Seminars in Fetal and Neonatal Medicine 24 (2019) 101038

Contents lists available at ScienceDirect

Seminars in Fetal and Neonatal Medicine

journal homepage: www.elsevier.com/locate/siny

Hemodynamic management in chronically ventilated infants

Shazia Bhombal[a], Shahab Noori[b,*]

[a] Division of Neonatal and Developmental Medicine, Department of Pediatrics, Stanford University, Palo Alto, CA, USA
[b] Fetal and Neonatal Institute, Division of Neonatology, Children's Hospital Los Angeles, Department of Pediatrics, Keck School of Medicine, University of Southern California, Los Angeles, CA, USA

ARTICLE INFO

Keywords:
Bronchopulmonary dysplasia
Diastolic dysfunction
Preterm infants
Pulmonary hypertension

ABSTRACT

Positive pressure ventilation can significantly alter hemodynamics. The reduction in systemic venous return and increase in right ventricular afterload in response to an inappropriately high mean airway pressure can decrease pulmonary blood flow and compromise systemic perfusion as a result. In addition to ventilator parameters, the degree of hemodynamic effects depends on the baseline cardiac function and lung compliance. Furthermore, the chronically ventilated infants often have a multitude of comorbidities which may also impact hemodynamics. These include pulmonary and systemic hypertension which can lead to myocardial dysfunction as a result of the increase in the right and left ventricular afterload, respectively. In this section, we aim to outline the hemodynamic changes associated with chronic lung disease and mechanical ventilation and discuss management options.

1. Introduction

An understanding of the heart lung interaction is crucial to grasping the impact chronic ventilation will have on the heart and circulation. The heart lung interaction is on a continuum, whether a patient is on mechanical support or breathing on their own. For a patient on assisted ventilation, lung overdistension can lead to hemodynamic alterations, with increased right ventricular (RV) afterload and decreased RV output, as well as decreased left ventricular (LV) filling and resultant decreased LV output [1]. While proximal airway pressure is routinely measured at the bedside, intrathoracic pressure is more difficult to estimate and therefore is not routinely monitored even though it has more hemodynamic relevance. The effect of respiratory cycle on the hemodynamics depends on whether the patient is spontaneously breathing or on mechanical ventilation (Fig. 1). For example, inspiration promotes systemic venous return in spontaneously breathing infant but could impede venous return in mechanically ventilated patients. On the other hand, mechanically ventilated patients have a more favorable intrathoracic interaction with the LV that allows for a lower transmural gradient and lower afterload thereby improving systemic perfusion [2].

In ventilated infants, it is important to closely monitor the lung expansion, as inappropriately high mean airway pressure (MAP) leads to lung overdistention and compression of alveolar vessels resulting in decreased pulmonary blood flow and decreased cardiac output (Fig. 2). Similarly, low lung volume can increase pulmonary vascular resistance by increasing tortuosity of extra-alveolar vessels [3] . To a lesser degree, even during the respiratory cycle pulmonary vascular resistance changes with the lowest pulmonary vascular resistance occurring at functional residual capacity, during end expiration [4]. In addition to the effect on pulmonary vascular resistance, inappropriately high mean airway pressure can also lead to decreased systemic venous return. In such a case, volume administration targeting a higher central venous pressure (CVP) may help with RV filling, though this is not well elucidated in the neonatal literature [5]. There is a fine balance in chronically ventilated patients to attain the optimal positive end-expiratory pressure (PEEP) to allow for aeration of heterogenous lung parenchyma to ensure the best ventilation/perfusion (V/Q) matching, without overdistending the lung. In a study evaluating changes in PEEP on hemodynamics in the preterm neonate after acute phase of respiratory distress syndrome, an increase in PEEP from 0 to 8 cmH_2O resulted in an approximately 25–30% decrease in biventricular stroke volume, with significant difference from 4 to 8 cmH_2O, without significant change in heart rate, thus resulting in decreased cardiac output [6] . On the other hand, in premature patients with a patent ductus arteriosus (PDA), an increase in PEEP from 5 to 8 cmH_2O did not altered systemic perfusion except for a mild reduction in LV output presumably due to reduction in PDA shunt [7]. Indeed, other investigators have also found milder effect PEEP or MAP on hemodynamic when the lungs have low compliance [8]. With a poorly compliant lungs, the airway pressure is not as readily transmitted to the pulmonary

* Corresponding author. Division of Neonatology, Children's Hospital Los Angeles, 4650 Sunset Blvd, MS#31 Los Angeles, CA 90027, USA.
E-mail address: snoori@chla.usc.edu (S. Noori).

