

# Evolution of left ventricular function in preterm infants: long-term significance

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The hemodynamic changes during the transition from fetal to neonatal circulation are probably the most significant and drastic adaptation in the human life.<sup>1</sup> These changes are well studied in term infants. However, the transition from fetal to neonatal circulation in preterm neonates is poorly understood. Preterm infants, especially extremely preterm ones, have immature myocardium with inherently impaired diastolic function at birth. Any subsequent impairment of myocardial function during the transitional circulation may increase the risk of hemodynamic instability. Therefore, understanding the transitional physiology and cardiac function is of paramount importance in managing preterm infants with hemodynamic instability.<sup>1</sup>

The transition process from fetal to neonatal circulation may be more challenging in preterm infants because of the following factors: 1) impaired myocardial performance due to immature myocardium possessing an inefficient contractile mechanism leading to inherited impaired cardiac functions; 2) higher incidence of persistent shunting across the patent ductus arteriosus, which plays an important role in cardiovascular physiology and affects cardiac functions; 3) limited ability to increase heart rate to increase cardiac output; 4) increased cardiac demand from higher baseline heart rate; and 5) premature myocardium may lack adequate adrenergic innervation and underdeveloped hypothalamic–pituitary–adrenal axis. Therefore, preterm infants may have limited ability to increase cardiac output during adverse adaptation and they may show inadequate response to stressful situations.<sup>1-3</sup>

Recently, there has been a great interest among clinicians to acquire skills in neonato-

logist-performed echocardiography, which can be used to understand cardiovascular physiology at the bedside.<sup>4-6</sup> In the last decade, the understanding of transitional physiology in preterm infants has vastly improved.<sup>4</sup> However, there are scarce data on the evolution of cardiac function in preterm infants during the neonatal period.

Bokiniec et al<sup>7</sup> have recently described the echocardiographic assessment of left ventricular (LV) function in term and preterm infants at 40 weeks of postconceptional age. They found preterm infants to have preserved systolic and diastolic function of the left ventricle at 40 weeks of postconceptional age. However, in comparison with term infants, preterm neonates, after their transition to neonatal circulation, had significantly reduced myocardial thickness, lower myocardial performance index, and low cardiac output.<sup>7</sup> The progression and impact of these significant changes during childhood and adult life are poorly understood.

There is a growing body of evidence from studies on adults showing that preterm infants have a higher risk of adverse cardiovascular events and heart failure during early adulthood.<sup>8,9</sup> The findings from these recently published studies are astonishing. They reinforce the importance to understand the cardiovascular physiology in preterm infants during transition to neonatal circulation and early childhood. A better understanding of cardiovascular physiology and evolution of cardiac function may help elucidate the impact of ex utero interventions on the premature myocardium and develop strategies to reduce the risk of adverse cardiovascular events during childhood and adult life.

From animal studies on cardiac modeling in preterm infants, Bensley et al<sup>10</sup> concluded that

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preterm birth leads to remodeling of the myocardium that alters its final structure. This may program the premature myocardium for the long-term cardiac vulnerability. In a human longitudinal study using serial echocardiography, Aye et al<sup>11</sup> reported that preterm infants have a disproportionate increase in ventricular mass from birth up to 3 months of postnatal age, and they suggested that early postnatal development may provide a window for interventions relevant to long-term cardiovascular health. Similar findings have been published by Cox et al.<sup>12</sup> who used cardiac magnetic resonance (CMR). They demonstrated significant differences in LV geometry between preterm infants at term-corrected age and term controls. They concluded that computational CMR demonstrates that significant LV remodeling occurs soon after preterm delivery and is associated with definable clinical situations. This suggests that targeted neonatal interventions could reduce long-term cardiac dysfunction.<sup>12</sup>

With advance in technology and echocardiographic techniques, it is possible to understand cardiovascular physiology at the bedside, and cardiac function can be reliably assessed even in preterm infants. It may help predict medium- to long-term prognosis. Czernik et al<sup>13</sup> demonstrated that preterm infants who developed bronchopulmonary dysplasia had significant cardiac deformation changes on day 1 and day 7 after birth on speckle-tracking echocardiography. They also concluded that serial speckle-tracking assessment is possible in preterm infants with low intra- and interobserver variability.

Echocardiography can help evaluate hemodynamics in neonates and children, and it may be reliably used at the bedside in the neonatal intensive care unit to assess cardiac output, cardiac function, presence of shunts and their hemodynamic significance, as well as pulmonary and systemic vascular resistance. Serial echocardiography may help evaluate the impact of interventions on the cardiovascular physiology.<sup>14</sup> In the last decade, there has been a tremendous interest in using neonatologist-performed echocardiography to gain physiological information and assess hemodynamic parameters for clinical decision making in sick neonates. Targeting therapy on the basis of altered cardiovascular physiology affecting hemodynamics and cardiac function, and monitoring response to intervention may help deliver individualized high-quality care to preterm infants with hemodynamic instability.<sup>15</sup>

In summary, the transition process from fetal to neonatal circulation in preterm infants is complex, and it can be more challenging in extremely low-birth-weight infants with hemodynamic instability. Despite preserved systolic LV function at 40 weeks of postconceptional age, preterm infants continue to have significant

differences in their myocardium and cardiac function at term-equivalent age when compared with term infants. Preterm infants have a higher risk of adverse cardiovascular events and heart failure in early adulthood. Bokinić et al<sup>17</sup> studied LV function at term-equivalent age in preterm infants. However, there is an urgent need for longitudinal studies to understand the evolution of cardiac function and myocardial changes in preterm infants from birth to early adulthood, to understand the preterm transitional physiology precisely, and to identify which interventions can alter the adverse physiology favorably to decrease the long-term cardiovascular risk in these populations.

## ARTICLE INFORMATION

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