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Comparing the clinical characteristics and risk factors of prognosis in pediatric ARDS with and without malignancies: a retrospective cohort study

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Abstract

Background The number of malignancy patients with respiratory failure is rising in pediatric intensive care units (PICU). Our study aims to compare the clinical characteristics and prognostic risk factors of acute respiratory distress syndrome (ARDS) with or without malignancies.

Methods This retrospective study reviewed medical records of 188 ARDS patients admitted to the PICU between January 2018 and December 2022, including 60 with malignancies and 128 without. Clinical data were collected within 48 h post-ARDS diagnosis. *Multivariate logistic regression analysis* and *receiver operating characteristic curve (ROC) analysis* were used to investigate the risk factors for PICU mortality in the malignancy and non-malignancy groups.

Results Compared with pediatric patients without malignancy, the ARDS patients with malignancy presented higher mortality (55.0% vs. 31.3%, $P=0.002$), a higher incidence of community-acquired fungal infection (36.1% vs. 6.3%, $P<0.001$) and multidrug resistance (MDR) bacteria (65.4% vs. 30.5%, $P=0.003$). There were substantial differences in levels of lactate [1.5 (0.8–3.7) vs. 1.0 (0.7-2.0) mmol/L, $P=0.008$], C-reactive protein (CRP) [150.0 (83.0-168.0) vs. 31.0 (10.0-108.0) mg/L, $P=0.02$], procalcitonin (PCT) [10.4 (2.0-27.5) vs. 1.2 (0.3–6.2) mg/L, $P<0.001$], counts of platelet [17.0 (8.0–73.0) vs. 232.0 (152.0-330.0) $\times 10^9$/μL, $P<0.001$], the distribution of CD8 + T [36.9 (26.0-53.6) vs. 21.9 (17.3–29.1) %, $P<0.001$], CD19 + T cells [9.9 (0.9–30.2) vs. 33.6 (22-46.6) %, $P<0.001$], and higher peak vasoactive–inotropic score (VIS) in ARDS with malignancy [73.0 (20–208) vs. 15.0 (5.0–82.0), $P<0.01$]. In multivariable analysis, only VIS independently predicted mortality in ARDS patients with malignancy (*OR*, 1.011; 95% *confidence interval [CI]*: 1.003–1.018; $P=0.005$). Neither pSOFA scores (*OR*, 1.249, *95% CI*: 0.958–1.628, $P=0.101$) nor lactate levels (*OR*, 1.192, *95% CI*: 0.928–1.531, $P=0.170$) showed significant associations.

Conclusion ARDS patients with malignancies exhibited poorer outcomes. VIS is only an independent predictor of mortality in pediatric ARDS patients with malignancies.

Keywords Malignancies, Acute respiratory distress syndrome, Vasoactive inotropic score, Children

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Background

ARDS significantly complicates the clinical management of patients with malignancies. Individuals with malignancy are 1.57-fold more likely to develop ARDS than those without malignancies [1]. Studies have demonstrated that the etiology of ARDS in this population is predominantly linked to infections, with pneumonia being the most common precipitating factor [2]. Approximately 50% of patients with hematological and solid tumors require ICU admission due to acute respiratory failure [3]. In pediatric cases, the severity and outcome of ARDS are significantly impacted by underlying malignancy, patients with leukemia/lymphoma undergoing induction chemotherapy have been shown to develop severe ARDS, with a mortality rate that remains concerning despite advancements in the use of extracorporeal membrane oxygenation (ECMO) [4]. It reported that hospital mortality rate excess 50% in children with hematological malignancies [5], emphasizing the urgent need to investigate the risk factors for the development of ARDS and improve prognosis for this unique group of patients.

Therapeutic interventions for malignancy, including chemotherapy, radiation, and bone marrow transplantation, can render pediatric patients immunocompromised, increasing their susceptibility to infections and ARDS [6]. Furthermore, the malignancies and treatment-related complications can exacerbate lung damage and affect the outcomes of ARDS [7]. While research has delved into the epidemiology, pathophysiology, and therapeutic strategies for ARDS, few studies have compared the differences between ARDS with and without malignancy, particularly regarding malignancy type, treatment strategy, and immune status. It's urgent for research to elucidate these differences and to develop targeted management strategies for high-risk patients.

We conducted a retrospective study in pediatric ARDS patients requiring invasive mechanical ventilation (MV) with and without malignancy, compared their clinical characteristics differences, and explored the risk factors for mortality.

Methods

Study design

This is a retrospective study that included patients diagnosed with ARDS who were admitted to the PICU under the supervision of Shanghai Children's Hospital from January 2018 to December 2022 according to the medical records. This study was approved by the Ethics Committee of Shanghai Children's Hospital (2024R149-E01). Informed consent was waived owing to the retrospective nature of this study.

Patients

The following were the inclusion criteria: (1) patients aged 1 month to 18 years; (2) those who met the diagnostic criteria for ARDS according to the Berlin definition [8]; and (3) those who received MV. The following were the exclusion criteria: (1) patients with cardiogenic pulmonary edema; (2) patients with lung lesions due to the infiltration of malignancy; and (3) patients hospitalized in PICU for less than 24 h. The patients were divided into two groups based on their underlying conditions: the malignancy and non-malignancy groups.

Outcomes

The primary outcome was PICU mortality. The second outcome was to investigate the risk factors associated with survival status including VIS, laboratory indicators and related parameters monitored during MV including positive end-expiratory pressure (PEEP), peak inspiratory pressure (PIP), dynamic lung compliance (Cdyn).

Data collection

Data were extracted from the electronic medical record system for each patient. We collected data, including age, sex, body mass index, source of admission, causes of ARDS, primary existing malignancy, blood transfusion, status of bone marrow transplant/hematopoietic stem cell transplantation, identified pathogens, PaO_2/FiO_2 levels, duration of MV, PEEP, PIP, Cdyn, length of PICU stay, length of hospital stay, PICU survival status, comorbidity of patients, continuous renal replacement therapy (CRRT) and ECMO support, and VIS. Disease severity was assessed using pSOFA. Laboratory indicators included CRP, PCT, indicators of inflammatory factors and cellular immunity. Clinical data (except length of PICU stay, length of hospital stay, intubation on the first day of entering PICU, MV days and PICU survival status) and VIS were measured within 48 h following ARDS diagnosis, and the worst values were selected. We defined agranulocytosis as granulocyte counts less than 500/μL [9]. The maximum value was selected for the VIS and calculated according to the following method: VIS = 1 × dobutamine (μg/kg/min) + 1 × dopamine (μg/kg/min) + 100 × norepinephrine (μg/kg/min) + 100 × epinephrine (μg/kg/min) + 10 × milrinone (μg/kg/min) + 10,000 × vasopressin [10]. Community-acquired infection was defined as a pathogen that led to ARDS acquired out of a hospital or within 48 h of hospitalisation [11]. Hospital-acquired infection was defined as an infection acquired following 48 h of hospitalisation [12].

