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Acute Respiratory Distress Syndrome (ARDS)

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Introduction

Acute respiratory distress syndrome (ARDS) is a life-threatening condition of seriously ill patients, characterized by poor oxygenation, pulmonary infiltrates, and acuity of onset. On a microscopic level, the disorder is associated with capillary endothelial injury and diffuse alveolar damage.

ARDS is defined as an acute disorder that starts within 7 days of the inciting event and is characterized by bilateral lung infiltrates and severe progressive hypoxemia in the absence of any evidence of cardiogenic pulmonary edema. ARDS is defined by the patient's oxygen in arterial blood (PaO2) to the fraction of the oxygen in the inspired air (FiO2). These patients have a PaO2/FiO2 ratio of less than 300. The definition of ARDS was updated in 2012 and is called the Berlin definition. It differs from previous American European Consensus definition by excluding the term Acute Lung Injury, it also removed the requirement for wedge pressure <18 and included the requirement of positive end-expiratory pressure (PEEP) or continuous positive airway pressure (CPAP) of greater than or equal to 5.

Once ARDS develops, patients usually have varying degrees of pulmonary artery vasoconstriction and, subsequently, may develop pulmonary hypertension. ARDS carries a high mortality, and few effective therapeutic modalities exist to combat this condition.[1][2]

Etiology

ARDS has many risk factors. Besides pulmonary infection or aspiration, extra-pulmonary sources include sepsis, trauma, massive transfusion, drowning, drug overdose, fat embolism, inhalation of toxic fumes, and pancreatitis. These extra-thoracic illnesses and/or injuries trigger an inflammatory cascade culminating in pulmonary injury.[3]

Lung Injury Prevention Score [1] is helpful in identifying low-risk patients, but a high score is less helpful.

Some risk factors for ARDS include:

- Advanced age
- Female gender
- Smoking
- Alcohol use
- Aortic vascular surgery
- Cardiovascular surgery
- Traumatic brain injury

Epidemiology

Estimates of the incidence of ARDS in the United States range from 64.2 to 78.9 cases/100,000 person-years. Twenty-five percent of ARDS cases are initially classified as mild and 75% as moderate or severe. However, a third of the mild cases go on to progress to moderate or severe disease.[4] A literature review revealed a mortality decrease of 1.1% per year for the period 1994 through 2006. However, the overall pooled mortality rate for all the studies evaluated was 43%.[5]The mortality of ARDS is commensurate to the severity of the disease, it is 27%, 32%, and 45% for mild, moderate, and severe disease, respectively.

Pathophysiology

ARDS represents a stereotypic response to various etiologies. It progresses through different phases, starting with alveolar-capillary damage, a proliferative phase characterized by improved lung function and healing, and a final fibrotic phase signaling the end of the acute disease process. The pulmonary epithelial and endothelial cellular damage is characterized by inflammation, apoptosis, necrosis, and increased alveolar-capillary permeability, which leads to the development of alveolar edema and proteinosis. Alveolar edema, in turn, reduces gas exchange, leading to hypoxemia. A hallmark of the pattern of injury seen in ARDS is that it is not uniform. Segments of the lung may be more severely affected, resulting in decreased regional lung compliance, which classically involves the bases more than the apices. This intrapulmonary differential in pathology results in a variant response to oxygenation strategies. While increased positive end-expiratory pressure (PEEP) may improve oxygen diffusion in affected alveoli, it may result in deleterious volutrauma and atelectrauma of adjacent unaffected alveoli. [6]

Histopathology

The key histologic changes in ARDS reveal the presence of alveolar edema in areas of diseased lung. The type I pneumocytes and vascular endothelium are injured, which results in leaking of proteinaceous fluid and blood into the alveolar airspace. Other findings may include alveolar hemorrhage, pulmonary capillary congestion, interstitial edema, and hyaline membrane formation. None of these changes are specific for the disease. [7]

History and Physical

The syndrome is characterized by the development of dyspnea and hypoxemia, which progressively worsens within hours to days, frequently requiring mechanical ventilation and intensive care unit-level care. The history is directed at identifying the underlying cause which has precipitated the disease. When interviewing patients that are able to communicate, often they start to complain of mild dyspnea initially, but within 12-24 hours, the respiratory distress escalates, becoming severe and requiring mechanical ventilation to prevent hypoxia. The etiology may be obvious in the case of pneumonia or sepsis. In other cases, however, questioning the patient or relatives on recent exposures may also be paramount in identifying the causative agent.

