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Morbidity and Mortality among Critically Injured Children with Acute Respiratory Distress Syndrome

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Abstract

Objective: To evaluate morbidity and mortality among critically injured children with acute respiratory distress syndrome (ARDS)

Design: Retrospective cohort study

Setting: 460 Level I/II adult or pediatric trauma centers contributing to the National Trauma Data Bank

Patients: 146,058 patients <18 years admitted to an intensive care unit with traumatic injury from 2007–2016

Interventions: None

Measurements and Main Results: We assessed in-hospital mortality and need for post-discharge care among patients with and without ARDS, and hospital resource utilization and discharge disposition among survivors. Analyses were adjusted for underlying mortality risk (age, Injury Severity Score, serious brain or chest injury, and admission heart rate and hypotension), and year, transfer status, and facility trauma level designation. ARDS occurred in 2590 patients (1.8%). Mortality was 20.0% among ARDS patients versus 4.3% among non-ARDS patients, with an adjusted relative risk (aRR) of 1.76 (95% CI 1.52–2.04). Post-discharge care was required in an additional 44.8% of ARDS patients versus 16.0% of non-ARDS patients (aRR 3.59, 2.87–4.49), with only 35.1% of ARDS patients discharging to home versus 79.8% of non-ARDS patients. ARDS mortality did not change over the ten-year study period (aRR 1.01/year, 0.96–1.06), nor did

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the proportion of ARDS patients requiring post-discharge care (aRR 1.04/year, 0.97–1.11). Duration of ventilation, ICU stay, and hospital stay were all significantly longer among ARDS survivors. Tracheostomy placement occurred in 18.4% of ARDS survivors versus 2.1% of non-ARDS patients (aRR 3.10, 2.59–3.70).

Conclusions: ARDS development following traumatic injury in children is associated with significantly increased risk of morbidity and mortality, even after adjustment for injury severity and hemodynamic abnormalities. Outcomes have not improved over the past decade, emphasizing the need for new therapeutic interventions and prevention strategies for ARDS among severely injured children.

Keywords

Acute Respiratory Distress Syndrome; Child; Intensive Care Units; Hospital Mortality; Outcome Assessment; Trauma Centers

Introduction

Traumatic injury is the leading cause of death and new disability in children and adolescents in the United States.[1] While most deaths occur immediately or within hours of the injury, over one-quarter of pediatric trauma deaths are characterized as “late mortality,” occurring after at least 24 hours of hospitalization.[2] Children who survive to hospital admission remain at risk for life-threatening complications of their initial injury, the most common being acute respiratory distress syndrome (ARDS).[2]

ARDS can be triggered by direct pulmonary insults such as pneumonia and aspiration, or by systemic inflammation, as with sepsis and trauma.[3] Mortality among children with ARDS of all etiologies ranges from 13–44% depending on the patient population,[4–12] highlighting the heterogeneity of the syndrome. A recent meta-analysis found a combined mortality rate of 27.3% for pediatric ARDS in Western countries.[13] Most pediatric ARDS studies have included very few trauma patients, however; while one recent study assessed in-hospital mortality among a mixed population of trauma, burn, and drowning patients,[14] none have evaluated outcomes among trauma patients specifically or assessed post-discharge morbidity. It therefore remains unclear whether mortality among children with post-traumatic ARDS is similar to that of ARDS due to other etiologies, or what the impact of ARDS is on survivors of pediatric trauma.

A challenge in studying post-traumatic ARDS is to distinguish the effect of ARDS on outcomes from the impact of the severity of the injury itself. While most adult studies have found that unadjusted mortality is higher among patients with ARDS than those without,[15–21] several have found no additional impact of ARDS on mortality after adjusting for confounding factors such as age, injury severity, and physiologic parameters on admission.[15,16] We therefore aimed to evaluate outcomes among pediatric patients with post-traumatic ARDS by estimating risk for all-cause hospital mortality after adjusting for underlying mortality risk, and assessing markers of morbidity among survivors including hospital resource utilization and need for ongoing post-discharge care. Improved understanding of how ARDS impacts outcomes in critically injured children will enable better assessment of the efficacy of interventions and allow identification of areas for targeted support for survivors.

Materials and Methods

We conducted a retrospective cohort study of children admitted to intensive care units (ICUs) at trauma centers included in the National Trauma Data Bank (NTDB)[21] from 2007–2016. This study was exempt from review by the University of Washington Institutional Review Board as data were de-identified and not considered to be human subjects research.

