



Predictive Value of Preoperative Neutrophil-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Serum Albumin for Postoperative Pneumonia after Thoracic Surgery

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Abstract

Background: Postoperative pneumonia (POP) is an important complication that occurs after thoracic surgeries and has been responsible for increased cases of morbidity and mortality. It is, therefore, important to identify those patients at high risk of developing it before the surgery, allowing for the implementation of preventive measures.

Purpose: This study aimed at examining the predictive significance of preoperative platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and serum albumin level in relation to the potential occurrence of postoperative pneumonia in patients sought for thoracic surgery.

Material and methods: The authors used a prospective cohort design to observe 287 patients who were to undergo thoracic surgery from January 2022 to December 2023. Blood samples for complete blood test and serum albumin were drawn not later than 48 hours prior to the operation. The diagnosis of postoperative pneumonia adhered to established diagnostic criteria. **Results:** Fifty-two patients developed postoperative pneumonia (cumulative incidence of 18.1%). The group of patients with POP was characterized by significantly higher NLR (4.8 ± 2.1 vs. 2.9 ± 1.3 , $p < 0.001$), higher PLR (134.7 ± 48.2 vs. 98.3 ± 35.6 , $p < 0.001$) and lower serum albumin levels (3.1 ± 0.6 vs. 3.7 ± 0.4 , $p < 0.001$). ROC analysis revealed the area under the curve for NLR, PLR, and serum albumin of 0.821, 0.764, 0.809 respectively. A combined score that covers all the three factors showed higher predictive significance (AUC 0.887).

Conclusion: The author concluded that NLR, PLR, and serum albumin are significant predictors for postoperative pneumonia occurrence. The combined score can help recognize the patients at risk and apply effective treatment methods.

Keywords:

Neutrophil-to-lymphocyte ratio; Platelet-to-lymphocyte ratio; Serum albumin; Postoperative pneumonia; Thoracic surgery; Predictive marker.

1. INTRODUCTION

Postoperative pneumonia (POP) has been one of the most frequently encountered complications of thoracic surgery according to studies that indicate incidence rates ranging from 5% to 40% depending upon the nature of surgery, details of the patients and diagnostic criterion.[1] The effects of this complication are significant in terms of postoperative complications and increase in hospital stay along with an increase in costs of healthcare and the mortality rate in high-risk

patient population.[2] However, despite the advancements achieved in surgical techniques, perioperative antibiotics, and respiratory care after surgery, there has been no prominent change in occurrence rate of POP in the last two decades indicating the need to enhance the prevention and treatment procedures.

The pathophysiology of postoperative pneumonia operates through various factors that include immunosuppression that is induced by surgical injury, unsatisfactory functioning of mucociliary clearance that is conditioned by anesthesia and mechanical ventilation, risk of aspiration, as well as ventilation of the airways with pathogens.[3] As for the patients undergoing thoracic surgery, they are facing additional problems caused due to the breach of the chest wall, surgical disturbance of lungs, and alterations in regarding pulmonary mechanics.[4] Commonly known risk factors of POP are older patients, patients suffering from obesity, COPD, decreased function of respiration, long time spent on surgery, and emergency surgery.[5] Nevertheless, despite several risk factors that can help identify risk patients preoperatively, it is not easily done as patients that are at risk may be missed. NLR implies the number of neutrophils divided by the number of lymphocytes. It indicates neutrophilia and lymphopenia, showing the state of systemic inflammation and stress.[6] A number of studies conducted among different population in surgical settings suggest that high NLR is tied to the probability of post-surgical complications, especially infections like pneumonia.[7,8]

Similarly, sorting because of PLR serves as an indicator of systemic inflammation and immune status. Specifically, PLR implies the ratio of platelets to lymphocytes and can demonstrate the occurrence of platelet activation and lymphopenia. In short, an elevated PLR may imply that the immune regulation is not balanced, leading to an increase of activity in platelets because of lymphocyte suppression.[9] Although some studies show that PLR may help to predict pre- and post-surgical complications in different surgical settings, hardly any research has been done in the field of thoracic surgery to evaluate PLR role in different surgical context.[10]

In addition, serum albumin can be considered a diagnostic criterion of nutritional status, hepatic function and systemic inflammation. Albumin is considered a negative acute phase reactant that decreases in levels under systemic inflammatory condition.[11] Several investigations have shown that low levels of albumin is independently linked with unfavourable surgical prognosis, such as increased risk of infections.[12] The possible methods explaining the association of low albumin levels with postoperative infections include impaired immune functions, reduced ability to produce antimicrobial peptides, change in wound healing and increased permeability of capillaries resulting in swelling of tissues.[13]

Even if each of these factors has been linked with the risk of postoperative complications individually, the research of their combined predictive value for pneumonia after thoracic surgery has not been carried out enough.[14] Moreover, the optimal values of these factors for predicting pneumonia have not been studied properly and defined for patients undergoing thoracic surgeries. Previous research involving these criteria has been mainly conducted in cardiac or abdominal surgeries and applied to thoracic procedures with limitations because of their specific pathophysiology of pneumonia.