https://doi.org/10.1016/j.siny.2019.101038

Abbreviations

ACE	angiotensin converting enzyme
BPD	bronchopulmonary dysplasia
CT	computerized tomography
CVP	central venous pressure
ELBW	extremely low birth weight
IUGR	intrauterine growth restriction
iNO	inhaled nitric oxide
LV	left ventricle
MAP	mean airway pressure
MRI	magnetic resonance imaging
PDA	patent ductus arteriosus
PEEP	positive end-expiratory pressure
RV	right ventricle
V/Q	ventilation/perfusion

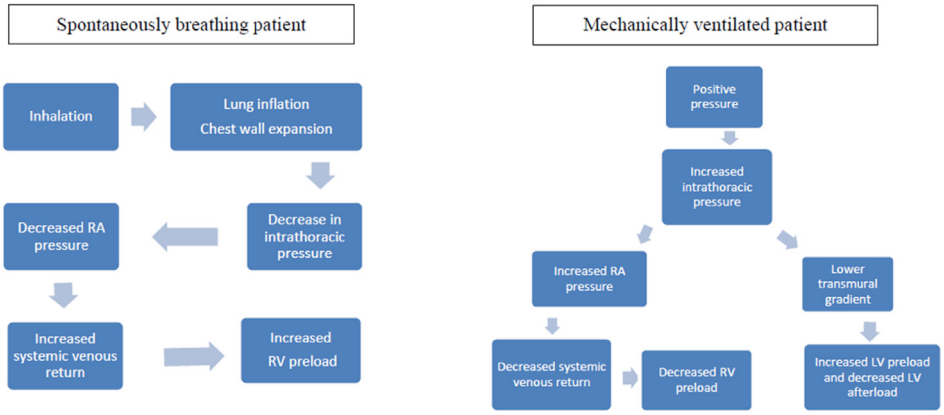

Fig. 1. The effect of spontaneous respiration versus mechanical ventilation on the hemodynamics.

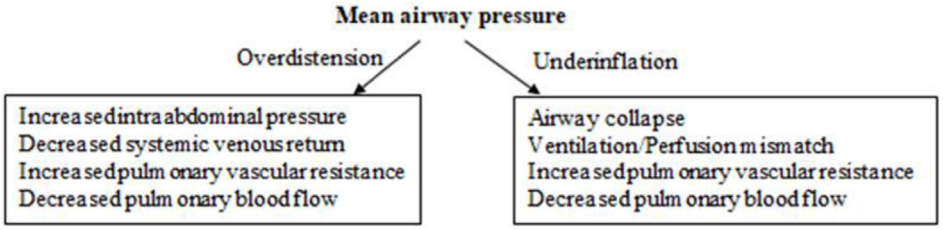

Fig. 2. Effect of mean airway pressure on hemodynamics.

vasculature as compared to a compliant lung. For example, an infant with chronic lung disease, may have little variability in hemodynamics with a change in PEEP from 6 to 8 cmH_2O, whereas a ventilated patient with an upper airway anomaly who has compliant lungs will have a more hemodynamic alteration with such a change. This must be kept in mind when considering increasing PEEP to affect pulmonary or systemic blood flow. The literature is contradictory regarding the effect of noninvasive mechanical ventilation on hemodynamics, perhaps due to differential transmission of pressure via noninvasive route. One study evaluating continuous positive airway pressure of 5 cmH_2O in preterm infants reported a decrease in RV output and reduction in the size of right and left sided structures, with no effect on PDA shunt [9]. However, a similar study did not find any effect on cardiac output and size [10].

In chronically ventilated infants with pulmonary hypertension, increased pulmonary vascular resistance due to lung overdistension may even be more problematic and could exacerbate the RV dysfunction prevalent in this population (see below). In addition, systemic circulation could be compromised due to ventricular interdependence. Indeed, distortion of the RV and septal flattening impacts LV function and filling through ventricular-ventricular interaction [4,11].

Chronically ventilated infants are comprised of broad differential diagnoses, including lung hypoplasia, neuromuscular disease, central hypoventilation disorders, airway anomalies, and bronchopulmonary dysplasia (BPD). Former preterm neonates comprise a majority of infants requiring mechanical support, and this patient population is particularly at risk for further comorbidities that will affect their hemodynamic management.

2. Pulmonary hypertension in chronic lung disease

Chronic lung disease of the premature neonate comprises a large number of chronically ventilated infants and is the most common complication of preterm birth. BPD was first described in 1967 by Northway and colleagues and comprised of patients with gestational ages ranging from 30 to 39 weeks with resultant inflammation, fibrosis and scarring of the pulmonary vascular bed due to factors including mechanical support and oxygen toxicity [12,13]. As the threshold of viability has moved to 22–24 weeks' gestation, a newer form of BPD has emerged. This “new BPD” is characterized by arrest in lung development [14]. Over the last decade, the development of pulmonary hypertension has increasingly been recognized in this population.

