admitted to a neonatal intensive care unit (NICU) with PDA detected by echocardiography. The Ain Shams University Ethical Committee gave ethical approval under reference number (FMASU M S 394/2020). All subjects' guardians or parents provided informed consent prior to inclusion. In addition, the inclusion criterion was preterm neonate (with left to right shunting PDA). The exclusion criterion was neonate with no PDA detected in echocardiography performed at 24 h of life. We also excluded infants with structural heart anomalies, excluding those with atrial septal defects or patent foramen ovale, as well as those with chromosomal anomalies. The sample size was calculated assuming a power of 80 % and alpha error of 5 %. A sample size of 70 neonates was sufficient to detect a significant difference between EC and echocardiography for HS-PDA detection.

Clinical assessment

Neonates were managed according to the NICU protocol. Complete history taking and full clinical examination were performed for all subjects, including clinical signs of respiratory distress syndrome (RDS) such as retractions, moaning sounds, or nasal flaring.

Hemodynamic monitoring

The hemodynamic states of all preterm neonates were continuously assessed from birth by continuously monitoring the mean arterial blood pressure (BP), oxygen saturation, heart rate (HR), and urinary output. Data were analyzed for babies who were later diagnosed as having PDA.

Noninvasive EC

Upon admission, all premature infants were immediately connected to the EC with a portable noninvasive electrical cardiometer (ICON®-Osypka Medical, Berlin, Germany). Four skin sensors were positioned on the thighs, forehead,

chest, and left side of the neck in order to continuously monitor changes in electrical conductivity within the thorax. The following electro-cardiometry parameters were recorded: SV, CO, systemic vascular resistance, index of contractility (ICON), and thoracic fluid content (TFC) and total fluid contents. Data were analyzed for infants who were subsequently diagnosed with PDA. In order to avoid bias, the echocardiologist and doctor who applied the EC were blinded to each other's measurements.

Echocardiography

Transthoracic two-dimensional echocardiography was performed at the age of 24 h using an electrocardiography machine and a Vivid-3 Pro-ultrasound scanner (GE Medical Systems, Milwaukee, WI, USA), with an 8–10 MHz (10S) probe (GE HealthCare Vivid, USA). Echocardiography was conducted based on parasternal, apical, subcostal, and suprasternal views. Color Doppler was also performed. The shunting direction and ductal diameter were determined, and the superior vena cava (SVC) flow was calculated. Echocardiographic measurements were performed according to the guidelines specified by the American Society of Echocardiography.¹⁶

Criteria for HS-PDA

The criteria for determining HS-PDA include the presence of at least one of the following: left pulmonary artery flow velocity >0.25 m/s, internal ductal diameter ≥ 1.5 mm, left atrium to aortic root ratio (LA/Ao ratio) ranging from 1.4 to 1.6 for moderate PDA and >1.6 for large PDA, and absent or reverse diastolic flow (in the descending aorta). In addition, clinical symptoms such as persistent hypotension, metabolic acidosis, or significant ventilator support may indicate HS-PDA. A baby was enrolled in the study after PDA diagnosis.^{17,18}

Group classification

Among the 218 preterm neonates evaluated for eligibility, 143 neonates were excluded because 102 had no PDA by echocardiography, 14 manifested congenital heart disease, 12 had multiple significant congenital anomalies, and 15 guardians declined participation.

Based on the echocardiography findings, the 75 neonates included in the study were categorized into two groups: the HS-PDA group included 33 neonates and the hemodynamically nonsignificant PDA group included 42 neonates.

Laboratory and radiological investigations

C-reactive protein, capillary blood gases, complete blood picture, chest X-ray with radiological assessment of grade of RDS, abdominal plain X-ray, and Doppler ultrasound were used to exclude NEC in suspected cases. In addition, cranial ultrasound was conducted to detect IVH (on days 3, 7, and 28).