The usefulness of developing an effective tool for predicting the possibility of pneumonia after surgery cannot be underestimated considering that patients who are likely to be at high risk could receive intensive treatment based on enhanced respiratory physiotherapy, preventive antibiotics, early mobilization and nutritional support.[15] Such efforts proved to be effective

concerning the prevention of complications after surgery. In addition, risk stratification allows making accurate predictions for patients, conducting appropriate consent discussions with patients and allocating resources properly when planning surgical interventions.

The reason for studying the correlation between NLR, PLR and fasting serum albumin is that pneumonia after a surgical procedure is caused by several factors such as impaired immune response reflected in lymphocyte rates, systemic inflammation reflected in high levels of neutrophils and platelets and lack of nutrients or stress reflected in low levels of albumin.[16]

The goal of the current research was to investigate the predictive ability of NLR, PLR and serum albumin concerning pneumonia development among patients who have had thoracic procedure surgeries at Al Hilla Teaching Hospital. It was stated in the hypothesis that the increase in NLR and PLR and decrease in serum albumin are statistically related to pneumonia development and, thus, the use of these three parameters together would ensure more accurate results than playing with parameters separately. The usage of results of the research can help identify high-risk patients earlier and, thus, provide them with preventive interventions to avoid the risk of pneumonia.

2. METHODOLOGY

2.1 Study Design and Patient Population

This prospective cohort study was performed at the Department of Thoracic Surgery, Al Hilla Teaching Hospital, Babylon, Iraq, from January 2022 to December 2023. The research was authorized by the institutional review board and ethics committee, and all participants signed a written informed consent form before being included in the study. The research procedure followed the rules stated in the Declaration of Helsinki and Good Clinical Practice.

Participants were adults (≥ 18 years) scheduled for elective thoracic surgery, such as lobectomy, segmentectomy, wedge resection, pneumonectomy, decortication, and other significant surgical treatments. Patients who were subjected to emergency surgical procedures were excluded from the study, as well as those who had respiratory diseases before the operation, and those who were undergoing immunosuppressive therapy. Patients who had any form of hematological cancer, ongoing cancer with systemic chemotherapy for the last three months, and major hepatic dysfunction (Child-Pugh class C) were excluded from the study. Participants whose telephone number was missing or whose laboratory findings were not sufficient were excluded from the research study.

2.2 Data Collection

At preoperative assessment, demographic information had been collected which covered the patient's age, sex, BMI, other health conditions that existed together with the primary health problem and results of the pulmonary function tests. All patients were evaluated in general practice and examined with CBC and metabolic panel. The laboratory samples were taken in the last two days preceding surgery after a period of fasting that lasts for the night. The blood samples for CBC tests were taken in the tubes made from EDTA and the blood was processed to analyze metabolism.

2.3 Laboratory Measurements

The complete blood count for participants in this study was determined through the use of Sysmex XN-1000 (Japan) automated hematological analyzers to enable the determination of differential counts required for the calculation of NLR. The absolute values of neutrophils and lymphocytes were recorded and NLR was determined by dividing the value of neutrophils with that of lymphocytes. Similarly, the PLR value was determined by dividing the value of platelets with that of lymphocytes. Serum albumin levels were measured using bromocresol green method on Roche Cobas c702 (Switzerland) automated chemistry analyzers. All laboratory tests were carried out by certified laboratory technicians working through any principles based on standard protocols.

2.4 Surgical Procedures and Perioperative Management

All surgery procedures conducted on the thorax underwent execution by proficient medical practitioners who made use of the standard surgical procedure. Anesthesia was induced using either thiopental or propofol and maintained with either sevoflurane or isoflurane in combination with opioids. Standard monitoring using electrocardiography and an electroencephalography was carried out. Prophylactic antibiotics were administered at the induction stage of anesthesia. Pain relievers were used postoperatively with opioids and non-opioids used.

Postoperative care entails provision of respiratory care through mobilization and physiotherapy given to patients. Chest tubes were managed with suction being used as indicated. Additionally, patients were encouraged to walk starting on the first postoperative day.

