

Are platelet volume indices related to mortality in hospitalized children on mechanical ventilation?

Journal of International Medical Research 2018, Vol. 46(3) 1197–1208 © The Author(s) 2018 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav DOI: 10.1177/0300060517737211 journals.sagepub.com/home/imr



Sheng Ye¹, Yanyi Zhang², Chenmei Zhang¹ and Dan Xu¹

Abstract

Objectives: To investigate platelet volume indices and in-hospital mortality in children on mechanical ventilation.

Methods: This retrospective study included children aged <16 years on mechanical ventilation, and compared parameters, measured on admission, between survivors and non-survivors. Dynamic platelet volume indices over the first 7 days were visualized. Independent risk factors of mortality were identified using multivariate logistic regression analysis.

Results: Out of 2319 children aged 28 days–3 years, serum albumin (odds ratio [OR] 0.9, 95% confidence interval [CI] 0.85, 0.96), bilirubin (OR 1.01, 95% CI 1.0, 1.77), and lactic acid (OR 1.22, 95% CI 1.05, 1.38) levels were associated with mortality. Out of 2415 children aged > 3 years, procalcitonin (OR 1.01, 95% CI 1.0, 1.01) and lactic acid (OR 1.22, 95% CI 1.09, 1.35) were associated with mortality. Platelet volume indices on admission were not independently associated with mortality in either group. Mean platelet volume (MPV) and platelet distribution width (PDVV) showed different trends in non-survivors versus survivors over 1 week in both age groups.

Conclusions: Platelet volume indices may be associated with mortality in critically ill children receiving mechanical ventilation.

Keywords

Mean platelet volume, platelet distribution width, mortality, children, mechanical ventilation

Date received: 17 July 2017; accepted: 13 September 2017

²Psychological Department, The Children's Hospital, Zhejiang University School of Medicine, Hangzhou, China

Corresponding author:

Dan Xu, Paediatric Intensive Care Unit, The Children's Hospital, Zhejiang University School of Medicine, 3333 Bingsheng Road, Hangzhou 310003, China. Email: 6514236@zju.edu.cn

¹Pediatric Intensive Care Unit, The Children's Hospital, Zhejiang University School of Medicine, Hangzhou, China

Creative Commons Non Commercial CC-BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (http://www.creativecommons.org/licenses/by-nc/4.0/) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (https://us.sagepub.com/en-us/nam/open-access-at-sage).

Introduction

Mechanical ventilation is frequently used for life support in intensive care units (ICUs). Acute respiratory failure requiring mechanical ventilation remains the most common reason for paediatric ICU (PICU) admission,¹ with most of these children requiring mechanical ventilation due to the severity of their illness. Albumin,^{2,3} lactic acid,^{4,5} procalcitonin,⁶ glucose,^{7,8} PaO₂,⁹ and nutritional status¹⁰ have been reported as predictors of mortality risk in critically ill patients, and some of these factors have been included in the score that estimates mortality risk.^{11,12} There is growing evidence to show that mean platelet volume (MPV), platelet distribution width (PDW), and red blood cell distribution width (RDW) are associated with mortality in adult populations.¹³⁻²¹ Few studies, however, have evaluated such risk factors for in-hospital mortality in critically ill children who have undergone mechanical ventilation.

Platelet volume indices have been shown to play an important role inflammation and infection,^{22,23} and mechanically ventilated patients are generally in a high state of inflammation.^{24,39} Ventilator associated pneumonia is the second most frequently occurring nosocomial infection in the PICU, accounting for up to 20% of all such infections.²⁵ The aim of the present study was to identify platelet volume indices associated with in-hospital mortality in children who receive mechanical ventilation. Platelet volume indices, measured during admission, were hypothesized to be associated with hospital mortality in children who required mechanical ventilation.

Patients and methods

Study population

This retrospective, observational, singlecentre study included paediatric patients, aged < 16 years, who were admitted to the 40-bed PICU at The Children's Hospital, Zhejiang University School of Medicine, Hangzhou, China, between January 2014 and June 2016. Data from patients who received mechanical ventilation during hospitalization were sequentially collected, and divided into two cohorts based on age at admission: patients aged > 3 years and patients aged from 28 days to 3 years. The following patients were excluded: (1) children who stayed in the PICU for < 24 h, (2) children without ventilator use during hospitalization, (3) new-borns aged < 28days, (4) children with haematology diseases such as aplastic anaemia, leukaemia, thrombocytopaenia, or hemophagocytic syndrome, (5) children with tumours, (6) children who received mechanical ventilation more than twice, (7) children whose parents refused treatment with mechanical ventilation, and (8) children for whom platelet indices were not obtained.

This study was approved by the Medical Ethics Committee of Zhejiang University School of Medicine Children's hospital: Ethics Committee reference number, 2016-IRBAL-042. Informed consent was not deemed to be required due to the retrospective nature of the study.

