DOI: 10.4274/jarem.galenos.2025.22590
J Acad Res Med 2025;15(3):112-21

Association of Pre-operative Hematological, Inflammatory Markers, and Myoma Characteristics with Post-operative Erythrocyte Suspension Requirement Following Myomectomy: A Retrospective Observational Study

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Cite this article as: Tercan C, Dağdeviren E, Tercan E, Tunç B, Güler OM, Güner G. Association of pre-operative hematological, inflammatory markers, and myoma characteristics with post-operative erythrocyte suspension requirement following myomectomy: a retrospective observational study. J Acad Res Med. 2025;15(3):112-21

ABSTRACT

Objective: To evaluate the association of pre-operative hematologic and inflammatory markers, fibroid burden, surgical factors, and surgeon experience with post-operative erythrocyte suspension (ES) transfusion risk in patients undergoing laparotomic (LM) and laparoscopic myomectomy (LSM).

Methods: This retrospective case-control study included patients undergoing LM or LSM. Baseline demographics, clinical characteristics, pre- and post-operative hematologic and inflammatory parameters, and surgical data were analyzed. Multivariate logistic regression identified independent predictors of ES transfusion. Receiver operating characteristic curves established the pre-operative hemoglobin cut-off values that predict transfusion risk.

Results: Transfusion groups had longer operation times, larger and heavier fibroids, and lower pre-operative hemoglobin in both LM and LSM cohorts. Myoma count and surgeon experience were independent predictors of transfusion only in the LM group, [odds ratio (OR) =1.128 and OR =0.916, respectively]. No inflammatory markers, including systemic immune-inflammation index, significantly predicted transfusion. Pre-operative hemoglobin cut-off of 11.75 g/dL predicted transfusion with moderate accuracy in both LM [area under the curve (AUC) =0.633] and LSM (AUC =0.639) groups. Surgeon experience reduced transfusion risk in LM, but not in LSM.

Conclusion: Fibroid burden, operation time, and surgeon experience significantly influence transfusion risk in myomectomy, especially in open surgery. A pre-operative hemoglobin level of 11.75 g/dL serves as a useful threshold for anemia management to minimize transfusion needs. Incorporating these clinical factors into perioperative planning may improve patient safety and reduce transfusion-related complications. Further prospective studies are needed to refine prediction models.

Keywords: Inflammatory markers, laparoscopy, laparotomy, myomectomy, siri, surgeon experience, transfusion risk

INTRODUCTION

Background

Uterine fibroids (leiomyomas) are the most common benign tumors among women of reproductive age, often presenting with heavy menstrual bleeding, pelvic pain, and infertility. Myomectomy the surgical removal of fibroids, is performed to relieve these symptoms while preserving the uterus, particularly in women desiring future fertility. By age 50, uterine fibroids have been reported in up to 70% of White women and 80% of Black women (1). Although hysterectomy remains the most frequently performed surgery for symptomatic fibroids, myomectomy is increasingly favored in younger women to maintain reproductive potential. However, compared to hysterectomy, myomectomy is associated with greater intraoperative blood loss due to uterine anatomic disruption and tumor-related neovascularization.

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Received Date: 13.06.2025 **Accepted Date:** 14.08.2025
Epub: 21.10.2025
Publication Date: 02.12.2025

J Acad Res Med 2025;15(3):112-21

Myoma size, location, and number significantly influence bleeding risk and thus transfusion rates. In a tertiary center, open (abdominal) myomectomy transfusion rates ranged from 4.7% to 6.4%, whereas laparoscopic myomectomy (LSM) transfusion rates were approximately 2.2% (2). Intraoperative transfusions not only increase morbidity but also impact recovery and resource utilization. Average blood loss in large multiple fibroids can approach 800 mL (2).

Recent research indicates that various platelet indices (PIs), including platelet count (PLT); plateletcrit (PCT); mean platelet volume (MPV); platelet-large cell ratio (P-LCR); platelet distribution width (PDW); and alongside the neutrophil-to-lymphocyte ratio (NLR), an indirect indicator of inflammation; as well as the systemic immune-inflammation index (SII) [SII = platelets × neutrophils (NEU)/lymphocytes] and the systemic inflammatory response index (SIRI) (SIRI = monocytes × NEUs/lymphocytes), undergo notable alterations in different clinical conditions. Elevated SII levels have been linked to unfavorable prognoses in cancer patients and in other diseases, such as ischemic stroke, where a high SII correlates with increased mortality and the likelihood of hemorrhagic transformation (2,3). These observations point to a potential role for SII in predicting outcomes during acute bleeding events, although additional studies are required to validate its diagnostic precision and determine appropriate cut-off values (4). Several publications have also investigated the prognostic utility of these biomarkers in predicting bleeding risk, including contexts like gastrointestinal hemorrhage and the need for platelet transfusions after cardiopulmonary bypass surgery (5,6). Given the considerable variability in surgical bleeding during myomectomy and the clinical impact of transfusion decisions, identifying reliable pre-operative predictors of erythrocyte suspension (ES) transfusion need is clinically important. Akay et al. (7) recently reported that SII may be a significant marker for predicting postpartum hemorrhage risk, underscoring the potential utility of this biomarker in hemorrhagic conditions. Therefore, assessing pre-operative SII and SIRI values could facilitate individualized risk stratification and optimize resource allocation in gynecologic surgery.

Objectives

This study aimed to examine the relationship between myoma characteristics, pre-operative hemogram parameters, PIs, and the need for post-operative ES transfusion in patients undergoing myomectomy. By analyzing these routinely collected laboratory parameters alongside demographic and pathological data, we sought to determine their potential utility as predictors of transfusion requirements in this surgical population.

