Hemodynamic Assessment and Monitoring of Premature Infants

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KEYWORDS

- Hemodynamic assessment
- Perivable
- Preterm infant
- Hypotension
- Echocardiography
- NICOM
- NIRS

KEY POINTS

- Management of the hemodynamic status of perivable premature infants is challenging owing to the multitude of etiologies and the unique characteristics of the circulatory system.
- There are difficulties in monitoring and identifying hemodynamic compromise and a lack of evidence supporting the current treatment approaches.
- A physiology-based approach to the diagnosis, monitoring and management of low blood flow states in perivable infants is likely to produce the best outcomes.

INTRODUCTION

The cardiovascular care of critically ill preterm infants, particularly around the perivable period, remains a significant challenge in the neonatal intensive care unit for a multitude of reasons. First, the etiologic causes of hemodynamic compromise in this population are heterogeneous; second, the phenotypic presentation is oftentimes modified by the complex physiologic processes that occur during transition from fetal to neonatal life; third, the pharmacologic effects of therapeutic intervention are developmentally regulated; finally, thresholds to guide intervention, predominantly based on mean arterial pressure, lack scientific validation. Consequently, the approach to infants with low blood flow states needs to be individualized. The use of regimented protocols, which usually recommend the administration of fluids followed by stepwise incremental addition of specific cardiovascular agents, without consideration of their...

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biological appropriateness for the active pathophysiologic state, have failed to produce tangible improvements in short- and long-term outcomes. In fact, recent evidence points toward causing harm.\(^1\) Another increasingly recognized challenge is the lack of feasible and robust measurements of systemic blood flow that facilitate the identification of hemodynamic compromise. The overreliance on blood pressure, which is a poor surrogate for systemic blood flow, may result in both overtreatment and undertreatment of infants in certain physiologic situations. Although methods for intermittent and/or continuous monitoring of cardiac output and systemic blood flow are becoming increasingly used, the unique physiologic environment of preterm infants (with the persistence of fetal shunts) add further challenges to using those methods. There remains a lack of reliable data on normal blood pressure and cardiac output values in the neonatal population during the early transitional period and beyond. Identification of thresholds or clinical scenarios where hemodynamic intervention may modify patient outcomes represents the most important challenge for neonatal intensivists. Relevant to the clinical decision making process are the active disease state, phase of physiologic transition, and competing interventions, yet these are often not considered.

**TRANSITIONAL PHYSIOLOGY: CARDIOVASCULAR AND PHYSIOLOGIC CONCEPTS**

The transition from fetal to neonatal life is accompanied by important physiologic changes in the circulatory system: There is a significant increase in systemic vascular resistance (SVR) resulting in an increase in left ventricular (LV) afterload. This increase is a consequence of the loss of low resistance placental circulation, and a surge in vasoconstrictor substances including vasopressin (through vasopressin receptors, which increase intracellular calcium release and upregulate adrenaline receptors) and thromboxane A\(_2\) (a potent vasoconstrictor).\(^2\) In addition, there is a decrease in pulmonary vascular resistance (PVR) as a consequence of pulmonary arterial vasodilatation. This decrease is facilitated by the increase in the partial pressure of oxygen accompanying lung aeration, and the increased production of potent pulmonary arterial vasodilators including prostaglandins, bradykinins, and histamine.\(^3\) The increase in SVR and decrease in PVR redirects right ventricular output from shunting across the ductus arteriosus (and supplying the brain) toward the pulmonary vascular bed (to supply the lungs). This is a crucial step during the early transition, which ensures that LV preload (which was derived from the placental circulation during fetal life) is maintained by adequate pulmonary venous return. The maintenance of adequate LV preload is essential for sustaining an adequate LV output (LVO) in the face of a rising LV afterload. Consequently, right ventricular preload becomes dependent on systemic venous return, and right ventricular afterload remains low owing to decreasing PVR (Figs. 1 and 2).

