Chapter 11
Acute Respiratory Failure and Management

Prakadeshwari Rajapreyar, Whitney Kopp, and Adrienne Randolph

Acute Respiratory Failure

Acute respiratory failure is a common reason for admission to the pediatric intensive care unit in oncology patients [1]. Acute respiratory complications are also common after pediatric hematopoietic stem cell transplant (HSCT), accounting for a high proportion of HSCT-related morbidity and mortality [2–4]. When pulmonary disease in HSCT patients progresses to acute respiratory failure, they often require emergent intubation and support with invasive mechanical ventilation (IMV) [3, 5]; many children develop refractory hypoxemia and multi-organ failure. Tamburro et al. reported outcomes in a cohort of mechanically ventilated pediatric oncology and HSCT patients. The non-HSCT patients had better outcomes than the HSCT patients with 6-month survival at 60% [6]. While the outcomes are better in the oncology patients, they are nevertheless worse than immunocompetent patients. Their immunocompromised status and chemotherapy-related multi-organ failure are likely complicating factors affecting outcomes in this cohort.

Focusing on the more complicated HSCT patients, intubation for HSCT-related acute lung injury (ALI) often led to early redirection of care due to high fatality two decades ago; recent reports show that outcomes have improved with improved

P. Rajapreyar (✉) · W. Kopp
Division of Pediatric Critical Care Medicine,
Medical College of Wisconsin/Children's Hospital of Wisconsin,
Milwaukee, WI, USA
e-mail: prajaprey@mcw.edu

A. Randolph
Division of Critical Care Medicine, Department of Anesthesia, Critical Care and Pain Medicine, Boston Children's Hospital, Boston, MA, USA

Departments of Anesthesia and Pediatrics, Harvard Medical School,
Boston, MA, USA

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survival [6–8]. Tamburro et al. demonstrated 6-month survival of 25% in the HSCT cohort, while van Gestel et al. showed a 6-month survival of 35% [6–9]. Improved outcomes are likely multifactorial, influenced by increased willingness to deliver intensive care therapies with earlier rescue and support and innovations in transplant management leading to less lung toxicity.

Acute respiratory failure with hypoxemia due to inflammation following a known clinical insult is defined as acute respiratory distress syndrome (ARDS). Oncology and HSCT patients should be closely monitored for development of pediatric ARDS (PARDS), with stratification of severity of illness to allow early and appropriate escalation of respiratory support. In 2015, the Pediatric Acute Lung Injury Consensus Conference (PALICC) guidelines defined PARDS and stratified severity [10] using the following definition:

1. Evidence of acute pulmonary parenchymal disease with unilateral of bilateral infiltrates on chest imaging
2. Hypoxemia as documented and stratified by measures of oxygenation (oxygenation index {OI}, oxygen saturation index {OSI}, arterial oxygen saturation/FiO2 ratio {P/F ratio}, oxygen saturation/Fio2 ratio {S/F ratio})
3. Symptoms of hypoxemia and chest imaging changes within 7 days of a known clinical insult
4. Above criteria not explained by left ventricular dysfunction

Lung injury in the pediatric oncology patients is related to their immunocompromised status and direct pulmonary toxicity from chemotherapy and/or radiation. Chemotherapeutic agents most commonly implicated in lung injury include bleomycin, cyclophosphamide, nitrosureas, cyclophosphamide, chlorambucil, methotrexate, procarbazine, mitomycin, cytarabine, vinca alkaloids, and alkylating agents such as busulfan [11]. Of these, bleomycin, busulfan, cyclophosphamide, and the nitrosureas are most commonly implicated in pediatric patients [11, 12]. Toxicity from radiation therapy is dose dependent with patients receiving fractionated doses having less risk for toxicity than patients receiving the same total dose given at one time. Patients typically develop symptoms within 1–3 months of receiving radiation therapy and present with cough, dyspnea, and pink-tinged sputum during the inflammatory phase. This can progress to the fibrotic stage which progresses over 1–2 years. Patients in this phase develop increasing dyspnea, oxygen requirement, and declining pulmonary function tests.

