Can We Predict Gastric Leaks After Laparoscopic Sleeve Gastrectomy by Evaluating the Complete Blood Count on Postoperative Day 1?

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Introduction: We assessed whether postoperative day-1 (POD-1) complete blood count (CBC) test parameters, including red cell distribution width (RDW), mean platelet volume (MPV), plateletcrit (PCT), platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR), could identify patients with gastric leaks after laparoscopic sleeve gastrectomy (LSG).

Methods: Patients with postoperative gastric leaks (n = 36) and patients with no complications who were selected by age-sex-BMI matching (n = 254) were included in the study. The levels of RDW, MPW, PCT, PLR, and NLR were compared between groups in univariate analyses. Receiver operating characteristic (ROC) curve analysis was run for CBC parameters with a P-value < 0.05 in univariate analyses. The area under the curve (AUC) was evaluated, and a cutoff value was determined. Sensitivity, specificity, likelihood ratio (LR), positive predictive value (PPV), negative predictive value (NPV), and accuracy were calculated.

Results: The level of PCT was significantly lower, while levels of PLR and NLR were significantly higher in patients with postoperative gastric leaks as compared with those without ($P < 0.05$). The AUC of both PCT and PLR was < 0.750, while the AUC of NLR was 0.911. NLR cutoff at 3.6 yielded 80% sensitivity, 92% specificity, and an LR of 10. In the study cohort, PPV of 59%, NPV of 97%, and an accuracy of 90% were found.

Conclusions: Our results suggest that NLR at POD-1, with a cutoff value of 3.6, is a useful indicator of postoperative gastric leak who underwent LSG. We recommend the use of this easily calculated parameter in clinical practice.

Key Words: sleeve gastrectomy, morbid obesity, neutrophil-to-lymphocyte ratio, gastric leak

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Laparoscopic sleeve gastrectomy (LSG), which was initially proposed as the first stage of a 2-step procedure for high-risk patients, has now been accepted as an effective, single-stage surgical treatment for morbid obesity. It has become the most commonly performed bariatric procedure,[1,2] showing improved short-term and long-term postoperative results since its introduction. However, short-term complications, such as stenosis, leakage, and bleeding, which require timely diagnosis and treatment, are still a matter of concern. Of these, suture line leaks are likely the most concerning complications and occur in 1% to 3% of patients in large published series.[3,4]

Many systemic inflammatory response (SIR) markers, such as C-reactive protein (CRP), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), red cell distribution width (RDW), mean platelet volume (MPV), and plateletcrit (PCT) have been studied in the literature.[5–10] In recent years, the use of both CRP and NLR as a predictive marker for postoperative complications following bariatric surgical procedures has been described.[8–10] However, there is scarce data on whether the SIR markers, which are obtained from a complete blood count (CBC) test, are beneficial in bariatric surgery for this purpose.

AIM

In this study, we aimed to evaluate changes in the laboratorial parameters in POD-1 CBC test, including RDW, MPV, PCT, PLR, and NLR, between the patients who experienced postoperative gastric leaks and the patients who did not experience any postoperative complications, and to determine whether these parameters could identify patients with gastric leaks after LSG. We hypothesize that there is value in these parameters, which may be useful for early detection of postoperative gastric leaks.

MATERIALS AND METHODS

The data of this study were obtained from a prospectively collected database between March 2014 and July 2019, and retrospectively reviewed. All operations were performed at a reference center and teaching hospital for bariatric surgery. The study was approved by the local ethics committee of our hospital. A written-informed consent was obtained from patients. From this database, patients who underwent primary LSG were identified and retrospectively reviewed using the bariatric surgery registry and electronic medical records.

Inclusion criteria were defined as individuals aged 18 and above with a complete blood count (CBC) result on postoperative day 1 (POD-1). Exclusion criteria encompassed patients with a history of chronic inflammatory diseases (eg, rheumatological diseases, chronic liver diseases, and chronic kidney diseases), as the presence of accompanying diseases could lead to misinterpretation of blood parameters. In addition, individuals using anti-inflammatory medications (such as corticosteroids, antibiotics, or nonsteroidal anti-inflammatory drugs that might impact blood count results) were excluded. Patients lacking a CBC on POD-1 or those experiencing complications other than

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gastric leak (such as pneumonia and soft tissue infection, which could influence laboratory blood work) were also excluded from the study.

