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Pediatric Emergency Blood with Effect Transfusion and Prognosis

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Abstract

Background: The COVID-19 pandemic has led to a shortage of blood supplies for children, resulting in prolonged waiting times for transfusions. This study aims to explore the effect of timely blood transfusion on the effect and prognosis of blood transfusion in children during the COVID-19 pandemic. **Methods:** This retrospective cohort study included children who were indicated for blood transfusion in the Pediatric Emergency Department of Guangzhou Women and Children's Medical Center between January 2020 and December 2020. The outcomes were the effect and the final clinical outcomes of blood transfusion. **Results:** This study included 260 children with non-traumatic non-surgical low Hb: 209 with timely transfusion, 40 with delayed transfusion, and 11 without transfusion; 80% of children were below 60 g/L (min 17 g/L), and the waiting time for transfusion within 100.5 hours ($P < 0.001$ among the three groups). Among 249 patients receiving blood transfusions, overall efficiency was 33.33%. There were no differences in the change in Hb value after transfusion ($P = 0.205$). The Hb improvement refractory group received more washed red blood cell suspensions ($P = 0.044$), lower post-transfusion Hb values ($P < 0.001$), and a smaller change in Hb value ($P < 0.001$) compared with the successful group. Timely transfusion rates (70% vs. 86.6% $P = 0.009$) and post-transfusion Hb values were smaller (64 vs. 78 g/L, $P < 0.001$); the post-transfusion Hb threshold of hypoxia improvement was 61.5g/L [Sensitivity: 47.5%, Specificity: 90.4%, AUC: 0.737, $P < 0.001$]. **Conclusions:** During the 100-h waiting time, there were no significant differences in outcomes among the timely, delayed, and no transfusion groups. A timely blood transfusion may not affect the clinical outcomes of children.

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Keywords

COVID-19, Blood Banks, Transfusion, Pediatrics, Outcomes

1. Introduction

The novel coronavirus disease COVID-19 was declared a global pandemic on March 11, 2020. As of March 6, 2022, over 443 million cases, including over 5.9 million deaths, have been reported worldwide [1]. Besides the important patient morbidity and mortality [2], COVID-19 directly imposed an important strain on healthcare systems all over the world due to the increases in hospitalizations and intensive care unit (ICU) admissions and limited hospital space, staffing, and supplies [3]. In addition, indirect strains of COVID-19 on healthcare systems and public health included delayed or even suspended disease screening programs, preventive and elective treatments, and anxiety and depression [4]. Patients with non-absolutely-emergent symptoms avoided hospitals because of fear of catching the disease, leading to a decrease in emergency department visits of 23% for myocardial infarction, 20% for stroke, and 10% for diabetic emergencies in the United States of America [4].

Another indirect strain of COVID-19 on healthcare resources was a sharp decrease in blood resources worldwide. Indeed, many countries implemented lockdowns and curfews during which citizens were strictly forbidden to leave their homes except for essential workers, seeking healthcare, or buying essential supplies [5]. Furthermore, even when allowed to leave their home, many people chose not to because of the fear of getting COVID-19 [6]. These factors directly led to a decrease in unpaid blood donations worldwide [7], including in China [8].

The blood supply has been seriously affected, leading to blood shortages in emergency departments, including pediatrics [9]. Children will require blood component transfusions for a wider variety of medical conditions, including acute hemorrhage, surgeries, cancers, hematological diseases, and stem cell transplants [10]. Delayed or lacking blood transfusion can affect the prognosis of pediatric patients [11].

Still, the impact of the blood supply shortage on pediatric patient outcomes is poorly documented. Therefore, this study aimed to explore the effect of timely blood transfusion on the effect and prognosis of blood transfusion in children in a state of strained blood bank resources during the COVID-19 pandemic.

2. Material and METHODS

Study design and patients

This retrospective cohort study included children who presented to the Pediatric Emergency Department of Guangzhou Women and Children's Medical Center (Zhujiang New Town Branch) between January 2020 and December 2020 and applied for blood transfusion. The inclusion criteria were 1) patients with hemoglobin

(Hb) < 70 g/L, accompanied by clinical symptoms of ischemia, and issuing a blood transfusion application form [12] [13] and 2) from 1 month to 18 years of age. The exclusion criteria were 1) loss of blood due to acute traumatic surgery, or 2) blood transfusion for preparing for surgery. This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. The study was approved by the Ethics Committee of Guangzhou Women and Children Medical Center (No. 251A01). The requirement for patients' informed consent was waived due to the retrospective nature of the study.

