Review Article

Management of severe respiratory failure in complex trauma patients

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Abstract: Acute respiratory failure represents a major challenge in the management of complex trauma patients. Both direct thoracic injury and extrathoracic injury can lead to respiratory failure. The pathophysiologic mechanisms underlying respiratory failure in this setting can vary. Successful management of severe respiratory failure in complex trauma patients requires an understanding of these pathophysiologic processes and careful attention to multiple treatment priorities. Lung-protective ventilation strategies, judicious fluid management, and the use of rescue modalities are discussed in this review.

Keywords: Trauma; acute respiratory distress syndrome (ARDS); chest; injury; extracorporeal membrane oxygenation (ECMO)

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Introduction

Acute respiratory failure represents a major challenge in the management of trauma, affecting up to 20% of complex trauma patients (1,2). Respiratory failure can progress to acute respiratory distress syndrome (ARDS), occurring in up to 5% of blunt trauma patients admitted to the intensive care unit in one large series (3). Independent predictors of development of ARDS include injury severity score (ISS) greater than 25, the presence of pulmonary contusion, age greater than 65, hypotension on admission, and blood product transfusion requirement of more than ten units. Severe respiratory failure develops following trauma in one of two settings: (I) direct chest injury leading to functional impairment of one or both lungs; or (II) indirect injury via a multi-factorial inflammatory—mediated response to severe extrathoracic injury.

Direct lung injury from trauma

Blunt chest injury

Pulmonary contusion represents a common cause of respiratory failure following blunt chest trauma. The parenchymal lung injury of blunt trauma may lead to respiratory failure via a constellation of pathophysiologic changes, including increased production of mucus and decreased clearance of mucus and blood from the airways, alterations in surfactant stabilization of alveolar units, alterations of lung compliance, and ventilation/perfusion mismatch (4).

Often (but not always) associated with pulmonary contusion, rib fractures lead to respiratory failure via alterations in the cohesive function of the chest wall as a unit to provide negative pressure and allow full lung expansion. As the atelectasis associated with rib fractures increases with number and severity of fractures, so too does the risk of pneumonia, respiratory failure, and death (5). This effect is particularly pronounced in the elderly population, for whom the presence of rib fractures conveys a mortality of at least 20% (6).

Management of blunt chest trauma generally focuses on pain control and pulmonary toilet in an effort to prevent respiratory failure. Treatment of pneumothorax and hemothorax with tube thoracostomy or surgical drainage,

when needed, optimizes pulmonary function. High level evidence for the optimal approach to these issues is lacking, however, as noted in a recent Eastern Association for the Surgery of Trauma (EAST) Practice Management Guideline providing only conditional recommendations, based on low quality evidence, for epidural and multimodal analgesia (7). In the absence of strong evidence, the generally accepted strategies of optimizing pain control and minimizing atelectasis seem to be appropriate.

Non-invasive positive pressure ventilation (NIV) using continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BIPAP), as well as high flow nasal cannula oxygen therapy, are sometimes used in an effort to prevent respiratory embarrassment following blunt thoracic trauma. Though commonly used, strong data is lacking for the use of these modalities in the treatment of blunt chest injury. Four randomized controlled trials (8-11), as well as several retrospective cohort studies and observational studies, have investigated the use of NIV in chest trauma. A meta-analysis of these trials (12) suggested that NIV may improve mortality, decrease intubation rate, decrease intensive care unit length of stay, improve oxygenation and respiratory rate. These results should be interpreted with caution, however, as the included studies displayed considerable heterogeneity and a paucity of high quality data. Additional research is needed to further delineate these modalities' roles in the management of blunt chest injury, but in the absence of convincing evidence they are still employed with some frequency.

