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Outcomes of Children With Cystic Fibrosis Admitted to PICUs*

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Abstract

Objectives: Data on outcomes of children with cystic fibrosis admitted to PICUs are limited and outdated. Prior studies cite PICU mortality rates ranging from 37.5% to 100%. Given the advances made in cystic fibrosis care, we expect outcomes for these patients to have changed significantly since last studied. We provide an updated report on PICU mortality and the factors associated with death among critically ill children with cystic fibrosis.

Design: Retrospective multicenter cohort analysis utilizing data from the Virtual Pediatric Systems database.

Setting: Data were collected from 135 PICUs from January 1, 2009, to June 20, 2018.

Patients: One-thousand six-hundred thirty-three children with cystic fibrosis accounting for 2,893 PICU admissions were studied.

Interventions: None.

Measurements and Main Results: The primary outcome was mortality during PICU admission. Predictors included demographics, anthropometrics, diagnoses, clinical characteristics, and critical care interventions. Odds ratios of mortality were calculated in univariate and multivariable analyses to assess differences in mortality associated with predictor variables. Generalized estimating equation models were used to account for multiple admissions per patient. The overall PICU mortality rate was 6.6%. Factors associated with increased odds of mortality included hemoptysis/pulmonary hemorrhage, pneumothorax, gastrointestinal bleeding, bacterial/fungal infections, lower body mass index/malnutrition, and need for noninvasive or invasive respiratory support. Intubation/mechanical ventilation occurred in 26.4% of the 2,893 admissions

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and was associated with a 19.1% mortality rate. Of the nonsurvivors, 20.7% died without receiving mechanical ventilation.

Conclusions: The mortality rate during PICU admissions for patients with cystic fibrosis is lower than has been reported in prior studies, both in the overall cohort and in the subset requiring invasive mechanical ventilation. These data provide updated insight into the prognosis for cystic fibrosis patients requiring critical care.

Keywords

critical care outcomes; cystic fibrosis; intensive care units; pediatric; pediatrics; pulmonary medicine; respiration; artificial

The management of patients with cystic fibrosis (CF) has changed drastically in recent years with the development of new medications, respiratory support strategies, and approaches to the treatment of CF exacerbations. With advances in care, there has been a coincident improvement in the overall morbidity and mortality of CF patients. Median survival has increased from 33.9 to 47.7 years from 2000 to 2016 (1). Despite these improvements, CF remains a chronic disease with a perpetual risk for complications that may require intensive care management, including respiratory failure, hemoptysis, pneumothorax, and gastrointestinal complications. It is unclear whether morbidity and mortality has also improved in the subset of CF patients that require critical care.

Studies examining outcomes of CF patients admitted to PICUs have not been conducted in the modern era of CF care. The first study of PICU mortality in this population was performed in 1978 and demonstrated a 69% mortality rate on mechanical ventilation, but 80% mortality at hospital discharge (2). There have been several studies since then that generally report improved outcomes in adults with CF requiring critical care (3–11). Fewer studies include pediatric patients (12–16) and only four of those studies focused solely on the pediatric population (13–16). All four studies report on outcomes relative to specific respiratory support strategies, with enrollments ranging from five to 33 patients. A 2002 report provided the most thorough assessment in a retrospective analysis of a cohort of 33 pediatric patients who required invasive mechanical ventilation. Overall hospital mortality was 61%, improved from the 1978 study though still quite high (14).

Management of respiratory exacerbations has changed significantly since this latest study was performed, primarily with regards to the growing popularity of noninvasive ventilatory strategies and the trend toward earlier referral for lung transplantation evaluation (17). We hypothesized that with these treatment advancements, outcomes in pediatric CF patients in the PICU have improved. We sought to use a large, multicenter database to update our understanding of PICU outcomes and the factors associated with mortality for children with CF requiring critical care.