Data collection and definition

Detailed demographic and clinical characteristics at admission and hematologic indicators of included patients were extracted from the structured electronic medical records system (EMRS). The demographic and clinical data of the patients were collected, mainly including age, sex, weight, waiting time for transfusion, pretransfusion Hb levels, posttransfusion Hb levels, Hb levels at the time of leaving the emergency department, changes in Hb, and red blood cell suspension amount and type.

The overall effect of blood transfusion was defined as the Hb rose to the expected value within 24 h after red blood cell transfusion, and hypoxia caused by anemia was improved. The expected value was calculated as:

Expected value of hemoglobin rising (g/L) = (Hb of donor (g/L) × Input volume (L))/(Weight of patients (kg) × 0.09 (L/kg)) × 90% [(donor's hemoglobin × blood input volume)/(patient's weight × 0.09)] × 90%. The input volume was based on whole blood, and the red blood cell preparation was approximately equal to the whole blood volume [14]. The symptoms of hypoxia include heart rate and respiratory rate increased above normal levels and/or the SpO_2 being below 90% [15].

The outcome was the clinical outcomes of this emergency department visit, such as death, heart failure, respiratory failure, shock, bleeding, etc., as poor clinical outcomes. Otherwise, the outcome was considered good. The studies showed that the mortality of critically ill children in Africa without blood transfusion in 8 hours was 15.7% [16], and ICU patients in the United States transfused later (24-48 h) were more likely to die [17]. We defined waiting more than 12 hours for blood transfusion as delayed blood transfusion based on safety and variability greater than the smallest node of waiting time (5 hours) in this study. According to the actual time of blood transfusion after applying for blood transfusion, the patients were divided into the timely blood transfusion group, the delayed blood transfusion group, which received a blood transfusion more than 12 hours after the application was issued, and the no blood transfusion group. According to the above two criteria of transfusion effectiveness, the patients were divided into Overall efficiency (Hb increased to the expected level with the improvement of hypoxia) and Overall invalidity group (Hb elevation did not reach the expected value and/or the hypoxia did not improve); Hb improved effective (Successful transfusion group) and ineffective group (Refractory transfusion group); hypoxia improved and no improved group.

Statistical analysis

Data were expressed as mean±SD for normally distributed variables, median (IQR) for non-normally distributed variables, and number (percentage) for categorical variables. The normality of the data distribution was examined by using the Kolmogorov-Smirnov tests. Baseline characteristics, transfusion profile, and outcomes were compared between different groups using the Mann-Whitney U-Test and Chi-square/Fisher's exact test to detect any differences. Logistic regression models were used to estimate the odds ratio (OR) and 95% confidence intervals (CIs) for improved hypoxia in different characteristics comparisons. The Receiver Operating Characteristic (ROC) Curve was also adopted to assess the predictive factors for hypoxia improvement in patients with transfusion. A two-sided P-value of < 0.05 was regarded as statistically significant. Data management and statistical analyses were conducted using SPSS 26.0 software.

3. Results

Baseline characteristics

A total of 260 pediatric patients with anemia and hypoxia were enrolled, whose baseline hemoglobin values were all below 70 g/L, in which 12% of children were below 40 g/L and 68% were below 60 g/L. The top five causes of blood transfusions were solid tumors, leukemia, aplastic anemia, hemolytic anemia, and cytopenias due to early complications of hematopoietic cell transplantation. As expected, the waiting time for transfusion was longer in the delayed group and the no transfusion group, compared with the timely group (38.6 ± 20.6 and 32.7 ± 18.6 vs. 4.3 ± 2.7 h, P < 0.001), and the waiting time for transfusion was within 100.5 hours. Except for two patients whose Hb values decreased by 2 and 3 g/L, respectively, the rest were maintained at the original level or increased to varying degrees in no transfusion patients (2.55 ± 4.2 g/L) until discharge from the emergency department. There were no differences in age, sex, weight, and baseline hemoglobin values among the three groups with different waiting times for transfusion, P = 0.914, 0.093, 0.945, and 0.208, respectively (**Table 1**).

Transfusion effectiveness

Overall efficiency

Among 249 patients receiving blood transfusions, overall efficiency was 33.33%. Compared with the overall effective group, the post-transfusion and expected increase in Hb value and hypoxia improvement rate were lower in the invalid group (all P < 0.001) (**Table 2**).