The additional effects of the timing of cord clamping after birth need to be considered as an important part of the transitional process. The placenta is thought to hold 30% to 50% of the fetal circulating volume at any one time; therefore, early clamping of the cord may result in a significant reduction of LV preload and effective LVO. This is a consequence of the reduction in blood flow to the left atrium from the placental circulation, which is not restored effectively until pulmonary flow blow is established.\(^4\) Deferring cord clamping until the infant begins to breath and establish pulmonary blood flow may result in fewer fluctuations in LVO by ensuring the maintenance of LV preload (from the placental circulation) until pulmonary venous return takes over.\(^5\) Knowledge of the approach taken in a particular infant (early or deferred clamping of the umbilical cord) will help with the individualized approach to managing that particular infant if a low blood flow state is identified.
The persistence of fetal shunts can add further complexity to the transitional circulation and may contribute to the evolution of hemodynamic compromise. During normal transition, the increasing left atrial pressure results in closure of foramen ovale flap with abolition of transatrial flow. In addition, owing to the increasing SVR and decreasing PVR, flow across the ductus arteriosus becomes exclusively left to right within the first 24 hours of life. The increase in oxygen tension, and decrease in prostaglandin levels postnatally, followed by local atherosclerotic-like processes within the ductal wall results in an arrest in flow across the ductus, usually within 48 hours.5,6

Fig. 1. The fetal circulation. See text for further details. LA, left atrium; PFO, patent foramen ovale; PVR, pulmonary vascular resistance; SVR, systemic vascular resistance.
Important Considerations in Preterm Infants

The periviable preterm infant is faced with additional challenges that increase the risk of hemodynamic compromise, especially during the early transitional period. The myocardium of the preterm infant possesses an inefficient contractile mechanism (impaired systolic performance) and a preponderance of noncontractile, poorly compliant collagen, leading to impaired diastolic performance (Fig. 3). In addition, owing to the relatively faster heart rate of preterm infants, the percentage of time spent in diastole (the time of LV filling) is considerably shorter. As a result, it is poorly tolerant of increased afterload, and lacks the necessary reserve to cope with reduced preload, both of which are common occurrences during the transitional period as outlined. In addition to those challenges, preterm infants exhibit a high resting peripheral vascular resistance.

Fig. 2. Circulation during early postnatal life. Ca++, calcium ions; cGMP, cyclic guanine monophosphate; COX, cyclooxygenase; LV, left ventricle; NO, nitric oxide; PVR, pulmonary vascular resistance; RA, right atrium; SVR, systemic vascular resistance.

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tone owing to the relatively higher concentration of vasoconstrictive (alpha) receptors at the expense of vasodilatory (beta receptors). The myocardium on the other hand lacks adequate adrenergic innervation limiting its ability to increase contractility (inotropy). Furthermore, preterm infants are unable to increase glucocorticoid production in response to stress owing to the underdeveloped hypothalamic–pituitary–adrenal axis. In combination, these factors limit the ability of the preterm myocardium to respond to inotropes, which generally result in a predominant vasopressor effect in this population. Finally, left-to-right shunting across a patent ductus arteriosus (PDA) and a patent foramen ovale (PFO) may further compromise systemic blood flow and effective cardiac output by short circuiting blood to the lungs (pulmonary overcirculation) at the expense of the systemic circulation (systemic hypoperfusion).

Preterm infants around the periviable period may be particularly vulnerable to the effects of left-to-right shunting associated with a significant PDA. Left heart diastolic function may play a key role in handling the increased blood volume returning to the heart. In the setting of compromised diastolic function, the increased pulmonary venous return to the left atrium may result in increased left atrial pressure and eventual pulmonary venous congestion. This process may explain the higher incidence of pulmonary hemorrhage in this population. Another important factor that compromises cardiac output is positive end-expiratory pressure. Infants born around the perivable period are more likely to have reduced respiratory drive at birth coupled with poor lung compliance and reduced thoracic wall muscle strength, resulting in a significant need for positive pressure support. Recent recommendations to maintain a relatively higher positive end-expiratory pressure may result in reduced cardiac output.