MATERIALS AND METHODS

Design

This was a retrospective multicenter cohort analysis utilizing data from 135 PICUs contributing to the Virtual Pediatric Systems database (VPS, LLC). VPS collects information regarding diagnoses, clinical characteristics, critical care interventions, and outcomes of patients admitted to a wide variety of PICUs, amassing the most robust pediatric intensive care database to date. Trained VPS analysts collect patient data from PICU admission through PICU discharge, transfer, or death. Diagnoses are assigned to patients based on review of attending physician documentation; some but not all sites additionally contribute *International Classification of Diseases*, 9th and 10th Edition (ICD-9 and ICD-10) codes. VPS takes several steps to assure high-quality data collection, including credential requirements for data collectors, a standardized definitions/operations manual, routine inter-rater reliability testing, and automated and manual data cleaning processes. This study was reviewed by our institutional review board and determined to be exempt, given that all patient information was de-identified prior to study team access.

Patients

We queried the VPS database for patients admitted to PICUs between January 1, 2009, and June 20, 2018. All PICU admissions associated with a diagnosis code of CF were included in the study.

Outcomes

The primary outcome was survival to PICU discharge or transfer.

Predictors

For each PICU admission, we queried patient demographic data, anthropometrics, patient origin prior to PICU admission, readmission status, Pediatric Risk of Mortality-3 (PRISM-3) data, diagnoses, and interventions performed in the PICU. PRISM-3 raw scores and probability of death (POD) were calculated within 12 hours of admission and served as estimates of admission illness severity (18, 19). Age was recorded in defined age ranges. Readmission status was coded in the VPS data and referred to any admission within the studied time frame that was preceded by a prior admission to a VPS site. Body mass index (BMI) was calculated for all admissions of patients over 2 years old that had both weight and height recorded. Diagnoses were grouped by corresponding ICD-10 (if available) or ICD-9 codes. For diagnoses without associated ICD codes, the VPS-assigned diagnosis code was used for categorization (Supplemental Table 1, Supplemental Digital Content 1, <http://links.lww.com/PCC/B317>). Bacterial, viral, and fungal infections were identified by VPS coders through review of medical record documentation; microbiologic data to support these diagnoses were not available to the study team. Respiratory support interventions were grouped into categories of invasive ventilation, noninvasive support only, and other. Invasive ventilation was defined as endotracheal intubation or tracheostomy insertion and any form of mechanical ventilation. Noninvasive support only represented the use of continuous positive airway pressure or bilevel positive airway pressure without the need for preceding or

subsequent invasive ventilation. All remaining admissions were categorized as “other.” Renal replacement therapy was defined as hemodialysis, continuous venovenous hemofiltration/hemodialysis, or peritoneal dialysis. Other procedures analyzed included tracheostomy tube insertion, chest tube insertion, bronchoscopy, and extracorporeal life support (ECLS). VPS mandates reporting of intubation, mechanical ventilation, and ECLS at all sites; reporting of the other procedures occurred at some but not all sites. Admissions during which a certain procedure’s data were not collected were excluded from analysis of the specified procedure.

Statistical Analysis

Standard comparative statistics were used to describe population norms, including means with sDs for normally distributed variables and medians with interquartile ranges (IQRs) for skewed distributions. Non-normal distributions were compared using Wilcoxon rank-sum tests and proportions were compared with chi-square and Fisher exact tests. Mortality rates were compared between groups using mortality odds ratios (ORs) with 95% CIs and two-tailed p values with a nominal significance level of α equals to 0.05. To account for patients having more than one PICU admission during the study period with certain patient-level data that would remain constant across admissions (i.e., sex, race/ethnicity) and other characteristics that would change on subsequent encounters (i.e., age, diagnosis codes), we used generalized estimating equation (GEE) models with a logistic link function and clustered PICU admissions by patient (20). Univariate GEE models were first calculated for each of the factors studied. We then created a multivariable GEE model to assess the independent association of certain predictors with mortality. Factors selected for inclusion in the model were patient/admission characteristics and diagnoses with p value of less than or equal to 0.10 in univariate analysis. Procedures performed during admission were not included to avoid the expected predictor dominance of these variables so that the model better reflects the effects of patient characteristics on outcome. PRISM-3 data were excluded from multivariable analysis as it has been previously validated as a predictor of PICU mortality (18, 19). Last, we performed a subgroup analysis of nonsurvivors comparing those who received mechanical ventilation to those who were not intubated or mechanically ventilated during their admission. We sought to compare clinical characteristics between these two groups with the assumption that those who died without intubation/mechanical ventilation had some limitation of care in place, that is, a do not intubate (DNI) order. All statistical analyses were performed using R statistical software (21).