Patients who experienced postoperative gastric leaks were grouped as "leakage group." The leak was defined as the leak of luminal contents from a surgical connection between 2 hollow viscera in accordance with the previously published criteria.[11] Subsequently, "leakage group" and "control group" were matched in regard to age, sex, and BMI (body mass index) to ensure that the control group closely resembled the leakage group.

For blood tests on POD-1, venous blood samples were drawn into EDTA tubes (5 mL). All samples were processed within 2 hours after vein puncture, using an automated hematology analyzer. Studied parameters from the complete blood count (CBC) test results include the following; white blood cell (WBC) count per microliter of blood, platelet (PLT) count per microliter of blood, neutrophil count, lymphocyte count, RDW measurements derived from the red blood cell distribution curves generated on automated hematology analyzers, MPV (fL), PCT (%). The PLR and NLR were calculated separately as the absolute counts of platelet and neutrophil, respectively, divided by the absolute lymphocyte count.

Statistical Analysis

Since the number of patients in the leakage group was known, we performed a priori power analysis to determine the required sample size for the control group, using the G-Power program (version 3.1.9.4). The alpha level, or the type I error rate, was set as 0.05. Power (1-beta), or type II error rate, was set at 0.80 level. Effect size d was set as 0.5. After the required sample size was calculated, the leakage group was matched with the control group according to their age, gender, and BMI. Comparative analysis was then run between the 2 groups.

Categorical variables were analyzed using Pearson χ^2 or Fisher Exact test, and continuous variables using the independent sample *t* test (for normal distributions) or Mann-Whitney *U* Test (for non-normal distributions). The normality of the distribution of continuous variables was assessed using histograms, skewness, and the Shapiro-Wilk test. Categorical variables were presented as the frequency with percentage [n (%)] and continuous variables as mean ± SD or median (interquartile range, IQR), as appropriate.

Receiver operating characteristic (ROC) curves were performed, and the area under the curve (AUC) was calculated for the markers, which showed statistical significance in a univariate analysis. The parameter with an AUC closest to 1 was the most predictive of a postoperative gastric leak. The sensitivity and specificity were calculated according to cutoff points determined by ROC curves. Further analyses were performed to determine the likelihood ratio, positive predictive value, negative predictive value, and accuracy of each studied variable at their cutoff values. To do this, all patients were categorized as above and below the cutoff value of the index variable, and bipartite comparisons were run between outcomes, predicted by the index variable and real outcomes. Statistical assessments were performed using SPSS software pack (Statistical Package for Social Sciences for Windows version 22 software). A *P*-value of <0.05 was considered statistically significant.

TABLE 1. Comparison of Patient Demographics

	Leakage group (n = 36)	Control group (n = 254)	*P*
Age, y, mean ± SD	41.86 ± 11.55	39.22 ± 10.92	0.178
Sex, female, n (%)	20 (55.6)	173 (68.1)	0.185
Body mass index (kg/m^2), mean ± SD	47.11 ± 4.77	46.85 ± 6.07	0.769
ASA score, median (IQR)	3 (2-3)	3 (2-3)	0.824
Comorbidities, n (%)			
Hypertension, yes	20 (55.6)	145 (57.1)	0.859
Dyslipidemia, yes	19 (52.8)	152 (59.8)	0.471
COPD, yes	7 (19.4)	44 (17.3)	0.815
Obstructive sleep apnea	14 (38.9)	89 (35)	0.711
Smoking, yes	12 (33.3)	79 (31.1)	0.848
Diabetes mellitus, yes	13 (36.1)	80 (31.5)	0.572

ASA indicates The American Society of Anesthesiologists; COPD, chronic obstructive pulmonary disease; IQR, interquartile range.

