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Evaluation of the Relationship Between Preoperative and Postoperative Platelet Values and Amount of Blood Transfusion in Cases with Craniosinocytosis

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ABSTRACT

AIM: This study aimed to demonstrate that decreased platelet count in patients with craniosynostosis increases the requirement for blood replacement, thus providing guidance to clinicians by revealing the time at which the platelet count decreases. Additionally, the relationship between the amount of blood transfusion and preoperative and postoperative platelet counts was evaluated.

MATERIAL and METHODS: This study included 38 patients with craniosynostosis who underwent surgery between July 2017 and March 2019 in the Neurosurgery Department. The patients exhibited no cranial pathologies except craniosynostosis. All surgeries were performed by a single surgeon. The demographic data, anesthesia and surgical durations, preoperative complete blood count and bleeding time, intraoperative blood transfusion amount, and postoperative complete blood count and total blood transfusion amount of the patients were recorded.

RESULTS: The preoperative and postoperative changes and the timing of changes in hemoglobin and platelet counts, amount and timing of postoperative blood transfusion, and relationship between the amount and timing of blood replacement and preoperative and postoperative platelet counts were evaluated. The postoperative platelet counts tended to decrease after 12, 18, 24, and 36 h, and began increasing after 48 h. Although decreased platelet count did not lead to platelet replacement, it influenced the erythrocyte replacement requirement in the postoperative period.

CONCLUSION: Platelet count was associated with the amount of blood replacement. The platelet counts decreased within the first 48 h following surgery and tended to elevate thereafter; thus, clinicians should closely monitor these platelet counts within 48 h after surgery.

KEYWORDS: Blood loss, Blood transfusion, Craniosynostosis, Platelet

ABBREVIATIONS: cc: Cubic centimeter, **cm:** Centimeter, **FFP:** Fresh frozen plasma, **g:** Grams, **Hb:** Hemoglobin, **kg:** Kilograms, **ml:** Milliliter, **mm:** Millimeter, **PRBC:** Packed red blood cell, **µl:** Microliter

INTRODUCTION

Craniosynostosis is a craniofacial malformation caused by the early closure of one or more cranial sutures. (17) The primary goals of craniosynostosis treatment involve restoring the deformity and preventing or treating cognitive disorders by relieving the intracranial pressure via decompressing the neural tissues.

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Hypovolemia secondary to bleeding constitutes the most crucial complication of craniosynostosis surgery (15). Numerous studies have been conducted to minimize these complications.

Several techniques and interventions have been developed to reduce blood loss and minimize the number of required allogeneic blood transfusions. Patients receiving whole blood transfusion may not need fresh frozen plasma (FFP), cryoprecipitate, fibrinogen concentrate, or platelet transfusions. However, the rate of whole blood use has progressively decreased to ensure efficient use and storage of donor blood. If packed red blood cell (PRBC) suspensions have been prepared for transfusion, platelet suspension and FFP also need to be prepared, with FFP being the most commonly used blood product for this purpose. Pieters et al.reported that prophylactic FFP use did not differ according to blood transfusion (14). Numerous clinics compensate blood and fluid losses via crystalloids, PRBC suspensions, and FFP.

Herein, we evaluated the relationship between the amount of blood transfusion and preoperative and postoperative platelet counts.

MATERIAL and METHODS

Study Population

We retrospectively evaluated 38 patients with craniosynostosis who underwent surgery at the Neurosurgery Department between June 2017 and March 2019. All surgical procedures were performed by a single surgeon. The surgical interventions included synovectomy, remodeling, vertex craniectomy, and barrel osteotomy. Barrel osteotomy was performed for all the patients. The demographic data, anesthesia and operation durations, preoperative complete blood count and bleeding time, and intraoperative blood transfusion, postoperative complete blood count, and total blood transfusion amounts of the patients were recorded.

The inclusion criteria were patients with syndromic or nonsyndromic craniosynostosis, patients aged <2 years, patients who had not undergone a previous cranial surgery, and patients without additional cranial pathology.

All patients underwent preoperative assessment, including physical and neurological examinations and their head circumferences were measured. The anterior and posterior fontanels were assessed for closure. In addition, preoperative complete blood count and bleeding time assessments were performed. All the patients underwent preoperative and postoperative pediatric consultations.

