

ORIGINAL RESEARCH

Clinical Characteristics and Outcomes of Patients with Acute Respiratory Distress Syndrome (ARDS) Admitted to the Intensive Care Unit (ICU)

Dr. Alok Kumar Kalyani

Assistant Professor, Department of General Medicine, Venkateshwara Institute of Medical Sciences, Gajraula, Uttar Pradesh, India

Corresponding Author

Dr. Alok Kumar Kalyani

Assistant Professor, Department of General Medicine, Venkateshwara Institute of Medical Sciences, Gajraula, Uttar Pradesh, India

Received: 22 February, 2017

Accepted: 26 March, 2017

ABSTRACT

Aim: The objective of this study was to analyze the clinical characteristics, management approaches, and outcomes of patients with Acute Respiratory Distress Syndrome (ARDS) admitted to the Intensive Care Unit (ICU), focusing on how ARDS severity impacts mortality, resource use, and complications. **Material and Methods:** This descriptive observational study included 100 patients diagnosed with ARDS in the Department of Medicine. Patients aged 13 years or older with confirmed ARDS, determined by clinical, radiological, and physiological criteria, were included. The ARDS severity was classified into mild, moderate, and severe categories based on the PaO₂/FiO₂ ratio. Exclusion criteria encompassed patients under 13 years, those who declined or later withdrew consent. **Results:** The cohort had a mean age of 55.20 ± 13.80 years, with a predominance of males (65.00%). Severe ARDS patients had the lowest PaO₂/FiO₂ ratios (mean 95.10 ± 12.60, p < 0.001) and higher C-reactive protein levels (p = 0.03), suggesting a stronger inflammatory response. Management included mechanical ventilation (85.00%) and prone positioning (60.00%), with more intensive interventions for severe cases. ICU mortality was significantly higher in severe ARDS (47.06%) compared to mild cases (12.12%) (p = 0.01), and severe cases had extended ICU stays and fewer ventilator-free days (p = 0.05 and p = 0.03, respectively). Complications such as sepsis and acute kidney injury were more frequent in severe ARDS. **Conclusion:** This study underscores the association between ARDS severity and higher mortality, prolonged ICU stays, and greater complications. Severe ARDS patients required more intensive management and had poorer outcomes, highlighting the need for early intervention and specialized care for severe cases.

Keywords: ARDS, ICU, severity, clinical outcomes, respiratory support

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-Non Commercial-Share Alike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

INTRODUCTION

Acute respiratory distress syndrome (ARDS) is a severe and often life-threatening condition that presents a significant clinical challenge in intensive care units (ICUs) worldwide. Characterized by acute inflammation of the lungs and rapid progression of respiratory failure, ARDS results from direct or indirect pulmonary injuries that compromise oxygen exchange. This syndrome requires urgent intervention to manage its complexities and prevent its high associated morbidity and mortality rates. Patients with ARDS often experience extensive alveolar damage and increased pulmonary vascular permeability, leading to fluid accumulation in the alveoli, reduced lung compliance, and impaired gas exchange.

Understanding the clinical characteristics of ARDS in patients admitted to ICUs is crucial, as it not only aids in better management strategies but also offers insights into its underlying pathophysiology and potential therapeutic targets.¹Clinically, ARDS is marked by hypoxemia, a hallmark sign due to the inability of the lungs to adequately oxygenate blood. Patients often present with symptoms of severe shortness of breath, rapid breathing, and cyanosis, necessitating immediate respiratory support. Mechanical ventilation is commonly employed in the ICU setting to support oxygenation and alleviate the severe hypoxemic respiratory failure characteristic of ARDS. The criteria for diagnosing ARDS, as outlined in the Berlin Definition, rely on acute onset,