Protocol for the management of HS-PDA

Infants diagnosed with HS-PDA by echocardiography were administered either oral acetaminophen or oral ibuprofen. Patients were administered oral ibuprofen (100 mg/5 mL ibuprofen suspension) at a dosage of 10 mg/kg/day for the initial day, followed by 5 mg/kg/day for the following two days. If HS-PDA persisted, a second course was administered at 5 mg/kg/day for an additional three days. In cases where ibuprofen is not recommended, patients were administered oral acetaminophen (acetaminophen suspension 250 mg/5 mL) at a dosage of 15 mg/kg (every 6 h) for three consecutive days. If ductal closure did not occur, a second acetaminophen course was prescribed. Surgical PDA ligation is an option when medical treatments have been unsuccessful in treating HS-PDA that has been confirmed by echocardiography.

Outcome measures

The primary outcome was to determine whether early hemodynamic parameters could predict HS-PDA in preterm neonates. The secondary outcome measures were NICU admission duration, IVH $>$ grade II based on the classification of Papile et al.,¹⁹ NEC $\geq$ stage 2 based on the classification of Bell modified by Kliegman and Walsh,²⁰ and mortality and bronchopulmonary dysplasia.

Statistical analysis

Collected data were coded, tabulated, and analyzed using Microsoft Office Excel (2007) and IBM SPSS V22.0 (IBM Corp.-Chicago-USA-2013). Quantitative data were analyzed based on descriptive statistics, including the mean $\pm$ standard deviation, and minimum and maximum of the range for quantitative data with normal distributions. Qualitative data were analyzed and expressed as numbers and percentages. Independent *t*-tests were performed to compare two independent groups with normal distributions. Qualitative data were analyzed by conducting inferential tests on independent variables. The Chi-square test was used to examine differences between proportions and Fisher's exact test for variables with small, expected numbers. A logistic regression model was utilized to identify HS-PDA predictors. Receiver operator characteristic (ROC) curve analysis was conducted to determine each test's diagnostic power and optimal cut-off point. Moreover, the area under the curve (AUC) was determined for each plot. The significance level was set at $p < 0.05$.

Results

The maternal and neonatal characteristics of both groups are presented in Table 1. GA, Apgar score, and birth weight were notably lower in neonates diagnosed with HS-PDA than those with hemodynamically nonsignificant PDA. No substantial differences were found between both groups in terms of chorioamnionitis and preeclampsia ($p > 0.05$). The urine output was significantly lower in neonates with HS-

Table 1: Maternal and neonatal characteristics of groups.

Variable	Hemodynamically significant PDA	Hemodynamically not significant PDA	<i>p</i> -value
	N = 33	N = 42	
Gestational age (wks), mean $\pm$ SD	32.76 $\pm$ 1.97	34.36 $\pm$ 1.87	0.001
Birth weight (kg), mean $\pm$ SD	1.74 $\pm$ 0.56	2.22 $\pm$ 0.56	0.001
Antenatal steroids, n (%)	5 (15.2)	21 (50.0)	0.002
Maternal chorioamnionitis, n (%)	3 (9.1 %)	5 (11.9)	0.695
Preeclampsia, n (%)	6 (18.2 %)	5 (11.9)	0.446
Apgar 1 min, median (IQR)	6 (6–7)	7 (7–7)	0.016
Apgar 5 min, median (IQR)	9 (8–9)	9 (9–9)	0.001
pH, mean $\pm$ SD	7.31 $\pm$ 0.05	7.27 $\pm$ 0.47	0.643
HCO ₃ , mean $\pm$ SD	16.99 $\pm$ 2.11	19.58 $\pm$ 3.19	<0.001
UOP (mg/kg/h), mean $\pm$ SD	2.45 $\pm$ 0.98	3.05 $\pm$ 0.79	0.005
Severe IVH, grade III or IV, n (%)	5 (18.18)	0 (0)	<0.001
Medical or surgical NEC, n (%)	4 (12.12)	1 (2.3)	<0.001
BPD, n (%)	1 (3.03)	0 (0)	0.256
Length of stay (days), median (IQR)	20 (15–30)	11 (7–15)	<0.001
Mortality, n (%)	7 (21.21)	2 (4.7)	<0.001

Abbreviations: SD, standard deviation; IQR, interquartile range; wks, weeks; kg, kilogram; pH, potential of hydrogen; HCO₃, bicarbonate; UOP, urine output; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; BPD, bronchopulmonary dysplasia. Data expressed as numbers (%) compared with chi-square test (χ^2). Values expressed as mean $\pm$ SD compared by one-way analysis of variance. Median values (IQR) used in Kruskal–Wallis test for comparison.

