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Health Care Utilization and the Cost of Post-Traumatic ARDS Care

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Abstract

Background—Post-traumatic acute respiratory distress syndrome (ARDS) is associated with prolonged mechanical ventilation and longer hospitalizations. The relationship between post-traumatic ARDS severity and financial burden has not been previously studied. We hypothesized that increasing severity is associated with incrementally higher health care costs.

Methods—Adults arriving as the highest level of trauma activation were enrolled in an ongoing prospective cohort study. Patients who survived ≥ 6 hours are included in the analysis. Blinded review of chest radiographs was performed by two independent physicians for any intubated patient with PaO₂:FiO₂ ratio (P/F) ≥ 300 mgHg during the first 8 days of admission. The severity of ARDS was classified by the Berlin criteria. Hospital charge data was utilized to perform standard costing analysis.

Results—ARDS occurred in 13% (203/1586). The distribution of disease severity was 33% mild, 42% moderate, and 25% severe. Patients with ARDS were older (41 vs 35 years, $p < 0.01$), had higher median ISS (30 vs 10, $p < 0.01$), more chest injury (AIS 3: 51% vs 21%, $p < 0.01$), and blunt mechanisms (85% vs 53%, $p < 0.01$). By ARDS severity, there was no significant difference in age, mechanism, or rate of traumatic brain injury. Increasing ARDS severity was associated with higher ISS and higher mortality rates. Standardized total hospital charges were four-fold higher for patients who developed ARDS compared to those who did not develop ARDS (\$434K vs \$96K,

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p<0.01). Furthermore, the daily hospital charges significantly increased across categories of worsening ARDS severity (mild \$20,451; moderate \$23,994; severe \$33,316, p<0.01).

Conclusions—The development of post-traumatic ARDS is associated with higher health care costs. Among trauma patients who develop ARDS, total hospital charges per day increase with worsening severity of disease. Prevention, early recognition, and treatment of ARDS after trauma are potentially important objectives for efforts to control health care costs in this population.

Level of Evidence—IV

Study Type—Economic and Value-based Evaluations

Keywords

ARDS; Berlin criteria; cost; trauma

Background

In the United States, injury is the leading cause of death for people 1-44 years of age (1) and a leading cause of death worldwide (2). The national economic burden of trauma is extensive as the total lifetime medical and work loss costs due to injury in the United States was estimated to be \$671 billion in 2013 (3, 4). There is a tri-modal distribution of deaths after injury (5, 6), with a significant proportion of late deaths due to multi-organ failure (MOF) (7, 8), frequently driven by lung dysfunction (9). Since the initial recognition of acute lung injury as a clinical entity by Ashbaugh et al. in 1967 (10), it has undergone multiple iterations. Acute respiratory distress syndrome (ARDS) was formally defined at the American-European Consensus Conference in 1994 (11) and most recently revised with the gradation of hypoxemia in the Berlin definition in 2012 (12). ARDS is associated with significant morbidity and mortality in critically ill patients, with an estimated national incidence of 200,000 cases per year, representing nearly 15% of all intensive care unit admissions (ICU) and with a mortality ranging from 30% to 60% (13-16).

The etiology of post-traumatic ARDS is hypothesized to be heterogeneous, related to both direct and indirect insults in addition to the complex milieu of systemic inflammation and infection (17). A recent meta-analysis showed an estimated incidence of ARDS after injury of 8.4%, with no change in incidence over the past three decades despite a myriad of changes in trauma systems, patient management and public health priorities (18). Further, lung injury after trauma continues to be associated with an extensive burden of mortality (19) with a nearly three-fold higher mortality rate in critically ill severely injured patients (20).

Although there are no data specific to trauma patients regarding the cost associated with ARDS, the cost outcomes of patients suffering ARDS from primarily medical illness demonstrate that many die after protracted and costly treatment courses (21-23). The incremental financial burden associated with increasing post-traumatic ARDS severity has not been previously studied. This study investigates the costs associated with post-traumatic ARDS and across ARDS categories classified by Berlin criteria.

Methods

This study is a secondary analysis of a prospective cohort study of all highest-level activation trauma patients at a single urban Level 1 trauma center. Comprehensive demographic, injury, clinical, and outcome data were collected upon arrival and up to 28 days for 1586 of the highest-level adult trauma activation subjects surviving more than six hours after injury from 2005-2016 at Zuckerberg San Francisco General Hospital. Patients were divided into those who developed ARDS by the Berlin criteria and compared to those without ARDS (Supplemental Digital Content 1: Study Design Figure). Subset analyses were performed in intubated patients with and without ARDS (Supplemental Digital Content 2 and 3). ARDS severity was classified by the degree of hypoxemia per the Berlin criteria: mild ($200 < \text{PaO}_2:\text{FiO}_2$ ratio (P/F) < 300), moderate ($100 < \text{P/F} < 200$), and severe ($\text{P/F} < 100$) (12). The Glasgow coma scores (GCS) used was the first recorded score in the Emergency Department (ED). Multi-organ failure (MOF) was defined using the Denver Post-Injury Multiple Organ Failure Score (24). Ventilator free days were counted for the first 28 days of hospitalization. Subjects who expired received zero ventilator free days.