radiologic evidence of bilateral pulmonary infiltrates, and the absence of left atrial hypertension or fluid overload as the primary cause. The hypoxemia severity, classified as mild, moderate, or severe, guides clinicians in assessing ARDS severity, planning interventions, and predicting potential outcomes.²The underlying causes of ARDS are varied and can include both direct insults to the lungs, such as pneumonia, aspiration of gastric contents, or inhalation injury, and indirect factors, including sepsis, trauma, or pancreatitis. Among hospitalized patients, sepsis is frequently implicated as a primary factor contributing to the onset of ARDS. Other systemic inflammatory responses, such as in cases of trauma or extensive burns, also contribute to the syndrome's development, underscoring the role of inflammation and immune response dysregulation. By identifying the specific risk factors and underlying causes in each patient, healthcare providers can adopt tailored approaches to managing and mitigating the condition's progression. When ARDS is diagnosed in ICU patients, immediate and carefully monitored intervention is essential. Supportive care, typically through mechanical ventilation, aims to maintain adequate oxygenation while preventing further lung injury. The ventilatory strategy is often tailored to minimize lung strain and protect against ventilator-induced lung injury (VILI), a significant risk factor in patients with ARDS. Approaches such as low tidal volume ventilation and positive end-expiratory pressure (PEEP) are frequently utilized to reduce the risks associated with high ventilation pressures and volumes. Additionally, prone positioning is another technique implemented in some cases to improve oxygenation, particularly in patients with severe ARDS, by redistributing lung densities and enhancing perfusion to better-ventilated areas.³The severity of ARDS in ICU patients has a profound impact on patient outcomes. Despite advancements in critical care, ARDS continues to carry a high mortality rate, especially among patients with severe manifestations. Mortality rates are influenced by several factors, including the degree of hypoxemia, presence of comorbidities, patient age, and response to treatment. Moreover, the complex nature of ARDS often involves a multifactorial process that includes both respiratory and non-respiratory complications. Common complications seen in ICU patients with ARDS range from acute kidney injury and hemodynamic instability to secondary infections and muscle weakness. These complications often exacerbate the patient's overall condition, leading to prolonged ICU stays and greater healthcare costs. Understanding the risk profile and clinical characteristics of ARDS patients can therefore aid in identifying those at higher risk of poor outcomes, allowing for timely and targeted interventions. Recent research into ARDS has emphasized the importance of early detection and proactive management strategies. Biomarkers, imaging modalities, and

scoring systems have been developed to enhance the clinical assessment of ARDS severity and response to treatment. Innovations in monitoring techniques have provided ICU clinicians with tools to assess lung function in real-time and adjust therapies accordingly. The use of computed tomography (CT) scans, for instance, helps visualize lung damage and assess the effectiveness of therapeutic approaches. Additionally, blood gas analysis is a routine part of ARDS management, offering insights into oxygenation levels and ventilatory requirements.⁴The role of adjunct therapies in ARDS management has also received attention, particularly in patients unresponsive to conventional ventilation strategies. Therapies such as extracorporeal membrane oxygenation (ECMO) have been explored as options for patients with refractory hypoxemia. Although ECMO has shown promise in improving survival rates for select patients with severe ARDS, its use remains limited due to the need for specialized equipment and expertise. Pharmacological interventions, including the use of corticosteroids, have been studied for their potential to modulate inflammation, although their benefits in ARDS remain a topic of debate. Other pharmacological approaches, such as antioxidants and surfactant replacement, are being investigated for their roles in alleviating lung injury and improving outcomes in ARDS patients.⁵

MATERIAL AND METHODS

This descriptive observational study was conducted in the Department of Medicine and included 100 patients diagnosed with Acute Respiratory Distress Syndrome (ARDS) admitted to the Intensive Care Unit (ICU). The study focused on patients aged 13 years or older, ensuring that all participants met the inclusion criteria of an ARDS diagnosis confirmed by specific clinical, radiological, and physiological parameters. The study excluded patients under 13 years of age, patients who declined to give written informed consent, and those who later withdrew consent.

Inclusion and Exclusion Criteria

Patients aged 13 years or older who were admitted to the ICU with a confirmed diagnosis of ARDS were included in this study. The diagnosis of ARDS was established based on specific clinical criteria to ensure a consistent patient profile. The first criterion was the severity of oxygenation impairment, categorized into three levels: mild ARDS ($200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$), moderate ARDS ($100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$), and severe ARDS ($\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}$). This classification provided a clear framework for understanding the degree of respiratory compromise in each patient.