METHODS

Study Design

This retrospective observational cohort study was conducted to assess the relationship between pre-operative hemogram and PIs and the post-operative requirement for ES transfusion in patients undergoing myomectomy.

Setting and Participants

The study was carried out in the Department of Gynecology and Obstetrics a tertiary care center between 01.04.2020 and 01.04.2024. Medical records of all women aged 20-60 years who underwent open [laparotomic (LM)] or LSM for symptomatic uterine fibroids during this period were reviewed. To eliminate potential confounding influences on PIs, patients with any additional conditions such as diabetes mellitus, malignancies other than sarcoma, autoimmune diseases, or known bleeding disorders were excluded. Other exclusion criteria included pre-operative anemia [defined as hemoglobin (Hb) <10 g/dL], pre-operative or intraoperative ES transfusion, conversion to hysterectomy during the procedure, or missing laboratory or surgical data. The selection process of study participants is summarized in Figure 1.

Ethical Considerations

The Institutional Review Board of University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital approved this retrospective study (approval no: KAEK/12.06.2024.27, date: 26.06.2024). Given the retrospective design, the requirement for informed consent was waived. The study adhered to the principles outlined in the Declaration of Helsinki.

Variables

The primary outcome of the study was the requirement for post-operative ES transfusion, defined as the administration of one or more units of ES within the first 48 hours following surgery.

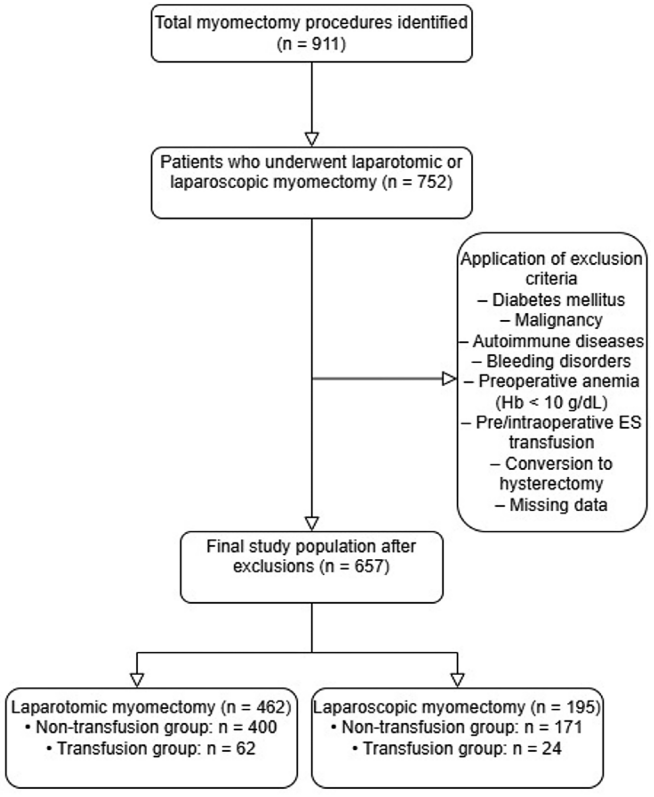

Figure 1. Flow diagram of participants
Hb: Hemoglobin, ES: Erythrocyte suspension

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Independent variables included laboratory parameters such as pre-operative and post-operative (6-hour) complete blood count values. These encompassed PLT; PCT; MPV; PDW; and P-LCR. The inflammatory markers, NLR, platelet-to-lymphocyte ratio (PLR), SIRI, and SII, were also calculated, along with Hb and hematocrit (HCT) levels.

Potential confounding variables considered were age, body mass index (BMI), surgeon experience (in years), surgical approach (laparoscopic vs. open), fibroid characteristics (size, number, and location), operative time, and estimated intraoperative blood loss.

Bias

To minimize selection bias, all consecutive eligible patients during the study period were included. Observer bias was mitigated by blinding the data analyst to transfusion outcomes until completion of statistical modeling.

Study Size

Based on the pilot study by Mohr et al. (6), an effect size of 0.997 was assumed. With an alpha level of 0.05 and a statistical power of 80%, the minimum required sample size was calculated to be 34 patients in total, with at least 17 patients in each group.

Quantitative Variables

Continuous variables were analyzed without transformation. Patients were grouped according to post-operative ES transfusion status (transfusion vs. no transfusion). The relationship between laboratory parameters and transfusion need was evaluated using univariate and multivariate methods.

Statistical Analysis

Statistical analyses were conducted using SPSS version 27.0. Descriptive statistics were used to summarize the data. Continuous variables were reported as mean ± standard deviation or as median with interquartile range (25^{th}-75^{th} percentiles), depending on the distribution. Categorical variables were presented as frequencies and percentages. The Kolmogorov-Smirnov test was used to assess the normality of data distribution. For data with a normal distribution, comparisons between two groups were made using the Student's t-test. For non-normally distributed data, the Mann-Whitney U test was applied for two-group comparisons. Categorical variables were analyzed using either the chi-square test or Fisher's exact test, as appropriate. To determine the optimal cut-off values of pre-operative parameters for predicting the need for ES transfusion, receiver operating characteristic curve analysis was performed, and the area under the curve (AUC) was used to evaluate diagnostic accuracy. Multivariate logistic regression was conducted to identify independent predictors of ES transfusion, with results expressed as odds ratios (OR) and 95% confidence intervals (CI).

