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Risk factors for mortality in children with moderate-to-severe ARDS with concurrent hematological or immune-related diseases: a retrospective analysis

Qingyue Wang[1,2], Hongxing Dang[1*], Yueqiang Fu[1], Chengjun Liu[1], Jing Li[1] and Feng Xu[1]

Abstract

Background As a heterogeneous syndrome, acute respiratory distress syndrome (ARDS) patients with comorbidities are significantly more severely ill. We aim to investigate the clinical characteristics and analyze the risk factors for mortality in children with moderate-to-severe acute respiratory distress syndrome (ARDS) who also have concurrent hematological or immune-related diseases.

Methods A retrospective observational study was conducted from September 2020 to May 2022 in the pediatric intensive care unit (PICU) at Children's Hospital of Chongqing Medical University (Chongqing, China). All children with moderate-to-severe ARDS were included and divided into two groups based on the presence or absence of hematological or immune-related diseases. Clinical characteristics, treatment, and outcome data were collected. Univariate logistic regression and multivariate Firth regression analysis were used to identify risk factors for mortality in children with moderate-to-severe ARDS with concurrent hematological or immune-related diseases.

Results A total of 215 children with moderate-to-severe ARDS were included in the study, of whom 65 had hematological or immune-related diseases (30.2%). These children were older ($p < 0.001$), had higher Pediatric Index of Mortality 3 scores ($p = 0.002$), higher lactate levels ($p = 0.042$), higher rates of positive pathogen detection ($p < 0.001$), shorter PICU stay ($p = 0.023$), higher incidence of multiple organ dysfunction syndrome ($p = 0.012$), and higher 28-day mortality rates ($p < 0.001$). Firth regression analysis showed that invasive fungal infection (OR = 4.954, 95% CI 0.245–3.158, $p < 0.05$), use of vasoactive drugs (OR = 7.638, 95% CI 0.524–3.811, $p < 0.05$), and high-frequency oscillatory ventilation (OR = 6.551, 95% CI 0.134–3.908, $p < 0.05$) were associated with increased mortality rates in children with moderate-to-severe ARDS with concurrent hematological or immune-related diseases.

Conclusion The incidence of moderate-to-severe ARDS is higher in children with concurrent hematological or immune-related diseases, and their prognosis is worse. In this group, children with invasive fungal infections, greater use of vasoactive drugs, or high-frequency oscillatory ventilation had a higher 28-day mortality rate.

Keywords Acute respiratory distress syndrome, Children, Mortality, Hematological or Immune-related diseases

*Correspondence:
Hongxing Dang
danghx@cqmu.edu.cn
[1]Pediatric Intensive Care Unit of Children's Hospital of Chongqing Medical University, National Clinical Research Center for Child Health and Disorders, Ministry of Education Key Laboratory of Child Development and Disorders, Chongqing, China
[2]Department of Pediatrics, West China Second University Hospital, Chengdu, China

Background

Acute respiratory distress syndrome (ARDS) is a heterogeneous syndrome characterized primarily by inflammatory injury to the alveolar epithelial cells and pulmonary capillary endothelial cells [1]. As one of the major critical illnesses in the pediatric intensive care unit (PICU), the mortality rate of children with ARDS remains high both domestically and internationally [2, 3, 4]. The nature and severity of underlying diseases have a substantial impact on the management and prognosis of ARDS, and children with comorbidities are significantly more severely ill [5, 6, 7, 8, 9, 10].

While the features and mortality risk factors of ARDS have been extensively studied in the general population, there is a lack of research on children with hematological or immune disorders who develop ARDS. Our objective is to investigate the clinical characteristics of moderate-to-severe ARDS in children with concurrent hematological or immune disorders, analyze the risk factors for mortality in this group, and explore potential strategies to improve outcomes.

