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Original Article

Patient blood management in pediatric cardiovascular surgery patients during the COVID-19 pandemic: Is it applicable?

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Abstract

Aim: To limit the spread of coronavirus disease (COVID-19), social isolation and reduced mobility have been recommended. However, this has led to the rapid depletion of blood stocks as people are afraid of catching the highly contagious disease. This study aimed to present blood management practices in pediatric cardiovascular surgery patients during the pandemic and the relationship between blood products and patient outcomes such as pediatric intensive care unit (PICU) stay and mortality.
Material and Methods: In this retrospective cohort study, we compared 201 patients who underwent pediatric cardiovascular surgery during the COVID-19 pandemic (11.03.2020-30.11.2020, pandemic group) with 206 patients operated during the same period in 2019 (pre-pandemic control group). We used R (version 4.2.2; R Core Team, R Foundation for Statistical Computing, Vienna, Austria) for statistical analysis. Continuous variables were presented as median and interquartile range or mean SD. Logistic regression predicted blood and blood product usage based on pre and postoperative time. Multivariable logistic regression was conducted with a p-value less than 0.10 for predicting mortality.
Results: In 2019 and 2020, 56% of patients who underwent surgery were male. The median age was 19.5 (5.4-92.6) months in 2019 and 10.3 (4.6-7.1) months in 2020, with a significant difference (p-value of 0.01). The RACHS score was higher in 2019 than 2020 (p-value < 0.001), and a similar percentage of patients required extracorporeal membrane oxygenation (ECMO) support in both years.
Conclusion: We continued to use patient blood management, which we started to use in the past as well. Patient Blood Management guidelines should be tailored to each centre to ensure optimal patient care based on needs and centre dynamics. Allogeneic transfusions pose a risk-benefit balance, and limited transfusions can benefit patients more significantly.

Keywords: Blood management, pediatric cardiovascular surgery, COVID-19

INTRODUCTION

The disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), first detected in Wuhan Province of China in December 2019, was diagnosed by the World Health Organization (WHO) on February 11, 2020, as coronavirus disease (COVID-19) and on March 11, 2020, this epidemic was declared as a pandemic (1). Although the SARS-CoV-2 pandemic infects more than 600 million people in the world today, our country's total number of cases has reached 16,671,848, and the number of lost patients has reached 100,000 (2).

In order to limit the spread of COVID-19, social isolation and reduced human mobility have been recommended as the main precautions. However, this has rapidly reduced blood stocks due to concerns about catching the virus and increasing infections and there is a need to evaluate the possibility of the virus threatening blood safety and take preventive measures. The incubation period of SARS-CoV-2 can range from 1-14 days (mean 3-5 days) and a reported maximum of 32 days (3).

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As COVID-19 continues to spread in communities, emergencies such as trauma, blood dyscrasias, and heart surgeries for adults and children still require transfusions.pediatric cardiovascular surgery (PCS) involves a significant risk of bleeding, thus requiring the use of allogeneic blood products. Several risk factors related to perioperative anemia and coagulopathy have been identified (4,5).