Statistical analyses

To express nonnormally distributed descriptive statistics data, the interquartile range (*IQR*) was employed; For cases where data were missing, we used the median

value of all available data points for each variable to fill in the gaps. To compare continuous variables, *Mann–Whitney U* tests were performed. To evaluate categorical variables, *Fisher's* exact or chi-square test was used. *Multivariate logistic regression analysis* was used to evaluate the risk factors for PICU mortality in the malignancy and non-malignancy groups. Variables that demonstrated statistically significant differences between survivors and non-survivors in univariate analyses were entered into further *multivariate logistic regression analysis*, conducted separately for malignancy and non-malignancy patients. To appreciate the accuracy of independent predictors of PICU mortality, *the ROC curve* and *Youden index* were generated. Statistical analyses were performed using SPSS 26.0. *P* values < 0.05 were considered statistically significant.

Results

Characteristics of ARDS patients with and without malignancies

A total of 188 children with moderate-to-severe ARDS were included in this study, of whom 60 had malignancies (Table 1). ARDS patients with malignancy were more likely to be older (median: 79.0 vs. 34.0 months) and have higher pSOFA scores (14.0 vs. 9.0 points) than those without malignancy (all *P* values < 0.05). Additionally, children with malignancy had a higher PICU mortality rate (55.0% vs. 31.3%, *P* = 0.002) and shorter length of PICU stay (10.0 vs. 13.0 days, *P* = 0.019) than those without malignancy.

In this study, 166 (88.3%) of the 188 patients with ARDS were culture-positive for one or more pathogen infections in sputum or bronchoalveolar lavage fluid (Table 1). The pathogen spectrum between patients with and without malignancies was different. For patients with community-acquired pneumonia, bacteria were the most

Table 1 Characteristics of moderate-to-severe ARDS patients grouping based on whether suffering malignancy

Characteristic	Total (*n* = 188)	Malignancy (*n* = 60)	Non-malignancy (*n* = 128)	*P*
Age (month)	42.0 (20.0–99.0)	79.0 (36.0-131.5)	34.0 (13.3–72.0)	<0.001
≤1 yrs	33.0 (17.6)	2.0 (3.3)	31.0 (24.2)	<0.001
1–3 yrs	49.0 (26.0)	14.0 (23.3)	35.0 (27.3)	0.559
3–6 yrs	45.0 (24.0)	13.0 (21.7)	32.0 (25)	0.618
6–18 yrs	61.0 (32.4)	31.0 (51.7)	30.0 (23.5)	<0.001
Male, n (%)	102.0 (54.3)	31.0 (51.7)	71.0 (55.5)	0.626
BMI	16.1 (14.4–18.2)	16.2 (14.4–18.4)	16.1 (14.3–18.2)	0.627
pSOFA	11.0 (8.0–14.0)	14.0 (12.0–15.0)	9.0 (8.0–11.0)	<0.001
Patients source, n (%)				
Emergency department	87.0 (46.3)	22.0 (36.7)	65.0 (50.8)	0.070
Transferred	101.0 (53.7)	38.0 (63.3)	63.0 (49.2)	
Cause of ARDS, n (%)				
Origin of pulmonary	152.0 (80.9)	44.0 (73.3)	108.0 (84.4)	0.073
Exogenous pulmonary	36.0 (19.1)	16.0 (26.7)	20.0 (15.6)	
Severe of ARDS, n (%)				
Moderate	87.0 (46.3)	27.0 (45.0)	60.0 (46.9)	0.810
Severe	101.0 (53.7)	33.0 (55.0)	68.0 (53.1)	
PaO_2/FiO_2, mmHg	89.0 (57.0-133.0)	90.0 (60.0-139.0)	86.0 (57.0-130.0)	0.314
PICU mortality, n (%)	73.0 (38.8)	33.0 (55.0)	40 (31.3)	0.002
Length of PICU stay (d)	12.0 (7.0–19.0)	10.0 (6.0–17.0)	13.0 (8.0–20.0)	0.019
Length of hospital stay (d)	23.0 (14.0–31.0)	22.0 (13.0–34.0)	23.0 (15.0–30.0)	0.647
Community-acquired infections, n (%)	131.0 (69.7)	36.0 (60.0)	95.0 (74.2)	
Bacteria	59.0 (45.0)	15.0 (41.7)	44.0 (46.3)	0.633
MDR	19.0 (32.2)	8.0 (53.3)	11.0 (25.0)	0.088
Virus	34.0 (26.0)	5.0 (13.9)	29.0 (30.5)	0.052
Fungal	19.0 (14.5)	13.0 (36.1)	6.0 (6.3)	< 0.001
Multi-infection	19.0 (14.5)	3.0 (8.3)	16.0 (16.9)	0.217
Hospital-acquired infections, n (%)	35.0 (18.6)	17.0 (28.3)	18.0 (14.0)	
Bacteria	26.0 (74.3)	11.0 (64.7)	15.0 (83.3)	0.383
MDR	16.0 (61.5)	9.0 (81.8)	7.0 (46.7)	0.158
Fungal	5.0 (14.3)	4.0 (23.5)	1.0 (5.6)	0.300
Multi-infection	4.0 (11.4)	2.0 (11.8)	2.0 (11.1)	1.000