Materials and methods

Study subjects

This study followed the consensus of the 2015 Pediatric Acute Lung Injury Consensus Conference (PALICC) [11] and included all children with ARDS admitted to the PICU of the Children's Hospital of Chongqing Medical University(Chongqing, China) between September 2020 and May 2022. The exclusion criteria are as follows: (1) age ≤ 28 days; (2) without invasive mechanical ventilation; (3) mild ARDS; (4) incomplete medical records; (5) lost to follow-up within 28 days after diagnosis. All children with moderate-to-severe ARDS were divided into the concomitant hematologic or immunologic-diseases group and the non-concomitant hematologic or immunologic-diseases group, based on the presence or absence of concomitant hematologic or immunologic diseases. Hematologic diseases mainly included hematopoietic stem cell diseases, erythrocyte diseases, granulocyte diseases, lymphatic or tissue diseases, and hemorrhagic diseases. Immunologic diseases mainly included organ-specific and systemic autoimmune diseases. None of the included patients received extracorporeal membrane oxygenation.

Data collection

Medical information about the patients, including sex, age, weight, and information about treatment measures (such as mechanical ventilation, corticosteroids, muscle relaxants, surfactants, pulmonary vasodilators, transfusions, and prone positioning), as well as blood and sputum pathogen results and blood gas analysis results on the first day after ARDS diagnosis, were collected through the medical record system. The Pediatric Logistic Organ Dysfunction 2 (PELOD 2), Pediatric Index of Mortality 3 (PIM3), and Z-scores of weight-for-age (WAZ) were calculated. All study subjects were followed up until 28 days after diagnosis. The primary outcome was 28-day mortality, and the secondary outcomes were mechanical ventilation time, PICU survival time, and Hospital stays.

Data analysis

Data were analyzed using IBM SPSS 26.0. Normally distributed data were described as mean ± standard deviation, tested by the *t*-test. Non-normally distributed data were described as the median with the 25–75% interquartile range, and the Mann-Whitney U-test was used for between-group comparisons. Categorical variables were compared by chi-squared test or Fisher exact test with counts and percentages. Univariate analysis using binary logistic regression and multivariate analysis using Firth regression were performed to identify risk factors for mortality. A p-value < 0.05 was considered statistically significant for all the tests.

Results

Population demographics and baseline information of patients with hematologic or immune-related diseases and those without

A total of 215 children with moderate-to-severe ARDS who met the inclusion criteria were collected in this study, and the case selection process is shown in Fig. 1. The patients were divided into the hematologic or immune-related diseases group and the non-concomitant hematologic or immune-related diseases group according to the presence or absence of hematologic or immune-related diseases, (Table 1). Nearly half of the children with moderate-to-severe ARDS who had hematologic or immune-related diseases had severe ARDS, and they were older with higher corresponding weight, weight-for-age Z-score, PIM3 score, lactate levels, and pathogen positivity rates (including blood and sputum) than those in the non-complicated group. Additionally, the incidence of MODS and 28-day mortality rate were significantly higher, while the PICU survival time was shorter in the group with hematologic or immune-related diseases.

Population demographics and baseline information of surviving and deceased children with moderate-to-severe ARDS and hematologic or immune-related diseases

We further analyzed the 65 children with moderate-to-severe ARDS and hematologic or immune-related diseases and divided them into surviving and deceased groups based on the prognosis 28 days after ARDS diagnosis, comparing their baseline data (Table 2). Primary immunodeficiency disease (18 [27.7%]) and acute

