

## Bedside Monitoring of Peripheral Circulation and its Significance in Management of Neonatal Cardiovascular Failure

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Very Low Birth Weight (VLBW) infants are at high risk for developing neurological complications. Circulatory instability, especially during the extrauterine transition, is considered to be a major underlying cause [1-4]. Not a few VLBW infants develop cardiovascular failure during the early postnatal period, and reports indicate that 4%-39% [5] and 16%-98% of VLBW infants and extremely low birth weight infants [6] have been managed with circulatory agents in Neonatal Intensive Care Units (NICUs).

Because several studies have determined an association between hypotension and poor neurodevelopmental outcomes in VLBW infants [7,8], circulatory management in NICUs mainly targets elevating blood pressure. However, data have not been generated from randomized controlled trials to support the notion that treating hypotension positively affects mortality rates or the incidence of IVH among preterm infants [9-11]. Thus, additional or alternative circulatory parameters associated with circulatory management in NICUs are required to improve the prognosis of such infants.

### Why peripheral perfusion should be measured

Cardiovascular failure was defined at an International Consensus Conference (2006) to determine hemodynamic monitoring and implications for the management of patients with shock [12] as a life-threatening, generalized maldistribution of blood flow resulting in failure to deliver and/or utilize adequate amounts of oxygen, leading to tissue dysoxia. According to the formula  $\text{Blood flow} = \text{Blood pressure} / \text{Vascular resistance}$ , elevating blood pressure does not always correspond to an adequate increase in organ blood flow.

These authors suggested that a definition of shock requires not hypotension but rather, physical evidence of inadequate tissue perfusion. They also recommended measuring markers of inadequate perfusion when shock is suspected from historical and physical findings. Because most clinical markers of inadequate perfusion are in fact peripheral, such as skin tone, blood lactate level, and capillary refill time, assessing peripheral perfusion is an important aspect of clinical examinations to determine cardiovascular failure.

### How to Evaluate Peripheral Perfusion

The importance of evaluating systemic blood flow and blood flow to all organs/tissues is being increasingly recognized. Some recent studies have demonstrated correlations between poor outcomes and low blood flow or the hypoperfusion of both vital and non-vital organs in preterm infants [13-15]. Dempsey et al. [16] suggested a correlation between poor outcomes and peripheral hypoperfusion that was comprehensively judged from parameters such as color, heart rate, capillary refill time, urine output, and absolute and temporal change in acidosis during the early neonatal period in preterm infants. The authors showed that the outcomes of hypotensive infants with good peripheral perfusion and normotensive infants did not differ and were better than those of hypotensive infants with poor peripheral hypoperfusion. Thus, they defined the concept as permissive hypotension. Although these findings led to the development of perfusion-oriented circulatory management,

the outcomes should be reconfirmed using more objective methods to generalize such findings among NICUs.

### Conventional Peripheral Parameters

Peripheral hemodynamics has been evaluated using several clinical parameters to manage cardiovascular failure. These parameters include temperature (central-peripheral temperature difference), capillary refill time, acid-base balance, skin color and urine output [17]. Despite their clinical importance, these conventional peripheral parameters are less quantitative, poorly reproducible, rather subjective, easily affected by other factors, and are difficult to continuously evaluate in real time. Several studies have found that these peripheral parameters are poor indicators of cardiovascular failure or low systemic blood flow, at least when the single parameter was assessed.

### Novel Methods of Measuring Peripheral Parameters

Several more objective, real-time, non-invasive methods of measuring peripheral perfusion have been developed, and they are being applied more frequently in research settings.

#### Near-infrared spectroscopy

Near-infrared spectroscopy can measure oxygenated hemoglobin, deoxygenated hemoglobin, and tissue oxygenation index. Changes in total hemoglobin (oxygenated hemoglobin+deoxygenated hemoglobin) represent changes in tissue blood volume. Fractional tissue oxygenation extraction can also be calculated from the tissue oxygenation index and  $\text{SpO}_2$  derived from pulse oximetry. Studies using this method have mainly evaluated cerebral perfusion in neonates, but it has also been applied to evaluate peripheral renal, abdominal [18] and forearm [19] perfusion in adult and in neonates.

#### Orthogonal polarization spectral imaging

Orthogonal polarization spectral imaging can visualize the microcirculation and measure capillary density noninvasively at the bedside. However, the method is unsuitable for continuous monitoring. This modality has demonstrated changes in capillary density in infants with sepsis [20].

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## Peripheral perfusion index

The peripheral perfusion index is calculated from values derived from pulse oximetry that is commonly applied in NICUs. The index is a ratio of the pulsatile (arterial compartment) and the non-pulsatile (other tissues; venous blood, bone, connective tissue) component of the light reaching the detector attached to the device. A low peripheral perfusion index reportedly indicates low peripheral perfusion and it is associated with low superior vena cava blood flow [21].

## Laser Doppler flowmetry

This method can continuously measure blood flow around a probe and in real time. Laser beams penetrate the skin and strike red blood cells in the capillaries, venules and arterioles within a hemispherical area. The beams are then converted into scattered light by frequency variations that are proportional to red blood cell velocity. A photodetector in the probe recognizes the light as electric signals. The relative value of blood flow is calculated from these signals and expressed as mL/100 g/min.

We used a CDF-2000 laser Doppler flowmeter (Nexis, Fukuoka, Japan) to demonstrate physiological changes in skin blood flow in VLBW infants during the extrauterine transition [22] and we found that blood flow in the skin correlated with systemic blood flow [23]. We also found that low blood flow in the skin of the feet at 18 and 24 hours after birth predicted the development of intraventricular hemorrhage [24].

## Research Direction

The routine clinical application of novel peripheral parameters in circulatory management requires further study. Many concerns should be addressed, such as physiological/pathophysiological changes in different types of cardiovascular failure, non-cardiovascular factors that influence the values of these parameters, associations between neurological complications and changes in values caused by circulatory agents. Whether circulatory management that aims to improve perfusion actually improves prognosis should also be determined. Most importantly, these issues should be investigated using not only peripheral parameters but also by simultaneously measuring correlating systemic and brain perfusion.

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