Viral Pneumonia and Acute Respiratory Distress Syndrome

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KEYWORDS

• Acute respiratory distress syndrome • Respiratory virus • Community-acquired pneumonia

KEY POINTS

- Respiratory viruses are increasingly recognized in patients with severe community-acquired pneumonia and acute respiratory distress syndrome (ARDS).
- Pandemic and seasonal respiratory viral infections have been implicated in the pathogenesis of ARDS in adults.
- Supportive care for adults with ARDS caused by respiratory viruses is similar to the care of patients with ARDS from other causes.
- Antiviral therapy is available for some respiratory viral infections; however, further research is needed to determine which groups of patients would benefit.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a severe form of inflammatory lung injury characterized by increased vascular permeability in the lung.[1] Clinically, ARDS is defined by the presence of severe hypoxemia and bilateral opacities on chest imaging that are not explained by the presence of cardiac failure or volume overload.[2,3] Community-acquired pneumonia (CAP) is the most common cause of ARDS that develops outside of the hospital.[4] Respiratory viruses are increasingly recognized in patients with severe CAP and ARDS.[5,6] This article reviews the epidemiology, diagnosis, and management of adult patients with severe pneumonia and ARDS caused by viral respiratory pathogens.

EPIDEMIOLOGY

Improved diagnostic testing, particularly multiplex reverse transcription polymerase chain reaction (RT-PCR) assays, have increased recognition that respiratory viruses cause critical illness in adults.[7–9] Although no studies have reported the incidence of ARDS specifically caused by viral pneumonia, epidemiologic surveys of adults admitted to the intensive care unit (ICU) with pneumonia and respiratory failure suggest that respiratory viruses are a common cause of severe pneumonia.[10,11] In the Etiology of Pneumonia in the Community (EPIC) study, a population-based surveillance for CAP, respiratory viruses were identified in 22% of adults admitted to the ICU with radiographically proven pneumonia.[12] In a prospective, observational study of consecutive patients admitted to an ICU with CAP in 6 hospitals in Kentucky, respiratory viruses were identified in 23% of adults.[13] In a retrospective study of 198 patients with pneumonia admitted to a single ICU in South Korea, 36.4% had evidence of viral pneumonia, including 23 patients with a virus identified in bronchoalveolar lavage (BAL).[5] In

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these series, influenza virus and rhinovirus were the most commonly detected respiratory viruses, identified in approximately 6% and 8% of cases of viral pneumonia respectively. The prevalence of identified bacterial coinfection was low, and in 1 series[5] the mortalities related to bacterial and viral pneumonia were comparable.

Epidemiologic studies have shown that respiratory viruses are an underappreciated cause of severe CAP. However, the results of these studies should be interpreted with caution for several reasons. First, the viruses most commonly detected in patients with CAP vary across reports, which likely reflects differences in patient populations, season, and geographic location. Although respiratory viruses are commonly detected in critically ill patients using RT-PCR, their role in the pathogenesis of severe pneumonia and ARDS is less clear.[14,15] Respiratory viruses may be the sole cause of CAP and ARDS in some patients, or may be a risk factor predisposing patients to infections with other organisms, or may also represent concurrent upper respiratory tract infection, colonization, or prolonged viral shedding.[16–20]

PATHOGENESIS

The pathogenesis of ARDS in patients infected with respiratory viruses is incompletely understood. Most adults with respiratory viral infections have mild symptoms. However, viral strains associated with ARDS, such as the 2009 pandemic influenza A virus strain, are the identical to those seen in mild cases.[21,22] A combination of variable host factors and the host immune response therefore likely leads to the development of severe pneumonia and ARDS. Detailed review of the pathologic mechanisms implicated in the development of ARDS caused by respiratory viruses is beyond the scope of this article, but several excellent reviews on this topic exist.[23–26] Respiratory viruses initially infect the nasal and bronchial epithelium. This point of entry leads to respiratory airway and alveolar endothelial injury, elaboration of cytokines and chemokines, and recruitment of both innate and adaptive immune cells.[27] Specific cytokine profiles vary by virus, but converge on a common end pathway, resulting in the pathologic hallmark of ARDS, diffuse alveolar damage.[28–30] The mechanisms of acute lung injury caused by viral pathogens have important clinical implications; if ARDS results from the inflammatory host response rather than viral-mediated injury, then antiviral therapy alone may not be central to resolution of lung injury.[31]

GENERAL APPROACH TO VIRAL PNEUMONIA AND ACUTE RESPIRATORY DISTRESS SYNDROME

Diagnosis

The diagnosis of ARDS should be considered in all patients with respiratory viral infection, hypoxemia, and bilateral opacities on chest radiography unless there is strong clinical suspicion for cardiogenic pulmonary edema or volume overload. Criteria for diagnosing ARDS, referred to as the Berlin criteria,[2] are listed in **Box 1**. In resource-limited settings, diagnostic testing to ensure that patients meet each criterion, such as echocardiography or arterial blood gas analysis, may not be possible. In such situations, any patient with hypoxemia and bilateral opacities on chest radiography should be considered to have ARDS unless strong clinical suspicion for cardiogenic pulmonary edema or volume overload is present.[32]

Diagnosis of respiratory viruses can be made using isolation of intact virus particles from cell culture, viral antigen detection by immunofluorescence, or multiplex RT-PCR. When available, multiplex RT-PCR provides more rapid diagnosis with equal or better sensitivity and specificity compared with viral culture and immunofluorescence testing.[33,34] Multiplex RT-PCR testing using specimens collected from nasopharyngeal (NP)

Box 1
Definition of acute respiratory distress syndrome, Berlin criteria

Within 1 week of known clinical insult or new or worsening respiratory symptoms.

Bilateral opacities on chest imaging not fully explained by effusions, lobar/lung collapse, or nodules.

Respiratory failure not explained by cardiac failure or fluid overload. Need objective assessment such as echocardiography to exclude hydrostatic edema if no risk factor present.

Impaired oxygenation:

Mild: 200< P_aO_2/FiO_2 ≤300 with PEEP or CPAP ≥5 cm H_2O

Moderate: 100< P_aO_2/FiO_2 ≤200 with PEEP ≥5 cm H_2O

Severe: P_aO_2/FiO_2 ≤100 with PEEP ≥5 cm H_2O

Abbreviations: CPAP, continuous positive airway pressure; FiO_2, fraction of inspired oxygen; PEEP, positive end-expiratory pressure.

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