2.1. Pathogenesis

Lung development spans five stages, embryonic (4–7 weeks), pseudoglandular (7–17 weeks), canalicular (17–24 weeks), saccular (24–36 weeks), and alveolar stages (36 weeks–2 years). Preterm birth results in arrest of lung development at the late canalicular or early saccular stages, resulting in abnormal pulmonary vascular development and remodeling. This arrest of development leads to impairment of the dual mechanisms of vascular growth, angiogenesis (extension of

existing vascular network with eventual formation of alveolar capillary network) and vasculogenesis (development and differentiation of mesenchymal cells into vascular networks) [15–17]. The pathogenesis of pulmonary vascular disease in preterm neonates is multifactorial, including prenatal and postnatal factors, hypoxia, hyperoxia, inflammation, and baro- and volutrauma associated with mechanical ventilation (Fig. 3). Many of these factors influence proangiogenic genes such as vascular endothelial growth factor (VEGF) [18]. VEGF is essential in vascular network development, with animal studies demonstrating that alterations in expression with mechanical ventilation and hyperoxia decrease VEGF expression [19,20]. Numerous other signaling pathways such as soluble fms-like tyrosine kinase-1 (sFlt-1) and hypoxia-inducible factor 1 (HIF-1) also play an important role in vascular development. Contributions of these factors in development of pulmonary vascular disease in BPD requires further studies [18,21].

In addition to alterations in vascular development, increased muscularization of the peripheral pulmonary vasculature is noted in the preterm neonate. Decreased vascular network and increased muscularization of the peripheral pulmonary vasculature places preterm neonates at risk for development of pulmonary hypertension [22]. Premature neonates with severe BPD have a higher incidence of pulmonary hypertension than those with mild or no BPD [23,24]. Thus, chronically ventilated preterm infants are at high risk of developing pulmonary hypertension. The propensity for development of pulmonary hypertension may be identified early in the postnatal course. Diagnosis of pulmonary hypertension ranges from 6 to 43% between 1 and 6 weeks after birth with this finding being predictive of both pulmonary hypertension at 36 weeks postnatal age and increased severity of BPD [23,24]. The observation that premature neonates with signs of pulmonary hypertension on echocardiography at 7 days of life have a higher incidence of pulmonary hypertension later on, suggests that early pulmonary vascular disease may play a role in development of pulmonary hypertension in the preterm population [23]. Another potential contributor for development of pulmonary hypertension in BPD is decreased placental perfusion leading to chronic hypoxia [25].

2.2. Diagnosis and screening

Identification of patients with pulmonary hypertension is crucial, as diagnosis of pulmonary hypertension in a preterm neonate is associated with an increased risk of morbidity and mortality, with one study reporting a survival rate of 64% at 6 months and 52% two years after diagnosis of pulmonary hypertension [26]. Until recently, diagnosis of pulmonary hypertension often occurred after the first few postnatal months [26]. However, with increased awareness, pulmonary hypertension is more likely to be recognized during the initial hospitalization. In one study, over a 5-year period, all the extremely low birth weight (ELBW) infants received an echocardiogram when BPD was diagnosed or prior to discharge and at least one more echocardiogram after discharge [27]. Eighteen percent of the ELBW infants had pulmonary hypertension with 41% identified after discharge [27] hence the recommendation of close follow up as outpatient [26,28]. In a recent study, adults with a history of prematurity at < 29 weeks' gestation but no notable cardiorespiratory compromise underwent catheterization and found to have increased resting pulmonary artery pressures and elevated pulmonary vascular resistance compared with adults born at term [29]. Eighteen percent of adults born preterm were diagnosed with pulmonary hypertension and an additional 27% had borderline elevated pulmonary artery pressures. The authors found that number of days with assisted ventilation (non-invasive and invasive) correlated more with incidence of elevated pulmonary artery pressures as an adult than gestational age. While further studies are needed to fully assess the impact pulmonary vascular disease has on an individual born preterm, screening for pulmonary hypertension in the chronically ventilated preterm neonate appears prudent.