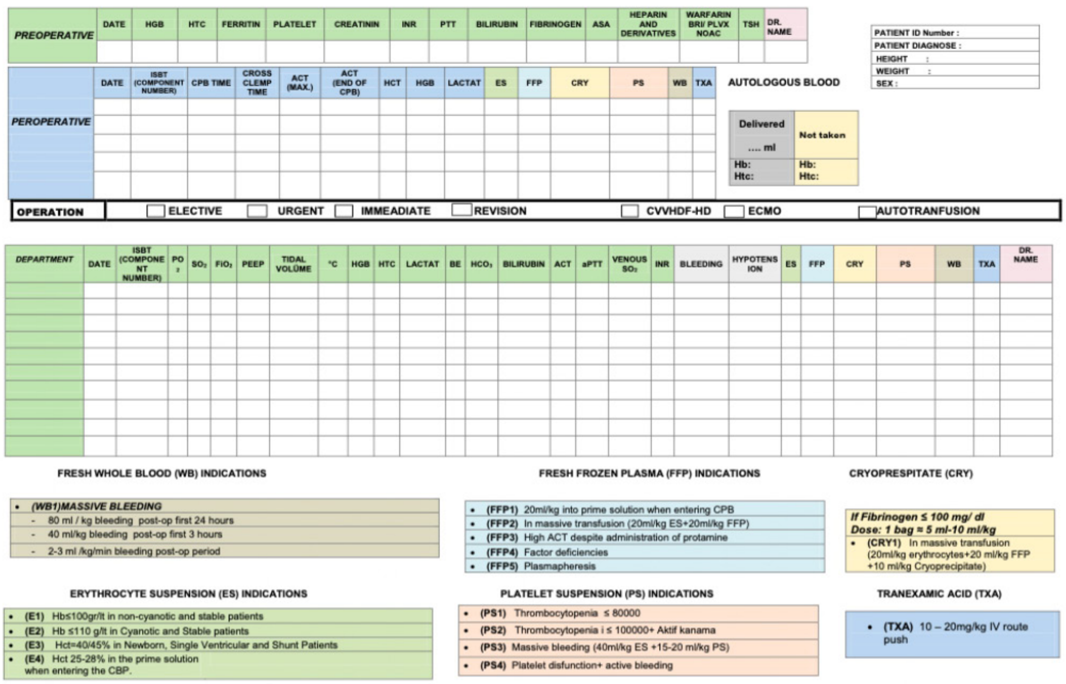
These mechanisms impact both adults and children, but the hemostatic system of pediatric patients differs significantly from that of adults. In cases of cyanotic heart disease, cardiopulmonary bypass (CPB) causes more hemodilution, and complex surgical procedures are often necessary (6). To address this, patient blood management (PBM) programs must optimize preoperative haemoglobin levels, minimize blood sampling, improve hemostasis, reduce bleeding, correct coagulopathy, and incorporate blood preservation techniques. These measures should also be applied to the pediatric cardiac surgery population, as they are in other medical fields (7).

In this study, we aimed to present our results of patient blood management practices in pediatric cardiovascular surgery patients during the COVID-19 pandemic and the relationship between the use of blood and blood products and pediatric intensive care unit (PICU) stay and mortality.

MATERIAL AND METHODS

Patient selection

This study was conducted at our institution, a tertiary referral center for adult and pediatric cardiovascular surgery with a total capacity of 450 beds, serving patients from across Türkiye. The center performs approximately 250 pediatric cardiac surgical procedures annually and includes a dedicated 12-bed pediatric cardiovascular intensive care unit. This retrospective study included 407 consecutive patients aged 0–18 years who underwent PCS. Of these, 201 underwent surgery between March 11 and November 30, 2020 (pandemic group), and 206 underwent surgery during the corresponding period in 2019 (pre-pandemic control group). Clinical, demographic, operative, and transfusion-related data were extracted from electronic hospital records and institutional blood bank and transfusion registries. We retrospectively collected data on various factors including age, gender, birth weight, type of operation, risk adjustment for congenital heart surgery (RACHS) scores preoperative hematocrit (Hct), PICU duration as well as erythrocyte suspension (ES), fresh whole blood (FWB), fresh frozen plasma (FFP), cryoprecipitate (CRY), and pooled platelet (HPLT) counts during the 48 hours before and after surgery. These variables, together with clinical outcomes (PICU stay, MV duration, and in-hospital mortality), were compared between the pandemic and pre-pandemic groups. All patients who underwent PCS during the COVID-19 pandemic were subject to the transfusion indications and threshold values found in our PBM form (Figure 1). Our study was conducted by the Helsinki Declaration and approved by the Kartal Koşuyolu Yüksek İhtisah Training and Research Hospital Clinical Research Ethics Committee (Desicion no: 2021/10/506, Date: 24.08.2021).