Participants:

We used the NTDB research datasets from 2007–2016 to identify pediatric trauma patients. The NTDB contains >7 million records from >1000 U.S. and Canadian facilities and is the largest trauma registry worldwide, representing nearly all Level I or II adult or pediatric trauma centers in the U.S.[22] Patients with traumatic injury who are transferred via Emergency Medical Services or sustain injuries resulting in hospital admission or death are eligible for inclusion. We included patients <18 years with ≥1 ICU day at a Level I or II adult or pediatric trauma center. We excluded patients admitted with burns/inhalation (n=6302) or drowning (n=429), as the physiologic mechanism for ARDS development is likely different in these patients than other trauma patients and the NTDB is not a representative database for these patients. Patients from nine facilities that do not routinely report hospital complications were excluded (n=1805).

Identification of ARDS:

ARDS is recorded in the NTDB as a hospital complication for patients who met American-European Consensus Conference criteria[23] through 2011, modified Berlin criteria[24] from 2012–2014, and full Berlin criteria from 2015–2016 (Supplemental Digital Content 1). The NTDB does not record whether an intervening event occurred between the injury and ARDS onset, and our findings are thus inclusive of the full scope of ARDS triggers that patients are susceptible to following traumatic injury, including direct chest trauma, severe systemic inflammation, transfusion-associated lung injury, aspiration, and pneumonia.

Covariates:

We used a modification of Haider et al.'s risk adjustment model for underlying risk of mortality among patients of all ages in the NTDB, which included six covariates (age, Injury Severity Score [ISS], admission heart rate, admission hypotension, total admission Glasgow Coma Scale [GCS] score, and ventilator use) with an area under the receiver operating characteristics curve of 0.9578 for mortality prediction.[25] In our cohort, however, 54% of ARDS patients were intubated, chemically paralyzed, or had an eye injury at admission, rendering total GCS unreliable. Additionally, 88% of patients with ARDS were mechanically ventilated, leading to collinearity between ventilator use and ARDS. We thus substituted total GCS and ventilator use with the presence of a serious brain or chest injury (defined by a region-specific Abbreviated Injury Scale (AIS) severity score ≥3), two factors that contribute substantially to GCS and need for mechanical ventilation but with more discriminative ability in this cohort. Our final set of covariates for risk adjustment thus included age, ISS, brain injury with AIS ≥3, chest injury with AIS ≥3, admission heart rate, and admission hypotension. Heart rate and hypotension were categorized using age-adjusted normative values.[26,27]

Outcomes:

We assessed in-hospital mortality and post-discharge care needs among survivors by categorizing patients by discharge disposition: 1) discharge to home with no homecare services; 2) ongoing care needs including transfer to a second acute care facility, inpatient rehabilitation, skilled nursing facility, long-term care facility, home care, or other (hospice, psychiatric care, left against medical advice, or unspecified facility); and 3) expired. We also assessed whether the frequency of mortality and need for post-discharge care changed from 2007–2016. Outcomes assessed among survivors were duration of mechanical ventilation, frequency of tracheostomy placement, ICU and hospital length of stay (LOS), and type of post-discharge care required.

Statistical analysis:

We calculated rates of each outcome for patients with and without ARDS. We estimated associations between ARDS and each outcome in bivariate analyses clustered by facility using generalized linear Poisson regression for death and tracheostomy, multinomial logistic regression for discharge disposition, and linear regression for duration of ventilation and LOS. We repeated each analysis as a multivariable model with the six pre-determined covariates, as well as admission year, transfer status, and facility trauma level designation, to estimate adjusted associations between ARDS and each outcome. We determined annual rates of mortality and post-discharge care among patients with and without ARDS, and estimated associations between year and discharge disposition in bivariate analyses and as multivariable models with the pre-determined covariates. All models were complete case analyses; no covariates had >5% missing data. We conducted all analyses using Stata/SE 14.2 statistical software (StataCorp LP, College Station, TX).

Results

A total of 146,058 patients from 460 facilities met inclusion criteria, with an ARDS incidence of 1.8% (n=2590). Two-thirds of patients were male, and just over half were non-Hispanic white. Patients with ARDS were slightly older than those without ARDS (mean 10.4 years vs 9.5 years), and a higher proportion were African American (20.8% vs 14.5%). Motor vehicle crashes were the most common mechanism of injury among ARDS patients, while falls were most common among non-ARDS patients. ARDS patients had a higher median ISS (26 vs 13), and higher frequency of brain injury, chest injury, abnormal admission heart rate, and admission hypotension (Table 1).