With a relatively high prevalence of pulmonary hypertension in the chronically ventilated preterm infant, the American Heart Association and American Thoracic Society in 2015 released guidelines recommending screening for pulmonary hypertension in the patient with BPD [30]. A recent expert consensus statement from the Pediatric Pulmonary Hypertension Network recommended screening

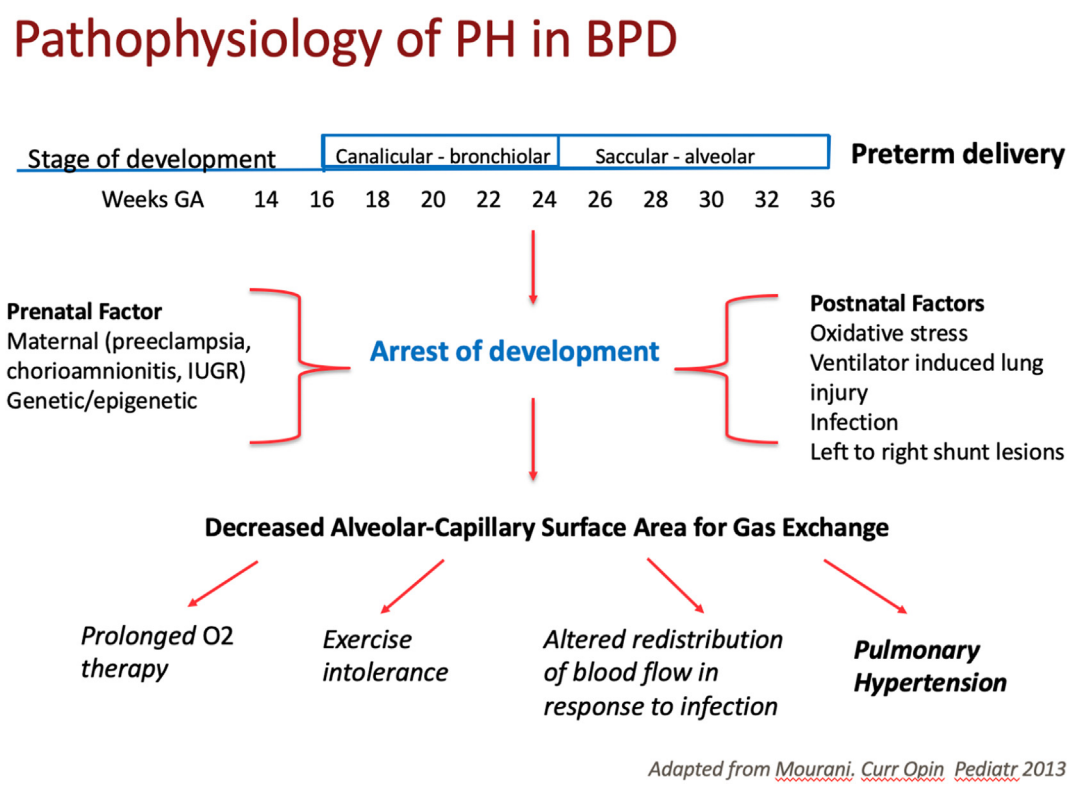

Fig. 3. Pathophysiology of BPD associated pulmonary hypertension [69,70].

echocardiograms in the patient with BPD, particularly in patient with persistent high oxygen requirements and prolonged mechanical ventilation at 36 weeks postmenstrual age [28]. In a recent survey of neonatologists, while a majority performed screening echocardiograms on their preterm neonates with BPD at 36 weeks gestational age, only 38% had an institutional screening protocol [31]. Patient characteristics that increase the risk of development of pulmonary hypertension and therefore warrant screening include hypercarbia, poor growth, and feeding difficulties [32].

2.2.1. Cardiac catheterization

Cardiac catheterization is considered the gold standard for assessment of pulmonary hypertension, with the 2015 AHA guidelines recommending cardiac catheterization for patients with BPD prior to initiation of medications. However, this procedure is not without risk, particularly in the population with chronic lung disease. In a retrospective study of children undergoing catheterization for pulmonary vasoreactivity testing, 6% resulted in resuscitation or death [33]. Institutional experience in the management of patients with pulmonary hypertension particularly important in chronically ventilated infants when performing catheterizations in this population as children under 2 years of age have an increased risk of complications from cardiac catheterization compared to the older pediatric population [34]. While catheterization at the time of initial diagnosis of pulmonary hypertension in the chronically ventilated infants may not be indicated, catheterization may be appropriate in cases such as need for multiple pulmonary vasodilators, evaluation of shunt lesions (atria and ventricular septal defect, PDA) or concern for impaired LV function and pulmonary vein stenosis. Goals of catheterization include assessment of severity of pulmonary hypertension, obtain pulmonary venous saturations for pulmonary contribution, assessment for pulmonary vein stenosis, and perform acute pulmonary reactivity testing [28].

2.2.2. Echocardiography

While cardiac catheterization is the gold standard for diagnosis of pulmonary hypertension, echocardiography is the most utilized and effective noninvasive method for assessment. Although inter- and intrarater agreement is fairly high in diagnosing pulmonary hypertension in the preterm infant [35,36], utilization of echocardiography for identification of pulmonary hypertension must be done with caution. In comparison to catheterization, only presence of tricuspid regurgitation jet and resultant estimated elevation in pulmonary artery pressure had good correlation with elevated pulmonary vascular resistance by catheterization. However, a reliable tricuspid regurgitation jet velocity is obtained only in approximately 61% of pediatric echocardiographic studies [37].