RESULTS

Of the 998,846 PICU admissions in the study period between January 1, 2009, and June 20, 2018, 2,893 included a diagnosis of CF. There were 1,633 patients accounting for these admissions. The median length of PICU stay was 2.15 days (IQR, 0.69–6.14 d). Readmissions accounted for 1,312 admissions (45.4%). One-hundred ninety-two admissions ended in death, accounting for an overall mortality rate of 6.6% of admissions. Of the 1,633 patients included in the study period, 11.8% died during a PICU admission (Fig. 1).

Demographics and Admission Characteristics

Patient demographics, readmission status, origin prior to PICU admission, BMI, PRISM-3 scores, survivors, and nonsurvivors are listed in Table 1. The largest groups of patients were between age 13–18 years old (39.0%), Caucasian (66.9%), and female (50.2%). Patients less than 2 years old had the lowest mortality. Race/ethnicity and gender did not differ between survivors and nonsurvivors. The greatest proportion of patients (34.8%) were admitted to the PICU from general care units. Admissions from intermediate care units, neonatal ICUs/delivery rooms, and transfers from other PICUs were associated with increased mortality while admission following a surgery/procedure was associated with lower mortality. Readmission status was not associated with mortality.

The median PRISM-3 score was 3 (IQR, 0–6) and the median PRISM-3 POD was 0.51 (IQR, 0.30–1.64). As expected, higher PRISM-3 scores and PODs were associated with increased odds of mortality in our cohort.

BMI data were available for 995 of the admissions and ranged from 9.6 to 45.8 (median, 17.8; IQR, 15.8–20.0). Increasing BMI was associated with decreased mortality ($p = 0.001$). Relative to normal-weight patients (BMI 18.5–25), underweight patients (BMI < 18.5) had increased mortality ($p = 0.028$). No patients with a BMI greater than 25.0 died ($n = 0/43$ admissions).

Diagnoses Associated With Mortality

In univariate analyses, diagnoses related to respiratory, gastrointestinal, and infectious complications were each significantly associated with increased odds of mortality (Table 2). Among respiratory diagnoses, hemoptysis/pulmonary hemorrhage, pneumothorax, and chronic airway obstruction were each associated with increased mortality ($p < 0.001$, $p < 0.001$, $p = 0.001$, respectively). Diagnoses pertaining to lung transplant were not significantly associated with mortality ($p = 0.380$). Among gastrointestinal diagnoses, hepatobiliary disease, gastrointestinal bleeding, and splenomegaly were associated with increased mortality ($p < 0.001$, $p < 0.001$, $p = 0.048$, respectively). Bacterial and fungal infections, but not viral infections, were associated with increased odds of mortality ($p < 0.001$, $p = 0.007$, respectively). Additionally, comorbidities including a diagnosis of malnutrition, cardiovascular comorbidities, and renal comorbidities were associated with increased mortality ($p < 0.001$, $p < 0.001$, $p < 0.001$, respectively).

Procedures Associated With Mortality

Invasive ventilation occurred in 763 of 2,893 (26.4%) of admissions and was associated with a mortality rate of 19.1% (Table 3). Median length of intubation for survivors was 1.62 days (IQR, 0.54–5.00 d) and for nonsurvivors 3.46 days (IQR, 1.09–8.57 d). Relative to patients not requiring any form of positive pressure ventilation, those treated with noninvasive ventilation and those treated with invasive ventilation both had increased mortality rates ($p < 0.001$, $p < 0.001$, respectively). Tracheostomy tube insertion (2.9% of admissions) and chest tube insertion (8.8% of admissions) were not associated with increased mortality. Bronchoscopy (9.3% of admissions) and renal replacement therapy (2.3% of admissions) were associated with increased mortality ($p < 0.001$, $p < 0.001$, respectively). ECLS was

used in 1.3% of admissions. Nineteen of the 37 admissions (51.3%) during which ECLS was performed ended in death ($p < 0.001$). Figure 2 summarizes the results of univariate analysis as a forest plot of the ORs of mortality.