Toxicity from chemotherapeutic agents may occur early in the form of a hypersensitivity reaction which presents with rales, fever, and dyspnea while receiving the medication. Patients typically respond well to stopping the medication and administration of steroids. Endothelial injury and vascular leak causing noncardiogenic pulmonary edema is another early pulmonary toxicity seen from drugs such as methotrexate, cytarabine, ifosfamide, cyclophosphamide, IL-2, ATRA (all trans-retinoic acid), and bleomycin. Both types of early toxicity respond well to supportive care and have a relatively good prognosis. Later pulmonary toxicity occurring several months to years after receiving the chemotherapeutic agent leads

to fibrotic lung injury and has a much worse prognosis [11]. If patients respond to steroids, weaning of steroids should occur slowly and cautiously as it can reactivate the underlying disease process.

The lung injury that occurs in post-HSCT patients can be grossly classified as infectious or noninfectious [3, 13], although it could be multifactorial in some patients. Alternatively, pulmonary complications can be classified as early and late [13]. The classification into early and late (within and beyond 100 days respectively) is not absolute but may help the clinician to develop a differential diagnosis [13]. Early complications tend to be related to immune suppression, endothelial/alveolar injury, and/or neutrophil recovery. For this review, we will first focus on early or acute complications of infectious and noninfectious etiologies and later address late complications.

HSCT Patients

Initial Workup of the HSCT Patient with Acute Pulmonary Complications

Noninfectious complications after HSCT are often treated with immune suppression. Therefore, the first step in management of a HSCT patient with acute hypoxia and/or hypercarbia is to perform a thorough workup to confirm or rule out infectious etiologies (Table 11.1). These children are at high risk of death if their infection is not identified early and treated and their immune dysregulation appropriately addressed. Bacterial, viral, and fungal infections are all considerations in

Table 11.1 Workup of a child presenting with acute lung injury after HSCT

A. Respiratory testing for respiratory pathogens:
(a) Viral testing extended panel of organisms with NP swab in non-intubated patients and endotracheal or bronchoalveolar lavage (BAL) when possible
(b) Sensitive polymerase chain reaction (PCR) testing for respiratory syncytial virus, HSV, VZV, influenza virus, parainfluenza virus, adenovirus, human metapneumovirus, rhinovirus, coronavirus, and HHV6 at a minimum
(c) Consider testing for acid fast bacilli, *Nocardia*, *Legionella*
(d) Polymerase chain reaction for *Chlamydia*, *Mycoplasma*, and *Aspergillus* species
(e) Consider PCP risk factors and send sensitive PCR test if present
B. Other testing to identify pathogens:
(a) Routine cultures of indwelling lines for bacteria and fungi
(b) Urine for legionella
(c) Shell vial culture for CMV
(d) Serum galactomannan ELISA for *Aspergillus* species
C. Rule out non-pulmonary causes or contributors of pulmonary dysfunction:
(a) Echocardiogram to rule out cardiac dysfunction
(b) Evaluation of renal function
(c) Evaluate fluid status and rule out and manage iatrogenic fluid overload

Modified from https://www.atsjournals.org/doi/pdf/10.1164/rccm.2007-413ST [14]

posttransplant patients given their immunosuppression and presence of indwelling catheters and invasive lines. Identification of specific organism can help clinicians target antimicrobial therapy. Unfortunately, broad-spectrum empiric treatment is often prolonged due to delays in turnaround times and insensitivity of microbiological testing.