Clinical and laboratory data

Data on patients' age, sex, date of hospital admission/discharge, date of transfer in/out of the PICU, duration of mechanical ventilation, admission diagnosis, and discharge status were collected. Relevant laboratory tests were obtained from Donglian Medical Information Systems (Hangzhou Donglian Software Co., Hangzhou, China). The following admission data were also collected: white blood cell (WBC) count, haemoglobin, platelet count, MPV, PDW, plateletcrit, RDW, serum high-sensitivity C-reactive protein (hs-CRP) and procalcitonin levels, and serum albumin, bilirubin, and lactic acid levels. Platelet indices and RDW were recorded daily until PICU discharge or death.

Blood samples from paediatric patients in the PICU are routinely sent for analyses by special care workers at the Zhejiang University School of Medicine Children's hospital. Blood samples relating to the present data were collected into tubes that contained ethylenediamine tetra-acetic acid for routine blood examination, and complete blood count results were usually obtained within half an hour of collection.

Definitions

Mechanical ventilation is the most effective treatment for critically ill children with respiratory failure requiring respiratory support. Mechanical ventilation is used in the Zhejiang University School of Medicine Children's hospital for patients with lung disease caused by respiratory failure and also for patients with neuromuscular disease and for those who need respiratory support, including the following range of conditions: (1) apnoea/weakening or disappearance of spontaneous breathing, (2) carbon dioxide retention with carbon dioxide partial pressure > 60 mmHg, (3) hypoxemia, with oxygen partial pressure < 50mmHg, and (4) in some patients, for prevention or to provide respiratory support, in cases of shock, anaesthesia, or coma.

Clinical outcome

The primary outcome measure was the PICU mortality rate, which was defined as deaths occurring during the PICU stay. Survivors were discharged to home or transferred to another department in Zhejiang University School of Medicine Children's hospital.

Statistical analyses

Based on the primary outcome measure, each age cohort was further subdivided

into two groups: survivors and nonsurvivors. Univariate analysis was used to compare variables for survivors versus nonsurvivors in each cohort, and all tests of significance were two tailed. Continuous variables were first tested for skewness and kurtosis. Normally distributed data are presented as mean \pm SD and skewed data are presented as median and interguartile range. Categorical variables are presented as n (% prevalence).²⁶ Unadjusted comparisons between survivors and nonsurvivors were performed, and the test results were confirmed with multivariate logistic regression analysis using a stepwise approach.²⁷ Results of the logistic regression analysis are reported as odds ratios (ORs) with 95% confidence intervals (CIs). All analyses were performed using the R-3.3.1 statistics package (http://www. r-project.org), and P-values of <0.05 were considered statistically significant.

Results

In this retrospective cohort study, 6488 children with mechanical ventilation were identified, and 1622 neonates and 143 patients with tumours were excluded. A total of 4723 children meeting the inclusion criteria were enrolled into the study (mean age, 3.31 ± 3.83 years; 54.5% male / 45.5% female), 184 of whom died during hospitalization, equating to an overall mortality rate of 3.90%. The subgroup aged 28 days to 3 years comprised 2319 children, with a mortality rate of 4.57% (106 deaths). In this subgroup, cardiovascular disease was found to be the main underlying reason for mechanical ventilation (Table 1). Univariate analysis revealed statistically significant differences between survivors and non-survivors in terms of CRP, WBC, haemoglobin, platelet count, RDW, and serum albumin, bilirubin, and lactic acid levels (P < 0.03; Table 1). Age was not found to differ between survivors and