Table 2: Echocardiographic parameters for neonates.

Echocardiographic parameters	Hemodynamically significant PDA	Hemodynamically not significant PDA	<i>p</i> -value
	N = 33	N = 42	
SVC flow (mL/kg/min)	135.24 $\pm$ 21.06	122.36 $\pm$ 23.69	0.017
LVO (mL/kg/min)	375.33 $\pm$ 59.23	246.71 $\pm$ 64.58	<0.001
RVO (mL/kg/min)	246.45 $\pm$ 34.22	206.36 $\pm$ 47.44	<0.001
LA/Ao ratio	1.40 $\pm$ 0.26	1.14 $\pm$ 0.23	<0.001

Abbreviations: LA/Ao, left atrium to aortic root ratio; SVC, superior vena cava; LVO, left ventricular output; RVO, right ventricular output; SD, standard deviation. Differences significant at *p*-value <0.01. Data expressed as mean $\pm$ SD compared with Student's *t*-test. Data expressed as numbers and percentages compared using chi-square (χ^2) test.

PDA ($p > 0.05$). Furthermore, the urine output ($p = 0.005$) and HCO₃ ($p < 0.001$) were significantly lower than those in the other group.

Neonates diagnosed with HS-PDA were also more likely to develop severe IVH, NEC, and Grade III or IV than those in the other group ($p < 0.001$). There was no significant difference between groups in terms of the incidence of BPD at 36-week gestation ($p > 0.05$). Neonates with HS-PDA had a longer duration of hospital stay than those with hemodynamically nonsignificant PDA (20 versus 11 days, respectively; $p < 0.001$). The mortality rate was higher among neonates with HS-PDA ($p < 0.001$).

Among the echocardiographic parameters, Table 2 shows that the SVC flow, left ventricular output (LVO), LA/Ao ratio, and right ventricular output (RVO) were significantly higher in neonates with HS-PDA than neonates with hemodynamically nonsignificant PDA.

Examination of the vital parameters for neonates showed that the mean BP, systolic BP, and diastolic BP were significantly lower in the HS-PDA group than the nonsignificant PDA group at each follow-up point

($p < 0.01$) (Figure 1a). Furthermore, the HR was significantly elevated in the HS-PDA group at each follow-up point ($p < 0.01$) (Figure 1b).

The SV and CO were significantly lower in neonates with HS-PDA according to the recordings obtained by EC upon admission and at 12 h ($p < 0.01$) (Figure 2; Tables 3 and 4). There were no significant differences in SVRI, ICON, and FTC between the two groups according to the EC measurements upon admission and at 12 h of life ($p > 0.05$ for all). TFC was significantly lower in neonates with hemodynamically nonsignificant PDA after 12 h ($p = 0.02$). Comparisons of the EC parameters at 12 h after birth showed that CO and SV were significantly elevated and TFC was significantly lower compared with those at admission (Table 5).

The ROC curve was analyzed to examine the capacity of the electrocardiometry parameters for predicting HS-PDA. The AUC for CO was 0.751 and the cut-off point was ≤ 0.53 L/min, with sensitivity of 63.64 %, specificity of 78.57 %, positive predictive value of 70.0 %, and negative predictive value of 73.3 %.