It is thought that a BAL should be strongly considered in patients with diffuse lung injury posttransplant [3]. However, it is prudent to consider the risk-benefit ratio and optimal timing of the BAL due to the potential for worsening lung mechanics. Triebwasser et al. in 2018 in a retrospective chart review of 593 patients of different age groups that underwent a BAL reported identification of pathogens in 30% of cases [15]. They reported that the BAL led to changes in patient management in 55% of cases, including alteration in antibiotics (37%) and immunosuppression (25%). BAL complications included hypoxemia (1%), hemorrhage (2%), and respiratory failure (1%) in patients not requiring mechanical ventilation prior to the BAL. This would suggest that an early BAL would be safe and may alter the treatment plan in more than half of cases. Prophylaxis and preemptive screening for invasive fungal and CMV infections have resulted in a decrease in their incidence posttransplant [3]. Improved molecular diagnostic techniques will likely result in improved testing yield and decreased need for prolonged empiric therapy.

Noninfectious Complications in HSCT Patients

Once infection is ruled out, children with lung injury are then categorized as either acute idiopathic pneumonia syndrome (IPS), engraftment syndrome, diffuse alveolar hemorrhage, or other lung injury syndromes. In 1993 a National Institutes of Health workshop defined IPS as widespread alveolar injury in the absence of active lower respiratory infection, cardiogenic causes, renal failure, or iatrogenic fluid overload after HSCT [3, 16]. This definition was further classified based on anatomy as interstitial, vascular, airway tissue, or unclassifiable [3, 14]. T-cell-mediated injury is supported as the primary pathophysiology by murine models. TNF-α levels have been shown to be increased in the BAL fluid of mice with IPS. This is supported by the clinical observation that patients who receive T-cell-depleted grafts have a lower incidence of pulmonary complications [13]. However other TNF- α-independent pathways may also contribute to the pathophysiology of IPS [3]. Given the TNF-α pathway-mediated injury, the soluble TNF-α-binding protein, etanercept, has been tested in a trial for treatment of IPS [17]. Early recognition of the disorder, ruling out other infectious etiologies, and initiation of corticosteroids along with other anti-inflammatory targeted therapies may improve outcomes after IPS [3].

Engraftment syndrome (ES) is characterized by fever, rash, and non-cardiogenic pulmonary edema occurring at the time of neutrophil recovery after HSCT [3, 18]. ES may be related to a graft-versus-host response or in some cases a host-versus-graft response [13]. Chang et al. reported a higher risk for developing GVHD and

non-relapse-related mortality in patients with ES [19]. Corticosteroids are often effective in patients with ES [3].

Diffuse alveolar hemorrhage (DAH) originates from the pulmonary microvasculature in response to alveolar injury which may be noninfectious etiology, secondary to chemotherapy, radiation, immune-mediated events, or other systemic/pulmonary infections [3, 20]. In some cases, it is a type of IPS. Progressive bloody return is noted on BAL when performed. High-dose corticosteroids were reported to not alter the outcomes in these patients in a prospective cohort study of 103 adult HSCT patients [3, 20]. However, Rathi et al. reported that patients who received low-dose steroids had lower mortality in comparison to medium- and high-dose steroids in a cohort study of 119 adult HSCT patients [3, 21]. Wanko et al. reported a decrease in 100-day mortality (44% versus 83%) in a small group of eight adult patients with DAH, treated with concomitant aminocaproic acid and steroids [22]. Recombinant factor VIIa has been used in some patients for refractory bleeding but has not shown to improve duration of mechanical ventilation or survival [3, 13, 23].

The other lung injury syndromes to consider include radiation pneumonitis, pulmonary veno-occlusive disease, pulmonary cytolytic thrombi, transfusion-related acute lung injury, pulmonary arterial hypertension, and pulmonary thromboembolism [3, 24, 25].

Specific Infectious Complications in HSCT Patients

The type of infection identified influences patient prognosis and treatment in HSCT patients. Preemptive antiviral therapy has reduced the incidence of cytomegalovirus (CMV) infection after HSCT. Ganciclovir is typically used for treatment of CMV infection. Foscarnet can be used when cytopenias are present. Newer drugs under evaluation are maribavir, letermovir, and brincidofovir [26].

