Neonatal Septic Shock and Hemodynamic Monitoring in Preterm Neonates in a NICU: Added Value of Electrical Cardiometry in Real-Time Tailoring of Management and Therapeutic Strategies

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Am J Perinatol

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Abstract

Objective Electrical cardiometry is an impedance-based monitoring technique that provides data on several hemodynamic parameters in a noninvasive way. There is limited information on clinical utility of the application of this technique in neonates.

Study Design In this study, we describe the case of a preterm neonate born at $30^{2/7}$ weeks of gestational age who developed severe systemic infection with fluid refractory septic shock on day 2 of life.

Discussion Electrical cardiometry was used and proved very helpful in real-time guiding the choice and the dosing of the most appropriate inotrope drugs in this patient. In addition, it promptly underlined an abrupt drop of systemic vascular resistances occurring after administration of the first dose of antibiotic, thus warning the attending neonatologist to institute appropriate treatment before the clinical conditions could further worsen.

Conclusion This case report suggests that electrical cardiometry could be a useful tool in assessing, monitoring, and guiding care of neonates who develop severe septic shock. We suggest that electrical cardiometry is a promising approach in the management strategies of such patients that warrants informative clinical trials.

Keywords

- electrical cardiometry
- septic shock
- newborn
- hemodynamic monitoring
- thoracic electrical bioimpedance
- cardiac output

Key Points

- Electrical cardiometry was helpful in real-time decision-making.
- Electrical cardiometry reported hemodynamic perturbations before worsening of clinical conditions.
- Electrical cardiometry should be included in the management of critical patients.

The ability to determine a patient's hemodynamics status is pivotal in intensive care medicine and is consistently recommended by authoritative guidelines for septic shock resuscitation.[1] Apart from invasive technique, such as pulse contour analysis and thermodilution by pulmonary artery catheter, transthoracic echocardiography is the most

received
November 21, 2020
accepted after revision
February 1, 2021

Thieme Medical Publishers, Inc.,
333 Seventh Avenue, 18th Floor,
New York, NY 10001, USA

DOI https://doi.org/10.1055/s-0041-1726123.
ISSN 0735-1631.

common noninvasive method to assess cardiac output (CO) in infants, but it is technically demanding and operator dependent and can only be obtained intermittently.

Electrical cardiometry (EC) is a noninvasive technique that measures thoracic electrical bioimpedance (TEB) and continuously derives hemodynamic parameters such as heart stroke volume (SV) and CO, contractility (expressed as contractility index, ICON), systemic vascular resistance (SVR), and thoracic fluid content. EC releases a high frequency and low amperage electric current through the thorax by two electrodes (placed on head and thigh). Erythrocytes are in random orientation before the aortic valve opening and then align in a parallel fashion with pulsatile blood flow. This parallel state results in increased conductance and conversely decreased impedance. Two electrodes (on the thorax and neck) receive these signals and the difference in conductance between these two stats.

The ability to determine a patient's hemodynamic status provides the baseline data that allow the calculation of hemodynamic parameters using mathematical algorithms.[2]

The accuracy of EC in determining CO in term and even preterm neonates has been demonstrated and validated through the use of transthoracic echocardiography.[3,4] Consequently, there has been a growing interest to apply this technology in the neonatal intensive care (NICU) setting.

Hence, this technique has been studied in different clinical scenarios including surgical ligation for patent ductus arteriosus,[5] hemodynamic transition after birth,[6] and circulatory modifications secondary to caffeine administration.[7] Reference ranges of values in hemodynamically stable neonates of different gestational age and body weight have been recently published.[8] Clinical applications of EC are very promising and could be useful in many areas.[9–11]

Septic shock in newborn is a critical condition associated with high mortality and morbidity. As it is a dynamic condition that changes markedly overtime, we have speculated that frequent or continuous measurement of CO, SVR, and other hemodynamic parameters using EC could be helpful to individualize the treatment and to adapt it over time.

Here, we report on a newborn with septic shock who underwent EC monitoring, allowing the attending neonatologists to continuously track not only CO, but also all hemodynamic parameters needed to enable optimization and adaptation of the inotropic therapy.

