

The Use of Neutrophil-to-Lymphocyte Ratio, Monocyte-to-Lymphocyte Ratio and Platelets-to-Lymphocyte Ratio in the Assessment of the Risk of Conversion and Complications After Cholecystectomy Performed Due to Symptomatic Cholelithiasis

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Purpose: Laparoscopic cholecystectomy is quite a safe procedure, as only about 2% of cases result in clinically significant postoperative complications. The occurrence of conversion and postoperative complications is associated with prolonged hospitalization and higher perioperative mortality. Some parameters assessed in preoperative laboratory tests are used to predict the risk of conversion and clinically significant postoperative complications. The aim of this study was to evaluate the usefulness of preoperative neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and platelets-to-lymphocyte ratio (PLR) values in predicting the risk of conversion and complications in laparoscopic cholecystectomy performed due to symptomatic cholelithiasis.

Patients and Methods: A retrospective analysis of patients operated on for symptomatic cholelithiasis was performed. The Results of preoperative laboratory tests were assessed – NLR, MLR and PLR. Their impact on early outcomes of surgical treatment was analyzed in the study population.

Results: The analysis concerned 227 patients operated on for symptomatic cholelithiasis. The study group included 61 (26.9%) men and 166 (73.1%) women. As the NLR, MLR and PLR values increase, the length of hospitalization increases (rS 0.226, 0.247 and 0.181, respectively), as well as the risk of converting the procedure to an open method ($p < 0.05$). Moreover, with increasing NLR and MLR values, the grade of postoperative complications according to the Clavien-Dindo scale increases ($p = 0.0001$ and 0.008 , respectively). The grade of postoperative complications does not depend on the PLR value.

Conclusion: The risk of conversion can be assessed based on preoperative NLR, MLR and PLR values in patients undergoing surgery for symptomatic cholelithiasis. Elevated preoperative NLR and MLR values are associated with a higher grade of postoperative complications in the Clavien-Dindo scale.

Keywords: laparoscopic cholecystectomy, conversion, complications, neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, platelets-to-lymphocyte ratio

Introduction

Cholecystolithiasis is one of the most common diseases requiring surgical treatment. Laparoscopic cholecystectomy is currently the gold standard in the treatment of this disease.¹ According to available literature, the cholecystectomy is converted to an open method in 5–15% of cases.^{1,2} The main reasons for conversion include the inability to obtain a critical view of safety or intraoperative complications such as hemorrhage or iatrogenic injury of biliary tree.³ Laparoscopic cholecystectomy

is quite a safe procedure, as only about 2% of cases result in clinically significant postoperative complications.⁴ Their frequency depends on the indications for surgery.⁴

The occurrence of conversion and postoperative complications is associated with prolonged hospitalization and higher perioperative mortality.^{5,6} Knowledge of the preoperative laboratory factors influencing the conversion rate and complications after cholecystectomy, allows determining the group at high risk of their occurrence and enables better preparation for the surgical procedure, increasing its safety.⁶ This affects the outcomes of surgical treatment in the case of symptomatic cholelithiasis.⁶ According to the available literature, some parameters assessed in preoperative laboratory tests are used to predict the risk of conversion and clinically significant postoperative complications.⁷

Hematological parameters such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR) and platelets-to-lymphocyte ratio (PLR) are markers of inflammation,^{8,9} also used in gallbladder surgery.^{7,10} The literature confirms the relationship between the values of these ratio's and the risk of gangrenous cholecystitis⁷ or with survival in the case of gallbladder cancer.^{10,11} A small number of analyses concern the use of these factors in the prediction of conversion and postoperative complications after laparoscopic cholecystectomy.

The aim of this study was to evaluate the use of preoperative NLR, MLR and PLR values in predicting the risk of conversion and complications in laparoscopic cholecystectomy performed due to symptomatic cholelithiasis.

Materials and Methods

A retrospective analysis of 245 patients operated on for symptomatic cholelithiasis from November 2021 to June 2023 in the Department of General Surgery of the St. Alexander Hospital in Kielce was performed. Of these, 227 were included in the study after meeting the inclusion and exclusion criteria.

The following inclusion criteria were defined:

- Age between 18 and 100 years.
- Presence of symptomatic cholelithiasis confirmed by imaging tests.
- Availability of documentation containing complete analyzed data.