Median (interquartile range) listed for continuous variables, n (%) for categorical variables

common pathogens overall. However, in patients with malignancies, the second most common pathogens were fungi (36.1%), with *Pneumocystis jirovecii* and *Aspergillus* being frequently detected in sputum or alveolar lavage fluid. In contrast, children without malignancies showed viruses as the second most common pathogens (30.5%), with *adenoviruses*, *respiratory syncytial virus*, and *influenza virus* being predominant. In hospital-acquired infections, a shift in pathogen distribution was observed. Gram-negative bacteria, including *Acinetobacter baumannii (A. baumannii)*, *Pseudomonas aeruginosa (P. aeruginosa)*, and *Klebsiella pneumoniae*, were the most prevalent pathogens in hospital-acquired pneumonia among malignancy patients, with MDR observed in 81.8% of cases (9/11 patients with bacterial infections). Conversely, among patients without malignancies, 13 out of 15 patients were infected with gram-negative bacteria, with a notable prevalence of *A. baumannii* and *P. aeruginosa*. This group exhibited a high mortality rate, with 8 of the 9 infected patients (88.9%) succumbing to their infections. Furthermore, when comparing the overall infection rates between hospital-acquired and community-acquired bacterial infections, patients with malignancies had a significantly higher rate of MDR bacteria. Specifically, 65.4% (17/26) of ARDS patients with malignancies were infected with MDR bacteria, compared to 30.5% (18/59) in patients without malignancies ($P = 0.003$).

Thirty-two (53.3%) patients were diagnosed with agranulocytosis within the first week of PICU stay. According to the different types of malignancy, 47 patients had hematological malignancies, including 25, 16, and 6 patients with acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), and non-Hodgkin's lymphoma, respectively. 13.3% of total patients with malignancy experienced recurrence (the patients relapsed before their admission to the PICU) and 18.2% of those with recurrence were dead (Supplemental Fig. 1).

Use of life-supporting interventions in patients with and without malignancies

Patients with ARDS and malignancy had a higher utilization rate of CRRT and a shorter duration of MV times than those without ($P < 0.05$). Survivors in the malignancy group were linked to lower CRRT use and longer MV durations than those in non-survivors, though not significantly. Survivors without malignancy also showed a non-significant trend towards CRRT use and MV durations. Ventilation parameters were noted between survivors and non-survivors in either group (Table 2).

Characteristic of non-pulmonary organ dysfunction in ARDS patients with and without malignancies

By comparing with ARDS patients with or without malignancies, we observed that although pSOFA scores in the nervous and cardiovascular systems did not differ significantly, they did differ in other non-pulmonary organs. Additionally, we noted that the peak VIS values were elevated in malignant patients as compared to non-malignancy counterparts. Furthermore, pronounced differences were identified between the two groups regarding rate of transfusion of red blood and platelet, levels of haematoglobin, absolute neutrophil count, absolute Platelet counts, lactate, CRP, PCT, as well as the distribution of $CD8^+$ and $CD19^+$ cells.

In patients with malignancy, survivors had lower VIS, pSOFA scores and Lactate levels than non-survivors (all $P < 0.05$). In patients without malignancy, survivors had lower pSOFA scores, serum CRP, Lactate, and IL-6 levels than non-survivors (all $P < 0.05$) (Table 3).

Table 2 The comparison of clinical treatments between malignancy and non-malignancy patients

Characteristic	Malignancy ($n = 60$)				Non-malignancy ($n = 128$)				*P*
	Total	Survivors ($n = 27$)	Non-survivors ($n = 33$)	*P*	Total	Survivors ($n = 88$)	Non-survivors ($n = 40$)	*P*	
Extracorporeal life support, n (%)									
CRRT	36.0 (60.0)	13.0 (48.0)	23.0 (70.0)	0.09	48.0 (38.0)	29.0 (33.0)	19.0 (48.0)	0.115	0.027
ECMO	5.0 (8.0)	2.0 (7.0)	3.0 (9.0)	1	26.0 (20.0)	19.0 (22.0)	7.0 (18.0)	0.594	0.296
Mechanical ventilation									
Intubation on the first day of entering PICU, n (%)	32.0 (53.0)	17.0 (63.0)	15.0 (46.0)	0.176	104.0 (81.0)	71.0 (81.0)	33.0 (83.0)	0.807	0.117
PEEP, cmH_2O	11.0 (9.0–15.0)	10.0 (8.0–14.0)	12.0 (10.0–15.0)	0.409	11.0 (7.0–16.0)	10.0 (6.0–16.0)	12.0 (9.0–16.0)	0.254	0.743
PIP, cmH_2O	28.0 (24.0–31.0)	25.0 (22.0–30.0)	29.0 (26.0–32.0)	0.119	28.0 (24.0–31.0)	28.0 (23.0–30.0)	30.0 (25.0–33.0)	0.09	0.936
Cdyn, ml/ cmH_2O/kg	0.5 (0.4–0.6)	0.5 (0.5–0.6)	0.5 (0.3–0.6)	0.464	0.5 (0.3–0.5)	0.5 (0.4–0.5)	0.5(0.2–0.6)	0.808	0.421
MV days (d)	5.0 (3.0–10.0)	7.0 (4.0–14.0)	5.0 (2.0–9.0)	0.071	8.0 (4.0–13.0)	8.0 (5.0–12.0)	10.0 (2.0–24.0)	0.465	0.007

Abbreviations: VIS, the score of vasoactive drugs; CRRT, continuous renal replacement therapy; ECMO, extracorporeal membrane oxygenation; PEEP, positive end-expiratory pressure; PIP, peak inspiratory pressure; MV, mechanical ventilation. Cdyn, dynamic compliance

Table 3 Characteristics of non-pulmonary organ dysfunction in ARDS patients with or without malignancy