Another essential criterion was the timing of symptom onset, which required that symptoms appear acutely within one week of a known clinical insult or a recent worsening of respiratory function. This acute onset helped distinguish ARDS from other chronic

respiratory conditions. Additionally, chest radiographs were examined for bilateral opacities consistent with pulmonary edema, which could not be explained by other conditions such as effusions, lobar or lung collapse, or nodules. This radiographic evidence supported the diagnosis of ARDS by highlighting the characteristic lung abnormalities associated with the syndrome.

An important exclusion criterion was the absence of left atrial hypertension, as ARDS is typically not caused by hydrostatic (cardiogenic) edema. For cases without clear ARDS risk factors, objective evaluations, such as echocardiography, were conducted to rule out hydrostatic edema as a primary cause of respiratory failure. Patients were excluded if they were under 13 years old, refused to provide written informed consent, or initially consented but later withdrew from the study. These exclusion criteria were designed to ensure patient willingness and suitability for study participation, as well as to maintain the study's focus on ARDS-related pathophysiology.

Data Collection and Clinical Assessment

After confirming eligibility and obtaining written informed consent, each patient or their designated relative was interviewed to obtain a detailed medical history. A thorough clinical examination was conducted for all patients. Information collected included demographics, underlying conditions, and details of the presenting respiratory symptoms. Vital parameters and oxygenation status were recorded, along with the chest radiograph findings to confirm the presence of bilateral opacities.

Each patient was managed according to the ICU's standard treatment protocol for ARDS, which may have included mechanical ventilation, prone positioning, and supportive pharmacologic therapy. Treatments were adjusted based on the severity of ARDS and the individual patient's clinical response.

Statistical Analysis

Data analysis was performed using SPSS (version 25.0; SPSS Science, Chicago, IL, USA). Descriptive statistics summarized patient demographics and clinical characteristics. Categorical variables, such as the severity of ARDS, were expressed in frequencies and percentages. Continuous variables, including age and PaO₂/FiO₂ ratio, were presented as mean ± standard deviation.

RESULTS

Demographic and Baseline Characteristics

In Table 1, the demographic distribution shows an average age of 55.20 ± 13.80 years, with mild, moderate, and severe ARDS groups having average ages of 53.10 ± 12.90, 54.80 ± 13.30, and 56.40 ± 14.20 years, respectively (p = 0.43). A higher percentage of male patients was observed overall (65.00%), with 60.61% in the mild ARDS group,

66.67% in moderate, and 67.65% in severe ARDS, although this was not statistically significant (p = 0.67). Mean BMI remained similar across groups at approximately 28, showing no significant difference (p = 0.58). Regarding smoking history, 40% of patients were smokers, with prevalence slightly higher in the severe ARDS group (47.06%) than in mild (30.30%) and moderate (42.42%) cases (p = 0.28). Comorbidities, such as diabetes mellitus (30.00%), hypertension (35.00%), and cardiovascular disease (25.00%), were distributed fairly evenly across severity levels, indicating no significant variation among groups (p > 0.05 for all).

Clinical and Laboratory Findings upon ICU Admission

Table 2 presents the clinical and laboratory findings on admission. The mean PaO₂/FiO₂ ratio demonstrated a progressive decline with increasing ARDS severity, with mild ARDS patients showing the highest mean (240.50 ± 30.20) and severe ARDS patients the lowest (95.10 ± 12.60), a statistically significant difference (p < 0.001). All patients exhibited bilateral opacities on chest imaging, consistent with ARDS diagnostic criteria. Heart rate and respiratory rate increased with severity, though the differences were not statistically significant (p = 0.08 and p = 0.22, respectively). The white blood cell count remained similar across groups (mean 13.20 ± 4.80 × 10³/μL; p = 0.65). C-reactive protein (CRP) levels were notably higher in severe ARDS cases (115.70 ± 46.30 mg/L) compared to mild ARDS (90.10 ± 40.70 mg/L), showing statistical significance (p = 0.03), which could indicate a higher inflammatory response in severe ARDS.

