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ORIGINAL ARTICLE

Does Transfusion of Blood and Blood Products Increase the Length of Stay in Hospital?

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Abstract We aimed to analyze the use of blood products in cardiac surgery and to investigate its effect on clinical outcomes. Perioperative transfusion requirement, survival and complication rates and the duration of hospitalization were noted. Patients were divided into two groups considering the duration of hospital and intensive care unit (ICU) stay. The cardiopulmonary bypass time and the cross clamp time, and the amount of used cryoprecipitate, fresh frozen plasma, platelet, red blood cell and the bleeding amount were significantly higher in groups that stayed at the hospital for > 7 days and at the ICU for > 2 days ($p > 0.05$). In the univariate model, to predict the patients who might stay at the hospital for more than 1 week and who might stay at the ICU for more than 3 days, we considered the significant efficacy of postoperative blood transfusion, bleeding amount, and the cardiopulmonary bypass time ($p < 0.05$). In the reduced multivariate model, however, we analyzed the significant-independent efficacy of the postoperative fresh frozen plasma use to determine the patients who would stay at the hospital for more than 1 week and who would stay at the ICU for more than 3 days ($p < 0.05$). We have concluded that increased use of blood products was associated with the cross clamp and cardiopulmonary bypass time and prolonged duration of hospital and ICU stays. In open cardiac surgeries, the use of blood products due to bleeding was identified as a predictor for staying longer than 3 days at the ICU and longer than 7 days at the hospital.

Keywords Blood transfusion · Length of hospital stay · Cardiac surgery · Complication

Introduction

Cardiac surgery has greatly improved over time due to improvements in medical and surgical practice and cardiac surgery critical care. On the other hand, as a result of aging of the population, heart surgery is currently performed in older, more complex patients with higher comorbidities [1]. Prolonged duration of hospitalization is often associated with increased hospital mortality and morbidity and long-term poor prognosis. Additionally, prolonged intensive care unit (ICU) stay after cardiac surgery has a major impact on overall cost and resource utilization [2, 3]. It has been also reported to simultaneously increase the incidence of rehospitalization [4].

A multivariate analysis determined 5 predictors that extend the duration of ICU stay after cardiac surgery in adult patients [5]. These predictors include ejection fraction $< 30\%$, pulmonary hypertension, prolonged ventilation over 12 h, postoperative acute renal insufficiency, and the amount of blood transfusion. Red blood cell (RBC) transfusion is associated with increased mortality and morbidity in both adult and pediatric patients. Despite

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raising oxygen carrying capacity by increasing hemoglobin (Hb) concentration of the blood, blood transfusion has risks and has been reported to have adverse consequences, such as prolonged hospitalization or increased hospital costs [6].

The quality- and material-related adverse effects caused by extended hospital stay have become more important today than ever before. The length of hospitalization after routine procedures has been specified as a measure of quality to reduce cost and hospital-acquired morbidity [7]. However, there is less data specifically related to the cardiac surgery patients. In this retrospective study, we aimed to analyze the use of blood and blood products in cardiac surgeries and to investigate its effect on clinical outcomes.

Materials and Methods

Patients who had open heart surgery at our clinic for coronary bypass and/or heart valve repair between 2006 and 2016 were included in our study after the approval of the Ethics Committee. Perioperative transfusion requirements were noted considering the amounts of transfused RBC, platelet (PLT), fresh frozen plasma (FFP) and cryoprecipitate (Cryo). Patients were also evaluated regarding survival complication rates and the duration of hospitalization. We divided patients into two groups considering the duration of hospital stay and the ICU stay. Their laboratory test results including Hb, Hct, INR, BUN and creatinine levels were compared. Patients who had missing data and underwent emergency surgery as well as those who were intervened with the beating heart technique or required re-operation were excluded from the study.