Characteristic	Malignancy ($n=60$)				Non-malignancy ($n=128$)				*P*
	Total	Survivors ($n=27$)	Non-survivors ($n=33$)	*P*	Total	Survivors ($n=88$)	Non-survivors ($n=40$)	*P*	
Total pSOFA score	14.0 (12.0–15.0)	12.0 (10.0–14.0)	15.0 (14.0–16.0)	<0.01	9.0 (8.0–11.0)	8.0 (7.0–10.0)	11.0 (9.0–13.0)	<0.01	<0.01
Nervous system									
pSOFA score > 0	50.0 (83.0)	22.0 (81.0)	28.0 (85.0)	0.728	115.0 (90.0)	77.0 (88.0)	38.0 (95.0)	0.193	0.204
Cardio Vascular system									
pSOFA score > 0	57.0 (95.0)	24.0 (89.0)	33.0 (100.0)	0.085	117.0 (91.0)	79.0 (90.0)	38.0 (95.0)	0.524	0.564
VIS at peak	73.0 (20–208)	35.0 (10.0–80.0)	180.0 (45.0-338.0)	<0.01	15.0 (5.0–82.0)	10.0 (5.0–39.0)	79.0 (10.0-195.0)	<0.01	<0.01
Renal									
pSOFA score > 0	22.0 (37.0)	7.0 (26.0)	15.0 (76.0)	0.118	28.0 (22.0)	16.0 (18.0)	12.0 (30.0)	0.134	0.032
Hematologic									
pSOFA score > 0	54.0 (90.0)	23.0 (85.0)	31.0 (94.0)	0.489	30.0 (23.0)	17.0 (19.3)	13.0 (32.5)	0.103	<0.001
Absolute neutrophil count ($\times 10^3/\mu L$)	0.37 (0.04–1.18)	0.37 (0.04–1.7)	0.3 (0.04–0.93)	0.618	5.34 (2.85–9.2)	4.57 (2.73–8.22)	7.12 (3.25-11.00)	0.068	<0.001
Haematoglobin	70.0 (55.0–82.0)	69.0 (58.0–87.0)	70.0 (55.0–80.0)	0.414	90.0 (76.0-106.0)	92.0 (78.0-108.0)	84.0 (62.0–98.0)	0.057	0.001
Transfusion of Red Blood	52.0 (87.0)	22.0 (81.0)	30.0 (91.0)	0.448	62.0 (48.0)	39.0 (44.0)	23.0 (58.0)	0.167	0.028
Absolute Platelet counts ($\times 10^9/\mu L$)	17.0 (8.0–73.0)	21.0 (10.0-110.0)	16.0 (8.0–43.0)	0.252	232.0 (152.0-330.0)	246.0 (167.0-335.0)	206.0 (103.0-309.0)	0.057	0.001
Transfusion of Platelet	44.0 (73.0)	17.0 (63.0)	27.0 (82.0)	0.100	18.0 (14.0)	10.0 (11.0)	8.0 (20.0)	0.193	<0.001
Liver									
pSOFA score > 0	37.0 (62.0)	16.0 (59.0)	21.0 (64.0)	0.729	24.0 (19.0)	14.0 (16.0)	10.0 (25.0)	0.222	<0.001
Lactate	1.5 (0.8–3.7)	1.2 (0.7-2.0)	2.7 (1.1–6.3)	0.006	1.0 (0.7-2.0)	0.9 (0.7–1.6)	1.6 (0.7–2.9)	0.02	0.008
Infection									
CRP	150.0 (83.0-168.0)	113.0 (78.0-160.0)	160.0 (100.0-170.0)	0.096	31.0 (10.0-108.0)	22.5 (9.3–98.8)	84.0 (10.0-170.0)	0.02	<0.001
PCT	10.4 (2.0-27.5)	3.5 (2.1–15.8)	16.6 (2.4–32.7)	0.193	1.2 (0.3–6.2)	0.9 (0.3–5.1)	2.8 (0.4–11.5)	0.052	<0.001
Cytokines									
IFN-γ	26.9 (9.1–146.0)	17.5 (7.3-182.9)	27.1 (8.0-115.3)	0.927	11.9 (4.9–55)	11.8 (4.6–41.3)	26.5 (5.2–62.3)	0.364	0.198
IL-6	206.3 (21.6-1257.8)	210.4 (17.5-598.1)	202.1 (44.4-7421.5)	0.371	99.6 (33.7-266.9)	96.2 (28.5-203.8)	109.4 (63-704.5)	0.032	0.205
IL-8	325.8 (9.0-1119.0)	84.7 (6.7-507.2)	540.1 (11.4-4449.5)	0.181	43.0 (18-103.8)	36.9 (19.0–96.0)	50.5 (16.1-159.4)	0.889	0.082
TNF-α	4.0 (2.0–10.0)	3.3 (2.4–10.2)	3.8 (1.9–9.5)	0.935	3.6 (2.4–8.2)	3.9 (2.4-8.0)	3.3 (2.4–11)	0.654	0.926
Cellular immunity									
CD4 + T	26.9 (18.5–37.2)	25.9 (19.2–37.9)	27.9 (16.4–37.9)	0.935	26.6 (20.0-35.2)	25.1 (17.2–27.8)	30.3 (21.6–39.5)	0.141	0.870
CD8 + T	36.9 (26.0-53.6)	41.6 (32.9–65.4)	35.9 (21.9–41.3)	0.113	21.9 (17.3–29.1)	21.4 (17.2–27.8)	26.3 (16.9–34.3)	0.202	<0.001
CD19 + T	9.9 (0.9–30.2)	6.1 (0.6–20.3)	18 (3.4–35.2)	0.173	33.6 (22-46.6)	34.6 (25.3–47.1)	27.4 (13.9–41.1)	0.055	<0.001
NK	4.0 (2.0–10.0)	3.7 (1.5–10.3)	4.9 (1.8–9.9)	0.705	5.6 (2.7-9.0)	5.6 (3.2–9.1)	5.0 (1.7–9.3)	0.210	0.210

Abbreviations: CRP, C-reactive protein (mg/L); PCT, procalcitonin (mg/L); Lactate, Lactic acid (mmol/L); IFN-γ, interferon-γ (pg/mL); IL-6, interlukin-6 (pg/mL); IL-8, interlukin-8 (pg/mL); TNF-α, Tumor Necrosis Factor-alpha (pg/mL)

The missing values were imputed with the median of available data points for each variable. The values were taken the worst within 48 h after being diagnosed with ARDS

Survival analysis and risk factor

The *Kaplan–Meier* curve indicated that the cumulative survival rate in the malignancy group was significantly lower than that in the non-malignancy group (Fig. 1). Using the *multivariable logistic regression models*, we explored the risk factors for PICU mortality in both patients with and without malignancies, and noted that the VIS (*OR*, 1.011; 95% *CI*: 1.003–1.018; $P=0.005$) was an independent risk factor for PICU mortality in patients with malignancy (Table 4).