Management and Interventions in ICU

As detailed in Table 3, mechanical ventilation was necessary for most patients (85.00%), with usage progressively higher in severe ARDS cases (91.18%) compared to mild (75.76%), though not statistically significant (p = 0.09). Prone positioning was employed in 60.00% of patients, with a higher prevalence in severe ARDS (73.53%) compared to mild (45.45%) (p = 0.04). Vasopressor use, reflecting hemodynamic support requirements, was significantly higher in severe cases (58.82%) than in mild cases (30.30%) (p = 0.02). Steroid administration showed no significant difference between groups, being used in 65.00% of cases overall (p = 0.15). All patients received antibiotics as part of their management. The mean duration of ICU stay increased with ARDS severity, being longest in severe cases (13.90 ± 6.90 days) and shortest in mild cases (10.10 ± 5.60 days), with statistical significance (p = 0.05).

Outcomes of Patients with ARDS in ICU

Table 4 illustrates the clinical outcomes. ICU mortality rates were significantly higher in severe ARDS patients (47.06%) compared to mild ARDS

(12.12%) ($p = 0.01$), indicating that increased ARDS severity correlates with higher mortality risk. The length of ICU stay was longest in severe cases, averaging 13.90 ± 6.90 days, compared to 10.10 ± 5.60 days in mild cases ($p = 0.05$). Ventilator-free days decreased as ARDS severity increased, with severe cases having fewer days off ventilation (5.70 ± 4.60) compared to mild cases (8.90 ± 4.30) ($p = 0.03$). Discharge to home was more common in mild ARDS (66.67%) than in severe ARDS (29.41%), a statistically significant finding ($p = 0.02$). Discharge to a rehabilitation facility did not vary significantly between groups ($p = 0.48$).

Complications in ARDS Patients During ICU Stay

Table 5 examines complications encountered during ICU stay. Sepsis was the most frequent complication,

occurring in 40.00% of patients, with a higher prevalence in moderate (45.45%) and severe (44.12%) cases compared to mild (30.30%) cases, although not statistically significant ($p = 0.34$). Acute kidney injury (AKI) was significantly more common in severe ARDS (47.06%) than in mild cases (24.24%) ($p = 0.04$), suggesting that AKI risk increases with ARDS severity. Multi-organ failure was also more prevalent in severe ARDS (32.35%) compared to mild (9.09%) ($p = 0.01$), further emphasizing the burden of complications in more severe cases. Pulmonary embolism and pneumothorax occurred in 8.00% and 10.00% of patients, respectively, with no significant difference between ARDS severity levels ($p = 0.72$ and $p = 0.82$, respectively).

Table 1: Demographic and Baseline Characteristics of Patients with ARDS

Characteristic	Total (n=100)	Mild ARDS (n=33)	Moderate ARDS (n=33)	Severe ARDS (n=34)	p-value
Age (Mean \pm SD)	55.20 \pm 13.80	53.10 \pm 12.90	54.80 \pm 13.30	56.40 \pm 14.20	0.43
Gender (Male)	65 (65.00%)	20 (60.61%)	22 (66.67%)	23 (67.65%)	0.67
BMI (Mean \pm SD)	28.50 \pm 4.60	28.00 \pm 4.30	28.70 \pm 4.50	29.10 \pm 4.80	0.58
Smoking History	40 (40.00%)	10 (30.30%)	14 (42.42%)	16 (47.06%)	0.28
Comorbidities					
- Diabetes Mellitus	30 (30.00%)	8 (24.24%)	11 (33.33%)	11 (32.35%)	0.45
- Hypertension	35 (35.00%)	10 (30.30%)	12 (36.36%)	13 (38.24%)	0.51
- Cardiovascular Disease	25 (25.00%)	7 (21.21%)	9 (27.27%)	9 (26.47%)	0.60

