



## Effectiveness of Platelet Markers in Estimating the Amount of Intraoperative Bleeding in Vertebra Surgery

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### 1. INTRODUCTION

Perioperative bleeding is an undesirable but inevitable complication of surgery. Bleeding control in the surgical field or insufficiency in hemostatic pathways are the two main causes of perioperative bleeding. One of the most important steps in perioperative bleeding management is the early identification of the patient at risk.

Coagulation tests and platelet counts are the parameters examined for preoperative evaluation before major surgery. Mean platelet volume (MPV, which indicates the size of platelets), platelet dis-

tribution width (PDW, which shows the size heterogeneity of platelets), plateletcrit (PCT, which is the percentage of platelets in circulation), MPV/lymphocyte count ratio (MPVLR), and platelet count/lymphocyte count ratio (PLR) are parameters that provide information about platelet functions.

As far as we know to date, there are no studies in the literature examining platelet markers as a predictor for intraoperative surgical bleeding in vertebra surgeries. In this study, we aimed to investigate the effectiveness of preoperative MPV,

**Purpose:** One of the most important steps in perioperative bleeding management is the predetermination of the patient at risk. Even if there is no hemostatic abnormality in vertebral surgery, which is a major surgery, severe bleeding can be encountered and many perioperative blood transfusions might be required. In this study; we investigated the effectiveness of preoperative mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), mean platelet volume lymphocyte count ratio (MPVLR), and platelet count to lymphocyte count ratio (PLR) values in predicting the amount of intraoperative bleeding in patients who will undergo vertebral surgery.

**Method:** Preoperative MPV, PDW, PCT, MPVLR, PLR values and demographic data such as gender, age, ASA score and body mass index (BMI) were recorded in patients scheduled for vertebral surgery in the neurosurgery clinic. In addition, the duration of surgery, the number of vertebral transpedicular screwing and laminectomy levels as surgical procedure were recorded. The amount of intraoperative bleeding was obtained by calculating the amount of blood accumulated in the aspirator and the amount of blood in the sponges during the operation.

**Results:** Of the 63 patients included in the study, 60.3% (n=38) were female and 39.7% (n=25) were male. The mean age of the patients was  $54.7 \pm 11$  years and the mean BMI was  $29.6 \pm 4.6$ . No correlation was found between the amount of bleeding and gender, age, MPV, PDW, PCT, MPVLR, or PLR values. A significantly high correlation was found between amount of bleeding and BMI, duration of surgery, and the number of transpedicular screwing segments.

**Conclusion:** Platelet markers do not appear to have an effect on the amount of bleeding. However; as the BMI increases, the duration of surgery prolongs and the number of transpedicular screw segments increases for which the amount of bleeding increases.

**Keywords:** Intraoperative bleeding amount, Mean platelet volume, Mean platelet volume lymphocyte ratio, Platelet distribution width, Plateletcrit, Platelet lymphocyte ratio

PCT, PDW, MPVLR and PLR values for predicting the amount of intraoperative bleeding in patients undergoing vertebra surgery.

## **2.MATERIALS and METHODS**

This prospective, clinical observational study was conducted at Sakarya University Training and Research Hospital in accordance with the Declaration of Helsinki, after receiving approval from the Sakarya University Faculty of Medicine Non-Interventional Ethics Committee on November 9, 2020 (decision no: 71522473/050.01.04/566).

### **2.1.Patient selection and exclusion criteria**

Patients between the ages of 18 and 65 years who were classified by the American Society of Anesthesiologists (ASA) to fall within I–III risk groups and who would undergo elective surgery for lumbar vertebra stabilization, were included in our study. Those who declined to participate in the study, patients under 18 years and over 65 years old, patients in the ASA IV and higher risk groups, with a body mass index (BMI) of 35 and above, with low platelet count (<150,000) or diagnosed with platelet dysfunction, those who received anti-coagulant or used antiplatelet drugs, who had previous vertebral surgery, patients with more than five segments of surgical level, and patients with liver failure and chronic renal failure were excluded from the study. Patients who met the inclusion criteria were identified from surgery lists. A day before the surgery, the patients were visited at the neurosurgery clinic. Written informed consent was obtained from patients who were informed about the study and agreed to participate. The study was conducted with a single surgical team to ensure standardization.

