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EPIDEMIOLOGY OF CAUSE OF DEATH IN PEDIATRIC ACUTE RESPIRATORY DISTRESS SYNDROME

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Abstract

Objective—Investigations of acute respiratory distress syndrome (ARDS) in adults suggest hypoxemia is an uncommon cause of death. However, the epidemiology of death in pediatric ARDS (PARDS) is not well characterized. We aimed to describe the cause, mode, and timing of death in PARDS non-survivors. We hypothesized that most deaths would be due to non-pulmonary factors, rather than hypoxemia.

Design—Retrospective, decedent-only analysis.

Setting—Two large, academic pediatric intensive care units.

Patients—Non-survivors with PARDS.

Interventions—None.

Measurements and Main Results—Of 798 subjects with PARDS, there were 153 non-survivors (19% mortality). Median time to death was 6 [IQR 3, 13] days after PARDS onset. Patients dying < 7 days after PARDS onset had greater illness severity and worse oxygenation. Patients dying < 7 days were more likely to die of a neurologic cause, including brain death. Patients dying ≥ 7 days after PARDS onset were more commonly immunocompromised. Multisystem organ failure (MSOF) predominated in deaths ≥ 7 days. Withdrawal of therapy was

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the most common mode of death at all timepoints, accounting for 66% of all deaths. Organ dysfunction was common at time of death, irrespective of cause of death. Refractory hypoxemia accounted for only a minority of PARDS deaths (20%).

Conclusions—In PARDS, early deaths were due primarily to neurologic failure, while later deaths were more commonly due to MSOF. Deaths from neurologic causes accounted for a substantial portion of non-survivors. Refractory hypoxemia accounted for only a minority of deaths. Our study highlights limitations associated with using death as an endpoint in therapeutic PARDS trials.

Keywords

children; ARDS; PARDS; mortality; multisystem organ failure; MSOF

INTRODUCTION

Adult acute respiratory distress syndrome (ARDS) short-term mortality remains high, up to 40% in recent observational studies (1, 2). In pediatric ARDS (PARDS), mortality rates are half of adult rates (3–6). Studies examining the epidemiology of cause of death in adults demonstrate that refractory hypoxemia is uncommon (7, 8), and that the majority of non-survivors die from multisystem organ failure (MSOF) or due to poor neurologic prognosis. This has relevance because interventions that target hypoxemia, such as inhaled nitric oxide (9), exogenous surfactant (10), and fluid-conservative therapy (11), have not improved mortality.

Few studies have investigated the cause of death in PARDS, and none with modern definitions and management (6). The degree to which mortality may be primarily attributable to PARDS, exacerbated by PARDS, or associated with the inciting insult or co-morbidities is unknown. Despite this uncertainty, all-cause mortality remains a common endpoint, either alone or as part of a composite (11–14). Understanding the epidemiology of death in modern PARDS is crucial for trial design, especially as it relates to subject eligibility and choice of endpoints.

We aimed to describe the cause, mode, and timing of death in a large, modern cohort of PARDS non-survivors. We hypothesized that the majority of deaths in PARDS would not be due to the underlying pulmonary injury, but rather due to non-pulmonary factors. A secondary aim was to describe the prevalence of specific organ dysfunctions at the time of death.

METHODS

Population

We performed a retrospective observational study on all pediatric intensive care unit (PICU) non-survivors with PARDS at the Children's Hospital of Philadelphia (CHOP) and the Children's Hospital of Los Angeles (CHLA). The study was approved by the respective Institutional Review Boards, and requirement for informed consent waived. The CHOP cohort is a prospectively enrolling study of invasively ventilated children meeting American-

European Consensus Conference acute lung injury criteria (two consecutive $\text{PaO}_2/\text{FIO}_2$ 300 separated by ≥ 1 hour with bilateral infiltrates) between July 1, 2011, and June 30, 2017. As the study was initiated prior to the Berlin definition (15), minimum PEEP was not specified; however, CHOP PICU does not utilize $\text{PEEP} < 5 \text{ cmH}_2\text{O}$. Thus, all patients met Berlin criteria. Similarly, as the study was initiated prior to the Pediatric Acute Lung Injury Consensus Conference (PALICC) definition of PARDS (16), we did not screen using oxygenation index (OI); however, all patients met PARDS criteria. The CHLA cohort was obtained by retrospective screen of the electronic health record and a local database for invasively ventilated children with qualifying PaO_2 or $\text{SPO}_2 \geq 97\%$ within the first week of ventilation between March 1, 2009, and April 30, 2013. For patients meeting the hypoxemia screening, chart review was performed to determine whether subjects met PALICC PARDS criteria by either OI (≥ 4) or oxygen saturation index ($\text{OSI} \geq 5$).