Hb improved efficiency

The Hb value successfully reached the expected level in 37.35% of patients, including 37.8% in the timely group and 35.0% in the delayed group (P = 0.737). There were no differences between the timely and delayed groups regarding the type of red blood cell suspension (P = 0.111) or the amount of suspension (P = 0.827), and no differences in the change in Hb value after transfusion (P = 0.205)

Table 1. Baseline characteristics and outcomes in patients with different timing of blood transfusion.

Characteristic	Timely transfusion (n = 209)	Delayed transfusion (n = 40)	No transfusion (n = 11)	P
Age, years, mean ± SD	6.1 ± 4.3	6.4 ± 4.1	5.9 ± 2.9	0.914
Sex, n (%)				0.093
Male	128 (61.2)	28 (70.0)	10 (90.9)	
Female	81 (38.8)	12 (30.0)	1 (9.1)	
Weight, kg, mean ± SD	20.2 ± 11.7	20.2 ± 9.4	21.4 ± 8.4	0.945
Waiting time for transfusion, hours, mean ± SD	4.3 ± 2.7	38.6 ± 20.6[a]	32.7 ± 18.6[*b]	**<0.001**
Baseline hemoglobin values, g/L, mean ± SD	53.44±10.06	52.85±5.94	58.36±2.01	0.208
Changes in hemoglobin values, g/L, mean ± SD	23.93 ± 16.39	20.48 ± 14.09	2.55 ± 4.2	0.205[c]
RBC suspension, U, mean ± SD	1.14 ± 0.44	1.13 ± 0.37	-	0.827
Type of RBC suspension, n (%)				0.111
RBC suspension	190 (90.9)	33 (82.5)	-	
Washed RBC suspension	19 (9.1)	7 (17.5)	-	
Hb improved efficacy, n (%)				0.737
Successful transfusion	79 (37.8)	14 (35.0)	-	
Refractory transfusion	130 (62.2)	26 (65.0)	-	
Hypoxia improved efficacy, n (%)				**0.009**
No-improved	28 (13.4)	12 (30.0)		
Improved	181 (86.6)	28 (70.0)		
Outcomes, n (%)				0.886
Favorable clinical outcome	208 (99.5)	40 (100)	10 (100)	
Not favorable clinical outcome	1 (0.5)	0	0	

*Length of stay in the emergency room without transfusion. RBC: red blood cell.
[a]Comparison of timely blood transfusion group and delayed blood transfusion group, P<0.001; [b] comparison of the timely blood transfusion and no blood transfusion groups, P<0.001; [c] comparison of the hemoglobin changes in the timely blood transfusion and delayed blood transfusion groups.

Table 2. Baseline characteristics and outcomes in patients with or without overall effective transfusion.

Characteristic	Overall invalidity (n = 166)	Overall efficiency (n = 83)	P
Age, years	5 (6)	5 (7)	0.821
Male (%)	100 (60.2)	56(67.5)	0.266
Weight, kg	16.1(13.0)	17.0 (15.9)	0.365
Malignant/Pernicious diseases (%)	111 (66.9)	52 (62.7)	0.509
Fever (%)	36 (21.7)	16 (19.3)	0.659
Waiting time for transfusion, hours	4.29 (4.9)	3.73(4.2)	0.103
RBC suspension, U	1 (0.6)	1 (0.0)	0.106
Type of RBC suspension (%)			0.065

Continued

RBC suspension	143 (86.1)	78 (94.0)	
Washed RBC suspension	23 (13.9)	5 (17.9)	
Pre-transfusion hemoglobin values, g/L	56.5 (11)	54 (11)	0.425
Post-transfusion hemoglobin values, g/L	73 (17)	85 (18)	**<0.001**
Outcomes			
Timely transfusion (%)	138 (83.1)	71 (85.5)	0.625
Hypoxia improved (%)	126 (75.9)	83 (100)	**<0.001**
Expected changes in hemoglobin values (%)	10 (6.0)	83 (100)	**<0.001**
Favorable clinical outcome (%)	165 (99.4)	83 (100)	1.000

Data are presented as median (IQR) or n (%). Significant values are showing in bold.
Abbreviations: RBC, red blood cell.

(Table 1). There were no differences between the successful and refractory groups regarding age, sex, weight, pernicious anemia, fever, waiting time, pre-transfusion Hb values, suspension amount, and timely transfusion or not (all P > 0.05), but the refractory group received more washed red blood cell suspensions (13.5% vs. 5.4%, P = 0.044), the post-transfusion Hb values were lower (median, 73 vs. 84 g/L, P < 0.001), and the change in Hb value was smaller (median, 18 vs. 30 g/L, P < 0.001) (Table 3). However, no relevant factors were found by analyzing the associations of different baseline characteristics with refractory (all P > 0.05) (Table 4).