### **2.2.Collection of data**

Patient demographic data was collected for the study: age, gender, ASA score, height, weight, and

BMI were recorded. MPV, PCT, PDW, PLR and MPV-LR values obtained from the hemogram sample taken in the ward before the operation was recorded. The total surgery time from the beginning to the end and the number of vertebral instruments and laminectomy levels performed as surgical procedures were recorded.

### **2.3.Calculation of bleeding amount**

The total amount of bleeding that occurred during the surgery was calculated. First, the amount of aspirated blood was calculated by subtracting the amount of washing solution in the graduated bottles used in the surgical area from the amount accumulated in the aspirator at the end of the surgical procedure. In addition, at the end of the surgical procedure, the amount of blood collected in the sponges was calculated by subtracting the total dry sponge weight from the total weight of the bloody sponges used. In the weighing calculation, the average density of the blood (plasma + blood cells) was taken as 1060 kg/m<sup>3</sup>, and each gram on the precision scale was considered as 1 milliliter.<sup>1</sup>

### **2.4.Anesthesia management**

After the patients were taken to the operating room, peripheral venous cannulation was performed and 0.9% NaCl infusion was started. Electrocardiogram (ECG), pulse oximetry (SpO<sub>2</sub>), and noninvasive arterial blood pressure monitoring were performed on the patients for routine monitoring. Anesthesia induction was achieved intravenously with 2 mg/kg propofol (2%), 2 mcg/kg fentanyl, and 0.6 mg/kg rocuronium. After sufficient muscle relaxation was achieved, intubation was performed with a spiral-cuffed endotracheal tube (ETT). Neuromuscular blockade in patients was maintained with rocuronium at doses of 0.15 mg/kg at 30–45 minute intervals. Anesthesia was maintained with sevoflurane and an oxygen and air gas mixture with a minimum alveolar con-

centration (MAK) value of 1, with was performed using remifentanil infusion at a dose range of 0.05–0.25 mcg/kg/min. Approximately 30 minutes before terminating anesthesia, 1 mg/kg tramadol and 1 g paracetamol were administered intravenously for postoperative analgesic treatment. After the surgery was completed, the sevoflurane vaporizer was turned off. The effect of the neuromuscular agent was antagonized with 2 mg/kg sugammadex and when patient breathing was at an adequate volume, they extubated and taken to the postoperative recovery unit.

## 2.5. Statistical analysis

The SPSS 20 software program was used for statistical analysis of the data. Qualitative data were expressed as numbers and percentages. Quantitative data were expressed as mean and standard deviation was given. The correlation of quantitative data was evaluated with the Pearson correlation test. Normality test of continuous data was performed with Kolmogorov–Smirnov test. Comparison of repeated measurements of continuous variables was made with Student’s t-test. Factors related to the total amount of bleeding were investigated by correlation test. Factors associated with the amount of intraoperative bleeding were examined by linear regression analysis. In all tests, the statistical significance level was taken as  $p < 0.05$ . The minimum sample size required to detect an effect size of 0.4 between the two variables of interest with an  $\alpha = 0.05$  type 1 error and 80% power under the  $H_0: p = 0$  hypothesis, was found to be 46 patients using G.Power-3.1.9.2.

