

Diagnosis and Management of Acute Respiratory Distress Syndrome in Adult

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Abstract

Introduction: Acute respiratory distress syndrome (ARDS) is distinct type of hypoxemic respiratory failure. It is characterized by acute abnormality of both lungs. In 2012, a new definition of ARDS was introduced and called Berlin definition. This definition has replaced the previous American-European Consensus Conference's definition of ARDS that was published in the nineties. Data suggest that approximately 190,000 cases of ARDS are annually seen in the United States. About 10 to 15 percent of admitted patients and up to 23 percent of mechanically ventilated patient meet criteria for ARDS.

The Aim of Work: In this review, we will summarize the latest evidence regarding the diagnosis and management of acute respiratory distress syndrome. A very detailed discussion of every aspect of the diagnosis and treatment may need several articles to be sufficiently addressed.

Methodology: This article is a comprehensive review of available full article regarding diagnosis and management of ARDS until May 2020.

Conclusion: Patients with ARDS present with the features of ARDS itself as well as features due to the inciting event. The manifestations of ARDS are extremely nonspecific which lead to frequent missing of the diagnosis until the disease progresses. Most cases of ARDS are caused by pneumonia and sepsis. The aim of investigation is to determine the presence of ARDS and its possible cause, and excluding potential mimicking etiologies. Initial assessment of patient with ARDS include a thorough history and clinical examination. Adequate management of acute respiratory distress syndrome include supportive care and management of hypoxemia.

Keywords: ARDS; Adult; Diagnosis; Management

Introduction

Acute respiratory distress syndrome (ARDS) is distinct type of hypoxemic respiratory failure. It is characterized by acute abnormality of both lungs. The condition was first recognized during the sixties of last century. Military clinicians in surgical hospitals in Vietnam

called it shock lung, while civilian clinicians referred to it as adult respiratory distress syndrome [1]. Subsequently, as the condition had been recognized in all age group, the term has changed to acute respiratory distress syndrome. In 2012, a new definition of ARDS was introduced and called Berlin definition. This definition has replaced the previous American-European Consensus Conference's definition of ARDS that was published in the nineties [2]. However, most available data are based upon prior definitions.

A multicenter, population-based, prospective cohort study was conducted to estimate the incidence of ARDS in the United States during a period of 15 months [3]. Data suggest that approximately 190,000 cases of ARDS are annually seen in the United States. The age-adjusted incidence increased from 16 per 100,000 person-years among individuals aged 15 to 19 years to 306 per 100,000 person-years among individuals 75 to 84 years of age. Within intensive care units (ICUs), about 10 to 15 percent of admitted patients and up to 23 percent of mechanically ventilated patients meet criteria for ARDS [4]. It has been suggested that the incidence of ARDS could be higher in US and Europe than in other countries [4]. One prospective cohort study has suggested a decrease in the incidence of ARDS based on analysis of data from single institution. According to this analysis, the incidence of ARDS changed from 82.4 cases per 100,000 person-years in 2001 to 38.9 cases per 100,000 person-years in 2008 [5]. This was basically due to a decline in hospital-acquired ARDS as the incidence at hospital presentation did not change.

In this review, we will summarize the latest evidence regarding the diagnosis and management of acute respiratory distress syndrome. A very detailed discussion of every aspect of the diagnosis and treatment may need several articles to be sufficiently addressed.

Methodology

We conducted a thorough systematic search on scientific database including PubMed search engine and Google Scholar for all studies related to the diagnosis and management of acute respiratory distress syndrome (ARDS). All relevant available full articles until May 2020 were reviewed and included. The terms used in the search were: ARDS, adult, diagnosis, management.

Clinical features

Traditionally, it has been conceptualized that ARDS follows the same pattern of lung injury and clinical manifestations that can be caused by a variety of conditions. However, the validity of this assumption has been questioned because multiple studies have found more severe reductions in lung compliance and less responsiveness to positive end-expiratory pressure (PEEP) when the ARDS was due to a pulmonary condition than to an extra pulmonary causes, such as sepsis [6].