RESULTS

Demographic and Clinical Characteristics

Baseline demographic and clinical characteristics, including age, BMI, and comorbidities, were comparable between transfusion and non-transfusion groups in both surgical approaches.

Age, BMI Obstetric History and Previous Abdominal Surgery

Age and BMI did not differ significantly between transfusion and non-transfusion groups in either cohort. In the LM group, mean age was 38.89 vs. 39.12 years (p=0.777), and BMI was 26.74 vs. 26.59 kg/m² (p=0.803). In the LSM group, age was: 38.25 vs. 34.80 years (p=0.468), and BMI was: 26.32 vs. 24.76 kg/m² (p=0.135) (Table 1).

Gravidity was significantly different in the LM group [2.00 (0.00-3.00) vs. 1.00 (0.00-2.00), p=0.033]. No significant differences in gravidity, parity, or previous abdominal surgery history were observed in the LSM group. Type of delivery was similar across all subgroups (Table 1).

Myoma Characteristics

In the LM group, myoma pathology differed significantly between the transfusion and non-transfusion groups (p=0.003), with higher leiomyoma prevalence in the non-transfusion group. No significant differences were found in myoma pathology between subgroups in the LSM group (p=0.982) (Table 1).

Surgical and Laboratory Characteristics

Table 2 summarizes the surgical, pathological, and laboratory characteristics of the study population, highlighting significant differences between transfusion and non-transfusion groups across both LM and LSM cohorts.

In the LM cohort, myoma pathology differed significantly between transfusion groups (p=0.003), with a higher prevalence of leiomyoma in the non-transfusion group. No such difference was observed in the LSM group (p=0.982).

Operation time was significantly longer in transfusion groups in both LM (132.21 vs. 95.77 minutes, p<0.001) and LSM (196.33 vs. 152.89 minutes, p=0.004) cohorts. In LM, more myomas were removed in the transfusion group (2.00 vs. 1.00, p=0.021), although this difference was not observed in LSM (p=0.633). The maximum myoma diameter was larger in transfused patients, in both LM (10.00 vs. 8.00 cm, p<0.001) and LSM (11.50 vs. 10.00 cm, p=0.012). Similarly, myoma weight was significantly higher in transfusion groups; 226.0 vs. 164.8 g in LM (p=0.008) and 167.4 vs. 125.5 g in LSM (p=0.015).

Surgeon experience was lower in the LM transfusion group (4.00 vs. 5.00 years, p=0.044), but no significant difference was found in LSM (p=0.261).

Pre-operative Hb levels were significantly lower in transfusion groups for both LM (11.36 vs. 11.98 g/dL, p=0.002) and LSM (11.47 vs. 12.08 g/dL, p=0.023). Post-operative Hb and HCT values declined in all groups, with a significantly greater drop among those who received transfusions (p<0.001).

White blood cell counts increased post-operatively across all groups (p<0.001), consistent with an inflammatory response, but there were no significant differences between transfusion and non-transfusion groups (p>0.05). Pre-operative PLTs were similar

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Table 1. Demographic and clinical characteristics of participants by transfusion status

Operation			Laparotomic myomectomy			Laparoscopic myomectomy		
			Non-transfusion group (n=400)	Transfusion group (n=62)	p-value	Non-transfusion group (n=171)	Transfusion group (n=24)	p-value
Age[a] (years)			38.89±5.81	39.12±5.64	p=0.777	38.25±6.55	34.80±8.46	p=0.468
BMI[a] (kg/m^2)			26.74±4.54	26.59±4.55	p=0.803	26.32±4.92	24.76±3.70	p=0.135
Previous abdominal surgery[c] (n)			136 (34.1%)	16 (26.2%)	p=0.224	66 (38.8%)	6 (25.0%)	p=0.189
Gravidity[b] (n)			2.00 (0.00-3.00)	1.00 (0.00-2.00)	**p=0.033**	1.00 (0.00-3.00)	2.00 (1.00-3.00)	p=0.493
Parity[b] (n)			1.00 (0.00-2.00)	1.00 (0.00-2.00)	p=0.078	1.00 (0.00-2.00)	2.00 (0.00-3.00)	p=0.181
Type of delivery[c] n (%)		Nulliparous	157 (39.3%)	30 (48.4%)	p=0.243	70 (40.9%)	7 (29.2%)	p=0.274
		VD	128 (32.0%)	20 (32.3%)		57 (33.3%)	12 (50.0%)	
		CS	115 (28.8%)	12 (19.4%)		44 (25.7%)	5 (20.8%)	
Myoma pathology[c] n (%)	*Leiomyoma*		200 (50.0%)	24 (38.7%)	**p=0.003**	89 (52.0%)	12 (50.0%)	p=0.982
	Degenerated leiomyoma		173 (43.3%)	29 (46.8%)		70 (40.9%)	11 (45.8%)	
	Cellular leiomyoma		15 (3.8%)	3 (4.8%)		8 (4.7%)	1 (4.2%)	
	Adenomyoma		4 (1.0%)	2 (3.2%)		-	-	
	Bizarre leiomyoma		5 (1.3%)	1 (1.6%)		1 (0.6%)	0 (0.0%)	
	Mitotically active leiomyoma		1 (0.3%)	0 (0.0%)		1 (0.6%)	0 (0.0%)	
	Fumarate hydratase deficiency		0 (0.0%)	1 (1.6%)		2 (1.2%)	0 (0.0%)	
	STUMP		2 (0.5%)	0 (0.0%)		-	-	
	Malignancy		0 (0.0%)	2 (3.2%)		-	-	

[a]: Normal distribution, mean ± standard deviation, [b]: Non-normal distribution, median (25-75%), [c]: Categorical data, number (%), BMI: Body mass index, VD: Vaginal delivery, CS: Cesarean section, STUMP: Smooth muscle tumor of uncertain malignant potential

between groups. However, post-operative PLTs were lower in the LM transfusion group (233.5 vs. 250×10^9/L, p=0.023) but not significantly different in LSM (p=0.096).

