Editorial

Left ventricular dysfunction in the newborn

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Introduction

Any ill baby is of concern to all. With the advent of non-invasive echocardiography increasing attention is being directed towards the understanding of left ventricular (LV) dysfunction in the newborn. What are the causes and how are they best recognised? At the outset it would be helpful to review the physiological changes at birth so as to understand the mechanisms whereby the left ventricle takes on a substantial increased workload soon after birth.

Neonatal transition

Point of Care Ultrasound (POCUS) is providing further information about newborns as they transition from an intrauterine existence (1). The vast majority of neonates traverse this transition on their own with little or no external assistance (2). In the normal infant breathing commences, the lungs expand with alveoli aeration and pulmonary vascular dilatation, dramatically dropping the pulmonary vascular resistance and diverting blood away from the ductus into the pulmonary circuit (1). That in turn raises the left atrial pressure causing the flap valve of the foramen ovale to shift to the right closing off the substantial atrial defect, further aided by the loss of the umbilical venous return via the ductus venosus into the inferior vena cava and right atrium as the umbilical cord is ligated (3). At the same time there is a rise in the systemic venous resistance as a result of the clamping of the umbilical arteries with loss of the large placental bed. Almost immediately the LV afterload increases substantially while the fetal dominant right ventricle begins to gradually lose its muscle mass as its afterload progressively decrease with a fall in the pulmonary vascular resistance over the next few weeks to months (4). In addition with the initial few breaths of the infant and the resultant dramatic fall in the pulmonary vascular resistance, the ductus arteriosus now begins to shunt left to right. It previously acted as a "pressure valve" whereby the right ventricle ejected close to 90% of its output via the patent ductus into the descending aorta which in turn supplied the placental bed via the umbilical arteries coming off the common iliac arteries. The duct now begins to constrict and with the drop in the pulmonary vascular resistance, shunts left to right into the pulmonary circuit until such time, varying from a few hours to a few days and occasionally a few weeks to months it closes initially functionally, and then in most cases permanently (5).

LV dysfunction in the immediate post-natal period

How well does the left ventricle cope with a dramatic

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increase in its function now sustaining all of the newborn's systemic circulation? Vijayashankar and colleagues (6) have penned an elegant paper drawing attention to a group of infants who were shown to have LV dysfunction as evidenced by cross-sectional echocardiograms, carried out to investigate newborns presenting with cyanosis, and/or hypotension, respiratory distress etc. None of the newborns presented with features suggestive of cardiac failure. Two-thirds out of their cohort of 19 neonates did not have an apparent underlying cause. Their study sample was derived from reviewing the database of echocardiograms done at their respective hospitals selecting out those infants that were found to have LV dysfunction as defined by a fractional shortening <28% or an ejection fraction <50% on M-mode measurements, or reduced function reported by a cardiologist. Excluded were babies who were asphyxiated, premature or had a structural heart abnormality. That this was potentially a seriously ill cohort was apparent in that 18 out of the 19 infants required care in the intensive care ward or special care nursery. Three infants died, those with marked LV dysfunction. The causes in each of them subsequently became apparent—one with an inborn error of metabolism, one with fulminating *E.coli* infection and a third with an enterovirus viraemia.

Of note, all the survivors except for 2 had recovery of their LV function within 2 weeks. Two thirds of the infants were male, 2 out of the 19 were small for gestational age while 4 of the mothers where the aetiology of the LV dysfunction was unclear, were on recreational drugs. Specific causes were found in 6 patients, 2 with early onset neonatal infection, 1 with an inborn error of mitochondrial metabolism, 1 with Barth's syndrome and 2 with arrhythmias.

Of interest, Vijayashankar *et al.* (6) did not include 15 newborns with structural heart disease and 11 with perinatal asphyxia who also demonstrated LV dysfunction as that was not the thrust of their review. It may however be prudent have to look at which babies may go on to develop LV dysfunction so that a timely diagnosis may be made allowing for appropriate interventions and treatment. When would one consider the possibility of LV dysfunction in the newborn?

