Common Neonatal Cardiac Problems in Neonatal Intensive Care Unit and Role of Targeted Neonatal Echocardiography

Wesam Ahmed, Lotfy Mohamed Elsayed, SoadAbdelsalamShedeed, HeshamSaad Mohamed Ramadan, Mohamed M Shehab

Pediatrics Department, Faculty of Medicine, Zagazig University, Egypt

Corresponding author: Hesham Saad Mohamed Ramadan

Email: heshamsaad198919@gmail.com, **Mobile:**+201006877784

Abstract:

Targeted neonatal echocardiography (TnEcho) is an emerging technique to aid characterization of the hemodynamics of sick neonates in the neonatal intensive care units (NICUs) around the world. Evidence is accumulating which supports the positive impact of TnEcho service on clinical management and patient outcomes.

Keywords:, NICU, Targeted Neonatal Echocardiography, cardiac.

Tob Regul Sci. ™ 2023 ;9(1): 5751 - 5770
DOI: doi.org/10.18001/TRS.9.1.400

Introduction:

The use of targeted neonatal echocardiography (TnECHO) forthe evaluation of the cardiovascular wellbeing is gaining interest.The purpose of TnECHO is to provide physiological informationin real time, in order to support clinical decision making(1).

This approach is designed to enhance clinical judgment, providea better understanding of active physiological processes andmonitor the response to treatment. Combination of clinicalexamination and bedside echocardiography has been shownto improve clinical diagnosis and patient management(2).

Inadult intensive care units, use of trans-esophageal echocardiography is common practice and has been shown tochange the clinical management in up to 30% of patientsbased on the results; in an additional 10% of patients it maydetect severe previously unknown diagnoses(3).

There is someevidence that routine use of TnECHO in the neonatal unitmay lead to identification of cardiovascular compromise,changes in management (4) and potentially improve short-termoutcomes(5).

Suspected PDA:

- Definition and Scope of the Problem:

Although essential for the normal fetal circulation, persistent ductal patency may have significant deleterious effects in preterm or ill term infants. PDAs are found in about half of babies born at less than 29 weeks of gestation and/or weighing less than 800 g and is therefore a common problem encountered in the NICU. Failure of ductal closure, coinciding with the normal postpartum fall in pulmonary vascular resistance, results in a left-to-right ductal shunt. ***(6)***

The consequences may include pulmonary overcirculation and/or systemic hypoperfusion, both of which may be associated with significant morbidity. The clinical impact is dependent on the magnitude of the shunt, comorbid conditions, and the ability of the neonate to initiate compensatory mechanisms. The increased pulmonary flow, and accumulation of interstitial fluid secondary to the large ductal shunt, contributes to decreased lung compliance.***(7)***

The cumulative effects of increasing or prolonged ventilator requirements may increase the risk for chronic lung disease. Preterm infants have a limited capacity for increasing stroke volume in response to increased volume load on the LV myocardium. A large left-to-right shunt increases LV filling pressures, and this might be more pronounced in preterm infants because LV compliance might be lower. The inadequate stroke volume response with the "steal" of blood from the systemic circulation contributes to a decreased systemic perfusion. ***(8)***

A large ductus results in significant diastolic shunting with retrograde diastolic abdominal aortic flow that influences renal and intestinal perfusion. Low diastolic aortic pressure can further compromise coronary perfusion, which is already influenced by increased LV diastolic pressures. All of these hemodynamic complications of a large PDA create significant potential morbidity, including renal insufficiency, necrotizing enterocolitis, intraventricular hemorrhage, and myocardial ischemia. ***(9)***

- Indications for Echocardiography:

If a PDA is suspected on clinical grounds, echocardiography may be indicated. The first study should always be a comprehensive echocardiographic study to exclude associated CHD. This study can be performed by a core TNE-trained person and interpreted by an advanced TNE physician. It is highly recommended that this initial study be reviewed by a pediatric cardiologist. TNE can subsequently be performed to follow either spontaneous closure of the ductus or to assess the effect of therapy on closure. ***(10)***

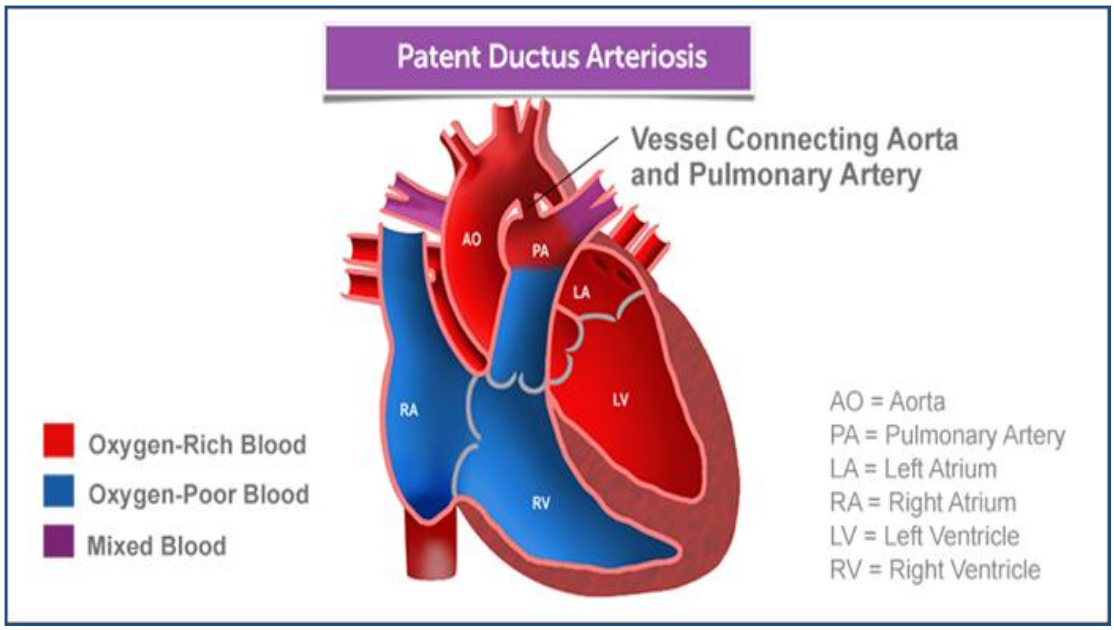

Figure (1): Patent ductus arteriosus. *(7)*

- Imaging Techniques:

The standard full targeted neonatal echocardiographic imaging protocol should be performed in the follow-up of patients with suspected PDA, including the different components. *(6)*

- Guidance of Clinical Decision Making:

Assessment of the hemodynamic significance of a PDA can be performed by combining different echocardiographic measurements.69 These include the following:

- ***Ductal size:***

A minimal ductal diameter more than 1.5 to 2.0 mm is generally considered a hemodynamically significant ductus. *(7)*

- ***Transductal flow:***

The direction and volume of the transductal shunt is dependent on the transductal (pulmonary vs systemic) gradient, which is influenced by the difference between the systemic and pulmonary vascular resistance and by the ductal size. Assessing shunt direction and gradient is important. *(8)*

- ***Left-heart size:***

The quantification of left-heart size reflects the chronic effect of LV volume loading due to the left-to-right shunt through the ductus. LV end-diastolic dimension can be measured on the basis of M-mode or 2D measurements. A dilated left ventricle indicates the presence of a large

shunt. The left atrial/aorta ratio can be used as an indicator of shunt size, with a ratio more than 1.4 indicating a significant left-to-right shunt.*(11)*

- ***Mitral inflow:***

In the presence of a ductal left-to-right shunt, pulmonary venous flow increases, and the rise in left atrial pressure will result in increased transmitral flow (in the absence of a significant atrial left-to-right shunt). Thus, an increase in early mitral inflow velocities can reflect the amount of ductal shunting, assuming the absence of an atrial shunt, mitral valve stenosis, or significant mitral regurgitation. *(11)*

In neonates with large left-to-right shunts, the increased early transmitral flow can result in an E/A ratio more than 1.0. The tracing reverts to the typical preterm E/A ratio less than 1.0 after PDA ligation. However, the measurement is of limited usefulness in isolation and is unlikely to be valuable in the presence of a patent foramen ovale. *(8)*

- ***Ductal "steal":***

A large ductus with left-to-right shunting will result in significant retrograde flow from the thoracic and abdominal aorta. The amount of retrograde diastolic flow may be more than 50% of total aortic flow in neonates with a large ductus. Several indices based on pulmonary, aortic, and peripheral artery flow velocity patterns have been proposed as objective methods in assessment of the magnitude of ductal steal. *(7)*

However, the utility of these indices to predict outcomes needs further validation. At present, only qualitative assessment of the descending aortic pulsed-wave Doppler tracing (for the presence or absence of retrograde diastolic flow) is recommended, because the presence of holodiastolic retrograde flow suggests at least a moderate amount of left-to-right ductal shunting. Early after ductus ligation, some preterm infants become hemodynamically unstable because of acute changes in preload and after-load. TNE can be helpful in determining the underlying mechanism. *(6)*

In every neonate with a clinical suspicion of a PDA, a comprehensive echocardiography study should be performed before medical or surgical treatment to exclude ductal-dependent congenital heart defects and define arch sidedness. Subsequent standard TNE helps in defining the hemodynamic significance of the PDA and is useful in clinical follow-up documenting spontaneous closure or the effect of treatment. In preterm infants with hemodynamic instability after ductus ligation, TNE can be helpful in identifying the cause. *(9)*

Perinatal Asphyxia:

- Definition and Scope of the Problem:

Hypoxic-ischemic encephalopathy is defined by persistent low Apgar scores (0-3) for more than 5 min and profound metabolic or mixed acidosis (pH less than 7.0) on an umbilical cord blood gas. Neonatal neurologic sequelae (e.g., seizures, coma) and multiple-organ involvement is a relatively common occurrence with an estimated incidence of 0.5% to 2% of live births despite modern intrapartum monitoring. ***(12)***

Birth asphyxia is the cause of 23% of all neonatal deaths worldwide. In recent years, there have been several randomized controlled trials investigating the impact of mild therapeutic hypothermia in reducing both morbidity and mortality in these infants.***(13)***

Asphyxia has been shown in several studies to result in clinically significant persistent pulmonary hypertension and in myocardial involvement including clinical, electrocardiographic, echocardiographic, and biochemical changes consistent with ischemic damage in up to two thirds of affected infants. Decreased cardiac output, as a direct result of insult to the myocardium, may significantly complicate perinatal management and contribute to morbidity and mortality.***(14)***

Additionally, therapeutic interventions, including whole-body hypothermia, selective head cooling, and the use of medications such as phenobarbital and midazolam can have additional hemodynamic effects. Therapeutic hypothermia alters systemic and/or pulmonary hemodynamics through increasing vascular resistance and lowering resting heart rate, which reduces cardiac output. ***(14)***

Therefore, assessment and appropriate management of cardiovascular manifestations of asphyxia and treatment, particularly in the setting of clinically evident low cardiac output state, may be helpful to clinicians caring for these patients. TNE may be useful, as data suggest that approximately 30% to 50% of infants with perinatal asphyxia exhibit echocardiographic evidence of ventricular dysfunction, suggested by decreased LV fractional shortening, decreased qualitative RV function, decreased peak systolic annular tissue Doppler velocities, and increased MPI. ***(13)***

- Indications for Echocardiography:

All neonates with clinical evidence of asphyxia should be evaluated for myocardial injury by clinical hemodynamic evaluation and the use of biomarkers for myocardial damage (e.g., troponin). If there is no clinical evidence of cardiovascular compromise and no elevation of biomarkers, echocardiography is unlikely to be useful. ***(12)***

If there are clinical manifestations suggesting poor end-organ perfusion, comprehensive echocardiography may be helpful for identifying possible underlying structural or functional heart disease. If abnormalities are detected, standard TNE can be used to monitor functional recovery and the hemodynamic effects of treatment. ***(10)***