Patients with ARDS present with the features of ARDS itself as well as features due to the inciting event [7]. Generally, the manifestations are extremely nonspecific which lead to frequent missing of the diagnosis until the disease progresses. Until now, more than 60 causes have been incriminated in the development of ARDS and increasing number of causes continue to emerge. However, most cases of ARDS are caused by few common conditions [8]. The most common etiologies are pneumonia (40 percent) and sepsis (32 percent) according to one report [9]. Other common inciting conditions include aspiration, trauma and burns, pancreatitis, Smoke inhalation, shock, transfusion-related acute lung injury, cardiothoracic surgery, hematopoietic stem cell transplant and drug toxicity. In addition, some factors have been suggested to possibly predispose patient to ARDS, but probably are not enough to cause ARDS by themselves. Sepsis is frequently counted as the most common cause of ARDS [8]. Hence, it should be promptly considered whenever ARDS develops in patient predisposed to serious infection or in association with a new fever or hypotension.

ARDS is suspected in patients with progressive dyspnea, increasing oxygen demand, and the presence of alveolar infiltration on chest imaging within 6 to 72 hours of inciting event. By history, ARDS patients typically present with dyspnea and a reduction in arterial oxygen saturation after 6 to 72 hours (or up to a week) following the primary etiology. On examination, patients may have tachypnea, tachycardia, and diffuse crackles. If these signs are severe, patient may appear with acute confusion, respiratory distress, cyanosis, and diaphoresis.

Other symptoms and signs as cough, chest pain, wheeze, hemoptysis, and fever are infrequently encountered and mostly driven by the underlying etiology.

Generally, most laboratory tests are nonspecific. A complete blood count (CBC) may show normal, elevated, or decreased white blood cell counts with or without a bacteremia. Evidence of organ injury could be seen in routine chemistries as a result of severe hypoxemia or associated shock and systemic inflammation. The prothrombin time and activated partial thromboplastin time may be prolonged, and D-dimer elevated, but laboratory evidence for disseminated intravascular coagulopathy (DIC) is usually limited to ARDS due to sepsis or malignancy. Typically, arterial blood gas (ABG) test reveals hypoxemia that is accompanied by acute respiratory alkalosis initially and an elevated alveolar to arterial oxygen gradient. Severe prolonged ARDS may present with acute hypercapnic respiratory acidosis which is an ominous sign with impending respiratory arrest. Metabolic acidosis from hypoxemia is unusual and, if present, is more likely to be due to the precipitating etiology as sepsis or associated organ injury as acute kidney injury rather than ARDS itself.

Imaging findings are inconsistent and vary according to the severity of ARDS. At first, simple chest radiograph typically has bilateral diffuse alveolar opacities with dependent atelectasis, however, these finding can be elusive [10]. Computed tomography (CT) of the chest may show widespread patchy and/or coalescent airspace opacities; these are usually more evident in the dependent part of the lung [11]. Similarly, the opacities can be subtle especially in early ARDS, but can become consolidative in appearance with disease progression [10]. The use of bedside lung ultrasound (US) is being studied and preliminary results show an 83 to 92 percent sensitivity for the diagnosis when compared with CT chest [12].

Patients with ARDS may present with clinical findings related to the underlying etiology. As an example, in patients with ARDS due to sepsis following pneumonia, there may be fever, hypotension, leukocytosis with left shift, lobar consolidation on chest radiograph, and lactic acidosis; patients with shock may also have evidence of organ failure, including elevated transaminases and renal insufficiency. Unfortunately, some features of the etiology could mask the manifestations of ARDS. As an example, the opacities from pancreatitis-related atelectasis may mimic ARDS, eventually delaying the diagnosis.

