ORIGINAL ARTICLE

Can neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, prognostic nutrition index, and albumin be used to predict cholecystectomy morbidity in super-elderly patients?

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ABSTRACT

BACKGROUND: This study aimed to evaluate the usability of neutrophil-lymphocyte ratio (NLR), platelet lymphocyte ratio (PLR), prognostic nutritional index (PNI), and serum albumin level in predicting cholecystectomy morbidity in elderly patients (85 years and older) who underwent cholecystectomy for acute cholecystitis.

METHODS: This retrospective study included super-elderly patients who underwent cholecystectomy due to acute cholecystitis at a tertiary health centre between January 2010 and January 2021. The patients were divided into two groups according to the presence of postoperative complications (morbidity). The differences between the two groups were evaluated. In addition, the role of NLR, PLR, PNI, and serum albumin level in predicting cholecystectomy morbidity for acute cholecystitis in super-elderly patients was assessed via ROC analysis.

RESULTS: Of 30 patients who met the study criteria, 22 (73.3%) were female, and the mean age of all patients was 87.43±2.66 years (range 85–94 years). 7 (23.3%) patients had at least one comorbid disease during the preoperative period. The mean value of NLR, PLR, albumin, and PNI were 8.31, 153.76, 3.45, and 48.37, respectively. The morbidity rate of the study was 23.3%. The area under the curve (AUC) for NLR was 0.466 ([95% confidence interval [CI]: 0.259–0.672]; P=0.787), and the AUC for PLR was 0.429 ([95% CI: 0.201–0.656]; P=0.573). These two factors were not suitable for predicting morbidity. The AUC for PNI was 0.780 ([95% CI: 0.568–0.991]; P=0.027), and the AUC for albumin was 0.894 ([95% CI: 0.770–1.000]; P=0.002). At the cut-off value of 3.05 g/dL, the sensitivity and specificity of albumin were 91.3% and 71.4%, respectively, while the sensitivity and specificity of PNI at the 41.70 cut-off value were 82.6% and 71.4%, respectively.

CONCLUSION: This study found that PNI and albumin can be used as predictive factors with high sensitivity and specificity for predicting cholecystectomy morbidity for acute cholecystitis in super-elderly patients. However, NLR and PLR had no significance in predicting cholecystectomy morbidity.

Keywords: Acute cholecystitis; albumin; morbidity; prognostic nutritional index.

INTRODUCTION

Cholecystectomy, surgical gallbladder removal, is mainly required in the presence of gallstones. Most people with gallstones are asymptomatic, while about 20% of patients with asymptomatic gallstones become symptomatic yearly.[1] Patients with symptomatic gallstones can apply to emergency services with the clinic of acute cholecystitis. The main surgi-

Cite this article as: Kartal M, Kalaycı T. Can neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, prognostic nutrition index, and albumin be used to predict cholecystectomy morbidity in super-elderly patients? Ulus Travma Acil Cerrahi Derg 2023;29:890-896.

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Ulus Travma Acil Cerrahi Derg 2023;29(8):890-896 DOI: 10.14744/tjtes.2023.31462 Submitted: 13.05.2023 Revised: 16.05.2023 Accepted: 06.07.2023

cal procedure for symptomatic gallstones or acute cholecystitis is laparoscopic cholecystectomy due to increased surgeons' skills and technological advances.

Due to the prolongation of lifespan, the concept of "old age" is divided into three subgroups: early senility, between the ages of 65 and 74; old age, between the ages of 75 and 84; and advanced old age (super-elderly), at ages 85 and older. Thanks to developments in and the increased availability of healthcare and improvements in healthcare delivery globally, life expectancy and the proportion of the population that is elderly are growing. Therefore, the number of cholecystectomies among the super-elderly population seems to increase.[2] In addition, due to the increase in comorbid diseases in this specific age group, surgeons are more likely to encounter morbidity and mortality after cholecystectomy.[3] Morbidity is reported to be 5–15% and mortality 0–1% in cholecystectomies performed in the geriatric population.[4] Elective surgery with acceptable morbidity and mortality is preferred over emergency procedures.[5] On the other hand, cholecystectomies performed in the elderly population cannot always be performed under elective conditions, but unfortunately, they are also performed under emergency conditions.

There are many publications in the literature on the use of biomarkers in kidney failure, inflammatory conditions such as appendicitis and cholecystitis, and cancer diseases to predict the current disease's course.[6] Although a few studies evaluate new markers to reduce morbidity and mortality in cholecystectomies performed in the geriatric population, the super-elderly population remains unexplored.[7,8] To fill this gap in the literature, we conducted a retrospective study to identify new parameters.