Pre-operative PIs and inflammatory markers [PDW, NEU, basophil (BAS), PCT, P-LCR, NLR, PLR, SII] showed no significant differences between transfusion groups in either cohort. Post-operatively, only PCT was significantly lower in the LM transfusion group (p=0.029); however, no significant differences were noted in the LSM cohort (p=0.169).

Intra-group Changes

Significant intra-group changes from pre-operative to post-operative periods were observed for most hematologic and inflammatory parameters (p<0.001). These changes indicate a robust inflammatory and hematologic response to myomectomy regardless of transfusion status. The median number of ES transfusion units was significantly higher in the transfusion groups in both LM and LSM [2.00 (1.00-2.00) units, p<0.001].

Multivariate binary logistic regression analysis results are shown in Table 3. For patients who underwent LM myomectomy, myoma count [regression coefficient (B)=0.120, OR=1.128, 95% CI: 1.045-1.217, p=0.002)] and surgeon experience (B=-0.088, OR=0.916, 95% CI: 0.851-0.986, p=0.020) were significant predictors. Age (B=0.006, OR=1.006, 95% CI: 0.949-1.066, p=0.848), BMI (B=-0.032, OR=0.968, 95% CI: 0.898-1.044, p=0.401), and pre-operative SIRI (B=-0.321, OR=0.725, 95% CI: 0.423-1.244, p=0.243) were not significant.

In the LSM group, none of the variables was statistically significant: age (B=0.022, OR=1.023, 95% CI: 0.929-1.126, p=0.649), BMI (B=-0.152, OR=0.859, 95% CI: 0.729-1.012, p=0.070), myoma count (B=-0.066, OR=0.936, 95% CI: 0.269-3.261, p=0.918), surgeon experience (B=-0.138, OR=0.871, 95% CI: 0.751-1.012, p=0.071), and pre-operative SIRI (B=0.018, OR=1.018, 95% CI: 0.854-1.213, p=0.843).

The pre-operative Hb cut-off values for predicting post-operative ES transfusion are presented in Table 4 and Figure 2. In the LM myomectomy group, the AUC was 0.633 (95% CI: 0.559-0.707, p=0.001), with a cut-off value of 11.75 g/dL, sensitivity of 58.1%, and specificity of 57.8%. In the LSM group, the AUC was 0.639 (95% CI: 0.512-0.767, p=0.027), with a cut-off value of 11.75 g/dL, sensitivity of 58.3%, and specificity of 60.8%.

DISCUSSION

Inflammation is a key factor in the development of bleeding disorders, especially during sepsis. The systemic inflammatory

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Table 2. Comparison of surgical and perioperative data based on ES transfusion status

Operation	Laparotomic myomectomy			Laparoscopic myomectomy		
	Non-transfusion group (n=400)	Transfusion group (n=62)	p-value	Non-transfusion group (n=171)	Transfusion group (n=24)	p-value
Operation duration[a] (min)	95.77±39.69	132.21±48.65	**p<0.001**	152.89±65.16	196.33±87.31	**p=0.004**
Myoma count[b] (n)	1.00 (1.00-3.00)	2.00 (1.00-5.00)	**p=0.021**	1.00 (1.00-1.00)	1.00 (1.00-1.00)	p=0.633
Maximum myoma diameter[b] (cm)	8.0 (7.0-10.0)	10.0 (9.5-11.0)	**p<0.001**	10.0 (8.0-12.0)	11.5 (11.5-15.0)	**p=0.012**
Myoma weight[b] (gr)	164.8 (83.7-267.8	226.0 (166.7-313.8)	**p=0.008**	125.5 (58.6-204.0)	167.4 (156.9-190.4)	**p=0.015**
Surgeon experience[b] (years)	5.00 (3.00-10.00)	4.00 (2.00-9.00)	**p=0.044**	6.00 (3.00-10.00)	4.00 (2.00-10.00)	p=0.261
ES transfusion unit[b] (n)	0.00 (0.00-0.00)	2.00 (1.00-2.00)	**p<0.001**	0.00 (0.00-0.00)	2.00 (1.00-2.00)	**p<0.001**
Hb differance[b] (g/dL)	1.25 (0.60-1.90)	2.10 (1.40-2.80)	**p<0.001**	1.00 (0.50-1.60)	2.50 (1.60-3.70)	**p<0.001**
Hb[a] (g/dL)						
Pre-operative	11.98±1.48	11.36±1.53	**p=0.002**	12.08±1.19	11.47±1.36	**p=0.023**
Post-operative	10.73±1.29	9.20±1.25	**p<0.001**	10.99±1.24	8.47±1.42	**p=0.023**
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
HCT[a] (%)						
Pre-operative	36.99±3.79	35.59±3.89	**p=0.089**	36.97±3.14	35.89±3.70	p=0.126
Post-operative	32.76±3.39	28.51±3.32	**p<0.001**	33.34±3.96	26.30±4.38	**p<0.001**
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
WBC[b] (109/L)						
Pre-operative	7.30 (6.17-8.66)	7.16 (5.47-8.23)	p=0.089	7.51 (6.39-8.86)	7.67 (6.41-8.71)	p=0.978
Post-operative	13.44 (11.21-15.77)	13.61 (11.52-15.49)	p=0.736	13.99 (11.89-16.66)	12.58 (11.71-16.08)	p=0.342
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
PLT[b] (10^9/L)						
Pre-operative	299.00 (251.00-344.50)	296.00 (236.00-332.00)	p=0.270	284.00 (234.00-323.00)	284.50 (240.50-352.50)	p=0.415
Post-operative	250.00 (211.00-297.50)	233.50 (189.00-270.00)	p=0.023	234.00 (192.00-280.00)	212.50 (157.50-265.50)	p=0.096
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
LYM[b] (10^9/L)						
Pre-operative	2.10 (1.69-2.67)	1.96 (1.60-2.49)	p=0.083	2.17 (1.79-2.77)	1.89 (1.60-2.38)	p=0.057
Post-operative	0.97 (0.68-1.40)	0.78 (0.61-1.10)	p=0.007	0.81 (0.62-1.20)	0.56 (0.47-0.97)	**p=0.030**
p-value	p<0.001	p<0.001		p<0.001	p<0.001	
MON[b] (10^9/L)						
Pre-operative	0.52 (0.42-0.64)	0.48 (0.37-0.58)	p=0.035	0.51 (0.43-0.65)	0.56 (0.42-0.67)	p=0.7487
Post-operative	0.65 (0.49-0.82)	0.64 (0.48-0.87)	p=0.780	0.65 (0.44-0.83)	0.70 (0.56-0.79)	p=0.510
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p=0.145**	
MPV[b] (fL)						
Pre-operative	10.50 (10.01-11.10)	11.01 (10.06-11.50)	p=0.067	10.50 (10.02-11.10)	10.70 (10.03-11.10)	p=0.668
Post-operative	10.40 (10.00-11.05)	10.75 (10.04-11.10)	p=0.240	10.10 (10.00-11.06)	10.55 (9.96-11.20)	p=0.624
p-value	**p<0.001**	**p=0.009**		**p<0.001**	**p=0.145**	