Statistical Analysis

The SPSS 22.0 program was used for the analysis of the study data. The descriptive statistics employed in the study were mean, standard deviation, median, minimum, maximum, frequency, and ratio. The Kolmogorov–Smirnov test was used to measure the distribution of variables. The Mann–Whitney U test was used to analyze quantitative independent data while the Chi-square test was used to assess the qualitative independent data. In cases where the Chi-square conditions were not met, the Fisher test was used for the qualitative data. A value of $p < 0.05$ was considered statistically significant.

Results

In total, the data of 117 patients was analysed. No significant difference was found between the groups staying at hospital for ≤ 7 days and for > 7 days regarding age, gender distribution, BMI and the cell saver blood as well as the levels of the hemoglobin (Hb), hematocrit (Hct), international normalized ratio (INR), blood urea nitrogen (BUN), and creatinine ($p > 0.05$). Nevertheless, patients staying at the hospital for > 7 days had significantly longer CPB time and Cx time and significantly higher Cryo, FFP, PLT, RBC, and bleeding in comparison with those who stayed at hospital for ≤ 7 days ($p > 0.05$, Table 1).

There was no significant difference between the groups with an ICU stay of ≤ 2 days and that with an ICU stay of > 2 days regarding age, gender distribution, BMI level, the cell saver blood, and the levels of Hb, Hct, INR, BUN, and creatinine ($p > 0.05$). However, the CPB time, Cx time, and the levels of Cryo, FFP, PLT, RBC, and the amount of bleeding were significantly higher among the patients who stayed at the ICU more than 2 days as compared to those staying at the ICU for ≤ 2 days ($p < 0.05$, Table 2).

In the univariate model, to predict the patients who would stay at the hospital for more than 1 week, we considered the significant efficacy of postoperative FFP, platelet, ES transfusion, bleeding amount, and the CPB time ($p < 0.05$). In the reduced multivariate model, however, we took the significant-independent efficacy of the postoperative FFP value into consideration to determine the patients who would stay at the hospital for more than 1 week ($p < 0.05$, Table 3).

Moreover, we considered the significant efficacy of postoperative FFP, postoperative PLT, postoperative RBC, bleeding amount, the CPB time and the Cx time to predict the patients who would stay at ICU for ≥ 3 days in the univariate model ($p < 0.05$). Furthermore, in the reduced multivariate model, we observed the significant-independent efficacy of the postoperative FFP value to determine the patients who would stay at the ICU for ≥ 3 days ($p < 0.05$, Table 4).

No significant correlation was found between the amount of used cell saver blood and age, BMI, the Cx time, the CPB time, Cryo, and the levels of FFP, PLT, RBC, Hb, Hct, INR, BUN, and creatinine and the amount of of bleeding ($p > 0.05$, Table 5).

Furthermore, there was no significant correlation between the length of hospital/ICU stay and age, BMI, Hb, Hct, INR, BUN, and creatinine levels ($p > 0.05$). Nevertheless, both the duration of hospitalization and that of ICU stay were significantly and positively correlated with the Cx time, CPB time, Cryo, FFP, PLT, RBC, and the amount of bleeding ($p < 0.05$, Table 5).