2.5 Postoperative Pneumonia Diagnosis

Postoperative pneumonia is identified as the emergence of pneumonia that occurs more than two days after the surgical procedure, based on clinical and radiological parameters. For the purposes of clinical diagnosis, the presence of minimum two symptoms like, a new troublesome cough, production of sphygmomanometer, body temperature more than 38 degrees Celsius, presence of noticeable blood in the sputum, etc., is required for diagnosis. In addition to that, during the process of radiological diagnosis, evidence of the new or progressing infiltrate was assessed by means of X-ray or computerized tomography. Also, sputum culture samples and blood culture samples were collected wherever necessary for the procedure. The diagnosis was made by physicians who were unaware of the preoperative laboratory results.

2.6 Statistical Analysis

Continuous variables were presented as mean $\pm$ standard deviation or median (interquartile range) based on normality of distribution determined by Shapiro-Wilk test. Categorical variables were presented as frequencies and percentages. Differences between groups were studied using independent samples t-test for normally distributed continuous variables or Mann-Whitney U test for non-normally distributed variables. Chi-square test was used for categorical variables.

Receiver operating characteristic (ROC) curves were drawn to assess predictive accuracy of NLR, PLR and serum albumin in the development of pneumonia after the operation. Area under the ROC curve (AUC) was calculated for all parameters. Optimal cutoff points were determined

based on Youden index. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated at optimal cutoff points.

Logistic regression analysis was conducted with pneumonia after the surgery being dependent variable and NLR, PLR and serum albumin being independent variables. Odds ratios with 95% confidence intervals were calculated. A scoring system was created using points for elevated NLR ($\geq$ cutoff), elevated PLR ($\geq$ cutoff), and low albumin ($\leq$ cutoff). ROC analysis was done for this combined score. All statistical analyses were performed using version 26 of SPSS (IBM Corporation, Chicago, Illinois) and version 9 of GraphPad Prism (GraphPad Software, San Diego, California).

2.7 Sample Size Calculation

According to the past study indicating 15% occurrence of postoperative pneumonia after thoracic surgery, and considering the possibility of finding a clinically relevant difference of 20% between high-risk and low-risk groups with 80% power, it necessitates collecting information from at least 250 patients. Yet to estimate the dropout rate of 10%, an intention was made to recruit 280 patients.

3. RESULTS

3.1 Patient Characteristics

Of the 287 patients who participated in this study, 281 patients completed the full period of follow-up and were included in the final statistical analysis. Six patients were excluded due to incompleteness of postoperative data. The average age of patients was 58.4 ± 11.2 years (age 28 to 82) with 167 males (59.4%) and 114 females (40.6%). The initial characteristics and comorbid conditions of the subjects were similar in both groups. In total, pneumonia developed in 52 patients (18.5%) as postoperative complications while the remaining 229 patients (81.5%) did not suffer any complications.

3.2 Laboratory Parameters and Postoperative Pneumonia

Table 1: Comparison of Preoperative Laboratory Parameters Between Patients With and Without Postoperative Pneumonia

Parameter	POP Group (n=52)	Non-POP Group (n=229)	p-value
NLR (mean $\pm$ SD)	4.8 ± 2.1	2.9 ± 1.3	<0.001
PLR (mean $\pm$ SD)	134.7 ± 48.2	98.3 ± 35.6	<0.001
Serum Albumin (g/dL)	3.1 ± 0.6	3.7 ± 0.4	<0.001
WBC ($\times 10^3/\mu\text{L}$)	7.4 ± 2.8	6.8 ± 2.1	0.089
Neutrophils (%)	68.4 ± 10.2	62.1 ± 8.9	<0.001
Lymphocytes (%)	18.2 ± 8.1	25.6 ± 9.3	<0.001
Platelets ($\times 10^3/\mu\text{L}$)	267.8 ± 89.4	245.2 ± 71.3	0.078

POP, postoperative pneumonia; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; WBC, white blood cell count; SD, standard deviation

3.3 Receiver Operating Characteristic Analysis

Table 2: Receiver Operating Characteristic Curve Analysis for Individual Parameters

Parameter	AUC	95% CI	Optimal Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
NLR	0.821	0.758-0.884	3.95	78.8	73.4	45.2	92.4
PLR	0.764	0.691-0.837	115.5	71.2	71.6	38.9	90.8
Albumin	0.809	0.745-0.873	3.45 g/dL	73.1	78.2	48.7	91.2

AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio

The receiver operating characteristic analysis revealed that NLR has the highest AUC being 0.821 (95% CI 0.758-0.884), thus having good predictive ability. PLR showed moderate predictive ability that was reflected in AUC value of 0.764 (95% CI 0.691-0.837), and serum albumin exhibited good predictive power with AUC of 0.809 (95% CI 0.745-0.873). The optimal cutoff value for NLR was found to be 3.95, with sensitivity being 78.8% and specificity being 73.4%. For PLR, the optimal cutoff was found to be 115.5, with sensitivity of 71.2% and specificity of 71.6%. For serum albumin, the cutoff of 3.45g/dL was found to be optimum and the sensitivity at this level was 73.1%, while the specificity was 78.2%.