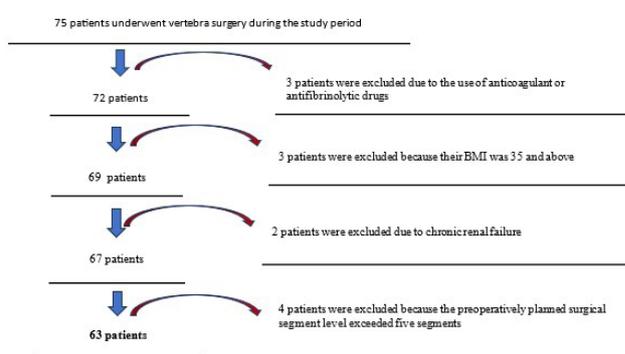
## 3. RESULTS

In our study, a total of 75 patients who underwent surgery for vertebra stabilization at the neurosurgery clinic of Sakarya Training and Research Hospital were evaluated. The data from 63 patients were analyzed, three patients were excluded from

the study due to the use of anticoagulant or anti-fibrinolytic drugs, three patients were excluded because their BMI was 35 and above, two patients were excluded because of existing chronic renal failure, and four patients were excluded because the preoperative planned surgical segment level exceeded five segments (Figure 1).

**Figure 1.**

### Workflow diagram



Demographic data and platelet parameters of the patients are given in Table 1. The average amount of intraoperative bleeding in the patients was  $298.73 \pm 170.3$  ml (60–920). The number of transpedicular screw segments and laminectomies performed as surgical interventions for vertebra stabilization and the amount of bleeding are given in Table 2.

The relationship between the amount of bleeding and the number of transpedicular screw segments was analyzed. Patients who underwent one and two segment transpedicular screw procedures lost  $213 \pm 95$  ml of blood, and patients who underwent three segments or more transpedicular screw procedures lost  $420 \pm 180$  ml of blood. The amount of bleeding was found to increase significantly in patients who underwent transpedicular screw procedures of three segments or more ( $p = 0.002$ ; Figure 2).

**Table 1.**

*Demographic data and platelet parameters of the patients*

*Values are given as mean  $\pm$  standard deviation, n, and percentage. n=number of patients. cm=centimeters. min=minutes. kg=kilogram. BMI=body mass index. MPV=mean platelet volume. PDW=platelet distribution width. PCT=Plateletcrit. MPVLR=mean platelet volume/lymphocyte count ratio. PLR=platelet count/lymphocyte count ratio.*

Total number of patients (n)	63
Gender, n (%)	
Female	38 (60.3%)
Male	25 (39.7%)
ASA, n (%)	
I	7 (11.1%)
II	31 (49.2%)
III	25 (39.7%)
Age (year)	54.0 $\pm$ 11.0
Size (cm)	161.6 $\pm$ 21.8
Weight (kg)	79.0 $\pm$ 12.0
BMI (kg/m <sup>2</sup> )	29.2 $\pm$ 4.6
Surgery duration (min)	125.3 $\pm$ 28.6
MPV	8.5 $\pm$ 1.3
PDW	18.2 $\pm$ 1.1
PCT	0.21 $\pm$ 0.06
MPVLR	4.0 $\pm$ 2.0
PLR	113.9 $\pm$ 46.7

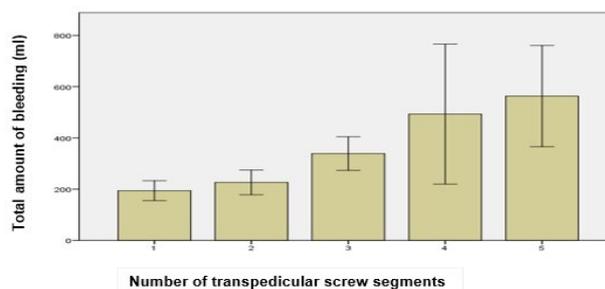
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When examining the demographic data of the pa-

tients and the amount of bleeding, no significant correlation was found between gender and age and the amount of bleeding ( $p=0.93$  and  $p=0.16$ , respectively). A significant and moderate correlation was detected between BMI and the amount of bleeding ( $p < 0.01$ ; Table 4). When the relationship between platelet markers and bleeding amount was evaluated; no correlation was found between MPV ( $p=0.83$ ), PDW ( $p=0.12$ ), PCT ( $p=0.13$ ), MPVLR ( $p=0.49$ ), and PLR ( $p=0.83$ ) values and the amount of bleeding (Table 3). On the contrary, a significantly high correlation was detected with the duration of surgery and the number of transpedicular screw segments, and a moderate correlation was detected with the number of laminectomies ( $p < 0.01$ ; Table 4).