Evaluation by echocardiography involves assessment of multiple parameters as a reflection of increased RV afterload in the presence of elevated pulmonary vascular resistance. Echocardiographic assessment of pulmonary hypertension in the patient with BPD includes assurance of normal intracardiac anatomy, assessment of right and left ventricular size and function, interventricular septal positioning, estimation of pulmonary artery pressure through evaluation of tricuspid and pulmonary regurgitation velocities as well as assessment of flow through shunts (ventricular septal defect, PDA) (Table 1 and Fig. 4) [28]. Recording systolic blood pressure at the time of the echocardiogram is utilized for comparison with pulmonary artery pressure estimation. Many of the standard measurements involve an imprecise qualitative judgement, and more advanced echocardiographic measures of pulmonary hypertension are being introduced in this population allowing for more quantifiable assessment (Table 1).

2.2.3. Other modalities

Other modalities of screening for pulmonary hypertension in the infant with BPD include electrocardiogram (EKG), with diagnosis of pulmonary hypertension consistent with right atrial enlargement, right axis deviation, and right ventricular hypertrophy, though right axis deviation is normal in the neonate, with right ventricle to left ventricle ratio normalizing by 6 months of age [38,39] . Serial EKGs may be useful in following for development of right sided changes [40]. High resolution contrast enhanced computerized tomography (CT) scan is quick, does not require anesthesia, and provides information on severity of the lung parenchyma disease, presence of pulmonary vein stenosis, thromboembolic disease and airway diseases [41,42]. While magnetic resonance imaging (MRI) is not routinely utilized in the assessment of pulmonary hypertension in the pediatric population, it has a role in assessment of RV size and function in the congenital heart disease realm. In a review of pediatric cardiac MRIs performed for pulmonary hypertension, RV ejection fraction and LV stroke volume index correlated most strongly with survival [43]. The ability to perform an MRI without sedation and radiation make it an attractive option, and further studies needed to demonstrate standardization of use in the pediatric pulmonary hypertension population.

2.3. Management

Treatment of pulmonary hypertension in the chronically ventilated infant encompasses optimizing ventilatory management and addressing inflammation and pulmonary edema prior to initiation of pulmonary vasodilator therapy. A thorough evaluation of the airway is warranted

Table 1
Echocardiographic parameters in patients with BPD associated pulmonary hypertension.

	Parameter	Markers of PH
Conventional Echocardiographic Measures	Right ventricular size	Dilation, hypertrophy
	Tricuspid regurgitation Doppler peak (Estimates RV systolic pressure)	> 3–3.5 m/s consistent with PH, compare pressure with systolic blood pressure
	Pulmonary insufficiency Doppler peak (Estimates mean pulmonary artery pressure)	> 25 mmHg
	Shunt assessment	Direction and velocity of flow across VSD, PDA provides pressure estimates
	Septal geometry	Flattening or bowing into LV consistent with PH
Advanced Echocardiographic Measures	LV Eccentricity index (Ratio of LV measured perpendicular compared to parallel in parasternal short axis)	Increased
	Tricuspid Annular Plane Systolic Excursion (TAPSE) (Movement of tricuspid valve along lateral RV wall as assessment of RV function)	Decreased
	RV Fractional area of change (RV FAC – measurement of RV function)	Decreased
	Pulmonary artery acceleration time (PAAT) and PAAT/ET (ejection time)	Decreased