Multivariable Model

Multivariable modeling identified six factors independently associated with increased mortality (Supplemental Table 2, Supplemental Digital Content 1, <http://links.lww.com/PCC/B317>). Transfer from an intermediate care unit ($p = 0.001$) or from another ICU ($p = 0.021$) were independently associated with increased mortality. BMI less than 18.5 was associated with increased mortality ($p = 0.007$). Hemoptysis/pulmonary hemorrhage ($p = 0.002$), hepatobiliary disease ($p = 0.007$), cardiovascular comorbidities ($p < 0.001$), and renal comorbidities ($p < 0.001$) were all associated with increased mortality. Admission following a surgery or procedure was associated with decreased mortality ($p < 0.001$) in multivariate modeling.

Stratified Analysis of Mechanically Ventilated Patients

Of the 192 admissions ending in death, 184 collected data on invasive and noninvasive ventilation. Thirty-eight nonsurvivors (20.7%) did not undergo intubation or mechanical ventilation during the terminal PICU admission (Supplemental Table 3, Supplemental Digital Content 1, <http://links.lww.com/PCC/B317>). Nonsurvivors who “did” receive mechanical ventilation had higher PRISM-3 scores and greater prevalence of cardiovascular comorbidities and renal comorbidities compared with those who “did not” receive invasive respiratory support ($p < 0.001$, $p < 0.001$, $p = 0.003$, respectively). These patients were also significantly different in terms of their origin prior to PICU admission ($p = 0.020$), with a higher percentage being admitted from other ICUs or the operating room/procedure suite. In contrast, nonsurvivors who never received mechanical ventilation were more likely to be admitted from general or intermediate care units. Other invasive procedures, including chest tube insertion, bronchoscopy, renal replacement, and ECLS, were rarely performed on nonsurvivors who never received mechanical ventilation.

DISCUSSION

In this contemporary multicenter cohort of pediatric CF patients requiring intensive care, we identified an overall PICU mortality rate of 6.6% and a subgroup PICU mortality rate of 19.1% for patients requiring mechanical ventilation. Roughly 20% of nonsurvivors never received mechanical ventilation; these patients presumably had limitations of care (i.e., a do not resuscitate and/or DNI order). Factors associated with PICU mortality included poor nutritional status at admission, specific respiratory complications (hemoptysis/pulmonary hemorrhage, pneumothorax, and chronic airway obstruction), and specific gastrointestinal complications (hepatobiliary disease, gastrointestinal bleeding, and splenomegaly). Young age, particularly the less than 2 years age group, showed a trend toward lower mortality. Consistent with general PICU populations, illness severity at admission, bacterial/fungal infections, renal or cardiovascular comorbidities, and use of invasive procedures were also associated with PICU mortality. These data provide updated epidemiological insight into outcomes for critically ill pediatric CF patients.

Our analysis reveals a significantly lower mortality rate for pediatric CF patients in the PICU compared with previous reports. The majority of prior investigation has reported outcomes relative to specific respiratory interventions. Our results confirm that respiratory support needs, and particularly invasive ventilation, are associated with an increased risk of mortality, although the mortality rate in this subgroup is also improved from historical figures. Since the study by Davis and di Sant'Agnese (2) reporting a 69% mortality rate among intubated CF children, reported mortality rates in this population have ranged from 37.5% to 100% (3, 4, 6–8, 10, 12, 14, 22). The most recent study in adults demonstrated a 44.5% mortality rate in intubated adults with CF (23). Our cohort showed a mortality rate of just 19.1% among those children receiving mechanical ventilation. A number of factors likely contribute to these improved outcomes in children, relative to both historical figures and to the adult CF population. The improvement in critical care outcomes mirrors the progress made in morbidity and survival of the CF population overall, which has come with advances in medications and technologies to support CF patients. Noninvasive respiratory support, available both at home and in the hospital, is likely to have contributed to this improvement. The evolving approach to chronic disease management with more focus being placed on early interventions and an emphasis on factors such as nutritional status also likely contributes to the better outcomes we see in children in this modern age of CF care. Last, advances in critical care interventions, including mechanical ventilation strategies, renal replacement therapy techniques, and ECLS, also likely contribute to the improvement in the overall mortality of the critically ill CF population.