The exclusion criteria were as follows:

- Qualification for cholecystectomy surgery for an indication other than symptomatic cholelithiasis.
- Performing surgery primarily using the open method.

Eighteen patients did not meet the study inclusion and exclusion criteria. In 16 cases, the documentation was incomplete, while in 2 cases the procedure was performed using the open method from the beginning.

The analyzed data included: age, gender, type of admission, American Society of Anesthesiologists (ASA) grade,¹² occurrence of conversion, duration of surgery and length of hospitalization, as well as the degree of postoperative complications determined according to the Clavien-Dindo scale.¹³ In addition, the results of preoperative laboratory tests were assessed - NLR, MLR and PLR. Their impact on early outcomes (up to 30 days after surgery) of surgical treatment was also analyzed in the study population.

Due to significant deviations from the normal distribution of quantitative variables, assessed with the Shapiro Wilk test and graphically with a q-q chart, non-parametric methods were used. Collected data were presented as median with interquartile range for quantitative variables and number of cases and percentage for qualitative variables. The U-Mann Whitney test was used to compare quantitative variables. The chi-square test was used to compare relationships in qualitative variables. Correlations were assessed using Spearman's rank correlation coefficient. The distribution of the values of the analyzed ratio's in particular grades of complications was assessed using the structure indicators test. P-values<0.05 were considered statistically significant.

The study was a retrospective study of patients medical records. All data was fully anonymized. Written informed consent was obtained from all participants. All procedures performed were in accordance with the 1964 Helsinki Declaration and its later amendments. Our study is exempted from institutional review board approval due to retrospective nature of the study, according to national Act on the medical and dental professions.

Results

The study group included 61 (26.9%) men and 166 (73.1%) women. The age of the patients ranged from 19 to 89 years (mean 54.9, median 58). Of the analyzed cases, 206 (90.75%) were operated on for elective indications. On the other hand, 21 (9.25%) were qualified for the procedure for urgent indications. In the study population, mainly ASA II was found - 171 (75.3%). ASA I was observed in 34 (15.0%) patients. In turn, ASA III was found in 22 (9.7%) cases. In the analyzed group there were no ASA IV or V.

In 28 (12.3%) cases, the procedure was converted to an open method. In 25 (89.3%) cases, the conversion was caused by the inability to obtain a critical view of safety.

In 2 (7.1%) cases it was caused by intraoperative hemorrhage and in 1 (3.6%) case by iatrogenic injury of biliary tree. The duration of the surgical procedure in the analyzed group ranged from 35 to 190 minutes (mean 76.3 minutes, median 70 minutes). The length of hospitalization ranged from 1 to 29 days (median 2 days). Clinically significant complications (grade III or higher) occurred in 8 (3.5%) patients. In the analyzed population, no complications of grade IV or V of the Clavien-Dindo scale were observed. The data described above are presented in [Table 1](#).

Table 1 Clinical Characteristics of the Analyzed Population

Variable		Total = 227
Gender	Men	61 (26.9%)
	Women	166 (73.1%)
Age	Mean	54.9
	Median	58
Type of admission	Elective	206 (90.8%)
	Emergency	21 (9.2%)
ASA grade	I	34 (15.0%)
	II	171 (75.3%)
	III	22 (9.7%)
	IV	0
	V	0
Conversion occurrence	No	199 (87.7%)
	Yes	28 (12.3%)
Duration of the procedure (minutes)	Mean	76.3
	Median	70
Length of hospitalization (days)	Median	2
The grade of postoperative complications according to the Clavien-Dindo scale	0	166 (73.1%)
	I	27 (11.8%)
	II	26 (11.5%)
	III	8 (3.5%)
	IV	0
	V	0

The values of the analyzed ratio's of the studied population were as follows (Table 2). There were no statistically significant differences in the NLR, MLR and PLR values depending on gender ($p>0.05$). The analysis of the correlation coefficient for quantitative variables showed that the values of the analyzed ratio's are not related to age and the duration of the surgical procedure, but are related to the length of hospitalization (Table 3). Higher NLR, MLR and PLR values are associated with longer hospitalization. However, these were weak relationships.

In the case of the analysis of the ratio's value depending on the occurrence of conversion, statistically significant differences were found in the compared groups ($p<0.05$). In the group of patients with conversion, higher values of NLR, MLR and PLR were found. The relationships are presented in Table 4.