**Figure 2**

*Relationship between total bleeding amount and number of transpedicular screw segments. Values are the mean and error bars represent standard deviation (95% CI).*



To examine the factors associated with the amount of intraoperative bleeding, linear regression analysis was performed between the amount of bleeding and factors with moderate or a high degree correlation. BMI ( $p < 0.01$ ,  $\beta=0.22$ ), surgical time ( $p < 0.01$ ,  $\beta=0.40$ ), and number of transpedicular screw segments ( $p < 0.01$ ,  $\beta=0.37$ ) were associated with the amount of bleeding. The effect of the number of laminectomies on the amount of bleeding was not found to be significant according to linear regression analysis ( $p=0.882$ ,  $\beta=0.01$ ; Table 5).

**Table 2.**

*Distribution of bleeding amount according to surgery type and level*

		n (%)	Amount of bleeding (ml)		
			Mean ± SD	Minimum (ml)	Maximum (ml)
Number of transpedicular screw segments	1	15 (23.8%)	194 ± 70	60	300
	2	22 (34.9%)	226 ± 108	90	475
	3	15 (23.8%)	339 ± 118	170	580
	4	5 (7.9%)	493 ± 220	270	720
	5	6 (9.5%)	563 ± 188	370	920
Laminectomy	0	5 (7.9%)	225 ± 197	60	500
	1	23 (36.5%)	229 ± 105	90	580
	2	28 (44.4%)	326 ± 151	95	700
	3	5 (7.9%)	369 ± 201	235	720
	4	2 (3.2%)	712 ± 293	505	920

Values are given as mean ± standard deviation, n, and percentage. n=number of patients. SD=standard deviation. ml=milliliter.

**Table 3.**

*Correlation of bleeding amount and platelet markers*

		MPV	PDW	PCT	MPVLR	PLR
Total amount of bleeding	r	0.03	0.19	0.19	0.09	0.27
	p	0.83	0.12	0.13	0.49	0.83

\*p<0.05 Pearson correlation test. MPV=mean platelet volume. PDW=platelet distribution width. PCT=platelet-crit. MPVLR=mean platelet volume/lymphocyte count ratio. PLR=platelet count/lymphocyte count ratio.

**Table 4.**

*Correlation of bleeding amount and operation characteristics*

		Gender	Age	BMI	Duration of surgery	Number of transpedicular screw segments	Number of laminectomies
Total amount of bleeding	r	0.01	0.18	0.46	0.67	0.69	0.47
	p	0.93	0.16	<0.01*	<0.01*	<0.01*	<0.01*

\*p<0.05 Pearson Correlation test. BMI=body mass index

**Table 5.**

*Factors affecting the amount of intraoperative bleeding according to the results of linear regression analysis*

	Not standardized		Standardized	T	p value
	β	SD	β		
BMI (kg/m2)	9.65	3.45	0.22	-3.81	<0.01*
Surgery duration	2.39	0.64	0.40	3.69	<0.01*
Number of transpedicular screw segments	52.55	14.77	0.37	3.55	<0.01*
Number of laminectomies	2.83	19.01	0.01	0.14	0.882

β=regression coefficient. BMI=body mass index. SD=standard deviation.

#### 4. DISCUSSION

Although no correlation was found between the amount of intraoperative bleeding and MPV, PDW, PCT, MPVLR, and PLR values, a correlation was observed between the duration of surgery and the number of transpedicular screw segments applied and the amount of bleeding. Additionally, while no correlation was found between gender and age and the amount of bleeding, a significant correlation was found between high BMI and the amount of bleeding.

We examined all of these parameters in our study separately and in relation to studies in the literature that address situations that are prone to intraoperative bleeding or coagulation. Evaluating our findings based on the results of studies on susceptibility to intraoperative bleeding or coagulation might be important to understand the relationship to the existing literature. We believe that such a comparison might help to better understand the findings of our current study and also allow us to identify consistency or differences between information in the literature and our own findings.