Case Report

A 1,475 g male infant was born at $30^{6/7}$ weeks of gestation via cesarean section due to prolonged premature rupture of membranes induced labor. A full course of betamethasone was administered and broad-spectrum antibiotic prophylaxis was given to the mother in the 9 days prior to delivery. Apgar's scores were 7 and 8 at 1 and 5 minutes, respectively. The patient was admitted to our neonatal intensive care unit in nasal continuous positive airway pressure (CPAP) and ampicillin and gentamicin were initiated as empirical antibiotics. A chest X-ray was obtained, and it was consistent with respiratory distress syndrome (low lung volumes, air bronchograms, and ground glass appearance). For this reason, surfactant was administered after 3 hours of life by using the intubation-surfactant-extubation technique with amelioration of oxygen need. On the day 2 of life, he suddenly showed mixed acidosis (pH = 7.11, $pCO_2 = 63$ mmHg, $PaO_2 = 35$ mmHg, $HCO_3 = 19$ mmol/L, lactate = 3.8 mmol/L) hypoactivity, apnea, prolonged refill time, and diuresis contraction. He was then intubated and ventilated in synchronized intermittent positive pressure ventilation with amelioration of the respiratory component of the acidosis. He showed low blood pressure (BP) 46/21 (29) mmHg despite two normal saline boluses of 10 mL/kg.

Laboratory test showed a total leukocyte count of 3.030 cells/μL (segmented neutrophil, 57.7%), platelet count of 84,000/L, elevated C-reactive protein level of 4.8 mg/dL (normal range < 0.5 mg/dL), and procalcitonin of 82.3 ng/mL (normal range < 10 ng/mL).

Blood culture sample taken at birth was at that moment negative but, under suspicion of septic shock, ampicillin was carried on and gentamicin was replaced by meropenem. Intravenous immunoglobulin was also used.

Functional echocardiography showed good heart contractility with CO of around 220 mL/kg/min and patent ductus arteriosus of 2 mm with a left to right shunt.

Hemodynamic monitoring was obtained by TEB-EC (ICON Osypka Medical GmbH, Berlin, Germany). The device was connected and patient demographic and anthropometric data (age, weight, and height) were entered. Four skin electrodes (iSense Electrical Cardiometry Skin Sensors; Osypka Medical) were applied per manufacturer recommendations. Information on CO, SVR, and cardiac contractility (ICON) were acquired. EC parameters are showed in ►**Table 1**.

Table 1 Electrical cardiometry parameters starting after two normal saline boluses of 10 mL/kg and how they changed according to our subsequent interventions.

	Before therapy	Start norepinephrine at 0.05 mcg/kg/min	Antibiotic therapy	Increasing norepinephrine to 1.5 mcg/kg/min	Tapering norepinephrine to 1 mcg/kg/min	Tapering norepinephrine to 0.6 mcg/kg/min	Stop therapy
ICON	7,308 ± 1,519	7,725 ± 1,726	9,708 ± 1,267	9,145 ± 1,277	8,735 ± 1,351	7,793 ± 1,209	5,224 ± 1,834
CO (mL/kg/min)	22,482 ± 4,067	2,425 ± 5,042	31,239 ± 5,705	32,486 ± 3,545	32,865 ± 6,059	31,864 ± 5,611	24,444 ± 7,010
SVR (dyn*s/cm^5)	594,557 ± 24,702	708,165 ± 163,741	481,266 ± 105,566	673,821 ± 68,251	644,866 ± 172,683	625,101 ± 116,867	726,302 ± 174,242
BP (mm Hg)	46/21/29	53/23/33	41/20/27	56/27/37	57/27/37	55/27/36	68/31/43

Abbreviations: BP, blood pressure; CO, cardiac output; ICON, contractility index; SVR, systemic vascular resistance.
Note: Data are expressed as means ± standard deviations.