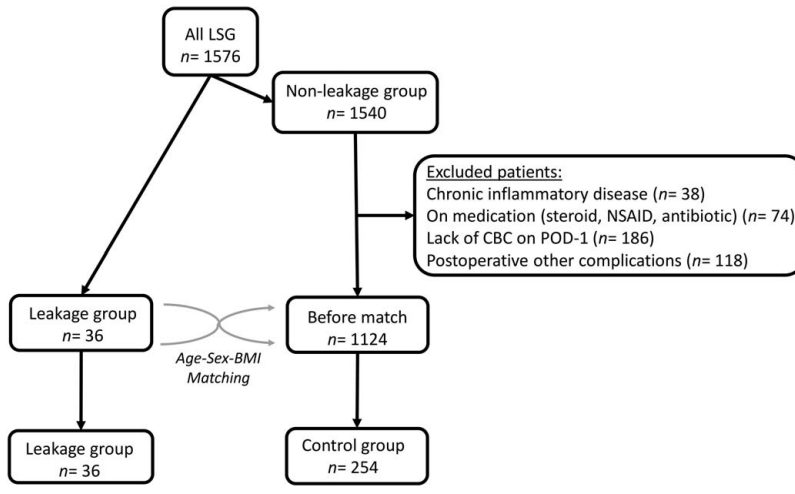

FIGURE 1. Patient selection flowchart. CBC indicates complete blood count; LSG, laparoscopic sleeve gastrectomy; NSAID, nonsteroidal anti-inflammatory drug; POD, postoperative day.

RESULTS

Out of 1576 patients who underwent LSG, 36 (2.2%) patients experienced a radiologically confirmed postoperative gastric leak, within a mean ± SD of 7 ± 2.8 days (min-max = 4-17 d). Using a priori power analysis with an allocation ratio of 7, the required sample size was found to be n = 254. Thus, patients in the leakage group were matched with selected patients (control group) using a 1:7 age-sex-BMI matching algorithm for patients who did not experience any postoperative complications (Fig. 1). Hospital stay was 3.2 days. The power of the study was found to be approximately 80% for a total sample size of 290.

After matching, the 2 groups were compared. There were no differences between the leakage group and control group in terms of patient demographics and comorbidities (Table 1).

Regarding CBC results on POD-1, there were no differences in platelet counts, the width of the red cell distribution curves, and the average size of platelets between the 2 groups. However, patients who experienced a postoperative gastric leak had a higher white cell neutrophil count as compared with the control group. On the other hand, the plateletcrit and lymphocyte counts were significantly lower in the leakage group. Accordingly, both PLR and NLR were found to be significantly higher in the leakage group. A comparison of laboratorial variables between the 2 groups is given in Table 2.

The ROC curve analyses were run for the outcome variables of PCT, PLR, and NLR, which were found to be statistically significant in univariate analysis (RDW and MPV were not). Although the PCT AUC showed statistical significance ($P = 0.008$) after ROC curve analysis, an AUC value of 0.637 indicated that it is a poor test (Fig. 2). Similarly, the AUC of PLR was 0.662, suggesting that it poorly predicts postoperative gastric leaks (Fig. 3). In comparison, the NLR AUC on POD-1 was 0.911, indicating that it is an excellent predictor for gastric leaks (Fig. 4), and an NLR cutoff at 3.59 yielded 80% sensitivity and 92% specificity. The results of the ROC curve analyses, including cutoff value sensitivity and specificity, likelihood ratios, positive predictive values, negative predictive values, and accuracy, are presented in Table 3.

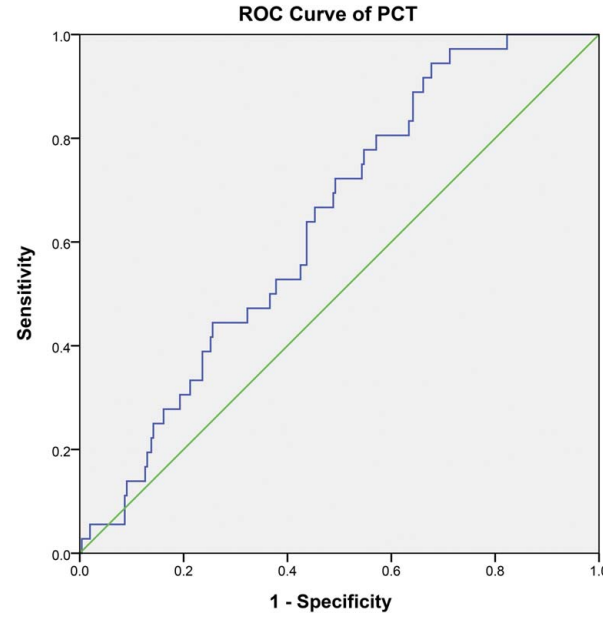

FIGURE 2. Plot of the receiver operating characteristic (ROC) curve of plateletcrit (PCT).