The physical examination will include findings associated with the respiratory system, such as tachypnea and increased work of breathing. Systemic signs may also be evident depending on the severity of illness such as central or peripheral cyanosis as a result of hypoxemia, tachycardia, and altered mental status. Despite 100% oxygen, patients have low oxygen saturation. Chest auscultation usually reveals rales, especially bibasilar, but are often auscultated throughout the chest.

Evaluation

The diagnosis of ARDS is made based on the following criteria: acute onset, bilateral lung infiltrates on chest radiography of a non-cardiac origin, and a PaO/FiO ratio of less than 300 mmHg. It is further sub-classified into mild (PaO2/FiO2 200 to 300mmHg), moderate (PaO2/FiO2 100 to 200mmHg), and severe (PaO2/FiO2 less than 100mmHg) subtypes. Mortality and ventilator-free days increase with severity. A CT scan of the chest may be required in cases of pneumothorax, pleural effusions, mediastinal lymphadenopathy, or barotrauma to properly identify infiltrates as pulmonic in location.

Assessment of left ventricular function may be required to differentiate from or quantify the contribution of congestive heart failure to the overall clinical picture. This assessment can be achieved via invasive methods such as pulmonary artery catheter measurements or non-invasively, such as with cardiac echocardiography or thoracic bioimpedance or pulse contour analysis. However, the use of pulmonary artery catheters (PAC) is controversial and should be avoided if clinically possible and noninvasive measures for assessment should be exhausted first, use PAC is discouraged by the new definition. The practice of using bronchoscopy may be required to assess pulmonary infections and obtain material for culture.

Other laboratory and/or radiographic tests will be guided by the underlying disease process, which has triggered the inflammatory process that has led to the development of ARDS. Also, laboratory tests will be needed as patients with ARDS are highly likely to develop or be affected by associated multi-organ failure, including but not limited to renal, hepatic, and hematopoietic failures. Regularly obtaining complete blood count with differential, comprehensive metabolic panel, serum magnesium, serum ionized calcium, phosphorus levels, blood lactate level, coagulation panel, troponin, cardiac enzymes, and CKMB are recommended if clinically indicated. [8][9][10]

Treatment / Management

Unfortunately, no drug has been proven to be effective in preventing or managing ARDS. The chief treatment strategy is supportive care and focuses on 1) reducing shunt fraction, 2) increasing oxygen delivery, 3) decreasing oxygen consumption, and 4) avoiding further injury. Patients are mechanically ventilated, guarded against fluid overload with diuretics, and given nutritional support until evidence of improvement is observed. Interestingly, the mode in which a patient is ventilated has an effect on lung recovery. Evidence suggests that some ventilatory strategies can exacerbate alveolar damage and perpetuate lung injury in the context of ARDS. Care is placed in preventing volutrauma (exposure to large tidal volumes), barotrauma (exposure to high plateau pressures), and atelectrauma (exposure to atelectasis). [1][11]

A lung-protective ventilatory strategy is advocated to reduce lung injury. The NIH-NHLBI ARDS Clinical Network Mechanical Ventilation Protocol (ARDSnet) sets the following goals: Tidal volume (V) from 4 to 8 mL/kg of ideal body weight (IBW), respiratory rate (RR) up to 35 bpm, SpO2 88% to 95%, plateau pressure (P) less than 30 cm H2O, pH goal 7.30 to 7.45, and inspiratory-to-expiratory time ratio less than 1. To maintain oxygenation, ARDSnet recognizes the benefit of PEEP. The protocol allows for a low or a high PEEP strategy relative to FiO2. Either strategy tolerates a PEEP of up to 24 cm HO in patients requiring 100% FiO2. The inspiratory-to-expiratory time ratio goal may need to be sacrificed and an inverse inspiratory-to-expiratory time ratio strategy instituted to improve oxygenation in a certain clinical situation.

Novel invasive ventilation strategies have been developed to improve oxygenation. These include airway pressure release ventilation (APRV) and high-frequency oscillation ventilation (children). Recruitment maneuver, along with APRV, has not shown to improve mortality but may improve oxygenation. Patients with mild and some with moderate ARDS may benefit from non-invasive ventilation to avoid endotracheal intubation and invasive mechanical ventilation. These modalities include continuous positive airway pressure (CPAP), bi-level airway pressure (BiPAP), proportional-assist ventilation, and high flow nasal cannula. Adequate care should be taken to intubate and mechanically ventilate these patients if they are getting worse on the above non-invasive ventilation.

A plateau pressure of less than 30 cm HO can be achieved using several strategies. Again, this is to reduce the risk of barotrauma. One strategy is to maintain as low a V and PEEP as possible. Also, increasing the rise and/or inspiration times can also help maintain the P goal. Finally, the flow rate can be decreased as an adjunct to decreasing the P. High P is also a product of decreased lung compliance from non-cardiogenic pulmonary edema, a salient feature of ARDS pathophysiology.