Hypoxia improved efficiency

Hypoxia caused by anemia was improved in 83.94% of the patients after blood transfusion. There were significant differences between the improved and no-improved groups regarding age, weight, and post-transfusion Hb values (all P < 0.001), and sex and timely transfusion also had significant differences (P = 0.031 and 0.009, respectively) (Table 5). Predictive factors with hypoxia improved, age, weight, timely transfusion, and post-transfusion Hb values had significant differences (P = 0.001, 0.024, 0.027, and 0.002, respectively) (Table 6). Combined with ROC curve analysis, it showed that older age and larger weight were unfavorable factors for the improvement of hypoxia. The threshold value of the former was 10.5 years old [Sensitivity: 52.5%, Specificity: 85.6%, AUC (95%CI): 0.731(0.641, 0.821), P < 0.001], and the latter was 18.95 kg [Sensitivity: 60.5%, Specificity: 65.6%, AUC (95%CI): 0.678(0.594, 0.762), P < 0.001]. In contrast, timely blood transfusion and high post-transfusion Hb value were favorable factors for hypoxia improvement, and the threshold of post-transfusion Hb value was 61.5 g/L [Sensitivity: 47.5%, Specificity: 90.4%, AUC (95%CI): 0.737 (0.647, 0.826), P < 0.001] (Figure 1). Figure 2 showed that, for blood transfusion, age was an unfavorable factor for hypoxia improvement (OR = 0.73 and P = 0.01), indicating that the probability of hypoxia improvement decreased by 27% for every 1-year increase in age; timely blood transfusion (OR = 2.86 and P = 0.027) was a favorable factor, and there was no gender correlation (OR = 0.69 and P = 0.318); the post-transfusion Hb value (OR = 1.05 and P = 0.02) is a favorable factor, for every

Table 3. Characteristics and outcomes of the patients, according to Hb, improved successfully vs. refractory.

Characteristic	Successful (n = 93)	Refractory (n = 156)	P
Age, years, median (IQR)	6 (7)	4.5 (6)	0.321
Sex, male, n (%)	62 (66.7)	94 (60.3)	0.312
Weight, kg, median (IQR)	17 (17)	16 (11.8)	0.128
Pernicious anemia, n (%)	61 (65.6)	102 (65.4)	0.974
Fever, n (%)	14 (15.1)	27 (17.3)	0.643
Waiting time for transfusion, hours, median (IQR)	3.78 (4.0)	4.29 (4.9)	0.108
Pre-transfusion hemoglobin values, g/L, median (IQR)	54 (11)	56 (11)	0.342
RBC suspension, U, median (IQR)	1 (0)	1 (0)	0.423
Type of RBC suspension, n (%)			**0.044**
RBC suspension	88 (94.6)	135 (86.5)	
Washed RBC suspension	5 (5.4)	21 (13.5)	
Timely transfusion, n (%)	79 (85.0)	130 (83.3)	0.737
Post-transfusion hemoglobin values, g/L, median (IQR)	84 (18)	73 (17)	**<0.001**
Change in hemoglobin values, g/L, median (IQR)	30 (17)	18 (13.5)	**<0.001**
Favorable clinical outcome	93 (100)	155 (99.36)	0.439

Table 4. Associations of different baseline characteristics with refractory.

Characteristic	Crude OR (95% CI)	P
Timely transfusion (vs. Delayed transfusion)	0.89 (0.44-1.80)	0.738
Age, years	0.97 (0.91-1.03)	0.273
Male sex (vs. Female sex)	0.76 (0.44-1.30)	0.312
Weight, kg	0.98 (0.96-1.00)	0.095
Pernicious anemia	0.99 (0.58-1.70)	0.974
Fever	1.18 (0.58-2.39)	0.643
Waiting time for transfusion, hours	1.01 (0.99-1.02)	0.562
Pre-transfusion hemoglobin values, g/L	1.01 (0.99-1.04)	0.360
RBC suspension, U	0.72 (0.39-1.31)	0.275
Washed RBC suspension (vs. RBC suspension)	2.74 (0.99-7.53)	0.051

Significant values are showing in bold.
Abbreviations: OR, odds Ratio; CI, confidence interval; RBC, red blood cell.

Table 5. Baseline characteristics and outcomes in patients with or without improved hypoxia.