Diagnostic evaluation

The aim of investigation is to determine the presence of ARDS and its possible cause, and excluding potential mimicking etiologies. Initial assessment of patient with ARDS include a thorough history and clinical examination. Clinicians should check for fever, productive cough, pleuritic chest pain, and history of aspiration that suggest pneumonia, orthopnea that may suggest cardiogenic pulmonary edema, and hemoptysis that may indicate the presence of cancer, vasculitis, or alveolar hemorrhage. History of asthma should be checked as well as this may suggest vasculitis. Other important conditions that could be suggested by history include cardiac dysfunction, cancer, stem cell transplant, or pulmonary fibrosis. Abdominal symptoms as pain, vomiting, or diarrhea may suggest pancreatitis, colitis, or viscus rupture. Evidence of recent trauma or surgery should be sought as well.

Examination should include full assessment for signs of acute cardiogenic pulmonary edema as raised jugular venous pressure, crackles, murmurs, S3/S4 gallops, and lower extremity edema. Signs that suggest pneumonia should be examined; this include dullness on percussion, rales, egophony, or bronchial breath sounds. Abdominal examination aims to check for tenderness and distension and/or absent bowel sounds to suggest subdiaphragmatic etiologies for ARDS. Relevant finding in skin examination include the presence of burns, rashes, wounds, track marks, and systemic manifestations of septic emboli. The size and tenderness of the lymph nodes may lead to suspect infections or cancer; the dentition should be checked for possible sepsis. Volume status could be examined by mucus membrane assessment, skin turgor assessment should also be assessed and fluid balance measured, whenever possible. Occasionally, volume status can be difficult to assess clinically, especially in older patients, and bedside hemodynamic tools may provide supplementary data to help inform the clinician in this regard.

Laboratory studies should include complete blood count (CBC), liver function tests, coagulation studies, and arterial blood gas (ABG) analysis. Some experts suggest that D-dimer, troponin, and lactate levels should be measured to exclude common etiologies that can cause or mimic ARDS. Brain natriuretic peptide (BNP) levels are frequently ordered for assessing cardiogenic pulmonary edema. Lipase should be checked in patients with abdominal symptoms, particularly if the patient has no other obvious risk factors for ARDS.

Radiograph is essential for all patients whom suspected to have ARDS. This is due to the fact that abnormal imaging is essential for the diagnosis of ARDS. Chest radiography plays additional role in the evaluation for etiologies of ARDS as well as for conditions that mimic ARDS, particularly acute cardiogenic pulmonary edema. Computed tomography (CT) of the chest is not necessary for the diagnosis, however, CT may be helpful when there is a need for a more detailed pulmonary evaluation as it demonstrates evidence for cavitation, pleural effusions, or chronic interstitial lung disease that may be missed on chest radiograph. Additional imaging may be performed when specific etiologies for ARDS are suspected. For example, magnetic resonance imaging of the brain (MRI) plays important role in trauma patients while abdominal CT has critical advantages in patients with suspected pancreatitis, abscess, colitis, peritonitis, appendicitis.

Electrocardiography should also be obtained in patient suspected to have ARDS to look for evidence of cardiac dysfunction, including arrhythmias, obvious changes consistent with right or left ventricular strain, or ST segment changes that suggest ischemia.

Sampling of the respiratory tract as sputum or endotracheal aspiration should be examined, when possible, for gram stain and sputum culture. Urinary legionella and streptococcal antigen should be checked as well when pneumonia is suspected as the etiology along with blood and urine cultures.

Acute cardiogenic pulmonary edema is the most important condition to be excluded as it is very difficult to distinguish it from ARDS. Hence, following all the previous evaluation techniques, the effort should be directed toward its exclusion. In practice, most clinicians use clinical evaluation and BNP or N-terminal proBNP (NT-proBNP), with or without transthoracic echocardiography to confirm or exclude pulmonary edema. Specific details about the process of excluding acute cardiogenic pulmonary edema will not be discussed here.

Initial evaluation is sufficient in most patients to establish a preliminary diagnosis of ARDS and its etiology and no further investigations are necessary. This process should be achieved while patients receive supportive therapy. However, further investigation may be required if the diagnosis remains unclear and conditions such as acute cardiogenic pulmonary edema could not be excluded; this occurs with smaller proportion of patients. Further testing may include reevaluation of fluid status, additional laboratory tests, right heart catheterization, bronchoscopy with broncho-alveolar lavage (BAL), and rarely, lung biopsy. The decision among these tests is individualized and is dependent upon the suspected condition that needs to be confirmed or excluded as well as the safety of testing and the therapeutic and prognostic value of the test.