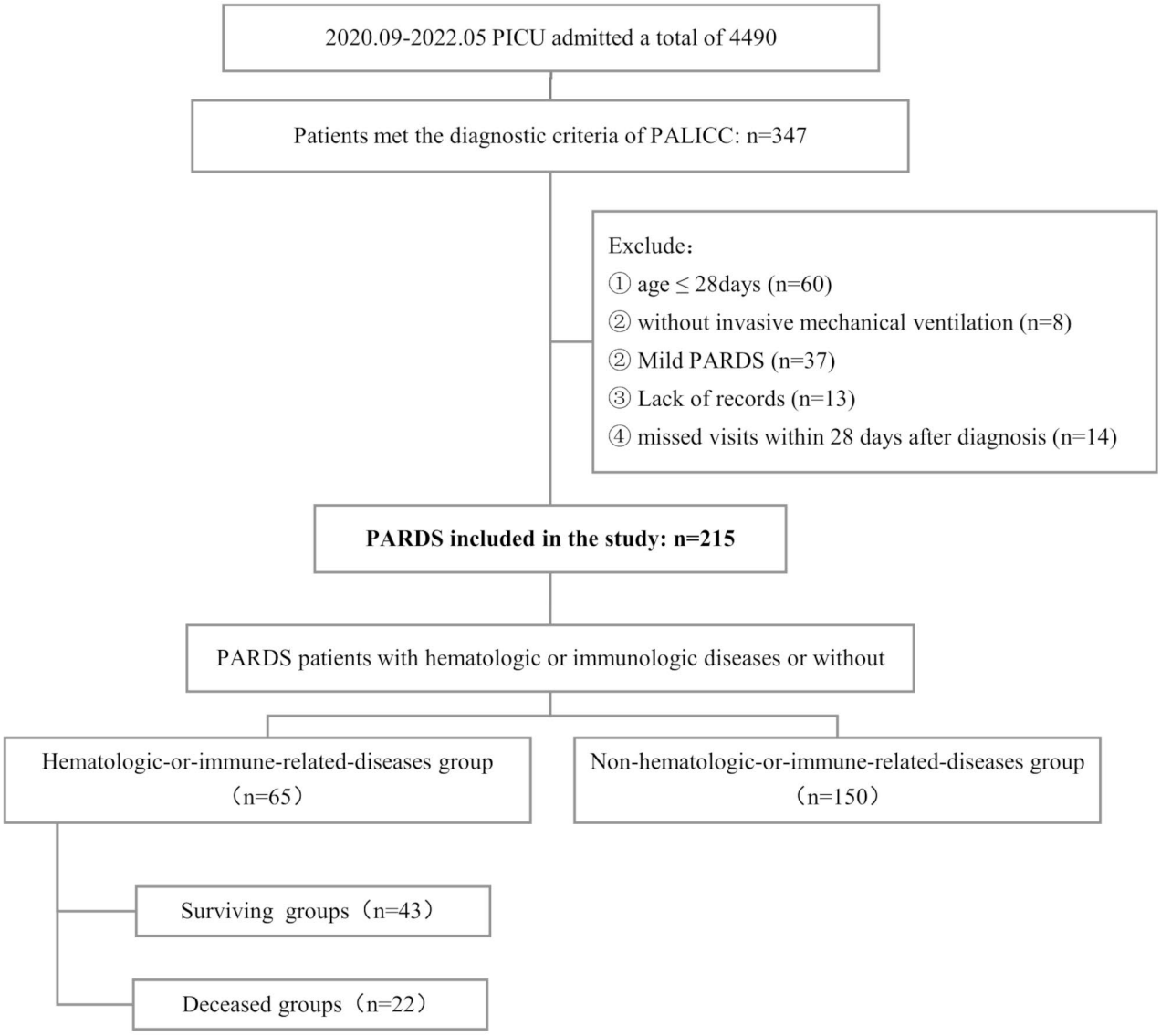

Fig. 1 Flow chart of screening
PICU: Pediatric Intensive Care Unit; PALICC, Pediatric Acute Lung Injury Consensus Conference; PARDS: Pediatric Acute Respiratory Distress Syndrome

leukemia (18 [26.2%]) were the most common underlying diseases, with other primary diseases including eight cases of lymphoma, six cases of Mediterranean anemia, four cases of systemic lupus erythematosus, four cases of juvenile idiopathic arthritis, and two cases of aplastic anemia. Neutrophil reduction was present in 36.9% of the children, and five cases had a history of Hematopoietic Stem Cell Transplantation (HSCT) prior to diagnosis. There were statistically significant differences between the two groups in terms of whether the age was under 6 years, PELOD2 score, Oxygenation Index (OI), whether septic shock or invasive fungal infection occurred, and the type of primary disease, but there was no significant difference in PIM3 score, HSCT, and blood gas lactate level between the two groups.