Improving lung compliance will improve P and oxygenation goal attainment. Neuromuscular blockade has been used in this endeavor. Neuromuscular blockers instituted during the first 48 hours of ARDS was found to improve 90-day survival and increase time off the ventilator.[12] However, the most recent trial published in 2019 showed no significant difference in mortality with continuous infusion of paralytics as compared to lighter sedation goals.

[2] Other causes of decreased lung compliance should be sought and addressed. These include, but are not limited to, pneumothorax, hemothorax, thoracic compartment syndrome, and intraabdominal hypertension. Prone position has shown benefits in about 50% to 70% of patients. The improvement in oxygenation is rapid and allows reduction in FiO2 and PEEP. The prone position is safe, but there is a risk of dislodgement of lines and tubes. It is believed that in the prone position, there is the recruitment of dependent lung zones, improved diaphragmatic excursion, and increased functional residual capacity. To derive the benefits, the patient needs to be maintained in the prone position for at least 8 hours a day.

Non-ventilatory strategies have included prone positioning [13] and conservative fluid management once resuscitation has been achieved.[14] Recently, extracorporeal membrane oxygenation (ECMO) has also been advocated as salvage therapy in refractory hypoxemic ARDS.[15] However, two major trials that compared venovenous (VV) ECMO to standard care showed no difference in mortality between the two groups. [3] Nutritional support via enteral feeding is recommended. A high-fat, low-carbohydrate diet containing gamma-linolenic acid and eicosapentaenoic acid has been shown in some studies to improve oxygenation. Care must also be taken to prevent pressure sores; thus, frequent patient repositioning or turning is recommended when feasible. Skin checks per nursing routine are also advised. Physical therapy should be involved in exercising the patient when they are liberated from mechanical ventilation and stable to participate in therapy.

Differential Diagnosis

- Cardiogenic edema
- Exacerbation of interstitial lung disease
- Acute interstitial pneumonia
- Alveolar hemorrhage
- Acute eosinophilic lung disease
- Organizing pneumonia

Prognosis

The prognosis for ARDS was abysmal until very recently. There are reports of a 30% to 40% mortality up until the 1990s, but over the past 20 years, there has been a significant decrease in the mortality rate, even for severe ARDS. These accomplishments are secondary to a better understanding of and advancements in mechanical ventilation, and earlier antibiotic administration and selection. The major cause of death in patients with ARDS was from sepsis or multiorgan failure. While mortality rates are now around 9% to 20%, it is much higher in older patients. ARDS has significant morbidity as these patients remain in the hospital for extended periods and have significant weight loss, poor muscle function, and functional impairment. Hypoxia from the inciting illness also leads to a variety of cognitive changes that may persist for months after discharge. Excitingly, for many survivors, there is an almost near-complete return of pulmonary capacity, as measured by functional testing. Nonetheless, many patients report feelings of dyspnea on exertion and decreased exercise tolerance. For these patients, this ARDS sequela makes returning to a normal life challenging as they adjust to a new baseline.[16][17]

Complications

- Barotrauma from high PEEP
- Prolonged mechanical ventilation -thus the need for tracheostomy
- Post extubation laryngeal edema and subglottic stenosis
- Nosocomial infections

- Pneumonia
- Line sepsis
- Urinary tract infection
- Deep venous thrombosis
- Antibiotic resistance
- Muscle weakness
- Renal failure
- Post-traumatic stress disorder

Postoperative and Rehabilitation Care

Tracheostomy and Percutaneous Endoscopic Gastrostomy (PEG)

Many patients with ARDS end up requiring a tracheostomy and a percutaneous feeding tube in the recovery phase. The tracheostomy facilitates weaning from the ventilator, making it easy to clear the secretions and is more comfortable for the patient. The tracheostomy is usually done at 2 to 3 weeks, followed by a percutaneous feeding tube.

Nutritional Support

The majority of patients with ARDS have difficulty eating, and muscle wasting is very common. These patients are either given enteral or parenteral feeding, depending on the condition of the gastrointestinal tract. Some experts recommend a low-carbohydrate high-fat diet as it has anti-inflammatory and vasodilating effects. Almost every type of nutritional supplement has been studied in patients with ARDS, but so far, none has proven to be the magic bullet.

Activity

Since patients with ARDS are bed-bound, frequent changes in position are highly recommended to prevent bedsores and deep venous thrombosis. In alert patients, one can minimize the sedation and sit them in a chair.