Increased airway pressure may lead to compression of the intraalveolar capillaries, increased PVR, and a reduction in effective pulmonary blood flow, pulmonary venous return, and LVO. This may occur with all modes of mechanical ventilation.

Neonatal sepsis may also modulate hemodynamic change, particularly during the transitional period. Sepsis in term infants is associated with a decrease in both systolic...
and diastolic function, measured using the myocardial performance index and pulsed wave Doppler studies of the mitral inflow. In addition, tissue Doppler–derived myocardial velocities reveal that both LV and right ventricular function are reduced in the presence of confirmed sepsis; nonsurvivors of neonatal sepsis have significantly higher troponin levels when compared with survivors. Group B Streptococcus is a leading cause of early neonatal sepsis and induces myocardial injury through a cytotoxin (beta-hemolysin/cytolysin), which has deleterious effects on cardiomyocyte viability, contractility, and calcium exchange. In addition to the direct myocardial effects, neonatal sepsis has a global effect on the cardiovascular system with the persistence of pulmonary arterial hypertension and an elevated SVR being the hallmarks of early disease (cold shock). Infants with Escherichia coli infection and other gram-negative organisms may present earlier with vasoactive shock (warm shock). The mortality in neonatal sepsis remains high. A similar pattern is observed in necrotizing enterocolitis, which can also result in vasoactive shock owing to the release of cytokines and the alteration in endothelial function.

Importance of Low Blood Flow States on Neonatal Outcomes

The rationale to correct hypotension and low blood flow states stems from their association with adverse outcomes. Hypotension during the early transitional period (defined as the lower mean arterial pressure over the first 24 hours) is associated with adverse outcomes including severe intraventricular hemorrhage, chronic lung disease, and death. However, several studies have also demonstrated that treatment of hypotension (irrespective of blood pressure) is also independently associated with death and significant neurodisability. Similarly, a low LVO and superior vena cava flow (surrogate markers for systemic blood flow) are also associated with adverse short- and long-term outcomes, including severe intraventricular hemorrhage and neurodisability. Correction of low blood flow states in an attempt to avoid those important outcomes has not been studied systematically. The continued uncertainty regarding the association between hypotension (and its treatment) with adverse outcome highlights the need for reliable and valid methods for monitoring the hemodynamic status of periviable infants. This information will enable more robust trials on interventions to be implemented with the aim of reducing those adverse outcomes.

CURRENT METHODS OF HEMODYNAMIC ASSESSMENT

The complexity of the pathophysiologic processes that contribute to hemodynamic compromise highlights the fact that no one marker, in isolation, can be reliably used to characterize the degree of compromise. However, a holistic appraisal of all the clinical and laboratory measures of cardiovascular homeostasis, in addition to the use of imaging modalities (such as echocardiography), may provide a more complete and accurate picture of the cause of hemodynamic instability and offer a possible therapeutic approach. Commonly used markers include heart rate, blood pressure, and capillary refill time in addition to measures of end-organ functionality (urinary output, muscle tone, and the level of consciousness) and laboratory parameters such as arterial pH, lactate, urea, and creatinine.