3.4 Multivariate Logistic Regression Analysis

Table 3: Logistic Regression Analysis for Predictors of Postoperative Pneumonia

Variable	Odds Ratio	95% CI	p-value
NLR (≥ 3.95)	3.84	1.92-7.67	<0.001
PLR (≥ 115.5)	2.51	1.31-4.82	0.006
Albumin (<3.45 g/dL)	3.12	1.58-6.14	0.001
Age (>65 years)	1.89	0.94-3.81	0.074
COPD	2.14	1.07-4.27	0.031
FEV ₁ (<60% predicted)	1.97	0.98-3.95	0.056

COPD, chronic obstructive pulmonary disease; FEV₁, forced expiratory volume in 1 second; CI, confidence interval

According to the findings of a logistic regression analysis, NLR, PLR, and serum albumin were detected to be independent predictors for development of postoperative pneumonia. Increased

NLR (≥ 3.95) was significantly associated with 3.84 times higher risk (95% CI 1.92-7.67, $p < 0.001$). Increased PLR (≥ 115.5) was found to be associated with 2.51 times increase in risk (95% CI 1.31-4.82, $p = 0.006$). Decreased serum albumin (< 3.45 g/dL) was related to 3.12 times increase in risk (95% CI 1.58-6.14, $p = 0.001$).

3.5 Combined Scoring System

Risk factors were combined to give the scores 1 point for having NLR ≥ 3.95 , PLR ≥ 115.5 and albumin < 3.45 g/dL each. Depending on the points, patients are categorized into low risk (0 points), intermediate risk (1 point), and high-risk categories (2 to 3 points).

Table 4: Combined Risk Score Analysis

Risk Category	Number (%)	POP Rate (%)	AUC	Sensitivity	Specificity
Low-risk (0 points)	134 (47.7%)	4.5	0.887	84.6	89.1
Intermediate-risk (1 point)	98 (34.8%)	17.3			
High-risk (2-3 points)	49 (17.4%)	53.1			

The results showed that the combined score achieved an AUC of 0.887 (95% CI 0.832-0.942) indicating its predictive ability was high. The high-risk group (2-3 points) had a postoperative pneumonia incidence of 53.1% while the low-risk group had 4.5% which translates to 11.8 times increased risk. The combined score demonstrated a sensitivity of 84.6% and specificity of 89.1%.

4. DISCUSSION

This report indicates that the preoperative measurement of NLR, PLR, and serum albumin can serve as a marker of the chance of developing pneumonia in the postoperative setting. Moreover, the application of a combined scoring system that includes these three parameters allows developing a substantially more precise predictive model for the detection of patients who are at high risk of complications. Therefore, the study can be considered to augment the existing knowledge about the relationship between inflammation and nutrition in surgical patients and presents the relevant results specifically for the thoracic surgery area.

The increase in NLR as a predicted factor of complication occurrence has been previously described in the literature.[17] What is interesting, from three previously mentioned parameters, NLR demonstrated the greatest predictive capacity with an AUC value equal to 0.821. The NLR cutoff value equal to 3.95 calculated in our study corresponds with values received for other types of surgical patients, but comparison is difficult due to different methodological approaches and patient population involved.[18] The mechanism of post-operative pneumonia occurrence can be explained by the combination of inflammatory process in the body and slight immunosuppression. Therefore, NLR level is an indicator of both the activation of neutrophils that lead to excessive inflammation and the occurrence of lymphopenia that negatively impacts

the immunity and the ability to recognize the pathogen.[19] In this regard, it should be noted that in patients who underwent thoracic surgery, the role of this decrease in immunity is even greater, because thoracic surgery implies severe damage to the area of the thoracic wall as well as the lung. The discovery that PLR can help predict post-surgery pneumonia helps strengthen evidence for the use of this element in risk assessments.[20] The predictive precision of PLR was found to be lower than that of NLR (the former had AUC of 0.764 against the latter whose AUC value was 0.821), but it is still useful in risk assessments, which is explained by the possibility to include the dynamic component of the platelet level. The platelet-lymphocyte ratio shows how platelets become active due to tissue damage and inflammatory processes occurring and show the level of immune suppression.[21] In patients undergoing thoracic surgery, the level of platelet activity is expected to be particularly high, as the surgeries involve considerable damage of soft tissues. Similarly, lymphopenia demonstrates the extent of immune suppression seen after the surgery.[22] Thus, the significance of PLR is indicative of severity of surgical injury and the corresponding immune dysfunction.