To adjudicate the criteria of bilateral infiltrates, two expert critical care physicians blindly reviewed all chest x-rays (CXRs) from the first 8 days of care for enrolled subjects with a documented P/F ratio of $< 300 \text{mgHg}$ (25). Confirmation of P/F ratio of $< 300 \text{mgHg}$ at time of positive CXR and positive end-expiratory pressure (PEEP) $> 5 \text{ mmHg}$ was performed on all subjects. Imaging studies were classified as “positive,” “negative,” or “equivocal” for the presence of bilateral infiltrates. “Equivocal” studies represented those images for which consensus could not be reached between expert reviewers. In the absence of volume overload or left heart failure, the time of onset of ARDS was determined as the first CXR adjudicated as “positive” for presence of bilateral infiltrates.

To exclude patients with CXR findings of bilateral infiltrates as a result of volume overload, left heart failure and volume status was adjudicated from echocardiogram reports and chart review. If an echocardiogram was performed for clinical care within 24 hours of the qualifying film for ARDS, reports were evaluated for the presence of moderate to severe left ventricular dysfunction or intravascular volume overload. If the subject did not have an echocardiogram performed, or if moderate systolic dysfunction was present, clinical records were reviewed for information regarding the clinical assessment of the presence of cardiogenic pulmonary edema. Subjects were excluded from analysis if cardiogenic pulmonary edema, gross volume overload requiring diuresis, or severe left ventricular systolic dysfunction was present.

Hospital charge data was utilized to perform standard costing analysis. Standard costing is a technique extrapolated from business where the practice of substituting an expected cost for an actual cost is done to benchmark future performance against or to compare current performance across groups (26-29). This analytic approach is commonly used in economic evaluations to minimize the effect of outliers and in situations where actual cost collection is challenging. In this method, data are grouped by common features to calculate the total cost for a group; either a mean per unit cost or a median cost can be calculated. This standardized cost is then applied to the members of the group to represent the expected cost for an

episode of care for patients with a similar feature of interest. Variance or differences in cost are then able to be calculated between and within groups for comparisons.

Total hospital charges were utilized in this standardized costing analysis. Hospital charge data provides a relative measure of the 'cost' of episodes of care, as actual cost data are generally not ascertainable in the health care setting. To estimate the median hospital charge per patient and minimize the effect of outliers due to prolonged and costly hospitalizations, we utilized this previously described standardized costing technique (26) through applying an expected daily standardized hospital charge to each patient's length of stay. The median standardized hospital charge was then analyzed by category to compare the attributable costs and differences related to ARDS development and by ARDS severity subtype.

Data are presented as mean (standard deviation), median (interquartile range), or percentage; univariate comparisons were made using Student's *t* test for normally distributed data, Wilcoxon rank sum or Kruskal-Wallis testing for nonparametric data, and Fisher's exact test for proportions. An $[\alpha] < 0.05$ was considered significant. All analysis was performed using Stata version 14 (StataCorp, College Station, TX). The study was approved by the Institutional Review Board.

Results

Total Cohort

During the ten-year study period, 1586 subjects were enrolled in the study and survived at least 6 hours after injury. Overall, 34 subjects were excluded due to the development of respiratory failure attributable to left heart failure or cardiogenic pulmonary edema ($n=12$), respiratory failure but equivocal CXR findings for bilateral infiltrates ($n=19$), or presence of bilateral infiltrates without hypoxemia ($n=3$). The remaining 1552 patients were included in the analysis. The cohort was primarily male (82%), white (58%), and bluntly injured (57%) with one third (34%) diagnosed with traumatic brain injury (TBI). The mean age of subjects was 40 years, the median injury severity score (ISS) was 13, and 28-day mortality was 13%. Overall, 53% were intubated on admission day. ARDS diagnosed by Berlin criteria was present in 13% (203/1586) of the cohort (Table 1). Of the ARDS patients, 33% ($n=67$) had mild hypoxemia ($200 < P/F < 300$), 42% ($n=86$) had moderate hypoxemia ($100 < P/F < 200$), and 25% ($n=50$) had severe hypoxemia ($P/F < 100$).

Those subjects who developed ARDS were older (41 vs 35 years, $p < 0.01$), had higher median ISS (30 vs 10, $p < 0.01$), and more suffered blunt mechanism of injury (85% vs 53%, $p < 0.01$: Table 1). There was no difference in gender. ARDS subjects were both more likely to have any chest injury (median abbreviated injury score (AIS): 3 vs 0, $p < 0.01$), severe chest injury (chest AIS ≥ 3 : 51% vs 21%, $p < 0.01$), suffered rib fractures (45 vs 20%, $p < 0.01$) and nearly all were intubated on admission day (96% vs 47%, $p < 0.01$). Subjects who developed ARDS had lower median GCS on presentation (8 vs 14, $p < 0.01$), were more likely to have head injury (median head AIS: 4 vs 0, $p < 0.01$) and be diagnosed with TBI (67% vs 28%, $p < 0.01$). Those who developed ARDS were more likely to be insured (77% vs 62%, $p < 0.01$).

At presentation, subjects who developed ARDS had greater hemodynamic instability, with more subjects having tachycardia (admission heart rate >110 bpm: 44% vs 26%, $p<0.01$) and hypotension (admission systolic blood pressure <90 mmHg: 13% vs 8%, $p<0.01$). Those with ARDS had worsened acidosis at presentation (admit base excess: -6.8 vs -3.1, $p<0.01$) and were more likely to require any transfusion at both six (69% vs 29%, $p<0.01$) and twenty-four hours (74% vs 33%, $p<0.01$; Table 1). In comparing the 880 patients who were intubated during their clinical course, the subjects who developed ARDS still had more blunt injury, higher ISS, higher rates of all head and thoracic trauma injury and were more likely to need transfusion at 6 and 24 hours (Supplemental Digital Content 2).