Table 1 Analysis of parameters associated with prolonged hospital stay

	Hospital stay ≤ 7 days			Hospital stay > 7 days			*p*
	mean ± S.D./n-%		Median	mean ± S.D./n-%		Median	
Age (years)	67.3 ± 9.7		68.0	66.7 ± 10.1		67.0	0.781[t]
Gender							
Female	34	42.5%		15	40.5%		0.842[X²]
Male	46	57.5%		22	59.5%		
BMI	26.7 ± 1.9		26.6	26.6 ± 2.0		26.0	0.677[m]
Cell saver blood volume (mL)	731.3 ± 199.7		700.0	791.9 ± 262.9		800.0	0.499[m]
CPB time	117.8 ± 55.3		110.0	145.8 ± 66.6		125.0	**0.020**[m]
CX time	81.7 ± 34.9		80.0	90.8 ± 28.8		90.0	**0.049**[m]
Cryoprecipitate							
Preoperative	0.28 ± 1.18		0.00	1.65 ± 4.60		0.00	0.157[m]
Postoperative	0.00 ± 0.00		0.00	0.86 ± 2.63		0.00	**0.000**[m]
FFP							
Preoperative	3.10 ± 2.84		2.50	4.65 ± 4.10		4.00	**0.045**[m]
Postoperative	0.36 ± 1.17		0.00	3.86 ± 5.96		0.00	**0.000**[m]
RBC							
Preoperative	2.48 ± 3.70		2.00	3.51 ± 3.70		3.00	**0.049**[m]
Postoperative	1.31 ± 1.42		1.00	7.84 ± 12.32		2.00	**0.001**[m]
Hb							
Preoperative	12.3 ± 2.2		12.4	12.5 ± 1.7		12.4	0.618[m]
Postoperative	10.7 ± 1.1		10.6	10.7 ± 1.3		10.7	0.817[m]
Hct							
Preoperative	36.1 ± 4.9		36.3	36.3 ± 4.7		36.6	0.629[m]
Postoperative	31.1 ± 3.2		31.0	30.8 ± 3.2		30.8	0.712[m]
Platelet							
Preoperative	231.3 ± 65.4		218.5	234.2 ± 80.3		217.0	0.995[m]
Postoperative	164.3 ± 69.2		159.5	163.5 ± 55.1		173.0	0.637[m]
INR							
Preoperative	1.13 ± 0.18		1.09	1.23 ± 0.42		1.13	0.225[m]
Postoperative	1.27 ± 0.12		1.25	1.34 ± 0.28		1.27	0.416[m]
BUN							
Preoperative	19.8 ± 8.1		17.0	18.2 ± 8.8		16.0	0.174[m]
Postoperative	21.1 ± 8.2		19.0	19.9 ± 8.0		18.0	0.444[m]
Creatinine							
Preoperative	0.97 ± 0.26		0.90	1.54 ± 3.30		0.90	0.398[m]
Postoperative	1.13 ± 0.40		1.00	1.17 ± 0.40		1.10	0.614[m]
Bleeding (mL)	562.9 ± 339.6		480.0	700.8 ± 345.5		600.0	**0.016**[m]

Bold values of $p < 0.05$ were considered statistically significant

ICU intensive care unit, *BMI* body mass index, *CPB* cardiopulmonary bypass, *CX* cross clamp, *FFP* fresh frozen plasm, *RBC* red blood cell, *Hb* hemoglobin, *Hct* hematocrite

[t]t test; [m]Mann–whitney u test; X^2Chi-square test

Discussion

This retrospective, observational cohort study indicated that the increased use of blood products in cardiac surgery patients was associated with the Cx time, the CPB time and prolonged hospital and ICU stays. The use of blood products due to blood loss in open heart surgeries was specified as a predictor for extended hospitalization and/or prolonged intensive care stay.

About 25% of blood transfusions in the United States occur in cardiac surgeries [8]. Despite the risks, more than 50% of patients undergoing CABG are given RBC

Table 2 Analysis of parameters associated with prolonged Intensive Care Unit stay