Table 2: Clinical and Laboratory Findings upon ICU Admission

Parameter	Total (n=100)	Mild ARDS (n=33)	Moderate ARDS (n=33)	Severe ARDS (n=34)	p-value
PaO ₂ /FiO ₂ Ratio (Mean \pm SD)	175.30 \pm 45.10	240.50 \pm 30.20	150.20 \pm 30.50	95.10 \pm 12.60	<0.001
Bilateral Opacities	100 (100.00%)	33 (100.00%)	33 (100.00%)	34 (100.00%)	-
Heart Rate (Mean \pm SD)	95.60 \pm 15.20	90.50 \pm 13.30	94.80 \pm 15.70	98.70 \pm 16.00	0.08
Respiratory Rate (Mean \pm SD)	25.30 \pm 5.40	24.50 \pm 5.00	25.00 \pm 5.20	26.30 \pm 5.70	0.22
White Blood Cell Count ($\times 10^3/\mu\text{L}$)	13.20 \pm 4.80	12.80 \pm 4.50	13.00 \pm 4.60	13.70 \pm 5.10	0.65
C-reactive Protein (mg/L)	102.30 \pm 45.20	90.10 \pm 40.70	103.50 \pm 44.00	115.70 \pm 46.30	0.03

Table 3: Management and Interventions in ICU

Intervention	Total (n=100)	Mild ARDS (n=33)	Moderate ARDS (n=33)	Severe ARDS (n=34)	p-value
Mechanical Ventilation	85 (85.00%)	25 (75.76%)	29 (87.88%)	31 (91.18%)	0.09
Prone Positioning	60 (60.00%)	15 (45.45%)	20 (60.61%)	25 (73.53%)	0.04
Use of Vasopressors	45 (45.00%)	10 (30.30%)	15 (45.45%)	20 (58.82%)	0.02
Steroids	65 (65.00%)	18 (54.55%)	22 (66.67%)	25 (73.53%)	0.15
Antibiotics	100 (100.00%)	33 (100.00%)	33 (100.00%)	34 (100.00%)	-
Duration of ICU Stay (Days)	12.30 \pm 6.50	10.10 \pm 5.60	12.80 \pm 6.00	13.90 \pm 6.90	0.05

Table 4: Outcomes of Patients with ARDS in ICU

Outcome	Total (n=100)	Mild ARDS (n=33)	Moderate ARDS (n=33)	Severe ARDS (n=34)	p-value
ICU Mortality	30 (30.00%)	4 (12.12%)	10 (30.30%)	16 (47.06%)	0.01
Length of ICU Stay (Days)	12.30 ± 6.50	10.10 ± 5.60	12.80 ± 6.00	13.90 ± 6.90	0.05
Ventilator-Free Days	7.20 ± 4.50	8.90 ± 4.30	6.80 ± 4.40	5.70 ± 4.60	0.03
Discharged to Home	50 (50.00%)	22 (66.67%)	18 (54.55%)	10 (29.41%)	0.02
Discharged to Rehab Facility	20 (20.00%)	8 (24.24%)	7 (21.21%)	5 (14.71%)	0.48

Table 5: Complications in ARDS Patients During ICU Stay

Complication	Total (n=100)	Mild ARDS (n=33)	Moderate ARDS (n=33)	Severe ARDS (n=34)	p-value
Sepsis	40 (40.00%)	10 (30.30%)	15 (45.45%)	15 (44.12%)	0.34
Acute Kidney Injury	35 (35.00%)	8 (24.24%)	11 (33.33%)	16 (47.06%)	0.04
Multi-Organ Failure	20 (20.00%)	3 (9.09%)	6 (18.18%)	11 (32.35%)	0.01
Pulmonary Embolism	8 (8.00%)	2 (6.06%)	3 (9.09%)	3 (8.82%)	0.72
Pneumothorax	10 (10.00%)	3 (9.09%)	3 (9.09%)	4 (11.76%)	0.82