Penetrating chest injury

Like blunt injury, penetrating thoracic injury can lead to respiratory failure. In addition to the systemic inflammatory mediated respiratory failure observed in severe injuries to other compartments, penetrating thoracic injury can affect lung parenchyma directly. In cases where surgical treatment is required, rates of respiratory failure and death vary according to the extent of lung resection required, with the highest mortality in cases requiring pneumonectomy (62%), as compared to lobectomy (35%) or wedge resection (22%) in one series of 669 patients (13). The lung-protective strategies highlighted throughout this review apply to penetrating lung trauma as well, as avoidance of further injury to the traumatized lung, with maintenance of function of spared lung, is desirable.

Indirect lung injury in severe trauma

In addition to direct traumatic injury to the thorax, severe extrathoracic injury can lead to respiratory failure through a variety of mechanisms. Traumatic brain injury (TBI) has a close association with respiratory failure, with up to 1/3 of severe TBI patients developing some degree of respiratory failure (14) and roughly 8% of patients with head abbreviated injury score (AIS) of 4 or greater developing ARDS (15,16). Acute respiratory failure from TBI can arise from impaired respiratory drive due to neural injury. Additionally, a syndrome of severe respiratory failure can arise from a complex interaction between the injured brain and injured lungs. The mechanisms underlying this brain-lung "cross-talk" association highlight the complex multifactorial nature of the care of severely injured patients. TBI induces increased endothelial permeability at both the blood-brain and the blood-lung barriers (17,18), and increased intracranial pressure has been shown to induce pulmonary edema (19,20). It is also important to note that conversely, lung injury can worsen brain injury. Animal studies suggest that the hippocampus, which plays an important role in cognition, is particularly vulnerable (21) to this type of injury.

Fat embolism from long bone fractures leads to lung injury via an incompletely understood pathophysiologic mechanism, most probably related to fat emboli occluding the microvasculature and triggering an inflammatory response (22).

Venous thrombosis can lead to pulmonary embolus, sometimes even in the immediate post-injury setting. One series noted 0.5% of initial trauma CT scans of the chest showed evidence of pulmonary embolus (23). Other series have documented the relatively common nature of pulmonary emboli in the trauma population, highlighting the fact that these emboli often occur early after the traumatic insult (24). While some uncertainty remains regarding the optimal management of these embolic events, in the setting of associated severe respiratory failure, the goals of treatment are similar—maintain lung recruitment and gas exchange while minimizing ventilator induced lung injury.

Severely injured trauma patients frequently require blood product transfusion. Blood product transfusion requirement directly correlates with risk of ARDS, both for the administration of packed red blood cells and fresh frozen plasma (25-27). Some authors have shown that transfusion

of blood products in critically ill or injured patients doubles the risk for the development of acute lung injury in the 6–72 hours after the transfusion (28), and this risk increases with each unit of blood products transfused. In patients with hemorrhagic shock, appropriate administration of blood products clearly must be performed, but in light of the increased risk of lung injury and infection, unnecessary transfusion should be fervently avoided. In the absence of active bleeding, a restrictive blood transfusion strategy in critically ill patients is clearly supported by the available literature (29).

Lung protection in severe respiratory failure

Respiratory support in the setting of both direct and indirect traumatic lung injury share the same management goals prioritized in care of other forms of respiratory failure: optimization of ventilation, oxygenation, and ventilation/perfusion matching, while avoiding ventilator associated lung injury. A considerable body of background work in both animal and human studies has established several pathways by which ventilator associated lung injury can occur. Alveolar overdistension predisposes patients to pneumothorax, pulmonary edema (30), and translocation of inflammatory mediators and bacteria. When ventilation volumes are low, lung injury occurs via the opening and closing of alveoli, known as atelectotrauma, with similarly injurious effects. These injurious forces result in surfactant dysfunction, sloughing of bronchial epithelium, and the release of inflammatory mediators which directly injure the lung and can lead to systemic inflammation, multi organ dysfunction, and death (31).