PREOPERATIVE	DATE	HGB	HTC	FERRITIN	PLATELET	CREATININ	INR	PTT	BILIRUBIN	FIBRINOGEN	ASA	HEPARIN AND DERIVATIVES	WARFARIN BRI/ PLVX NOAC	TSH	DR. NAME

PATIENT ID Number :
PATIENT DIAGNOSE :
HEIGHT :
WEIGHT :
SEX :

PEROPERATIVE	DATE	ISBT (COMPONENT NUMBER)	CPB TIME	CROSS CLEMP TIME	ACT (MAX.)	ACT (END OF CPB)	HCT	HGB	LACTAT	ES	FFP	CRY	PS	WB	TXA

AUTOLOGOUS BLOOD

Delivered .... ml	Not taken
Hb: Htc:	Hb: Htc:

OPERATION ☐ ELECTIVE ☐ URGENT ☐ IMMEADIATE ☐ REVISION ☐ CVVHDF-HD ☐ ECMO ☐ AUTOTRANFUSION

DEPARTMENT	DATE	ISBT (COMPONENT NUMBER)	PO_2	SO_2	FiO_2	PEEP	TIDAL VOLÜME	°C	HGB	HTC	LACTAT	BE	HCO_3	BILIRUBIN	ACT	aPTT	VENOUS SO_2	INR	BLEEDING	HYPOTENSION	ES	FFP	CRY	PS	WB	TXA	DR. NAME

FRESH WHOLE BLOOD (WB) INDICATIONS

- *(WB1)MASSIVE BLEEDING*
  - 80 ml / kg bleeding post-op first 24 hours
  - 40 ml/kg bleeding post-op first 3 hours
  - 2-3 ml /kg/min bleeding post-op period

FRESH FROZEN PLASMA (FFP) INDICATIONS

- (FFP1) 20ml/kg into prime solution when entering CPB
- (FFP2) In massive transfusion (20ml/kg ES+20ml/kg FFP)
- (FFP3) High ACT despite administration of protamine
- (FFP4) Factor deficiencies
- (FFP5) Plasmapheresis

CRYOPRESPITATE (CRY)

If Fibrinogen ≤ 100 mg/ dl
Dose: 1 bag ≈ 5 ml-10 ml/kg
- (CRY1) In massive transfusion (20ml/kg erythrocytes+20 ml/kg FFP +10 ml/kg Cryoprecipitate)

ERYTHROCYTE SUSPENSION (ES) INDICATIONS

- (E1) Hb≤100gr/lt in non-cyanotic and stable patients
- (E2) Hb ≤110 g/lt in Cyanotic and Stable patients
- (E3) Hct=40/45% in Newborn, Single Ventricular and Shunt Patients
- (E4) Hct 25-28% in the prime solution when entering the CBP.

PLATELET SUSPENSION (PS) INDICATIONS

- (PS1) Thrombocytopenia ≤ 80000
- (PS2) Thrombocytopenia i ≤ 100000+ Aktif kanama
- (PS3) Massive bleeding (40ml/kg ES +15-20 ml/kg PS)
- (PS4) Platelet disfunction+ active bleeding

TRANEXAMIC ACID (TXA)

- (TXA) 10 – 20mg/kg IV route push

Figure 1. Hospital patient blood management follow-up form for pediatric cardiac surgery patients

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Microbiological evaluation

Patients and their attendants had a sample taken from the back of their nose and nostril, following the guidelines of the National Health Ministry (8). Those who tested negative at least 48 hours before the operation were allowed to proceed with the council's decision. COVID-19 was confirmed through laboratory testing using Real Time-Polymerase Chain Reaction (RT-PCR). During the study period, two patients tested positive for SARS-CoV-2. One patient tested positive postoperatively. The other tested positive preoperatively; given the underlying restrictive cardiomyopathy and presentation with a hypercyanotic spell, this patient was managed conservatively in the PICU rather than undergoing surgery, and subsequently died. This patient was therefore not included among the 407 patients who underwent PCS. No patient in the surgical cohort underwent cardiac surgery while testing positive for COVID-19.