	ICU stay ≤ 2 days			ICU stay > 2 days			*p*
	mean ± S.D./n-%		Median	mean ± S.D./n-%		Median	
Age (years)	67.4 ± 9.9		68.0	65.3 ± 9.2		65.0	0.420[t]
Gender							
Female	40	40.0%		9	52.9%		0.3170.842[X2]
Male	60	60.0%		8	47.1%		
BMI	26.7 ± 1.8		26.3	26.7 ± 2.2		26.0	0.985[m]
Cell saver blood (mL)	740.0 ± 222.0		700.0	811.8 ± 220.5		800.0	0.163[m]
CPB time	118.9 ± 54.8		115.0	170.6 ± 72.0		180.0	**0.004**[m]
CX time	81.2 ± 33.5		80.0	103.5 ± 24.7		100.0	**0.004**[m]
Cryoprecipitate							
Preoperative	0.53 ± 2.45		0.00	1.76 ± 4.35		0.00	0.136[m]
Postoperative	0.14 ± 1.30		0.00	1.06 ± 2.33		0.00	**0.000**[m]
FFP							
Preoperative	3.47 ± 3.42		3.00	4.29 ± 2.85		4.00	0.149[m]
Postoperative	0.70 ± 2.21		0.00	6.00 ± 7.10		3.00	**0.000**[m]
RBC							
Preoperative	2.69 ± 3.77		2.00	3.47 ± 3.39		3.00	0.196[m]
Postoperative	2.00 ± 3.60		1.00	11.47 ± 16.04		2.00	**0.002**[m]
Hb							
Preoperative	12.4 ± 2.2		12.4	12.2 ± 1.7		12.3	0.798[m]
Postoperative	10.7 ± 1.2		10.7	10.5 ± 1.1		10.6	0.626[m]
Hct							
Preoperative	36.4 ± 4.9		36.6	35.0 ± 4.3		36.5	0.345[m]
Postoperative	31.2 ± 3.3		31.1	30.2 ± 2.4		30.1	0.233[m]
Platelet							
Preoperative	230.9 ± 66.0		219.0	239.8 ± 92.7		213.0	0.856[m]
Postoperative	166.0 ± 65.9		167.0	152.8 ± 58.8		145.0	0.363[m]
INR							
Preoperative	1.13 ± 0.17		1.10	1.34 ± 0.58		1.13	0.131[m]
Postoperative	1.28 ± 0.16		1.25	1.34 ± 0.30		1.29	0.659[m]
BUN							
Preoperative	19.8 ± 8.1		17.0	16.7 ± 9.3		15.0	0.063[m]
Postoperative	21.0 ± 8.4		19.0	19.2 ± 6.9		18.0	0.510[m]
Creatinine							
Preoperative	0.98 ± 0.26		0.90	2.14 ± 4.87		0.90	0.800[m]
Postoperative	1.14 ± 0.40		1.00	1.14 ± 0.42		1.10	0.879[m]
Bleeding (mL)	565.2 ± 321.7		490.0	849.4 ± 392.6		750.0	**0.003**[m]

Bold values of $p < 0.05$ were considered statistically significant

INR international normalised ratio, *BUN* blood urea nitrogen, *ICU* intensive care unit, *BMI* body mass index, *CPB* cardiopulmonary bypass, *CX* cross clemp, *FFP* fresh frozen plasm, *RBC* red blood cell, *Hb* hemoglobin, *Hct* hematocrite, *INR* international normalised ratio, *BUN* blood urea nitrogen

[t]t test; [m]Mann–whitney u test; X^2Chi-square test

transfusion [9]. Different transfusion applications are carried out in different clinics. Studies conducted in recent years have indicated that, rather than enhancing the survival of cardiac patients, transfusion elevates the morbidity and mortality due to the risks it carries, such as the increased need for inotropic agent and prolonged mechanical ventilation. It was reported in a study involving 802 patients under pediatric cardiac intensive care that 46% of the patients received RBC transfusion within 48 h following the admission to the intensive care unit [10]. There was a significant elevation in the hospitalization period of patients in both the low transfusion group receiving < 15 mL/kg blood and the high transfusion group receiving > 15 mL/kg blood.