This study was approved by the Erciyes University Clinical Research Ethics Committee (license number: 2019/627), and all the procedures conducted herein that involved human participants were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Imaging and Assessment Methods

In the patients with clinically diagnosed craniosynostosis, diagnostic transcranial Doppler sonography, thin-section, and three-dimensional brain computed tomography scans were performed to radiologically confirm the diagnosis of craniosynostosis. The patients were classified as sagittal, metopic, unicoronal, bicoronal, and multiple synostoses.

Before surgery, the patients were premedicated with midazolam (0.5 mg/kg) via a nonparticulate fruit juice.

A Foley catheter was inserted to monitor the urinary output of the patients. Peripheral venous catheterization was performed. Further, 1/3 dextrose (1700 cc m^2/kg/day) was administered as maintenance fluid. The amount of blood loss was estimated on the basis of the gauze count, hematocrit monitoring, amount of blood in aspirator, and surgeon experience. The lost blood was replaced with PRBC suspensions.

Under general anesthesia, a bicoronal skin incision was made. Cutaneous bleeding was controlled using bipolar cautery. Skin was removed as periosteum from the remaining bone. Then, the periosteum over the bone was removed, and osseous bleeding sites were covered with bone wax. Frontal craniotomy, fronto-orbital advancement, remodeling, and biparietal barrel osteotomy were performed in metopic synostosis. In unilateral coronal synostosis, bifronto-orbital advancement, bifrontal craniotomy, bilateral barrel osteotomy, and orbital apex osteotomy were performed. Furthermore, coronal synosectomy, fronto-orbital remodeling, and bifrontal and biparietal barrel osteotomy were performed in bilateral coronal synostosis. Barrel stave osteotomy was performed with incisions of 1–2 mm (4–6 cm in length).

All the patients were monitored in the intensive care unit for at least 24 h following surgery. Electric blankets were used to prevent heat loss during the early postoperative period. At 1 h postoperation, complete blood count and blood gas analysis were performed and the results were applied in the pediatric consultation. During the follow-up, fluid replacement was maintained at 1700 cc m^2/kg/day. For all patients, complete blood count was performed 1, 6, 12, 18, 24, 36, 48, and 73 h postoperation and at 6- or 8-h intervals thereafter. PRBC replacement was performed per the amount of blood collected from the drain.

PRBC replacement (10 cc/kg) was performed when the hemoglobin level decreased to <10 g/dl, whereas platelet suspension replacement (10 cc/kg) was performed when the platelet count decreased to <100,000/µl.

Statistical Analyses

To summarize the study data, descriptive statistical data are presented as mean ± standard deviation and median (range) for continuous variables based on data distribution. Categorical variables are summarized as count and percentage. Kolmogorov–Smirnov test was used to assess the normal distribution of numerical variables. One-way analysis of variance with repeated measures was used to assess differences among the dependent measurements repeated more than twice. Spearman rho correlation coefficient was used to evaluate the correlation between the preoperative platelet count and PRBCs at a certain timepoint. Statistical

Table I: Distribution of the Demographic and Clinical Characteristics of the Patients

	n (%)	Mean ± SD	Median [min–max]
Gender			
Male	22 (57.9)	-	-
Female	16 (42.1)	-	-
Age (month)		6.03 ± 4.21	4 [2–23]
Weight (g)		7207.89 ± 1983.63	7200 [4000–14000]
Duration of anesthesia (min)		130 ± 23.91	130 [75–210]
Duration of surgery (min)		105.66 ± 21.97	110 [60–180]
Closed suture			
Metopic	17 (44.7)	-	-
Sagittal	11 (28.9)	-	-
Unicoronal	5 (13.2)	-	-
Bicoronal	2 (5.3)	-	-
Multi-synostosis	3 (7.9)	-	-

***SD:** Standard deviation; **Min:** Minimum; **Max:** Maximum. Descriptive statistics are expressed as count (%) for categorical variables while mean ± SD and median (min–max) for numerical variables.*

Table II: Amount of Blood Replacement (ml)

	Mean ± SD
Perop. PRBC	83.82 ± 22.49
1 h	50 ± 0
6 h	56.58 ± 16.75
12 h	48.44 ± 15.78
18 h	58.64 ± 13.98
24 h	61 ± 23.66
30 h	54 ± 17.55
36 h	51.67 ± 25.62
48 h	51.15 ± 11.57
60 h	48.33 ± 4.08

***PRBC:** Packed red blood cells.*

analyses were performed using Jamovi [Jamovi project (2019)]. Jamovi (Version 1.0.7), computer software, retrieved from https://www.jamovi.org) and JASP Team (2019, Version 0.11.0.0, computer software). A p value <0.05 was considered statistically significant.