Primary outcome

The primary outcome was blood and blood product utilization before and after PBM implementation, comparing the pandemic (2020) and pre-pandemic (2019) periods.

Statistical Analysis

We used R (version 4.2.2; R Core Team, R Foundation for Statistical Computing, Vienna, Austria) for statistical analysis. Continuous variables were presented as a median and interquartile range [IQR] [quartile 1-quarter 3] or mean standard deviation. We used either Mann-Whitney U or a t-test to compare the two groups. We used logistic regression to predict blood and blood product utility based on preoperative and postoperative time (primary outcome). We conducted a multivariable logistic regression analysis to predict mortality, including variables with a p-value lower than 0.10 in the model. The regression output presents an odds ratio (OR) and confidence interval (CI). Inverse probability weighting (IPW) methods were also used to assess the robustness of the findings. Accordingly, in this study, IPW methods were used to adjust for confounders, with admission year status selected as the outcome condition in the logistic regression model. Age and total ES counts were used as covariates. The probabilities estimated by the model were used to calculate stabilized IPW weights, which were then used to weight each patient's contribution to the evaluation of death. The model was adjusted for the plausible confounders age, total ES counts, operating year, and RACHS score. The "ipw" and "survey" packages were used with R 4.2 (Vienna, Austria).

RESULTS

Table 1 presents a comparison of the demographic and clinical characteristics of patients. Out of 206 patients who underwent surgery between 11.03.2019-30.11.2019, 116 (56%) were male. In 2020, out of 201 patients, 114 (56%) were male, representing an overall 2.4% decrease in surgical volume compared to 2019. The proportion of elective to urgent/emergent procedures was similar between the two years (elective: 163/206 [79.1%] in 2019 vs 171/201 [85.1%] in 2020; urgent/emergent: 43/206 [20.9%] in 2019 vs 30/201 [14.9%] in 2020, $p = 0.12$). The median age for the two groups was 19.5 (5.4-92.6) and 10.3 (4.6-7.1) months, respectively ($p = 0.01$). The RACHS score was significantly higher in 2019 compared to 2020 (2.9 ± 0.9 vs 2.4 ± 1.1, respectively, $p < 0.001$). There was a significant difference in revision numbers between the two years (23 (11.2%) vs 41 (20.4%), $p = 0.01$). The mean PICU stay was five days (2-21 days), and mechanical ventilation (MV) duration was 3.4 days (1-18 days). Initial hematocrit values were higher in 2019 and showed a statistically significant difference (44.5 ± 4.5 vs 36.2 ± 5.7, $p < 0.001$).

Table 1. Comparison of patients' clinical characteristics operated in 2019 and 2020

Variable	2019, n = 206	2020, n = 201	P value
Age (month)*	19.5 (5.4-92.6)	10.3 (4.6-7.1)	**0.01**
Elective procedures, n (%)	163 (79.1)	171 (85.1)	**0.12**
Urgent/emergent procedures, n (%)	43 (20.9)	30 (14.9)	0.12
RACHS score	2.9 ± 0.9	2.4 ± 1.1	< 0.001
ICU LOS (days)*	5 (3-18)	5 (2-21)	**0.44**
Mortality n, (%)	23 (11.2)	24 (11.9)	0.81
Revision n, (%)	23 (11.2)	41 (20.4)	0.01
ECMO n, (%)	15 (7.3)	14 (7)	**0.90**
Weight (kg)	15.4 ± 9.5	11.2 ± 6.1	0.35
Initial hematocrit	44.5 ± 4.5	36.2 ± 5.7	< 0.001
Aortic cross-clamp time (min)	68.2 ± 22.5	70.5 ± 20.7	0.66
CPB time (min)	105.3 ± 22.2	109.7 ± 25.5	0.53
Total ES count* median (IQR) / mean	2 (0-3) / 3.37	2 (1-3) / 2.18	0.87