Adenovirus can cause a disseminated infection with significant mortality in HSCT patients [27]. Adenovirus titers in the serum are often used to monitor viral load and response to treatment. Cidofovir and brincidofovir have been used to treat adenoviral infection with the latter not demonstrating significant nephrotoxicity [27].

Respiratory syncytial virus (RSV) infection in immunocompromised children can rapidly progress to lower respiratory tract infection. Lower respiratory tract infection in these children has been associated with mortality attributed to RSV [28]. A recent multicenter investigation reported a low incidence of RSV infections in posttransplant patients with low utilization of critical care services and mortality [29]. It should however be noted that all patients who required critical care received treatment with ribavirin, although its benefit has not been rigorously proven in this population.

Invasive fungal infections in HSCT patients are associated with poor outcomes. Abassi et al. reported an 85% mortality within the first year after diagnosis of aspergillus infection in immunosuppressed pediatric patients [3, 30]. However, invasive fungal infections of the lung have decreased with better antifungal prophylaxis [3,

30–33]. Fungal infections also often require aggressive surgical intervention due to the patients underlying immunosuppression.

Pneumocystis jiroveci pneumonia (PJP) develops in 5–15% of pediatric HSCT patients, without prophylaxis, with a mortality rate higher than 50%. However this is rare with the advent of routine prophylaxis [34].

Late Pulmonary Complications in HSCT Patients

Bronchiolitis obliterans syndrome (BOS) and cryptogenic organizing pneumonia (COP) are late-onset noninfectious pulmonary complications of HSCT [13] often requiring chest computed tomography (CT) or lung biopsy to make the diagnosis. BOS is a progressive obstructive disease with onset 3–24 months posttransplant. Patients typically present with wheezing and dyspnea. Chest CT may demonstrate air trapping, centrilobular nodules, or bronchiectasis. Histology demonstrates bronchiolar inflammation with luminal obstruction [3]. COP is a restrictive lung disease with onset 2–12 months posttransplant with acute onset fever, cough, and dyspnea. Chest CT may demonstrate patchy airspace disease or nodular opacities. Histology reveals intraluminal organizing fibrosis in distal airspaces with mild interstitial inflammation [3]. Both BOS and COP are related to T-cell-mediated injury to lung epithelial cells, and Initial therapy is usually high-dose corticosteroids burst with a prolonged taper over months [3, 13]. Other therapies such as azithromycin, cyclosporine, and etanercept have been described and need further evaluation [3, 13]. A recent trial of inhaled fluticasone, azithromycin, and montelukast in patients with new-onset bronchiolitis obliterans showed that the combination therapy had improvement in ability to stabilize disease progression when compared to historical controls [35].

Respiratory Support

The transition from negative pressure ventilation to positive pressure ventilation results in significant changes in cardiopulmonary interactions. This is well known in patients with mediastinal masses impinging on great vessels or large pericardial effusions. Maintaining spontaneous ventilation, using specialized equipment (fiber-optic bronchoscope), avoiding the use of paralytics, and having extracorporeal membrane oxygenation (ECMO) equipment on standby are important considerations [13]. This transition can also result in cardiopulmonary collapse in patients with right heart failure and in patients who are intravascularly depleted such as patients in septic shock or hypovolemic shock. The former may be seen due to cardiac toxicity from chemotherapy and/or radiation or from pulmonary hypertension. Optimization of intravascular volume, use of inotropes to augment ventricular function, and availability of inhaled nitric oxide to avert a pulmonary hypertensive crisis might help prevent the need for cardiopulmonary resuscitation during this transition.