Consultations

Management of patients with ARDS requires an interprofessional team of healthcare workers that include:

- Pulmonologist
- Respiratory therapist
- Intensivist
- Infection disease
- Dietitian

Deterrence and Patient Education

Even though many risk factors for ARDS are known, there is no way of preventing ARDS. However, careful management of fluids in high-risk patients can be helpful. Steps should be taken to prevent aspiration by keeping the head of the bed elevated before feeding. Lung protective mechanical ventilation strategy in patients without ARDS who are high risk would help prevent ARDS.

Enhancing Healthcare Team Outcomes

ARDS is a serious disorder of the lung which has the potential to cause death. Patients with ARDS may require mechanical ventilation because of hypoxia.[18] The management is usually in the ICU with an interprofessional healthcare team. ARDS has effects beyond the lung. Prolonged mechanical ventilation often leads to bedsores, deep venous thrombosis, multi-organ failure, weight loss, and poor overall functioning. It is important to have an integrated approach to the management of ARDS because it usually affects many organs in the body. These patients need nutritional support, chest physiotherapy, treatment for sepsis if present, and potentially hemodialysis. Many of these patients remain in the hospital for months and even those who survive face severe challenges as a result of a loss of muscle mass and cognitive changes (due to hypoxia). There is ample evidence showing that an interprofessional team approach leads to better outcomes as it facilitates communication and ensures timely intervention.[19] The team and responsibilities should consist of the following:

- Intensivist for managing the patient on the ventilator and other ICU-related issues like pneumonia prevention, deep venous thrombosis prophylaxis and gastric stress prevention
- Dietitian and nutritionist for nutritional support
- Respiratory therapist to manage the ventilator settings
- Pharmacist to manage the medications which include antibiotics, anticoagulants, diuretics, among others
- Pulmonologist to manage the lung diseases
- Nephrologist to manage the kidneys and oversee renal replacement therapy if needed
- Nurses to monitor the patient, move the patient in bed, educate the family
- Physical therapist to exercise the patient, regain muscle function
- Tracheostomy nurse to assist with maintaining tracheostomy and weaning
- Mental health nurse to assess for depression, anxiety, and other psychosocial issues
- Social worker to assess the patient financial situation, transfer for rehab and ensure there is an adequate follow-up
- Chaplain for spiritual care

Outcomes

Despite advances in critical care, ARDS still has high morbidity and mortality. Even those who survive can have a poorer quality of life. While many risk factors are known for ARDS, there is no way to prevent the condition. Besides the restriction of fluids in high-risk patients, close monitoring for hypoxia by the team is vital. The earlier the hypoxia is identified, the better the outcome. Those who survive have a long recovery period to regain functional status. Many continue to have dyspnea even with mild exertion and thus are dependent on care from others. [21]

Questions

To access free multiple choice questions on this topic, click here.

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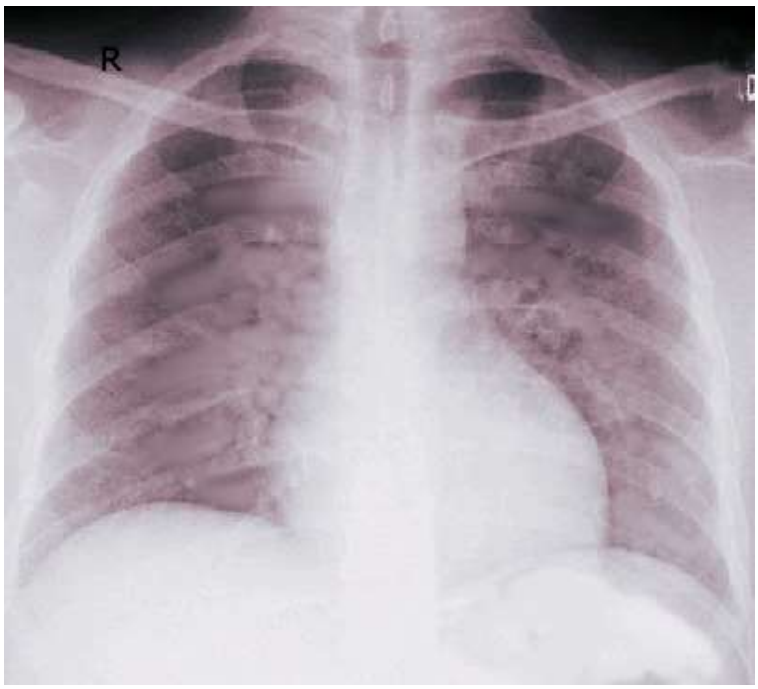
Figures



Acute Respiratory Distress Syndrome. Image courtesy S Bhimji MD

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