The mortality rate among ARDS patients was 20.0% versus 4.3% among patients without ARDS. Among patients without a serious brain injury, 9.2% of ARDS patients and 0.9% of non-ARDS patients died. Median time to death was 3 days (IQR 1–6) among ARDS patients and 2 days (IQR 1–4) among non-ARDS patients. Ongoing post-discharge care was required in an additional 44.8% of ARDS patients, compared to 16.0% of non-ARDS patients. Only

35.1% of patients with ARDS discharged to home without need for further care, while 79.8% of patients without ARDS discharged to home without services (Figure 1).

The relative risk (RR) of mortality among ARDS patients compared to those without ARDS was 4.70 (95% confidence interval [CI] 4.14–5.34). The RR of requiring post-discharge care (versus discharge home without homecare services) was 6.37 (95% CI 5.26–7.72). After adjusting for the selected covariates, the adjusted RR (aRR) for mortality was 1.76 (95% CI 1.52–2.04), and the aRR for post-discharge care was 3.59 (95% CI 2.87–4.49) (Table 2).

Hospital complications and procedures:

Patients with ARDS experienced higher rates of other hospital complications than non-ARDS patients, including pneumonia (20.6% vs 2.3%), sepsis or bacteremia (4.5% vs 0.4%), other infections (4.5% vs 1.1%), and cardiac arrest (8.2% vs 0.8%), though it is unknown whether these complications preceded ARDS onset (Supplemental Digital Content 3). Among patients with ARDS, development of pneumonia was associated with a lower risk of death relative to patients without pneumonia (aRR 0.45, 95% CI 0.36–0.58), while cardiac arrest was associated with a higher risk of death (aRR 3.03, 95% CI 2.46–3.72). Neither sepsis/bacteremia nor other infections were associated with risk of death. All hospital complications evaluated were associated with higher risk for post-discharge care.

Patients with ARDS more frequently underwent surgical procedures within 24 hours of hospital arrival, but none of the procedures assessed were associated with higher mortality risk among ARDS patients (Supplemental Digital Content 3). Spinal fusion was associated with higher risk of post-discharge care.

Trends over time:

Annual ARDS mortality ranged from 16.2–24.9% over the ten-year study period, but had no significant linear trend over time before risk adjustment (RR 1.01/year, 95% CI 0.96–1.05) and after adjustment (aRR 1.01/year, 95% CI 0.96–1.06). The proportion of ARDS patients who required post-discharge care also did not significantly change over time, ranging from 40.5–55.1% annually with no linear trend before or after risk adjustment (RR 1.01/year, 95% CI 0.95–1.07; aRR 1.04/year, 95% CI 0.97–1.11) (Figure 2).

Treatment and outcomes among ICU survivors:

Among patients who survived to hospital discharge, the duration of mechanical ventilation, ICU LOS, and hospital LOS were all significantly longer among patients with ARDS in both unadjusted and risk-adjusted analyses (Figure 3). Median ventilator duration was 6 days (IQR 3–12) for ARDS patients compared to 2 days (IQR 1–6) for non-ARDS patients. After risk adjustment, the average duration of mechanical ventilation was 3.10 days (95% CI 2.74–3.47) longer among ARDS patients than non-ARDS patients. Median ICU LOS among ARDS patients was 10 days (IQR 4–18) versus 2 days (IQR 1–3) in non-ARDS patients, with an average adjusted ICU LOS that was 6.53 days (95% CI 6.29–6.78) longer among ARDS patients. ARDS patients had a median 16-day hospital stay (IQR 9–26) compared to 4 days (IQR 2–7) among non-ARDS patients. The average adjusted hospital LOS was 9.08 days (95% CI 8.67–9.49) longer among ARDS patients than non-ARDS patients.

Tracheostomy placement occurred in 18.4% of ARDS patients who survived to hospital discharge compared to 2.1% of survivors without ARDS. Among survivors without a serious brain injury, 13.7% of ARDS patients and 1.1% of non-ARDS patients received a tracheostomy.

Tracheostomy was most common among patients aged 12–17 years (26.4% ARDS, 3.5% non-ARDS) and least common in patients ≤4 years (7.2% ARDS, 0.7% non-ARDS). Frequency of tracheostomy varied by facility type; while 20.5% of ARDS patients treated at adult-only facilities received a tracheostomy, 17.6% of those treated at mixed adult and pediatric facilities and only 11.3% of those treated at pediatric-only facilities did.