In traumatic conditions such as pulmonary contusion, pulmonary laceration, and bronchial disruption, a loss of homogeneity occurs in the lung, with healthy areas receiving more ventilation than injured lung units. This mimics the findings noted in ARDS, in which some areas, particularly dependent portions of the lung, are poorly expanded, while other areas become overdistended. In many cases, the pathophysiology, and therefore the management, of direct thoracic trauma mimics that of ARDS.

Since the ARDSNet trial (32), the mainstays of ARDS management have focused on avoidance of ventilator induced lung injury. This has manifest in the use of lower tidal volume ventilation and permissive hypercapnia. The ARDSNet protocol includes use of tidal volumes of 6–8 mL/kg of PBW, uses standardized PEEP/FiO_2 ratios based on oxygenation, and avoids elevation of the plateau pressure beyond 30 cmH_2O. This approach has been shown to have a mortality benefit.

Proponents of an "open lung" approach to management of injured lungs often advocate for use of relatively higher levels of PEEP in addition to the low tidal volume approach to ventilation. The physiologic reasoning behind this approach is that higher PEEP should maintain recruited lung units and recruit additional lung units, providing a higher functional residual capacity and minimizing atelectotrauma. Despite demonstrating improved oxygenation with a higher PEEP strategy, several studies have failed to demonstrate a mortality benefit to this approach (33-35). A recent multi-center, randomized controlled trial further called into question the high PEEP strategy (36). In this study, the use of an aggressive recruitment maneuver was paired with a stepwise PEEP titration. The results of the study, with higher mortality in the recruitment maneuver/high PEEP group, highlights the potential hazards of suboptimal PEEP or recruitment maneuvers. It is unclear which portion of the study's open lung protocol conferred the increased mortality (recruitment maneuvers or higher PEEP levels). One explanation for the inability to demonstrate mortality benefit with higher levels of PEEP may involve the concept of driving pressure. Driving pressure, determined by the tidal volume and compliance, can be calculated by subtracting the PEEP from the plateau pressure. In a recent patient level analysis of patients from the ARDSNet data set, Amato and colleagues demonstrated a survival benefit to patients managed with lower driving pressures (37). When PEEP was increased with no associated decrease in driving pressure, no mortality benefit was found. This may help to explain the lack of survival benefit to higher PEEP noted in prior studies—increasing the PEEP may only be helpful if it decreases the driving pressure. The question of what is the optimal PEEP for each individual patient remains challenging.

Prone positioning

Prone positioning has been used to optimize ventilator support in patients with severe respiratory failure. By decreasing the effect of the weight of the lungs, heart, and chest wall on the dependent posterior aspects of the lungs, aeration of these atelectatic segments can occur more easily. Several investigations into the use of prone positioning for ARDS demonstrated physiologic benefits, including improved oxygenation (38,39) and decreased ventilator-induced lung injury (40,41). These physiologic benefits

presumably stemmed from increasing end expiratory lung volume, with associated improvement in V/Q matching and decreased ventilator-induced lung injury.

Building on this work, the PROSEVA trial (42), a randomized, controlled investigation of prone positioning in moderate to severe ARDS, demonstrated a mortality benefit to the use of prone positioning. Patients were positioned prone for 16 hours per day. The results of the foundation work on physiologic benefits, compounded by the mortality benefit noted in PROSEVA, led to the inclusion of a strong recommendation for prone positioning by the 2017 ATS/ESICM/SCCM international consensus guidelines for management of ARDS (43).

Of note, exclusion criteria of the PROSEVA trial pertinent to the trauma population included ICP >30, unstable fractures of the spine, femur, or pelvis, burn >20% TSBA, facial trauma, and recent sternotomy or anterior chest tube presence with active air leak. Accordingly, extrapolation of the benefits of prone positioning to patients meeting these criteria should be performed with caution. The improved oxygenation associated with prone positioning has been reproduced in trauma patients without associated adverse effects (44). At many trauma centers, prone positioning is frequently used in trauma patients with severe respiratory failure, and the best available evidence suggests that it is safe in the trauma population as well as in patients who underwent abdominal surgery (45).