For those with ARDS, there was no difference in age, gender, body mass index (BMI), mechanism of injury, or presence of TBI by ARDS severity (Table 2). At presentation, there was also no difference in initial hemodynamics. With regards to torso trauma, there was no difference in median chest AIS, proportion of subjects with any chest injury or severe chest injury, nor percentage of subjects with rib fractures. Although there was a statistically significant difference across ARDS severity by median ISS (mild 29, moderate 34, severe 30, $p=0.04$), in comparing the moderate to the severe ARDS group, there was no significant difference in ISS ($p=0.82$). There was no difference in transfusion at 6 hours but there was a significant increase in receiving any transfusion at 24 hours by ARDS severity (mild 64%, moderate 76%, severe 84%, $p=0.05$).

Hospital Charges & Outcomes

Although there was no statistically significant difference in charge per day between those with and without ARDS, median actual total hospital charge was over three-fold higher in subjects with ARDS (\$451K vs \$106K, $p<0.01$). Standardized total hospital charges were four-fold higher in those with ARDS compared to those without (\$434K vs \$96K, $p<0.01$; Table 3). This increase in overall hospital charges reflects the longer hospital (18 vs 4 days, $p<0.01$) and ICU stays (14 vs 2 days, $p<0.01$), and reflects the severity of illness of the ARDS patients (ventilator-free days 3 vs 27 days, $p<0.01$; MOF 41% vs 3%, $p<0.01$). ARDS patients had markedly higher mortality, with one-third of ARDS patients deceased at 28 days (33%) and discharge (36%), compared to 10% of patients at both time points without ARDS (both $p<0.01$). In comparing only patients who were intubated during their clinical course, there continued to be no significant difference in charge per day between those with and without ARDS, with ARDS patients continuing to have higher total and standardized hospital charges, length of hospital and ICU admissions, and mortality (Supplemental Digital Content 3).

Amongst the patients with ARDS, the highest total standardized charge per day was associated with severe ARDS (mild \$20,451; moderate \$23,994; severe \$33,316; $p<0.01$, Table 4). Severe ARDS patients had increased mortality with half of the subjects with severe ARDS dying by 28 days (50%), compared to one-third of those with moderate ARDS (33%) and almost a quarter of those with mild ARDS (21%, $p<0.01$ for both). The total standardized hospital charge for the entire episode of care was therefore inversely related to ARDS severity (mild \$580K, moderate \$495K, severe \$338K, $p<0.01$) because the number of hospital days were lower in the severe ARDS patients ($p<0.01$). In fact, compared to

those with mild/moderate ARDS, those with severe ARDS had only 14 total hospital days versus 24 days for the mild group and 21 days for the moderate group ($p<0.01$).

Impact of Survival Status on Hospital Charges

For those with ARDS, subgroup analyses were performed assessing the role of mortality on length of stay and cost. For ARDS survivors, there was no statistically significant difference by severity for hospital or ICU length of stay; there was also no difference in charge per day (Table 5). In contrast, for those ARDS patients deceased at discharge, there was a significant increase in charge per day by ARDS severity (mild \$26,925; moderate \$31,783; severe \$43,380; $p=0.01$; Table 6). Those with severe ARDS died sooner than those suffering mild or moderate ARDS, incurring less total hospital charges (mild \$266K, moderate \$217K, severe \$121K, $p=0.08$), with a trend towards fewer hospital (mild/moderate 9 days, severe 5 days, $p=0.10$) and ICU days (mild 11 days, moderate 9 days, severe 5 days, $p=0.08$). In those without ARDS, we also investigated the impact of survival status on hospital costs and found that those who died were especially costly at \$38,801 per day. In contrast, those who survived without ARDS only cost \$22,476 per day.

Discussion

The impact of ARDS on mortality after injury is well-established (7-9, 11, 12, 24, 30), however, there is no previous data in trauma patients focusing on the cost associated with developing post-traumatic ARDS by Berlin criteria. In this study, those who developed ARDS were more likely to be older, suffer blunt injury, be severely injured, and have severe chest and head injury. Similar to cost analyses in medical patients, ARDS patients in this study had significantly longer ICU and hospital stays and fewer ventilator free days compared to those without ARDS. The net economic effect was higher total hospital charges in those with post-traumatic ARDS compared to patients without ARDS.

Using a standard costing approach, this study found that length of stay appears to be a major driver of the total health care charges associated with ARDS. The net standardized charge per day between those with and without ARDS was not statistically different. This finding supports that length of stay is a potential modifiable driver of total cost of caring for ARDS patients. However, once one develops ARDS, there is a proportional increase in the charge per day that is incurred with increasing disease severity – especially in those who die during the index trauma hospitalization. It is likely that the increased charges per day are not only related to ARDS but also reflect the overall injury severity and critical illness after injury that contribute to the development and severity of ARDS. This is supported by the findings of increasing ISS, mortality, and incidence of MOF with worsening hypoxemia category by Berlin criteria. Unfortunately, injury factors are largely non-modifiable as they are fixed by the initial injury pattern and there is an increased cost of caring for sicker patients (15, 31, 32).