Characteristic	no Hypoxia improved (n = 40)	Hypoxia improved (n = 209)	P
Age, years	11 (9)	4 (5)	**<0.001**
Male (%)	19 (47.5)	137 (65.6)	**0.031**
Weight, kg	23.0 (21.5)	16.0 (13.4)	**<0.001**

Continued

Malignant/Pernicious diseases (%)	28(70.0)	135 (64.6)	0.510
Fever (%)	11 (27.5)	41 (19.6)	0.261
Waiting time for transfusion, hours	4.18 (21.37)	4.13 (4.26)	0.885
RBC suspension, U	1 (1.0)	1 (0.5)	0.207
Type of RBC suspension (%)			0.172
RBC suspension	33 (82.5)	188 (90.0)	
Washed RBC suspension	7 (17.5)	21 (10.0)	
Pre-transfusion hemoglobin values, g/L	53.5 (14)	56.0(10)	0.101
Post-transfusion hemoglobin values, g/L	64.0 (23)	78.0 (18)	**<0.001**
Outcomes			
Timely transfusion (%)	28 (70.0)	181 (86.6)	**0.009**
Expected hemoglobin values (%)	10 (25.0)	83 (39.7)	0.078
Favorable clinical outcome (%)	40 (100.0)	209 (100.0)	1.000

Data are presented as median (IQR) or n (%). Significant values are showing in bold.
Abbreviations: RBC, red blood cell.

Table 6. Predictive factors with hypoxia improved in patients with transfusion.

Characteristic	Crude OR (95% CI)	P	Adjusted OR (95% CI)	P
Age	0.82 (0.76-0.89)	<0.001	0.73 (0.60-0.87)	**0.001**
Male	0.48 (0.24-0.94)	0.033	0.69 (0.30-1.48)	0.318
Weight	0.96 (0.93-0.98)	0.002	1.08 (1.01-1.16)	**0.024**
Timely transfusion	2.77 (1.26-6.07)	0.011	2.86 (1.13-7.26)	**0.027**
Post-transfusion hemoglobin values	1.06 (1.04-1.09)	<0.001	1.05 (1.02-1.08)	**0.002**

Significant values are showing in bold.
Abbreviations: OR, odds Ratio; CI, confidence interval; RBC, red blood cell.

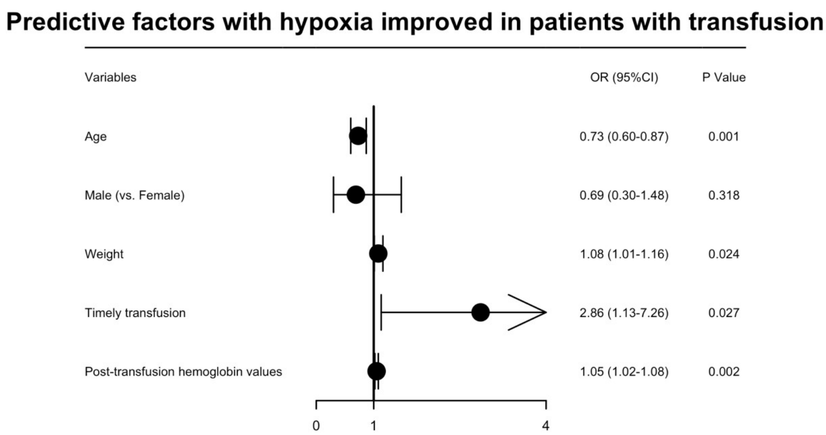

Figure 1. **A: ROC curves of age for hypoxia improved in patients with transfusion.** Cutoff: 10.5; Sensitivity: 52.5%, Specificity: 85.6%; AUC (95%CI): **0.731**(0.641, 0.821) P < 0.001; **B: ROC curves of weight for hypoxia improved in patients with transfusion.** Cutoff: 18.95; Sensitivity: 65.0%, Specificity: 65.6%; AUC (95%CI): 0.678 (0.594, 0.762) P < 0.001; **C: ROC curves of post-transfusion hemoglobin values for hypoxia improved in patients with transfusion.** Cutoff: 61.5; Sensitivity: 47.5%, Specificity: 90.4%; AUC (95%CI): **0.737** (0.647, 0.826) P = 0.046.