DISCUSSION

Numerous efforts have been made to identify useful markers for the prediction of adverse postoperative events.[12] Taking into account standard protocols of the enhanced recovery program, which warrants discharge of bariatric patients by the second postoperative day,[13] highlights the importance of obtaining early SIR markers and predicting postoperative leaks with sufficient. To the best of our knowledge, this is the first study to investigate whether the POD-1 RDW, MPV, PCT, PLR, and NLR are predictive of gastric leaks in patients undergoing LSG.

SIR markers have been studied separately as prognostic and predictive tools in various diseases. Kilincalp et al[14] reported that NLR, PLR, and MPV were useful and easily available biomarkers in the screening of colorectal cancer as well as in postoperative follow-up. AUCs of these parameters were 0.921, 0.853, and 0.717, respectively. Yücel and Ustun[7] evaluated the use of CBC parameters, including RDW, MPV, PCT, PLR, and NLR, in the prediction of the severity of preeclampsia. In an ROC curve analysis of the NLR, PLR, and RDW AUC, no statistically significant difference was found ($P = 0.636$, 0.104, and 0.36, respectively). However, the AUC of MPV and PCT were determined as 0.641 and 0.712, respectively, showing statistical significance ($P = 0.028$ and 0.001). The authors

TABLE 2. Comparison of Laboratorial Variables

Variable	Abbr.	Normal range	Leakage group (n = 36) mean ± SD	Control group (n = 254) mean ± SD	*P*
White blood cell (10^3/uL)	WBC	3.7-10.01	13.35 ± 3.69	9.57 ± 2.32	**< 0.001**
Platelet (10^3/uL)	PLT	155-366	289.81 ± 60.29	298.44 ± 69.09	0.455
Neutrophil (%)	NEU	1.63-6.96	11.81 ± 3.43	5.35 ± 1.67	**< 0.001**
Lymphocyte (%)	LYM	1.09-2.99	2.36 ± 0.98	2.99 ± 0.92	**0.001**
Red blood cell distribution width (%)	RDW	11.5-14.5	13.26 ± 1.48	13.18 ± 1.45	0.754
Mean platelet volume (fL)	MPV	6.9-16	8.52 ± 1.85	8.99 ± 5.87	0.355
Plateletcrit (%)	PCT	0.0-9.99	0.23 ± 0.04	0.26 ± 0.06	**0.008**
Platelet-to-lymphocyte ratio	PLR		154.09 ± 95.27	114.13 ± 65.07	**0.019**
Neutrophil-to-lymphocyte ratio	NLR		6.49 ± 5.07	2.14 ± 1.17	**< 0.001**

Bold values are statistically significant ($p < 0.05$).

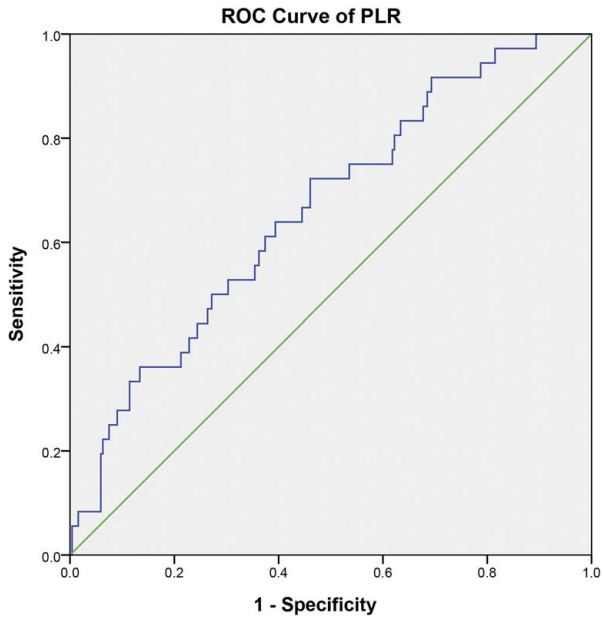

FIGURE 3. Plot of the receiver operating characteristic (ROC) curve of platelet-to-lymphocyte ratio (PLR).

concluded that MPV or PCT may be clinically useful markers in the prediction of severe preeclampsia. In the current study, RDW and MPV did not differ between the leakage and control groups in univariate analysis ($P = 0.754$ and 0.355). Therefore, they were not selected for a ROC analysis. Furthermore, the AUC of PCT and PLR was found to be 0.637 and 0.662, respectively, indicating that they do not possess clinical utility for patients undergoing LSG.