Bronchoscopy plays essential role when the cause of ARDS is uncertain and concern is raised about some conditions that need specific treatment. Patient suspected to have infection, particularly pneumonia, as an inciting condition could especially benefit from bronchoscopy as it provides specimens for culture when sputum is unavailable or unrevealing. Bronchoscopy may also help clinicians diagnose specific noninfectious causes of ARDS as acute eosinophilic pneumonia (AEP) or conditions that mimic ARDS as diffuse alveolar hemorrhage by providing specimens for cytology or biochemical analysis. Bronchoscopy in mechanically ventilated patients with hypoxemia has a similar spectrum of complications as in spontaneously breathing patients. These include barotrauma, bleeding, hypotension, hypoxemia, however, the risk of complications is believed to be higher in these patients. The decision to proceed with bronchoscopy mainly depends on weighing the risk against the diagnostic sensitivity for the suspected condition. Bronchoscopy has high sensitivity for detecting infections, DAH, and AEP. In contrast, it has limited benefits for many other conditions such as interstitial lung diseases, acute exacerbations of idiopathic pulmonary fibrosis (AEIPF), cryptogenic organizing pneumonia (COP), acute fibrinous organizing pneumonia (AFOP) or pulmonary vasculitis. Mini Broncho alveolar lavage (mini-BAL) may be an alternative of bronchoscopy carries a high risk rendering it unfeasible. However, the sensitivity of mini-BAL is likely lower than bronchoscopy.

Clinical diagnosis and Berlin definition

Acute respiratory distress syndrome is a diagnosis of exclusion. Hence, the diagnosis could be established once cardiogenic pulmonary edema and alternative causes of acute hypoxemic respiratory failure and bilateral infiltrates have been excluded. The Berlin Definition of ARDS sets a number of criteria to be present for diagnosis establishment [13]. These criteria are: (a) Respiratory symptoms must have begun within one week of a known clinical insult, or the patient must have new or worsening symptoms during the past week; (b) Bilateral opacities must be present on a chest radiograph or computed tomographic (CT) scan. These opacities must not be fully explained by pleural effusions, lobar collapse, lung collapse, or pulmonary nodules; (c) The patient's respiratory failure must not be fully explained by cardiac failure or fluid overload. An objective assessment to exclude hydrostatic pulmonary edema is required if no risk factors for ARDS are present; (d) moderate to severe impairment of oxygenation must be present, as defined by the ratio of arterial oxygen tension to fraction of inspired oxygen ($\text{PaO}_2/\text{FiO}_2$).

As no parameters relating to the underlying etiology are defined in the international consensus definition of ARDS, some confusion remains as to which conditions should or should not be included under the ARDS diagnostic umbrella. Generally, disorders that are known to cause diffuse alveolar damage and have the potential to resolve over time are included. Thus, viral or diffuse bacterial pneumonia and acute inhalational injuries are included, whereas eosinophilic pneumonia and diffuse alveolar hemorrhage associated with collagen vascular diseases are not.

Management

Adequate management of acute respiratory distress syndrome include supportive care and management of hypoxemia. Small number of ARDS patients die from respiratory failure alone [14]. On the other hand, ARDS patients commonly die as a result of their primary illness or due to secondary complications such as sepsis or multiorgan system failure.

Supportive care

Supportive care for patients with ARDS should be scrupulous with adequate sedation and neuromuscular blockade (paralysis), hemodynamic management, nutritional support, control of blood glucose levels, efficient evaluation and treatment of nosocomial pneumonia, glucocorticoid (in some patients), and prophylaxis against deep venous thrombosis (DVT) and gastrointestinal (GI) bleeding.