This study is aimed to search the significance of neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), prognostic nutritional index (PNI), and serum albumin level in predicting cholecystectomy morbidity operated on for acute cholecystitis in super-elderly patients.

MATERIALS AND METHODS

This retrospective study was conducted after ethical committee approval (KAEK 2021/13-225). It included super-elderly patients (85 years and over) who underwent cholecystectomy due to acute cholecystitis between 2010 and 2021 at Erzurum Regional Training and Research Hospital. During the study period, 50 patients underwent cholecystectomy. Patients who were operated on at external centres and then admitted to our centre due to complications (n=2) and those who underwent cholecystectomy for elective cholelithiasis (n=7), and patients who underwent non-gallstone cholecystectomy (n=11) were excluded. As additional data, we found that 7 patients underwent percutaneous cholecystostomy due to a high American Society of Anaesthesiologists (ASA) score.

Patients' preoperative, perioperative, and postoperative data were collected from our hospital's electronic archive. The preoperative factors included patients' ages, gender, comorbidities, and laboratory parameters. The basic haematological (white blood cell count, haemoglobin, platelet counts, and rates of neutrophil and lymphocyte) and biochemical parameters, including liver function tests and serum albumin levels, were identified. NLR, PLR, and PNI values were calculated. NLR is calculated by dividing the neutrophil count by the lymphocyte count, while PLR is calculated by dividing the platelet count by the lymphocyte count. The PNI is calculated using a simple mathematical formula: PNI= (10 × serum albumin [g/dL]) + (0.005 × lymphocytes/μL). In addition, surgery types and hospital stays (total and intensive care unit) were searched.

Patients were divided into two groups according to postoperative complications: patients who developed complications in the first 30 days were considered the morbidity-positive (+) group, and those without complications were considered the morbidity-negative (-) group. The differences between the two groups regarding the parameters investigated were evaluated.

Statistical Analysis

SPSS v23.0 (IBM, Armonk, NY, USA) program was used for statistical evaluation. While quantitative variables were expressed using mean±standard deviation, median, minimum-maximum, interquartile range, and range, qualitative variables were reported using numbers and percentages. Kolmogorov-Smirnov and Shapiro-Wilk tests were used to search the normality distribution of quantitative variables. According to these normality tests, the independent samples t-test or Mann-Whitney U test was used to compare the quantitative variables. On the other hand, the qualitative variables were compared with the Chi-square test and Likelihood ratio test. A P-value below 0.05 was considered statistically significant. <0.05 was considered statistically significant. In addition, the area under the curve (AUC) and the sensitivities and specificities of NLR, PLR, albumin, and PNI were calculated using the receiver operating characteristic (ROC) curve.

Ethics committee approval was received from the Non-invasive Clinical Research Ethics Committee of Erzurum Regional Training and Research Hospital (KAEK 2021/13-225).

RESULTS

Of 30 patients, 22 (73.3%) were female, and the mean age of all patients was 87.43±2.66 years (range 85–94 years). 7 (23.3%) patients had at least one comorbid disease during the preoperative period. The mean value of NLR, PLR, albumin, and PNI were 8.31, 153.76, 3.45, and 48.37, respectively. The most common surgery type was the fully open procedure, with 53.3%. The clinical parameters of the patients are shown in Table 1.

Table 1. The clinical parameters of the patients

Parameters	n (%) or value
Age[a]	87.00 (3.75)
Gender[b]	
Female	22 (73.3)
Male	8 (26.7)
Comorbidity[b]	
Present	7 (23.3)
Absent	23 (76.7)
Hematological parameters	
White blood count cell (10^3/mm^3)[c]	13.14±6.12 (4.60–25.78)
Haemoglobin[a]	13 (1.42)
Platelet count (10^3/mm^3)[c]	265.00±60.01 (170.00–434.00)
Neutrophil count (Neu)[a]	9.81 (8.51)
Lymphocyte count (Lym)[a]	2.10 (2.15)
Neutrophil (%)[c]	74.60±13.36 (47.00–96.60)
Lymphocyte (%)[c]	18.72±10.01 (5.00–40.00)
Neutrophil-lymphocyte ratio[a]	3.94 (6.81)
Platelet-lymphocyte ratio[a]	130.66 (144.77)
Biochemical parameters	
Alanine transaminase[a]	47.00 (153.50)
Aspartate transaminase[a]	50.00 (141.00)
Gamma-glutamyl transferase[a]	50.00 (152.00)
Alkaline phosphatase[a]	81.00 (70.75)
Total bilirubin[a]	1.05 (1.69)
Direct bilirubin[a]	0.60 (0.99)
Amylase[a]	62.50 (71.25)
Albumin[a]	3.40 (0.67)
Prognostic nutritional index[a]	45.75 (13.58)
Surgery type[b]	
Full open	16 (53.3)
Full laparoscopy	12 (40)
Conversion to open surgery	2 (6.7)
Morbidity[b]	
Present	7 (23.3)
Absent	23 (76.7)
Mortality[b]	
Present	1 (3.3)
Absent	29 (96.7)
Hospital stays (days)	
Intensive care unit[a]	1.00 (2.00)
Total[a]	5.00 (4.50)