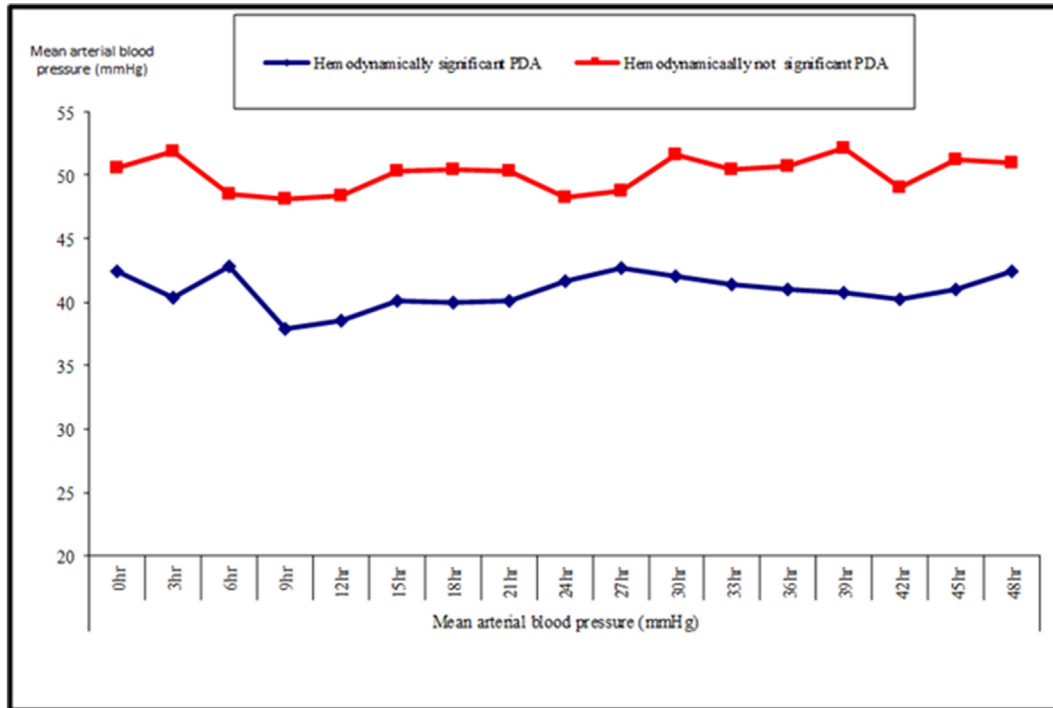
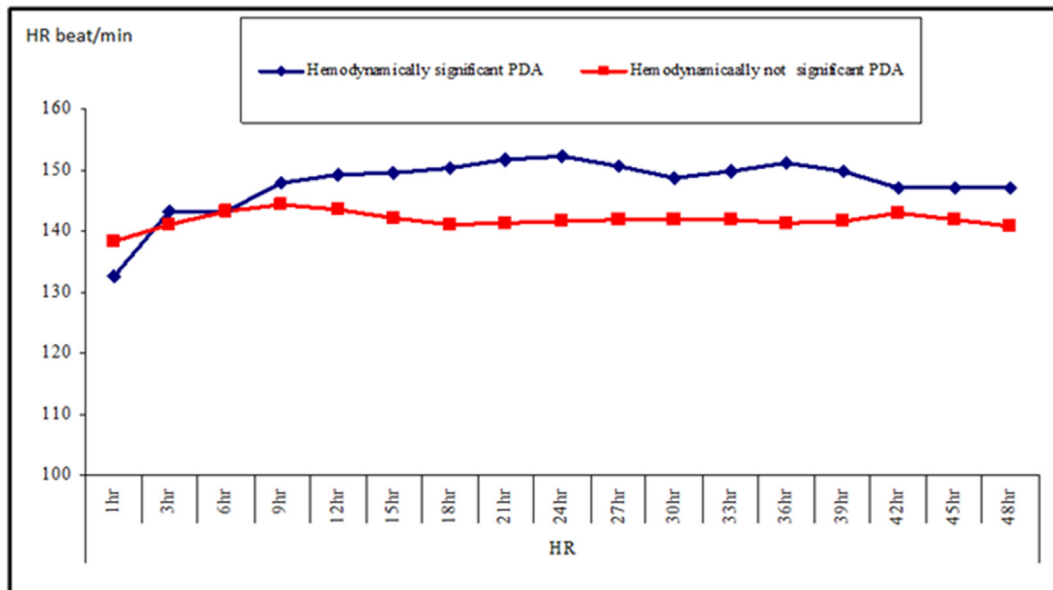
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Figure 1: (a) Comparison of mean arterial blood pressure in both groups. (b) Comparison of heart rate in both groups.