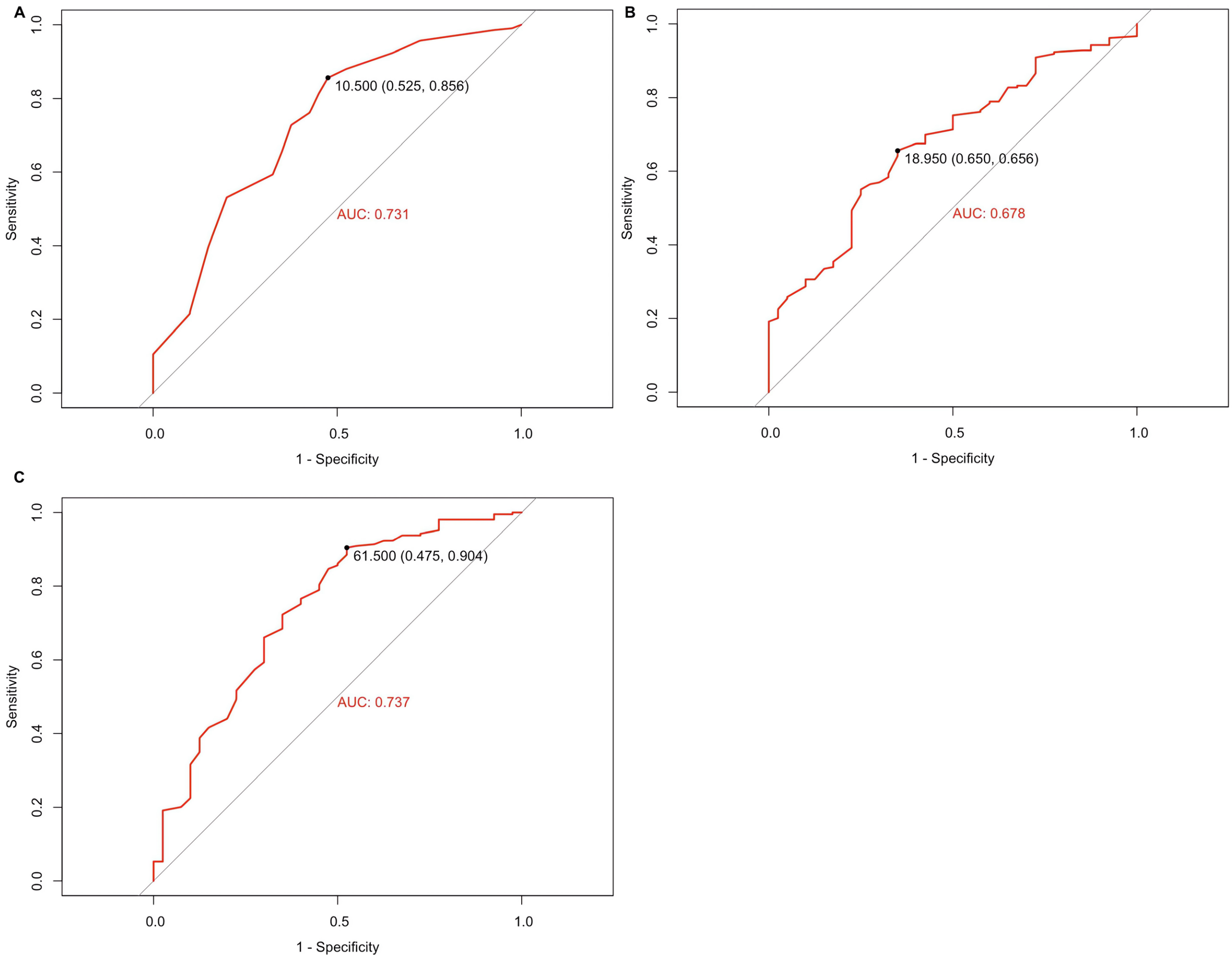

Figure 2. Forestpolt of predictive factors with hypoxia improved in patients with transfusion.

1 g/L increase in Hb, the probability of hypoxia improvement increases by 5%; similarly, for every 1 kg of weight loss (OR = 1.08 and P = 0.024), the probability of hypoxia improvement increases by 8%.

The outcome of this visit

Only one patient whose cause of death was heart failure secondary to myocardial damage in the timely transfusion group had an unfavorable outcome (P = 0.886 among the three groups) (Table 1). There were no differences in outcomes between the Hb-improved successful and refractory groups, hypoxia improved, and no-improved groups also (P = 0.439 and 1.000 respectively) (Table 3 and Table 5). In this study, no relevant factor could be found from the baseline characteristics with the outcome (all P > 0.05).

4. Discussion

There were no differences in the change in Hb value after transfusion. Only one patient in the timely transfusion group had an unfavorable outcome. There were no differences in outcomes among different groups despite indications for transfusion.