Albustar values also showed high predictive ability, which was comparable to the levels of NLR as it showed AUC of 0.809. Low levels of albumin in the body show signs of malnutrition and acute phase response during surgery.[23] Albumin is involved in immune mechanisms by acting as a transporter of anti-infection substances, increasing oncotic pressure in the body needed for healthy perfusion of tissues, and acting as a source of nitrogen used in synthesizing immune cells.[24] The optimal levels of albumin identified in this study (3.45 g/dL) correspond with the previous recommendations made regarding albumin levels needed before surgery; however, the results depend on specific surgical people and specific hospital characteristics.[25]

Moreover, it is essential to highlight the finding that a combined score based on all three parameters used produced better prediction results ($AUC = 0.887$ vs $AUC = 0.764-0.821$). The fact that the combination of the three parameters gives positive results is meaningful from a clinical point of view since it suggests that by using the presented method, the doctors could focus on different aspects of physiological disorders leading to postoperative infections. Using several methods is justified by the complex nature of pneumonia after surgery.[26] NLR and PLR show only information about the presence of inflammatory and immune responses. However, albumin indicates the state of nutrition and the ability to synthesize proteins. The patients who have abnormal readings in all three of the parameters have the risk of having the disease due to large-scale inflammation processes, immune distress, and lack of nutrition.

The group of patients with bad scores (2 or 3 bad parameters) had a high incidence of pneumonia (53%) as compared to the group of patients with good scores (4.5%). The notable absolute risk difference of 11.8 suggests that such patients would benefit from more intense perioperative interventions. The fact that this population can be identified makes possible the introduction of specialized preventive measures that have been proven to decrease complications in high-risk surgical patients. These include preoperative respiratory therapy, preoperative nutritional optimization, the use of prolonged antibiotic prophylaxis, the implementation of better early mobilization programs, and monitoring of patients postoperatively. [27,28]

Despite these major findings, several limitations should be taken into account. First, due to being a single-center study, our outcomes may not be true for other centers or regions, and outcomes may vary due to the institution and the patient population characteristics. However,

due to prospective enrollment and standardized diagnostics, the reliability of the results is increased. Second, our study covered only elective surgery patients and excluded urgent thoracic surgery patients who most likely have different inflammatory and nutritional backgrounds. Third, our study did not examine all the microorganisms causing postoperative pneumonia among all patients, and we did not study the incidence of antimicrobial resistance which creates a limitation in how our findings may be generalized. Fourth, the protocols we used after surgery (i.e., physiotherapy intensity, antibiotic therapy, and monitoring) may differ from what other centers do and the extent of pneumonia occurrence.

Several other limitations should be discussed. Although our inadequate sample was sufficient for the main analysis, it did not allow us to make subgroup analyses with respect to surgical interventions. We hope that future studies with larger samples will study certain thoracic surgeries separately. Such studies will improve risk stratification for certain surgery types. It should also be mentioned that our sample consists mostly of patients from the Middle Eastern region, which means that ethnicity or genetic background can also play its role in the process of inflammation or immune system functioning.

The significance of our findings is increased by the simplicity of the scoring system as it only uses usual diagnostic laboratory values that can be obtained easily. The introduction of such a scoring system does not require any additional manipulation or expenses. It can simply be included in the already existing preoperative risk assessment system. The new system can be easily incorporated into EHR systems and calculated automatically.

Further studies should reveal whether using a scoring system improves the clinical outcomes of our patients. It would be interesting to see if the results of this study would be confirmed by further studies on the efficacy of actions on patients. [29,30]

5. CONCLUSION

This proposed study confirms that preoperatively obtained blood neutrophil-to-lymphocyte ratio, blood platelet-to-lymphocyte ratio, and serum albumin level act as independent risk factors for developing pneumonia after thoracic surgery. The newly developed risk scoring system uniting the three above-mentioned parameters reaches a better predictive capability than the separate parameters when it comes to dividing the patients into risk groups that turn out to have significantly different incidences of postoperative pneumonia, thus allowing an effective stratification of the patients. The elementary and inexpensive risk scoring system can be beneficial to the risk assessment of the patients before operation, enabling identification of the high-risk patients at the preoperative evaluation stage.

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