ARDS survivors had an unadjusted RR of 8.74 (95% CI 7.30–10.47) for tracheostomy placement compared to non-ARDS patients with an adjusted RR of 3.10 (95% CI 2.59–3.70). The median time to tracheostomy placement was 10 days for both ARDS and non-ARDS patients (IQR 6–17 ARDS, 5–15 non-ARDS). Median time to tracheostomy was shortest among patients aged 12–17 years (9 days [IQR 6–15] ARDS; 9 days [5–14] non-ARDS) and longest among patients ≤4 years (19.5 days [11.5–28] ARDS; 16 days [9–21] non-ARDS). Among patients who received a tracheostomy, 91.6% of ARDS patients and 81.1% of non-ARDS patients required post-discharge care.

Of patients who survived ARDS, 56.0% required ongoing post-discharge care. Inpatient rehabilitation was the most common type (29.7% of survivors), followed by care in long-term care facilities (10.6%). In contrast, only 16.7% of survivors without ARDS required post-discharge care. Half (8.6% of survivors) received inpatient rehabilitation, with home healthcare the second most common (2.9%) type of post-discharge care (Supplemental Digital Content 2).

Among survivors without a serious brain injury, 44.1% of ARDS patients and 13.0% of non-ARDS patients required post-discharge care. Patients with ARDS remained significantly more likely than patients without ARDS to experience all types of post-discharge care after risk adjustment, especially for care in long-term care facilities (aRR 5.10, 95% CI 3.21–8.11) and skilled nursing facilities (aRR 4.91, 95% CI 3.48–6.94) (Table 2).

Discussion

While ARDS is a known complication of severe traumatic injury, its impact on outcomes in the pediatric trauma population has not previously been described. The findings of this ten-year cohort of nearly 150,000 critically injured children suggest that the development of ARDS is significantly associated with all-cause morbidity and mortality even after adjusting for important confounding factors. This study also demonstrates that little progress has been made over the past decade in improving outcomes for pediatric trauma patients with ARDS.

Several studies of adult ARDS have found lower in-hospital mortality among patients with post-traumatic ARDS compared to other etiologies,[28,29] but this has not been evaluated in children. The all-cause mortality rate of 20.0% among patients with post-traumatic ARDS in our cohort is similar to the overall pediatric ARDS mortality rate found in many recent studies,[5,7,8,10–12] and the 9.2% mortality among ARDS patients without serious brain injury is consistent with the mortality rate among general pediatric ARDS patients who did not die from neurologic causes.[12] There was a nearly five-fold higher risk of death among ARDS patients compared to those without ARDS, and a 76% higher risk for mortality after adjusting for confounding factors.

Furthermore, the impact of ARDS on survivors of pediatric trauma is substantial, with less than half of ARDS survivors discharging to home. While injury severity and serious neurologic injury contribute greatly to post-discharge care needs after trauma, ARDS patients remained over three times more likely to require ongoing care after discharge than non-ARDS patients after adjusting for these factors. Prolonged duration of mechanical ventilation, high rates of tracheostomy placement, and markedly longer lengths of stay in ARDS patients likely contributed to deconditioning and ongoing respiratory care needs.

The finding that 18.4% of ARDS survivors underwent tracheostomy placement is striking, especially considering that the median time to tracheostomy was only 10 days. Tracheostomy placement is a relatively rare event in pediatric ICU patients in general; a recent study of over 13,000 children mechanically ventilated for at least 72 hours found that only 6.6% received a tracheostomy, at a median 14.4 days after admission.[30] Tracheostomy placement in children, including trauma patients, has been shown to decrease ventilator duration and length of stay.[31,32] Unsurprisingly however, over 90% of ARDS survivors in our cohort who had a tracheostomy placed required ongoing post-discharge care, highlighting the fact that despite potential in-hospital benefits of tracheostomy placement, it is accompanied by a high burden of post-discharge care. Among pediatric patients in general, fewer than 50% of those with a tracheostomy are ever decannulated, and the average time to decannulation is two years.[33] This has not been evaluated in the trauma population specifically however, and further work is necessary to better understand the risks and benefits of tracheostomy placement among pediatric trauma patients both during and after hospitalization.

Neither mortality nor the need for ongoing post-discharge care in pediatric post-traumatic ARDS significantly changed over the ten-year study duration. This is consistent with findings demonstrating that while there has been a significant decrease in overall pediatric ARDS mortality in Western countries since the 1980s, the downward trend is no longer observed among cohorts after 1994.[13] While improvements in ventilator strategy, fluid management, and transfusion practices likely contributed to initial declines,[34] a plateau seems to have been reached for both pediatric ARDS mortality overall and for the trauma subpopulation, emphasizing the need for new therapeutic interventions and prevention strategies.