We initially hypothesized that ARDS patients would have higher costs per day due to apparent greater severity of illness by median ISS, increased need for transfusion, and incidence of severe TBI compared to the non-ARDS patients. However, our data demonstrated similar per day patient costs when analyzed in aggregate categories and

therefore, we performed further subset analysis to elucidate the potential underlying contributing factors. The severe ARDS patient median cost per day exceeds that of the non-ARDS patients (severe ARDS \$33,316 vs. non- ARDS \$23,514), consistent with the finding of severe ARDS patients being more ill overall. In addition, when we further separated the non-ARDS patients by those who survived or died by discharge, a similar pattern was found wherein the non-survivors had markedly higher costs (\$38,801 vs. \$22,476); suggesting that degree of illness is the major driver of hospital costs. In addition, these non-ARDS patients included a higher percentage of penetrating trauma where ISS can often underrepresent severity of injury.

There are multiple interconnected factors that impact the cost of intensive care and ARDS. Unfortunately, when ARDS develops care is largely supportive and there are minimal modifiable risk factors identified thus far that can be changed to augment the disease course or decrease mortality in this patient population, despite many advances in modern critical care. This supportive ICU care expends a significant amount of hospital resources; patients in the intensive care unit have higher total costs and longer lengths of stay than patients who do not require ICU care (33) and ICU care is estimated to be responsible for at least 13.4% of total yearly U.S. hospital costs (34). In addition, critically ill patients who require mechanical ventilation incur an estimated national cost of \$27 billion yearly, representing nearly one-third of all ICU costs, 12% of all hospital costs and consume a significant proportion of hospital and critical care resources (35). Studies on the outcomes and costs of ARDS have shown that the index ICU stay is responsible for much of the incremental cost associated with an episode of care (36-38). Further, studies have shown that the majority of ICU costs are “fixed” and occur regardless of patient quantity and thoroughfare, making efforts to minimize cost fraught with institutional barriers and complexities (39).

Since the introduction of the Berlin definition, there is increasing literature regarding the epidemiology and outcomes of modern ARDS patients fulfilling the Berlin definition. Two studies have been recently published on the expected distribution of ARDS severity; a German-based cross sectional observational study (40) most frequently reported moderate ARDS (48%), followed by severe (38%) and mild (14%) disease. In contrast, a recent large, international prospective observational ARDS study by Bellani et al. (41) reported a more even distribution of mild (30%), moderate (47%), and severe (23%) ARDS with an ARDS prevalence of 10.4% of ICU admissions and a nearly 40% mortality. Using blindly adjudicated chest radiograph findings, we found a similar distribution of ARDS severity with 33% of our patients suffering mild ARDS, 42% moderate, and 25% severe. Our mortality was also similar with 33% overall and 53% in the severe ARDS group.

Examining charges by ARDS severity is important given that similar to Bellani et al. we found those suffering severe ARDS died sooner and more often than those with mild or moderate disease. Thus, total hospital charges were lower due to the shorter overall hospital stays. If one were to only examine total hospital charges and not perform a standard costing analysis or a per unit charge analysis, the net economic impact of ARDS severity would be grossly underestimated. However, with standard costing, it is clear that these patients incur markedly more charges than those with less severe disease per unit of health care consumed as represented by the standard per day hospital charge. This is most prominently

demonstrated by the effect of ARDS severity on hospital charges per day for patients who died with severe illness compared with mild or moderate illness.

Our study has several strengths including the rigorous adjudication of ARDS. We used a standardized costing approach which allows for understanding the effect of length of stay and associated procedures, and minimizes the impact of outliers with lengthy or disproportionately costly hospitalizations. There is limited information regarding the cost of post-traumatic ARDS; prior cost analyses have also not assessed the impact of the Berlin categories on cost and hospital length of stay. This study is an important contribution towards defining the cost of ARDS development in trauma patients by severity and assessing the contributions of mortality and length of stay on resource utilization.

Our study has some limitations. It is a single center study and this may limit the generalizability of our findings, although the distribution of ARDS by severity category and non-economic outcomes are consistent with the recent large study of ARDS patients in 50 countries by Bellani et al. (41). Although using absolute charges would not be translatable to other regions of the country and centers, a standard costing approach allows for comparison of expected to observed costs as a method of relative benchmarking similar to cost to charge ratios. While standardized costing analysis controls for important drivers of health care costs and is a well-accepted method to account for the total burden of resources required for an episode of care, it is not possible with this methodology to definitively demonstrate that ARDS is the isolated cause of the difference in standardized charges as we cannot describe the incremental cost of each potential risk factor and are limited to the goal of assessing only overall effect. Further, it is not possible due to limitations in the data to definitely conclude why the non-ARDS patients per day cost is similar. Importantly, only select operative data was collected and it is possible that the non-ARDS patients required either more interventions overall or costlier operative interventions such as orthopedic surgeries with hardware. As ARDS is associated with increasing injury severity, the charge difference also likely reflects in part the differences in the care rendered for specific injuries and increased severity. Additionally, our hospital system is limited in providing only summary total hospital charges and not itemized charges for each patient; therefore, we are unable to determine incremental breakdown of costs related to the total hospital charge, which would be an important analysis in assessing interventions to reduce the costs of care.