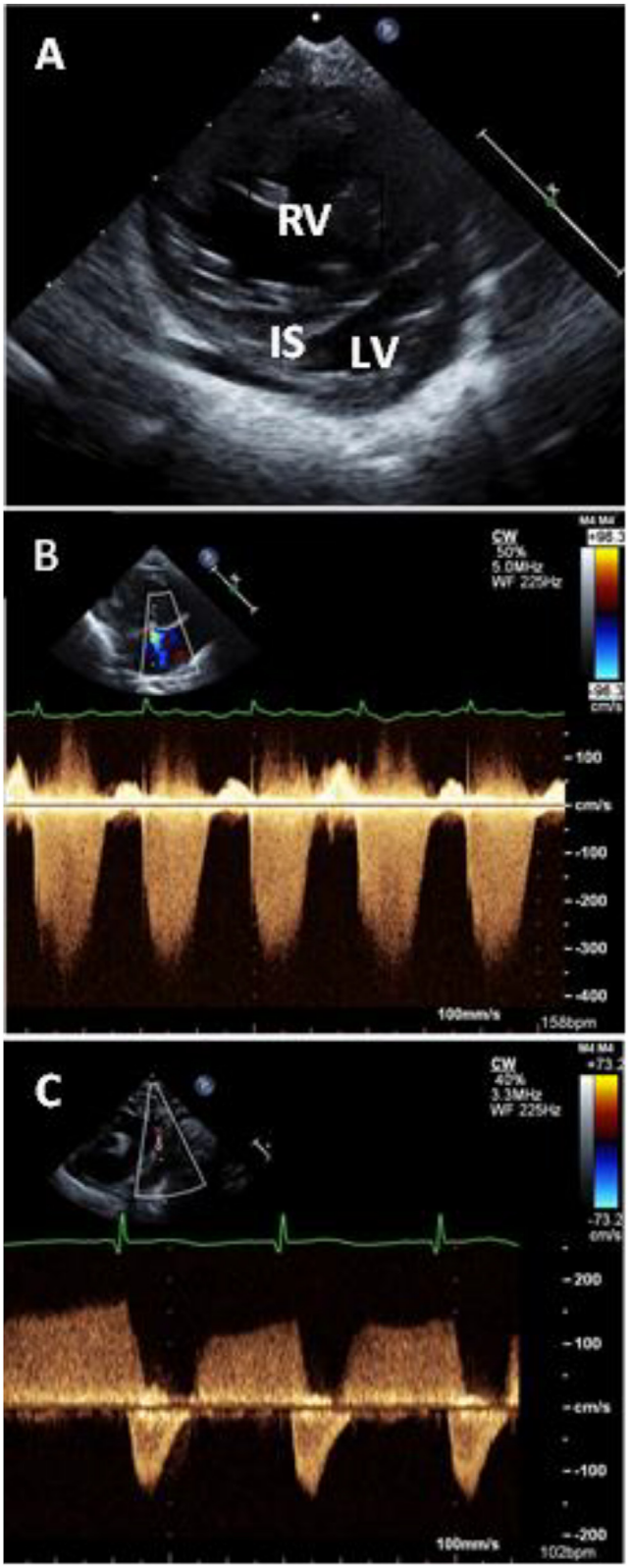

Fig. 4. Echocardiographic images of pulmonary hypertension. A. Parasternal short axis view demonstrating dilated right ventricle (RV) and flattened interventricular septum into the left ventricle, consistent with severe pulmonary hypertension. B. Tricuspid regurgitation Doppler demonstrating peak regurgitant velocity. C. Bidirectional flow across the PDA with flow below the baseline demonstrating right to left flow during systole, consistent with elevated pulmonary pressures. *RA = right atrium, RV = right ventricle, IS = interventricular septum, LV = left ventricle.*

including assessment for malacia and vocal cord paralysis (particularly in patients who have undergone PDA ligation, with incidence of vocal cord paralysis ranging from 11 to 67%) [44,45]. Oxygen saturation target in this population is 92–95%, with even brief, intermittent periods of hyperoxia associated with elevated pulmonary artery pressures by catheterization [28,46]. While there is no silver bullet for management of BPD associated pulmonary hypertension, numerous pulmonary vasodilators have been utilized (Table 2) [28,47]. Sildenafil is the most studied in this population, though data is limited. It is the most readily administered agent and is generally well tolerated orally. Of note, sildenafil has the potential to worsen V/Q mismatch in patients with significant lung disease and heterogeneity, as well as increase gastroesophageal reflux symptoms and close monitoring is warranted to assess effect on the individual patient. Further studies are needed to determine the choice and duration of the best medications for management of pulmonary hypertension in this population.

2.4. Outcome

In a multicenter retrospective cohort study of 1677 patients < 32 weeks' gestational age, increased morbidity and mortality were noted among infants with BPD and pulmonary hypertension (22%). In addition, 38% of infants with BPD and pulmonary hypertension were readmitted over the first year of life. Furthermore, they were more likely to be discharged home with tube feeds, a tracheostomy, and supplemental oxygen [48]. Therefore, a multidisciplinary team approach is warranted in this complex population. Indeed, coordination of care is needed to facilitate transition from inpatient to outpatient care with optimization of cardiorespiratory management and nutritional support, and to ensure neurodevelopmental follow-up [28,49].

3. Pulmonary vein stenosis

When imaging the chronically ventilated infant with BPD and pulmonary hypertension, pulmonary veins should also be evaluated. Pulmonary vein stenosis (PVS) is estimated to occur in approximately 2 cases per 100,000 annually, with most cases associated with preterm birth [50]. Infants with BPD and PVS have a mortality risk of 45–50% within the first two years of diagnosis [51,52]. PVS in the preterm neonate appears to be an acquired disease, diagnosed at an average of 6.5 months with approximately 3–5 echocardiograms obtained prior to finding PVS. Thus, continued evaluation of the pulmonary veins on serial echocardiograms is important for diagnosis. If echocardiogram is difficult to obtain (for example, poor acoustic windows), and there is a concern about presence of PVS, CT angiography should be considered. A recent study found the risk of increased mortality to be associated with stenosis of more than 2 pulmonary veins, bilateral PVS, small for gestational age, and < 6 months of age at diagnosis [52]. There is recent intriguing research on utilizing chemotherapy agents to impact multivessel pulmonary vein disease resulting in increased survival of 77% at 72 weeks [53]. Further studies are needed to understand the etiology and potential targets for prevention and therapy, as catheterization or surgical intervention is unsatisfactory, with restenosis often occurring in up to 44% [52].