There were several limitations to this study. All patients included in this cohort pre-date the pediatric ARDS consensus criteria published in 2015,[35] which have not yet been adopted by the NTDB. Instead, ARDS is identified in the NTDB based on adult ARDS consensus definitions, which likely underestimate ARDS occurrence in children[36] and may represent a more severely ill subpopulation of the patients who would have been identified by pediatric criteria.[37,38] Risk adjustment was based on previously published recommendations for mortality risk adjustment in the NTDB, but was not specific to pediatric ICU patients.

Additionally, we substituted ventilator use and total GCS with presence of serious chest and brain injuries given the high prevalence of mechanical ventilation and GCS modifiers in our cohort; this approach has not been validated. It is possible that there are additional confounders of the association between ARDS and mortality that were not included in our risk adjustment strategy. We also elected to use the same covariates developed for mortality risk adjustment to adjust for morbidities, which has not been validated. Finally, we assumed that discharge to home without homecare services was due to lack of need for services, but it is possible that patients could not obtain services due to insurance limitations or lack of availability, and that hospital stay was lengthened due to inability to discharge to a post-acute care facility.

Conclusions

Development of ARDS after trauma in pediatric patients is accompanied by high rates of morbidity and mortality that have not decreased over the past decade. ARDS is associated with increased risk of mortality in critically injured children even after adjustment for injury severity, brain and chest injuries, and hemodynamic abnormalities, in contrast to several recent adult studies that have not found an independent effect of ARDS after risk adjustment. The burden of ARDS on trauma survivors is also substantial, with high rates of in-hospital morbidity and low frequency of discharge to home without post-discharge health services. Characterization of the types of long-term morbidities that survivors of pediatric trauma-related ARDS face and identification of the potentially modifiable factors associated with morbidity are essential to guide interventions to improve long-term outcomes among severely injured children.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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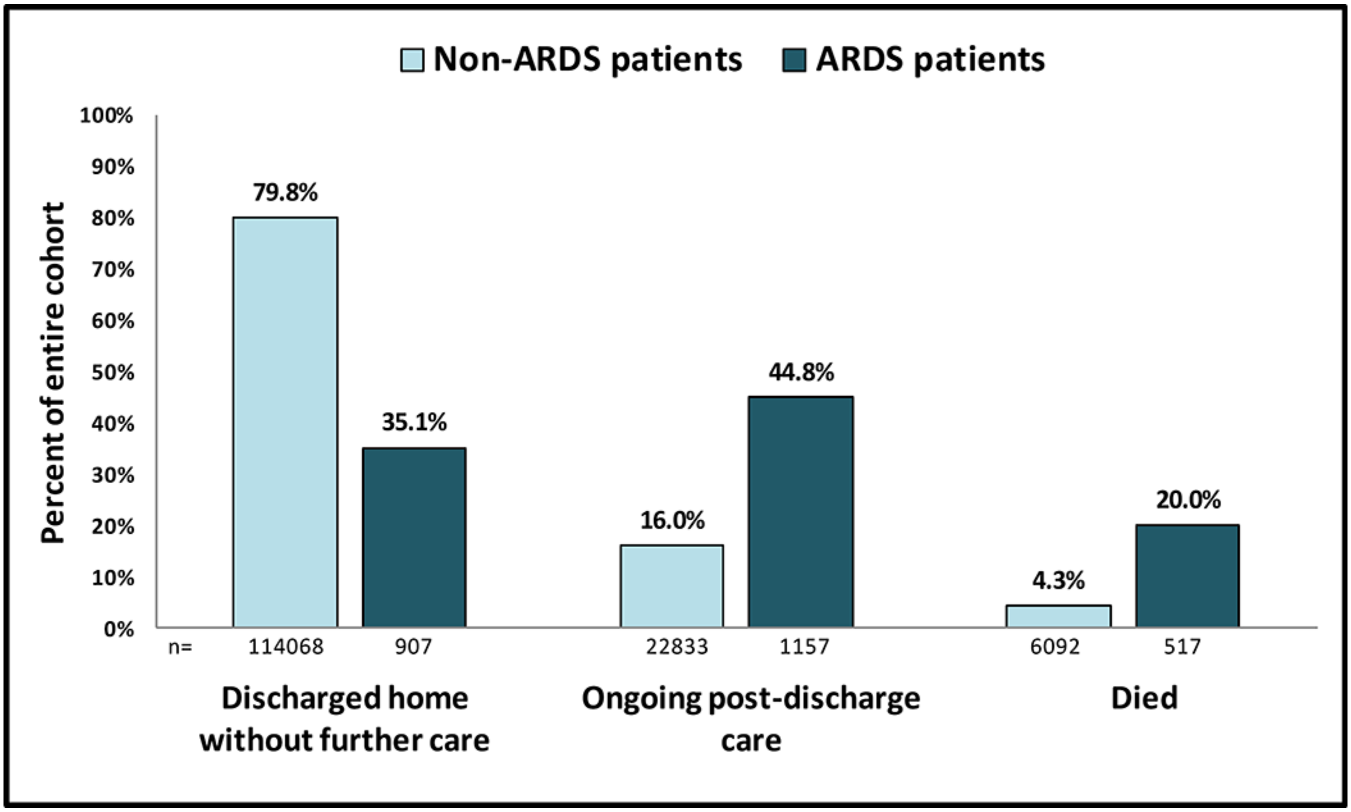