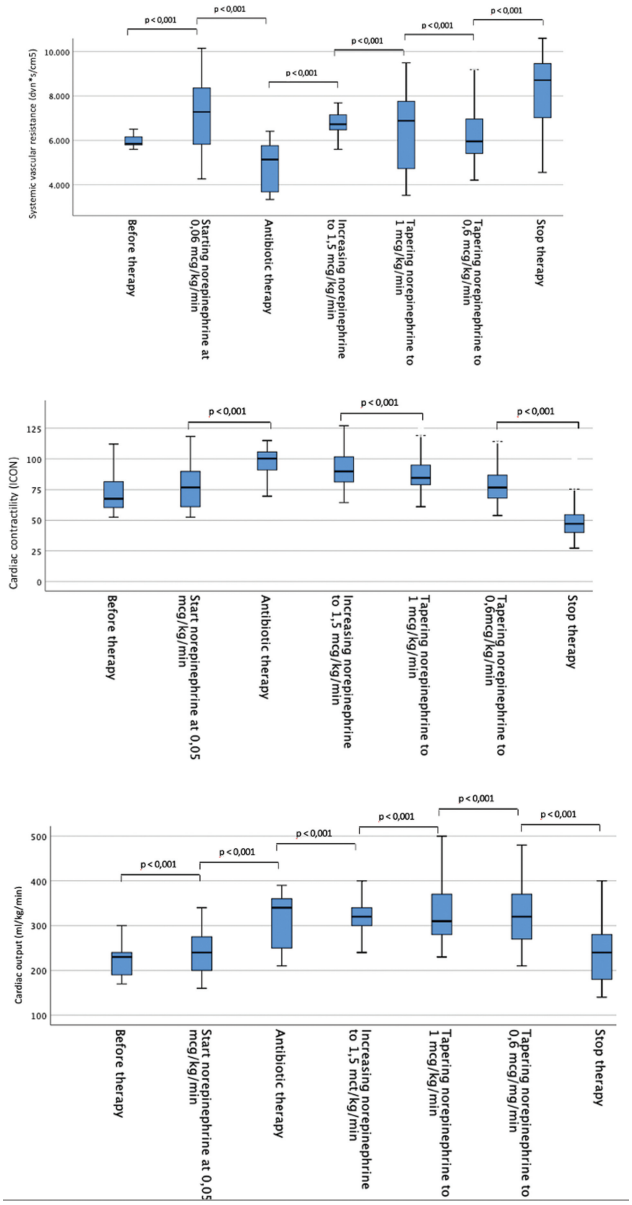

Fig. 1. Graphical representation of differences between cardiac output, cardiac contractility index, and systemic vascular resistance in the different phases of the therapy. Data were analyzed with non-parametric tests, p value was considered significant if $p < 0.001$.

Considering the clinical picture, characterized by low BP (49/21/29 mmHg), and SVR around 5,900 dyn*s/cm^5, CO = 220 mL/kg/min, and ICON of approximately 70 after two normal saline bolus, norepinephrine was started and raised up to 1.5 mcg/kg/min to obtain hemodynamic stability. SVR initially showed a significative increasing trend with increasing BP values (53/23/33 mmHg). However, shortly after, the EC showed a dramatic and statistically significant collapse of SVR (from a maximum of 8,453 dyn*s/cm^5 to a minimum of 3,375 dyn*s/cm^5; ►**Fig. 1**).

A corresponding significative increase in CO (from 2,425 ± 5,042 to 31,239 ± 5,705 mL/kg/min) and ICON (from 7,725 ± 1,726 to 9,708 ± 1,267) occurred as a response to support BP, nonetheless BP was reduced to 41/20/

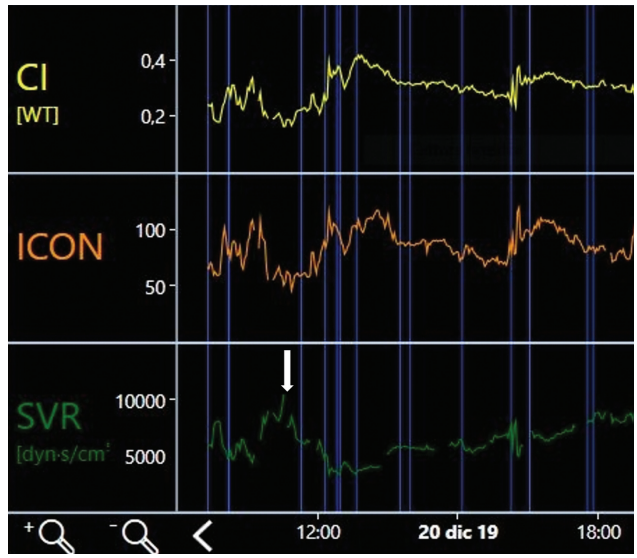

Fig. 2 . Graphical representation of cardiac output (indexed for body surface, CI), contractility index, and SVR trends values over the early hours of interventions. The arrow marks the fall of SVR following antibiotic therapy. Note the contextual rise of interaction context and CI. SVR, systemic vascular resistance.