Variable	Patient subgroup			
	Total n = 2 3 1 9	Survivors $n = 2213$	Non-survivors $n = 106$	Statistical significance
Age, months	$\textbf{10.6} \pm \textbf{9.55}$	10.6 ± 9.56	11.2 \pm 9.22	NS
CRP, mg/dl	$\textbf{15.2} \pm \textbf{32.9}$	14.5 ± 31.63	14.6 ± 58.46	P < 0.00 I
Procalcitonin, ng/ml	5.3 ± 38.61	$\textbf{3.7} \pm \textbf{26.22}$	$\textbf{0.3} \pm \textbf{I} \textbf{33.26}$	NS
Albumin, g/l	$\textbf{39.2} \pm \textbf{5.01}$	$\textbf{39.3} \pm \textbf{4.89}$	$\textbf{40.5} \pm \textbf{8.00}$	P < 0.00 I
Bilirubin, µmol/l	17.8 ± 28.57	17 ± 26.62	14.2 ± 66.02	P < 0.00 I
Lactic acid, mmol/l	2.2 ± 2.46	$\textbf{2.1} \pm \textbf{2.12}$	1.7 ± 6.23	P < 0.00 I
WBC, × 10 ⁹ /I	11.1 ± 6.68	11 ± 6.68	10.1 ± 11.08	P = 0.03
Haemoglobin, g/l	116.9 \pm 22.09	117.2 ± 147.05	120.2 ± 29.40	P < 0.00 I
PLT, $\times 10^{9}/l$	$\textbf{337.9} \pm \textbf{148.48}$	$\textbf{340.6} \pm \textbf{147.05}$	319.6 ± 168.14	P < 0.00 I
MPV, fl	$\textbf{40.3} \pm \textbf{38.46}$	$\textbf{41.7} \pm \textbf{38.05}$	$\textbf{40.4} \pm \textbf{37.24}$	NS
Plateletcrit, %	0.32 ± 0.13	0.32 ± 0.13	$\textbf{0.3}\pm\textbf{0.14}$	P < 0.00 I
PDW, %	$\textbf{57} \pm \textbf{30.79}$	$\textbf{57} \pm \textbf{30.74}$	$\textbf{53.3} \pm \textbf{32.34}$	NS
RDW, %	14.5 ± 2.51	14.5 ± 2.52	13.9 ± 2.06	P < 0.00 I
Primary diagnosis, n (%)				
Respiratory disease	398 (17.2)	357 (16.1)	41 (38.7)	
Heart disease	545 (23.5)	524 (23.7)	21 (19.8)	
Neurologic disease	400 (17.2)	380 (17.2)	20 (18.9)	
Sepsis	80 (3.4)	71 (3.2)	9 (8.5)	
Other external disease	645 (27.8)	640 (28.9)	5 (4.7)	
Other internal disease	251 (10.8)	241 (10.9)	10 (9.4)	

 Table 1. Demographic and clinical characteristics of surviving and non-surviving children, aged from 28 days to 3 years, admitted to a paediatric intensive care unit and who received mechanical ventilation

Data presented as mean \pm SD or *n* (%) patient prevalence.

CRP, C-reactive protein; WBC, white blood cell; MPV, mean platelet volume; PLT, platelet count; PDW, platelet distribution width; RDW, red blood cell distribution width.

External disease, condition requiring surgery; internal disease, condition not requiring surgery.

NS, no statistically significant between-group difference (P > 0.05; unadjusted comparisons).

non-survivors. In subsequent multivariate logistic regression analyses (Table 2), serum albumin (OR 0.9, 95% CI 0.85, 0.96; P < 0.001), bilirubin (OR 1.01, 95% CI 1.0, 1.77; P < 0.001) and lactic acid (OR 1.22, 95% CI 1.05, 1.38; P < 0.001) levels were found to be related to mortality.

The subgroup aged >3 years comprised 2404 patients, with a mortality rate of 3.24% (78 deaths). Neurologic disease was the primary condition requiring mechanical ventilation, however, respiratory diseases were the leading cause of death (41% of non-survivors; Table 3). Procalcitonin, CRP, haemoglobin, platelet count, RDW,

plateletcrit, PDW, lactic acid levels and patient age were found to be significantly different between survivors and nonsurvivors ($P \le 0.03$; Table 3). Subsequent multivariate logistic regression analysis (Table 4) revealed that procalcitonin (OR 1.01, 95% CI 1.0, 1.01; P = 0.02), platelet count (OR 1.01, 95% CI 1.00, 1.01; P = 0.02) and lactic acid (OR 1.22, 95% CI 1.09, 1.35; P < 0.001) were related to mortality.

In patients > 3 years of age, trend in MPV in non-survivors appears to decrease over the first 72 h, followed by an increase up to day 7 (Figure 1). In patients aged

Table 2. Logistic regression analysis of factors associated with mortality in children, aged from 28 days to 3 years (n = 2319) admitted to a paediatric intensive care unit and who received mechanical ventilation

Variable	OR (95% CI)	Statistical significance
CRP, mg/dl	1.00 (0.99, 1.01)	NS
Albumin, g/l	0.90 (0.85, 0.96)	P < 0.001
Bilirubin, μmol/l	1.01 (1.00, 1.17)	P < 0.00 I
Lactic acid, mmol/l	1.22 (1.05, 1.38)	P < 0.00 I
WBC, × 10 ⁹ /I	1.00 (0.95, 1.02)	NS
Haemoglobin, g/l	0.99 (0.98, 1.01)	NS
PLT, $\times 10^{9}/l$	0.99 (0.99, 1.00)	NS
MPV, fl	0.98 (0.96, 1.01)	NS
Plateletcrit, %	12.85 (0.00, 13711.72)	NS
RDW, %	1.08 (0.94, 1.19)	NS

OR, odds ratio; CI, confidence interval; CRP, C-reactive protein; WBC, white blood cell; MPV, mean platelet volume; PLT, platelet count; RDW, red blood cell distribution width.