Table 2 NLR, MLR and PLR Values in the Analyzed Population

Variable	Total (N=227)			Men (N=61)			Women (N=166)			P value
	Mean	Median	Min-max	Mean	Median	Min-max	Mean	Median	Min-max	
NLR	2.89	2.15	0.48 30.50	2.67	2.12	0.71 18.60	2.98	2.16	0.48 30.50	0.44
MLR	0.27	0.22	0.05 1.50	0.27	0.21	0.08 1.30	0.26	0.22	0.05 1.50	0.89
PLR	134.89	124.00	58.07 518.89	128.71	119.38	58.06 303.90	137.16	124.52	59.52 518.89	0.29

Abbreviations: P, statistical significance level; min-max, minimum-maximum range; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelets-to-lymphocyte ratio.

Table 3 Spearman Correlation Analysis Between Quantitative Variables and NLR, MLR and PLR Values in the Study Population

Variable	Age	Duration of the Procedure (Minutes)	Length of Hospitalization (days)
	rS		
NLR	0.018	0.130	0.226
MLR	0.131	0.064	0.247
PLR	0.027	0.099	0.181

Abbreviations: rs, Spearman's rank correlation, NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelets-to-lymphocyte ratio.

Table 4 NLR, MLR and PLR Values Depending on the Occurrence of Conversion

Variable	Total (N=227)			Group Without Conversion (N=199)			Group with Conversion (N=28)			P value
	Mean	Median	Min-max	Mean	Median	Min-max	Mean	Median	Min-max	
NLR	2.89	2.15	0.48 30.50	2.41	2.10	0.48 9.70	6.31	3.05	1.06 30.50	0.0005
MLR	0.27	0.22	0.045 1.50	0.23	0.21	0.05 0.90	0.49	0.31	0.08 1.50	0.0002
PLR	134.89	124.00	58.07 518.89	128.36	122.50	58.06 334.55	181.27	141.42	73.20 518.89	0.001

Abbreviations: P, statistical significance level; min-max, minimum-maximum range; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelets-to-lymphocyte ratio.

Table 5 The Relationship Between the Grade of Postoperative Complications and the NLR, MLR and PLR Values

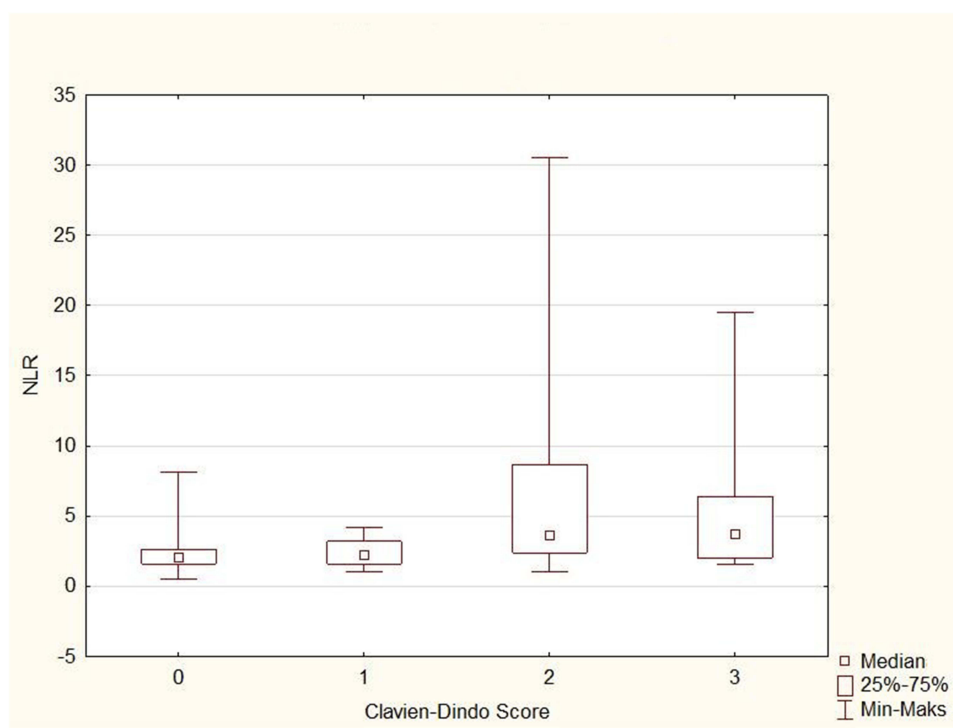
Variable	The Grade of Complications in the Clavien-Dindo Scale												P value
	0 (N=166)			I (N=27)			II (N=26)			III (N=8)			
	Mean	Median	Min-Max	Mean	Median	Min-Max	Mean	Median	Min-Max	Mean	Median	Min-Max	
NLR	2.30	2.01	0.48 8.15	2.37	2.20	1.00 4.17	6.37	3.58	1.06 30.50	5.65	3.68	1.54 19.50	0.0001
MLR	0.23	0.21	0.05 0.62	0.24	0.23	0.11 0.44	0.47	0.33	0.06 1.50	0.45	0.37	0.15 1.30	0.008
PLR	128.54	122.03	58.06 334.55	137.47	132.00	76.39 282.73	166.02	137.33	68.85 518.89	156.57	118.24	99.34 303.86	0.2253