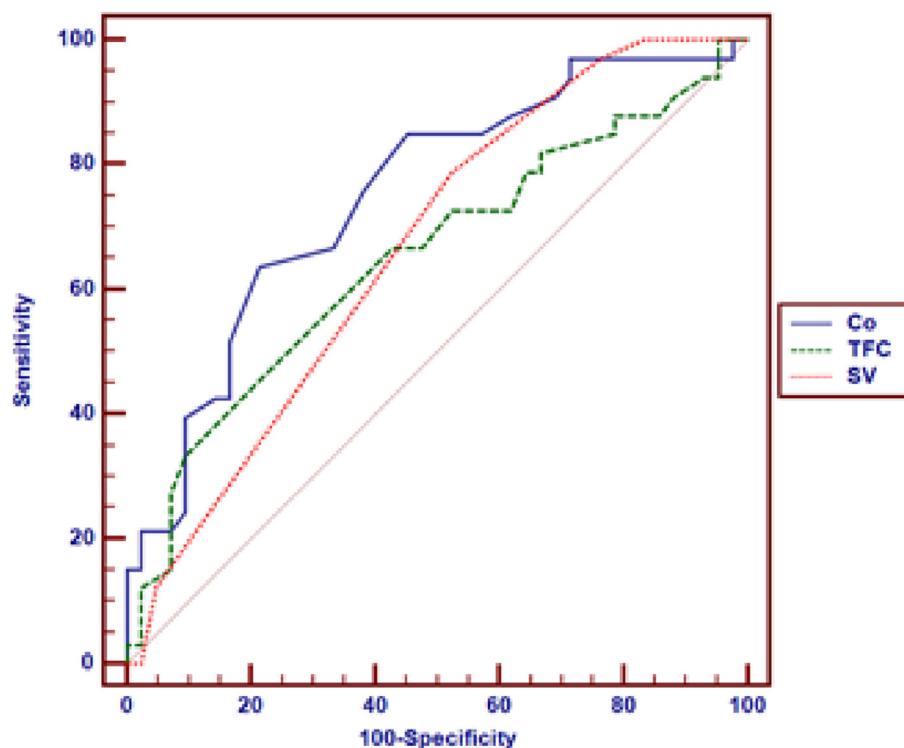


Figure 2: Comparison of cardiac output in both groups by electrical cardiometry.

Table 3: Electrical cardiometry parameters for groups on admission.

	Hemodynamically significant PDA N = 33	Hemodynamically not significant PDA N = 42	p-value
FTC, mean $\pm$ SD	262.52 $\pm$ 45.64	273.40 $\pm$ 49.80	0.333
CO (L/min), median (IQR)	0.34 (0.31–0.38)	0.55 (0.15–0.77)	0.036
ICON, mean $\pm$ SD	99.79 $\pm$ 25.82	95.52 $\pm$ 29.39	0.513
TFC, median (IQR)	30 (24–36)	29 (22–37)	0.676
SV (mL), mean $\pm$ SD	3.59 $\pm$ 0.64	4.55 $\pm$ 1.21	<0.001
SVRI (mL/min/m ²), median (IQR)	7801 (3333–11930)	5935 (1321–11285)	0.247

Abbreviations: FTC, fluid total content; CO, cardiac output; TFC, thoracic fluid content; ICON, index of contractility; SV, stroke volume; SVRI, systemic vascular resistance index. Differences significant at $p < 0.01$. Data expressed as numbers and percentages compared using chi-square (χ^2) test.

Table 4: Electrical cardiometry parameters for both groups at 12 h of age.