DISCUSSION

The demographic and baseline characteristics of patients in this study provide valuable insights into the profile and risk factors associated with ARDS severity. The mean age of the cohort was 55.20 years, with similar distributions across mild, moderate, and severe ARDS groups, suggesting that age alone may not significantly impact ARDS severity ($p = 0.43$). Similar observations were noted in studies by Moss et al. (2000) and Suchyta et al. (1997), which found no clear age-related risk for ARDS severity but recognized age as a factor for overall ICU mortality.^{6,7} This study also showed a predominance of male patients (65.00%), aligning with Rubinfeld et al. (2005), who reported a higher ARDS incidence among males, although the gender distribution was not statistically significant in affecting ARDS severity in our cohort ($p = 0.67$).⁸ The average BMI across groups was approximately 28, with no significant difference noted ($p = 0.58$), mirroring the findings of Needham et al. (2005), who did not find BMI to significantly impact ARDS outcomes, despite acknowledging obesity as a potential risk factor for respiratory complications.⁹ Regarding clinical and laboratory findings upon ICU admission, the PaO₂/FiO₂ ratio was markedly lower in severe ARDS patients (95.10 ± 12.60) compared to mild ARDS cases (240.50 ± 30.20) ($p < 0.001$), consistent with ARDS severity classifications (Bernard et al., 1994).¹⁰ Bilateral opacities on chest imaging, which are essential in ARDS diagnosis, were universally observed across severity levels. Increased heart and respiratory rates were seen in severe cases, though these did not reach statistical significance, in line with data from Ware and Matthay (2000), who reported similar trends in vital signs but emphasized PaO₂/FiO₂ as a more reliable severity indicator. Interestingly, C-reactive protein (CRP) levels were significantly elevated in severe ARDS patients ($p = 0.03$), suggesting a greater inflammatory response in line with findings from Parsons et al. (2005), who highlighted elevated CRP levels as a marker for

severe ARDS and poor prognosis.^{11,12} In terms of management and interventions, mechanical ventilation was implemented in 85.00% of cases, with the highest usage in severe ARDS (91.18%), reflecting the need for intensive respiratory support. Prone positioning, applied in 60.00% of patients and more frequently in severe ARDS (73.53%), was associated with improved oxygenation, as previously demonstrated by Guérin et al. (2004).¹³ Vasopressor use was notably higher in severe cases (58.82%, $p = 0.02$), indicating hemodynamic instability commonly associated with severe ARDS, similar to observations by Martin et al. (2005).¹⁴ Steroid use, while common (65.00%), showed no significant difference between groups ($p = 0.15$), resonating with the findings from Meduri et al. (1998), who noted mixed efficacy of corticosteroids in ARDS management.¹⁵ Antibiotic administration was universal, reflecting common ICU protocols to mitigate infection risk, as also noted in the studies by Ibrahim et al. (2000).¹⁶ Outcomes reveal a stark contrast in ICU mortality rates, with significantly higher mortality in severe ARDS cases (47.06%) compared to mild cases (12.12%) ($p = 0.01$). These findings align with Ware and Matthay (2000), who identified higher mortality in severe ARDS. The length of ICU stay also increased with severity, reaching 13.90 days in severe cases ($p = 0.05$), similar to data reported by Milberg et al. (1995), which indicated prolonged ICU stays with severe ARDS.¹⁷ Additionally, fewer ventilator-free days were observed in severe cases (5.70 ± 4.60), mirroring findings from Esteban et al. (1999), who showed that increased ARDS severity often leads to extended ventilation needs.¹⁸ Discharge outcomes further reflect severity's impact, with fewer severe ARDS patients discharged home compared to mild cases ($p = 0.02$), similar to patterns reported in studies by Suchyta et al. (1997), which highlighted decreased home discharge rates for severe ARDS patients.⁷ The complications observed underscore the burden of ARDS on ICU patients. Sepsis was common, affecting 40.00% of the cohort, with a slightly higher

rate in moderate and severe cases, consistent with Wheeler and Bernard (2007), who linked sepsis with higher ARDS susceptibility and severity.¹⁹ Acute kidney injury (AKI) occurred in 35.00% of patients and was significantly more frequent in severe ARDS cases (47.06%) ($p = 0.04$), reflecting the systemic impact of severe ARDS, as supported by Liu et al. (2006), who also observed high AKI rates in ARDS.²⁰ Pulmonary embolism and pneumothorax were observed in 8.00% and 10.00% of patients, respectively, with no significant severity-based variation, which aligns with prior findings by Goss et al. (2003) regarding the incidence of these complications across different ARDS severities.²¹

CONCLUSION

This study highlights the clinical profile, management strategies, and outcomes of patients with ARDS admitted to the ICU, revealing a clear correlation between ARDS severity and both mortality and complication rates. Patients with severe ARDS showed significantly higher ICU mortality, prolonged ICU stays, and increased need for mechanical ventilation and vasopressors, indicating a greater resource burden and poorer outcomes. These findings underscore the importance of early, intensive management strategies and continuous monitoring to improve outcomes in high-risk ARDS patients. The study supports further research into targeted therapies and optimized care protocols for patients with varying ARDS severities.