Conclusion

The development of post-traumatic ARDS is associated with higher health care costs. Among trauma patients who develop ARDS, hospital charges per day increase with worsening severity of disease and hypoxemia. The majority of factors contributing to the development or severity of post-traumatic ARDS are non-modifiable risk factors. The only modifiable risk factors identified for the development or severity of ARDS were transfusion variables within the first 24 hours. Given the profound morbidity and mortality associated with post-traumatic ARDS, ongoing investigations of ideal transfusion parameters and practices in the era of balanced resuscitation will be critical to alleviating the cost and burden of ARDS in trauma populations. Further, protective strategies to prevent or mitigate ARDS after trauma are essential to controlling health care costs and should be prioritized.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

- Centers for Disease Control and Prevention, National Center for Injury Prevention and Control. [cited 2017 April 27, 2017] 10 Leading Causes of Death by Age Group, United States – 2015. 2015. Available from: https://www.cdc.gov/injury/wisqars/pdf/leading_causes_of_death_by_age_group_2015-a.pdf
- Norton R, Kobusingye O. Injuries. *N Engl J Med*. 2013; 368(18):1723–30. [PubMed: 23635052]
- Florence C, Simon T, Haegerich T, Luo F, Zhou C. Estimated Lifetime Medical and Work-Loss Costs of Fatal Injuries--United States, 2013. *MMWR Morb Mortal Wkly Rep*. 2015; 64(38):1074–7. [PubMed: 26421530]
- Florence C, Haegerich T, Simon T, Zhou C, Luo F. Estimated Lifetime Medical and Work-Loss Costs of Emergency Department-Treated Nonfatal Injuries--United States, 2013. *MMWR Morb Mortal Wkly Rep*. 2015; 64(38):1078–82. [PubMed: 26421663]
- Trunkey DD. Trauma. Accidental and intentional injuries account for more years of life lost in the U.S. than cancer and heart disease. Among the prescribed remedies are improved preventive efforts, speedier surgery and further research. *Sci Am*. 1983; 249(2):28–35. [PubMed: 6623052]
- Demetriades D, Kimbrell B, Salim A, Velmahos G, Rhee P, Preston C, Gruzinski G, Chan L. Trauma deaths in a mature urban trauma system: is “trimodal” distribution a valid concept? *J Am Coll Surg*. 2005; 201(3):343–8. [PubMed: 16125066]
- Sauaia A, Moore FA, Moore EE, Moser KS, Brennan R, Read RA, Pons PT. Epidemiology of trauma deaths: a reassessment. *J Trauma*. 1995; 38(2):185–93. [PubMed: 7869433]
- Cothren CC, Moore EE, Hedegaard HB, Meng K. Epidemiology of urban trauma deaths: a comprehensive reassessment 10 years later. *World J Surg*. 2007; 31(7):1507–11. [PubMed: 17505854]
- Ciesla DJ, Moore EE, Johnson JL, Burch JM, Cothren CC, Sauaia A. The role of the lung in postinjury multiple organ failure. *Surgery*. 2005; 138(4):749–57. discussion 57-8. [PubMed: 16269305]
- Ashbaugh DG, Bigelow DB, Petty TL, Levine BE. Acute respiratory distress in adults. *Lancet*. 1967; 2(7511):319–23. [PubMed: 4143721]
- Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, LeGall JR, Morris A, Spragg R. Report of the American-European Consensus conference on acute respiratory distress syndrome: definitions, mechanisms, relevant outcomes, and clinical trial coordination. Consensus Committee. *J Crit Care*. 1994; 9(1):72–81. [PubMed: 8199655]
- Force ADT, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS. Acute respiratory distress syndrome: the Berlin Definition. *JAMA*. 2012; 307(23):2526–33. [PubMed: 22797452]
- Rubenfeld GD, Caldwell E, Peabody E, Weaver J, Martin DP, Neff M, Stern EJ, Hudson LD. Incidence and outcomes of acute lung injury. *N Engl J Med*. 2005; 353(16):1685–93. [PubMed: 16236739]
- Frutos-Vivar F, Ferguson ND, Esteban A. Epidemiology of acute lung injury and acute respiratory distress syndrome. *Semin Respir Crit Care Med*. 2006; 27(4):327–36. [PubMed: 16909367]
- Goss CH, Brower RG, Hudson LD, Rubenfeld GD, Network A. Incidence of acute lung injury in the United States. *Crit Care Med*. 2003; 31(6):1607–11. [PubMed: 12794394]
- Erickson SE, Martin GS, Davis JL, Matthay MA, Eisner MD, Network NNA. Recent trends in acute lung injury mortality: 1996-2005. *Crit Care Med*. 2009; 37(5):1574–9. [PubMed: 19325464]