Data Collection

Medical records were independently reviewed by two investigators at each site. A data dictionary was developed prior to chart abstraction (Supplementary Table 1). Cause of death was assigned to one of three exclusive categories: 1) persistent hypoxemia, 2) MSOF, or 3) neurologic dysfunction. Mode of death was also assigned one of three exclusive categories: 1) withdrawal or withholding of life-sustaining therapies, 2) unsuccessful cardiopulmonary resuscitation (CPR), or 3) brain death, as has been described previously in PICU non-survivors (17, 18). Organ failures present at time of death were defined using Goldstein criteria for septic children (19). Disagreements in classification of cause of death, mode of death, or presence of organ failures were resolved by consensus discussion among investigators. The primary outcome was time to death counted from days after PARDS onset, stratified into < 7 days (early) and ≥ 7 days (late) after PARDS onset. In a secondary analysis, we explored more granular timepoints, divided into ≤ 3 days, 4 to < 7 days, 7 to 14 days, and > 14 days after PARDS onset.

Equations and Definitions

Oxygenation was measured using OI ($\text{mean airway pressure [mPaw]} \times \text{FIO}_2 \times 100 / \text{PaO}_2$) or OSI ($\text{mPaw} \times \text{FIO}_2 \times 100 / \text{SPO}_2$) ensuring $80\% > \text{SPO}_2 \geq 97\%$. The designation “immunocompromised” required presence of an immunocompromising diagnosis (oncologic, immunologic, rheumatologic, or transplant) and active chemotherapy, or a congenital immunodeficiency (3, 20). Severity of illness score used was the Pediatric Risk of Mortality (PRISM) III at 12 hours.

Statistical Analysis

Analyses were performed using Stata 14.2 SE (StataCorp LLC, College Station, Texas). Data are expressed as medians [interquartile range] or percentages. Non-parametric tests or Fisher exact tests were used to compare continuous and categorical variables, respectively.

RESULTS

Cause and Mode of Death in PARDS

Of 798 subjects with PARDS, there were 153 non-survivors (19% mortality; Table 1). Of the CHLA cohort ($n = 254$), 110 (43%) were diagnosed using OSI, including 26 of 60 (43%) non-survivors. Median time to death was 6 [IQR 3, 13] days after PARDS onset (Figure 1). Patients dying earlier had higher PRISM scores ($p < 0.001$) and greater PARDS severity ($p = 0.037$). Immunocompromised subjects comprised 35% of all non-survivors and constituted 51% of late (> 7 days) deaths.

Patients dying < 7 days after PARDS onset were more likely to die of a neurologic cause of death ($p < 0.001$; Table 1). MSOF predominated as cause of death > 7 days after PARDS onset. Fourteen of 17 (82%) of subjects with aspiration died of neurologic causes. Of these 17 subjects, 1 (6%) had chronic neurologic dysfunction and 14 (82%) had acute neurologic dysfunction coincident with PARDS onset. Withdrawal of therapy was the most common mode of death, accounting for 66% of deaths. Unsuccessful CPR and brain death were more common < 7 days after PARDS onset, while withdrawal of therapy became more common as a mode of death > 7 days ($p < 0.001$). Twenty-three of 59 (39%) subjects with a neurologic cause of death underwent withdrawal; the remaining 36 (61%) were brain dead. Withdrawal also occurred in 87% of those dying of hypoxemia, and 80% of those dying of MSOF.

Organ dysfunction at time of death was common in all non-survivors (Table 1; Figure 2). Neurologic and cardiovascular failure were more common in patients dying < 7 days after PARDS onset. Respiratory and hepatic failure were more common in patients dying > 7 days.

Detailed Analysis of Time to Death

We examined the association of variables with time to death stratified into smaller epochs (Supplementary Table 2). As with the primary analysis, subjects dying earlier had higher PRISM scores and were less likely to be immunocompromised (both $p < 0.001$). There were differences between PARDS etiology and time to death ($p = 0.023$). Non-pulmonary sepsis was the most common etiology for subjects who died < 3 days after PARDS onset, while pneumonia was the most common for subjects who died between 4 and < 7 days.