Comparison of treatment and outcome information between surviving and deceased children with moderate-to-severe ARDS and hematologic or immune-related diseases

High-frequency oscillation ventilation (HFOV), transfusion, and vasoactive drugs were used more frequently in the deceased group, and the incidence of multiple organ dysfunction syndrome (MODS) was higher in the deceased group (Table 3).

Risk factor analysis for mortality in children with moderate-to-severe ARDS and hematologic or immune-related diseases

Univariate analysis using binary logistic regression and multivariate analysis using Firth regression were

Table 1 Population demographics and baseline information of patients with hematologic or immune-related diseases and those without

	Patients with hematologic or immune-related diseases (*n* = 65)	Patients without hematologic or immune-related diseases(*n* = 150)	x^2	*p*
Male/Female, *n*	34/31	91/59	1.302	0.254
Age, median and quartile, m	39.0(10.0,97.5)	13.0(5.8,36.3)	-3.608	<0.001
Weight, median and quartile, kg	14.0(9.0,24.0)	9.0(6.0,14.3)	-4.058	<0.001
WAZ, median and quartile	-0.37(-1.395,0.34)	-1.38(-2.78,-0.13)	-2.845	0.004
PIM3, median and quartile	20.9(7.1,89.3)	8.3(3.0,52.8)	-3.118	0.002
PELOD2, median and quartile	7(4,12)	6(2,11)	-1.290	0.197
OI, median and quartile	15.67(9.44,24.31)	12.28(9.12,21.17)	1.324	0.186
Severe PARDS, *n*(%)	32(49.2)	60(40.0)	1.578	0.209
Examination				
Lactate, mmol/L	0.8(0.6,1.9)	1.0(0.7,1.7)	-2.038	0.042
PaO2, mmHg	60.4(50.5,80.4)	64.0(52.5,81.6)	-0.226	0.821
PaCO2, mmHg	44.5(35.2,58.9)	43.0(36.0,53.0)	-0.652	0.514
Glu, mmol/L	6.0(5.0,7.6)	5.6(4.1,7.4)	-1.859	0.063
Positive Blood Pathogen, *n*(%)	21(32.3)	16(10.7)	14.907	<0.001
Positive Sputum Pathogen, *n*(%)	45(75.4)	56(37.3)	26.278	<0.001
MODS, *n*(%)	23(35.4)	29(19.3)	6.372	0.012
Outcomes				
Intubation time, median and quartile, d	8(3,16)	10(6,16)	-1.216	0.224
PICU survival time, median and quartile, d	9(5,18)	14(7,22)	-2.268	0.023
Hospital stays, median and quartile, d	19(10,28)	23(12,34)	-1.424	0.154
28-day mortality, *n*(%)	43(66.2)	55(36.7)	15.896	<0.001

WAZ, weight-for-age Z-score; PARDS: Pediatric Acute Respiratory Distress Syndrome; PIM3, Pediatric Index of Mortality 3 score; PELOD2, Pediatric Logistic Organ Dysfunction 2 score; OI, oxygenation index; PaO2, partial pressure of oxygen of arterial blood; PaCO2, partial pressure of carbon dioxide of arterial blood; MODS, multiple organ dysfunction syndrome

performed to identify risk factors for mortality (Tables 4 and 5). The univariate analyses suggested that the following factors(P<0.05): Age<6 years old, PELOD2, Septic Shock, IFIs, HFOV, Blood Transfusion, and Vasopressor differed significantly in the survival and non-survival groups. And we included these factors in multivariate analysis. The results showed that invasive fungal infection, HFOV, and the use of vasoactive drugs were associated with an increased mortality rate in children with moderate-to-severe ARDS and hematologic or immune-related diseases (Table 5).

Discussion

ARDS is the most severe form of acute hypoxic respiratory failure, which can be caused by various factors, with a wide variation in the course and prognosis of the disease in different pediatric patients [12, 13, 14]. Studies have shown that most children with ARDS have comorbidities and the different comorbidities are closely related to the prognosis of the disease [5, 15, 16]. In this study, the mortality rate of children with moderate-to-severe ARDS who had comorbid hematologic or immune diseases was as high as 66.2%, significantly higher than that of other pediatric ARDS populations [3, 17], so we emphasize the importance of timely diagnosis and appropriate treatment for these conditions.