NS, no statistically significant association (P > 0.05).

between 28 days and 3 years, trend in MPV in non-survivors appeared to decrease slightly over the first 48 h then increase slightly to day 7 (Figure 1). The trend in platelet count over time did not appear to differ between survivors and non-survivors during the first week following PICU admission in either age subgroup (Figure 2). For patients older than 3 years of age, trend in PDW in nonsurvivors increased in the first 48 h. For nonsurviving patients aged 28 days to 3 years, PDW increased over the first 96 h (Figure 3). There were similar trends in plateletcrit over time in survivors and non-survivors in both patient groups during the first week following admission to the PICU (Figure 4). There was no observable difference in trends in RDW between survivors and non-survivors in either patient group (Figure 5). Compared with survivors, MPV and PDW showed an increasing trend in non-survivors of both age cohorts during the first week following admission to the PICU.

Discussion

In the present retrospective, observational study comprising data collected from a tertiary children's teaching hospital, respiratory, heart, and neurological diseases were found to be the major underlying conditions for mechanical ventilation in children admitted to the PICU. Mechanical ventilation is a common practice in the ICU and is used as a therapeutic intervention, particularly in patients with acute respiratory failure.²⁸ Mechanical ventilation not only provides respiratory support but also improves gas exchange and alleviates the work of breathing. According to the present study, respiratory, heart, neurological, and surgical diseases can all result in respiratory failure, and these were shown to be the leading causes of PICU admission.

Various factors have been identified that impact the risk of mortality in critically ill children. For example, vitamin D deficiency in critically ill children was found to be associated with illness severity and clinical outcomes.²⁹ An investigation into the association between obesity and PICU mortaliusing a large, multicentre PICU ty database, found that risk-adjusted PICU mortality significantly increases as body mass index increases into the overweight and obese ranges.30 Several factors should be considered when assessing risk factors for death in critically ill children, particularly in children who require mechanical ventilation, such as those admitted to the PICU, who often present with, or develop, respiratory failure.31

In the present study, children of different ages were found to have different mortality risk factors. In children aged 28 days to 3 years, serum albumin (OR 0.9, 95% CI 0.85, 0.96), bilirubin (OR 1.01, 95% CI 1.0, 1.77), and lactic acid (OR 1.22, 95%

	Patient subgroup			
Variable	Total n = 2 404	Survivors $n = 2326$	Non-survivors $n = 78$	Statistical significance
Age, years	$\textbf{7.24} \pm \textbf{4.86}$	$\textbf{7.15} \pm \textbf{4.91}$	$\textbf{8.45} \pm \textbf{2.95}$	P < 0.00 I
CRP, mg/dl	$\textbf{17.0} \pm \textbf{36.40}$	$\textbf{17.0} \pm \textbf{35.18}$	$\textbf{49.9} \pm \textbf{59.39}$	P < 0.00 I
Procalcitonin, ng/ml	1.9 ± 7.04	1.9 ± 7.18	$\textbf{0.9} \pm \textbf{0.96}$	P = 0.03
Albumin, g/l	$\textbf{39.0} \pm \textbf{5.04}$	39.0 ± 4.9 l	$\textbf{35.4} \pm \textbf{8.69}$	NS
Bilirubin, µmol/l	12.8 ± 11.83	12.8 ± 11.74	16.1 ± 15.49	NS
Lactic acid, mmol/l	2.2 ± 1.80	2.2 ± 1.48	$\textbf{4.7} \pm \textbf{5.57}$	P < 0.00 I
WBC, × 10 ⁹ /I	$\textbf{9.7} \pm \textbf{20.43}$	$\textbf{9.7} \pm \textbf{20.56}$	12.5 ± 14.76	NS
Haemoglobin, g/l	120.5 \pm 18.58	120.5 ± 18.27	107.3 ± 24.30	P < 0.00 I
PLT, $\times 10^{9}/I$	$\textbf{292.2} \pm \textbf{104.35}$	$\textbf{292.2} \pm \textbf{102.25}$	192.5 \pm 129.36	P < 0.00 I
MPV, fl	$\textbf{42.4} \pm \textbf{38.25}$	$\textbf{42.3} \pm \textbf{38.26}$	$\textbf{41.6} \pm \textbf{38.20}$	NS
Plateletcrit, %	$\textbf{0.3} \pm \textbf{0.09}$	$\textbf{0.3} \pm \textbf{0.08}$	0.2 ± 0.11	P < 0.00 I
PDW, %	$\textbf{58.0} \pm \textbf{23.01}$	$\textbf{58.0} \pm \textbf{23.00}$	$\textbf{48.1} \pm \textbf{24.65}$	P = 0.01
RDW, %	13.2 ± 1.71	13.2 ± 1.69	14.1 ± 2.15	P < 0.00 I
Primary diagnosis, n (%)				
Respiratory disease	441 (18.3)	409 (17.6)	32 (41)	
Heart disease	512 (21.3)	500 (21.5)	12 (15.4)	
Neurologic disease	545 (22.7)	531 (22.8)	14 (17.9)	
Sepsis	84 (3.5)	78 (3.4)	6 (7.7)	
Other external disease	427 (17.8)	420 (18.1)	7 (9)	
Other internal disease	406 (16.9)	399 (17.2)	7 (9)	

Table 3. Demographic and clinical characteristics of surviving and non-surviving children, aged between >3 and ≤ 16 years, admitted to a paediatric intensive care unit and who received mechanical ventilation

Data presented as mean \pm SD or *n* (%) patient prevalence.