[a]: median (IQR); [b]: n (%); [c]: mean±standard deviation (range).

The morbidity rate of the study was 23.3%. Postoperative atelectasis was seen in 3 patients, acute pancreatitis in 2 patients, abdominal collection in one patient, and pleural effusion in one patient. The patients with pulmonary complications were treated with inhaler therapy and pulmonary exercises. In addition, in patients with pleural effusion, diuretic treatment was added to inhaler therapy and pulmonary exercises. The patients with acute pancreatitis were treated with sphincterotomy and stone extraction from the common bile duct with endoscopic retrograde cholangiopancreatography. The patient with the abdominal collection was treated with antibiotherapy, and the group spontaneously regressed.

The mortality rate of the study was 3.3%. This patient had gangrenous cholecystitis with cholecysto-colonic fistula, and she was treated with laparotomic cholecystectomy and right hemicolectomy anastomosis and died due to multi-organ failure. The NLR, PLR, albumin, and PNI values were 7.35, 79.26, 3.5 and 48, respectively.

Among the preoperative parameters, the presence of comorbidity (P=0.033) was higher, but the mean rank of the serum albumin (P=0.001) and PNI (P=0.025) was lower in morbidity-positive patients. In addition, the mean rank of the intensive care unit stay was higher in the morbidity-positive group (P=0.048). The comparison of the morbidity groups is shown in Table 2.

Evaluation of the factors affecting the morbidity of cholecystectomy performed on super-elderly patients by ROC analysis is shown in Table 3. At the cut-off value of 3.05 g/dL, the sensitivity and specificity of albumin were 91.3% and 71.4%, respectively, while the sensitivity and specificity of PNI at the 41.70 cut-off value were 82.6% and 71.4%, respectively. Figure 1 shows the ROC curves of NLR, PLR, albumin, and PNI.

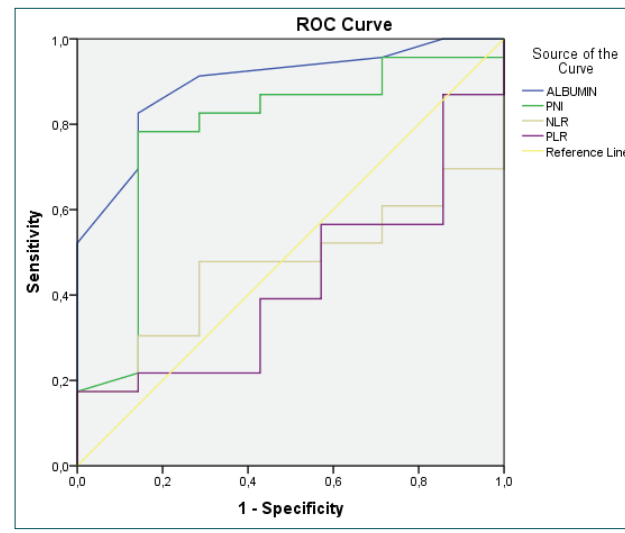

Figure 1. ROC curves of NLR, PLR, albumin, and PNI.