- Imaging Techniques:

The initial study should be a comprehensive study. Follow-up studies should use the standard targeted neonatal echocardiographic imaging protocol. *(14)*

- Guidance of Clinical Decision Making:

Evaluating the effect of therapy: Early (less than 6 hours of life) mild to moderate hypothermia improves survival without disability in moderately to severely asphyxiated infants. Early experience with therapeutic hypothermia reported hypotension and hypertension, vasodilation, bradycardia, and low cardiac output. Several large randomized controlled trials of both whole-body hypothermia and selective head cooling could not demonstrate significant differences between cooled infants and normothermic asphyxiated infants in the degree of hypotension and the need for volume and inotropic support. *(12)*

Although careful mild hypothermia does not seem to decrease blood pressure or impair cardiac function, asphyxia itself may have an effect on both, producing hypotension and poor cardiac output requiring the use of combinations of inotropes, vasodilators, and volume replacement. During the cooling and rewarming phases, the assessment of hemodynamics may be challenging, and there may be a place for the use of TNE in optimizing hemodynamic management. Prospective studies are required to further define normative data and therapeutic thresholds during the cooling and rewarming phases. *(9)*

Comprehensive echocardiography is indicated in neonates with perinatal asphyxia with clinical or biochemical signs of cardiovascular compromise. Standard TNE, including the assessment of LV function, pulmonary hypertension, and ductal shunting, can help in optimizing therapy. The role of TNE in monitoring the cooling and rewarming phases of hypothermia needs further investigation. *(12)*

Neonatal shock and hypotension:

- Definition and Scope of the Problem:

The diagnosis and management of shock in the newborn infant presents many challenges to neonatologists. The determination of the adequacy of overall circulatory well-being remains predominantly subjective, and there are no validated clinical scoring systems available. Despite its many limitations, mean arterial blood pressure remains the most commonly used marker for circulatory compromise. *(15)*

Reliance on mean blood pressure values alone to determine circulatory well-being is an overly simplistic approach to a much more complex problem. A normal blood pressure does not equate to normal end-organ blood flow. There has been a recent move in other areas of medicine to incorporating multimodal monitoring in the management of complex clinical problems, such as neurocritical care. *(16)*

Multimodal monitoring provides the opportunity to overcome some of the shortcomings of each monitoring technique and ultimately achieves more accuracy in determining appropriate interventions. Echocardiography represents an objective tool to assist with the assessment of shock in the newborn infant. Functional echocardiography is rational and non-invasive and may have a very important part to play in the overall assessment and management of newborn shock.*(17)*

Shock is defined as a state of impaired cellular energy (ATP) synthesis when tissue oxygen delivery no longer satisfies tissue oxygen demand.1 In the first phase of shock, perfusion and oxygen delivery is maintained towards the so-called vital organs (heart, brain, and adrenal glands) by selective regional vasodilation in combination with vasoconstriction to non-essential tissues, such as muscles, skin, kidneys, and the splanchnic tissues. *(15)*

This compensated stage of shock is the result of neuroendocrine mechanisms. As the product of cardiac output (which falls) and systemic vascular resistance (which increases), blood pressure actually remains in the normal range in a compensated shock. When this redistribution fails, perfusion and oxygenation of the vital organs will become impaired, resulting in multi-organ dysfunction. It is in this phase of uncompensated shock that systemic hypotension might be expected. *(16)*

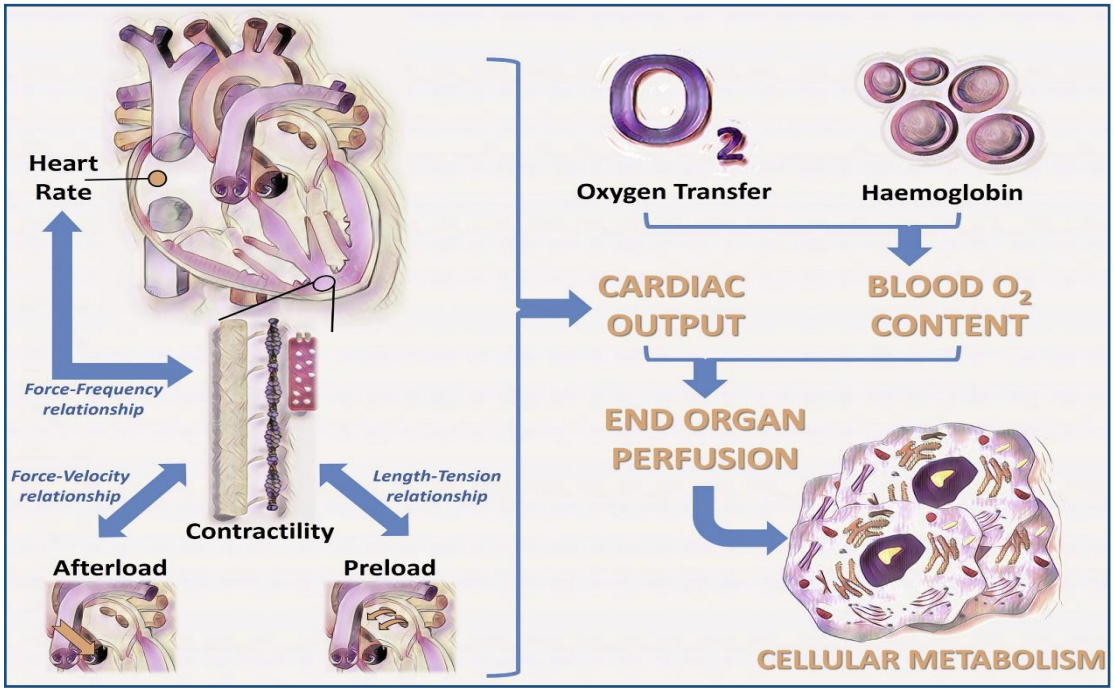

Figure (2): Neonatal hypotension.*(18)*

It should however be noted that—although controversial—data suggest that in very preterm infants the forebrain might be considered a non-vital organ, since the vasculature supplying the forebrain constrict in response to a decrease in perfusion. Moreover, cerebral autoregulation may

be impaired in sick preterm infants, potentially resulting in (periods of) a pressure-passive cerebral perfusion. ***(16)***