Malnutrition, along with renal comorbidities and cardiovascular comorbidities, were all associated with increased mortality in our cohort. Each of these factors could be considered markers of more severe underlying disease, highlighting the importance of longitudinal disease control in PICU CF care. Multiple indicators of nutritional status, including calculated BMI and diagnostic codes for malnutrition, were significantly associated with mortality in our study. Prior studies have also shown a direct correlation between BMI and outcomes such as mortality and pulmonary function in CF patients (24). For this reason, nutritional guidance and interventional programs have long been a staple of chronic CF management. Our study demonstrates the importance of extending those principles into the ICU. Current literature lacks investigation into the specifics of optimal nutritional support for CF patients in the ICU, and this study was not able to discern enteral and/or parenteral nutrition practices for the cohort. Future studies are needed to investigate how to best maintain and improve nutrition in these patients before and during periods of critical illness.

Of the respiratory diagnoses examined, hemoptysis/pulmonary hemorrhage, pneumothorax, and chronic airway obstruction were associated with increased odds of mortality. Several recent studies have shown increased mortality associated with hemoptysis (5, 14). This finding, along with our finding of increased mortality associated with pneumothoraces, contrasts with earlier literature, which often referred to hemoptysis and pneumothoraces as having more favorable outcomes compared with other etiologies of acute respiratory failure (3, 6, 22, 25). Only hemoptysis/pulmonary hemorrhage maintained a significant association with increased mortality as an independent factor in multivariate analysis. Hemoptysis is a common complication of CF, present in 6.4% of the PICU admissions in our cohort and reported to affect about 8% of the total CF population (23). The severity of hemoptysis can

vary widely and the approach to management is similarly varied, ranging from antibiotics and withholding respiratory clearance therapies to procedural interventions including bronchial artery embolization. Despite these available therapies, mortality remains high for these patients and improvement in the management of this specific complication of CF is needed.

Of the gastrointestinal diagnoses, hepatobiliary diseases (including cirrhosis, noncirrhotic liver failure, hepatic necrosis, cholecystitis/cholangitis, and other liver disorders), gastrointestinal bleeding, and splenomegaly were found to have higher odds of mortality. Only hepatobiliary disease maintained significance as a factor independently associated with mortality in multivariable analysis. CF patients with severe gastrointestinal disease represent a unique subset of the CF population. There are known differences in the rates of gastrointestinal complications between the different CF mutation classes (1). Mutation data, however, was not available for review in our data set. Future studies that include patient mutation classes and their associations with complications and outcomes are needed to further characterize these distinct subgroups of the PICU CF population.

Younger age has been shown to be associated with increased survival in intubated CF patients in previous studies (10, 12–14). Our data showed a trend toward significantly lower mortality in the less than 2 years old cohort, regardless of respiratory support needs. This is not unexpected given the natural history of CF, with the expectation of declining respiratory function and increasing comorbidities over time.

A number of factors were notably not associated with mortality in our study group. Sex and racial/ethnic background were two of these factors, despite known differences in CF genotypes, rates of complications, and mortality between these groups (26). It may be that once critically ill, the differences between demographic groups lose significance, however, our study was not designed to address this question specifically. We also did not see a significant association between mortality and diagnoses pertaining to lung transplant. One-hundred forty-seven patients accounted for the 349 encounters with lung transplant diagnoses coded. This higher readmission rate may reflect a lower threshold to admit posttransplant patients to the ICU given their overall high risk, even if the acute presentation is less severe or their preadmission lung function is not as compromised. This could contribute to a lower mortality rate in the transplanted group. These patients are also being compared in our study to other CF patients in the PICU who did not receive a lung transplant. These nontransplanted patients are still critically ill, and may in fact be worse off than their transplanted counterparts if they are not being considered candidates for transplant. Further studies focused specifically on the postlung transplant population are warranted to better characterize their indications for and outcomes of PICU admission.