*Variables that were not normally distributed are given as median (25–75 interquartile range); Categorical variables (elective vs urgent/emergent procedures) were compared using the chi-square test; RACHS: Risk adjustment for congenital heart surgery; ICU: Intensive care unit; LOS: Length of stay; ECMO: Extracorporeal membrane oxygenation; CPB: Cardiopulmonary bypass

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The usage of blood and blood products during the perioperative and postoperative periods is shown in Table 2. In 2019, more patients did not require any blood or blood products on the day of surgery compared to 2020, with a significant difference (172 (83.5%) vs 126 (62.7), p < 0.001). However, in 2020, there were significantly more patients who did not need blood or blood products on the first day after surgery and beyond compared to 2019 (162 (80.6) vs 113 (54.9), p < 0.001).

Table 2. Use of blood and blood products according to perioperative and postoperative time

Number of ES		2019, n (%)	2020, n (%)	P value
	0	80 (38.8)	57 (28.4)	
Peroperative	**1**	57 (27.7)	78 (38.8)	0.055
	≥ 2	69 (33.5)	66 (32.8)	
	0	172 (83.5)	126 (62.7)	
Postoperative day 0	**1**	21 (10.2)	56 (27.9)	**< 0.001**
	≥ 2	13 (6.3)	19 (9.5)	
	0	113 (54.9)	162 (80.6)	
Postoperative day 1 and after	**1**	51 (24.8)	25 (12.4)	**< 0.001**
	≥ 2	42 (20.4)	14 (7)	

ES: Erythrocyte suspension; Blood usage numbers — 0: never used; 1: 1 unit used; ≥ 2: 2 units or more used

In Table 3, we used logistic regression analysis to determine the probability of mortality. Our results show that the likelihood of death increases significantly with age, ES, and RACHS scores. In the multivariable (adjusted) model, the corresponding ORs are 0.98 (95% CI: 0.97-0.99, p = 0.002), 1.18 (95% CI: 1.09-1.27, p < 0.001), and 2.31 (95% CI: 1.58-3.37, p < 0.001), respectively.

Table 3. Probability of death according to crude and adjusted logistic regression analysis

Variable	Crude OR (CI)	P value	Adjusted OR (CI)	P value
Age (per month increase)	0.98 (0.97-0.99)	**0.003**	0.98 (0.97-0.99)	**0.002**
Total ES counts (per one unit increase)	1.17 (1.10-1.26)	**< 0.001**	1.18 (1.09-1.27)	**< 0.001**
Operating date (2020 vs 2019)	1.08 (0.58-1.98)	0.807	1.34 (0.67-2.66)	0.402
RACHS score	2.40 (1.72-3.35)	**< 0.001**	2.31 (1.58-3.37)	**< 0.001**

RACHS: Risk adjustment for congenital heart surgery, OR: Odds ratio, CI: Confidence interval

To predict mortality, we analyzed the marginal means of total ES (Table 4). Without using any ES, the probability of mortality was 0.027 (CI: 0.013-0.055). However, when three and eight units were used, it increased to 0.059 (CI: 0.035-0.096) and 0.13 (CI: 0.078-0.215), respectively.

To assess the robustness of the results, we also used inverse probability weighted (IPW) conditional multivariable logistic regression, which revealed that the increase in the risk of death was associated with total ES count (OR: 1.19, 95% CI: 1.04-1.35; p = 0.003). However, the increase in the risk of death was not found to be associated with age and operating year (OR: 1.68, 95% CI: 0.79-3.59; p = 0.194).