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Table 2. Continued

Operation	Laparotomic myomectomy			Laparoscopic myomectomy		
	Non-transfusion group (n=400)	Transfusion group (n=62)	p-value	Non-transfusion group (n=171)	Transfusion group (n=24)	p-value
PDW[b] (10^9/L)						
Pre-operative	12.10 (11.05-14.00)	13.05 (11.09-14.90)	p=0.116	12.09 (11.05-14.04)	13.10 (11.55-14.04)	p=0.178
Post-operative	12.03 (11.00-13.10)	12.20 (11.40-13.30)	p=0.159	12.03 (10.70-13.60)	12.34 (10.19-14.04)	p=0.687
p-value	**p<0.001**	**p=0.041**		**p<0.001**	**p=0.032**	
NEU[b] (10^9/L)						
Pre-operative	4.42 (3.59-5.37)	4.33 (3.26-5.05)	p=0.202	4.44 (3.75-5.59)	5.01 (3.65-5.50)	p=0.561
Post-operative	11.79 (9.53-14.03)	12.03 (10.31-13.77)	p=0.912	12.31 (10.33-15.10)	11.63 (10.80-14.13)	p=0.633
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
BAS[b] (10^9/L)						
Pre-operative	0.03 (0.02-0.04)	0.02 (0.01-0.04)	p=0.003	0.03 (0.02-0.04)	0.03 (0.02-0.03)	p=0.780
Post-operative	0.02 (0.01-0.02)	0.01 (0.01-0.02)	p=0.017	0.01 (0.01-0.02)	0.01 (0.01-0.02)	P=0.352
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
PCT[b] (%)						
Pre-operative	0.32 (0.28-0.36)	0.33 (0.28-0.37)	p=0.704	0.30 (0.26-0.35)	0.31 (0.27-0.38)	p=0.102
Post-operative	0.27 (0.23-0.31)	0.26 (0.21-0.29)	p=0.220	0.25 (0.22-0.29)	0.24 (0.18-0.28)	p=0.096
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
P-LCR[b]						
Pre-operative	30.20 (25.50-36.20)	32.35 (26.20-36.90)	p=0.158	30.80 (25.70-36.60)	31.90 (26.55-37.20)	p=0.190
Post-operative	29.20 (25.30-35.20)	31.55 (25.30-36.70)	p=0.624	29.80 (25.00-35.30)	33.50 (24.95-36.20)	p=0.386
p-value	**p=0.001**	**p=0.036**		**p=0.007**	**p=0.513**	
NLR[b]						
Pre-operative	2.07 (1.61-2.69)	1.96 (1.60-2.42)	p=0.444	2.05 (1.59-2.57)	2.61 (1.64-3.17)	**p=0.044**
Post-operative	12.31 (7.58-18.49)	14.42 (9.27-21.54)	p=0.097	14.90 (9.49-22.27)	19.91 (11.20-29.28)	**p=0.048**
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
PLR[b]						
Pre-operative	136.59 (108.33-181.91)	143.49 (114.45-182.63)	p=0.593	124.34 (104.37-158.16)	152.81 (125.57-196.69)	p=0.190
Post-operative	250.10 (169.32-375.00)	269.77 (204.82-375.95)	p=0.011	291.35 (195.08-406.25)	298.62 (221.83-514.17)	p=0.224
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
SII[b]						
Pre-operative	596.11 (457.20-842.12)	572.22 (444.79-734.77)	p=0.220	573.40 (423.67-770.13)	777.39 (495.43-1260.68)	p=0.339
Post-operative	2976.81 (1688.15-4853.92)	3220.41 (2151.56-4789.23)	p=0.037	3560.20 (2274.61-5236.63)	3226.46 (2557.44-5977.21)	p=0.444
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	
SIRI[b]						
Pre-operative	1.08 (0.82-1.48)	0.95 (0.70-1.33)	p=0.113	1.04 (0.78-1.43)	1.30 (0.90-1.89)	**p=0.007**
Post-operative	7.17 (4.48-11.51)	9.72 (5.86-14.31)	p=0.140	8.59 (5.06-14.15)	10.85 (7.71-16.12)	p=0.060
p-value	**p<0.001**	**p<0.001**		**p<0.001**	**p<0.001**	