This all implies that in the vulnerable, very preterm infant a pressure-based approach might lead to an impaired perfusion and oxygenation of the cortex during the initial, compensated state of shock. The combination of low cardiac output with normal-to-high blood pressure suggests a compensated stage of shock, while low cardiac output in the presence of hypotension is indicative of an uncompensated stage of shock. ***(15)***

A hyperdynamic circulation is characterized by a normal-to-high cardiac output in combination with hypotension. In transitional preterm physiology following birth, there is a physiological phenomenon that exists, where blood flow is normal with low blood pressure.***(17)***

There is increasing recognition in the neonatal literature that blood pressure, as the dependent variable defining organ perfusion, is only one of the end points of interest. The use of blood pressure monitoring is based on an assumed proportionality between blood pressure and systemic blood flow. The relationship between hypotension, cerebral perfusion, and adverse neurodevelopmental sequelae is open to question. First, the preterm cerebral circulation has been proposed to become pressure passive below a critical blood pressure. ***(15)***

Although there is evidence suggesting that neonates with hypotension and impaired cerebral oxygenation are at increased risk for brain injury, other investigators have demonstrated a lack of relationship between blood pressure and cerebral blood flow. Second, although some studies have suggested a relationship between adverse neurologic consequences and systemic hypotension, recent studies have failed to demonstrate any positive association between blood pressure and adverse neurologic outcomes. ***(16)***

This discrepancy suggests that the association is much more complex than any direct effect of blood pressure on cerebral blood flow and may represent the fact that hypotension is but an epiphenomenon and a marker of possible injury. In addition to blood pressure, other cardiovascular parameters, such as heart rate and capillary refill time, can be monitored. However, these are poorly validated and nonspecific measures of systemic flow. ***(17)***

Hemodynamic assessment using echocardiography has the potential of first identifying structural heart disease as an underlying cause, and when the heart is anatomically normal, it can provide insight into the underlying physiology of hypotension. This includes the assessment of LV function, pulmonary hypertension, and ductal patency. First a comprehensive echocardiographic examination needs to be performed in a child with hypotension. ***(17)***

When structural heart disease has been excluded, follow-up standard TNE can be used in the care of the hypotensive preterm neonate. This is currently considered an important area for

research, and current data are still too limited to promote serial TNE as a standard of care for this population.*(15)*

- Indications for Echocardiography:

In any neonate presenting with signs of hypotension, CHD needs to be excluded by comprehensive echocardiography. In the absence of structural heart disease, standard TNE can be used in the management of persistent hypotension, because it can be helpful in identifying the underlying mechanisms. *(9)*

- Guidance of Clinical Decision Making:

Traditionally, blood pressure-based assessment and intervention for neonates with hypotension and clinical shock states fail to address the importance of providing adequate systemic perfusion. Initial clinical experience suggests that TNE could be useful in guiding therapeutic decisions such as fluid administration and the use of inotropic and vasoactive agents. *(16)*

TNE might provide useful additional information for defining the underlying causes and guiding medical management in the follow-up of hypotensive neonates in whom structural heart disease has been ruled out. Further study regarding the role and use of standard TNE for this indication is required before it can be considered a standard of care in the NICU for this indication. *(19)*

Suspected Persistent Pulmonary Hypertension of the Newborn (PPHN):

- Definition and Scope of the Problem:

Persistent PPHN is a common problem, with an incidence of approximately 1 in 500 live births and mortality of up to 20%. It may be associated with perinatal asphyxia and meconium aspiration with pulmonary parenchymal disease. It is defined by a failure of the normal post-natal fall in pulmonary vascular resistance leading to impaired oxygenation, RV failure, and pulmonary-to-systemic shunting. *(20)*

Secondary consequences include low cardiac output because of left-heart preload compromise, itself a result of decreased pulmonary venous return and the mechanical effects of a pressure/volume-loaded right ventricle on left-heart filling. The right heart is functioning at higher pressure and volume, which can cause RV hypertrophy, dilation, and failure in severe cases. *(21)*

Inadequate ventilation and decreased LV output can lead to respiratory and metabolic acidosis, which in turn causes myocardial dysfunction, worsening pulmonary hypertension, progressive hypoxia, systemic hypoperfusion, and hypotension. This vicious cycle can then

worsen to the point that cardio-pulmonary or pulmonary bypass with venoarterial or venovenous ECMO becomes necessary. *(22)*

Pulmonary hypertension can also be seen in premature infants. Pulmonary hypertension in this setting is characterized by an abnormal vascular bed that has increased muscularization of vascular smooth muscle cells, distal extension of muscle into non-muscularized vessels, arrested vascular growth, and increased collagen and elastin deposition in the medial arterial layers. *(21)*

These changes are also seen in preterm infants with advanced bronchopulmonary dysplasia leading to chronic pulmonary hypertension, which in extreme cases may progress to corpulmonale by the first or second year of life. Factors contributing to this pathologic pulmonary vascular remodelling include oxygen toxicity, hypoxemia, and mechanical ventilation. *(22)*

- Indications for Echocardiography:

Echocardiography should be considered in any premature infant or neonate with clinically suspected pulmonary hypertension. The first comprehensive echocardiographic study should be aimed at excluding structural heart defects associated with pulmonary hypertension (especially total abnormal pulmonary venous return or left-sided heart problems). For pulmonary hypertension with no structural heart disease, standard follow-up using TNE can be indicated to assess the effect of treatment on PA pressures, RV function, ductal patency, and shunt direction at the ductal and atrial levels. *(10)*

- Imaging Techniques and Guidance of Clinical Decision Making:

Echocardiography in the setting of PPHN may be challenging because of the presence of coexisting lung disease and mechanical ventilation but imaging the heart from the multiple standard views should be attempted. Serial evaluations may be helpful in documenting response to therapy, particularly when the clinical response is equivocal or difficult to appreciate because of the complexity of the medical situation. *(21)*

In every child with suspected pulmonary hypertension, comprehensive echocardiography should be performed to rule out structural heart disease. In neonates with PPHN, TNE allows assessment of the effect of treatment on PA pressures, RV function, and shunt direction at the atrial and ductal levels. *(20)*

Congenital diaphragmatic hernia (CDH):

- Definition and Scope of the Problem:

Compared with persistent PPHN, CDH is less common, occurring between in 1 in 2,500 to 1 in 4,000 live births. The primary problem stems from the herniation of abdominal organs into

the chest cavity during early fetal life, leading to lung hypoplasia and maldevelopment of the pulmonary vasculature and, in some cases, cardiac ventricular hypoplasia.*(23)*

In contrast to neonates with PPHN who have normal gross pulmonary anatomy but abnormal vascular reactivity with or without remodelling of the pulmonary vascular architecture, patients with CDH typically have unilateral PA hypoplasia, ipsilateral to the hypoplastic lung, although in some cases, the contralateral lung and its vasculature may also be affected. *(24)*

Abnormal pulmonary flow in utero and mechanical distortion of the thoracic organs can in turn lead to decreased LV filling and relative LV hypoplasia. The exact mechanisms for these effects remain unclear,108 and the hypoplasia noted in utero will often resolve postnatally.109 Clinically, pulmonary hypertension is the hallmark of CDH, with similar secondary effects such as low cardiac output, inadequate ventilation, and cardiorespiratory collapse necessitating ECMO support.*(25)*

- Indications for Echocardiography:

All infants with CDH should undergo a comprehensive echocardiographic assessment of cardiac anatomy early in the course of postnatal management. Early diagnosis of CHD is mandated in the setting of CDH, which has a 10% to 18% incidence of associated CHD ranging from persisting atrial communications (patent foramen ovale and atrial septal defect) to more complex lesions, which impart a significantly higher mortality. *(25)*

More severe forms of CHD, especially those involving functionally single ventricles, are associated with such a poor prognosis that aggressive management may not be justified. Once CHD has been excluded, standard targeted neonatal echocardiographic studies can be used in follow-up. In CDH, TNE with focused imaging can also be used for checking line placement, which may be particularly difficult to assess radiographically because of distorted thoracic anatomy. *(10)*

- Guidance of Clinical Decision Making:

Before surgical repair, a comprehensive echocardiographic study should exclude associated CHD and include a baseline assessment of cardiac function and PA pressures. Subsequent preoperative standard TNE studies should focus on the assessment of pulmonary hypertension, right and LV function, and the presence and direction of ductal and atrial shunting. Although the ductus arteriosus is closing, it is essential to image the aortic arch to exclude the development of a juxtaductalcoarctation. *(23)*

After surgical repair, the focus of full TNE will be on pulmonary hypertension and cardiac function but should also include a more detailed assessment of branch pulmonary anatomy and pulmonary venous return. The presence of a pleural effusion on the side of the repair can be

easily assessed. If central lines are still present, confirmation of their position should be performed. *(24)*

Every child with a CDH should undergo a comprehensive echocardiographic study to rule out CHD and to assess the severity of PPHN. Standard TNE can be used to assess the effect of treatment on PA pressures, RV function, and shunt direction at the atrial and ductal levels. Focused TNE can be useful for line placement or in case of ECMO. *(25)*

Suspected Effusion:

- Scope of the Problem and Indications for Echocardiography:

Pericardial and pleural effusions in preterm or ill term infants in the NICU may have a variety of aetiologies, including infectious, neoplastic, obstructive (usually of the lymphatic system), idiopathic, and iatrogenic (due to perforation associated with indwelling lines or catheters or extravasation of intravenous fluids from an erosion of an indwelling catheter). The use of focused TNE in an acutely hemodynamically unstable neonate, particularly one with electromechanical dissociation, may be lifesaving if cardiac tamponade is present. *(26)*

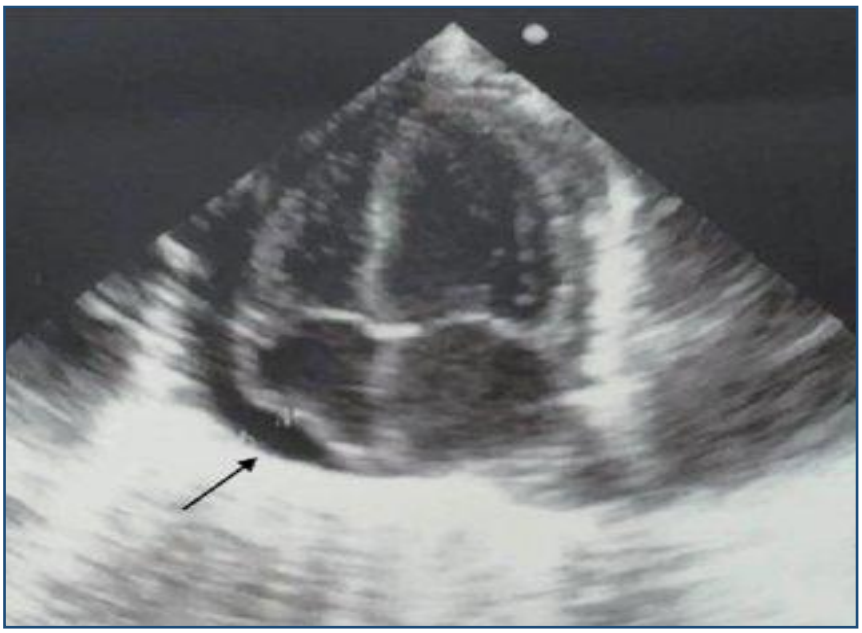

Figure (3): Echocardiogram showing the pericardial effusion.