It has been shown that male gender is a risk factor for intraoperative bleeding in patients with proximal humerus fractures.<sup>2</sup> Two different studies conducted on patients undergoing vertebra surgery showed that gender did not affect the amount of bleeding.<sup>3,4</sup> Similarly, in our study, no significant difference was detected between male and female patients in terms of the amount of intraoperative bleeding. It has been reported that increasing age correlates with an increase in the amount of bleeding in colon surgery, gastrectomy, and nephrectomy surgeries.<sup>5-6</sup> Furthermore, increasing age is a risk factor for bleeding during bariatric surgeries.<sup>7,8</sup> In patients who underwent retropublic prostatectomy and hepatic resection, age was not associated with the amount of bleeding.<sup>9</sup> Another

study reported no correlation between perioperative blood loss and age in patients who underwent percutaneous kyphoplasty due to vertebral fracture.<sup>10</sup> In our study, no relationship was found between the age of the patients and the amount of surgical bleeding. This could be because the age distribution of the patients in our study was not homogeneous and that patients over the age of 65 were excluded from the study. In other studies involving prostatectomy and cystectomy surgeries, BMI has been reported to be a predictive variable in predicting increased blood loss.<sup>11-12</sup> Villavicencio et al. investigated the factors associated with blood loss of 172 patients who underwent vertebra surgery, and reported that patients with a BMI of more than 30 kg/m<sup>2</sup> were associated with more intraoperative blood loss.<sup>13</sup> According to the data of a retrospective study on the possible causes of surgical occult bleeding in 143 patients who underwent vertebra surgery, the amount of bleeding increased in patients with a BMI greater than 24 kg/m<sup>2</sup>.<sup>14</sup> Similar to the results of various studies in the literature, a moderately significant correlation was found between BMI and bleeding amount in our study.

High platelet volume is an important variable in the pathophysiology of thrombosis. Large platelets produce more prothrombotic substances, such as thromboxane A<sub>2</sub>, B-thromboglobulin, P-selectin, glycoprotein-IIIa, and serotonin compared with normal-sized platelets.<sup>15</sup> For this reason, large volume platelets are more prone to adhesion and aggregation compared with smaller ones. In the literature, high MPV value is accepted as an independent risk factor for different clinical conditions.<sup>16-17</sup> It was observed that patients with pulmonary embolism had higher MPV values than those in the control group without a diagnosis of pulmonary embolism.<sup>18</sup> Increased MPV has been observed in cardiovascular diseases, cerebral

stroke, respiratory diseases, chronic renal failure, and rheumatoid diseases.<sup>20</sup> It has been reported that an MPV 11.6 fL or greater might be an independent risk factor for heart infarction in patients with coronary heart disease and that patients with high MPV have a higher risk of acute stroke than patients with normal MPV values.<sup>19</sup> In the literature, it was seen that high MPV value was associated with susceptibility to coagulation. In our study, no correlation was found between MPV values and the amount of bleeding. More studies are needed to confirm that the MPV value is not effective in predicting the amount of bleeding.

There are various studies in the literature investigating the relationship of PDW value with the prothrombotic process. It has been shown that platelet activity plays a central role in myocardial infarction and that high PDW is associated with prognosis in patients with CAD (coronary artery disease).<sup>20,21</sup> PDW was found to be higher in patients with ST-elevation myocardial infarction (STEMI) compared with those with stable CAD.<sup>20</sup> In one study; the PDW value was an independent marker of STEMI in young patients and might reflect the prothrombotic state in this specific population, given that it has been reported that a 1 fL increase in PDW levels corresponds with 13.5% greater likelihood to be associated with STEMI in young people.<sup>21</sup> Also, PCT value, another platelet marker, is an independent marker for STEMI and might reflect the prothrombotic state, especially in the young patient population.<sup>23</sup> In the literature, we see that an increase in PDW and PCT values causes susceptibility to prothrombotic conditions such as myocardial infarction. In our study, we found that PDW and PCT values did not have a positive or negative effect on the amount of bleeding. More studies are needed to determine if these values are not effective in estimating the amount of bleeding.