Table 4. Marginal means of total erythrocyte suspension (ES) units for predicting mortality according to logistic regression

Total ES	Probability of mortality	Standard error	Confidence interval of probability
0	0.027	0.01	0.013-0.055
3	0.059	0.017	0.035-0.096
8	0.13	0.024	0.078-0.215

ES: Erythrocyte suspension

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DISCUSSION

The principal findings of this study are threefold. First, implementation of patient blood management (PBM) strategies during the COVID-19 pandemic was feasible without significantly reducing pediatric cardiac surgical activity. Second, perioperative blood product utilization, particularly in the postoperative period, decreased significantly following PBM implementation. Third, erythrocyte suspension transfusion requirement and RACHS score were independently associated with in-hospital mortality.

The COVID-19 pandemic caused significant disruption to global blood donation systems. Many centers reported reductions in elective surgical activity due to limited blood availability. In contrast, our center experienced only a minimal decrease in surgical volume (2.4%), likely reflecting the urgent nature of congenital cardiac procedures. These findings highlight the importance of structured blood conservation strategies during healthcare crises.

As many guidelines recommend, the timing of triage methods and interventions for CHD has been adjusted according to patients' physiological and hemodynamic needs (9-11). Due to the pandemic, there has been a significant reduction in congenital cardiac surgeries, ranging from half to two-thirds compared to the previous year (12-14). However, our cardiac intervention rates decreased by 2.4% in 2020 compared to 2019. Despite a higher decrease in the first months of the shutdown, the overall difference between pre-pandemic and pandemic periods was slight. Early intervention is crucial for many CHDs, as they may become fatal or inoperable if not addressed on time. Modified intervention timings based on physiological and hemodynamic requirements have been proposed to address this (15,16). The Pediatric Cardiovascular Surgery and Pediatric Cardiology Departments evaluate patients born in our hospital or referred from other centres with the participation of the minimum number of physicians, either in person or via video conferencing, to determine the need for surgery. National guidelines have established a priority order for patients who require surgical intervention during the COVID-19 pandemic, as well as identifying which operations can be postponed (17).

The availability of blood products is a crucial factor to consider when deciding on pediatric emergency cardiac surgery (18). The COVID-19 outbreak has caused a decrease in blood supply due to the cancellation of a significant number of blood donations and a decrease in the number of regular donors who were either infected or unable to visit health institutions (19). This has resulted in a 16% decrease in blood donations during the first six months of 2020 compared to the previous year (20). In addition, during the pandemic, the expanded donor selection criteria mean that volunteers with symptoms of an acute viral illness or a confirmed diagnosis of SARS-COV 2 in the previous four weeks cannot donate blood (21).

Determining whether the SARS-CoV-2 virus can be transmitted through blood transfusion is crucial due to the possibility of asymptomatic carriers donating blood. There have been cases where viral RNA was found in the serum of COVID-19 patients, indicating the potential for blood to be a transmission route (22). More research is needed to confirm this, and programs should be established to provide enough blood products for high-risk surgeries (18). In our centre, we informed relatives of patients undergoing surgery about the importance of blood donation, which helped to ensure sufficient blood donations to the Turkish Red Crescent.

In pediatric cardiac surgery, focusing on patient blood management principles such as improving hemostasis, reducing bleeding, and incorporating blood conservation techniques is essential. Additionally, a meta-analysis found that the impact of red blood cell (RBC) transfusions on mortality and morbidity in pediatric patients with congenital heart disease undergoing cardiac surgery is unclear. In this trial, we hypothesized that the presence or absence of cyanosis could impact trial outcomes and require different clinical management for the two groups. Therefore, in our study, ES replacement is based on different haemoglobin cut-off values for cyanotic and noncyanotic patients.