[a]: Normal distribution, mean ± standard deviation, [b]: Non-normal distribution, median (25-75%), ES: Erythrocyte suspension, Hb: Hemoglobin, HCT: Hematocrit, WBC: White blood cell count, PLT: Platelet count, LYM: Lymphocyte, MON: Monocyte, NEU: Neutrophil, BAS: Basophil, MPV: Mean platelet volume, PDW: Platelet distribution width, PCT: Plateletcrit, P-LCR: Platelet-large cell ratio, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index

response triggered by sepsis closely interacts with coagulation pathways, potentially resulting in disseminated intravascular coagulation (DIC). DIC is characterized by extensive fibrin buildup and impaired fibrinolysis. Inflammatory agents, including cytokines and chemokines, stimulate tissue factor expression on monocytes and endothelial cells, which promotes thrombin production and concurrently inhibits natural anticoagulant systems like protein C and antithrombin (8). This imbalance causes microvascular clotting and tissue ischemia, leading to organ dysfunction. Furthermore, increased levels of inflammatory markers such as interleukins and tumor necrosis factor-α are associated with the severity of DIC, highlighting the importance of inflammation in diagnosing and predicting outcomes in sepsis-related coagulopathy (9). Although bleeding disorders in sepsis have been extensively studied, emerging evidence emphasizes the critical interaction between inflammation and coagulation in driving disease progression and contributing to morbidity and mortality.

The SII, introduced by Huang et al. (10) in 2019, represents the involvement of platelets, NEUs, and lymphocytes in inflammation, with the first two promoting inflammation and lymphocytes regulating immune responses. Elevated SII values have been linked to poor prognosis in cancer patients and other conditions such as ischemic stroke, where they predict mortality and hemorrhagic transformation (3,11). These observations imply that SII might also serve as a prognostic marker in acute bleeding events, though additional studies are needed to confirm its diagnostic accuracy and define cut-off points (4).

Moreover, the absence of significant differences in SII values across American Society of Anesthesiologists groups (p=0.821) indicates similar inflammatory states among risk categories, supporting cohort uniformity. Nevertheless, further investigation is required to clarify the influence of inflammation on transfusion outcomes, as chronic inflammatory conditions may affect anemia severity and transfusion responses (12).

This study's strengths include its matched case-control design, which reduces selection bias, and its use of routinely available blood markers to predict transfusion needs, thereby enhancing clinical applicability. Additionally, focusing on a clearly defined patient group improves relevance to comparable surgical populations. Importantly, this is the first study to evaluate PIs, inflammatory markers, and SII as predictors of ES transfusion in patients undergoing myomectomy.

Key Findings

Comparison with Existing Literature

Recent studies suggest systemic inflammation plays a role in fibroid pathogenesis and growth. In a retrospective case-control study of 357 patients, Çınar et al. (13) stratified cases by fibroid diameter (≤5 cm vs. >5 cm) and found that larger fibroids were associated with altered clinical parameters. In our cohort, larger and more numerous fibroids increased transfusion needs. In the LM group, transfused patients had more fibroids (median 2.0 vs. 1.0; p=0.021), but no difference was seen in LSM (p=0.633). Maximum fibroid diameter and weight were higher in transfused patients in both the LM (10.0 vs. 8.0 cm, 226.0 vs. 164.8 g) and the LSM (11.5 vs. 10.0 cm, 548.8 vs. 125.5 g) groups (all p<0.05). These results align with Çınar et al. (13) indicating fibroid size and burden increases the risk of bleeding and transfusion. The fibroid count

Table 3. Multivariate binary logistic regression analysis for predicting post-operative ES transfusion need

Variable	B	OR	95% CI	p-value
Laparotomic myomectomy				
Age (years)	0.006	1.006	0.949-1.066	p=0.848
BMI (kg/m²)	-0.032	0.968	0.898-1.044	p=0.401
Myoma count	0.120	1.128	1.045-1.217	p=0.002
Surgeon experience (years)	-0.088	0.916	0.851-0.986	p=0.020
SIRI pre-operative	-0.321	0.725	0.423-1.244	p=0.243
Laparoscopic myomectomy				
Age (years)	0.022	1.023	0.929-1.126	p=0.649
BMI (kg/m²)	-0.152	0.859	0.729-1.012	p=0.070
Myoma count	-0.066	0.936	0.269-3.261	p=0.918
Surgeon experience (years)	-0.138	0871	0.751-1.012	p=0.071
SIRI pre-operative	0.018	1.018	0.854-1.213	p=0.843

B: Regression coefficient, OR: Odds ratio, CI: Confidence interval, BMI: Body mass index, ES: Erythrocyte suspension, SIRI: Systemic inflammatory response index

Table 4. Hb cut-off values for predicting post-operative ES transfusion

Parameters	AUC (95% CI)	Cut-off (youden index)	Sensitivity (%)	Specificity (%)	p-value
Laparotomic pre-operative Hb	0.633 (0.559-0.707)	11.75	58.1	57.8	p=0.001
Laparoscopic pre-operative Hb	0.639 (0.512-0.767)	11.75	58.3	60.8	p=0.027

AUC: Area under the curve, CI: Confidence interval, ES: Erythrocyte suspension, Hb: Hemoglobin

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difference in LM may reflect surgical preference for laparotomy with higher fibroid burden, not an inherent risk of the approach.