CRP, C-reactive protein; WBC, white blood cell; MPV, mean platelet volume; PLT, platelet count; PDW, platelet distribution width; RDW, red blood cell distribution width.

External disease, condition requiring surgery; internal disease, condition not requiring surgery.

NS, no statistically significant between-group difference (P > 0.05; unadjusted comparisons).

CI 1.05, 1.38) levels were found to be associated with mortality. In children aged over 3 years, serum procalcitonin (OR 1.01, 95% CI 1.0, 1.01), platelet count (OR 1.01, 95% CI 1.00, 1.01) and lactic acid (OR 1.22, 95% CI 1.09, 1.35) levels were associated with mortality. The predictive value of blood lactic acid levels at admission have been evaluated previously, to determine the cut-off values for predicting in-hospital mortality in the critically ill paediatric population.⁴ A high blood lactic acid level at admission is independently associated with, and predictive of, in-hospital mortality in the general population of critically ill children.⁵ In another study, procalcitonin was associated with 28-day mortality in children with severe sepsis or septic shock.⁶ Hypoalbuminaemia at admission was found to predict poor outcomes in critically ill children, and shown to be associated with a higher mortality rate,² and hypoalbuminaemia at admission to a PICU is associated with higher 60-day mortality rate.³ As described above, serum albumin, bilirubin, lactic acid, and procalcitonin are shown to be related to mortality in critically ill children. The present study found that in both age groups of critically ill children, higher lactic acid levels were associated with a higher mortality rate. Although univariate analysis

Table 4. Logistic regression analysis of factors associated with mortality in children, aged between >3 and ≤ 16 years (n = 2404), admitted to a paediatric intensive care unit and who received mechanical ventilation

Variable	OR (95% CI)	Statistical significance
Age, years	1.00 (0.99, 1.00)	NS
CRP, mg/dl	1.00 (0.98, 1.01)	NS
Procalcitonin, ng/ml	1.01 (1.00, 1.01)	P = 0.02
Lactic acid, mmol/l	1.22 (1.09, 1.35)	P < 0.001
RDW, %	1.05 (0.84, 1.27)	NS
Haemoglobin, g/l	0.98 (0.97, 1.00)	NS
PLT, $\times 10^{9}$ /l	1.01 (1.00, 1.01)	P = 0.02
Plateletcrit, %	0.0 (0.00, 469.97)	NS
PDW, %	1.00 (0.98, 1.02)	NS

OR, odds ratio; CI, confidence interval; CRP, C-reactive protein; PLT, platelet count; PDW, platelet distribution width; RDW, red blood cell distribution width. NS, no statistically significant association (P > 0.05).

showed significant associations between plateletcrit and mortality in both groups, in children aged > 3 years, we found univariate analysis also showed a significant association between PDW and mortality, although the adjusted analysis failed to show such a trend. The present authors suggest that the association between mortality and plateletcrit or PDW may be dependent on other variables such as serum albumin, bilirubin, lactic acid.

In studies involving adult patients, platelet indices have been found to be related to mortality and disease severity. These studies demonstrated that patients with a low platelet count and high MPV and PDW survived for a shorter time than those with normal platelet indices, and thus platelet indices were proposed as a novel prognostic indicator in critically ill patients.^{19,20,32} The MPV is an indicator of platelet volume and activity, and altered MPV levels have been associated with mortality in patients with various diseases. For example, MPV has been

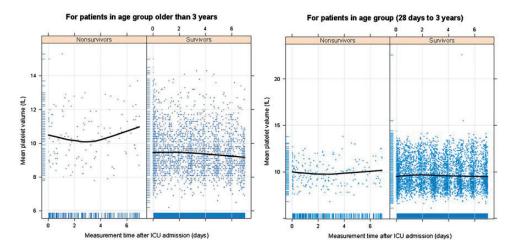


Figure 1. Scatter plots showing trend in mean platelet volume (MPV) between survivors and non-survivors in paediatric patients aged 28 days to 3 years (n = 2319 at admission) or aged between >3 and ≤ 16 years (n = 2404 at admission), who were receiving mechanical ventilation, measured during the first week following intensive care unit admission: In non-surviving patients aged >3 years, there was a decreasing trend in MPV during the first 72 h, followed by an increasing trend in MPV; In non-surviving patients aged 28 days to 3 years, MPV showed a very slight decreasing then increasing trend