Subjects dying < 3 days after PARDS onset died mostly of MSOF or neurologic causes ($p < 0.001$). Neurologic causes predominated between 4 and < 7 days. MSOF was the most common cause for subjects dying between 7 and 14 days, while hypoxemia and MSOF were most common for subjects dying after 14 days. Withdrawal of therapy was the most common mode of death, with the prevalence of unsuccessful CPR markedly diminished after 3 days. Neurologic failure was less common in later deaths, particularly > 14 days ($p < 0.001$).

Comparison between Institutions

When comparing the two institutions (Supplementary Table 3), they were similar with respect to demographics, severity of illness, and severity of PARDS. CHOP had more

immunocompromised subjects ($p = 0.003$), more pneumonia ($p < 0.001$), and more inhaled nitric oxide use ($p < 0.001$), whereas CHLA had more indirect PARDS ($p = 0.002$). CHOP had more acute neurologic failure, whereas CHLA had more chronic (Supplementary Table 4; both $p < 0.001$). Cause of death differed between institutions ($p = 0.050$), with more neurologic deaths at CHOP, and more MSOF deaths at CHLA.

Excluding Brain Death

If excluding subjects with brain death ($n = 36$, 24% of all deaths), mortality for the PARDS cohort reduced to 15%, and time to death increased to 8 [3, 17] days after PARDS onset (Table 2). Similar to the larger cohort, patients dying < 7 days had higher PRISM scores. Immunocompromised subjects now comprised 44% of all non-survivors and were more prevalent in later deaths ($p = 0.009$). MSOF was the most prominent cause of both early and late deaths. However, neurologic deaths were more common < 7 days after PARDS onset, while hypoxemia became more common > 7 days. Withdrawal of therapy predominated as mode of death, with a lower prevalence of unsuccessful CPR in later deaths. Organ dysfunction at time of death remained common.

Excluding Death Due to Neurologic Causes

Acute neurologic failure coincident with PARDS diagnosis was associated with mortality ($p < 0.001$; Supplementary table 4). Of the 63 non-survivors with acute neurologic failure, 52 (82%) ultimately died of a neurologic cause, and 60 (95%) had neurologic dysfunction present at time of death. If excluding patients with any neurologic cause of death ($n = 59$, 39% of all deaths), mortality for the PARDS cohort reduced further to 12%, and time to death increased to 10 [2, 19] days after PARDS onset (Table 3). As before, patients dying < 7 days had higher PRISM scores. Immunocompromised subjects now constituted 49% of non-survivors and were more prevalent among later deaths. MSOF was the most common cause of death, and withdrawal of therapy was the most common mode of death, with decreasing proportion of unsuccessful CPR among later deaths. Organ dysfunction at time of death remained common.

Excluding Subjects on Extracorporeal Support

Because extracorporeal membrane oxygenation (ECMO) can affect the attribution of death due to hypoxemia, we examined subjects placed on ECMO in more detail. Of the 153 non-survivors, seven received ECMO. Of these subjects, two died of hypoxemia, three of MSOF, and two of neurologic failure. All ECMO subjects died > 7 days after PARDS onset. Results were unchanged when analyzing the cohort excluding these seven subjects (Supplementary Table 5).

DISCUSSION

We describe the epidemiology of the cause of death in children with PARDS, capitalizing on a combined dataset of 798 subjects with PARDS from two academic centers using current management. Children who died < 7 days after PARDS onset predominantly died from neurologic causes, including brain death. Later deaths were more commonly due to MSOF. Deaths from neurologic causes accounted for 39% of all non-survivors. Organ dysfunction

was common at time of death, irrespective of cause of death. Refractory hypoxemia accounted for only 20% of PARDS deaths and was more common in those who died 7 days after PARDS onset. Given the retrospective nature of the study, as well as the subjective aspects of assigning cause of death, we interpret these findings with caution.