The NLR is an emerging biomarker gaining attention across many fields. It can be easily calculated from the differential CBC test, and it is also simple and inexpensive.[15] NLR provides information on both immune and inflammatory pathways that could make it a potential marker for predicting intraabdominal infections, such as acute appendicitis, gastrointestinal leakage from suture lines.[6,10,15,16] In a study with a total of 100 patients who underwent open colorectal procedures, Cook et al[6] reported that the ROC curve analysis of POD-1 NLR suggested a cutoff of 9.3 for the prediction of overall complications, with an area under the curve of 0.66. At this cutoff point, sensitivity, specificity, and likelihood ratio were 66%, 69%, and 2.12, respectively. In a study with 789 patients, 88.6% of which underwent Roux-en-Y gastric bypass versus 11.4% LSG, POD-1 NLR ≥ 10 was found to be significantly associated with adverse postoperative 30-day outcomes, including a higher incidence of overall complications and major complications, readmission rate, and reoperation rate.[10] This NLR threshold was chosen by the authors after referring to a study by Cook et al,[6] as the cutoff value of POD-1 NLR in bariatric surgery was unexplored previously.

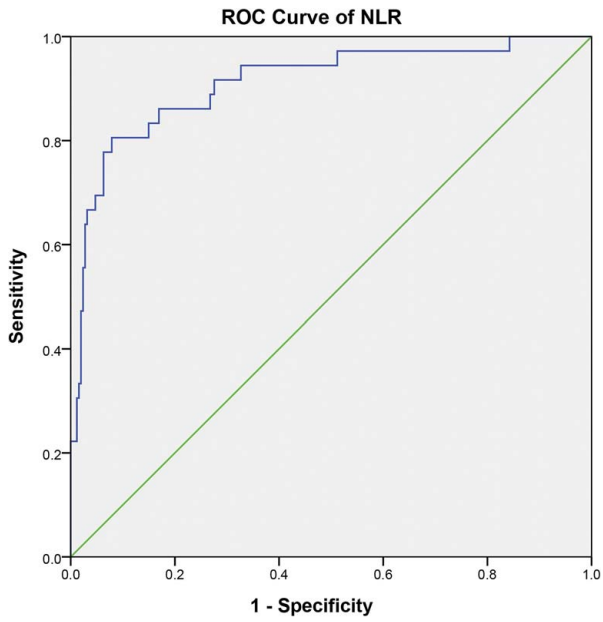

FIGURE 4. Plot of the receiver operating characteristic (ROC) curve of neutrophil-to-lymphocyte ratio (NLR).

In a study conducted by 't Hart et al,[17] they investigated the utility of the NLR as a predictive marker for early complications in metabolic-bariatric fast-track surgery, where patients are typically scheduled for discharge on POD-1. The prospective analysis included data from 829 patients who underwent primary metabolic surgery between April 2018 and April 2019, encompassing various procedures such as Roux-en-Y gastric bypass, sleeve gastrectomy, and 1 anastomosis gastric bypass. Among the patient cohort, 4.1% experienced major complications, and a significant association was observed between elevated postoperative NLR, delta-NLR, leukocyte count, and C-reactive protein (CRP) levels and the occurrence of early complications ($P < 0.001$, < 0.001, < 0.001, and 0.008, respectively). The study identified optimal cutoff points for predicting complications after metabolic surgery, with 6.73 for postoperative NLR (sensitivity 74% and specificity 70%) and 4.68 for delta-NLR (sensitivity 77% and specificity 75%). The findings suggest that postoperative NLR and delta-NLR independently correlate with early major complications after metabolic surgery. These markers exhibit potential clinical utility in identifying patients at risk for complications, thereby aiding in decision-making processes related to the safe discharge of patients on POD-1 or the need for early intervention. The study contributes valuable insights into risk assessment strategies in the context of fast-track metabolic surgery, emphasizing the importance of these hematological markers in predicting postoperative outcomes.