The results of this study suggest that children with moderate-to-severe ARDS who have comorbid hematologic or immune-related diseases are more common than other patients. These children tend to be older and have correspondingly higher weight and weight-for-age Z scores, which may be associated with a slightly later onset of their primary disease [18, 19] and a longer medical history. Since high lactate levels are consistent with the progression of ARDS [20], children with moderate-to-severe ARDS who have comorbid hematologic or immune-related diseases have significantly higher lactate levels than other children, but the increase in lactate levels in this study did not significantly affect the mortality rate of these children, possibly due to the fact that only lactate values from the first day after diagnosis were collected. The PIM3 score of children with moderate-to-severe ARDS who had comorbid hematologic or immune-related diseases was significantly higher in this study, which may be related to the characteristics of the PIM3 scoring system itself, with either severe combined immunodeficiency or hematologic system diseases after initial induction therapy being extremely high-risk factors in the PIM3 scoring system [21]. Additionally, high pathogen positivity rate is also a prominent feature of children with moderate-to-severe ARDS who have comorbid hematologic or immune-related diseases, with a 75.4%

Table 2 Population demographics and baseline information of surviving and deceased children with moderate-to-severe ARDS and hematologic or immune-related diseases

	Surviving group (*n* = 22)	Deceased group (*n* = 43)	x^2/Z	*p*
Male/Female, *n*	12/10	22/21	0.067	0.796
Age, median and quartile, m	75(18,100)	30(6,88)	-1.180	0.238
Age<6 years old	10(45.5)	31(72.1)	4.434	0.035
Weight, median and quartile, kg	17.0(10.4,29.3)	12.0(8.0,20.0)	-1.318	0.188
WAZ, median and quartile	-0.52(-1.40,0.725)	-0.43(-0.20,0.18)	-0.053	0.958
PIM3, median and quartile	13.5(5.6,86.7)	23.1(7.8,90.2)	-1.192	0.233
PELOD2, median and quartile	5(2,9)	8(5,12)	-2.237	0.025
OI, median and quartile	9.98(8.58,21.41)	16.80(11.00,26.33)	-2.218	0.027
Sever PARDS, *n*(%)	8(36.4)	24(55.8)	2.203	0.138
Septic Shock, *n*(%)	3(13.6)	20(46.)	6.880	0.009
Neutropenia, *n*%	5(22.7)	19(44.2)	2.878	0.090
Invasive Fungal Infections, *n*(%)	5(22.7)	22(53.5)	5.616	0.018
HSCT, *n*(%)	1(4.5)	4(9.3)	/	0.496
Primary Diseases				
PID	6(27.3)	12(27.9)	0.003	0.957
Leukemia	4(18.2)	13(30.2)	1.094	0.296
Lymphoma	1(4.5)	7(16.3)	/	0.248
SLE	4(18.2)	0(0)	/	0.011
MA	0(0)	6(14.0)	/	0.088
AA	0(0)	2(4.7)	/	0.545
JIA	3(13.6)	1(2.3)	/	0.109
Other*	4(18.2)	2(4.7)	/	0.168
Examination				
WBC ($\times 10^9$/L)	8.43(6.18,16.63)	8.45(1.09,22.47)	-0.094	0.925
PCT ($\times 10^9$/L)	0.77(0.38,2.94)	2.22(0.54,4.86)	-1.365	0.172
Creatine, μmol/L	26.0(19.4,67.0)	33.0(20.5,40.0)	-0.247	0.805
Lactate, mmol/L	1.0(0.6,1.9)	0.7(0.5,1.8)	-0.584	0.559
PaO2, mmHg	62.3(52.3,84.0)	60.0(50.0,75.6)	-0.603	0.546
PaCO2, mmHg	38.5(32.8,51.4)	48.0(37.7,60.0)	-1.754	0.079
Glucose, mmol/L	6.8(5.1,7.6)	5.94.8,7.7)	-0.488	0.626
Positive Blood Pathogen, *n*(%)	8(36.4)	13(30.2)	0.250	0.617
Positive Sputum Pathogen, *n*(%)	18(881.)	31(72.7)	0.742	0.389