Electrical cardiometry parameter		Hemodynamically significant PDA N = 33	Hemodynamically not significant PDA N = 42	p-value
FTC	Mean $\pm$ SD	275.12 $\pm$ 40.36	286.74 $\pm$ 33.39	0.177
CO (mL/min)	Mean $\pm$ SD	500 (410–550)	580 (540–690)	<0.001
ICON	Mean $\pm$ SD	109.91 $\pm$ 20.63	108.88 $\pm$ 21.98	0.837
TFC	Median (IQR)	27 (25–35)	25 (22–30)	0.026
SV (mL)	Mean $\pm$ SD	4.12 $\pm$ 0.65	4.86 $\pm$ 1.34	0.005
SVRI (mL/min/m ²)	Median (IQR)	5299 (4767–6978)	5689 (5255–9384)	0.076

Abbreviations: FTC, fluid total content; CO, cardiac output; TFC, thoracic fluid content; ICON, index of contractility; SV, stroke volume; SVRI, systemic vascular resistance index. Differences significant at $p < 0.01$. Data expressed as numbers and percentages compared using chi-square (χ^2) test.

Table 5: Comparison of EC parameters on admission and after 12 h in hemodynamically significant PDA group.

Hemodynamically significant PDA		EC parameters on admission	EC parameters 12 h	p-value
FTC	Mean $\pm$ SD	262.52 $\pm$ 45.64	275.12 $\pm$ 40.36	0.176
CO (L/min)	Median (IQR)	0.34 (0.31–0.38)	0.50 (0.41–0.55)	0.011
ICON	Mean $\pm$ SD	99.79 $\pm$ 25.82	109.91 $\pm$ 20.63	0.105
TFC	Median (IQR)	30 (24–36)	27 (25–35)	0.034
SV (mL)	Mean $\pm$ SD	3.59 $\pm$ 0.64	4.12 $\pm$ 0.65	0.003
SVRI (mL/min/m ²)	Median (IQR)	7801 (3333–11930)	5299 (4767–6978)	0.136

Abbreviations: FTC, fluid total content; CO, cardiac output; TFC, thoracic fluid content; ICON, index of contractility; SV, stroke volume; SVRI, systemic vascular resistance index. Differences significant at $p < 0.01$. Data expressed as numbers and percentages compared using chi-square (χ^2) test.

Discussion

In this study, we monitored hemodynamic changes during the first 12 h of life utilizing noninvasive EC and vital parameters. In addition, we attempted to assess whether these changes could predict HS-PDA in preterm infants with GA ≤ 35 weeks.

GA and birth weight were significantly lower in neonates with HS-PDA than those with hemodynamically nonsignificant PDA. Similar to our results, Terrin et al. reported that the GA and birth weight were significantly lower in neonates with HS-PDA than the controls.²¹ In the present study, we found a significantly higher incidence of IVH, and previous studies also observed an association between PDA and IVH.²² The incidence of NEC was higher in neonates with HS-PDA. Similarly, many previous studies reported NEC as a complication of HS-PDA.²³ We found that neonates with HS-PDA had significantly longer hospital stays. In a previous study, multivariate logistic regression analysis demonstrated that the average length of stay was correlated with HS-PDA, where it was longer in the HS-PDA group than the hemodynamically nonsignificant PDA group.²⁴ Mortality was higher among neonates with HS-PDA. In agreement with these findings, a previous study showed that HS-PDA was associated with considerably elevated mortality rates (25.6 %) compared with hemodynamically nonsignificant PDA (13.9 %).²⁵

Among the vital parameters, we found that the mean arterial BP, diastolic BP, and systolic BP were significantly lower and HR was significantly higher in the HS-PDA group than the hemodynamically nonsignificant PDA group. These findings agree with those obtained by Verma et al. who showed that HS-PDA was associated with decreased diastolic BP and systolic BP.²⁶ Furthermore, Lemmers et al. found that the mean BP was lower in infants with HS-PDA than those without PDA ($p < 0.05$). Moreover, the mean BP remained substantially lower at 6 h after initiating indomethacin treatment.²⁷ Numerous mechanistic pathways result in the circulatory imbalance with HS-PDA, characterized by systolic and/or diastolic hypotension.²⁸ The risk of refractory hypotension is considerably elevated in preterm neonates with HS-PDA.²⁹