Heart rate is an important determinant of cardiac output. However, stroke volume may play a more important role in maintaining cardiac output; recent data suggest that the increase in LVO seen soon after birth is a result of an increasing stroke volume rather than heart rate. The value of elevated heart rate as a marker of hemodynamic instability, particularly in the setting of hypovolemia, needs to be considered in the context of confounders; specifically, these include pain, fever, caffeine...
use, anemia, and arrhythmias. Capillary refill time, as a sign of hemodynamic compromise, is also very unreliable, and does not indicate the adequacy of blood flow to internal organs. Although prolonged capillary refill time is associated with low blood flow, the correlation with echocardiography measurements of cardiac output is loose at best. The assessment of renal perfusion in the early neonatal period is fraught with challenges. Urine output may indicate reduced renal perfusion in the absence of other pathologies (renal parenchymal disease and obstructive uropathies). Relative oliguria, may be normal in premature infants owing to renal tubular immaturity. Urine function tests may not reflect true neonatal renal function especially if taken within the first 24 hours of life. Anaerobic metabolism as a consequence of poor perfusion may lead elevated plasma lactate levels; however, its interpretation must be in combination with other markers of reduced perfusion. For example, an elevated lactate in isolation may be a consequence of increased glycogenolysis and inborn errors of metabolism. There may also be a delayed increase in serum lactate levels because poorly perfused areas will not mobilize the produced lactate until after adequate blood flow is restored. The relative time lag between the onset of shock and the change in those markers as outlined can make their clinical use less helpful.

### A Focus on Blood Pressure

Mean blood pressure is most common bedside measure used by clinicians as a measure of the adequacy of perfusion in the neonates. The appeal stems from the relative simplicity of the measurement (both invasive and noninvasive) and its continuous nature. Theoretically, this enables care providers to monitor for hemodynamic compromise when it arises, and to monitor treatment response once therapy is instituted. However, there are several limitations to the current approach of the use of blood pressure to monitor and treat low blood flow states in preterm and term infants. Those limitations include a lack of robust normative dataset in both term and preterm populations, the dissociation between blood pressure and systemic blood flow when SVR is not taken into account, and the overreliance on mean blood pressure rather than the more important components of the measurement (systolic and diastolic blood pressures).

The definition of systemic hypotension is highly controversial, with several iterations currently in use. This lack of uniformity stems from the relative lack of a clear threshold below which autoregulation is impaired and organ perfusion (and cellular metabolism) are compromised. In fact, a single threshold may not even exist because it is likely to vary across different gestations, physiologic phases, and disease states. In practical terms, clinicians generally use 1 of 3 thresholds to define hypotension. The most widely used definition of hypotension is unfortunately the one with the least amount of supportive evidence: a mean blood pressure in mm Hg below the numerical gestational age of the infant in weeks. This arbitrary definition, although easy to remember, is not useful for identifying low blood flow states owing to the nonlinear and inverse relationship between these parameters. Another threshold, used to define hypotension, is a mean blood pressure of less than 30 mm Hg. This cutoff is based on small studies that suggest there is a loss of cerebral autoregulation and cerebral white matter damage below this threshold. There are, however, a lack of studies demonstrating any benefit to institution of treatment, using either inotropes and/or vasopressors, to correct blood pressure above those thresholds. A less commonly used approach to define hypotension that has recently been advocated is the use of normative centiles, derived from a large population set, of systolic and diastolic blood pressures. This approach may be a more appropriate method of screening for potential hemodynamic compromise, especially when blood pressure falls below...
the third centiles for any given gestation; however, this approach is yet to be assessed systematically.

Appraisal of the relationship between blood pressure and cardiac output (systemic blood flow) must consider the SVR because blood pressure is proportional to the product of cardiac output and SVR (blood pressure = cardiac output × SVR). A normal arterial pressure in the setting of a high SVR is usually accompanied by low cardiac output (such as infants with hypoxic ischemic encephalopathy). Conversely, a low blood pressure in the setting of low SVR may indicate normal or high cardiac output (such as infants with warm shock). As there are no ways to directly measure SVR in neonates, all assumptions are implied.

Considering blood pressure by its 2 distinct components, systolic and diastolic, may lead to a more physiologic basis for diagnosis and treatment of low blood flow states. Systolic blood pressure may reflect LV contractile force and effective cardiac output; therefore, a low value may indicate reduced stroke volume (which is influenced by preload, contractility, and afterload). Conversely, diastolic blood pressure may be more reflective of resting vascular tone (SVR) and intravascular blood volume (fluid status). Combined systolic and diastolic hypotension may be reflective of circulatory system failure, which may or may not have antecedent systolic or diastolic hypotension in isolation. The physiologic impact of therapeutic intervention, based on these thresholds, and its relevance to neonatal outcomes needs prospective evaluation.