Noninvasive Ventilation (NIV)

Endotracheal intubation is associated with many complications, with highest concern being that of ventilator associated pneumonia [36]. Noninvasive positive pressure ventilation consists of continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP). These modalities can assist in oxygenation and ventilation in patients with respiratory distress and acute respiratory failure while potentially avoiding the complications of invasive mechanical ventilation (IMV) [37]. Continuous positive airway pressure (CPAP) maintains positive pressure and prevents airway and alveolar collapse in patients who are spontaneously breathing [38]. BiPAP is triggered by the patient's breath and an inspiratory positive airway pressure (IPAP) is provided while preventing airway and alveolar collapse with expiratory positive airway pressure (EPAP) [36–38]. A respiratory rate is also set on BiPAP, which can sometimes lead to dysynchrony between the mandatory breaths and the patient's innate respiratory efforts.

While NIV can potentially allow the avoidance of intubation and IMV, there are certain clinical scenarios that are considered contraindications to the use of NIV [36, 39]. The contraindications relate to the patient's inability to protect their airway with risk of aspiration, worsening gastric distension, and/or inability to provide consistent intrathoracic positive pressure with associated risks. The contraindications for NIV use can be listed as follows:

1. High risk of respiratory or cardiac arrest
2. Hemodynamic instability (dysrhythmias or shock)
3. Absent or weak cough or gag with inability to protect airway
4. Glasgow coma score < 8
5. Rapidly progressive neuromuscular weakness
6. Inability for good mask fit (facial surgery, trauma, burns, etc.)
7. Untreated pneumothorax
8. Vomiting and risk of aspiration
9. Poor skin integrity leading to skin breakdown

Much of NIV data available is in the immunocompromised patients with a dearth of data in the more specific hematopoietic stem cell transplant (HSCT) patients. NIV has been shown in some adult studies to reduce intubation rates, shorten ICU length of stay, and reduce the cost of hospitalization [40–44]. A meta-analysis by Wang et al. [45] looked at NIV versus IMV in all immunocompromised patients; the ICU length of stay was significantly shorter in the NIV group. This was however in patients with lower severity of illness scores [45]. Additionally, this group found a significant decrease in hospital mortality in NIV groups compared to IMV groups though there was high degree of heterogeneity. Within the hematologic and solid tumors subgroups, the 30-day mortality was significantly reduced with OR 0.34 (95% CI 0.22–0.54) when NIV was compared to IMV [45, 46]. Similarly, in a retrospective review of immunocompromised pediatric patients receiving NIV, Pancera et al. found that in the NIV group, there was a higher prob-

ability of 30-day survival (46.8%) when compared to the IMV (23.3%) [37]. However, more patients in the IMV group had markers of higher illness severity as evidenced by more than two organ failure, cardiovascular dysfunction, and therapeutic interventions scoring system score of ≥40.

NIV is not uniformly successful, and a growing body of evidence is aimed at determining factors that lead to failure of this modality in this at-risk population [37, 39, 47]. Literature reports a NIV success rate in immunocompromised pediatric patients of 54.5% with diagnosis of acute respiratory distress syndrome and up to 74.2% with diagnosis of respiratory failure [37, 47]. Among all patients with acute respiratory failure who received NIV, $FiO_2 > 80\%$ 1 h after initiation predicted failure of NIV [48]. Within pediatric immunocompromised patients, those who failed NIV were more likely to have severe sepsis and septic shock than those in the success group [47]. Patients in the NIV success group had early and sustained improvement compared to those who failed; therefore, lack of early improvement is discussed with the threshold of improvement being between 1 h and 2–4 h [47–50]. Munoz-Bonet et al. determined that an improvement in respiratory rate and pCO_2 2–4 h after NIV was associated with NIV success. Patients who had improvement of their PaO_2/FiO_2 ratio within the first hour of NIV initiation also were more likely to be in the NIV success group [49]. Therefore, a lack of improvement in physiologic parameters, such as weaning FiO2 or decreasing respiratory rate, within 2–4 h of NIV initiation should be considered an indication for endotracheal intubation (Fig. 11.1) [36]. Additionally, it appears prudent to consider patients with escalating hemodynamic support to have failed NIV trial.