Additionally of note in our data are the proportion of nonsurvivors that were intubated—79.3%. This seems to imply that 20.7% of the nonsurvivors were DNI status. The decision of whether or not to intubate a patient with CF is complicated and has been debated for years (27, 28). Factors affecting the decision to be DNI are individualized and likely depend on numerous considerations for a CF patient including baseline lung function, change in lung function over time, lung transplant candidacy, hypothesized reversibility of an acute

exacerbation, accrual of nonrespiratory comorbidities, family/social factors, and the efficacy and projected outcomes of available critical care interventions. Our findings support the general consensus that outcomes for intubated CF patients are improving, although there is still a significant risk of mortality. As CF and critical care practices continue to advance, patient and provider perspectives on limitations of care in the CF population must also continue to evolve.

There are a number of limitations to our study. The VPS data lack some of the clinical details included in many studies on CF, including mutation data and pulmonary function testing results. The database additionally does not include data on deaths that occur outside of the PICU, which may mask mortality especially for those patients with limitations of care. In analyzing outcomes by diagnosis, we must consider that CF patients often have numerous diagnosis codes that reflect chronic conditions as opposed to active problems contributing to an acute decompensation (e.g., *Pseudomonas aeruginosa* pneumonia may be coded to represent chronic pseudomonal colonization). There were additionally several diagnoses with relatively small sample sizes (i.e., chronic obstructive airway disease, splenomegaly), presumably due to inconsistent use of these diagnosis codes as well as overlap with other codes. Last, the study team did not have access to data on exact dates of admissions. With such an extended timeframe studied, we expect there to have been changes in outcomes over time as CF care advanced.

CONCLUSIONS

In conclusion, we have analyzed the largest cohort of pediatric patients with CF requiring intensive care studied to date. The PICU mortality rate is much improved compared with previous reports, in both the entire population and in the subset requiring mechanical ventilation. Specific respiratory complications (hemoptysis/pulmonary hemorrhage, pneumothorax, chronic airway obstruction), gastrointestinal complications (hepatobiliary disease, gastrointestinal bleeding, splenomegaly), bacterial and fungal infections, and renal or cardiovascular comorbidities were associated with increased mortality. Nutritional status additionally played a significant role in outcomes. There is a significant proportion of the critically ill CF population with apparent limitations of care, specifically DNI orders. As practices continue to advance, it will be important to continue to update our epidemiological understanding of the critically ill CF population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Flow chart depicting inclusion/exclusion in analysis and outcomes of the PICU admissions included from the Virtual Pediatric Systems data set. CF = cystic fibrosis.

Figure 2.

Forest plot depicting odds ratios (ORs) from unadjusted analysis. **Red:** significantly increased OR. **Green:** significantly decreased OR. **Gray:** reference group or OR incalculable. BMI = body mass index, ECLS = extracorporeal life support, PACU = post-anesthesia care unit, POD = probability of death, PRISM-3 = Pediatric Risk of Mortality-3.

TABLE 1.

Patient Demographics and Outcomes

Demographic/Clinical Characteristic	Survivors, <i>n</i> (%)	Nonsurvivors, <i>n</i> (%)	OR (95% CI)	<i>p</i>
Age ^a , yr				
< 2	355 (13.1)	16 (8.3)	0.59 (0.34–1.02)	0.057
2–5	199 (7.4)	11 (5.7)	0.72 (0.38–1.38)	0.327
6–12	570 (21.1)	37 (19.3)	0.85 (0.57–1.27)	0.430
13–18	1,047 (38.8)	80 (41.7)	Reference	
> 18	530 (19.6)	48 (25.0)	1.19 (0.82–1.72)	0.371
Sex				
Female	709 (49.2)	110 (57.3)	Reference	
Male	732 (50.8)	82 (42.7)	0.80 (0.60–1.08)	0.140
Race/ethnicity ^{b,c}				
White	965 (67.0)	128 (66.7)	Reference	
Hispanic/Latino	134 (9.3)	18 (9.4)	1.06 (0.65–1.73)	0.820
Black/African American	58 (4.0)	11 (5.7)	1.14 (0.61–2.14)	0.670
Asian/Indian/Pacific Islander	9 (0.6)	2 (1.0)	1.16 (0.28–4.76)	0.840
American Indian/Alaska Native	6 (0.4)	0 (0)	NA ^d	NA ^d
Other/mixed	36 (2.5)	4 (2.1)	1.16 (0.43–3.13)	0.770
Readmission ^e				
No	1,488 (55.1)	93 (48.4)	Reference	
Yes	1,213 (44.9)	99 (51.6)	1.31 (0.97–1.76)	0.077
Patient origin ^a				
General care unit	936 (34.7)	71 (37.0)	Reference	
Emergency department	860 (31.8)	58 (30.2)	0.89 (0.62–1.28)	0.529
Intermediate care unit	101 (3.7)	27 (14.1)	3.52 (2.20–5.65)	< 0.001
Operating room/procedure suite/ post-anesthesia care unit	575 (21.3)	12 (6.3)	0.28 (0.15–0.51)	< 0.001
Other ICU	87 (3.2)	19 (9.9)	2.88 (1.67–4.96)	< 0.001
Other	142 (5.3)	5 (2.6)	0.46 (0.18–1.18)	0.106
BMI ^e			0.88 (0.81–0.95)	0.001