Platelet Indices and Inflammatory Markers

Several studies have examined PIs and inflammatory markers in gynecologic and other tumors. For instance, clinicians have observed that low PCT and elevated PDW (≥23%) independently predict increased risk of postpartum hemorrhage (14). In patients with gynecologic malignancies, elevated PLT and PCT, along with decreased MPV, have been reported (6). Papillary thyroid carcinoma patients exhibit significantly higher PCT and lower PDW (15). In endometriosis, PCT increases while MPV and PDW decrease (5). Advanced breast cancer is associated with changes in platelet-related indices, with low PCT portending better survival outcomes (16). PCT has also been proposed as a sensitive biomarker for Crohn's disease activity (17).

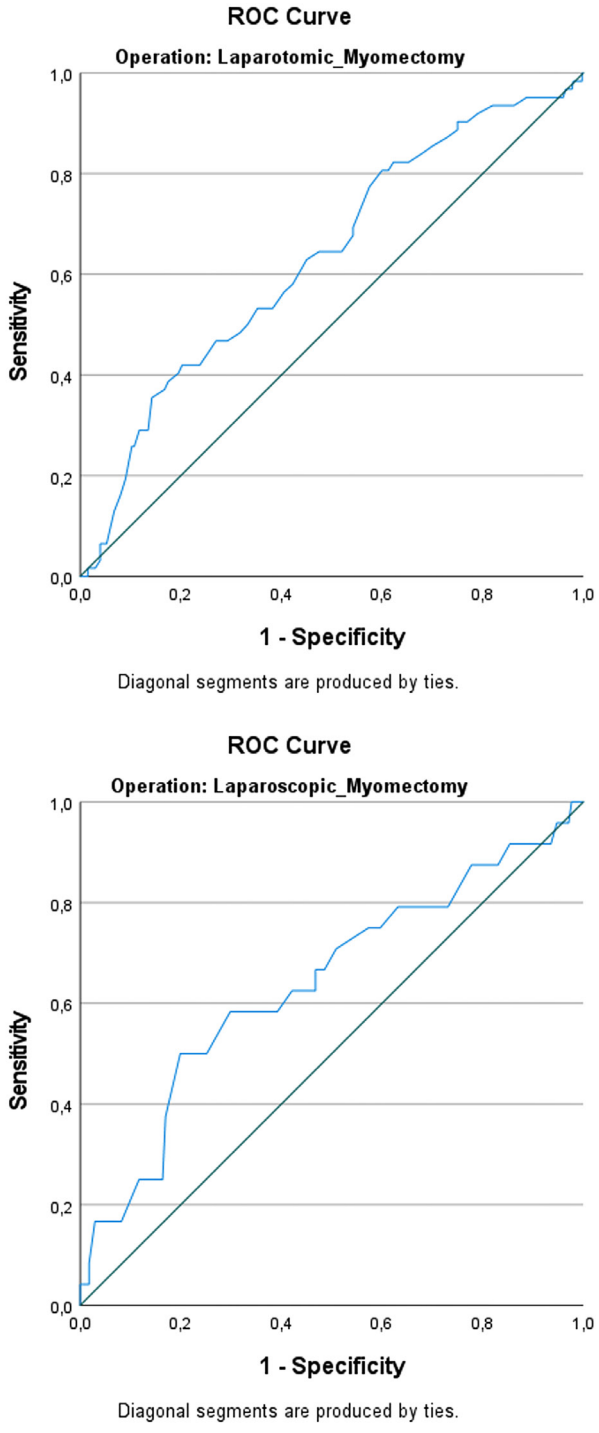

Figure 2. ROC curve of hemoglobin (Hb) cut-off values for predicting post-operative erythrocyte suspension (ES) transfusion in laparotomic and laparoscopic myomectomy
ROC: Receiver operating characteristic

Regarding perioperative settings, Mohr et al. (6) reported that low MPV (<7.7 fL) and low PCT (<0.01) are significant cut-off values for predicting platelet transfusion after cardiopulmonary bypass. van Dijk et al. (15) found that PLT and indices serve as risk factors for postpartum hemorrhage (7). Elevated NLR, as an indirect marker of inflammation, has been associated with gastrointestinal bleeding in children with Henoch-Schonlein purpura (5). In uterine leiomyomas, chronic inflammation plays a pivotal role in pathogenesis, and NLR has been proposed to differentiate myomas from sarcomas or endometriosis (18,19).

Çaltekin et al. (20) retrospectively evaluated 102 patients with uterine leiomyomas and found that compared to those with smaller fibroids (≤5 cm), patients with larger fibroids (>5 cm) exhibited a significant increase in NLR and a decrease in lymphocyte/monocyte ratio, whereas PLR did not differ significantly between size groups. In our cohort, pre-operative PDW, NEU, BAS, PCT, P-LCR, NLR, PLR, and SII showed no significant difference between transfused and non-transfused patients (all p>0.05). Post-operatively, only PCT was lower in the transfused LM subgroup (p=0.029), with no differences in LSM (p=0.169). Thus, while fibroid size affects some inflammatory markers, pre-operative markers did not predict transfusion need, though, post-operative PCT reduction may indicate platelet depletion from bleeding.