RESULTS

Of the 38 patients, 22 (57.9%) were boys and 16 (42.1%) were girls (Table I) and the mean age, weight, and anesthesia duration were 6.03 ± 4.21 months, 7207.89 ± 1983.63 g, and 130 ± 23.91 min, respectively. The mean surgical duration was 105.66 ± 21.97 min. Of the patients, 17 (44.7%) were classified as metopic, 11 (28.9%) as sagittal, 5 (13.2%) as unicoronal, 2 (5.3%) as bicoronal, and 3 (7.9%) as multiple synostosis.

Table II shows the mean amount of PRBC replacement in the preoperative period and at 1, 6, 12, 18, 24, 30, 48, and 60 h postoperation. The mean amount of PRBC replacement was 83.82 ± 22.49 ml during the peroperative period and 50, 56.58 ± 16.75, 48.44 ± 15.78, 58.64 ± 13.98, 61 ± 23.66 ml, 54 ± 17.55, 36.51.67 ± 25.62, 51.15 ± 11.57, and 48.33 ± 4.08 ml at 1, 6, 12, 18, 24, 30, 36, 48, and 60 h postoperation, respectively.

The mean Hb levels at baseline (preoperative period) and 1, 6, 12, 18, 24, 30, 36, 48, 60, and 72 h postoperation differed significantly ($p<0.001$) (Table III). The mean Hb levels at 60 and 72 h postoperation were significantly higher than those at 12, 18, 24, and 30 h postoperation ($p<0.05$ for each; Table III). The mean Hb level at 1 h postoperation was significantly higher than those at 6, 12, 18, 24, and 30 h postoperation ($p<0.05$ for each; Table III). Conversely, the mean Hb level at baseline was significantly higher than those at 6 and 12 h postoperation ($p<0.05$ for each; Table III). The change in preoperative and postoperative Hb values is illustrated in Figure 1.

The data presented in Table 3 indicate a significant difference between the mean platelet counts at baseline (preoperative period) and at 1, 6, 12, 18, 24, 30, 36, 48, 60, and 72 h postoperation ($p<0.001$). The mean platelet counts at baseline and 1 h postoperation were significantly higher than those at 6, 12, 18, 24, 30, 36, 48, 60, and 72 h postoperation ($p<0.05$ for each; Table III). Similarly, the mean platelet count at 6 h postoperation was significantly higher than those at 18, 24, 30, 36, 48, 60, and 72 h postoperation ($p<0.05$ for each; Table III).

The mean platelet count at 12 h postoperation was significantly higher than those at 36, 48, and 60 h postoperation (p<0.05 for each; Table III). Finally, the mean platelet count at 18 h postoperation was significantly higher than those at 48 and 60 h postoperation (p<0.05 for each; Table III). The change in preoperative and postoperative platelet counts is shown in Figure 2.

Table IV presents the relationship between the platelet count at baseline (perioperative period) and the amounts of PRBC replacement at 1, 6, 12, 18, 24, 30, 36, 48, 60, and 72 h postoperation. Accordingly, a significant negative correlation was detected between the baseline platelet count and amount of PRBC replacement at 36 h postoperation (*r*=−0.672; p=0.047). This suggests that the amount of PRBC replacement at 36 h postoperation decreased by increasing the baseline platelet count. When assessing other comparisons, no significant linear correlation was found between the baseline platelet count and amount of PRBC replacement at certain timepoints (p>0.05 for each).

DISCUSSION

Craniosynostosis represents a relatively common disorder, with an estimated incidence of 1 in 2000 births. The cranial deformity results from the early closure of cranial sutures.