ENHANCED METHODS FOR ASSESSMENT OF THE HEMODYNAMIC STATUS

The limitations of clinical and laboratory indices support the need for a more comprehensive approach to the monitoring of hemodynamic status of sick neonates, identification of states of hemodynamic compromise, and evaluation of treatment response. Several new modalities have emerged over the last 15 to 20 years and are becoming increasingly used in daily clinical practice.

Neonatal Echocardiography

The use of echocardiography to evaluate cardiovascular well-being in neonates is common in many tertiary neonatal intensive care units. When used in combination with clinical findings (to place the examination in context), neonatal echocardiography may be an invaluable tool for the identification of hemodynamic compromise, guiding therapeutic intervention, and monitoring treatment response. Over the last decade, there has been an increasing use of echocardiography performed by neonatologists around the world. Neonatal echocardiography is most commonly used for the assessment of PDA significance, determining treatment benefit, and confirming PDA closure after treatment; the prediction and management of hemodynamic instability after PDA ligation in preterm infants; assessment of myocardial performance and monitoring treatment response in neonates with persistent pulmonary hypertension of the newborn and hypoxic ischemic encephalopathy; and the assessment of central line positioning. There are an increasing number of prospective studies that highlight the potential merits of neonatal echocardiography in identification of cardiovascular compromise and guiding neonatal cardiovascular care. Regular use of echocardiography in the neonatal setting can lead to tangible improvement in the provision of care. Regular daily echocardiography once indomethacin treatment is instigated for PDA closure results in a reduction on the number of indomethacin doses given (and exposure to potential adverse effects) without increasing the number of treatment failures. In addition, the use of echocardiography to provide targeted PDA treatment may result in a reduction of severe
intraventricular hemorrhage and pulmonary haemorrhages.\textsuperscript{51,52} For neonates undergoing PDA ligation, echocardiography is now used to identify potential infants at risk of hemodynamic compromise after the procedure and provide targeted therapy to avoid this compromise with significant success.\textsuperscript{14,45} A detailed description of the use of echocardiography in various clinical scenarios in the preterm neonatal setting and its use to guide therapy has been described in detail by our group previously.\textsuperscript{36,40} There is a clear need for the systematic evaluation of a targeted approach that guides an individualized treatment regimen of hypotension and low blood flow states and is physiologically based. This is of particular importance to the perivable infant population.

To ensure safe and effective use of this modality in the neonatal intensive care unit, there needs to be structured training programs designed to ensure competency and build clinical expertise in this field. There are currently 3 guidelines in existence with recommendations for training in basic and advanced echocardiography skills, building clinical expertise, maintenance of the acquired skills, and the infrastructure required for the implementation of a successful training program.\textsuperscript{54–56} The only accredited training pathway for neonatal echocardiography currently in existence is the Neonatal Certificate in Clinician Performed Ultrasound, which is run by the Australian Society of Ultrasound Medicine (available from \url{www.asum.com.au}). The relative heterogeneity of these training programs (which is largely explained by the differing training needs across the various jurisdictions) highlights the need for the development of further accredited training bodies that hold the responsibility for training and ongoing maintenance of skills. The introduction of clinical programs should consider local expertise, patient populations, and proximity to pediatric echocardiography service; wherever possible, collaboration with pediatric echocardiography programs should be encouraged.