WAZ, weight-for-age z-score; PIM3, Pediatric Index of Mortality 3 score; PELOD2, Pediatric Logistic Organ Dysfunction 2 score; HSCT, Hematopoietic Stem Cell Transplantation; OI, oxygenation Index; PID, primary immunodeficiency diseases; SLE, systemic lupus erythematosus; MA, Mediterranean anemia; AA, aplastic anemia; JIA, juvenile idiopathic arthritis; PaO2, partial pressure of oxygen of arterial blood; PaCO2: partial pressure of carbon dioxide of arterial blood;

*Other: 1myelodysplastic syndromes,1 idiopathic thrombocytopenic purpura,1 acquired immune deficiency syndrome, 1 Behcet' syndrome, 1 hemophagocytic lymphohistiocytosis, 1 Autoimmune hemolytic anemia

positivity rate for respiratory pathogens in these children in this study, and a relatively high number of opportunistic pathogens such as *Pseudomonas aeruginosa*, cytomegalovirus, and Epstein-Barr virus, as well as drug-resistant bacteria, which may be closely related to their significant immune suppression.

Further analysis of the 65 cases of moderate-to-severe ARDS with concurrent hematologic or immune-related diseases revealed that the occurrence of invasive fungal infections (IFIs) may lead to increased mortality. IFIs are most commonly secondary to acquired immune deficiency states [22], and in this study, cases of acquired immune deficiency diseases resulting from HSCT or immunomodulatory therapy were prevalent. At this point, the patients may already be in a state of immunosuppression, and IFIs may further worsen their condition, which is also a known major adverse prognostic factor for critically ill pediatric patients with hematologic diseases [23]. Additionally, pediatric patients with primary immunodeficiency are also susceptible to IFIs. Due to the occurrence of immunosuppression during the course of many immune deficiency diseases and the treatment of hematologic diseases, prevention, early diagnosis, and appropriate management of IFIs may have significant implications for improving the prognosis of these patients. We also found that the use of high-dose chemotherapy drugs and immunodeficiency disorders can lead to low levels of granulocytes in patients, so these children are often treated with more advanced, broad-spectrum antimicrobial drugs, resulting in an increased

Table 3 Treatment and outcome between surviving and deceased children with moderate-to-severe ARDS and hematologic or immune-related diseases

	Surviving group (*n* = 22)	Deceased group (*n* = 43)	x^2/Z	*p*
MV>7 days	12(54.5)	22(51.2)	0.067	0.796
HFOV, *n*(%)	4(18.2)	20(46.5)	5.015	0.025
Pulmonary Vasodilators, *n*(%)	1(4.5)	3(7.0)	/	1.000
Neuromuscular Blocking Agents, *n*(%)	20(90.9)	37(86.0)	/	0.706
Prone Ventilation, *n*(%)	3(13.6)	8(18.6)	/	0.737
Systemic Steroid, *n*(%)	9(40.9)	9(20.9)	2.901	0.089
β-Receptor Agonist, *n*(%)	9(40.9)	18(41.9)	0.005	0.941
Diuretic, *n*(%)	17(77.4)	38(88.4)	1.377	0.241
Blood Transfusion, *n*(%)	9(40.9)	30(69.8)	5.050	0.025
Intravenous Immunoglobulin, *n*(%)	3(14.3)	14(32.6)	2.698	0.100
CRRT, *n* (%)	1(4.5)	7(16.3)	/	0.248
Vasopressor, *n*(%)	12(54.5)	39(90.7)	11.256	0.001
Parenteral Nutrition, *n*(%)	3(13.6)	5(11.6)	/	1.000
Outcomes				
Intubation time, median and quartile, d	9(3,16)	8(3,16)	0.292	0.770
Days of PICU, median and quartile, d	13(7,21)	8(4,16)	-1.375	0.169
Hospital stays, median and quartile, d	20(8,30)	19(10,28)	-0.305	0.760
MODS, *n*(%)	4(18.2)	19(44.2)	4.304	0.038