(27)

At the same time, echocardiography can be used to guide pericardiocentesis. After the child has been hemodynamically stabilized, the cause of the pericardial effusion needs to be established, and this requires the performance of comprehensive echocardiographyto rule out underlying heart disease such as pericardial tumors, pericarditis, and myocarditis.*(28)*

- Imaging Techniques and Guidance of Clinical Decision Making:

Pericardial effusion was discussed in Chapter (1). Echocardiography may be of use in detecting the presence of pleural effusions that are not evident on supine chest x-rays; however, it is of limited utility in determining the volume of fluid in the pleural space. If pleural effusions are detected (usually on subxiphoid axial, coronal, and sagittal 2D imaging), clinical and radiographic correlations are suggested. ***(10)***

TNE with focused imaging is a useful technique for diagnosing pericardial and pleural effusions, assessing their hemodynamic impact, and guiding interventional procedures. For infants with pericardial effusions, comprehensive echocardiography must be performed after hemodynamic stabilization. Focused TNE can also be helpful in monitoring treatment. ***(26)***

Central Line Placement:

- Definition and Scope of the Problem:

Many sick neonates (preterm or full term) require invasive intravascular circulatory monitoring and treatment via central venous and arterial vessels. Because of immaturity of the thrombogenic and fibrinolytic pathways, neonates are at an increased risk for the development of arterial or venous thrombosis in the presence of an indwelling vascular catheter.***(29)***

In critically ill children, the risk for deep thrombosis or infection is reported be relatively low, but in VLBW neonates (less than 1,500 g) with central venous line catheters, the reported frequency of thrombosis is about 10%, and catheter infections occur in up to 20% of infants. ***(30)***

Other studies have estimated the incidence of umbilical vein catheter-related thromboembolic events to be approximately 13%,117 while autopsy studies have estimated that 20% to 65% of infants who die with umbilical vein catheter in situ have evidence of thromboembolic events. The insertion of catheters and vascular cannulation is associated with a significant risk for vascular, cardiac, or pericardial injury and infection, including endocarditis, and mycotic aneurysm. ***(30)***

It has been well documented that detailed 2D echocardiography with Doppler assessment detects a much higher frequency of thrombotic complications if routinely performed in all neonates with central catheters. However, the clinical impact of performing scans to look for "silent" thrombi is uncertain.***(19)***

Before each scan, the examiner should obtain information about vascular access points, the type of catheter used, and its course. At least one study has demonstrated poor performance of routine echocardiography in the detection of vascular thrombosis associated with central venous

lines in the upper-body venous system in children, with sensitivity of only 4% compared with specific vascular ultrasound techniques (which had sensitivity of 88%). ***(31)***

Therefore, it is recommended that in case of suspected thrombus, a specific vascular study with special focus on identifying thrombi be performed. In some cases, it can be difficult to localize the tip of the catheter. The use of a small amount of agitated saline injected through the catheter during the echocardiographic exam may be helpful in identifying the line tip. For catheters that are radiopaque, the x-ray findings may also be helpful. ***(29)***

- Indications for TNE With Focused Imaging:

Focused TNE may be useful in identifying both appropriate catheter position and complications such as thrombosis, infection, abnormal position, line fracture, embolization and vessel occlusion. The identification of vegetations is a major criterion for diagnosing infective endocarditis, but the sensitivity of echocardiography has not been well established in neonates. Therefore, this type of study should be performed by a fully trained pediatricechocardiographer as the evaluation for endocarditis goes beyond the classic indications for TNE. ***(9)***

- Imaging Techniques:

- Umbilical arterial catheter:

The catheter may be seen in the subxiphoid views. The best view is the subxiphoid long-axis view below and above the diaphragm. The position of the catheter tip should be identified. The tip should be without thrombus and the flow in the aorta should be unobstructed, with laminar flow on color flow mapping and with antegrade systolic peak pulse wave of velocity less than 1 m/sec on pulsed Doppler. ***(19)***

- Umbilical venous catheter:

The locations of the hepatic segment of the inferior vena cava, hepatic vein, and ductus venosus are determined from the subxiphoid long-axis view below and above the diaphragm. The tip of the catheter should be without thrombus, and the inferior vena cava and hepatic veins should be unobstructed with laminar flow on color flow mapping. Phasic respiratory variation on pulsed Doppler interrogation should be seen in spontaneously breathing children. ***(29)***

- Central venous catheters:

For catheters inserted into femoral or saphenous vein, the hepatic segment of the inferior vena cava, the hepatic vein, and the junction of the inferior vena cava with the right atrium are imaged using the subxiphoid long-axis sweeps below and above the diaphragm. Imaging and functional assessment are similar to the catheter placed through the umbilical vein. ***(31)***

For catheters placed into the SVC, the proximal SVC connection with the right atrium is visualized from the subxiphoid "bicaval" view, from the high right parasternal view, and from suprasternal views. The suprasternal coronal or short-axis plane is used to visualize the left innominate vein and its connection to the SVC. The presence of a left SVC should be excluded by suprasternal views with leftward angulation. ***(30)***

In the same view, blood return from left subclavian vein can be detected by color flow mapping. Suprasternal coronal and sagittal views tilted rightward are used to determine the connection of the right SVC with the right atrium. The catheter tip should be without thrombus, and all systemic veins patent with laminar flow on color flow mapping, with phasic respiratory variation on pulsed Doppler interrogation in spontaneously breathing children.***(30)***

Focused TNE can be used for identifying catheter tip position after line placement and potential complications such as line thrombosis or infection. Echocardiography to rule out vegetations should be performed or interpreted by a pediatric cardiologist. ***(29)***

ECMO cannulation:

- Definition and Scope of the Problem:

Venovenous or venoarterial ECMO is an important treatment tool in the management of near-term and term neonates with severe hypoxemic respiratory failure, circulatory failure, or both. More than 19,000 patients in the registry of the Extracorporeal Life Support Organization are under the category of neonatal respiratory failure, with 77% overall survival reported to discharge.***(32)***

- Indications for Echocardiography:

Proper cannula position is essential for optimal function of the ECMO circuit; therefore, accurate determination of cannula position is essential. Recent literature has suggested that echocardiography is more accurate than chest radiography for determining cannula position, and there was higher need for reintervention when cannula position was actively screened by echocardiography. ***(10)***

The use of intraoperative imaging during cannula insertion significantly reduces the rate of repositioning. TNE with focused imaging is therefore indicated after cannula placement and when problems with the function of the cannula are suspected. In addition to the assessment of cannula position, echocardiography can be indicated to assess cardiac function, the presence of an atrial communication, and ductal shunting. ***(9)***

- Imaging Techniques:

TNE with focused imaging is performed immediately after cannulation is finished, the cannulae are fixed, and the patient placed back into the "resting" position. Scanning is generally performed in sterile or semisterile environment, though protocols may vary by institution. Neonates may be cannulated via the neck vessels (internal jugular for venovenous, internal jugular and internal carotid for venoarterial) or via sternotomy directly (RA and aortic). ***(33)***

- Venous cannulation:

The venous cannula is placed percutaneously or via surgical cut-down in the right internal jugular vein and through the SVC into the right atrium. Complications can include cannula misplacement or dislodgment (in the azygous vein, abutting the atrial septum, occluding the coronary sinus, protruding through the tricuspid valve, or penetrating into the inferior vena cava), intrapericardial penetration, thrombosis, and infection. ***(32)***

The tip of the venous cannula is visualized from subxiphoid views, four-chamber views, parasternal right inflow views, and modified short-axis views. Left suprasternal coronal or short-axis planes tilted rightward (not interfering with cannula insertion area) with color flow mapping are used to determine the patency of the SVC. The tip of the cannula with metallic and plastic component separation should be identified. ***(34)***

Color flow aliasing, caused by flow acceleration at the site of perforations, will help correctly identify the catheter tip, which should be without thrombus and separate from surrounding structures. The flow within the cannula is monophasic and without respiratory variation on pulsed-wave Doppler interrogation. ***(35)***

Proper function of the cannula can be demonstrated by a relatively small right atrium, a nondilated inferior vena cava, and flow on color flow mapping diverted into the cannula from the inferior vena cava as well as from left atrium (through an atrial communication). ***(32)***

Re-evaluation of cannula position should be performed whenever there is evidence of inadequate drainage despite appropriately sized venous cannulae. Inadvertent cannulation of the azygous vein should be suspected and excluded in cases of CDH or when there is significant compression or absence of the inferior vena cava resulting in dilation of the azygous vein. ***(35)***

- Aortic cannulation:

The aortic cannula is inserted into the right carotid artery with the tip ideally placed high in the ascending aorta. Complications may include cannula misplacement (deep in the aortic root, in the left ventricle through the aortic valve, or intrapericardial perforation), aortic regurgitation, aortic wall dissection, and cannula infection. Parasternal long-axis and suprasternal aortic arch views are used to ensure that the arterial cannula is well away from the aortic valve and sinuses of Valsalva. ***(34)***

Color flow mapping with aliasing helps identify the tip of the cannula and the direction of the jet, which dominantly supplies the descending aorta. Abnormal aortic cannula position should be suspected when there is evidence of inadequate oxygen delivery (low mixed venous saturations, poor perfusion, or hypotension) despite seemingly adequate circuit flow. ***(32)***

Focused TNE with focused imaging is a useful tool for neonates on ECMO, especially for evaluation of cannula position. When assessing PA pressure and ventricular performance, the impact of venoarterial ECMO on ventricular filling must be considered. Every child on ECMO must undergo comprehensive echocardiography.***(36)***

References:

[1] El-Khuffash, A. F., & McNamara, P. J. (2011, February). Neonatologist-performed functional echocardiography in the neonatal intensive care unit. In *Seminars in Fetal and Neonatal Medicine* (Vol. 16, No. 1, pp. 50-60). WB Saunders.

[2] Jain, A., Sahni, M., El-Khuffash, A., Khadawardi, E., Sehgal, A., & McNamara, P. J. (2012). Use of targeted neonatal echocardiography to prevent postoperative cardiorespiratory instability after patent ductus arteriosus ligation. *The Journal of pediatrics*, *160*(4), 584-589.

[3] Marcelino, P. A., Marum, S. M., Fernandes, A. P. M., Germano, N., & Lopes, M. G. (2009). Routine transthoracic echocardiography in a general Intensive Care Unit: an 18 month survey in 704 patients. *European Journal of Internal Medicine*, *20*(3), e37-e42.

[4] Sehgal, A., & McNamara, P. J. (2008). Does point-of-care functional echocardiography enhance cardiovascular care in the NICU?. *Journal of perinatology*, *28*(11), 729-735.

[5] O'Rourke, D. J., El-Khuffash, A., Moody, C., Walsh, K., & Molloy, E. J. (2008). Patent ductus arteriosus evaluation by serial echocardiography in preterm infants. *Acta Paediatrica*, *97*(5), 574-578.

[6] Benitz, W. E., Watterberg, K. L., Aucott, S., Cummings, J. J., Eichenwald, E. C., Goldsmith, J., ... & Wang, K. S. (2016). Patent ductus arteriosus in preterm infants. Pediatrics, 137(1).

[7] Gillam, M., & Reese, J. (2018). Diagnosis and management of patent ductus arteriosus. Neoreviews, 19(7), e394-e402.

[8] Deshpande, P., Baczynski, M., McNamara, P. J., & Jain, A. (2018). Patent ductus arteriosus: the physiology of transition. In Seminars in Fetal and Neonatal Medicine (Vol. 23, No. 4, pp. 225-231). WB Saunders.

[9] Papadhima, I., Louis, D., Purna, J., Deshpande, P., Diambomba, Y., Lee, S., ... & Jain, A. (2018). Targeted neonatal echocardiography (TNE) consult service in a large tertiary perinatal center in Canada. Journal of Perinatology, 38(8), 1039-1045.