NIV is associated with pressure-related pain/skin breakdown due to face masks and straps which at extremes may necessitate intubation if not addressed early [49]. NIV requires synchrony between the patient and ventilator, without which a patient may also fail NIV; however, there is little to no mention of this in the literature [36]. NIV can also be used in palliative care situations to alleviate air hunger [36] and in adult studies has been shown to decrease dyspnea and reduce the amount of morphine used [51].

NIV is a viable method of oxygenation and ventilation in immunocompromised patients with respiratory failure. However, controversy exists on the use of NIV in patients with acute respiratory failure due to potential for prolonging time to intubation, ultimately leading to worse outcomes [52].

It is therefore important to understand that while NIV potentially avoids complications of IMV, its utilization requires constant monitoring of the patient to ensure improvement. Lack of physiologic improvement should be considered an indication for endotracheal intubation, provided that would be reasonable for the patient's underlying disease and consistent with goals of care outlined by the family.

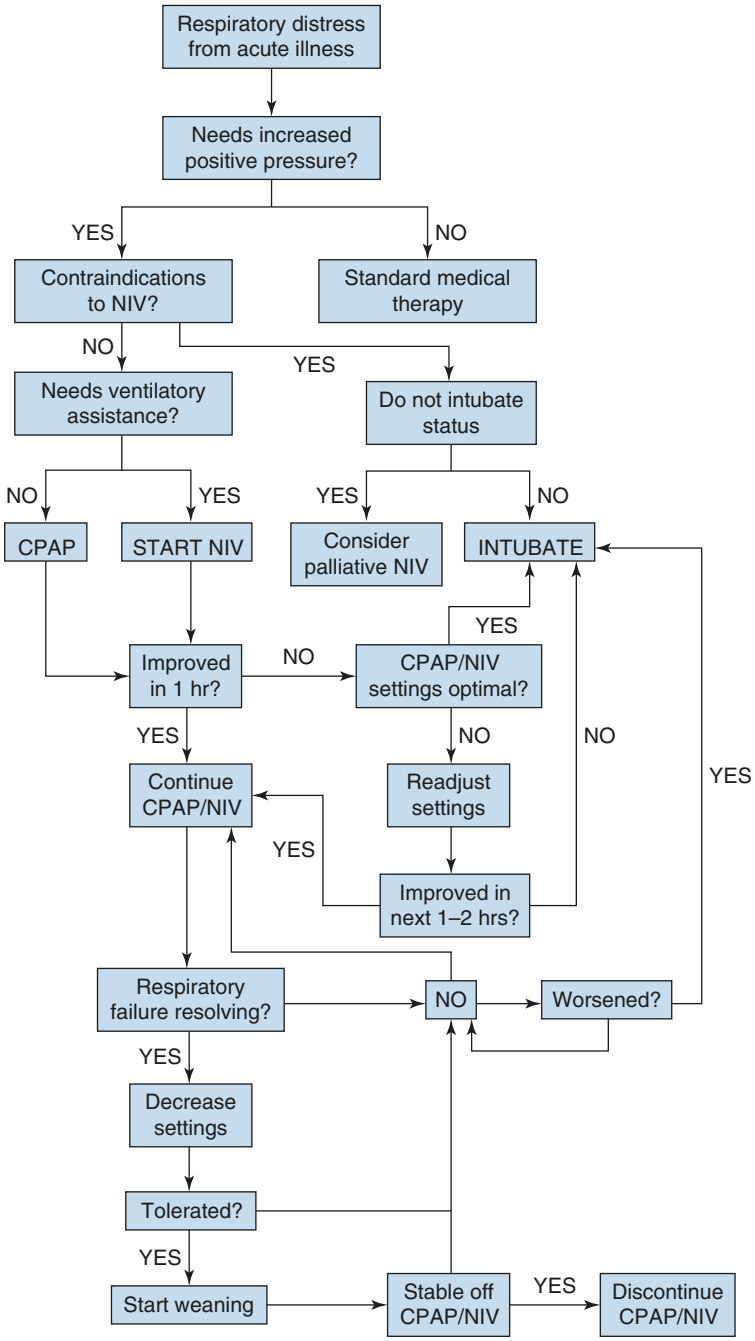

Fig. 11.1 Algorithm for initiation and weaning of NIV [36]. (Used with permission)