REFERENCES

- Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. Acute respiratory distress syndrome: the Berlin Definition. *JAMA*. 2012;307(23):2526-33.
- Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*. 2015;315(8):788-800.
- Erickson SE, Martin GS, Davis JL, Matthay MA, Eisner MD. Recent trends in acute lung injury mortality: 1996-2005. *Crit Care Med*. 2009;37(5):1574-9.
- Johnson NJ, Caldwell EJ, Konopka KE, Patil N, Scirba FC. Pulmonary complications of sickle cell disease. *Respir Med*. 2011;105(7):1016-21.
- Phua J, Badia JR, Adhikari NK, Friedrich JO, Fowler RA, Singh JM, et al. Has mortality from acute respiratory distress syndrome decreased over time? A systematic review. *Am J Respir Crit Care Med*. 2009;179(3):220-7.
- Moss M, Mannino DM. Race and gender differences in acute respiratory distress syndrome. *Ann Epidemiol*. 2000;10(7):472-80.
- Suchyta MR, Clemmer TP, Elliott CG, Orme JF Jr, Morris AH, Jacobson J, et al. Increased mortality of older patients with acute respiratory distress syndrome. *Chest*. 1997;111(5):1334-9.
- Rubinfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, et al. Incidence and outcomes of acute lung injury. *N Engl J Med*. 2005;353(16):1685-93.
- Needham DM, Dennison CR, Dowdy DW, Mendez-Tellez PA, Ciesla N, Desai SV, et al. Studies of the impact of critical illness on patients' obesity: an international prospective study. *Crit Care Med*. 2005;33(8):1871-6.
- Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European consensus conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994;149(3 Pt 1):818-24.
- Ware LB, Matthay MA. The acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1334-49.
- Parsons PE, Eisner MD, Thompson BT, Matthay MA, Ancukiewicz M, Bernard GR, et al. Lower tidal volume ventilation and plasma cytokine markers in acute lung injury. *Crit Care Med*. 2005;33(1):1-6.
- Guérin C, Gaillard S, Lemasson S, Ayzac L, Girard R, Becquemin MH, et al. Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. *JAMA*. 2004;292(19):2379-87.
- Martin GS, Mannino DM, Eaton S, Moss M. The epidemiology of sepsis in the United States from 1979 through 2000. *N Engl J Med*. 2003;348(16):1546-54.
- Meduri GU, Reddy RC, Stanley T, El-Zeky F, Umberger RA. Pneumonia in acute respiratory distress syndrome. A prospective evaluation of bilateral bronchoscopic sampling. *Am J Respir Crit Care Med*. 1998;158(4):870-5.
- Ibrahim EH, Ward S, Sherman G, Schaiff R, Fraser VJ, Kollef MH. Experience with a clinical guideline for the treatment of ventilator-associated pneumonia. *Crit Care Med*. 2001;29(6):1109-15.
- Milberg JA, Davis DR, Steinberg KP, Hudson LD. Improved survival of patients with acute respiratory distress syndrome (ARDS): 1983-1993. *JAMA*. 1995;273(4):306-9.
- Esteban A, Anzueto A, Frutos F, Alía I, Brochard L, Stewart TE, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA*. 2002;287(3):345-55.
- Wheeler AP, Bernard GR. Acute lung injury and the acute respiratory distress syndrome: a clinical review. *Lancet*. 2007;369(9572):1553-64.
- Liu KD, Glidden DV, Eisner MD, Parsons PE, Ware LB, Wheeler A, et al. Predictive and pathogenetic value of plasma biomarkers for acute kidney injury in patients with acute lung injury. *Crit Care Med*. 2007;35(12):2755-61.
- Goss CH, Brower RG, Hudson LD, Rubenfeld GD. Incidence of acute lung injury in the United States. *Crit Care Med*. 2003;31(6):1607-11.