Table III: Changes in Hb and Platelet Counts During the Preoperative and Postoperative Periods

	Hb	p	Platelet	p
Preop.	11.67 ± 1.07		410.55 ± 107.17	
1 h	12.18 ± 1.30		407.53 ± 123.74	
6 h	10.54 ± 1.38		352.32 ± 101.35	
12 h	10.82 ± 1.10		316.84 ± 78.06	
18 h	11.03 ± 0.95		309.00 ± 82.06	
24 h	11.23 ± 1.18	**<0.001**	299.50 ± 80.24	**<0,001**
30 h	11.02 ± 1.23		284.63 ± 80.48	
36 h	11.54 ± 1.44		272.63 ± 88.68	
48 h	11.64 ± 1.43		265.84 ± 71.83	
60 h	12.08 ± 1.16		267.82 ± 70.90	
72 h	12.38 ± 1.01		298.37 ± 77.07	

One-way analysis of variance was used in repeated measurements. Descriptive statistics are presented s standard deviation. P values marked as bold were considered as significant (p<0.05).

Table IV: Comparison of the Peroperative Platelet Count and Amount of PRBC Replacement During Postoperative Hours

	PRBC	r	p
Platelet	**1 h**	NaN	NaN
	6 h	−0.283	0.240
	12 h	0.064	0.813
	18 h	0.044	0.897
	24 h	0.078	0.830
	30 h	0.201	0.474
	36 h	−0.672	**0.047**
	48 h	0.308	0.305
	60 h	−0.131	0.805
	72 h	NaN	NaN

***NaN:** Not a number, Spearman Rho correlation coefficient was used. P values marked as bold were considered as significant (p<0.05).*

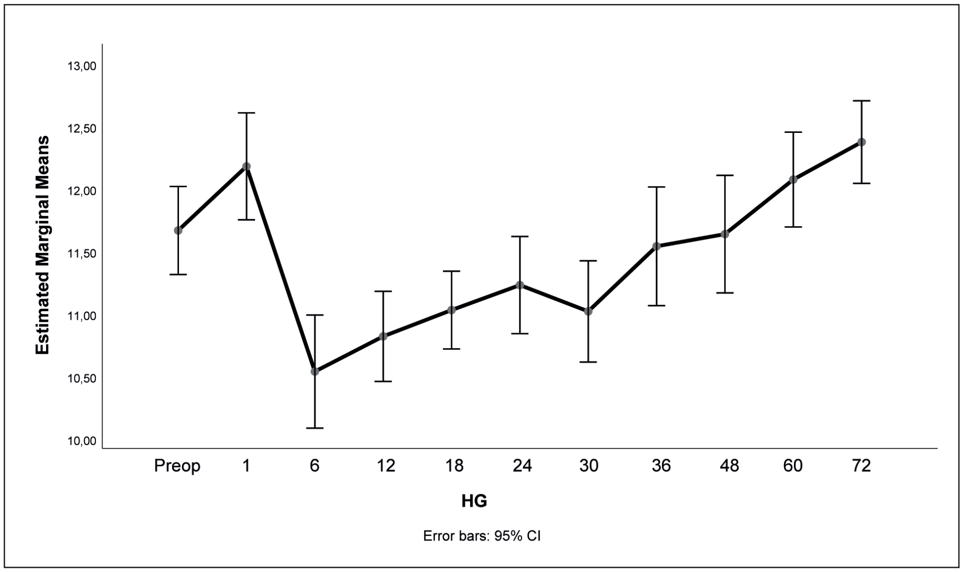

Figure 1: Change in preoperative and postoperative hemoglobin values.