17. Ware LB. Pathophysiology of acute lung injury and the acute respiratory distress syndrome. *Semin Respir Crit Care Med.* 2006; 27(4):337–49. [PubMed: 16909368]
18. Pfeifer R, Heussen N, Michalewicz E, Hilgers RD, Pape HC. Incidence of adult respiratory distress syndrome in trauma patients: A systematic review and meta-analysis over a period of three decades. *J Trauma Acute Care Surg.* 2017; 83(3):496–506. [PubMed: 28590348]
19. Daurat A, Millet I, Roustan JP, Maury C, Taourel P, Jaber S, Capdevila X, Charbit J. Thoracic Trauma Severity score on admission allows to determine the risk of delayed ARDS in trauma patients with pulmonary contusion. *Injury.* 2016; 47(1):147–53. [PubMed: 26358517]
20. Shah CV, Localio AR, Lanken PN, Kahn JM, Bellamy S, Gallop R, Finkel B, Gracias VH, Fuchs BD, Christie JD. The impact of development of acute lung injury on hospital mortality in critically ill trauma patients. *Crit Care Med.* 2008; 36(8):2309–15. [PubMed: 18664786]
21. Byrick RJ, Mindorff C, McKee L, Mudge B. Cost-effectiveness of intensive care for respiratory failure patients. *Crit Care Med.* 1980; 8(6):332–7. [PubMed: 6768495]
22. Bellamy PE, Oye RK. Adult respiratory distress syndrome: hospital charges and outcome according to underlying disease. *Crit Care Med.* 1984; 12(8):622–5. [PubMed: 6744902]
23. Carson SS, Bach PB. The epidemiology and costs of chronic critical illness. *Crit Care Clin.* 2002; 18(3):461–76. [PubMed: 12140908]
24. Sauaia A, Moore FA, Moore EE, Haanel JB, Read RA, Lezotte DC. Early predictors of postinjury multiple organ failure. *Arch Surg.* 1994; 129(1):39–45. [PubMed: 8279939]
25. Hendrickson CM, Dobbins S, Redick BJ, Greenberg MD, Calfee CS, Cohen MJ. Misclassification of acute respiratory distress syndrome after traumatic injury: The cost of less rigorous approaches. *J Trauma Acute Care Surg.* 2015; 79(3):417–24. [PubMed: 26307875]
26. Drummond, MF., Sculpher, MJ., Torrance, GW., O'Brien, BJ., Stoddart, GL. *Methods for the Economic Evaluation of Health Care Programmes.* 3rd. Oxford: Oxford University Press; 2005.
27. Ezenduka C, Ichoku H, Ochonma O. Estimating the costs of psychiatric hospital services at a public health facility in Nigeria. *J Ment Health Policy Econ.* 2012; 15(3):139–48. [PubMed: 23001282]
28. Islam MM, Shanahan M, Topp L, Conigrave KM, White A, Day CA. The cost of providing primary health-care services from a needle and syringe program: a case study. *Drug Alcohol Rev.* 2013; 32(3):312–9. [PubMed: 23194468]
29. Kaplan, RS., Porter, ME. [cited 2017 11/20/17] *The Big Idea: How to Solve the Cost Crisis in Health Care:* Harvard Business Review. Sep. 2011. Available from: <https://hbr.org/2011/09/how-to-solve-the-cost-crisis-in-health-care>
30. Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. *Crit Care Med.* 1995; 23(10):1638–52. [PubMed: 7587228]
31. Wind J, Versteegt J, Twisk J, van der Werf TS, Bindels AJ, Spijkstra JJ, Girbes AR, Groeneveld AB. Epidemiology of acute lung injury and acute respiratory distress syndrome in The Netherlands: a survey. *Respir Med.* 2007; 101(10):2091–8. [PubMed: 17616453]
32. Tyburski JG, Collinge JD, Wilson RF, Eachempati SR. Pulmonary contusions: quantifying the lesions on chest X-ray films and the factors affecting prognosis. *J Trauma.* 1999; 46(5):833–8. [PubMed: 10338400]
33. Cooper LM, Linde-Zwirble WT. Medicare intensive care unit use: analysis of incidence, cost, and payment. *Crit Care Med.* 2004; 32(11):2247–53. [PubMed: 15640637]
34. Halpern NA, Pastores SM. Critical care medicine in the United States 2000-2005: an analysis of bed numbers, occupancy rates, payer mix, and costs. *Crit Care Med.* 2010; 38(1):65–71. [PubMed: 19730257]
35. Wunsch H, Linde-Zwirble WT, Angus DC, Hartman ME, Milbrandt EB, Kahn JM. The epidemiology of mechanical ventilation use in the United States. *Crit Care Med.* 2010; 38(10):1947–53. [PubMed: 20639743]
36. Cameron JI, Herridge MS, Tansey CM, McAndrews MP, Cheung AM. Well-being in informal caregivers of survivors of acute respiratory distress syndrome. *Crit Care Med.* 2006; 34(1):81–6. [PubMed: 16374160]

37. Cheung AM, Tansey CM, Tomlinson G, Diaz-Granados N, Matte A, Barr A, Mehta S, Mazer CD, Guest CB, Stewart TE, et al. Two-year outcomes, health care use, and costs of survivors of acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 2006; 174(5):538–44. [PubMed: 16763220]
38. Herridge MS, Tansey CM, Matte A, Tomlinson G, Diaz-Granados N, Cooper A, Guest CB, Mazer CD, Mehta S, Stewart TE, et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med.* 2011; 364(14):1293–304. [PubMed: 21470008]
39. Kahn JM, Rubenfeld GD, Rohrbach J, Fuchs BD. Cost savings attributable to reductions in intensive care unit length of stay for mechanically ventilated patients. *Med Care.* 2008; 46(12):1226–33. [PubMed: 19300312]
40. Dodoo-Schittko F, Brandstetter S, Brandl M, Blecha S, Quintel M, Weber-Carstens S, Kluge S, Meybohm P, Rolfes C, Ellger B, et al. Characteristics and provision of care of patients with the acute respiratory distress syndrome: descriptive findings from the DCAPO cohort baseline and comparison with international findings. *J Thorac Dis.* 2017; 9(3):818–30. [PubMed: 28449491]
41. Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A, Gattinoni L, van Haren F, Larsson A, McAuley DF, et al. Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries. *JAMA.* 2016; 315(8):788–800. [PubMed: 26903337]