Lung protective strategies in the presence of brain injury

The presence of TBI complicates the management of severe respiratory failure, as the priorities of avoiding worsening brain injury and avoiding ventilator induced lung injury can be construed as being in conflict. Where ARDSNet protocols allow permissive hypercapnia in an effort to reduce ventilator induced lung injury, the desire to protect blood flow regulation in the injured brain mandates maintenance of pCO_2 in the normal range. Additionally, theoretical concern exists regarding the use of higher PEEP, owing to presumed risk of worsening elevated intracranial pressure by impairing venous return. In practice, however, as long as the MAP is maintained, increased levels of PEEP do not appear to significantly impact cerebral perfusion pressure or even intracranial pressure (46). High tidal volumes were found to be associated with increased risk of acute lung injury in patients with brain injury (47). Generally speaking, what is best for the injured lung is best for the injured brain, so "lung-protective" ventilator management strategies are usually used in brain injured patients as well.

Fluid management

Essential to the management of severe respiratory failure, particularly in the severely injured trauma patient, is proper fluid management. A conservative fluid management strategy was shown in a randomized trial to improve lung function and decrease duration of mechanical ventilation in patients with acute lung injury (48), without impacting non-lung organ failure. Restrictive fluid administration has been associated with decreased rates of VAP (49), and, when combined with damage control techniques, has been associated with improved operative mortality (50).

While intravenous fluid therapy is commonly used in severely injured patients in order to mitigate kidney injury, excess fluid administration and its associated elevated venous pressures may in fact worsen kidney function through increased renal parenchymal congestion (51). Analogous to the brain-lung interactions described above, the lungs and kidneys interact via similar "crosstalk" mechanisms whereby injury to one organ affects the function of the other. In totality, these and other studies highlight the importance of extremely judicious fluid management in the setting of severe traumatic respiratory failure. Optimization of fluid management can be facilitated through the use of critical care ultrasound. Multiple approaches have been described, including the use of bedside echocardiography and the use of lung ultrasound to detect development of pulmonary edema (52).

Alternative modes of ventilation in severe respiratory failure

High frequency oscillatory ventilation (HFOV), a mode characterized by the high frequency application of very small tidal volumes, should theoretically produce minimal ventilator induced lung injury. For some time, considerable enthusiasm existed for the mode's application in severe respiratory failure, including from traumatic injury. Unfortunately, two recent large randomized controlled trials failed to show benefit to the use of HFOV (53,54), so the mode has begun to fall out of favor.

VDR, the volumetric diffusive respirator, has been used as rescue therapy for refractory ARDS. This ventilator uses a high frequency percussive mechanism to deliver pulses of gas. These high frequency pulses create a "to and fro"

effect well-suited to clearance of the airways. Naturally, the mode was applied to burn/inhalational injuries, where the airway clearance benefits were most pronounced. Because many burn centers also care for other trauma patients, VDR ventilation remains a regularly utilized approach in the trauma population.

In airway pressure release ventilation (APRV), a CPAP is applied, with intermittent releases to allow for convective CO_2 removal. The patient can spontaneously breathe throughout the entirety of the cycle. The key to success in the use of APRV lies in the proper choice of release time. When the release time is set too short, convective CO_2 removal is inadequate and the patient can become very uncomfortable. When the release time is set too long, excessive exhalation occurs, resulting in large tidal volumes and atelectotrauma, loss of lung homogeneity, and the type of ventilator-induced lung injury shown to be harmful by ARDSNet. Guidelines for setting APRV settings can be found in multiple sources (55), but it is the authors' opinion that the mode, when set correctly, is a highly effective ventilatory strategy both for the treatment and prevention of ARDS.