Figure 1: Frequency of discharge outcomes in patients with and without ARDS

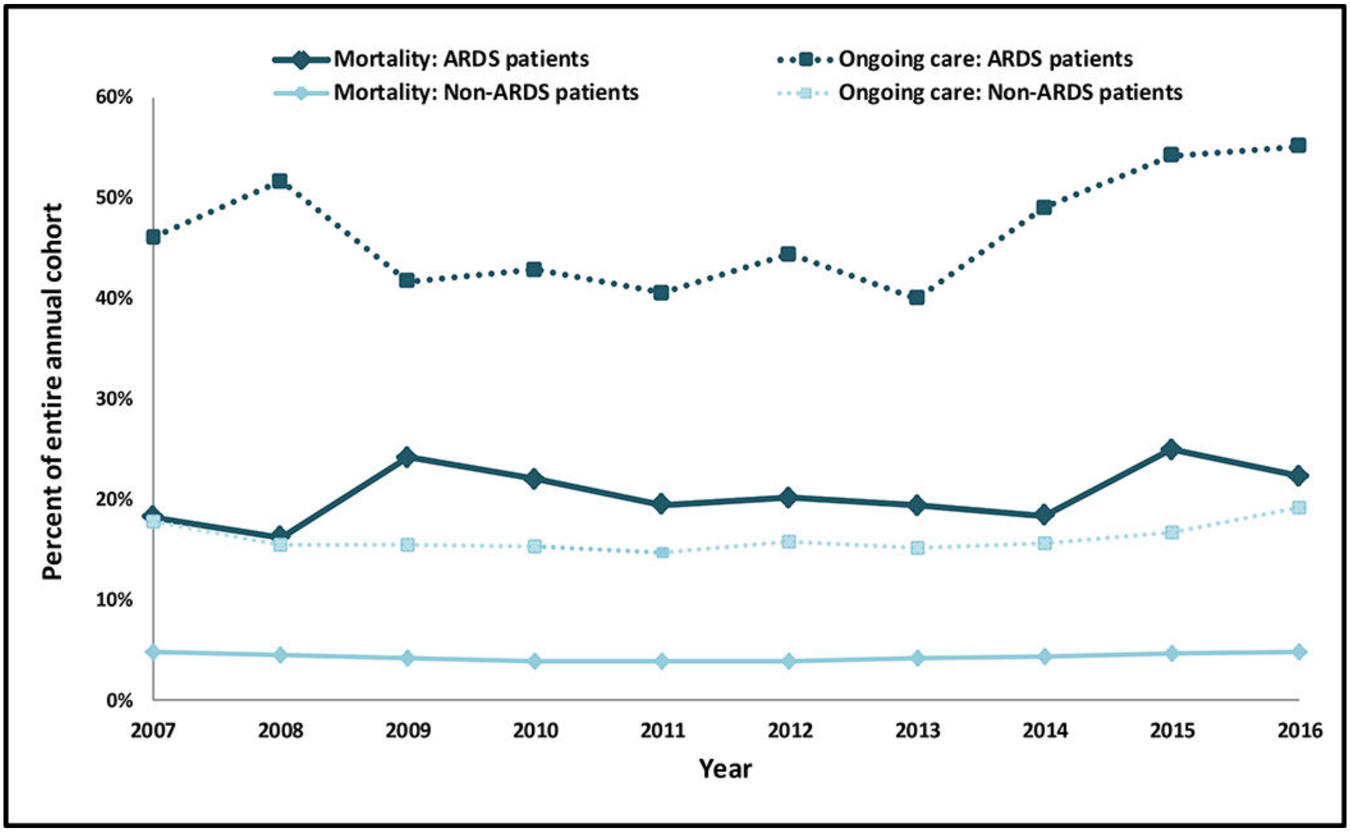

Figure 2: Trends in mortality and need for ongoing care among ARDS patients from 2007–2016.
Dark blue lines represent mortality and need for ongoing care among ARDS patients. Light blue lines represent mortality and need for ongoing care among non-ARDS patients.