Table 3 The prediction of patients who will stay in hospital for more than 1 week in a univariate model

	Univariate model			Multivariate model		
	OR	95% confidence interval	*p*	OR	95% confidence interval	*p*
Postoperative FFP	1404	1144–1723	**0.001**	1404	1144–1723	**0.001**
Postoperative Platelet	1269	1073–1501	**0.005**			
Postoperative RBC	1314	1103–1564	**0.002**			
Bleeding (mL)	1002	1001–1030	**0.049**			
CPB time (min)	1008	1001–1014	**0.027**			

Logistic regression. Bold values of $p < 0.05$ were considered statistically significant

FFP fresh frozen plasm, *RBC* red blood cell, *CPB* cardiopulmonary bypass

Table 4 The prediction of patients who will stay in Intensive Care Unit for more than 3 days in a univariate model

	Univariate model			Multivariate model		
	OR	95% confidence interval	*p*	OR	95% confidence interval	*p*
Postoperative FFP	1299	1135–1486	**0.000**	1264	1106–1445	**0.001**
Postoperative Platelet	1210	1062–1379	**0.004**			
Postoperative RBC	1150	1056–1253	**0.001**			
Bleeding (mL)	1002	1001–1003	**0.004**	1001	1000–1003	**0.016**
CPB time (min)	1012	1004–1020	**0.003**			
Cx time (min)	1019	1003–1035	**0.016**			

Logistic regression. Bold values of $p < 0.05$ were considered statistically significant

FFP fresh frozen plasm, *RBC* red blood cell, *Cx* cross clamp, *CPB* cardiopulmonary bypass

The aim of blood transfusion is to enhance the oxygen carrying capacity of blood. However, it is still unclear at what level of anemia this physiological effect can be transformed into an improved clinical outcome. Furthermore, transfusions are performed using blood from the blood banks which is known to have potential adverse effects. Nevertheless, it has been demonstrated that 25–60% of patients are given excessive transfusion [11]. Schwann et al. [12] reported that patients receiving blood transfusions had 21% higher risk for coronary artery graft failure. The restrictive transfusion regimen is the recommended intraoperative transfusion strategy in the European Society of Anesthesiology (ESA) guidelines [13]. This regimen intends to keep Hb concentration at a level of 7–8 g/dl. On the other hand, the level of 9–11 g/dl, known as the liberal regimen, has been indicated to be ineffective and is no longer recommended.

In a meta-analysis involving 6 randomized controlled trials of cardiac surgical patients (3352 patients), 19 non-cardiac surgical trials (8361 patients), and 39 observational studies (232.806 patients) demonstrated significantly increased mortality and morbidity among patients receiving RBC transfusions in cardiac surgery as compared to those who do not receive any blood transfusion [14]. A comparison was made between the Hct thresholds of 24% and 28% for blood transfusions in cardiac surgery; however, no significant difference was detected regarding side effects and complications [15]. For this reason, aggressive blood conservation is recommended for cardiac surgeries.

In the present study, our purpose was to create a risk estimation model to be used to create accurate and reliable clinical predictions to advocate the perioperative decision-making process. In this way, clinicians can be prevented from making predictions based on misestimation, intuitions and cognitive biases [16]. Our study showed that not only RBC transfusion, but also postoperative FFP and PLT transfusion, the amount of bleeding, and the CPB time had a predictive value in the projection of patients that would stay at the hospital for more than a week and at the intensive care unit for more than 3 days. It was also concluded that besides the above-mentioned risk factors, the Cx time was also a predictor for extended stay at the intensive care unit. Cross-clamp time is an independent predictor of mortality and morbidity in cardiac patients and may affect the blood transfusion rate (ref).

Table 5 Determination of parameters related to blood products transfusion, hospital and intensive care unit stay

		Cell saver blood (mL)	Age (years)	BMI	Cx time (min)	CPB time (min)
Cell saver blood (mL)	r		− 0.107	0.097	0.016	0.053
	p		0.249	0.298	0.865	0.571
ICU stay time (days)	r	0.154	− 0.017	− 0.064	0.242	0.245
	p	0.098	0.855	0.491	**0.009**	**0.008**
Hospital stay time (days)	r	0.074	− 0.011	− 0.019	0.178	0.204
	p	0.430	0.907	0.839	0.057	0.052