Comparison of Surgical Approaches for Myomectomy

When comparing LM and LSM in terms of transfusion risk, our findings highlight notable differences that align with and expand upon existing knowledge. In both surgical approaches, longer operative times were significantly associated with increased transfusion rates, with LM transfused patients averaging 132.2±48.7 minutes compared to 95.8±39.7 minutes in non-transfused cases (p<0.001); LSM transfused patients demonstrated even longer durations, 196.3±87.3 minutes versus 152.9±65.2 minutes, respectively (p=0.004). These results are consistent with Hamilton et al. (21) who identified the operation time exceeding 197 minutes as a key intraoperative risk factor for transfusion during LSM. Hamilton's study, highlights pre-operative factors (race, bleeding disorders, HCT) and intraoperative variables (specimen weight, intramural myomas) in a risk stratification tool. Our study adds real operative time data to the LM and LSM groups, emphasizing surgical duration and the impact of complexity on transfusion needs. These findings emphasize the need for tailored surgical planning to reduce transfusion risks.

In our cohort, fibroid burden (number, size, weight) predicted transfusion only in LM patients, with transfused cases showing higher myoma count (2.0 vs. 1.0; p=0.021), diameter (10.0 vs. 8.0 cm; p<0.001), and weight (226.0 vs. 164.8 g; p=0.008). In LSM, only diameter and weight differed significantly, not myoma count (p=0.633). This aligns with Pundir et al. (22) who found increased bleeding and transfusion risks with larger uteri (≥20 weeks), ≥10 fibroids, and more extensive surgery, including repeat myomectomies. Their analysis further highlights increased complications and blood loss in repeat myomectomies, emphasizing fibroid burden and surgical complexity, as critical factors influencing perioperative transfusion risk. Together, these data underscore the importance of fibroid load assessment and surgical planning, particularly in open approaches, to mitigate bleeding risks and optimize patient safety.

Surgeon experience significantly affected transfusion risk in LM, with transfused patients operated on by less experienced surgeons (median 4.0 vs. 5.0 years, p=0.044); each additional year of surgeon experience reduced transfusion odds by 8.4% (OR= 0.916, p=0.020). Experience had no significant effect in LSM cases. This reflects LM's technical challenges, especially with multiple fibroids. A recent meta-analysis supports that LSM causes less blood loss and fewer complications than open surgery, despite the longer operative times due to a steeper learning curve and higher technical demands (23). Bipolar diathermy, vasopressin injection, and temporary uterine artery clipping reduce bleeding during laparoscopy. Odejinmi et al. (24) reported shorter operative times and less blood loss in laparoscopic hysterectomy versus myomectomy, underscoring the roles of patient selection and surgeon expertise. While laparoscopic methods reduce blood loss and complications, surgeon experience remains key, especially in open surgery. Larger fibroid size and weight increase bleeding risk in both approaches, but multiple fibroids and surgeon experience are especially critical in LSM (LM). LSM appears less affected by fibroid multiplicity, likely due to better visualization and hemostatic control (24).

Clinical Implications

Longer operative times and larger fibroid burden, particularly larger size, increase transfusion risk in LM, where surgical experience independently lowers this risk. In LSM, fibroid size remains a risk factor, but myoma count and surgeon experience do not.

A pre-operative Hb cut-off of 11.75 g/dL (LM AUC: 0.633; LSM AUC: 0.639) provides a useful threshold for anemia correction to reduce transfusions. Incorporating fibroid characteristics, surgical approach, and surgeon experience into risk models can improve perioperative care.

Study Limitations

This retrospective study evaluated the association between pre-operative hemogram parameters, PIs, and the need for post-operative ES transfusion in patients undergoing myomectomy. Lower pre-operative Hb levels, prolonged operative time, and greater estimated blood loss were independently associated with an increased likelihood of ES transfusion. In the open (LM) cohort, both myoma count and surgeon experience emerged as additional independent predictors.

Strengths of this study include a comprehensive analysis of hematologic and coagulation parameters in a large, consecutively sampled cohort, as well as blinded data review to minimize bias. However, limitations include its retrospective, single-center design, which restricts causal inference and generalizability, along with the absence of coagulation biomarkers such as fibrinogen and D-dimer that could enhance transfusion risk prediction

CONCLUSION

Our study highlights that the size and number of fibroids, alongside operative time and surgeon experience, are key determinants of transfusion risk in myomectomy patients. While larger fibroids increase bleeding risk across both LM and laparoscopic approaches, the cumulative effect of multiple fibroids and surgical expertise notably impacts outcomes in open surgery. Pre-operative Hb level serves as a practical threshold to guide anemia management and reduce transfusion needs. Incorporating these clinical factors into perioperative risk assessments can enhance surgical planning, minimize transfusion-related complications, and improve patient safety. Further prospective studies including additional biomarkers are warranted to refine prediction models and optimize care.

Ethics

Ethics Committee Approval: The Institutional Review Board of University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital approved this retrospective study (approval no: KAEK/12.06.2024.27, date: 26.06.2024).

Informed Consent: Due to the retrospective nature of the study, the requirement for informed consent was waived. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Footnotes

Author Contributions: Surgical and Medical Practices - C.T., G.G.; Concept - C.T., E.D., E.T., B.T., O.M.G., G.G.; Design - C.T., E.D., E.T., B.T., O.M.G.; Data Collection and/or Processing - E.D., B.T., O.M.G.; Analysis and/or Interpretation - C.T., E.T., G.G.; Writing - C.T., E.D., E.T., B.T., O.M.G., G.G.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors report that no financial support was received for this study

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