Our finding that hypoxemia is an uncommon cause of death is consistent with prior studies. In a study of 470 children with acute hypoxemic respiratory failure (203 deaths, 43%) in 1991, hypoxemia as cause of death was attributed to 41 (20%) subjects (6). Fifty-one subjects (25%) had withdrawal of care, lower than this present study. However, children with poor neurologic prognosis were excluded from this cohort, thus precluding a direct comparison with our study. Furthermore, specific organ failures contributing to MSOF were not described, and etiologies of respiratory failure relied on administrative coding, with less granularity than in the current study. Dahlem et al described 12 PARDS non-survivors (21), seven of whom died from neurologic injury, while respiratory failure accounted for two deaths. In a PARDS cohort of 146 patients (38 deaths), MSOF was the cause of death in 40%, while respiratory failure was the cause in 26% (22). Adult studies have reported similar findings (7, 8, 23, 24), with MSOF accounting for the majority of deaths (over 40%), and respiratory failure accounting for a minority (less than 25%).

Neurologic failure was the cause of death in 39% of cases, including 36 subjects with brain death. Neurologic dysfunction was present in nearly half of non-survivors, somewhat higher than reported for adults. Stapleton et al reported that neurologic dysfunction was the cause of death in 29% of adult ARDS mortalities (7). Interventional PARDS trials commonly exclude subjects with limitations of care orders, or exceedingly poor neurologic prognosis (13, 14, 25). This, along with other commonly applied exclusion criteria in clinical trials, likely contributes to why mortality rates extrapolated from observational studies systematically overestimate the observed mortality rates in trials.

The predominance of neurologic and MSOF as causes of death in our study reinforce that PARDS management should be considered in the context of a broader systemic illness. Given the time-course in which these deaths occurred in our cohort, it is unlikely that trials focused on PARDS-specific therapies would have any impact on subjects dying 3 days of PARDS onset. MSOF has been linked to the damaging effects of mechanical ventilation in adults (12, 26). However, this link is more tenuous in PARDS, with no demonstration of an association between either tidal volume (27) or ventilator pressures (28) with mortality in observational studies. Together, these findings highlight the uncertainty of whether interventions predominantly targeting the injured lung will have major impacts on mortality in PARDS.

Reporting mortality as the primary endpoint, or as a component of a composite (such as VFD), is problematic for interventions primarily postulated to improve lung injury. Mortality in PARDS appears to be primarily related to non-pulmonary organ failures, including neurologic, rather than refractory or persistent hypoxemia. Eligibility criteria for trials excluding subjects with poor neurologic prognosis, refractory shock, or significant co-morbidities may mitigate some of these concerns, albeit at the cost of reduced mortality rates and reduced generalizability. Methods exist to deal with studying functional outcomes when

some subjects will have unmeasurable outcomes because of death, such as restricting analyses to survivors only, or computing a survivor average causal effect (SACE)(29). In the case of PARDS, the primary outcome of interest could be duration of ventilation. However, survivor-only analyses and SACE require assumptions that may not be plausible (no effect of intervention on mortality) or may be untestable (identification of subjects who would survive irrespective of treatment arm). Clearly, selection of an appropriate outcome for PARDS trials is problematic, potentially requiring further development of statistical methodologies.

Our study has limitations. The retrospective and subjective nature of assigning cause of death could introduce misclassification bias. Additionally, the two-center nature may limit generalizability, although PARDS etiologies and severity were comparable to others (22, 30–32). CHOP and CHLA had differences in case mix, with more immunocompromised subjects and acute neurologic failure at CHOP, and more indirect PARDS at CHLA. This likely contributed to more neurologic deaths at CHOP, and more MSOF at CHLA. These differences may affect the generalizability of our study; however, the combined cohort is potentially more representative of the actual heterogeneity of PARDS. In both institutions hypoxemia was the least common cause of death. The use of ECMO may alter the cause, mode and timing of death, although exclusion of these subjects did not alter results. Finally, as we could not interview providers or families in real-time, the reasons underlying actual withholding or withdrawal of care remain unknown. Thus, whether decisions to limit care were based on specific organ failures, such as neurologic, or because of the severity of an underlying co-morbidity, such as malignancy, remain speculative.

However, our study has several strengths. This was the first study to describe the epidemiology of death in PARDS using modern ventilator management and PARDS definitions. We also provided a detailed description of failing organs at the time of death. Lastly, we used two independent investigators at each site and a common data dictionary to minimize misclassification and ensure consistency.

CONCLUSION

In PARDS, early deaths are due primarily to neurologic failure, while later deaths are more likely to be due to refractory hypoxemia or MSOF. Deaths from neurologic causes accounted for a substantial portion of non-survivors. Organ dysfunction is common at time of death, irrespective of cause of death. Hypoxemia accounted for only a minority of deaths. Our study highlights limitations associated with using death as an endpoint in PARDS trials. Therefore, death should be reconsidered as a primary outcome, especially for interventions targeting lung injury. Most subjects appear to die with, but not necessarily from, PARDS.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1. Frequency histogram of days from PARDS onset to death. The inset shows time to death restricted to the first 30 days.

