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Prognostic significance of NLR in acute cholecystitis, treated with laparoscopic cholecystectomy

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Abstract: Introduction: Acute cholecystitis (AC) is a condition that requires surgical treatment. Laparoscopic cholecystectomy (LC) is considered the gold standard. Based on routine blood tests, it is possible to determine the neutrophil-to-lymphocyte ratio (NLR), which accurately characterizes the body's systemic inflammatory response. The NLR is used as a prognostic tool in many gastrointestinal diseases and may therefore be useful in the diagnosis of AC.
Aim: The objective of this study is to assess the prognostic value of the NLR index in the course of AC.
Materials and Methods: This is a retrospective analysis of patients with AC who underwent LC. The study analyzed the following factors: emergency or elective admission, white blood cell count and bilirubin levels which are the part of preoperative laboratory tests, intraoperative complications such as gallbladder perforation and empyema formation, surgery duration, and length of hospital stay.
Results: The study involved 306 patients treated with LC. In the group of patients with NLR >5, there was a statistically significant correlation with higher risk of emergency admission, elevated bilirubin levels, higher risk of empyema, longer surgery time and hospital stay. We did not find an association between the NLR index and the risk of gallbladder perforation or patient gender.
Conclusions: High NLR values are associated with an increased risk of complications during AC. Therefore, this predictor can be successfully used in clinical practice to identify the severe course of cholecystitis.

Keywords: neutrophil-to-lymphocyte ratio (NLR), acute cholecystitis (AC), gallbladder diseases, digestive system diseases, laparoscopy, cholecystectomy, blood test.

Introduction

Acute cholecystitis (AC) is an inflammatory disease that affects the gallbladder [1]. AC is also one of the most frequent gastrointestinal conditions that requires surgical intervention [2]. Laparoscopic cholecystectomy is considered to be the gold standard for the treatment of AC [3]. Nowadays, there are a variety of methods used to assess the prognosis, severity and individualize the management of AC. However, not all of these methods are cheap, simple and easy to use. Complex biochemical and hematological indicators such as neutrophil-to-lymphocyte ratio (NLR) can be the solution to this problem offering clinically efficient and cost-effective risk stratification method.

The NLR is calculated by dividing the number of neutrophils by the number of lymphocytes in whole blood per 1 ml. Both components of the aforementioned ratio are basic and inexpensive laboratory parameters, which are a part of standard hematological laboratory tests performed upon admission to all emergency or surgical departments. This makes the application of NLR possible in the context of many diseases. It is considered that the NLR index accurately assesses the systemic inflammatory response of the body [4]. Additionally, it provides a measure of both the innate and adaptive regulatory response of the immune system to inflammation, infection, and tissue damage [5].

Predictive value of NLR has been described in gastrointestinal conditions, such as acute pancreatitis [6] and acute appendicitis [7]. For that reason it is reasonable to evaluate the prognostic value of NLR in AC as well. The literature on that particular application of NLR is scant. Therefore we had conducted a study based on the unselected group of patients admitted to the general surgical department in order to test the utility of NLR.

The aim of this study was to determine the prognostic value of NLR in the assessment of the severity of AC and the likelihood of intraoperative complications during laparoscopic cholecystectomy.

Materials and Methods

A retrospective study was conducted at the Department of General and Oncological Surgery, 5th Military Hospital, Cracow, Poland, from January 2016 to December 2017. The study population consisted of 306 patients operated on for AC by laparoscopic cholecystectomy. We recorded baseline preoperative laboratory tests (WBC, bilirubin level), mode of surgery (elective or emergency), intraoperative complications (i.e. gallbladder perforation and/or empyema formation), time of surgery and length of hospital stay.

NLR was calculated by dividing the absolute number of neutrophils by the absolute number of lymphocytes in the whole blood. Laboratory tests used for NLR calculations were performed on the admission day.

The cutoff value of 5 for NLR was determined based on the literature; according to the majority of studies, NLR values equal to or greater than 4 [2, 8] or greater than 5 [4, 9, 10] indicate the risk of complications and severe course of gastrointestinal diseases.

All data were analyzed using IBM SPSS Statistics v29 software (IBM, Armonk, New York, USA). Results were presented as numbers with percentage or median with minimum and maximum ranges. The study of categorical variables used the chi-square test of independence. Normal distribution was checked using the Shapiro-Wilk test. Quantitative data were compared using the Mann–Whitney test. Results were considered statistically significant at $p < 0.05$.

Results

In the total group of 306 patients undergoing laparoscopic cholecystectomy there were 195 women (63.7%) and 111 men (36.3%). The median age was 56.6 (19–96) years. Fifty two (17%) patients were admitted as an emergency, while the remaining 254 (83%) were admitted electively. All 306 patients were operated by laparoscopy. The median operation time was 60 (24–230) minutes. The median length of stay was 4 (2–24) days. Laboratory tests detected elevated levels of bilirubin in 46 patients (15%). Intraoperative complications like gallbladder perforation or empyema, occurred in 70 (23%) and 39 (13%) patients respectively.