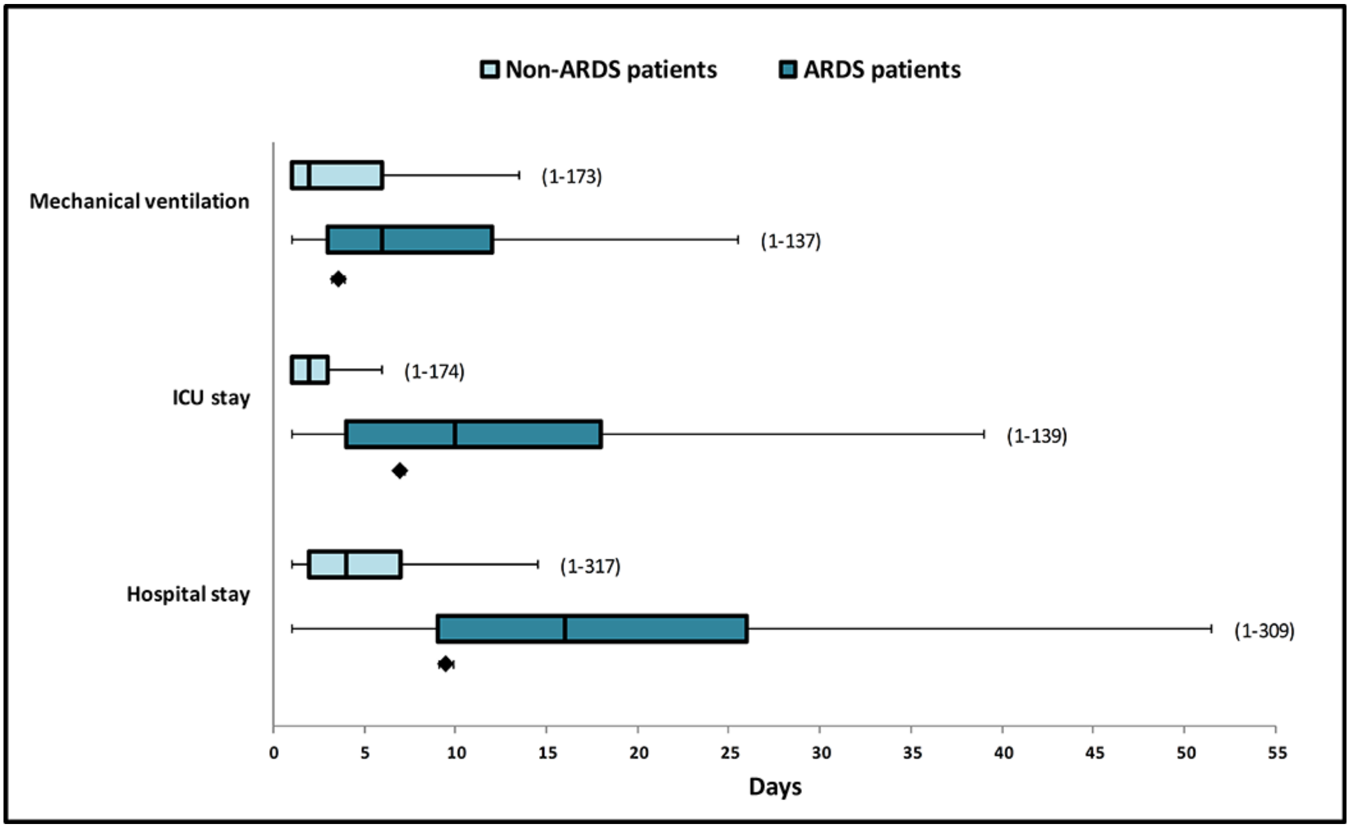

Figure 3: Duration of mechanical ventilation, ICU length of stay, and hospital length of stay among patients with and without ARDS who survived to hospital discharge.

Box-plots demonstrate median and interquartile range, with whiskers representing upper and lower adjacent values (1.5x the interquartile range). Outliers are included in calculations but not illustrated; the range of data points are indicated in parentheses. Black diamonds represent the average number of additional days for ARDS patients compared to non-ARDS patients after risk adjustment, with error bars representing 95% confidence intervals.