		Cryoprecipitate	FFP	Platelet	RBC	Hb
Cell saver blood (mL)	r	0.173	0.161	0.111	0.106	− 0.027
	p	0.062	0.083	0.233	0.258	0.776
ICU stay time (days)	r	0.306	0.284	0.336	0.282	− 0.035
	p	**0.001**	**0.002**	**0.000**	**0.002**	0.707
Hospital stay time (days)	r	0.344	0.400	0.343	0.299	0.037
	p	**0.000**	**0.000**	**0.000**	**0.001**	0.692

		Hct	INR	BUN	Creatine	Bleeding (mL)
Cell saver blood (mL)	r	− 0.063	− 0.148	− 0.098	− 0.139	0.089
	p	0.501	0.112	0.295	0.134	0.338
ICU stay time (days)	r	− 0.027	0.029	− 0.086	0.000	0.234
	p	0.774	0.754	0.354	0.998	**0.011**
Hospital stay time (days)	r	− 0.005	0.068	− 0.048	− 0.003	0.222
	p	0.956	0.468	0.609	0.978	**0.043**

Spearman correlation. Bold values of $p < 0.05$ were considered statistically significant

ICU intensive care unit, *FFP* fresh frozen plasm, *RBC* red blood cell, *Hb* hemoglobin, *Hct* hematocrit, *INR* international normalized ratio, *BUN* blood urea nitrogen, *BMI* body mass index, *Cx* cross clamp, *CPB* cardiopulmonary bypass

As stated in the EACTS/EACTA (European Association for Cardio-Thoracic Surgery) Guidelines on patient blood management, creating a close collaboration between surgeons, anesthetists, clinical perfusionists, and intensivists is the key factor for reducing the frequency of blood transfusions in cardiac surgeries [17].

Cell saver is a device recommended to be employed for patients in cardiac surgery. Previous studies reported that cell saver blood transfusion increases the FFP requirement [18, 19]. Our study, on the contrary, did not show a significant correlation between the amount of cell saver blood usage and the Cryo, FFP, PLT, RBC transfusions or the amount of bleeding.

Limitations

The retrospective nature is the major limitation of this study because, in analyses, we might have ignored other factors that potentially influenced patients' hospitalization period. Furthermore, as there was no information on the waiting time of transfusions, it was not possible to analyze the effects of waited blood transfusions on patient survival or complications. A meta-analysis including 16 studies with a total of 31359 patients compared old blood transfusion with fresh blood transfusion and concluded that transfusing old or fresh blood did not elevate mortality among inpatients [20]. Nevertheless, fresher RBC transfusion has been shown to be associated with increased risk of transfusion reaction and transfusion-mediated infection. We think that the effect of fresher or older RBC transfusion on the duration of hospital or intensive care unit stay may be a good topic for further prospective researches. The lack of information on whether patients had received medications in the preoperative period, such as erythropoietin or iron, is another limitation.

Another major limitation that can be attributed to this study is that we were not able to assess the impact of the use of viscoelastic tests on blood transfusion. A meta-analysis involving 8737 patients from 15 clinical trials suggested a reduction in the frequency of RBC and platelet transfusions as a result of the use of viscoelastic point-of-care (POC) testing to guide transfusion in patients

undergoing cardiac surgery [21]. However, according to the results of that meta-analysis, POC tests are not recommended for routine usage because employing TEG or ROTEM did not affect mortality, bleeding-reoperation for bleeding, stroke, ventilation time or the duration of hospitalization when compared with standard care.

Conclusion

In conclusion, the strategy of restrictive blood transfusion is a recommended method in cardiac surgeries as well as in non-cardiac surgeries. Any increase in the amount of transfused blood and blood products was specified as a predictor for a hospital stay of > 7 days and an intensive care stay of > 3 days in patients undergoing cardiac surgery.

Compliance with Ethical Standards

Conflict of interest There are no conflicts of interest to declare.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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