MV, mechanical ventilation; HFOV, high frequency oscillation; CRRT, continuous renal replacement therapy; PICU, Pediatric Intensive Care Units; MODS, multiple organ dysfunction syndrome

incidence of antibiotic-resistant and multiple infections. In clinical practice, treatment measures such as granulocyte colony-stimulating factor, which are often used to shorten the duration of low levels of granulocytes in these patients, may increase the risk of developing ARDS during the recovery phase of granulocyte levels [24], ultimately leading to a worse prognosis.

The use of HFOV is positively correlated with increased mortality in children with moderate-to-severe ARDS combined with hematological or immune-related diseases, in line with some previous studies [17, 25, 26]. Mechanical ventilation is the mainstay of treatment for ARDS, and as an alternative mode of ventilation, HFOV can prevent lung volume injury and atelectasis and improve short-term oxygenation. However, the negative impact of HFOV on airway barrier function is unavoidable, and it can also cause hemodynamic damage and worsen cardiac function [27]. In addition, due to the difficulty of controlling the underlying disease and other complications in these patients, it is challenging to fundamentally improve the prognosis even if short-term oxygenation can be maintained. Since HFOV is typically used as a rescue ventilation strategy when conventional ventilation fails to maintain oxygenation, it more strongly reflects the severity of the illness. We also found that the use of vasoactive drugs was positively correlated with increased mortality in these children, with a higher dosage or greater need for vasoactive drugs indicating a higher risk of circulatory failure. In addition to invasive mechanical ventilation, some invasive hemodynamic monitoring may also affect the circulation of these patients, and severe infections may cause hemodynamic instability, which may affect the outcome.

In addition to the above factors, the mechanism of ARDS in children with hematological malignancies is unique [28, 29], and tumor cells may cause severe damage to lung tissue, leading to a high incidence of severe lung infection and weak recovery after infection. Since HSCT is a powerful curative method for hematological malignancies, the unique inflammatory disorder that occurs after transplantation can lead to worse outcomes [30]. Previous studies have indicated that HSCT itself is a high-risk factor for mortality in patients with hematological malignancies [31]. Although relatively few patients with post-transplantation hematological disease were included in our study, only one out of the five patients with HSCT survived.

The number of cases in this study was relatively small, and mechanical ventilation parameters and other indicators that may also affect the prognosis of these patients were not further explored. More large-scale, prospective, multicenter clinical studies are needed in the future to continue to study this population.

Conclusion

In summary, a higher 28-day mortality rate is observed in children with moderate-to-severe ARDS and hematological or immune-related diseases who have more invasive fungal infections, more severe lung injury, and greater circulatory impairment. These patients tend to have a shorter survival time and a poorer prognosis. Clinical staff should pay attention to the early identification and

Table 4 Univariate logistic regression models for mortality in children with moderate-to-severe ARDS and hematologic or immune-related diseases