Table 1:

Characteristics of pediatric intensive care unit patients with and without ARDS included in the National Trauma Data Bank, 2007–2016

Patient or Injury Characteristic	Patients with ARDS No. (%) (n=2590, 1.8%)	Patients without ARDS No. (%) (n=143468, 98.2%)
Age (years)		
<1	334 (14.0)	18661 (16.3)
1 – 4	294 (12.3)	14856 (13.0)
5 – 11	449 (18.8)	26268 (22.9)
12 – 17	1308 (54.8)	54879 (47.9)
Mean (± SD)	10.4 (± 6.3)	9.5 (± 6.2)
Race/ethnicity		
Non-Hispanic White	1466 (56.6)	81421 (56.8)
Non-Hispanic African American	539 (20.8)	20714 (14.5)
Hispanic	363 (14.0)	23799 (16.6)
Asian/Pacific Islander	48 (1.9)	3179 (2.2)
Other/Unknown/Multiracial	174 (6.7)	14152 (9.9)
Male gender	1688 (65.2)	95372 (66.6)
Mechanism of injury		
Fall	1095 (42.9)	34809 (24.6)
Motor vehicle crash	202 (7.9)	37610 (26.6)
Pedestrian/cyclist	370 (14.5)	20280 (14.3)
Firearm	195 (7.6)	7334 (5.2)
Struck by/against	102 (4.0)	14076 (10.0)
Other	591 (23.1)	27397 (19.4)
Injury Severity Score		
1 – 8	133 (5.3)	33679 (24.1)
9 – 15	342 (13.5)	44466 (31.8)
16 – 24	551 (21.8)	34986 (25.0)
25 – 39	1096 (43.3)	22607 (16.2)
40 – 75	411 (16.2)	4122 (3.0)
Median (IQR)	26 (17–35)	13 (9–20)
Traumatic brain injury with AIS ≥3	1701 (66.6)	68733 (49.1)
Chest injury with AIS ≥3	1269 (49.7)	28847 (20.6)
Heart rate on admission		
Pulseless	24 (1.0)	376 (0.3)
Bradycardic	190 (7.6)	7024 (5.1)
Normal	781 (31.3)	64039 (46.1)
Tachycardic	1504 (60.2)	67341 (48.5)
Hypotension on admission	253 (10.3)	4831 (3.6)
Facility trauma level designation		
Pediatric Level 1	1280 (49.4)	66058 (46.0)

Patient or Injury Characteristic	Patients with ARDS No. (%) (n=2590, 1.8%)	Patients without ARDS No. (%) (n=143468, 98.2%)
Adult Level 1	771 (29.8)	36389 (25.4)
Pediatric Level 2	219 (8.5)	22760 (15.9)
Adult Level 2	320 (12.4)	18261 (12.7)

ARDS, acute respiratory distress syndrome; SD, standard deviation; IQR, interquartile range; AIS, Abbreviated Injury Scale severity score

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Table 2:

Discharge outcomes among patients with ARDS relative to patients without ARDS

Outcome	Unadjusted RR	95% CI	Adjusted RR[a]	95% CI
Mortality[b]				
Survived	Ref		Ref	
Died	4.70	4.14 – 5.34	1.76	1.52 – 2.04
Discharge Disposition: Entire Cohort[b]				
Home without further care	Ref		Ref	
Ongoing post-discharge care	6.37	5.26 – 7.72	3.59	2.87 – 4.49
Died	10.67	8.93 – 12.75	4.56	3.51 – 5.92
Discharge Disposition: Survivors[c]				
Home without further care	Ref		Ref	
Home healthcare	3.93	2.70 – 5.73	2.97	2.12 – 4.15
Long-term care facility	13.70	8.79 – 21.35	5.10	3.21 – 8.11
Skilled nursing facility	10.61	7.49 – 15.03	4.91	3.48 – 6.94
Inpatient rehabilitation	6.55	5.10 – 8.41	3.27	2.37 – 4.50
Transfer to second acute care facility	4.49	3.20 – 6.32	2.76	2.02 – 3.79
Other	2.25	1.31 – 3.88	3.28	1.77 – 6.09

ARDS, acute respiratory distress syndrome; RR, relative risk; CI, confidence interval

[a]Adjusted relative risks are adjusted for age, Injury Severity Score, presence of a traumatic brain injury with an Abbreviated Injury Scale severity score ≥3, presence of a chest injury with an Abbreviated Injury Scale severity score ≥3, admission heart rate, admission hypotension, year, transfer status, and facility trauma level designation

[b]Assessed among all patients in cohort (n=146,058)

[c]Assessed among survivors to hospital discharge (n=139,449)