Demographic/Clinical Characteristic	Survivors, <i>n</i> (%)	Nonsurvivors, <i>n</i> (%)	OR (95% CI)	<i>p</i>
BMI categorized				
< 18.5	546 (20.2)	50 (26.0)	1.95 (1.07–3.53)	0.028
18.5–24.9	340 (12.6)	16 (8.3)	Reference	
25.0–29.9	33 (1.2)	0 (0.0)	NA ^d	NA ^d
> 29.9	10 (0.4)	0 (0.0)	NA ^d	NA ^d
PRISM-3 score ^f			1.17 (1.14–1.20)	< 0.001
PRISM-3 score				
< 3	1,318 (50.4)	25 (13.6)	Reference	
3–5	601 (23.0)	38 (20.7)	3.33 (1.99–5.57)	< 0.001
6–10	446 (171)	43 (23.4)	5.08 (3.07–8.42)	< 0.001
> 10	248 (9.5)	78 (42.4)	16.58 (10.32–26.63)	< 0.001
PRISM-3 probability of death ^f			1.07 (1.04–1.09)	< 0.001

BMI = body mass index, NA = not available, OR = odds ratio, PRISM-3 = Pediatric Risk of Mortality-3.

^aReference group chosen based on highest absolute number of patients per group.

^bReference group chosen based on highest absolute number of patients per group.

^cHispanic race and Latino ethnicity are not separated in Virtual Pediatric Systems database.

^dIncalculable due to insufficient numbers.

^eFifty-two admissions were coded as readmissions without data from a prior admission included in the studied data set; this is presumably due to the prior admission occurring prior to January 1, 2009.

^fOR represents change in odds for every 1 point increase in independent variable.

Boldface values indicates significant with *p* < 0.05.

OR and 95% CIs represent ratio of odds of mortality between groups.

TABLE 2.