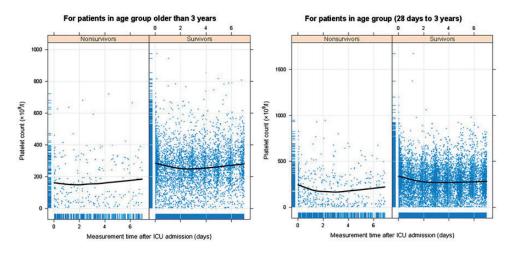


Figure 2. Scatter plots showing trend in platelet count between survivors and non-survivors in paediatric patients aged 28 days to 3 years (n = 2319 at admission) or aged between >3 and ≤ 16 years (n = 2404 at admission), who were receiving mechanical ventilation, measured during the first week following intensive care unit admission: There was no obvious difference between survivors and non-survivors in either patient group

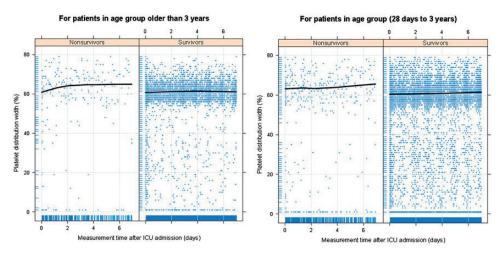


Figure 3. Scatter plots showing trend in platelet distribution width (PDW) between survivors and nonsurvivors in paediatric patients aged 28 days to 3 years (n = 2319 at admission) or aged between >3 and ≤ 16 years (n = 2404 at admission), who were receiving mechanical ventilation, measured during the first week following intensive care unit admission: In non-surviving patients aged >3 years, PDW showed an increasing trend in the first 48 h; In patients aged 28 days to 3 years, PDW showed a slight gradual increase over 7 days

reported as valuable for predicting mortality, and the severity of disease, among patients with community-acquired pneumonia,³³ and MPV has been related to mortality in cases of sepsis and myocardial infarction.^{34,35} Some studies, however, have suggested that initial MPV values may not be useful as a prognostic marker of mortality

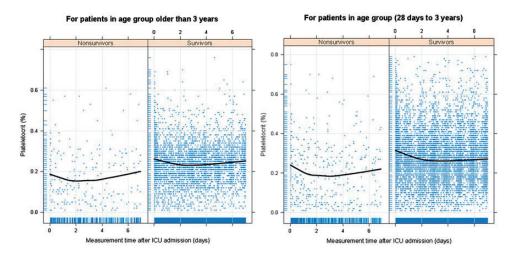


Figure 4. Scatter plots showing trend in plateletcrit between survivors and non-survivors in paediatric patients aged 28 days to 3 years (n = 2319 at admission) or aged between >3 and ≤ 16 years (n = 2404 at admission), who were receiving mechanical ventilation, measured during the first week following intensive care unit admission: There were similar trends in plateletcrit over time between survivors and non-survivors in both patient age groups

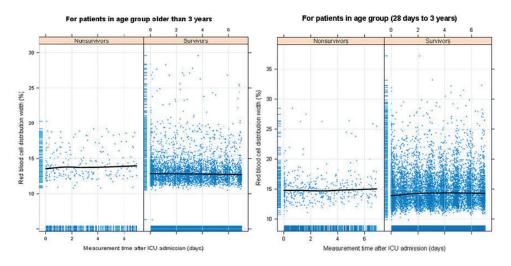


Figure 5. Scatter plots showing trend in red blood cell distribution width (RDW) between survivors and non-survivors in paediatric patients aged 28 days to 3 years (n = 2319 at admission) or aged between >3 and ≤ 16 years (n = 2404 at admission), who were receiving mechanical ventilation, measured during the first week following intensive care unit admission: There was no observable difference in RDW trends between survivors and non-survivors in either patient age group

in critically ill patients, but subsequent MPV values following admission may be useful in predicting mortality.^{15,18} A previously published study found that PDW was increased in neonates with late onset sepsis,³⁶ and higher MPV and PDW values have been reported in non-survivor preterm infants with sepsis.³⁷ One study found no correlation between mortality and MPV, determined in the first h of PICU admission, but an increase in MPV values following PICU admission was correlated with higher hospital mortality.³⁸ Of note, the present study found that the MPV value decreased slightly in the first 72 h, followed by an increase up to day 7, and the PDW increased during the first 48 h in non-surviving patients aged > 3 years. Among patients aged 28 days to 3 years, however, the MPV value in non-survivors only showed a minimal decrease then increase over 7 days, and the PDW value increased over the first 96 h. Platelet count, plateletcrit, and RDW displayed no obvious differences in change, however, between survivors and non-survivors in children of either age group. Thus, the present authors suggest that subsequent MPV and PDW values following admission may be related to mortality in critically ill children receiving mechanical ventilation, and this should be investigated further.