Extracorporeal support

Extracorporeal membrane oxygenation (ECMO) is a salvage therapy for patients with hypoxemia refractory to mechanical ventilation. The use of ECMO for a trauma patient was first described in 1972 by Hill *et al.* (56). Since then, numerous case reports and small case series and a few large case series have described strategies for the use of ECMO for trauma patients, the complications suffered by those patients, and have attempted to identify factors associated with survival to hospital discharge.

No randomized trials of ECMO have been conducted exclusively for populations of trauma patients. The best data come from retrospective analyses, the largest of which include 10 to 46 patients. Anderson *et al.* reported the support of 24 trauma patients, 12 of whom were adults, with ECMO at the University of Michigan (57). Seventeen patients were liberated from the ECMO circuit and 15 (63%) survived to discharge. All patients were anticoagulated with heparin infusions. Major bleeding complications occurred in 75% of patients and 20.8% of patients had cerebral infarcts or hemorrhage. In 2010, Arlt *et al.* at University Hospital Regensburg, Germany showed ECMO could support patients with respiratory failure also suffering hemorrhagic shock by using a heparin coated system (58). Other large, single institution series have reported survival to hospital discharge rates of 44–70%, with bleeding complication rates up to 35% (59-62). Guirand *et al.* compared trauma patients supported with ECMO at Wake Forest School of Medicine to patients supported with mechanical ventilation at Los Angeles County and University of Southern California Medical Center to assess whether ECMO was associated with a survival benefit (63). The patients supported with ECMO had higher Murray Lung Injury Scores, lower PaO_2/FiO_2 ratios, higher rate of open abdomens, higher rate of renal replacement therapy, and higher pre-ECMO fluid balance reflecting the overall worse condition of patients selected to undergo ECMO support. The rates of survival to discharge were 58% and 55% for the ECMO and mechanical ventilations groups, respectively. When the investigators adjusted for fluid balance, PaO_2/FiO_2 ratios, Murray Lung Injury Score, open abdomen, renal replacement therapy, hemorrhagic complications (15% of ECMO patients suffered complications), and pulmonary complications a survival benefit associated with ECMO support was observed. The survival benefit associated with ECMO should be interpreted with caution because the trial was not randomized and the risk of confounding factors unaccounted for by the statistical analysis is great.

TBI is not an absolute contraindication to ECMO support. Muellenbach *et al.* described support of 3 patients with TBI using ECMO without anticoagulation for 5, 1, and 2 days without thromboembolic events (64). Additional cases of supporting patients with TBI with ECMO report delaying or holding anticoagulation or attaining lower aPTT goals (65-68). Particularly with the use of veno-venous ECMO, delaying or avoiding systemic anticoagulation is performed at many centers. No large, single series has focused on ECMO for patients with TBI, but many of the large trials include patients with traumatic brain injuries and no increased risk of mortality has been found (59,62,69). ECMO has even been successfully employed during and shortly after decompressive craniotomy (70,71). Despite measures to reduce anticoagulation duration or intensity, there remains a risk of cerebrovascular complications for trauma patients supported with ECMO as high as 14–16% (60,69).

ECMO has also been used to support patients with endobronchial hemorrhage (72,73), aortic injuries (74-76), bronchial transections (77-82), and drowning (83,84).

Once considered too unsafe, ECMO has proved to be a valuable tool to support and salvage patients who likely

would not have survived with conventional mechanical ventilation. Reports have expanded ECMO to not only trauma patients in general, but also to patients with injuries once thought to be absolute contraindications to ECMO support. Further improvements in care may be made by defining which patients are most likely to benefit from ECMO or those beyond the capabilities of ECMO and centralizing care for patients on ECMO in specialized units (85).

Conclusions

Severe respiratory failure represents a considerable problem in patients with complex traumatic injuries. Optimal management of these patients requires a thorough understanding and application of the pathophysiology of the complex interactions between the lungs and multiple organ systems. Many questions remain unanswered and the field is ripe with areas in need of additional investigation.

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Footnote

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