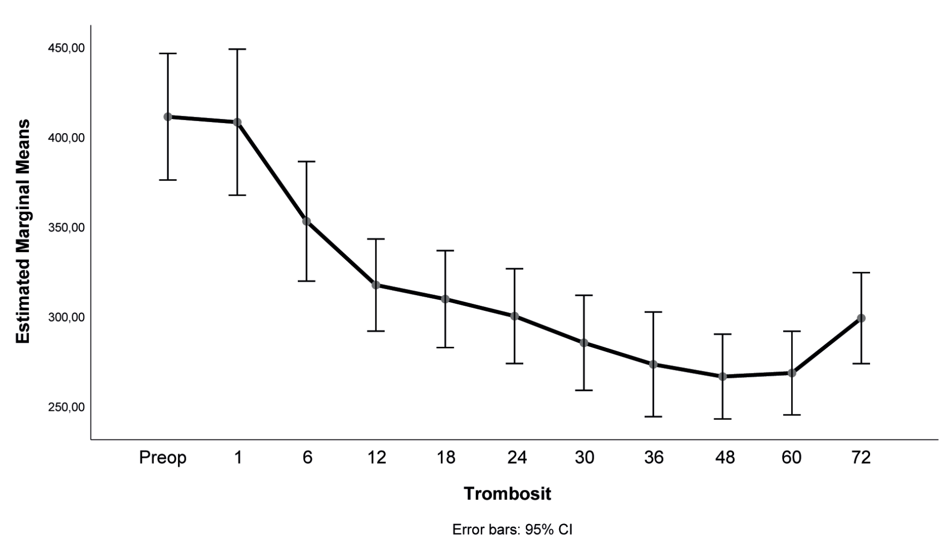

Figure 2: Change in preoperative and postoperative platelet counts.

Rapid brain growth within the first year of life consequently results in intracranial hypertension and cognitive disorders later in life. Primary surgical repair is generally recommended within the first year of life (7). Despite the low circulatory blood volume, surgery is performed at least within 6 months of life. Thus, the relatively small blood loss significantly impacts hemodynamics and blood clotting.

Numerous studies have been conducted with the aim of minimizing complications related to hemorrhage. Although several centers apply autologous blood collected during the preoperative period intraoperatively, (6) antifibrinolytic agents intraoperatively, (1,3,12) recombinant human erythropoietin preoperatively, (5) and fibrin glue (21), no procedure is widely accepted (9). Generally, surgery for craniosynostosis is performed within the first 6 months of life. However, some authors have proposed that surgery should be postponed until 6–9 months of age to minimize bleeding complications, unless increased intracranial pressure is a concern (2,9,19).

Park et al. reviewed 40 cases of craniosynostosis, which included 31 boys and 9 girls, and found that the mean age and weight were 14.6 months and 10,300 g, respectively, in the study population (13). Dahmani et al. reviewed 41 cases of craniosynostosis, which included 13 boys and 29 girls, and found that the mean age was 7.2 months, ranging from 4 to 19 months (2). Kucuk et al. reported that the mean age and weight were 7.4 months and 8,269 g, respectively, in the 143 cases reviewed that included 100 boys and 43 girls (9). Herein, the mean age was 6.03 ± 4.21 months in the 38 patients of craniosynostosis. Of the patients, 22 (57.9%) were boys and 16 (42.1) were girls. The mean weight was 7207.89 ± 1983.63 g. The demographic characteristics of our study population were consistent with those reported in the literature.

Herein, the most common forms of craniosynostosis included metopic synostosis (44.7%), followed by sagittal (28.9%) and unicoronal synostosis (13.2%). However, a few studies reported sagittal synostosis as the most common (13,18). Herein, the higher prevalence of metopic synostosis may have been due to the demographic characteristics of our patients.

Massimi et al. reported that the patients who underwent surgery involving a smaller scalp incision and shorter operative duration exhibited lower transfusion requirement than those with open sagittal synostosis, consistent with our results (10).

Prolonged surgical duration is an important factor affecting the amount of bleeding. Surgical team experience may indirectly reduce the amount of bleeding by shortening the surgical duration. (20,22) Herein, the mean surgical duration was 105.66 ± 211.97 min (range, 60–180 min). Numerous studies reported longer surgical duration. White et al. reported that the mean duration of fronto-orbital advancement surgeries was 5.11 h (22). In a study by Kang et al., the mean surgical duration was 3.5 h (8). Herein, the surgical duration was shorter than those reported in the literature, presumably owing to the collective experience of the surgical team who have been working together for many years.

The mean intraoperative PRBC replacement amount and surgical duration were 61.2 ml and 124.4 min, respectively, in a case series involving 143 patients in a study by Kucuk et al. (9). In a study targeting the reduction of postoperative bleeding via intraoperative fibrin glue application, White et al. reported that the amount of PRBC replacement was >300 ml in 116 cases (21). In a study comparing endoscopic and open surgeries, Shah et al. reported that the mean intraoperative PRBC replacement amount and surgical duration were 218 ml and 179 min, respectively (16). A study by Moon et al. involving patients with sagittal synostosis who underwent barrel and Z osteotomies reported a mean blood transfusion amount and surgical duration of 451 ml and 6.5 h, respectively (11). In a study by Zakhary et al. involving 100 patients who underwent barrel osteotomy, the mean intraoperative PRBC transfusion amount and surgical duration were 302.8 ml and 216.7 min, respectively (24).