Outcomes by Diagnosis Group

Diagnosis	Survivors, n (%)	Nonsurvivors, n (%)	OR (95% CI)	p
Any respiratory diagnosis	2,230 (82.6)	179 (93.2)	2.91 (1.64–5.16)	< 0.001
Hemoptysis/pulmonary hemorrhage	159 (5.9)	25 (13.0)	2.39 (1.52–3.76)	< 0.001
Pneumothorax	174 (6.4)	25 (13.0)	2.17 (1.40–3.38)	< 0.001
Bronchiectasis	287 (10.6)	27 (14.1)	1.38 (0.88–2.15)	0.160
Pleural effusion	128 (4.7)	14 (7.3)	1.58 (0.91–2.74)	0.100
Asthma	281 (10.4)	16 (8.3)	0.78 (0.46–1.32)	0.360
Chronic airway obstruction	25 (0.9)	7 (3.6)	4.05 (1.76–9.31)	0.001
Tracheostomy/chronic vent dependence	82 (3.0)	7 (3.6)	1.21 (0.52–2.84)	0.660
Lung transplant	322 (11.9)	27 (14.1)	1.21 (0.79–1.85)	0.380
Any gastrointestinal diagnosis	1,633 (60.5)	133 (69.3)	1.47 (1.07–2.03)	0.017
Pancreatic disease	762 (28.2)	64 (33.3)	1.27 (0.93–1.75)	0.140
Gastroesophageal reflux disease	457 (16.9)	36 (18.8)	1.13 (0.78–1.64)	0.510
Intestinal malabsorption/obstruction/ileus	376 (13.9)	22 (11.5)	0.80 (0.50–1.27)	0.340
Hepatobiliary disease	275 (10.2)	42 (21.9)	2.47 (1.71–3.58)	< 0.001
Portal hypertension	106 (3.9)	13 (6.8)	1.78 (0.98–3.23)	0.059
Gastrointestinal bleeding	59 (2.2)	13 (6.8)	3.25 (1.81–5.83)	< 0.001
Splenomegaly	41 (1.5)	7 (3.6)	2.45 (1.01–5.98)	0.048
Gastrostomy/enterostomy	481 (17.8)	39 (20.3)	1.18 (0.80–1.73)	0.410
Liver transplant	92 (3.4)	5 (2.6)	0.76 (0.30–1.91)	0.560
Any infection	1,600 (59.2)	150 (78.1)	2.46 (1.73–3.48)	< 0.001
Bacterial infection	948 (35.1)	98 (51.0)	1.93 (1.44–2.58)	< 0.001
Viral infection	324 (12.0)	28 (14.6)	1.25 (0.82–1.92)	0.300
Fungal infection	298 (11.0)	34 (17.7)	1.74 (1.16–2.59)	0.007
Malnutrition	534 (19.8)	57 (29.7)	1.71 (1.25–2.36)	< 0.001
Diabetes	758 (28.1)	63 (32.8)	1.25 (0.92–1.71)	0.160
Psychiatric comorbidities	421 (15.6)	38 (19.8)	1.34 (0.91–1.96)	0.140
Cardiovascular comorbidities	511 (18.9)	91 (47.4)	3.86 (2.80–5.33)	< 0.001
Renal comorbidities	293 (10.8)	56 (29.2)	3.38 (2.32–4.94)	< 0.001

OR = odds ratio.

OR and 95% CIs represent ratio of odds of mortality between groups. Boldface values indicates significant with $p < 0.05$.

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TABLE 3.

Procedures and Outcomes

Procedure/Intervention ^a	Survivors, <i>n</i> (%)	Nonsurvivors, <i>n</i> (%)	OR (95% CI)	<i>p</i>
Respiratory support ^a				
Noninvasive support only	575 (21.3)	34 (17.7)	15.94 (5.68–44.70)	<0.001
Invasive ventilation	617 (22.8)	146 (76.0)	63.77 (23.66–172.00)	<0.001
Other ^b	1,078 (39.9)	4 (2.1)	Reference	
Tracheostomy tube insertion ^c				
Yes ^d	75 (2.8)	9 (4.7)	1.69 (0.79–3.63)	0.180
No	1,664 (61.6)	118 (61.5)		
Chest tube insertion ^e				
Yes	231 (8.6)	24 (12.5)	1.35 (0.85–2.14)	0.210
No	1,282 (47.5)	99 (51.6)		
Bronchoscopy ^f				
Yes	236 (8.7)	32 (16.7)	2.09 (1.37–3.19)	<0.001
No	1,498 (55.5)	97 (50.5)		
Renal replacement therapy ^g				
Yes	42 (1.6)	25 (13.0)	9.82 (5.61–17.17)	<0.001
No	1,847 (68.4)	112 (58.3)		
Extracorporeal life support				
Yes	18 (0.7)	19 (9.9)	16.37 (8.44–31.74)	<0.001
No	2,683 (99.3)	173 (90.1)		

OR = odds ratio.

^aRespiratory support data collected in 1,691 admissions, excluding admissions during which mechanical ventilation occurred.^bNo bilevel positive airway pressure, continuous positive airway pressure, or invasive mechanical ventilation used.^cTracheostomy tube insertion data collected in 1,866 admissions.^dIncludes tracheostomy tube changes.^eChest tube insertion data collected in 1,636 admissions.

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^f Bronchoscopy data collected in 1,863 admissions.

^g Renal replacement therapy data collected in 2,026 admissions.

Boldface values indicates significant with $p < 0.05$.

OR and 95% CIs represent ratio of odds of mortality between groups.