Abbreviations: P, statistical significance level; min-max, minimum-maximum range; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelets-to-lymphocyte ratio.

Based on the grade analysis of postoperative complications, it was found that the NLR and MLR values in particular grades are not the same ($p = 0.0001$ and 0.008 , respectively). As the NLR and MLR values increase, the grade of postoperative complications according to the Clavien-Dindo scale increases. On the other hand, the distribution of PLR values in particular grades of postoperative complications is the same ($p > 0.05$). The described relationships are presented in Table 5 and Figures 1–3.

Based on the multiple comparison test, it was found that in the case of the NLR, statistically significant differences occur between the ratio values in grades 0 and II of the Clavien-Dindo scale ($p = 0.0001$) and in grades I and II ($p = 0.02$). There were no statistically significant differences between grades 0 and I. Moreover, no statistically significant differences were found for grade III complications due to the small number of cases in this grade.

In the case of the MLR ratio, statistically significant differences were found between the ratio value in grades 0 and II of the Clavien-Dindo scale ($p = 0.007$). Between grades 0 and I as well as I and II, no statistically significant differences

**Figure 1** The relationship between the grade of postoperative complications and the NLR value.

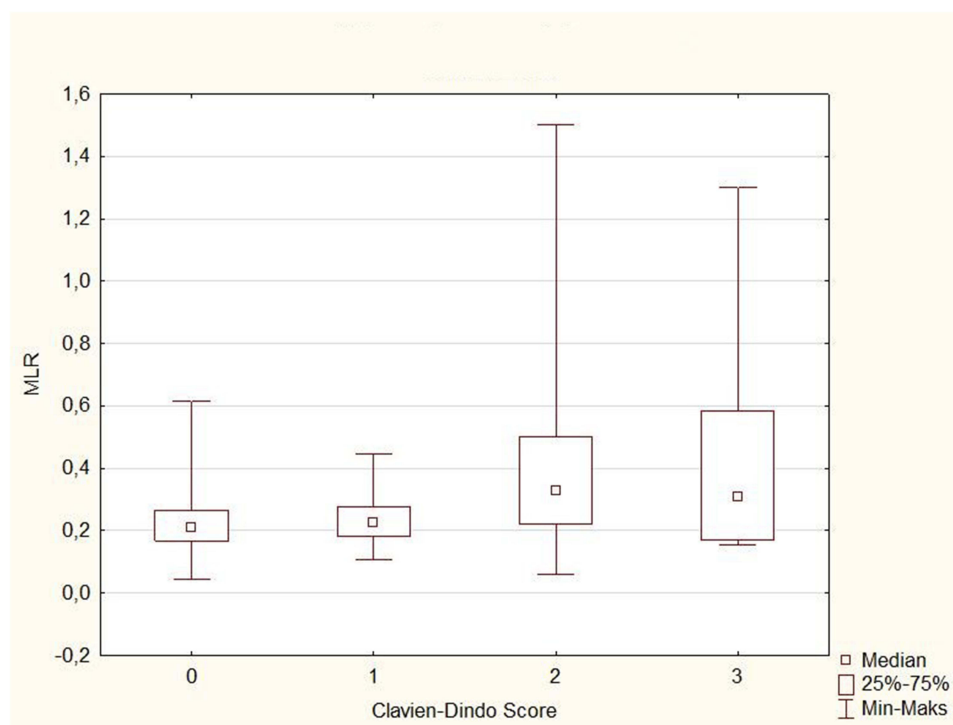


Figure 2 The relationship between the grade of postoperative complications and the MLR value.