Prenatal predictors

Most women in established centres have routine fetal ultrasounds. It not only provides information related to the wellbeing of the fetus by reviewing their somatic growth and physiological markers but also provides considerable information about ventricular function and anatomy (7). As the earlier paper suggested (6), small for dates infants are more likely to develop cardiac dysfunction, though that is rarely manifest in utero (8). Signs of ventricular failure may be evident by ventricular enlargement and poor ventricular contractility. In the more severe cases atrioventricular valve incompetence and the development of a pericardial effusion with a "rocking" movement of the ventricles may become apparent. In severe cases of cardiac failure a hydropic fetus may be seen with pleural effusions, ascites and scalp oedema, all of which may be ominous signs of possible intrauterine death. In addition to the morphological changes, multiple abnormal Doppler indices have been described by Davey *et al.* who have extensively reviewed the causes, diagnosis and management of fetal cardiac failure (9). Cardiac failure may arise from a cardiomyopathy whether familial, dilated or hypertrophic (10).

Intrauterine viral infections such as due to Parvovirus or Coxsackie virus may cause a fetal myocarditis leading to a dilated cardiomyopathy and progressive cardiac failure (8). Parvovirus may also lead to severe anaemia (11), which may also be caused by alloimmunization from Rh incompatibility or a genetic haemoglobinopathy (12). Twin to twin transfusion may lead to cardiac failure and fetal demise for both twins—the recipient and donor twin (13). Restrictive or premature closure of the ductus venosus or ductus arteriosus, or a restrictive foreman ovale may lead to cardiac failure, which may manifest in the newborn period if the fetus survived (9). Persistent or recurrent fetal tachyarrhythmias and/or profound bradycardia due to a congenital complete heart block may lead to cardiac failure (14). Large AV fistulae for example in the brain, liver or lung may cause aortic runoff which persists into the newborn period (9).

Finally one needs to consider critical congenital heart disease which may in specialised centres almost uniformally be picked up by fetal scans mid-pregnancy, though may still be missed by screening services (15-17). If a duct dependent pulmonary circulation such as pulmonary atresia or severe Fallot is missed, they present with cyanosis in the newborn usually readily recognised by the clinician. However a duct dependent systemic circulation seen in infants with a tight coarctation of the aorta, hypoplastic or interrupted aortic arch, hypoplastic left heart syndrome, and/or critical aortic valve stenosis, while resulting in early LV dysfunction, may still not be suspected in the newborn if the duct remains wide open (17). The clinician may be prewarned of such an abnormality

though they are not always picked up on fetal scans even in skilled hands (15,18). Finally a history of illicit drug use may also be an important risk factor for the development of LV dysfunction as Vijayashankar *et al.* have noted (6).

Newborn

Aortic runoff

While the majority of neonates who present with early tachypnoea have a respiratory cause, one need be cognisant of those who develop LV dysfunction and cardiac failure from a large aortic runoff, for example as seen in a vein of Galen fistula. The large left to right shunt from the fistula is not dependent on the drop in the pulmonary vascular resistance and therefore may present within the first day or two of newborn life (9,17). Full pulses and a soft, high frequency continuous murmur heard over the temporal region or eye using the stethoscope bell may suggest the diagnosis readily confirmed on imaging.

Critical congenital heart disease

As noted above, left sided congenital heart lesions that are duct dependent may present with acute LV dysfunction and if severe enough will lead to cardiac failure once the ductus arteriosus closes (17). If the duct closes rapidly the infant may develop cardiogenic shock with acute decompensation, hypotension, increasing metabolic acidosis, elevated lactate levels and death, often at times misdiagnosed as due to sepsis. If the duct closes gradually the baby may develop increasing tachypnoea, poor feeding, a blotchy appearance, with somewhat weak pulses once the left ventricle is unable to sustain the increase in cardiac afterload, for example with a tight coarctation, hypoplasia or interruption of the aortic arch or critical aortic valve stenosis. Such findings may also be noted if the left ventricle is marginally small or truly hypoplastic. A prenatal diagnosis if made forewarns the clinicians. Once born the loss of support provided by the right ventricle through the patent duct places the full systemic circulation onto the left ventricle which in turn decompensates (1,17).

Myocarditis

Acute cardiac failure arising from enterovirus or Coxsackie virus needs to be considered in any baby that develops increasing tachypnoea with a poor cardiac output and signs of cardiac failure. The baby may become increasingly unwell and may require extracorporeal membrane oxygenation (ECMO) support in the hope that recovery comes about as highlighted by Vijayashankar *et al.* (6) and noted by others (19).

Bacterial infection

One of the 19 patients earlier described was subsequently diagnosed with a fulminating infection (6). Poor feeding, fever and/or hypothermia, vomiting, a dusky/blotchy appearance and mild tachypnoea warrants further investigation of any neonate, which will include blood cultures ± a lumbar puncture, urine examination, chest X-ray, and monitored by the level of inflammatory markers (20). Early treatment of the infection is mandatory. Any suggestion of poor pulses or hypotension or persistent tachypnoea warrants further investigation including a review of LV function as suggested by Vijayashankar *et al.* (6).