According to the *ROC curve* of VIS in predicting the survival status in patients with malignancy (Fig. 2a), the area under the curve (*AUC*) was 0.800 (95% *CI*: 0.69–0.91, $P<0.05$), and the best cutoff value of the VIS was

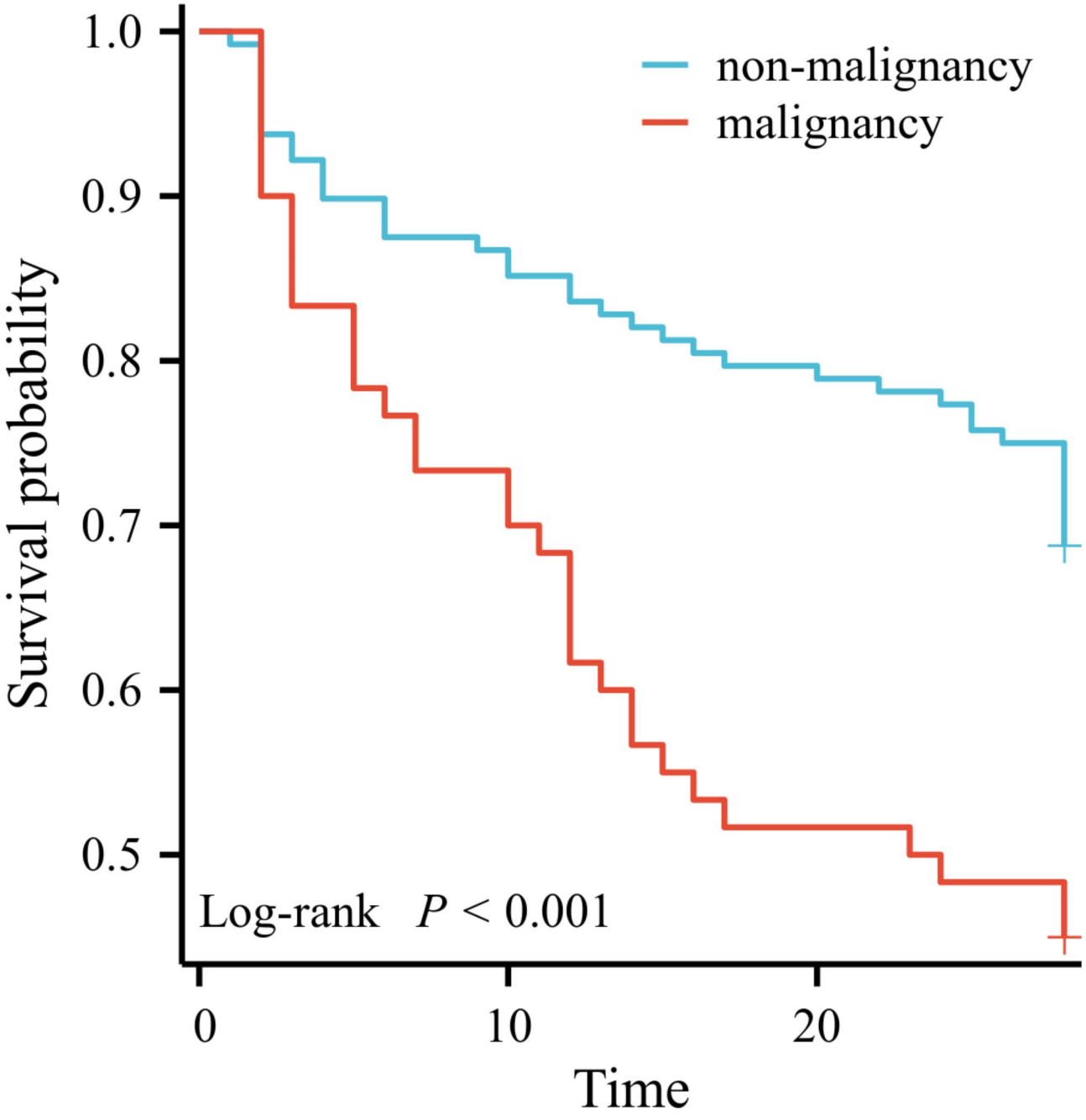

Fig. 1 Kaplan–Meier curve of the PICU mortality in patients with and without malignancies

137.5, with a sensitivity of 0.606, specificity of 0.889, accuracy of 0.733, positive predictive value of 0.870, and negative predictive value of 0.649. The *Kaplan–Meier curve* and *log-rank test* (< 0.001) also showed a significant difference in the survival rate between patients with subgroups stratified by the VIS (< 137.5 vs.≥137.5) (Fig. 2b).

Discussion

Our study found that ARDS with malignancy children had a significantly higher risk of death than those without malignancy. Children with malignancy who develop ARDS are more prone to complications, including community-acquired fungal infection, MDR bacterial infection, and organ dysfunction. To the best of our knowledge, this is the first research report comparing mortality rates and clinical characteristics between ARDS patients with and without malignancy in a large-scale

Table 4 Risk factors associated with PICU mortality in patients with and without malignancy

Variables	Odds Ratio	95% CI	*P*
Malignancy group			
pSOFA	1.249	0.958–1.628	0.101
VIS	1.011	1.003–1.018	0.005
Lactate	1.192	0.928–1.531	0.170
Non-malignancy group			
pSOFA	1.132	0.952–1.345	0.160
VIS	1.002	0.996–1.008	0.495
CRP	1.006	0.999–1.014	0.095
Lactate	0.960	0.739–1.246	0.628
IL6	1.000	1.000–1.000	0.624

The models adjusted for all variables listed in the table

PICU population in China. The populations with compromised immune systems, especially those with malignancy, are more susceptible to infections and drug resistance [13–15]. MDR infections not only prolong the hospital stay and intensive care requirements for malignancy patients but also significantly increase mortality [2]. In the case of ARDS, MDR infections worsen clinical outcomes, especially in immunosuppressed patients [16]. Study have shown that that patients with malignancy are prone to infections, particularly those caused by drug-resistant pathogens, after undergoing immunosuppressive treatments such as chemotherapy and radiotherapy [17]. A large retrospective study found that approximately 90% of ARDS cases in patients with malignancy were related to infections, with a significant portion caused by invasive fungal infections [2]. Moreover, the immunosuppressed state following chemotherapy significantly reduces these patients' resistance to infections, leading to an increased incidence of MDR infections [18]. MDR infections often present atypically, which may delay diagnosis and treatment, increasing risks for patients [19]. Therefore, early identification and proactive management of these infections are key to improving outcomes. Future research should focus on optimizing these patients' management strategies to reduce the worsened outcome of MDR infections.