Red blood cells transfusion threshold in children

The restrictive red blood cell (RBC) transfusion threshold for adult inpatients recommended by the AABB in 2018 was Hb level ≤ 70 g/L, including critically ill patients [12]. The exploration of blood transfusion thresholds for different diseases, including sepsis shock, cardiac surgery, tumors, etc., was carried out in the range of Hb 70 to 100 g/L [18]. For ethical reasons, prospective clinical cohort studies with lower transfusion thresholds would be hard. However, the COVID-19 pandemic has led to a shortage of blood supply, and patients in need cannot obtain blood transfusions in time. China had also been affected by the 2020 COVID-19 epidemic, and blood donation in Guangzhou decreased by 10% compared with 2019 [19], while we had the opportunity to observe the effect of lower transfusion thresholds and longer waiting transfusion time on clinical outcomes of children in passive randomized during the pandemic.

There are pros and cons of red blood cell transfusion in each patient. In the setting of acute uncontrollable hemorrhage, red blood cell transfusion frequently saves lives [20]. This common understanding is based on strong clinical experience, albeit on weak study evidence, because denying transfusions in a life-threatening condition for the sake of a trial would be undoubtedly unethical. Studies have shown that minimalized transfusion through an institutional PBM—for example, lowering the transfusion threshold below 7 g/dL—can positively affect the prognosis of patients who are receiving chemotherapy for advanced colorectal cancer [21]. In our study, 80% of patients' pre-transfusion hemoglobin values were below 60 g/L, which is lower than the restrictive RBCs transfusion threshold for adult inpatients recommended by the AABB. Due to the influence of multiple factors, such as the type of RBCs transfused, the post-transfusion Hb value did not reach the expected level in most patients. Even so, in these patients, the hypoxia caused by anemia was still improved and had a good outcome. By analyzing the post-transfusion Hb value that improved hypoxia, we found that the threshold for hypoxia improvement was Hb, reaching 61 g/L after blood transfusion. For most children with hematology-oncology diseases in our study, the transfusion threshold of 60 g/L is relatively safe, which was similar to another study in which children suffering from chronic anemia with Hb < 60 g/L were relatively stable [22]. In addition, a single transfusion threshold criterion is not suitable for all individuals, and personalized transfusion strategies are required to save lives while reducing unnecessary blood consumption and transfusion complications. Therefore, retrospective data on large samples can be collected in multiple centers or further studied through meta-analysis to adjust the criteria for restrictive transfusion according to the individual's different tolerance to hypoxic ischemia or disease, such as increasing the urgency weight of transfusion in the event of acute blood loss. A review by Mo & Delaney [10] highlighted the need for evidence-based criteria for managing blood transfusion in children. The evidence from trials in adults is often applied to children, which might be improper [23]. In addition, the available trials suffer from important biases [24].

Timing of RBCs transfusion in children

It has been shown that delays in obtaining blood products contribute to hypovolemia in the acute trauma setting and cardiac arrest in children [25]. In the surgical setting, the age of the children (even small blood loss will be more significant in younger children than in older ones) and the nature of the surgery will affect the need for blood transfusion [26]. In addition, even if Hb levels are often used as an indication for transfusion, anemia is more easily tolerated than hypovolemia [27]. In the present study, the amount of red blood cells was similar between the two transfusion groups, and the Hb change was also similar between the two groups. When considering all three groups, there were no differences in the occurrence of poor outcomes among the timing groups. Of course, the group of patients without transfusion was small, introducing a bias. Nevertheless, the results indicate that the timing of transfusion or receiving a transfusion did not affect the outcomes in children in the emergency department. Nevertheless, it is worth noting that timely blood transfusion was a favorable factor for hypoxia improvement; therefore, the waiting time for blood transfusion cannot be extended indefinitely. The longest waiting time for blood transfusion of the patients in this study was 100.5 hours. During this time, there was no difference between the timely and the delayed groups in terms of blood transfusion volume and post-transfusion Hb level. Except for two patients whose Hb values decreased by 2 and 3 g/L, respectively, the rest were maintained at the original level or increased to varying degrees in no transfusion patients (2.55 ± 4.2 g/L) until discharge from the emergency department. The exact indications for transfusion might be inappropriate for all children. For children whose blood transfusion application has been unsuccessful for more than 12 hours, it is necessary to dynamically review the hemoglobin level, especially after the delay. Re-examination of the blood routine before blood transfusion will help to judge whether to carry out the transfusion order and accurately evaluate the blood transfusion effect.

In our study, transfusion decisions were based on several key criteria, including hemoglobin levels below 7 - 8 g/dL, the presence of specific clinical symptoms, and other relevant clinical assessments. We followed the blood management protocols established by Guangzhou Women and Children's Medical Center, which outlined the process for transfusions under these indications.