4. Systemic hypertension

Patients with chronic lung disease are at increased risk for developing systemic hypertension which affects LV afterload and could alter hemodynamics. The incidence of systemic hypertension in the neonatal period has been reported from 0.2 to 3%, however patients with BPD have been noted to have an increased incidence of systemic hypertension [54]. The association of systemic hypertension with BPD was initially reported in 1984 with 43% of preterm neonates developing systemic hypertension in their first year of life, with a mean onset of 4.8 months [55]. While a later study demonstrated a lower incidence of

Table 2
Pharmacotherapy for pulmonary hypertension in the chronically ventilated infant.

Pathway	Medication	Mechanism of action (MOA)
cGMP	Inhaled nitric oxide	Lead to production of cGMP, relaxation of vascular smooth muscle, vasodialtion
	Sildenafil	Phosphodiesterase 5 inhibitor, prevents breakdown of cGMP, potentiating vasodilation by relaxation of vascular smooth muscle
cAMP	Iloprost (inhaled, IV)	Activates adenylate cyclase leading to increased cAMP and vascular smooth muscle relaxation, half-life 20–30 min by inhalation
	Treprostinil (inhaled, IV, SC)	Remodulin, same MOA as Iloprost, half-life 3 h
	Eproprostenol IV	Flolan, Same MOA as Iloprost, short half-life of 6 min, continuous infusion
	Milrinone IV	Phosphodiesterase 3 inhibitor, prevents breakdown of cAMP, potentiating vasodilation by relaxation of vascular smooth muscle
Endothelin	Bosentan	Endothelin 1 antagonist, affecting both endothelin A (ET_A, vasoconstriction) and B (ET_B, vasodilation) receptors

13% diagnosed in the first year, it is reasonable to conclude that patients with BPD should be monitored for development of systemic hypertension. Patients with severe BPD (as defined in early studies by home oxygen requirement) comprised the majority of premature patients with systemic hypertension, with early studies defining hypertension as systolic blood pressure greater than 115 mmHg [55,56]. A recent multicenter study reviewed incidence of systemic hypertension in 18 institutions over nearly 20 years and found a similar incidence of unexplained systemic hypertension in preterm patients with and without chronic lung disease. Patients developed systemic hypertension between 3.5 and 4 months of age and generally resolved over the subsequent two years [57].

Numerous potential causes have been suggested for development of systemic hypertension in the preterm neonate. Umbilical artery catheter thrombosis is recognized as the most common renovascular cause of systemic hypertension in neonates, potentially resulting from endothelial damage at the time of catheter placement [54]. Another intriguing prospect is the effect lung disease has on circulating levels of norepinephrine. In the lamb model, norepinephrine was found to have decreased clearance during periods of hypoxia [58]. It is plausible that increased levels of circulating norepinephrine could contribute to elevated systolic blood pressure in the preterm neonate. In the adult population with chronic lung disease, increased arterial stiffness has been noted [59]. Interestingly, a recent study in the BPD population also demonstrated increased aortic wall thickness and stiffness [60]. The authors surmised that increased systemic vascular thickness could be a factor in elevated systolic blood pressure. Recognition of systemic hypertension in patients with BPD is important as it may affect LV structure and systolic and diastolic function [61].

Given the impact on the LV function and the risk for cardiac hypertrophy and heart failure early recognition and treatment of hypertension is recommended [62,63].

Vasodilators such as hydralazine are among the most commonly used antihypertensive agents, followed by angiotensin-converting enzyme (ACE) inhibitors, calcium channel blockers, and alpha- and beta-blockers [64]. In neonates, ACE inhibitors can evoke an exaggerated response leading to hypotension and therefore should be started with a low dose. Furthermore, due to possible adverse effect on renal development, some have recommended it only after 44 weeks postmenstrual age [63]. While there is a dearth of literature on the management of systemic hypertension in the setting of chronic lung disease, use of diuretics such as spironolactone, at times paired with a thiazide agent, may be a useful first line treatment. In chronically ventilated neonates, beta blockers should be used with caution as it can exacerbate the chronic lung disease.