In the current study, we found that a POD-1 NLR cutoff of 3.6 with an AUC of 0.911 produced a sensitivity of 80%, specificity of 92%, likelihood ratio of 10, and accuracy of 90%. Of note, this threshold serves to predict postoperative gastric leaks after LSG and not overall complications. Furthermore, when interpreting the results of this study, it should be taken into account that the positive and negative predictive values may alter depending on the prevalence of the disease. The prevalence of the disease in this study was determined to be 12.4%, as 36 out of 290 patients experienced gastric leak. As is expected, the lower the leakage rate is, the higher the negative predictive value is, and consequently, the lower the positive predictive value is. In a sense, calculating the NLR < 3.6 in a low prevalence setting confidently rules out the presence of a gastric leak,

TABLE 3. Receiver Operating Characteristic Curve Analyses

Variable	*P*	AUC	95% CI		Cutoff value	Sensitivity (%)	Specificity (%)	LR (%)	PPV (%)*	NPV (%)*	Accuracy (%)*
			Lower bound	Upper bound							
PCT	0.008	0.637	0.555	0.720	0.25	66.7	54.7	1.47	17.2	92	56.2
PLR	0.002	0.662	0.569	0.754	104.13	72.2	52.8	1.53	17.8	93	55.2
NLR	< 0.001	0.911	0.854	0.969	3.59	80.5	92.1	10.23	59.1	97.1	90.6

*These values are dependent on the prevalence of disease, which is 12.4% gastric leak for the study cohort.

AUC indicates area under curve; LR, likelihood ratio; NLR, neutrophil-to-lymphocyte ratio; NPV, negative predictive value; PCT, plateletcrit; PLR, platelet-to-lymphocyte ratio; PPV, positive predictive value.

whereas the NLR of ≥ 3.6 may be due to a false positive rather than a true positive.

The clinical implementation of the NLR as an early predictor for major complications after metabolic surgery holds promising implications for improving patient outcomes and postoperative management. By incorporating NLR assessments into routine preoperative and postoperative evaluations, health care practitioners can potentially identify patients at a higher risk of developing major complications promptly. This proactive approach allows for timely intervention, personalized care, and optimized decision-making regarding postoperative discharge or additional monitoring. The simplicity and cost-effectiveness of NLR measurements make them an attractive tool for integration into clinical practice, offering a valuable and accessible biomarker to enhance risk stratification in the context of metabolic surgery. Further research and validation of NLR as a reliable predictor could contribute to establishing standardized protocols, ultimately enhancing the quality of care and patient safety in the field of metabolic surgery.

The main limitations of this study are related to its design, in that it is retrospective in nature, although the data was collected prospectively. Also, the study represents a single center's outcomes, which could be a concern for its generalizability. Another potential limitation pertains to the method employed for selecting the control group. Despite the authors' efforts to mitigate selection biases through a matching approach, there remains a possibility of imbalance between the 2 groups. For instance, while there was no statistically significant difference in gender distribution between the 2 groups, the proportion of male patients was higher in the leakage group compared with the control group. It is noteworthy that epidemiological studies have demonstrated gender-related influences on laboratory results, encompassing parameters such as PLT, MPV, and PCT.[18] However, in our present study, no differences were observed between male and female patients in any of the studied laboratory parameters ($P > 0.05$). Similarly, Furuncuoğlu et al[19] found that complete blood count (CBC) parameters could be significantly influenced by BMI status. Their study included participants from various BMI groups, and when we categorized patients based on a BMI below and above 40 kg/m^2, no statistical significance in CBC parameters was observed ($P > 0.05$). Despite attempts to address these considerations, the potential for residual imbalances and confounding variables should be acknowledged when interpreting the study results.

CONCLUSIONS

Both PCT and PLR on POD-1 were not found to be as clinically reliable parameters in this cohort. However, NLR with a cutoff value of 3.6 may be a useful predictor of postoperative gastric leak risk in patients undergoing LSG. This observation might enable timely, targeted intervention, and may be particularly useful when evaluating patients scheduled for early discharge postoperatively. Further prospective studies with larger sample sizes are warranted to better elucidate the utility of the NLR in bariatric surgery.

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