There was a significant correlation between the NLR score and the majority of analyzed factors. In the group of patients with NLR >5, the length of surgery ($p < 0.001$) and hospital stay were significantly longer ($p < 0.001$). NLR >5 also correlated with a higher risk of empyema ($p < 0.001$), high bilirubin levels ($p < 0.001$) and emergency admission ($p < 0.001$). There was no statistically significant difference according to gender or gallbladder perforation (Table 1).

Table 1. Correlation between NLR score and analyzed factors in the study group.

	Total	NLR >5	NLR <5	p
Total	306	32	274	
Females	195	17	178	0.187
Emergency	52	20	32	<0.001
Perforation	70	7	63	0.887
Empyema	39	16	23	<0.001
Bilirubin	46	14	32	<0.001
Operative time	60 (24–230)	87.5 (35–230)	60 (24–210)	<0.001
Length of stay	4 (2–24)	5 (2–16)	4 (2–24)	<0.001

Discussion

The aim of this study was to determine the prognostic significance of the NLR in the course of acute cholecystitis (AC). Although the clinical significance of the NLR has been described in various both malignant and non-malignant disorders, including gastrointestinal malignancies [4, 11], acute appendicitis [7], and gallstone pancreatitis [12], its potential application in the context of AC is not supported by sufficient data. The results of our study point out that NLR could also be applied in patients with AC diagnosis, showing prognostic value.

According to epidemiological studies, female gender is a risk factor for developing cholelithiasis, which can lead to AC [13]. However, no data suggest an association between the NLR index and gallstones. Both our study and the literature [2] conclude that the level of NLR in AC is not related to the gender of the patient. However, one study showed a statistically significant association between NLR >3 and male gender [14]. Due to these conflicting results, further studies are needed to analyze the association of gender with NLR levels in the course of AC.

In our study, we found that emergency surgery mode was significantly associated with NLR >5. However, it is important to note that in the literature, even lower NLR values, such as NLR >3,

correlate with emergency department admission [14]. Therefore, the NLR index may be a useful tool in making decisions about further treatment and ultimately the mode of presumed surgery.

Our study also showed that higher NLR values were associated with a longer hospitalization time. The median length of hospitalization for patients with NLR >5 was 5 days, which was 1 day longer than the group of patients with NLR <5. This prolongation of hospitalization time was also confirmed by another study, which found that an NLR value >5 was associated with a hospitalization time of up to 7 days [9]. Importantly, an NLR >3 also increases hospital length of stay by approximately 1 day [14].

The NLR index also correlates with time of surgery. In our study, the median surgery time in patients with NLR >5 was 90 minutes, which was approximately 30 minutes longer than in patients with NLR <5. Other studies suggest that the median operative time may reach 100 minutes in patients with NLR >5 [9]. The NLR index, as an indicator of prolonged surgery and hospitalization time, can be useful in the management of hospital departments and operating rooms.

Bilirubin level is part of the routine admission tests for the diagnosis of AC [15]. This is the first study to report a direct correlation between NLR >5 and markedly elevated bilirubin levels in the course of AC. The bilirubin level has previously been shown to be prognostically significant for the severity of AC [15, 16].

To date, studies have investigated the relationship between the NLR index and the risk of postoperative complications. Different results have been obtained, postulating a lack of statistical significance [14] or poor predictive value, with the exception of the good predictive value of NLR for Clavien-Dindo grade IV complications [16].

Our study analyzed the risk of intraoperative complications. We showed for the first time that an NLR >5 on admission in patients with AC indicates an increased risk of empyema, whereas we found no correlation between the risk of gallbladder perforation and NLR level, which is also confirmed in the literature [9].

Our study has some limitations, including: heterogeneous structure of the studied population, limited number of parameters analyzed, retrospective type of the study. On the other hand this study is based on an unselected AC population that represents the typical profile of AC patients admitted to ER/surgical departments and thus our conclusion supporting the use of NLR as a prognostic indicator can be generalized and applied in routine practice.

We have shown that elevated NLR values (>5) at admission in patients with AC were associated with emergency mode of surgery, prolonged surgery time, prolonged hospital stay and increased risk of empyema. In clinical practice, this means that NLR could serve as an easily accessible predictor of more severe course of AC. In addition, the NLR value is easy to calculate and does not require any additional tests beyond the standard ones, performed in every patient in every ER. As a result, the NLR can be added to the diagnostic work-up, resulting in faster and more accurate diagnosis of cases of severe AC, thus increasing the chances of successful treatment for patients.

Author Contributions

Study Design and Conceptualization: Wojciech M. Wysocki, Data Collection: Katarzyna A. Kowalczyk, Rafał Robak, Jakub Pośpiech, Statistical Analysis and Methodology: Tomasz Stefura, Wojciech M. Wysocki, Data Interpretation: Katarzyna A. Kowalczyk, Wojciech M. Wysocki, Jakub Pośpiech, Tomasz Stefura, Manuscript Preparation: Jakub Pośpiech, Katarzyna A. Kowalczyk,

Tomasz Stefura, Wojciech M. Wysocki, Resources and literature search — Rafał Robak, Jakub Pośpiech, Supervision: Wojciech M. Wysocki.

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Conflict of interest

None declared.

Abbreviations

AC — acute cholecystitis
ER — emergency department
LC — laparoscopic cholecystectomy
NLR — neutrophil-to-lymphocyte ratio

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