The results of the present study may be limited by several factors. First, the study was retrospective, and because of data limitations, factors such as duration of mechanical ventilation, ventilator setting parameters, duration of ICU stay, and other factors that affect mortality were not acquired. Secondly, although risk factors for death were found to vary between the different age groups, receiver operating characteristic curves were not used to establish the predictive value of each studied parameter for mortality. Thirdly, many factors may affect mortality in mechanically ventilated children, and a larger sample size is needed to better investigate mortality risk. Finally, dynamic MPV and PDW in non-survivors was found to increase slightly in both cohorts during the first week following PICU admission, however, this trend may only be a phenomenon of assay variability, or normal variability within the study population. The strengths of the present study include the following: the study was conducted in a children's hospital, and provides the first analysis of the influence of platelet parameters on mortality in children receiving mechanical ventilation, revealing that platelet parameters may have different clinical significance in critically ill children of different ages. As the children in the present study were divided into two cohorts based on age, it was shown that mortality in different age groups may be affected by different factors. The present authors suggest that clinicians should monitor the relevant clinical indicators according to patient age.

In conclusion, this single-centre, retrospective, cohort study revealed that risk factors for mortality in critically ill children may differ at different ages. Increased lactic acid levels appear to be the main risk factor for mortality in all critically ill children, and platelet count was found to be associated with mortality in patients aged > 3 years only. No association was found between platelet volume indices on PICU admission and mortality in critically ill children receiving mechanical ventilation, however, subsequent MPV and PDW values following admission may be related to mortality in patients aged < 16 years. A larger prospective study is needed to further investigate these factors, and the age of the child should be taken into consideration when evaluating mortality risk.

Acknowledgments

The authors would like to thank Dr Yugang and his colleagues in the Department of Information Section of the Children's Hospital, Zhejiang University School of Medicine, for enabling data collection to support this study.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

Funding

Sheng Ye received grants from the Zhejiang Medical and Health Science and Technology Plan Project (2007 B119), the Zhejiang Medical and Health Science and Technology Plan Project (2012 KYB119), and the Natural Science Foundation of Zhejiang Province (LY12 H19006).

References

- 1. Krmpotic K and Lobos AT. Clinical profile of children requiring early unplanned admission to the PICU. *Hosp Pediatr* 2013; 3: 212–218.
- Horowitz IN and Tai K. Hypoalbuminemia in critically ill children. *Arch Pediatr Adolesc Med* 2007; 161: 1048–1052.
- Leite HP, Rodrigues da Silva AV, de Oliveira Iglesias SB, et al. Serum albumin is an independent predictor of clinical outcomes in critically ill children. *Pediatr Crit Care Med* 2016; 17: e50–e57.
- 4. Vincent JL, Quintairos E Silva A, Couto L Jr., et al. The value of blood lactate kinetics in critically ill patients: a systematic review. *Crit Care* 2016; 20: 257.
- Bai Z, Zhu X, Li M, et al. Effectiveness of predicting in-hospital mortality in critically ill children by assessing blood lactate levels at admission. *BMC Pediatr* 2014; 14: 83.
- Poddar B, Gurjar M, Singh S, et al. Reduction in procalcitonin level and outcome in critically ill children with severe sepsis/septic shock-a pilot study. *J Crit Care* 2016; 36: 230–233.
- Li Y, Bai Z, Li M, et al. U-shaped relationship between early blood glucose and mortality in critically ill children. *BMC Pediatr* 2015; 15: 88.
- Nayak PP, Davies P, Narendran P, et al. Early change in blood glucose concentration is an indicator of mortality in critically ill

children. *Intensive Care Med* 2013; 39: 123–128.

- 9. Raman S, Prince NJ, Hoskote A, et al. Admission PaO2 and mortality in critically ill children: a cohort study and systematic review. *Pediatr Crit Care Med* 2016; 17: e444–e450.
- Bechard LJ, Duggan C, Touger-Decker R, et al. Nutritional status based on body mass index is associated with morbidity and mortality in mechanically ventilated critically ill children in the PICU. *Crit Care Med* 2016; 44: 1530–1537.
- Singhal D, Kumar N, Puliyel JM, et al. Prediction of mortality by application of PRISM score in intensive care unit. *Indian Pediatr* 2001; 38: 714–719.
- 12. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the working group on sepsis-related problems of the European society of intensive care medicine. *Intensive Care Med* 1996; 22: 707–710.
- Akca S, Haji-Michael P, de Mendonca A, et al. Time course of platelet counts in critically ill patients. *Crit Care Med* 2002; 30: 753–756.
- Gao YX, Li Y, Yu XZ, et al. The impact of various platelet indices as prognostic markers of septic shock. *PLoS One* 2014; 9: e103761.
- Kim CH, Kim SJ, Lee MJ, et al. An increase in mean platelet volume from baseline is associated with mortality in patients with severe sepsis or septic shock. *PLoS One* 2015; 10: e0119437.
- 16. Kutlucan L, Kutlucan A, Basaran B, et al. The predictive effect of initial complete blood count of intensive care unit patients on mortality, length of hospitalization, and nosocomial infections. *Eur Rev Med Pharmacol Sci* 2016; 20: 1467–1473.
- Sezgi C, Taylan M, Kaya H, et al. Alterations in platelet count and mean platelet volume as predictors of patient outcome in the respiratory intensive care unit. *Clin Respir J* 2015; 9: 403–408.
- Tajarernmuang P, Phrommintikul A, Limsukon A, et al. The role of mean platelet volume as a predictor of mortality in

critically ill patients: a systematic review and meta-analysis. *Crit Care Res Pract* 2016; 2016: 4370834.