In a retrospective study, Willems et al. compared children receiving prophylactic transfusion (ES transfusion in the CPB prime to maintain calculated hematocrit above 20% after administration of cardioplegia) with children receiving therapeutic transfusion (RBC transfusion in the postoperative period to compensate for blood loss or signs of inadequate tissue oxygen delivery) (24). They found that children who received therapeutic transfusions had a higher risk of severe morbidity and mortality than those who received prophylactic transfusions. In our study, we did not use a preventive transfusion regimen, and we observed that the baseline hematocrit levels were higher in 2019 than in 2020. This difference was likely due to more urgent cases being admitted to hospitals during the pandemic. Given the ongoing debate about the risks and benefits of prophylactic transfusions, it may be best to adopt a more restrictive transfusion approach for children undergoing cardiac surgery. As a result, total blood and blood product utilization decreased by 25.8% between the two years (1563 vs 1159 units) (Table 5, Figure 2), although the discard rate increased from 9.4% to 12.3%, possibly reflecting smaller inventory buffers during the pandemic.

Table 5. Total numbers of blood and blood products used and discarded between March–November 2019 and 2020

	2019, n (%)	2020, n (%)
Blood and blood products used, n	1563	1159
Blood and blood products discarded, n (%)	147 (9.4)	143 (12.3)

Discard rate increased from 9.4% (2019) to 12.3% (2020) despite an overall 25.8% reduction in total blood and blood product utilization

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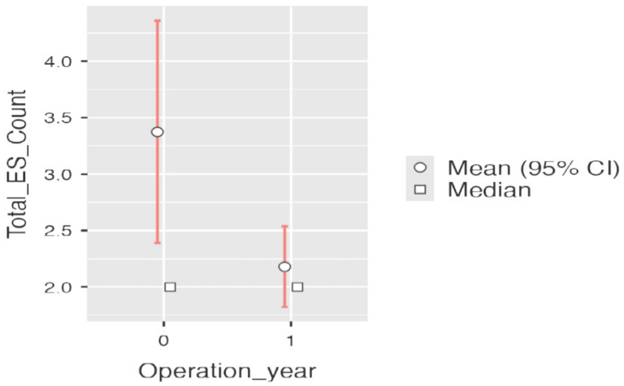

Figure 2. Median and mean values of erythrocyte suspension (ES) units used in 2019 and 2020

Although the mortality rates of both years were similar, the probability of mortality calculated in the univariate (crude) logistic regression analysis showed that each one-month increase in age, 1 unit ES increase and 1 point increase in the RACHS scores significantly affected the mortality (OR 0.98 (CI0.97-0.99), $p = 0.003$, OR 1.17(CI 1.10-1.26) $p < 0.001$, OR 2.40 (CI 1.72-3.35) $p < 0.001$ respectively). This finding was found to be compatible with those in the literature.

Study Limitation

This study has several limitations. First, its retrospective, single-centre design carries an inherent risk of selection bias. Second, the 2019 cohort served as a historical rather than a randomized control group, and the more urgent case-mix admitted during the pandemic may have introduced confounding by indication that could not be fully accounted for in the multivariable model. Third, no a priori power calculation was performed, and the relatively small sample size limits the precision of some subgroup comparisons. Fourth, this study evaluated only in-hospital outcomes and did not include post-discharge follow-up data. Finally, although all patients underwent COVID-19 screening as part of institutional protocol, only two patients tested positive for SARS-CoV-2 during the study period, which was too small a number to permit separate statistical analysis of the relationship between COVID-19 status and transfusion requirements or outcomes. Prospective, multicentre studies with larger patient populations are needed to confirm these findings and to further refine patient blood management protocols during future healthcare crises.

CONCLUSION

As a result, we used the patient blood management procedure, which we started to use before, even if we had to operate in emergency cases, even during the pandemic period. Patient Blood Management is a set of rules that should be planned and applied specifically to each centre according to the patients or the dynamics of the centres. Considering the risk-benefit balance of allogeneic transfusion, limited transfusion will benefit patients.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: The authors declare that they received no financial support.

Ethics Committee Approval: Our study was conducted by the Helsinki Declaration and approved by the Kartal Koşuyolu Yüksek İhtisah Training and Research Hospital Clinical Research Ethics Committee (Desicion no: 2021/10/506, Date: 24.08.2021).

Informed Consent: Written informed consent was obtained from the parents or legal guardians of all pediatric patients included in the study.

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