Figure 2.
Frequency histogram of number of organ failures at time of death.

Table 1

Demographics of the non-survivors

Variable	All	Days between PARDS onset and death		p value
		< 7 days	7 days	
n	153	83	70	
Age (years)	7.2 [2.2, 14.5]	7 [1.6, 14.7]	7.3 [2.8, 13.5]	0.796
Female (%)	66 (43)	37 (45)	29 (41)	0.745
PRISM III at 12 hours	20 [11, 30]	27 [16, 33]	14 [8, 21]	< 0.001
Immunocompromised (%)	53 (35)	17 (20)	36 (51)	< 0.001
Cause of PARDS (%)				
Pneumonia	47 (31)	21 (25)	26 (37)	0.335
Aspiration	17 (11)	13 (16)	4 (6)	
Drowning	7 (5)	4 (5)	3 (4)	
Trauma	9 (6)	4 (5)	5 (7)	
Non-pulmonary sepsis	49 (32)	27 (33)	22 (31)	
Other	24 (16)	14 (17)	10 (14)	
Cause of PARDS (%)				
Direct	71 (46)	38 (46)	33 (47)	0.872
Indirect	82 (54)	45 (54)	37 (53)	
PARDS severity at onset (PALICC)				
Mild	47 (31)	25 (30)	22 (31)	0.037
Moderate	31 (20)	11 (13)	20 (29)	
Severe	75 (49)	47 (57)	28 (40)	
Ancillary therapies				
Inhaled nitric oxide	66 (43)	34 (41)	32 (46)	0.624
High frequency oscillation	36 (24)	20 (24)	16 (23)	> 0.999
Extracorporeal support	7 (5)	0	7 (10)	0.004
Cause of death (%)				
Persistent hypoxemia	31 (20)	11 (13)	20 (29)	< 0.001
MSOF	63 (41)	28 (34)	35 (50)	
Neurologic	59 (39)	44 (53)	15 (21)	
Mode of death (%)				
Withdrawal/withholding therapy	101 (66)	43 (52)	58 (83)	< 0.001
Unsuccessful CPR	16 (10)	12 (14)	4 (6)	
Brain death	36 (24)	28 (34)	8 (11)	
Organ dysfunctions at death (%)				
Neurologic	75 (49)	52 (63)	23 (33)	< 0.001
Cardiovascular	123 (80)	73 (88)	50 (71)	0.014
Respiratory	134 (88)	68 (82)	66 (94)	0.026
Renal	78 (51)	38 (46)	40 (57)	0.195
Hepatic	61 (40)	26 (31)	35 (50)	0.021
Hematologic	63 (41)	33 (40)	30 (43)	0.743

^aP values represent results of a Wilcoxon rank sum or Fisher exact test.

CPR: cardiopulmonary resuscitation; MSOF: multisystem organ failure; PALICC: Pediatric Acute Lung Injury Consensus Conference; PARDS: Pediatric Acute Respiratory Distress Syndrome; PRISM III: Pediatric Risk of Mortality III