Inborn errors of metabolism

Three infants from their study were found to have inborn errors of metabolism (6), often picked up by the development of tachypnoea associated with a metabolic acidosis. Again there is a need to look at LV function as that may become significantly impaired, even leading to the demise of the infant. Pompe's disease (glycogen storage II) is the archetypal inborn error and needs early consideration especially if the electrocardiogram shows marked LV hypertrophy (21).

Perinatal asphyxia

Vijayashankar *et al.* (6) have drawn attention to perinatal hypoxia as a cause of LV dysfunction. The troponin level rises, there may be electrocardiographic changes, and evidence of reduced LV function and coronary artery flow (22,23). These cardiac findings may be a guide to the associated but less readily assessable hypoxic ischaemic encephalopathy. Of note blood pressure measurements may not necessarily reflect the degree of LV dysfunction (24) which once again raises the importance of POCUS (1).

Clinical features

As highlighted by Vijayashankar *et al.*, the clinical features that might suggest the need for reviewing LV function are often non-specific and include cyanosis, a low or high blood pressure, respiratory distress, an irregular pulse,

Table 1 Echocardiographic parameters evaluating systemic (cardiac and vascular) function

Component of function	Technique	View	Cursor position	Comments
Inter-ventricular septal hypertrophy	M-mode	Parasternal long axis	Distal to mitral valve leaflet tips at end-diastole	Septal thickness indexed to LV posterior wall thickness in diastole
Relative left ventricular dilatation	M-mode	Parasternal long axis	Distal to mitral valve leaflet tips at end-diastole	Wall thickness relative to end-diastolic LV cavity dimension
Fractional shortening	M-mode	Parasternal long axis	Distal to mitral valve leaflet tips at end-diastole	LVEDD-LVESD/LVEDD
Stroke volume	PWD	Apical 5-chamber	Aligned with the flow, sample just beyond aortic valve	Angle and cursor position dependant, LVO = heart rate × stroke volume
Cardiac inflow	2D & PWD	Apical 4-chamber	Use mitral cross-sectional area and trans-mitral Doppler VTI	Include both E and A waves in VTI measurement

LV, left ventricular; LVEDD, left ventricular end diastolic dimension; LVESD, left ventricular end systolic dimension; PWD, pulse wave Doppler; LVO, left ventricular output; 2D, two-dimensional; VTI, velocity time integral.

pre and post ductal saturation differences etc. (6,15). A significant readily heard murmur would make one seek an echocardiogram looking for a congenital heart abnormality. A prenatal diagnosis would also point to the need for further study especially if the baby develops signs of cardiac failure, tachypneoa, a large liver as assessed by the liver span, differential or poor pulses with or without tachypnoea (17,25). A chest X-ray which shows cardiomegaly ± congestion and/or plethora may also be an indicator for further study as well as abnormal pulse oximetry screening (15).

Echocardiographic parameters

What then are the minimal echocardiographic requirements in order to arrive at a diagnosis of LV dysfunction? Few are trained or for the busy clinician, have the time to carry out the extensive examination as formulated by Sehgal and Menahem (personal communication)[1]. LV size and fractional shortening/ejection fraction remain essential. A good M mode would allow for measurement of free wall and septal thickness, LV and to some extent right ventricular size (*Table 1*). Stroke volume and cardiac inflow would also be helpful. The other indices would be dependent on the skill and training of the clinicians and the time available.

Management strategies

Management of LV dysfunction is beyond the scope of this editorial. Suffice to say it will depend on the cause of the LV dysfunction, whether it is to treat a systemic infection, provide inotropic support, consider catheter or surgical intervention for a structural abnormality or just to observe awaiting improvement.

Conclusions

Tachypnoea arising from the many causes of respiratory distress is by far more common than that due to cardiac failure from LV dysfunction (17). While there are multiple features pre and postnatally that may alert the newborn clinician to the possibility of LV dysfunction, many present with non-specific symptoms and signs suggestive of an unwell baby (6). Increasingly neonatal clinicians are being trained and are able to carry out functional echocardiograms (POCUS), rather than relying on the goodwill of their cardiology colleagues. That capability will allow for greater recognition of LV dysfunction which once diagnosed, may lead to timely intervention and improved outcomes. In addition it is prudent to remember that any sick neonate from whatever cause, whether due to an infection, asphyxia etc., warrants an echocardiogram to assess cardiac function.

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