Echocardiography is widely regarded as the most reliable method for directly evaluating the PDA diameter and shunt pattern.³ However, there is a possibility of inconsistent measurements due to differences in interpretation among observers.³⁰ Among the echocardiography parameters, we found that the SVC flow, RVO, LVO, and LA/Ao ratio

were higher in neonates with HS-PDA than neonates with hemodynamically nonsignificant PDA. Similarly, a previous study showed that LVO was higher in a HS-PDA group than a hemodynamically nonsignificant PDA group, which was attributed to the changes in the LVO levels in the HS-PDA group following PDA closure.³¹ Another study found that cardiovascular parameters, including the LA/Ao ratio, left ventricular dimensions and volumes, left atrium volume index, CO, and SV were substantially elevated in a HS-PDA group than those with hemodynamically nonsignificant PDA and non-PDA.³²

Furthermore, another study of infants who underwent early functional echocardiography showed that LVO was higher in infants who required treatment for PDA.⁷ In addition, a study determined that the elevated LVO observed in individuals with PDA was responsible for increasing their SV but without affecting their HR.³³ Moreover, an elevated LVO was associated with a notable ductal shunt in another study.³⁴

LVO assesses the extent of pulmonary overcirculation, which may account for related morbidities, including pulmonary hemorrhage and an increased need for respiratory support.³⁵

Interest is increasing in implementing EC technology in neonatal intensive care units because it facilitates continual hemodynamic monitoring in neonatal critical care.³⁶ EC is based on the concept of electrical bioimpedance, which is determined by measuring changes in the blood flow within the aorta through adhesive electrodes applied to the scapular area or neck and thorax.³⁷

In the present study, we found that the SV and CO values recorded by EC were significantly lower upon admission and at 12 h of life in neonates with HS-PDA than neonates with hemodynamically nonsignificant PDA. In this context, Lu et al. reported that the CO differed significantly among premature infants with variations in GA and birth weight. Lower GA and BW values corresponded to decreased CO values.²⁴ Rodríguez et al. used EC to observe infants with PDA in need of treatment and they reported a significant reduction in the CO index ($p = 0.03$).¹⁸ In addition, Hsu et al. found that the baseline CO measured by EC was higher in infants diagnosed with PDA than infants without PDA.³⁸ The perinatal transition results in significant changes in CO. A decrease in CO may be caused by myocardial dysfunction and an inability to adequately respond to higher demand.³⁹

We showed that CO and SV were markedly higher at 12 h than on admission. Similarly, Miletin et al. measured CO by

bioreactance in preterm infants between 6 h and 48 h of life. They observed decreased CO levels at 6 h, which subsequently increased during the second day of life.⁴⁰ Furthermore, Cappelleri et al. investigated the changes in LVO in preterm infants within the first two days of life by using bioreactance to estimate the left ventricular CO and SV. They observed a gradual increase in both of these measurements while a consistent HR was maintained.⁴¹

The main strength of the present study is its prospective design. The echocardiogram-derived estimates served as surrogate measures to compare with the gold standard and validate the results based on our measurements. The limitations of the study are the relatively small sample size and short-term follow-up of patients. Further studies are needed with a larger number of patients and longer follow-up periods to better understand the early hemodynamic changes in neonates with HS-PDA.

In conclusion, the SV and CO values recorded by EC were significantly lower in neonates with HS-PDA. The electrocardiographic CO and SV values were also significantly higher at 12 h compared with those on admission. EC could be beneficial for the early detection and monitoring of hemodynamic changes in high-risk neonates.

Conflict of interest

There is no conflict of interest.

Ethical approval

The study protocol was approved by Ain Shams University Ethical Committee under the reference number (FMASU M S 394 / 2020). All the legal guardians or parents of included neonates provided informed consent prior to inclusion in the study.

Authors contribution

RAE and AME conceived and designed the study. MNF collected and organized data and wrote the initial manuscript. DMS and RAE analyzed and interpreted data, wrote final draft of article, and provided logistic support. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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