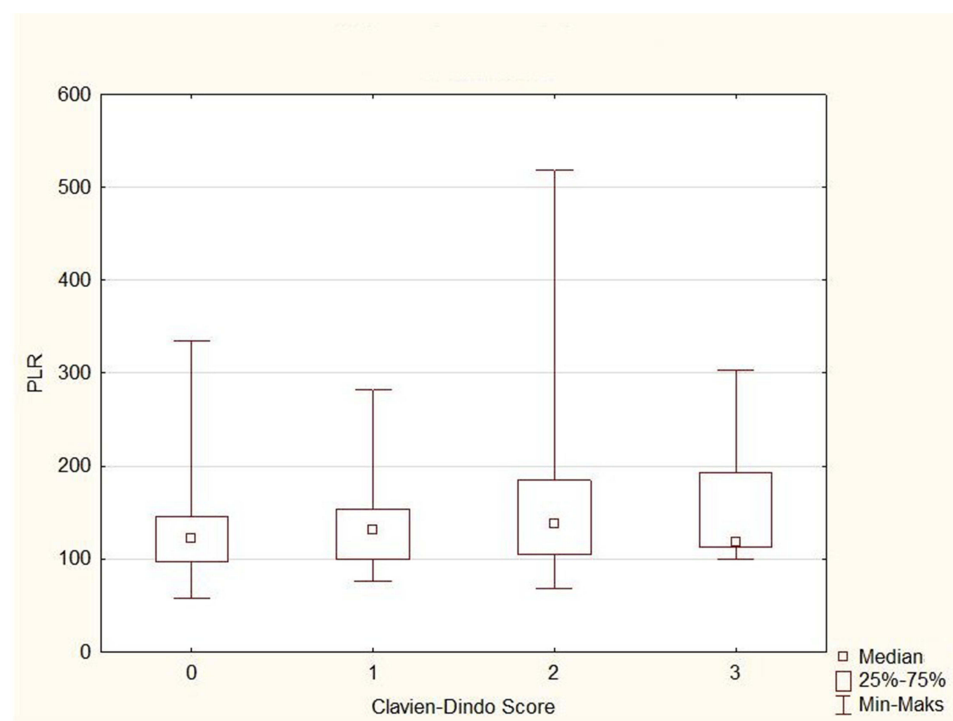


Figure 3 The relationship between the grade of postoperative complications and the PLR value.

were found in the case of MLR values. As in the case of NLR, no statistically significant differences were found for grade III complications due to the small number of cases in this grade.

Discussion

In this study, we analyzed and confirmed the usefulness of the neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio and platelets-to-lymphocyte ratio in the assessment of the risk of conversion and complications after cholecystectomy performed due to symptomatic cholelithiasis.

The study group included 61 (26.9%) men and 166 (73.1%) women. The age of the patients ranged from 19 to 89 years (mean 54.9, median 58). In the analyzed population, there was no relationship between NLR, MLR and PLR values depending on gender and age. According to Izumisawa et al, NLR and MLR values determined before surgery depend on age, while there is no such relationship in the case of PLR.¹⁴ In the same analysis, no relationship between the values of the analyzed biochemical parameters and gender was confirmed.¹⁴ On the other hand, according to Lee et al, in the case of older age and male gender, NLR has higher values.¹⁵ Durak et al showed that NLR >5 is only associated with older age and is not related to gender.¹⁶