- Zhang S, Cui YL, Diao MY, et al. Use of platelet indices for determining illness severity and predicting prognosis in critically ill patients. *Chinese Med J (Engl)* 2015; 128: 2012–2018.
- Zhang Z, Xu X, Ni H, et al. Platelet indices are novel predictors of hospital mortality in intensive care unit patients. *J Crit Care* 2014; 29: 885.e1–6.
- Rosas-Cabral A, Viana-Rojas JA, Prieto-Macias J, et al. The association between red cell distribution width (RDW) and short-term mortality risk in patients with acute coronary syndrome (ACS). *Gac Med Mex* 2016; 152: 70–77 [In Spanish, English abstract].
- 22. Joshi S and Whiteheart SW. The nuts and bolts of the platelet release reaction. *Platelets*, 2017; 28: 129–137.
- 23. Suades R, Padro T and Badimon, L. The role of blood- borne microparticles in inflammation and hemostasis. *Semin Thromb Hemost* 2015; 41: 590–606.
- 24. Pinheiro de Oliveira R, Hetzel MP, dos Anjos Silva M, et al. Mechanical ventilation with high tidal volume induces inflammation in patients without lung disease. *Crit Care* 2010; 14: R39.
- 25. Foglia E, Meier MD and Elward A. Ventilator-associated pneumonia in neonatal and pediatric intensive care unit patients. *Clin Microbiol Rev* 2007; 20: 409–425.
- 26. Zhang Z. Univariate description and bivariate statistical inference: the first step delving into data. *Ann Transl Med* 2016; 4: 91.
- Zhang Z. Variable selection with stepwise and best subset approaches. *Ann Transl Med* 2016; 4: 136.
- Cartin-Ceba R, Kojicic M, Li G, et al. Epidemiology of critical care syndromes, organ failures, and life-support interventions in a suburban US community. *Chest* 2011; 140: 1447–1455.
- 29. Shah SK, Kabra SK, Gupta N, et al. Vitamin D deficiency and parathyroid response in critically-ill children: association

with illness severity and clinical outcomes. *Indian Pediatr* 2016; 53: 479–484.

- Ross PA, Newth CJ, Leung D, et al. Obesity and mortality risk in critically ill children. *Pediatrics* 2016; 137: e20152035.
- Farias JA, Fernaíndez A, Monteverde E, et al. Mechanical ventilation in pediatric intensive care units during the season for acute lower respiratory infection: A multicenter study. *Pediatr Crit Care Med* 2012; 13: 158–164.
- 32. Zampieri FG, Ranzani OT, Sabatoski V, et al. An increase in mean platelet volume after admission is associated with higher mortality in critically ill patients. *Ann Intensive Care* 2014; 4: 20.
- 33. Golcuk Y, Golcuk B, Bilge A, et al. Combination of mean platelet volume and the CURB-65 score better predicts 28-day mortality in patients with communityacquired pneumonia. *Am J Emerg Med* 2015; 33: 648–652.
- 34. İşgüder R, Ceylan G, Ağın H, et al. Increased mean platelet volume in children with sepsis as a predictor of mortality. *Turk J Pediatr* 2016; 58: 503–511.
- 35. Tekbas E, Kara AF, Ariturk Z, et al. Mean platelet volume in predicting shortand long-term morbidity and mortality in patients with or without ST-segment elevation myocardial infarction. *Scand J Clin Lab Invest* 2011; 71: 613–619.
- Patrick CH and Lazarchik J. The effect of bacteremia on automated platelet measurements in neonates. *Am J Clin Pathol* 1990; 93: 391–394.
- Catal F, Tayman C, Tonbul A, et al. Mean platelet volume may simply predict the severity of sepsis in preterm infants. *Clin Lab* 2014; 60: 1193–1200.
- Erdogan S, Oto A and Bosnak M. The relation between mean platelet volume and mortality in critical pediatric patients. *Turk J Pediatr*.2015; 57: 605–610.
- Retamal J, Bergamini B, Carvalho AR, et al. Non-lobar atelectasis generates inflammation and structural alveolar injury in the surrounding healthy tissue during mechanical ventilation. *Critical Care* 2014; 18: 505.