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Table 2

Demographics of the non-survivors when excluding brain death

Variable	All	Days between PARDS onset and death		<i>p</i> value ^a
		< 7 days	7 days	
n	117	55	62	
Age (years)	7.2 [2.6, 14.7]	7 [1.6, 14.7]	7.3 [2.8, 15]	0.868
Female (%)	46 (39)	21 (38)	25 (40)	0.851
PRISM III at 12 hours	17 [11, 25]	21 [13, 32]	13 [8, 20]	< 0.001
Immunocompromised (%)	52 (44)	17 (31)	35 (56)	0.009
Cause of PARDS (%)				
Pneumonia	42 (36)	16 (29)	26 (42)	0.357
Aspiration	7 (6)	5 (9)	2 (3)	
Drowning	3 (3)	2 (4)	1 (2)	
Trauma	5 (4)	1 (2)	4 (6)	
Non-pulmonary sepsis	43 (37)	23 (42)	20 (32)	
Other	17 (14)	8 (15)	9 (15)	
Cause of PARDS (%)				
Direct	52 (44)	23 (42)	29 (47)	0.710
Indirect	65 (56)	32 (58)	33 (53)	
PARDS severity at onset (PALICC)				
Mild	32 (27)	14 (25)	18 (29)	0.072
Moderate	29 (25)	9 (16)	20 (32)	
Severe	56 (48)	32 (58)	24 (39)	
Ancillary therapies				
Inhaled nitric oxide	56 (48)	28 (51)	28 (45)	0.581
High frequency oscillation	32 (27)	17 (31)	15 (24)	0.534
Extracorporeal support	6 (5)	0	6 (10)	0.029
Cause of death (%)				
Persistent hypoxemia	31 (26)	11 (20)	20 (32)	0.039
MSOF	63 (54)	28 (51)	35 (56)	
Neurologic	23 (20)	16 (29)	7 (11)	
Mode of death (%)				
Withdrawal/withholding therapy	101 (86)	43 (78)	58 (94)	0.029
Unsuccessful CPR	16 (14)	12 (22)	4 (6)	
Brain death	-	-	-	
Organ dysfunctions at death (%)				
Neurologic	39 (33)	24 (44)	15 (24)	0.032
Cardiovascular	92 (79)	48 (87)	44 (71)	0.042
Respiratory	105 (90)	46 (84)	59 (95)	0.064
Renal	68 (58)	30 (55)	38 (61)	0.574
Hepatic	54 (46)	21 (38)	33 (53)	0.137
Hematologic	53 (45)	25 (45)	28 (45)	> 0.999

^aP values represent results of a Wilcoxon rank sum or Fisher exact test.

CPR: cardiopulmonary resuscitation; MSOF: multisystem organ failure; PALICC: Pediatric Acute Lung Injury Consensus Conference; PARDS: Pediatric Acute Respiratory Distress Syndrome; PRISM III: Pediatric Risk of Mortality III

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Table 3

Demographics of the non-survivors when excluding neurologic causes of death

Variable	All	Days between PARDS onset and death		<i>p</i> value ^d
		< 7 days	7 days	
n	94	39	55	
Age (years)	7.2 [1.9, 15]	6.3 [1.6, 14.7]	7.7 [2.2, 15.2]	0.534
Female (%)	39 (41)	15 (38)	24 (44)	0.674
PRISM III at 12 hours	14 [8, 24]	21 [12, 32]	11[7, 19]	0.003
Immunocompromised (%)	46 (49)	13 (33)	33 (60)	0.013
Cause of PARDS (%)				
Pneumonia	35 (37)	11 (28)	24 (44)	
Aspiration	3 (3)	2 (5)	1 (2)	
Drowning	2 (2)	2 (5)	0	0.174
Trauma	4 (4)	1 (3)	3 (5)	
Non-pulmonary sepsis	37 (39)	19 (49)	18 (33)	
Other	13 (14)	4 (10)	9 (16)	
Cause of PARDS (%)				
Direct	40 (43)	15 (38)	25 (45)	0.532
Indirect	54 (57)	24 (62)	30 (55)	
PARDS severity at onset (PALICC)				
Mild	24 (25.5)	8 (21)	16 (29)	0.076
Moderate	25 (26.5)	7 (18)	18 (33)	
Severe	45 (48)	24 (62)	21 (38)	
Ancillary therapies				
Inhaled nitric oxide	45 (48)	21 (54)	24 (44)	0.403
High frequency oscillation	26 (28)	12 (31)	14 (25)	0.643
Extracorporeal support	5 (5)	0	5 (9)	0.074
Cause of death (%)				
Persistent hypoxemia	31 (33)	11 (28)	20 (36)	
MSOF	63 (67)	28 (72)	35 (64)	0.506
Neurologic	-	-	-	
Mode of death (%)				
Withdrawal/withholding therapy	78 (83)	27 (69)	51 (93)	
Unsuccessful CPR	16 (17)	12 (31)	4 (7)	0.004
Brain death	-	-	-	
Organ dysfunctions at death (%)				
Neurologic	16 (17)	8 (21)	8 (15)	0.571
Cardiovascular	79 (84)	38 (97)	41 (75)	0.003
Respiratory	91 (97)	37 (95)	54 (98)	0.568
Renal	59 (63)	22 (56)	37 (67)	0.387
Hepatic	46 (49)	14 (36)	32 (58)	0.038
Hematologic	48 (51)	20 (51)	28 (51)	> 0.999

^aP values represent results of a Wilcoxon rank sum or Fisher exact test.

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