[10] Giesinger, R. E., Stanford, A. H., Rios, D. R., Bhombal, S., Fraga, M. V., Levy, V. Y., & McNamara, P. J. (2019).Targeted neonatal echocardiography in the United States of

America: the contemporary perspective and challenges to implementation. Pediatric research, 85(7), 919-921.

[11] Mitra, S., & McNamara, P. J. (2020). Patent ductus arteriosus time for a definitive trial. Clinics in Perinatology, 47(3), 617-639.

[12] Ahearne, C. E., Boylan, G. B., & Murray, D. M. (2016). Short- and long-term prognosis in perinatal asphyxia: An update. World journal of clinical pediatrics, 5(1), 67.

[13] Popescu, M. R., Panaitescu, A. M., Pavel, B., Zagrean, L., Peltecu, G., &Zagrean, A. M. (2020). Getting an early start in understanding perinatal asphyxia impact on the cardiovascular system. Frontiers in pediatrics, 8, 68.

[14] Sendeku, F. W., Azeze, G. G., & Fenta, S. L. (2020). Perinatal asphyxia and its associated factors in Ethiopia: a systematic review and meta-analysis. BMC pediatrics, 20(1), 1-11.

[15] Kalish, B. T., & McPherson, C. (2017). Management of neonatal hypotension. Neonatal Network, 36(1), 40-47.

[16] Wu, T. W., & Noori, S. (2021). Recognition and management of neonatal hemodynamic compromise. Pediatrics & Neonatology, 62, S22-S29.

[17] Sahni, M., & Jain, S. (2016). Hypotension in neonates. NeoReviews, 17(10), e579-e589.

[18] Barrington, K., El-Khuffash, A., & Dempsey, E. (2020). Intervention and Outcome for Neonatal Hypotension. Clinics in Perinatology, 47(3), 563-574.

[19] Singh, Y., Katheria, A., & Tissot, C. (2018). Functional echocardiography in the neonatal intensive care unit. Indian pediatrics, 55(5), 417-424.

[20] Mathew, B., &Lakshminrusimha, S. (2017). Persistent pulmonary hypertension in the newborn. Children, 4(8), 63.

[21] Mandell, E., Kinsella, J. P., & Abman, S. H. (2021).Persistent pulmonary hypertension of the newborn. Pediatric Pulmonology, 56(3), 661-669.

[22] Fuloria, M., & Aschner, J. L. (2017). Persistent pulmonary hypertension of the newborn. In Seminars in Fetal and Neonatal Medicine (Vol. 22, No. 4, pp. 220-226). WB Saunders.

[23] Chandrasekharan, P. K., Rawat, M., Madappa, R., Rothstein, D. H., &Lakshminrusimha, S. (2017). Congenital Diaphragmatic hernia–a review. Maternal health, neonatology and perinatology, 3(1), 1-16.

[24] Puligandla, P. S., Skarsgard, E. D., Offringa, M., Adatia, I., Baird, R., Bailey, J. M., ... & Traynor, M. (2018). Diagnosis and management of congenital diaphragmatic hernia: a clinical practice guideline. CMAJ, 190(4), E103-E112.

[25] Dingeldein, M. (2018). Congenital diaphragmatic hernia: management & outcomes. Advances in pediatrics, 65(1), 241-247.

[26] Chioukh, F. Z., Ameur, K. B., Hmida, H. B., & Monastiri, K. (2016).Pericardial effusion with cardiac tamponade caused by a central venous catheter in a very low birth weight infant. Pan African Medical Journal, 25(1).

[27] Liz, C. F., Domingues, S., Pinho, L., Lopes, L., Carvalho, C., Magalhães, M., & Proença,

E. (2020). Neonatal pericardial effusion: case report and review of the literature. Journal of Pediatric and Neonatal Individualized Medicine (JPNIM), 9(1), e090111-e090111.
[28] Tissot, C., Muehlethaler, V., & Sekarski, N. (2017). Basics of functional echocardiography in children and neonates. Frontiers in pediatrics, 5, 235.
[29] Mcmullan, R., & Gordon, A. (2016). Impact of a central line infection prevention bundle in newborn infants. infection control & hospital epidemiology, 37(9), 1029-1036.
[30] Cho, H. J., & Cho, H. K. (2019). Central line-associated bloodstream infections in neonates. Korean journal of pediatrics, 62(3), 79.
[31] Zaghloul, N., Watkins, L., Choi-Rosen, J., Perveen, S., &Kurepa, D. (2019). The superiority of point of care ultrasound in localizing central venous line tip position over time. European journal of pediatrics, 178(2), 173-179.
[32] Macchini, F., Di Cesare, A., Morandi, A., Ichino, M., Raffaeli, G., Conigliaro, F., ... & Cavallaro, G. (2019). Surgical expertise in neonatal extracorporeal membrane oxygenation (ECMO): a single center experience. Frontiers in pediatrics, 7, 398.
[33] Alammary, D., Narvey, M., Soni, R., Elsayed, Y., & Louis, D. (2021). Targeted neonatal echocardiography service in neonatal intensive care in Manitoba, Canada. Journal of Perinatology, 1-5.
[34] Stewart, L. A., Klein-Cloud, R., Gerall, C., Fan, W., Price, J., Hernan, R. R., ... & Duron, V. P. (2022). Extracorporeal Membrane Oxygenation (ECMO) and its Complications in Newborns with Congenital Diaphragmatic Hernia. Journal of Pediatric Surgery.
[35] Moscatelli, A., Febbo, F., Buratti, S., Pezzato, S., Bagnasco, F., Lampugnani, E., ... & Castagnola, E. (2019). Intensivists performed percutaneous bicaval double-lumen echo-guided extracorporeal membrane oxygenation cannulation at bedside in newborns and children: a retrospective analysis. Pediatric Critical Care Medicine, 20(6), 551-559.
[36] Mukerji, A., Diambomba, Y., Lee, S. K., & Jain, A. (2016). Use of targeted neonatal echocardiography and focused cardiac sonography in tertiary neonatal intensive care units: time to embrace it?. Journal of Ultrasound in Medicine, 35(7), 1579-1591.