27 mmHg, despite perfusion maintained adequate as by sufficient capillary refill and diuresis.

The above mentioned, abrupt fall in SVR (►**Figs. 1** and **2**) prompted to increase the dosage of inotropes and occurred immediately after commencing meropenem therapy, hypothetically related to an effect of bacterial toxin release on vascular tone.

Due to clinical and hemodynamic stability, the inotropic support was gradually tapered and suspended after 48 hours, the patient was then extubated and nCPAP was resumed.

Blood culture resulted positive for *Escherichia coli* and antibiotic therapy was carried on for 10 days with full recovery.

Discussion

Our assumption was that continuous hemodynamic monitoring with EC in a patient with septic shock would be helpful in choosing and dosing the appropriate inotrope. The present case report corroborates this assumption, being—to our knowledge—the first ever report of such a use in a neonatal setting.

The use of clinical assessment alone to differentiate between "cold" and "warm" shock and to select the adequate inotropic and vasoactive medications is fraught with errors since this is a dynamic condition that changes markedly overtime. Such subjective classification of shock as "warm" or "cold" was found to be inaccurate, with up to 66% of shock diagnosed as being "cold" shock by experienced clinicians were found to have vasodilation by invasive measurement.[12]

Moreover, as BP is the product of CO × SVR, a decrease in SVR triggers a reactive increase in CO to maintain an adequate BP. A patient with septic shock and still normal BP is not necessarily reassuring as it does not always equate adequate vital organ perfusion.

For the whole of the above-mentioned reasons, continuous hemodynamic monitoring can be useful in guiding the most appropriate cardiovascular medications during management of these critical patients.

In our case, considering patient's clinical condition, good heart function demonstrated by functional echocardiography, low BP, and hemodynamic parameters on EC after two normal saline bolus, the inotrope of choice was norepinephrine for its activity on vascular α-adrenoreceptor stimulation. As reported in the case report section, SVR initially showed an increasing trend with increasing BP values. This supports our hypothesis that we were facing a "warm" fluid refractory shock with low SVR. There are limited studies on norepinephrine therapeutic use in preterm neonatal shock. In one of the few such studies,[13] patients with fluid refractory shock with BP $<$10th centile and urine output $<$1 mL/kg/h were enrolled. The authors concluded that norepinephrine therapy could be considered to improve BP and urine output in these patients.

It is however important to remark that diuresis reduction and BP drop are late results of a series of hemodynamic imbalances that can be highlighted at an earlier stage with EC.

In particular, we have witnessed the drop of SVR a few minutes after the first dose of antibiotic, likely showing that the release of bacterial endotoxins and inflammatory cytokines is responsible for vasodilation in case of gram-negative sepsis. Thanks to real-time monitoring through EC, this abrupt fall in SVR was immediately counteracted at bedside by increasing the norepinephrine dosage to prevent clinical worsening. Similar to previous reports, the need for inotrope support lasted approximately 48 hours.[13]

In conclusion, since variability in inotrope use is more closely associated with local clinician expertise rather than patients clinical and hemodynamic condition, EC can play an important role to give continuously hemodynamic function assessment in newborn with septic shock guiding in the choice of the most appropriate inotrope. It is reasonable to assume that EC may be useful in all those situations where continuous hemodynamic monitoring is necessary, such as perinatal asphyxia, management of patent ductus arteriosus, or congenital heart disease where the altered structure of the heart can make functional echocardiographic evaluation difficult. Therefore, EC can enable timely and targeted interventions to restore the hemodynamic balance in several situations. Continued evidence-based research is necessary to validate specific EC-based interventions in targeted neonatal populations and to clarify the role of EC in improving patient outcomes and if it could be useful also to reduce duration of inotrope support in septic patients.

Funding
None.

Conflict of Interest
None declared.

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