The use of sedative agent in patients with ARDS follows the same principle that in critically ill patients. Adequate sedation and analgesia may improve tolerance of mechanical ventilation and decrease oxygen consumption according to one study [15]. The duration of sedation in patients with severe ARDS may be needed for several days or longer. The choice of sedative agent should be driven by the patient's specific needs. Narcotics may be most useful in patient with pain and for suppression of the respiratory drive; benzodiazepines may be used for anxiety; and antipsychotic agents are especially helpful for agitated patient with delirium [16]. Intermittent injections of sedative agents are preferred method, while continuous infusions are usually reserved for patients who require repeated doses to achieve adequate sedation. Sedation scales such as the Richmond Agitation-Sedation Scale (RASS) could be used for precise sedation goals; decreasing the likelihood of over or under-sedation [17].

Neuromuscular blockade (induced paralysis) in patients with ARDS can have favorable effects as improving oxygenation [18] and undesirable effects as prolonged neuromuscular weakness [19]. Therefore, the impact of these competing effects on patient-important outcomes has remained unclear since data are conflicting. While a relatively old randomized trial reported a mortality benefit, a new trial published in 2019 reported no mortality benefit in patients with moderate to severe ARDS. Thus, experts recommend not to routinely using neuromuscular blockade in patients with moderate to severe ARDS, unless other indications are present. Indications that justify such use include severe ventilator dyssynchrony.

Glucocorticoids can be administered in some patients with ARDS. Patients who may benefit from glucocorticoid include patients with non-ARDS-related indications for systemic glucocorticoid therapy as patient with acute eosinophilic pneumonia. Similarly, glucocorticoids may also be beneficial to patients with ARDS due to refractory sepsis or community-acquired pneumonia if they meet indications. Glucocorticoid is also effective in patients presenting -or early in the disease- with moderate to severe ARDS and fail standard therapies. Glucocorticoids are generally not used in patients with less severe ARDS and in patients late in the disease course (more than 14 days). Similarly, Glucocorticoid is not administered in patients with certain viral infections as it is associated with worse outcomes in these patients [20].

Management of hypoxemia

By definition, patients with ARDS are severely hypoxemic. Hypoxemia could be managed to improve arterial oxygen saturation (SaO_2) by using high fractions of inspired oxygen (FiO_2), decrease oxygen consumption, improve oxygen delivery, and manipulate mechanical ventilator support. Usually, these options are applied in combination. Unfortunately, each method has its unquantifiable risk. The choice depends mostly on insuring adequate oxygenation and minimizing the inevitable risks.

Most acute respiratory distress syndrome patients require a high fraction of inspired oxygen (FiO_2), especially early in the disease course when pulmonary edema is most severe [21]. Prior to intubation, high flow oxygen can be provided through a face mask or high flow nasal cannula. This method could be sufficient to prevent subsequent intubation [22]. However, most patients with ARDS will require intubation and mechanical ventilation. During the attempt for intubation, 95 to 100 percent oxygen should be given to ensure an adequate SaO_2 . Some experts believe that using slightly less than 100 percent oxygen is preferred to reduce the risk of absorptive atelectasis [23]. It is believed that high FiO_2 supplementation carries a significant risk in patient with ARDS, however, there is no data to support this believe. This believe has emerged from studies in animals and normal humans that showed that high concentrations of oxygen damage the lung within hours [24]. It is uncertain at which threshold oxygen toxicity occurs, but appears to begin above 50 percent, and the risk rises as concentrations approach 100 percent [25]. Accordingly, the FiO_2 should be maintained at range of 50 to 60 percent as soon as safely possible.

Conclusion

Acute respiratory distress syndrome (ARDS) is distinct type of hypoxemic respiratory failure. It is characterized by acute abnormality of both lungs. In 2012, a new definition of ARDS was introduced and called Berlin definition. Patients with ARDS present with the features of ARDS itself as well as features due to the inciting event. The manifestations of ARDS are extremely nonspecific which lead to frequent missing of the diagnosis until the disease progresses. Most cases of ARDS are caused by pneumonia and sepsis. The aim of investigation is to determine the presence of ARDS and its possible cause, and excluding potential mimicking etiologies. Initial assessment of patient with ARDS include a thorough history and clinical examination. Adequate management of acute respiratory distress syndrome include supportive care and management of hypoxemia

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