When we examined the literature, we found that similar to the other platelet markers we discussed in our study, that there are no studies on MPVLR and PLR values regarding the amount of bleeding. Attention has been drawn to the importance of these values in various diseases associated with the thrombotic process. In a study of 266 stroke patients who received intravenous thrombolysis, it was thought that MPVLR could be used as an activity marker for prognosis in acute ischemic stroke patients receiving intravenous thrombolysis.<sup>22</sup> Studies have reported that patients with acute deep vein thrombosis have increased MPVLR and PLR values compared with the control group.<sup>23</sup> Also, patients with retinal vein occlusion had higher PLR values than the control group.<sup>24</sup> A meta-analysis by Wang et al. conducted in 2017, recommended PLR to be used routinely in the prognostic evaluation of pulmonary embolism.<sup>25</sup> Similarly, Telo et al. concluded that the PLR value increased in patients at high risk for acute pulmonary embolism and that the PLR value had an estimated predictive value for 3-month mortality.<sup>26</sup> Although there is no specific study in the literature on whether MPVLR and PLR values are directly related to the amount of bleeding, these markers could be valuable indicators in many diseases and are associated with thrombotic conditions. In our study, we did not detect a relationship between MPVLR and PLR values and the amount of bleeding. Various surgical clinical studies are needed to elucidate whether these values are predictive in estimating the amount of bleeding.

We examined the relationship between surgical time and the number of transpedicular screw segments and the amount of intraoperative bleeding. Zheng et al., in their study involving patients undergoing lumbar spine surgery, reported the number of surgical vertebra segments as a predictive factor in terms of intraoperative blood loss.<sup>27</sup> In

another study, Thompson et al. in their study of 311 patients who underwent vertebra surgery, reported that the amount of bleeding increased as the number of vertebral segments underwent surgery and the surgical time increased.<sup>28</sup> In agreement with similar vertebral surgery studies in the literature, we concluded in our study that the amount of bleeding increases proportionally with the surgical time and the number of transpedicular screw segments.

Our study has some limitations. To ensure standardization, we planned our study to be conducted in a single center and with a single surgical team to eliminate differences in operating room conditions, surgery, and anesthesia protocols. For these reasons, our most important limitation was that we performed a single-center study with a small number of patients. Another limitation was that the number of laminectomy and transpedicular screw segments performed in the patients was not distributed homogeneously.

## 5. CONCLUSION

We did not detect a correlation between the amount of intraoperative bleeding and patient gender, age, and platelet markers MPV, PCT, PDW, MPVLR, and PLR values. However, with secondary inferences we found that the amount of bleeding increased corresponding to increased patient BMI, surgery time, and the number of transpedicular screw segments applied.

In many clinics around the world; conventional coagulation parameters and platelet counts are first evaluated in terms of bleeding risk during preoperative routine anesthesia evaluation. With this study, we wanted to draw attention to platelet markers that we think are ignored with the aim of gaining a broader perspective during the preoperative evaluation process. Although we did

not determine the predictive relationship between platelet markers and the amount of intraoperative bleeding, we believe that many different clinical studies are needed to confirm this.

### **Ethics Committee Approval**

Sakarya University Faculty of Medicine Non-Interventional Ethics Committee November 9, 2020 (decision no: 71522473/050.01.04/566). The study was carried out following the international declaration and guidelines.

### **Conflict of Interest**

No conflict of interest was declared by the authors.

### **Author Contributions**

Concept – SÇ, OP; Supervision – OP, HK, ATT; Materials – SÇ, DC; Data Collection and Processing – SÇ, OP, HK; Analysis and Interpretation – OP, ATT; Writing –SÇ

### **Peer-review**

Externally peer-reviewed.

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