In present cohort study, we found that children with malignancy have a significantly higher incidence of organ dysfunction compared to non-malignancy patients. Consistent with previous reports, malignancy is more likely to impair the lungs, liver, kidneys, and coagulation functions, thereby directly impacting patients' overall quality of life and prognosis [20]. Malignancy patients in our PICU have lower hemoglobin and platelet levels compared to non-malignancy patients, leading to a greater need for blood transfusions. This further reflects the fragility of their hematological system. The frequency of CRRT use in ARDS patients with malignancies has significantly increased in our center, possibly due to the more widespread occurrence of kidney or liver dysfunction in this particular population. Furthermore, CRRT

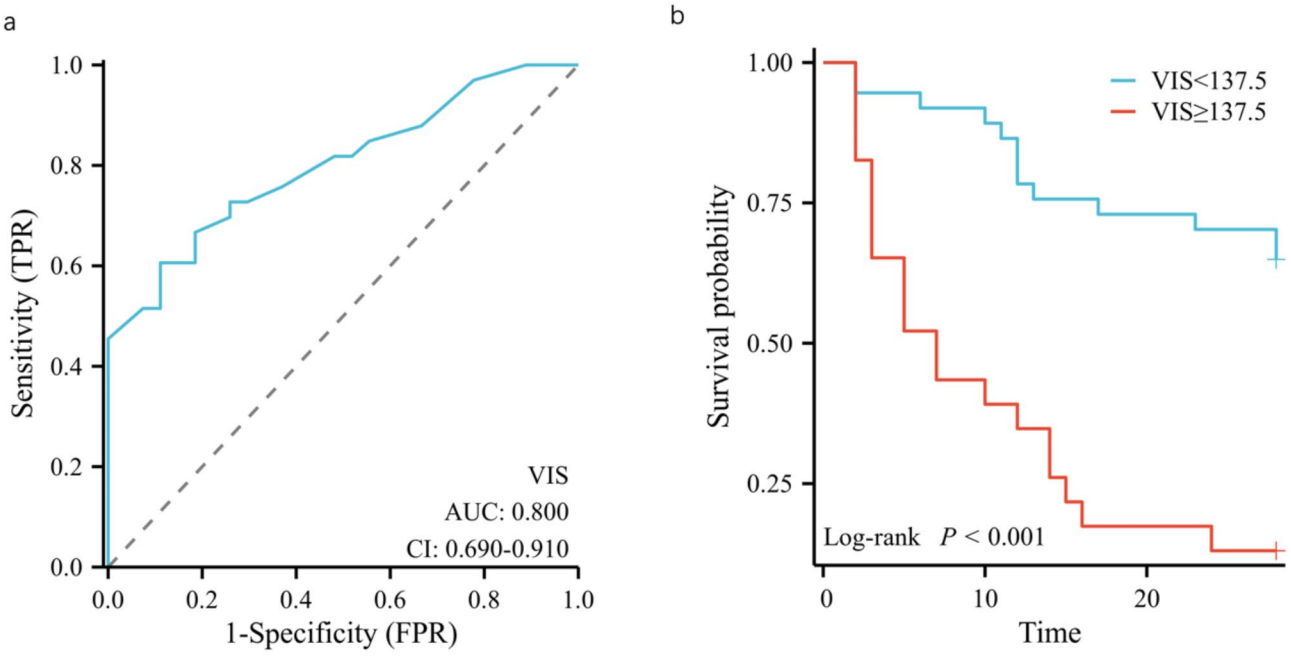

Fig. 2 VIS is an independent predictor of PICU mortality in patients with malignancy. (**a**) The receiver operating characteristic curve of the vasoactive–inotropic score (VIS) in predicting the survival status in patients with malignancy. The sensitivity is 0.606, specificity is 0.889, accuracy is 0.733, positive predictive value is 0.870 and negative predictive value is 0.649. (**b**) the Kaplan–Meier curve of the PICU mortality in the subgroups stratified by the VIS (cutoff value, 137.5) in patients with malignancy

can effectively correct metabolic imbalances, study in pediatric malignancy patients found that CRRT has a rapid effect in correcting hyperphosphatemia and hyperuricemia in tumor lysis syndrome. Most patients returning to normal electrolyte levels within 12 h after CRRT initiation [21]. Moreover, a retrospective study involving patients with AKI and malignancy revealed that the overall mortality rate remains alarmingly high, particularly among those with hematological malignancies [22]. Factors such as the timing of CRRT initiation, severity of illness as indicated by the SOFA score, and the presence of oliguria were significant predictors of outcomes in this population [23, 24]. Notably, early initiation of CRRT has been correlated with improved survival rates [25]; emphasizing the importance of timely intervention in critically ill patients.

In our study, children with malignancy had a shorter duration of ventilation than their non-malignancy counterparts. This difference may be closely linked to the higher mortality risk that malignancy patients experience in the PICU. Additionally, evidence indicates that non-invasive ventilation can effectively lower mortality rates in patients with hematological malignancies compared to invasive mechanical ventilation [26]. The literature has also validated the effectiveness of non-invasive ventilation in pediatric immunocompromised patients [27]. This further emphasizes the importance of minimizing the reliance on invasive support for this vulnerable population. Unfortunately, our study did not track ventilator-free days, leading to missing data that limits our ability to conduct an in-depth analysis of the potential benefits of non-invasive ventilation. The variables of CRP and PCT levels and the distribution of $CD8^+$ T cells and $CD19^+$ B cells indicate unique infection and immune response characteristics in patients with malignancies. This immune characteristic may reflect the complexity of the tumor microenvironment and the tumor cells' escape mechanisms from the host immune system. Immune system in malignancy patients is often in a state of continuous activation, leading to immune suppression and increased risk of infection, which can adverse outcomes [28]. Therefore, monitoring immune status of malignancy patients will help optimize treatment plans and improve patient prognosis. Identifying VIS as a risk factor for mortality in ARDS patients with malignancies represents a pivotal finding in our research. Elevated VIS levels are typically associated with hemodynamic instability in patients, which is particularly pronounced in those with malignancy, the presence of malignancy affects the patient's physiological state and can cause hemodynamic changes during treatment, potentially worsening the condition and increasing mortality risk [29]. Previous research has demonstrated that VIS is highly sensitive and specific in predicting mortality in PICU [30]. For instance, one study showed a significant correlation between VIS and mortality risk in patients with septic shock, with an AUC of 0.88, further validating the effectiveness of VIS as a prognostic indicator [31]. Additionally, higher VIS levels are linked to organ dysfunction and increased mortality, highlighting the importance of VIS in guiding clinical management [32, 33]. In patients with malignancy, a higher VIS likely reflect the hemodynamic changes caused by the malignancy and its treatment; for instance, a study of pediatric patients with hematological malignancies found a positive correlation between high VIS and mortality [5]. Moreover, prolonged mechanical ventilation time and higher VIS may impact the prognosis of children with hemophagocytic lymphohistiocytosis, further emphasizing the necessity of monitoring VIS in clinical practice [34]. In summary, as an independent prognostic indicator, VIS holds broad application prospects in ARDS with malignancy. Clinicians should consider incorporating it into routine monitoring to better assess changes in the patient's condition and optimise treatment strategies.