	p	OR	95CI
Sex (Male)	0.796	1.145	0.409–3.210
Age<6 years old	0.039	3.100	1.062–9.052
Weight	0.258	0.978	0.940–1.017
PIM3	0.310	2.072	0.507–8.468
PELOD2	0.035	1.136	1.009–1.279
OI	0.146	1.043	0.985–1.104
Sever PARDS	0.141	2.211	0.768–6.360
PID	0.957	1.032	0.327–3.263
Leukemia	0.300	1.950	0.551–6.901
Lymphoma	0.202	4.083	0.469–35.524
Septic Shock	0.045	3.562	1.032–12.303
Neutropenia	0.096	2.692	0.840–8.627
Invasive Fungal Infections	0.022	3.910	1.222–12.514
Hematopoietic Stem Cell Transplantation	0.505	2.154	0.226–20.529
WBC	0.288	1.016	0.987–1.046
PCT	0.191	1.161	0.928–1.454
Creatine	0.681	0.998	0.988–1.008
Lactate, mmol/L	0.691	1.102	0.684–1.774
PaO2, mmHg	0.845	0.998	0.976–1.020
PaCO2, mmHg	0.482	1.010	0.982–1.039
Glu, mmol/L	0.315	0.940	0.833–1.060
Positive Blood Pathogen	0.617	0.758	0.256–2.245
Positive Sputum Pathogen	0.392	0.574	0.161–2.048
MV>7	0.796	0.873	0.312–2.446
HFOV	0.031	3.913	1.135–13.496
Length of HFOV	0.417	1.100	0.874–1.383
Pulmonary Vasodilators	0.702	1.575	0.154–16.091
Neuromuscular Blocking Agents	0.575	0.617	0.114–3.343
Prone Ventilation	0.615	1.448	0.343–6.108
Systemic Steroid	0.093	0.382	0.124–1.176
β-Receptor Agonist	0.941	1.040	0.366–2.953
Diuretic	0.248	2.235	0.571–8.754
Blood Transfusion	0.027	3.333	1.143–9.722
Intravenous Immunoglobulin	0.111	3.057	0.773–12.088
CRRT	0.202	4.083	0.469–35.524
Vasopressor	0.002	8.125	2.154–30.654
Parenteral Nutrition	0.816	0.833	0.180–3.863

WAZ, weight-for-age Z-score; PIM3, Pediatric Index of Mortality 3 score; PELOD2, Pediatric Logistic Organ Dysfunction 2 score; OI, oxygenation Index; PaO2, partial pressure of oxygen of arterial blood; PaCO2: partial pressure of carbon dioxide of arterial blood; HFOV, high frequency oscillation ventilation; CRRT, continuous renal replacement therapy

Table 5 Multivariate logistic regression models for mortality in children with moderate-to-severe ARDS and hematologic or immune-related diseases

	P	OR	95CI	Tolerance	VIF
Age<6 years old	0.354	2.173	0.421–11.209	0.641	1.56
PELOD2	0.983	0.998	0.85–1.173	0.706	1.416
Septic Shock	0.222	3.005	0.514–17.553	0.84	1.19
IFIs	0.018	7.008	1.396–35.171	0.848	1.179
HFOV	0.031	10.024	1.239–81.107	0.622	1.607
Blood Transfusion	0.329	2.267	0.439–11.707	0.727	1.375
Vasopressor	0.008	11.779	1.899–73.05	0.851	1.175

PELOD2, Pediatric Logistic Organ Dysfunction 2 score; IFIs, invasive fungal infections; HFOV, high frequency oscillation ventilation; VIF, variance inflation factor

diagnosis of these patients. In the treatment process, caution should be exercised when using HFOV, and attention should be paid to the stability of hemodynamics in these patients and the prevention of IFIs, with the aim of improving their prognosis.

Abbreviations

ARDS	Acute respiratory distress syndrome
PICU	Pediatric Intensive Care Unit
PELOD 2	Pediatric Logistic Organ Dysfunction 2
PIM3	Pediatric Index of Mortality 3
WAZ	Z-scores of weight-for-age
HSCT	Hematopoietic Stem Cell Transplantation
MODS	Multiple organ dysfunction syndrome
MV	Mechanical ventilation
HFOV	High-frequency oscillation
CRRT	Continuous renal replacement therapy
IFIs	Invasive fungal infections
VIF	Variance inflation factor

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QW and HD: conceptualization, writing review, and editing. QW: data curation and investigation. JL: formal analysis, methodology, software, QW: writing-original draft. HD: project administration and supervision. JL, CL, YF, and XF: resources, visualization, and validation. All authors contributed to the article and approved the submitted version.

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Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The study was conducted in accordance with the Declaration of Helsinki. This study obtained ethical approval from the Ethics Committee of the Children's Hospital of Chongqing Medical University [File No.: (2019) Ethics Review (Research) No.(172)]. Informed consent was not applicable because the data were anonymized. Ethics Committee of the Children's Hospital of Chongqing Medical University waived the need for patient informed consent due to retrospective analysis of medical records.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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