Invasive Mechanical Ventilation

Mortality with respiratory failure in pediatric oncology and HSCT patients varies depending on the underlying clinical diagnosis and etiology. Tamburro et al. reported an overall survival of 59% to extubation and discharge, in mechanically ventilated pediatric oncology patients and HSCT patients [6]. Aspesberro et al. cited 25% survival at 6 months in pediatric HSCT patients who were mechanically ventilated [53]. The reason for intubation such as elective for a procedure or emergent due to lung failure and the degree of lung injury is important to consider. Given the high mortality, it is important to urgently rediscuss goals of care and code status for patients with irreversible underlying disease and a few months or less to live, where it may prolong suffering. In a multicenter retrospective cohort study between 2009 and 2014 of 242 HSCT patients, the PICU mortality was noted to be 60.4%. Patients ventilated longer than 15 days had 2.4 times higher odds of death, and 40% of patients were placed on high-frequency oscillatory ventilation (HFOV) with a higher mortality of 76.5%. Transition to HFOV within 2 days of start of invasive mechanical ventilation resulted in a 76% decrease in the odds of death compared to those who were transitioned later [52]. The study suggests that early and aggressive lung protective ventilation strategies may result in improved outcomes in these patients.

In hypoxemic respiratory failure, the more common reason for hypoxemia is likely alveolar derecruitment. Optimizing alveolar recruitment using adequate positive end expiratory pressure (PEEP) while limiting peak inspiratory pressures (PIP) thereby avoiding further ventilator-induced lung injury (VILI) should be the goal with invasive mechanical ventilation. Permissive hypercapnia and hypoxia while ensuring adequate end-organ oxygen delivery would help achieve these goals in these patients. Severity of lung injury in intubated patients with hypoxemic respiratory failure can be estimated using OI and OSI [10]. OI has shown to also be a predictor of mortality [54–56]. An OI $\geq$ 20 at any point during ventilation in post-transplant patients has been shown to be associated with 94% mortality, while an OI $\geq$ 25 was associated with 100% mortality [55].

Consistent with optimizing lung recruitment and preventing further ventilator-induced lung injury, the Pediatric Acute Lung Injury Consensus Conference (PALICC) guidelines recommend utilization of moderately elevated levels of PEEP titrated to observed oxygenation and hemodynamic response and recommend tidal volumes of 3–6 and 5–8 ml/kg ideal body weight based on respiratory system compliance. High PEEP levels may be required in children with large abdominal masses or ascites causing significant mechanical constraints on the diaphragm, interfering with lung mechanics and causing significant lung derecruitment.

PALICC guidelines recommend consideration of HFOV when plateau pressures exceed 28 cm H_2O. Thereby, if one is not able to achieve lung recruitment without utilization of high ventilation strategies, one should consider escalation to other non-conventional modalities that are considered lung protective [10]. Airway pressure release ventilation (APRV) is another modality that has been used by some centers. Rowan et al. in a retrospective multicenter database study reported on 85 pediatric

HSCT patients with severe PARDS managed with HFOV. The study suggested that in that cohort, early use of HFOV was associated with improved survival compared to late implementation of HFOV, and the subjects had outcomes similar to those treated only with conventional mechanical ventilation [57]. There continues to be a need for more outcome data with HFOV and APRV use in pediatric patients with respiratory failure. Yehya et al. in a cohort of pediatric patients, refractory to conventional mechanical ventilation requiring transition to HFOV or APRV, demonstrated that HFOV was associated with more frequent neuromuscular blockade with no difference in mortality [56]. Perhaps more important is to observe the improvement in OI at 6–24 h after transition to HFOV and APRV which has been associated with survival, likely reflecting severity of lung disease and/or the ability to re-recruit the lungs [54, 56, 58]. In conclusion, lung protective ventilation should be implemented early in this cohort of children given the high risk of mortality and morbidity.