Our study has several limitations. Firstly, as a single-center, limited-scale retrospective study, its conclusions need to be confirmed by a multi-center, well-designed, and prospective study with a larger population. Secondly, the lack of data on ventilator-free days hampers a comprehensive assessment of patients' respiratory support needs and recovery times. Lastly, due to limitations in data collection, we could not include information on MDR genes in this study.

Conclusion

ARDS patients with malignancies present higher mortality rates and more organ dysfunction than those without malignancies. The VIS only serves as an independent predictor of mortality in ARDS patients with malignancy.

Abbreviations

ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
ARDS	Acute respiratory distress syndrome
AUC	The area under the curve
BMT	Bone marrow transplantation
Cdyn	Dynamic lung compliance
CRP	C-reactive protein
CRRT	Continuous renal replacement therapy
CI	Confidence interval
ECMO	Extracorporeal membrane oxygenation
HSCT	Hematopoietic stem cell transplantation
OR	Odds ratio
IFN-γ	Interferon-γ
IL-6	Interlukin-6
IL-8	Interlukin-8
IQR	The interquartile range
MDR	Multidrug resistance
MV	Mechanical ventilation
PCT	Procalcitonin
PEEP	Positive end-expiratory pressure
PICU	Pediatric intensive care unit
PIP	Peak inspiratory pressure

pSOFA	Pediatric sequential organ failure assessment score
ROC	Curve, receiver operating characteristic curve
TNF-α	Tumor necrosis factor alpha
VIS	Vasoactive–inotropic score

Supplementary Information

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Supplementary Material 1: **Supplemental Fig. 1**. Type and clinical characteristics of ARDS patients with malignancy depending on PICU mortality. (a) Different types of malignancy, (b) disease status of malignancy, (c) agranulocytosis and BMT/HSCT of ARDS patients with malignancy. *, indicates $P < 0.05$, ns, indicates $P > 0.05$. Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; BMT, bone marrow transplantation; HSCT, hematopoietic stem cell transplantation. a Other malignancies including Hodgkin's lymphoma, chronic myeloid leukemia, myelodysplastic syndromes, and chronic eosinophilic leukemia

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Author contributions
Yucai Zhang designed and supervised the research. Pin Li provided guidance and helped construct the article's framework. Xi Xiong, Xiaoxuan Ma and Yiping Zhou collected clinical data. Xi Xiong and Xiaoxuan Ma analyzed the data. Xi Xiong wrote the manuscript. Pin Li, Yun Cui, Yucai Zhang and Chunxia Wang reviewed and edited the manuscript. All authors contributed to the work and approved it for publication. Yucai Zhang is the guarantor of this research and takes responsibility for the integrity and accuracy of the work.

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Data availability
The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of Shanghai Children's Hospital (2024R149- E01). Informed consent was waived because of the retrospective nature of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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References

1. Ho K, Gordon J, Litzenberg KT, Exline MC, Englert JA, Herman DD. Cancer is an independent risk factor for acute respiratory distress syndrome in critically ill patients: A single center retrospective cohort study. J Intensive Care Med. 2022;37(3):385–92.
2. Azoulay E, Lemiale V, Mokart D, Pène F, Kouatchet A, Perez P, Vincent F, Mayaux J, Benoit D, Bruneel F, et al. Acute respiratory distress syndrome in patients with malignancies. Intensive Care Med. 2014;40(8):1106–14.
3. Azoulay E, Mokart D, Kouatchet A, Demoule A, Lemiale V. Acute respiratory failure in immunocompromised adults. Lancet Respir Med. 2019;7(2):173–86.
4. Zhang Y, Zhou Y, Shi J, Shan Y, Sun T, Wang C, Shao J, Cui Y. Extracorporeal membrane oxygenation for severe acute respiratory distress syndrome in children with leukemia/lymphoma: A retrospective case series. Front Pediatr. 2022;10:955317.
5. Zhang Q, Hu WT, Yin F, Qian H, Wang Y, Li BR, Qian J, Tang YJ, Ning BT. The clinical characteristics of ARDS in children with hematological neoplasms. Front Pediatr. 2021;9:696594.
6. Gertz SJ, Bhalla A, Chima RS, Emeriaud G, Fitzgerald JC, Hsing DD, Jeyapalan AS, Pike F, Sallee CJ, Thomas NJ, et al. Immunocompromised-Associated pediatric acute respiratory distress syndrome: experience from the 2016/2017 pediatric acute respiratory distress syndrome incidence and epidemiology prospective cohort study. Pediatr Crit Care Med. 2024;25(4):288–300.
7. Prasertsan P, Anuntaseree W, Ruangnapa K, Saelim K, Geater A. Severity and Mortality Predictors of Pediatric Acute Respiratory Distress Syndrome According to the Pediatric Acute Lung Injury Consensus Conference Definition. Pediatr Crit Care Med 2019;20(10):e464-e472.
8. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS. Acute respiratory distress syndrome: the Berlin definition. JAMA. 2012;307(23):2526–33.
9. Kobayashi S, Noh JY, Mukasa K, Kunii Y, Watanabe N, Matsumoto M, Ohye H, Suzuki M, Yoshihara A, Iwaku K, et al. Characteristics of agranulocytosis as an adverse effect of antithyroid drugs in the second or later course of treatment. Thyroid. 2014;24(5):796–801.
10. McIntosh AM, Tong S, Deakyne SJ, Davidson JA, Scott HF. Validation of the Vasoactive-Inotropic score in pediatric sepsis. Pediatr Crit Care Med. 2017;18(8):750–7.
11. Chang YT, Lin CY, Lu PL, Lai CC, Chen TC, Chen CY, Wu DC, Wang TP, Lin CM, Lin WR, et al. Stenotrophomonas maltophilia bloodstream infection: comparison between community-onset and hospital-acquired infections. J Microbiol Immunol Infect. 2014;47(1):28–35.
12. Lanks CW, Musani AI, Hsia DW. Community-acquired pneumonia and Hospital-acquired pneumonia. Med Clin North Am. 2019;103(3):487–501.
13. Baden LR, Swaminathan S, Almyroudis NG, Angarone M, Baluch A, Barros N, Buss B, Cohen S, Cooper B, Chiang AD, et al. Prevention and treatment of Cancer-Related infections, version 3.2024, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2024;22(9):617–44.
14. McNeil JC. Staphylococcus aureus - antimicrobial resistance and the immunocompromised child. Infect Drug Resist. 2014;7:117–27.
15. Moreau AS, Martin-Loeches I, Povoa P, Salluh J, Rodriguez A, Thille AW, Diaz Santos E, Vedes E, Lobo SM, Mégarbane B et al. Impact of immunosuppression on incidence, aetiology and outcome of ventilator-associated lower respiratory tract infections. Eur Respir J 2018;51(3).
16. Paramythiotou E, Dimopoulos G, Koliakos N, Siopi M, Vourli S, Pournaras S, Meletiadis J. Epidemiology and incidence of COVID-19-associated pulmonary aspergillosis (CAPA) in a Greek Tertiary Care Academic Reference Hospital. Infect Dis Ther 2021;10(3):1779–92.
17. Vázquez-López R, Rivero Rojas O, Ibarra Moreno A, Urrutia Favila JE, Peña Barreto A, Ortega Ortuño GL, et al. Antibiotic-resistant septicemia in pediatric oncology patients associated with post-therapeutic neutropenic fever. Antibiotics (Basel) 2019;8(3).
18. Thampy LK, Remy KE, Walton AH, Hong Z, Liu K, Liu R, et al. Restoration of T cell function in multi-drug resistant bacterial sepsis after interleukin-7, anti-PD-L1, and OX-40 administration. PLoS One 2018;13(6):e0199497.
19. Lujan M, Gallego M, Rello J. Healthcare-associated infections. A useful concept? Curr Opin Crit Care 2009;15(5):419–24.