Table 1
Subjects without and with ARDS

| | No ARDS n=1349 (87%) | ARDS n=203 (13%) | <i>p</i> -value |
|--|-------------------------|---------------------|-----------------|
| Age (years) | 35 (25-51) | 41 (27-54) | <0.01 |
| Male gender (%) | 82% | 83% | 0.77 |
| BMI (kg/m ²) | 27 +/- 5 | 27 +/- 6 | 0.07 |
| Blunt mechanism (%) | 53% | 84% | <0.01 |
| Uninsured (%) | 38% | 23% | <0.01 |
| ED GCS | 14 (8-15) | 8 (3-14) | <0.01 |
| Admit SBP <90 mmHg (%) | 8% | 13% | 0.02 |
| Admit HR >110 BPM (%) | 26% | 44% | <0.01 |
| ISS | 10 (2-24) | 30 (25-41) | <0.01 |
| Head AIS | 0 (0-3) | 4 (2-5) | <0.01 |
| Chest AIS | 0 (0-2) | 3 (0-4) | <0.01 |
| Any chest injury (AIS>0), n (%) | 413 (31%) | 123 (61%) | <0.01 |
| Any severe chest injury (AIS 3), n (%) | 284 (21%) | 103 (51%) | <0.01 |
| Any rib fracture(s), n (%) | 276 (20%) | 92 (45%) | <0.01 |
| Intubated on admission day, n (%) | 632 (47%) | 195 (96%) | <0.01 |
| Any TBI, n (%) | 384 (28%) | 137 (67%) | <0.01 |
| Admit base excess | -3.1 +/- 5.9 | -6.8 +/- 6.2 | <0.01 |
| Any transfusion within 6h, n (%) | 391 (29%) | 137 (69%) | <0.01 |
| Any transfusion within 24h, n (%) | 439 (33%) | 148 (74%) | <0.01 |

* Data are mean +/- SD, median (inter-quartile range), or n (%) as indicated. Data for skewed variables reported as median with inter-quartile ranges. Injury Severity Score (ISS); Abbreviated injury score (AIS), traumatic brain injury (TBI)

Table 2
Patient Demographics/Outcomes by ARDS severity

| | Mild ARDS n=67 | Moderate ARDS n=86 | Severe ARDS n=50 | <i>p</i> -value |
|--|-------------------|-----------------------|---------------------|-----------------|
| Age (years) | 45 (27-60) | 41 (27-54) | 36 (27-52) | 0.18 |
| Male gender | 88% | 77% | 86% | 0.16 |
| BMI (kg/m ²) | 27 +/- 5 | 28 +/- 7 | 28 +/- 5 | 0.78 |
| Blunt mechanism (%) | 79% | 88% | 84% | 0.32 |
| Uninsured (%) | 19% | 21% | 32% | 0.23 |
| ED GCS | 10 (5-14) | 8 (4-11) | 7 (3-14) | 0.37 |
| Admit SBP <90 mm Hg (%) | 7% | 12% | 24% | 0.29 |
| Admit HR >110 BPM (%) | 48% | 49% | 36% | 0.45 |
| ISS | 29 (22-34) | 34 (25-43) | 30 (25-45) | 0.04 |
| Head AIS | 4 (2-5) | 5 (2-5) | 5 (0-5) | 0.15 |
| Chest AIS | 2 (0-3) | 3 (0-4) | 3 (0-4) | 0.12 |
| Any chest injury (AIS>0), n (%) | 36 (54%) | 54 (63%) | 36 (66%) | 0.35 |
| Any severe chest injury (AIS 3), n (%) | 28 (42%) | 47 (55%) | 28 (56%) | 0.20 |
| Any rib fracture(s), n (%) | 24 (36%) | 44 (52%) | 24 (48%) | 0.15 |
| Intubated on admission day (%) | 62 (93%) | 84 (98%) | 49 (98%) | 0.30 |
| Any TBI, n (%) | 46 (67%) | 59 (69%) | 32 (64%) | 0.84 |
| Any transfusion within 6h, n (%) | 40 (62%) | 59 (69%) | 38 (78%) | 0.20 |
| Any transfusion within 24h, n (%) | 42 (64%) | 65 (76%) | 41 (84%) | 0.05 |

* Data are mean +/- SD, median (inter-quartile range), or n (%) as indicated. Data for skewed variables reported as median with inter-quartile ranges. Injury Severity Score (ISS); Abbreviated injury score (AIS), traumatic brain injury (TBI).