Extracorporeal Membrane Oxygenation (ECMO) as Rescue Therapy

Pediatric oncology and HSCT patients with severe PARDS should be evaluated for possible ECMO support when lung protective strategies result in inadequate gas exchange [10]. Immunocompromised status was demonstrated to be an independent risk factor for hospital mortality in adult patients with respiratory failure on ECMO [59]. Establishing set criteria for ECMO cannulation in this population is challenging given their immunocompromised status, thrombocytopenia, unique/varying range of pathologies, and multi-organ dysfunction. Gow et al. in 2006 reported a 21% survival rate to decannulation in a small cohort of 19 pediatric HSCT patients [60]. Renal complications and multi-organ dysfunction were reported to be risk factors for death. It thereby appears prudent to make the decision regarding cannulation by utilizing a multidisciplinary approach early in the disease process, to determine candidacy and timing of cannulation and allow serial evaluation. The patient's family should be appropriately counseled and informed consent obtained prior to ECMO cannulation given the high risk of complications in this patient population.

Ancillary Therapies (Fluid Management, Inhaled Nitric Oxide, and Surfactant)

Fluid overload is common in HSCT patients who develop PARDS. Initiation of empiric broad-spectrum antimicrobial treatment often exacerbates this situation. Tight fluid management is imperative along with initiation of diuretics in many patients. Clinical orders to limit total fluids at maintenance, to concentrate all

medications and infusions, and to evaluate the need for medications that have a high volume of fluid should be done early to avoid worsening fluid overload. Acute renal failure is not an uncommon complication in posttransplant patients, and it makes fluid management extremely challenging. Fluid overload associated with acute renal failure leads to worsening respiratory function, prolonged ventilation, increased ICU stay, and mortality [61–66]. Early consultation of renal specialists and intervention with diuretics and advanced therapies for fluid removal is imperative. In a retrospective chart review of 113 critically ill pediatric patients receiving continuous veno-venous hemofiltration, median fluid overload percentage was significantly lower in survivors versus non-survivors (7.8% vs. 15.1%) [65]. Michael et al. reviewed 26 HSCT patients with acute renal failure and noted a fluid overload of <10% was associated with improved survival [66]. Ellbahlawan et al. demonstrated a significant improvement in the PaO2/FiO2 ratio in HSCT patients after initiation of continuous renal replacement therapy, which significantly correlated, with reduction of fluid balance [67]. Initiation of CRRT for treatment of fluid overload may improve oxygenation and survival [3].

The use of inhaled nitric oxide can be considered in patients with documented pulmonary hypertension or severe right ventricular dysfunction [10]. PALICC guidelines also recommend consideration of use as a rescue or bridge to ECMO [10].

Surfactant use in immunocompromised children with acute lung injury was associated with improved oxygenation in a post hoc analysis of data from a previous randomized control trial [68]. A subsequent FDA-funded multicenter trial that attempted to investigate utility of surfactant in this cohort was unfortunately stopped due to low enrollment. Therefore, there remains a lack of evidence supporting the efficacy of surfactant use in this patient population.

Conclusion

Immunocompromised oncology patients, including HSCT patients are a unique patient population with unique pathologies and other organ dysfunction leading to respiratory failure. Evaluation of a HSCT patient with acute hypoxia and/or hypercarbia requires a workup to confirm or rule out infectious etiologies prior to treatment for potential noninfectious causes. Utilization of NIV requires constant monitoring of the patient to ensure improvement. The lack of physiological improvement on NIV should be considered an indication for endotracheal intubation. Early and aggressive lung protective ventilation strategies upon intubation with close monitoring for fluid overload may result in improved outcomes in these patients. Further research is required to look at other modifiable clinical factors/management techniques and to assess outcomes after the use of NIV, IMV, and ECMO in this unique population.

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