\textit{Noninvasive Techniques for Monitoring Cardiac Output}

Although there are many advantages to imaging-guided care, the techniques required considerable skill and can only provide discrete intermittent measurements. The ability to provide continuous monitoring of cardiac output and possibly SVR in the neonatal population would be a welcome addition. In older children, and in adults, this can be achieved using thermodilution with a pulmonary artery catheter, an arterial catheter for pulse contour analysis, an intratracheal tube for partial CO\textsubscript{2} rebreathing, or an intraoesophageal probe for continuous Doppler velocity flow assessment. Thermodilution is regarded as the gold standard for continuous hemodynamic monitoring; however, this method is not feasible in the neonates owing to the invasive nature of the technique and the size constrains of the population of interest. Two relatively new noninvasive approaches for continuous monitoring of cardiac output based on the expanded theory of bioimpedance have recently emerged, namely, transthoracic bioreactance (TBR) and electrical velocimetry (EV).

TBR derives an estimate of stroke volume of the blood ejected from the aorta by measuring the degree of phase shift of an electrical current as it traverses the thorax (rather than measuring the attenuation of amplitude—bioimpedance). The system contains an algorithm that uses the degree of phase shift to derive stroke volume. Cardiac output can be derived by multiplying stroke volume by the heart rate. Interestingly, TBR can also be used to derive the SVR when invasive blood pressure readings are known, adding the potential advantage of knowing the 3 components that determine flow. This method has been validated extensively in the adult population against thermodilution with good agreement demonstrated.\textsuperscript{57} TBR also possesses high sensitivity and specificity for predicting significant hemodynamic changes in critically ill
adults, with good precision and responsiveness, in a wide range of intensive care circulatory situations when compared with thermodilution. Validation studies in neonates have focused on comparing this technique with echocardiography. There is a strong correlation between TBR-derived LVO and both stroke volume and echocardiography derived parameters; however, there seems to be a systematic underestimation in TBR-derived values on the order of 30%. TBR may also detect important hemodynamic changes occurring after PDA ligation in preterm infants. Validation in small animal models with stroke volumes comparable to those in neonates (1–3 mL) demonstrated good agreement between TBR and invasive measurement of aortic blood flow. The effect of significant intracardiac (PFO) and extracardiac (PDA) shunts on this technique has not been investigated to date in sick neonates. Current research using TBR is directed at delineating the hemodynamic profile on infants with hypoxic ischemic encephalopathy and persistent pulmonary hypertension of the newborn, with an assessment of the impact of therapeutic interventions on those parameters.

EV is based on the theory that the conductivity of blood in the aorta is higher during systole when all red blood cells are aligned in the direction of flow and lower in diastole when the red blood cells are randomly oriented. The mean rate of change in conductivity may be used to derive aortic stroke volume. There is evidence that EV-derived estimates of cardiac output are comparable with those obtained using echocardiography, with a mean difference of 4 mL/min. This method, however, demonstrates relatively wide limits of agreement ranging between −234 and 242 mL/min, with an adjusted percentage bias of 31.6%. In addition, EV estimates of cardiac output are significantly influenced by a PDA and PFO. The presence of a high-volume shunt across the PDA increased the bias between the 2 methods from −6 to −36 mL/min in 1 study. In another study, a PDA and PFO had a cumulative effect on EV measurements leading to an overestimation of EV-derived values when compared with echocardiography. Further studies are required for both modalities to further demonstrate their potential benefit in the management of the hemodynamic status of neonates before widespread clinical use.

Near Infrared Spectroscopy

Near infrared spectroscopy (NIRS) offers the ability to assess target organ blood flow. It offers additional information regarding organ perfusion, which supplements data provided by echocardiography and other modalities. The use of NIRS to assess cerebral perfusion is also subject to scientific adjudication. Early studies from adults demonstrated the benefit of NIRS in measuring cerebral perfusion during therapeutic hypothermia after cardiac arrest and during cardiac surgery. Cerebral NIRS may also possess important prognostic abilities after cardiac arrest in adults. Some of the first studies of NIRS in neonates also examined its use after cardiac surgery.