Table 3
Hospital Charges & Outcomes for those without and with ARDS

| | No ARDS n=1349 (87%) | ARDS n=203 (13%) | <i>p</i>-value |
|--|---------------------------------|-----------------------------|-----------------------|
| Total hospital charge (\$) | 106,430 (49,453-225,623) | 450,888 (224,901-827,5290) | <0.01 |
| Charge per day (\$) | 23,514 (17,389-31,291) | 24,446 (14,989-34,044) | 0.66 |
| Standard total hospital charge (\$) | 96,588 (48,294-265,617) | 434,646 (21,7323-990,027) | <0.01 |
| Ventilator free days | 27 (25-28) | 3 (0-17) | <0.01 |
| ICU days | 2 (0-4) | 14 (6-23) | <0.01 |
| Hospital days | 4 (2-11) | 18 (9-41) | <0.01 |
| MOF (%) | 3% | 41% | <0.01 |
| Mortality at 28 days (%) | 10% | 33% | <0.01 |

* Data are mean +/- SD, median (inter-quartile range), or n (%) as indicated. Data for skewed variables reported as median with inter-quartile ranges. Ventilator free days are counted for the first 28 days of hospitalization. Subjects who expired received 0 ventilator free days. Intensive care unit (ICU); multiple organ failure (MOF).

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Table 4
Hospital Charges & Outcomes of ARDS Patients by Disease Severity

| | Mild ARDS n=67 | Moderate ARDS n=86 | Severe ARDS n=50 | <i>p</i> -value |
|--|---------------------------|-----------------------------|---------------------------|-----------------|
| Total hospital charge (\$) | 462,417 (264,993-920,018) | 489,330 (254,829-773,073) | 311,017 (179,427-802,498) | 0.35 |
| Charge per day (\$) | 20,451 (13,398-28,133) | 23,994 (14,989-32,768) | 33,316 (17,175-120,735) | <0.01 |
| Standard total hospital charge (\$) | 579,528 (265,617-123,497) | 495,013 (265,617-1,014,174) | 338,058 (120,735-603,675) | <0.01 |
| Ventilator free days | 10 (0-21) | 3 (0-15) | 0 (0-10) | 0.03 |
| ICU days | 14 (7-24) | 14 (8-24) | 10 (4-22) | 0.14 |
| Hospital days | 24 (11-51) | 21 (11-42) | 14 (5-25) | 0.01 |
| MOF (%) | 23% | 45% | 58% | <0.01 |
| Mortality at 28 days (%) | 21% | 33% | 50% | <0.01 |

* Data are mean +/- SD, median (inter-quartile range), or n (%) as indicated. Data for skewed variables reported as median with inter-quartile ranges. Ventilator free days are counted for the first 28 days of hospitalization. Subjects who expired received 0 ventilator free days. Intensive care unit (ICU); multiple organ failure (MOF).

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Table 5
Outcomes for ARDS Survivors at Discharge

| | Mild ARDS n=51 | Moderate ARDS n=55 | Severe ARDS n=24 | p-value |
|--|-----------------------------|-------------------------------|-----------------------------|----------------|
| Total hospital charge (\$) | 598,373 (294,475-933,216) | 590,800 (402,658-861,691) | 673,565 (394,118-1,028,822) | 0.74 |
| Charge per day (\$) | 17,127 (12,154-26,297) | 18,913 (12,298-28,449) | 19,096 (13,613-34,225) | 0.42 |
| Standard total hospital charge (\$) | 724,410 (338,058-1,448,820) | 724,410 (410,499-1,303,938) | 591,602 (386,352-1,002,101) | 0.69 |
| Ventilator free days | 16 (0-23) | 12 (3-19) | 10 (6-20) | 0.35 |
| ICU days | 14 (9-24) | 18 (11-26) | 20 (11-27) | 0.35 |
| Hospital days | 30 (14-60) | 30 (17-54) | 25 (16-42) | 0.70 |
| MOF (%) | 27% | 45% | 54% | 0.05 |

* Data are mean +/- SD, median (inter-quartile range), or n (%) as indicated. Data for skewed variables reported as median with inter-quartile ranges. Ventilator free days are counted for the first 28 days of hospitalization. Subjects who expired received 0 ventilator free days. Intensive care unit (ICU); multiple organ failure (MOF).

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Table 6
Outcomes for Deceased ARDS Patients at Discharge

| | Mild ARDS n=16 | Moderate ARDS n=31 | Severe ARDS n=26 | p-value |
|--|---------------------------|---------------------------|---------------------------|-----------------|
| Total hospital charge (\$) | 309,149 (184,706-475,944) | 287,408 (125,047-474,431) | 210,630 (145,417-305,520) | 0.52 |
| Charge per day (\$) | 26,925 (22,592-34,985) | 31,783 (19,559-40,272) | 43,380 (31,550-58,992) | 0.01 |
| Standard total hospital charge (\$) | 265,617 (108,662-495,013) | 217,323 (72,441-338,058) | 120,735 (72,441-265,617) | 0.08 |
| Ventilator free days | 0 (0-0) | 0 (0-0) | 0 (0-0) | 0.32 |
| ICU days | 9 (5-21) | 9 (3-13) | 5 (3-11) | 0.10 |
| Hospital days | 11 (5-21) | 9 (3-14) | 5 (3-11) | 0.08 |
| MOF (%) | 6% | 45% | 62% | <0.01 |

* Data are mean +/- SD, median (inter-quartile range), or n (%) as indicated. Data for skewed variables reported as median with inter-quartile ranges. Ventilator free days are counted for the first 28 days of hospitalization. Subjects who expired received 0 ventilator free days. Intensive care unit (ICU); multiple organ failure (MOF).

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