Moreover, during the COVID-19 pandemic, we implemented adjustments to our blood management strategies, such as specific adjustments, to address specific challenges brought by the pandemic. These measures ensured that we continued to deliver safe and timely transfusion services to patients during this period.

Influencing factors of blood transfusion effect

Blood transfusion effectiveness varies due to donor, component, and recipient factors [28]. Due to the shortage of blood supply in this study, the diversity of donors and the time of red blood cell inventory were both limited, and the recipients' overall effect of blood transfusion was mainly affected by the elevated Hb. The expected level of Hb improvement is calculated and does not always correspond to the magnitude of the actual state after transfusion due to effects such as changes in blood volume and destruction of allogeneic RBCs. The Hb-improved refractory group received more washed RBCs suspensions, which may be related to the destruction of the input-washed RBCs. Among these blood transfusion patients, the improvement rate of hypoxia after blood transfusion was much higher than the expected rate of Hb increase, and the improvement of hypoxia was more toward a good clinical outcome. At this level, hypoxia improvement may be more important for the clinical outcomes of transfusion children. In our blood transfusion study, larger age was an unfavorable factor for hypoxia improvement. Timely blood transfusion, lower weight, and the post-transfusion Hb value were favorable factors (**Figure 2**) that may be related to higher oxygen consumption in older and heavier children.

Considering the ethical implications of delayed transfusion and the necessity for personalized transfusion strategies involves several key aspects:

Ethical Implications of Delayed Transfusion

1. Patient Safety and Harm: Ethically, healthcare providers have a duty to avoid harm and ensure patient safety. Delayed transfusion can lead to adverse outcomes, such as exacerbated anemia or organ dysfunction, especially in vulnerable populations like children. Ensuring timely transfusion is crucial to prevent negative health impacts.

2. Informed Consent and Autonomy: Patients or their guardians should be fully informed about the benefits and risks of both receiving and delaying a transfusion. Respecting patient autonomy means allowing them to make decisions based on complete and understandable information.

3. Equity and Resource Allocation: During events like the COVID-19 pandemic, resource allocation becomes critical. Deciding who receives a limited blood supply raises ethical questions about fairness and equity, especially if delays are due to scarcity rather than clinical indication.

Necessity for Personalized Transfusion Strategies

1. Individual Health Needs: Every patient has unique health needs and may respond differently to anemia or transfusion. Personalized strategies consider individual factors such as underlying health conditions, severity of symptoms, and risk of transfusion reactions.

2. Optimizing Outcomes: Personalized transfusion strategies aim to optimize patient outcomes by tailoring treatment to individual circumstances. This approach can help improve recovery times and overall quality of care.

In summary, addressing the ethical and personalized aspects of transfusion decisions involves balancing timely medical interventions with respect to individual patient needs and broader ethical considerations. It's about delivering safe, equitable, and effective healthcare while respecting patient rights and optimizing resource use.

5. Limitations

This study has limitations. First, it was a retrospective study, prone to selection bias, and it was impossible to collect some influencing factors. Second, it was an observational study. Due to the small size of patients and cumbersome data, it is easily affected by subjective concepts. Third, the children had various types of diseases, and there may be selection bias. Fourth, the time for blood transfusion might be related to the supply of blood products on that day, which is an uncertain and force majeure factor. Finally, the judgment of clinical symptoms and clinical outcomes in outcome measures may be greatly influenced by the subjective concept.

In Conclusion, during the 100-h waiting time, there were no significant differences in outcomes among the timely, delayed, and no transfusion groups despite indications for transfusions, and the Hb value in 80% of patients was below 60 g/L. Timely blood transfusion or not may not affect the final clinical outcomes of this emergency department visit of children with non-traumatic, non-surgical children.

Author Contribution

Yanmei Song and Fang Yu collected data and wrote articles; Jing Sun and Guangming Liu conducted statistical analysis. Xiaowei Fan and Peiqing Li conducted clinical quality control; Daoju Jiang for image processing; Yumei Xiong and Haomei Yang modified the article; Xuan Shi conducted research design; Qiang Wang revised and reviewed the article. All authors read and approved the final manuscript.

Data Availability Statement

All data generated or analysed during this study are included in this published article.

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Ethics Approval Statement

This work has been carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association. The study was approved by the Ethics Committee of Guangzhou Women and Children Medical Center (No. 251A01). The requirement for patients' informed consent was waived due to the retrospective nature of the study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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