Herein, the mean PRBC replacement amount was 83.82 ± 22.49 ml perioperatively and 50, 56.58 ± 16.75, 48.44 ± 15.78, 58.63 ± 13.98, 61 ± 23.66, 51.67 ± 25.62, 51.15 ± 11.57, and 48.33 ± 4.08 ml at 1, 6, 12, 18, 24, 26, 48, and 60 h postoperatively, respectively.

Our results are in agreement with those reported by Kucuk et al. (9). The smaller amount of blood replacement in our study may have been due to the shorter surgical duration owing to the several years of collective experience of the surgical and anesthetic teams.

Pieters et al. reported that FFP infusion preoperatively did not differ from the on-demand use of FFP perioperatively regarding the need for blood transfusion (14).

During surgery for craniosynostosis, the estimated blood loss ranged from 20% to 500% of the total blood volume (23). Following the blood loss of 150%–200% of the total blood volume, a significant dilution effect on other clotting factors becomes apparent, with thrombocytopenia developing in general, resulting in increased need for blood transfusion. To reduce the amount of the transfusion of any type of blood product, clotting time (clot formation velocity), clot formation time (seconds; platelet level/function and fibrinogen/polymerization level), alpha degree, and maximum clot firmness (seconds; platelet/fibrinogen/factor XIII, fibrinolysis) can be assessed via thromboelastography or rotational thromboelastometry. In a study on fibrinogen by Haas et al., the preoperative platelet count was 332 × 10^3. The authors reported that the platelet count decreased to 179 × 10^3 intraoperatively and to 143 × 10^3 postoperatively (4).

Herein, the preoperative platelet count was 410 × 10^3, which tended to decrease at 12, 18, 24, and 36 h postoperation, similarly to that reported by Haas et al (4).

In a study that evaluated prophylactic FFP preoperatively, Pieters et al. reported a preoperative platelet count of 341.1 × 10^3 in the study group and 351.4 × 10^3 in the control group (14). Similar to the findings of our study, the platelet count was 176.4 × 10^3 and 179.6 × 10^3 in the study and control groups, respectively. Herein, the platelet count started to increase 48 h postoperation, consistent with the findings of previous reports.

Herein, we assessed the relationship between preoperative platelet count and amount of postoperative blood replacement and found that the amount of PRBC replacement at 36 h postoperation significantly decreased by increasing the preoperative platelet count; however, no such relationship was observed at the other timepoints. This suggests that the reduction in platelet count affects the amount of erythrocyte replacement in the postoperative period, although not resulting in platelet replacement.

In the 38 patients included in this study, platelet replacement was required in 2 patients at 36 and 60 h postoperation. In the study by Pieters et al., 2 of the 40 patients in the control group and 2 of the 39 patients in the study group received postoperative platelet replacement (14). The platelet replacement rate in our study was in agreement with that reported in the study by Pieters et al.

As surgery for craniosynostosis is usually performed within the first 6 months of life when the total blood volume is lower, the estimated postoperative blood loss increases owing to the hemodilutional coagulopathy caused by blood loss and intraoperative fluid replacement. We consider that preoperative and postoperative platelet counts affect the estimated amount of blood loss. In numerous clinics, blood replacement is achieved via blood products. However, blood loss during surgery is replaced using whole blood, thereby suggesting that although platelet counts do not indicate the need for blood replacement, the amount of blood replacement is low in patients with high platelet counts. However, we believe that prospective controlled studies are warranted to further clarify this issue.

As patients with craniosynostosis are generally younger than 1 year, preoperative preparation is greatly important. Thus, increasing platelet counts in the preoperative period is essential to minimize bleeding and the amount of blood replacement.

CONCLUSION

The platelet counts decreased within the first 48 h postsurgery and tended to elevate thereafter; thus, clinicians should closely monitor these platelet counts within 48 h after surgery. A correlation was reported between the baseline platelet counts and the amount of blood replacement at 36 h postoperation; thus, clinicians should be more careful in this regard.

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AUTHORSHIP CONTRIBUTION

Study conception and design: NAD, ISO
Data collection: AS
Analysis and interpretation of results: ZFK, AS
Draft manuscript preparation: NAD, AK
Critical revision of the article: NAD, AK, ISO
All authors (NAD, AK, AS, ZFK, ISO) reviewed the results and approved the final version of the manuscript.

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