In preterm infants, NIRS-derived fractional tissue oxygen extraction and regional cerebral oxygen saturation reference values, particularly over the first 72 hours of life, are emerging. NIRS may provide novel insights into the effect of various disease states on end-organ flow. Recently, the use of NIRS was studied in infants with a hemodynamically significant PDA and demonstrated a decrease in regional cerebral oxygen saturation when a PDA persisted. NIRS can also be used to assess regional saturations and fractional tissue oxygen extraction in the splanchnic vasculature with evidence, suggesting that this technique may be able to distinguish between complicated and uncomplicated necrotizing enterocolitis. However, one of the most exciting uses of NIRS is its use in guiding the treatment of potential hemodynamic compromise and cerebral hypoxia in the preterm population. In a multicenter,
randomized, controlled trial, infants monitored with NIRS and treated for evolving cerebral hypoxia had a lower cerebral hypoxic burden when compared with infants who were not treated based on NIRS findings.75,76 The long-term benefit of this approach has yet to be elucidated. The role of NIRS as an ancillary monitoring device to support cardiovascular decision making in the neonatal intensive care unit is yet to be elucidated and should remain an investigative tool.

**Cardiac MRI**

Cardiovascular MRI, using balanced steady-state free precession, has been used recently in preterm infants to provide a more accurate delineation of myocardial volume, function, dimension, and flow across important shunts, such as a PDA. It has been validated recently in the neonatal population.77,78 Its use in the preterm population remains in the research area at present, but this technique may provide novel insights.

**A PATHOPHYSIOLOGY-BASED APPROACH TO THE MANAGEMENT OF LOW BLOOD FLOW STATES**

Advances in neonatal intensive care, coupled with our enhanced understanding of preterm infant transitional physiology and the introduction of the enhanced methods of assessment as outlined, can pave the way for a more holistic approach to the management of low blood flow states and hypotension. Periviable preterm infants, with their inherent challenges, are the population most likely to benefit from this approach. The principles of this approach include a more objective assessment of the cardiovascular system as a whole, including a focus of target organ flow. This objective assessment needs to be performed on a continuous basis during the critical transitional period. This monitoring will enable a targeted and tailored approach to each physiologic situation (Fig. 4).

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**Fig. 4.** The complexity of comprehensive monitoring of the hemodynamic status of periviable infants. ECHO, echocardiography; LV, left ventricular; NICOM, noninvasive cardiac output monitoring; NIRS, near infrared spectroscopy; SVR, systemic vascular resistance.
Treatment of low blood pressure in isolation may not necessarily translate into an improvement in systemic blood flow, because many cardiotropic agents (eg, dopamine) act by increasing SVR but at the expense of cardiac output. This approach does not take into account the maturity of the infant, the underlying cause, the presumed physiology, or other potential iatrogenic influences on systemic blood flow, including other medications, mechanical ventilation, or the presence of a PDA. There is limited evidence supporting the use of current therapeutic agents. Rather, the ultimate goal of treatment should be to maintain adequate oxygen delivery and tissue oxygenation to ensure normal cellular metabolism and not “normalizing” the blood pressure. Other factors influencing the adequacy of cellular oxygen delivery include hemoglobin and oxygen saturation, as well as factors influencing myocardial performance. Oxygen consumption should also be minimized by ensuring adequate sedation if necessary, pain control, and normothermia. A suggested approach to management is summarized in Fig. 5.

![Fig. 5. Physiology-based approach to management of low blood flow states. BP, blood pressure; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; PPHN, persistent pulmonary hypertension of the newborn; SVR, systemic vascular resistance.](image-url)
SUMMARY

Preterm infants, particularly infants around the periviable period, provide a considerable challenge in the management of hemodynamic compromise. The pathophysiology and etiology is varied and depends on a variety of antenatal factors, transitional events, and postnatal stressors. This variation has precluded the benefit of a standardized approach to management. Individualized care is likely to be the most appropriate pathway to ensure optimal outcomes. To achieve this care and devise an initialized approach, reliable, precise and valid methods are needed to offer optimal and continuous monitoring.

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