20. Soeteman M, Fiocco MF, Nijman J, Bollen CW, Marcelis MM, Kilsdonk E, et al. Prognostic factors for multi-organ dysfunction in pediatric oncology patients admitted to the pediatric intensive care unit. Front Oncol 2023;13:1192806.
21. Anderson A, Shoulders L, James V, Ashcraft E, Cheng C, Ribeiro R, et al. Benefit of continuous kidney replacement therapy for managing tumor lysis syndrome in children with hematologic malignancies. Front Oncol 2023;13:1234677.
22. Al-Ayed T, Rahman NU, Alturki A, Aljofan F. Outcome of continuous renal replacement therapy in critically ill children: a retrospective cohort study. Ann Saudi Med 2018;38(4):260–68.
23. Dos Santos TOC, Oliveira MAS, Monte JCM, Batista MC, Pereira Junior VG, Dos Santos BFC, et al. Outcomes from a cohort of patients with acute kidney injury subjected to continuous venovenous hemodiafiltration: the role of negative fluid balance. PLoS One 2017;12(4):e0175897.
24. Ma X, Dou J, Wang C, Miao H, Shi J, Cui Y, et al. The death risk of pediatric patients with cancer-related sepsis requiring continuous renal replacement therapy: a retrospective cohort study. J Pediatr (Rio J) 2024;100(6):614–21.
25. Oh HJ, Shin DH, Lee MJ, Koo HM, Doh FM, Kim HR, et al. Early initiation of continuous renal replacement therapy improves patient survival in severe progressive septic acute kidney injury. J Crit Care 2012;27(6):743.e749–718.
26. Belenguer-Muncharaz A, Albert-Rodrigo L, Ferrandiz-Sellés A, Cebrián-Graullera G. Ten-year evolution of mechanical ventilation in acute respiratory failure in the hematogical patient admitted to the intensive care unit. Med Intensiva 2013;37(7):452–60.
27. Wang T, Zhang L, Luo K, He J, Ma Y, Li Z, et al. Noninvasive versus invasive mechanical ventilation for immunocompromised patients with acute respiratory failure: a systematic review and meta-analysis. BMC Pulm Med 2016;16(1):129.
28. Malek E, de Lima M, Letterio JJ, Kim BG, Finke JH, Driscoll JJ, et al. Myeloid-derived suppressor cells: the green light for myeloma immune escape. Blood Rev 2016;30(5):341–8.
29. Baizabal-Carvallo JF, Alonso-Juárez M, Salas I. Pretruncal subarachnoid hemorrhage and high cerebral blood flow velocities with bevacizumab therapy. Clin Neuropharmacol 2010;33(5):268–9.
30. Musick MA, Loftis LL, Kennedy CE. Comparing vasoactive-inotropic score reporting strategies in the PICU relative to mortality risk. Pediatr Crit Care Med 2018;19(12):1130–6.
31. Kallekkattu D, Rameshkumar R, Chidambaram M, Krishnamurthy K, Selvan T, Mahadevan S. Threshold of inotropic score and vasoactive-inotropic score for predicting mortality in pediatric septic shock. Indian J Pediatr 2022;89(5):432–7.
32. Lee EP, Zhao LL, Hsia SH, Chan OW, Lin CY, Su YT, et al. Vascular reactivity index as an effective predictor of mortality in children with refractory septic shock. J Intensive Care Med 2021;36(5):589–96.
33. Sun YT, Wu W, Yao YT. The association of vasoactive-inotropic score and surgical patients' outcomes: a systematic review and meta-analysis. Syst Rev 2024;13(1):20.
34. Parajuli B, Angurana SK, Awasthi P, Nallasamy K, Baranwal A, Bansal A, et al. Hemophagocytic lymphohistiocytosis in a PICU of a developing economy: clinical profile, intensive care needs, outcome, and predictors of mortality. Pediatr Crit Care Med 2021;22(1):e44–e57.

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