5. Diastolic dysfunction in chronic lung disease

Diastolic dysfunction is a well-known entity in the adult literature. However, in infants this diagnosis is not well defined, though is becoming more recognized in neonates, especially in preterm infants with chronic lung disease. Diastolic dysfunction includes decreased myocardial compliance and impairment in relaxation of the myocardium and can result from numerous etiologies. Premature myocardium is inherently poorly compliant. As for impairment in myocardial relaxation, other than cases of cardiomyopathy such as hypertrophic cardiomyopathy of infants of diabetic mothers [65], the underlying cause is unclear. In the adult population, diastolic dysfunction is considered in many disease states, including in patients with pulmonary hypertension or increased pulmonary edema.

In fetal life, the RV is the dominant ventricle and provides about 60% of the combined cardiac output. As a result, and the RV is thickened at birth, with improvement in relaxation occurring over time. Shortly after birth, LV afterload increases with removal of the low resistance placental circulation, and the LV is suddenly faced with an increased workload. In addition, the LV is exposed to a large change in volume with increased pulmonary venous return. The left ventricle adapts to postnatal life, with the LV diastolic function improving in the neonate over time. Echocardiography allows for assessment of the left ventricular diastolic flow parameters and changes over time. Normal LV filling occurs primarily through passive filling (E wave on Doppler of mitral valve inflow). The late atrial contraction (A wave on Doppler of mitral inflow) provides a smaller portion of the LV filling. However, with decreased LV compliance particularly in the first month of life in the preterm neonate, there is E/A wave reversal, with more flow entering the LV from the atrial contraction (Fig. 5). Preterm and term waveforms differ initially, with differences disappearing by the first month of life [66]. LV diastolic dysfunction has been associated with steroid use, particularly with dexamethasone, leading to LV hypertrophy in the preterm population, though this appears to normalize over time [67]. As discussed earlier, the higher prevalence of systemic hypertension in patients with chronic lung disease may result in diastolic dysfunction. Indeed, diastolic dysfunction has been reported in patients with severe BPD. This is important as treatment of BPD-associated pulmonary hypertension with pulmonary vasodilators could potentially worsen respiratory status in the subset with diastolic dysfunction. Addressing diastolic dysfunction utilizing afterload reduction and diuretics may be helpful in this population [68].

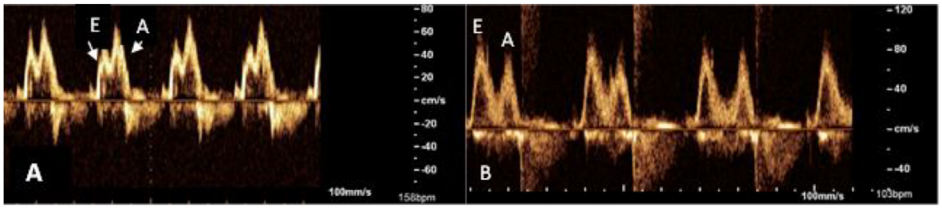

Fig. 5. Mitral valve inflow Doppler. A. Normal E/A ratio in a 7 day old preterm neonate with a larger atrial kick component of ventricular filling (A wave), compared with initial passive filling (E wave) B. Normal E/A ratio in a 10 month old infant, with majority of left ventricular filling occurring passively during initial opening of the valve (E wave).

6. Conclusions

Chronic mechanical ventilation has direct effects on hemodynamics by altering the loading condition and pulmonary vascular resistance. However, multiple comorbidities in the infants that require mechanical ventilation, notably those with a history of prematurity, have the potential to affect cardiac function. Comprehensive evaluation and assessment of hemodynamics in the chronically ventilated infant, especially for pulmonary and systemic hypertension, is essential, as they affect cardiorespiratory function over time. In addition, assessment of diastolic function and treatment targeting diastolic dysfunction may be helpful in management of chronically ventilated infants.

Declaration of competing interest

No conflict of interest for either or the authors and no funding source.

Learning Points

1. Positive pressure ventilation impacts cardiac mechanics and must be considered when managing a chronically ventilated infant.
2. Patients with chronic lung disease have an increased risk of developing pulmonary hypertension.
3. Patients with chronic lung disease are at risk for developing systolic hypertension.
4. Diastolic dysfunction with elevated left sided pressures can impact ventilatory management and pulmonary edema in the chronically ventilated patient and should be recognized and managed appropriately.

Research Directions

1. Identifying chronically ventilated infants at risk for development of pulmonary hypertension.
2. The long-term effects of pulmonary vasodilators in chronically ventilated infants with pulmonary hypertension.
3. The interaction between systemic hypertension and chronic lung disease; particularly in chronically ventilated infants with LV diastolic dysfunction.
4. The role of diastolic dysfunction in pathogenesis of chronic lung disease.

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