According to Lee et al, in the group of patients with NLR >3 compared to patients with NLR <3, the average duration of the laparoscopic cholecystectomy is approximately 15 minutes longer.¹⁵ Moloney et al also confirmed the association of NLR values >3 with prolonged surgical procedure duration.⁸ Moreover, NLR >3 is associated with a higher risk of prolonged hospitalization.^{8,15} Similar relationships were confirmed by Ares et al and Ahmed et al in their analyses, but according to these authors, this relationship occurs in the case of NLR >5.^{17,18} Elevated NLR values are associated with advanced inflammation,^{11,15} most pronounced in cases of gangrenous cholecystitis.¹⁷ MLR values also depend on the severity of inflammation.¹¹ There are no analyses of the impact of this ratio on the duration of surgery and length of hospitalization. However, Durak et al showed that increased MLR values correlate with a greater severity of inflammatory adhesions making surgery more difficult.¹⁶ On the other hand, the duration of the surgical procedure does not depend on the PLR value, but the length of hospitalization does.¹⁷ In the study group, it was found that the values of the analyzed ratio's were not correlated with the duration of the surgical procedure. However, elevated preoperative NLR, MLR and PLR values are associated with longer hospitalization.

According to available literature, in 5–15% of laparoscopic cholecystectomies the procedure is converted to an open method.^{1,2} In the analyzed population, conversion occurred in 28 (12.3%) cases. Shimoda et al showed that increased NLR and PLR values correlate with a greater risk of the bailout surgery¹⁹ – partial or subtotal cholecystectomy recommended by the Tokyo Guidelines when total cholecystectomy is not possible due to acute cholecystitis.²⁰ Gupta et al showed that the risk of not achieving the critical view of safety, which is one of the main causes of conversion, does not depend on the NLR value.²¹ In the analyzed literature regarding the risk of conversion during laparoscopic cholecystectomy performed for acute cholecystitis, there is no relationship between increased NLR values and a higher risk of conversion.^{7,15,17,22} Ares et al also showed no such relationship in the case of PLR values.¹⁷ However, the analysis by Moloney et al regarding the risk of conversion in the case of elective laparoscopic cholecystectomy showed that NLR values >3 are associated with a higher risk of conversion.⁸ The analyzed literature did not include any analyses regarding the use of MLR and PLR values in the assessment of conversion risk, especially in relation to elective cholecystectomy. In the analyzed population, a relationship was found between the occurrence of conversion and the values of the analyzed ratio's ($p < 0.05$). In the group of patients with conversion, higher values of NLR, MLR and PLR were found.

In the analyzed population, no complications of grade IV or V of the Clavien-Dindo scale were observed. On the other hand, grade III complications occurred in 8 (3.5%) cases. The literature analyzing the usefulness of NLR, MLR and PLR values in the assessment of mortality and the occurrence of postoperative complications after laparoscopic cholecystectomy is limited.^{15,17,23,24} According to Kartal et al, mortality after cholecystectomy does not depend on the NLR and PLR values.²⁴ However, this analysis included only patients over 85 years old.²⁴ According to Lee et al, in the case of NLR >3, there was no greater risk of major postoperative complications.¹⁵ Also Ares et al showed no such relationship with NLR and PLR values.¹⁷ In both analyses, the occurrence of postoperative complications was not assessed according to the Clavien-Dindo scale.^{15,17} Moreover, these analyses included only patients operated on for acute cholecystitis.^{15,17} According to Kubat et al, in geriatric patients with

acute cholecystitis, in the case of NLR value >9.9 , early cholecystectomy should be performed due to the lower risk of complications compared to the group of patients who underwent delayed cholecystectomy.²³ Based on the analysis, it was found that the NLR and MLR values in the various grades of complications are not the same. As the NLR and MLR values increase, the grade of postoperative complications according to the Clavien-Dindo scale increases. On the other hand in the case of PLR, no such relationship was found. It was not possible to determine the exact relationship between the NLR and MLR values and the occurrence of clinically significant postoperative complications determined according to the Clavien-Dindo scale due to the small number of cases in grade III and higher in the analyzed group.

An undoubted limitation is retrospective nature of this study and the limited size of the analyzed population, taking into account the incidence of cholelithiasis. However, despite these limitations, it was possible to identify the influence of the values of the analyzed biochemical parameters on the early outcomes in group of patients undergoing laparoscopic cholecystectomy due to symptomatic cholelithiasis.

Conclusions

The risk of conversion can be assessed based on preoperative NLR, MLR and PLR values in patients undergoing surgery for symptomatic cholelithiasis. Elevated NLR and MLR values are also associated with a higher grade of postoperative complications in the Clavien-Dindo scale. The influence of NLR and MLR values on the occurrence of clinically significant postoperative complications requires further analyses.

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