Table 2: The comparison of the morbidity groups according to clinical parameters

Parameters	Morbidity (+) (n=7)	Morbidity (-) (n=23)	P-value
Age[a]	86.00 (3.00)	87.00 (6.00)	0.564*
Gender[b]			0.345**
Female	4 (57.1)	18 (78.3)	
Male	3 (42.9)	5 (21.7)	
Comorbidity[b]			**0.033****
Present	4 (57.1)	3 (42.9)	
Absent	3 (13.0)	20 (87.0)	
Hematological parameters			
White blood count cell ($10^3/mm^3$)[c]	14.09	12.85	0.704***
Haemoglobin (g/dL)[a]	12.60 (0.70)	13.00 (1.80)	0.666*
Platelet count ($10^3/mm^3$)[c]	268.42	263.95	0.871***
Neutrophil count (Neu)[a]	9.37 (15.81)	10.08 (5.82)	0.962*
Lymphocyte count (Lym)[a]	2.00 (2.30)	2.36 (2.00)	0.737*
Neutrophil (%)[c]	73.81	74.84	0.875***
Lymphocyte (%)[c]	21.11	17.99	0.545***
Neutrophil-lymphocyte ratio[a]	4.00 (4.81)	3.88 (7.86)	0.811*
Platelet-lymphocyte ratio[a]	165.71 (131.67)	100.00 (146.91)	0.598*
Biochemical parameters			
Alanine transaminase (U/L)[a]	36.00 (191.00)	52.00 (145.00)	0.471*
Aspartate transaminase (U/L)[a]	26.00 (147.00)	50.00 (131.00)	0.413*
Gamma-glutamyl transferase (U/L)[a]	25.00 (251.00)	51.00 (129.00)	0.886*
Alkaline phosphatase (U/L)[a]	77.00 (108.00)	81.00 (68.00)	0.962*
Total bilirubin (mg/dL)[a]	1.00 (2.10)	1.10 (1.73)	0.598*
Direct bilirubin (mg/dL)[c]	0.60 (1.00)	0.60 (1.07)	0.924***
Amylase (U/L)[a]	89.00 (190.00)	61.00 (58.00)	0.532*
Albumin (g/dL)[a]	3.00 (0.20)	3.50 (0.80)	**0.001***
Prognostic nutritional index[a]	40.50 (6.00)	48.50 (12.20)	**0.025***
Surgery type[b]			**0.030******
Full open	2 (28.6)	14 (60.9)	
Full laparoscopy	3 (42.9)	9 (39.1)	
Conversion to open surgery	2 (28.6)	0 (0)	
Hospital stays (days)[a]			
Intensive care unit	4.00 (4.00)	0.00 (2.00)	**0.048***
Total	10.00 (8.00)	5.00 (3.00)	0.266*

[a]: median (IQR); [b]: n (%), [c]: means; *: Mann Whitney U test; **: Chi-square test; ***: Independent samples t-test; ****: Likelihood ratio test.

Table 3. Evaluation of the factors affecting morbidity of cholecystectomy performed at super-elderly patients by ROC analysis

Parameters	P-value	The area under the curve	95% Confidence interval	
			Lower	Upper
Neutrophil-lymphocyte ratio	0.787	0.466	0.259	0.672
Platelet-lymphocyte ratio	0.573	0.429	0.201	0.656
Serum albumin	0.002	0.894	0.770	1.000
Prognostic nutritional index	0.027	0.780	0.568	0.991

DISCUSSION

This study is aimed to search the role of NLR, PLR, PNI, and serum albumin level in the morbidity analysis of cholecystectomy for acute cholecystitis in super-elderly patients. The present study is pioneering in being the first study on this subject. According to the current study results, only PNI and serum albumin levels are independent factors in predicting the mortality of acute cholecystitis. On the other hand, no effect of NLR and PLR on acute cholecystitis morbidity was found in patients aged 85 years and over.

Although cholecystectomy is acceptable for the general population as the definitive and final treatment for acute cholecystitis, there is insufficient data on this for the elderly.[9] Because of chronic diseases that may affect the results of surgical treatment in this patient group, less invasive treatment methods have been tried recently. To avoid the risk of emergency surgery, percutaneous cholecystostomy and elective cholecystectomy are two treatment approaches for acute cholecystitis. Percutaneous cholecystostomy is a curative treatment method in elderly patients with acute cholecystitis with high ASA scores.[10] Although percutaneous cholecystostomy prevents sepsis in some patients with antibiotic treatment, it is not a choice in gangrenous and perforated gallbladders, and cholecystectomy is the only alternative in these patients.[11] In the present study, 7 patients underwent percutaneous cholecystostomy due to high ASA scores.

The morbidity and mortality of cholecystectomy performed in the elderly vary according to the type of surgery performed. While the incidence of open cholecystectomy morbidity reported in the elderly population is 23–28%, mortality is 1.5–2%.[12] However, the overall morbidity rate of laparoscopic cholecystectomy was 5–15%, and the overall mortality rate was 0–1%.[13] The morbidity and mortality rates of the present study were 23.3% and 3.3%, respectively.

Neutrophils represent innate immunity, while lymphocytes represent the adaptive immune system. NLR, the ratio of two values, represents both parts of the immune system.[14] Based on complete blood count values, NLR is a manifestation of the systemic inflammatory response, usually elevated in advanced inflammatory or malignant diseases. In addition, some studies report that NLR is associated with proinflammatory cytokines such as IL-6, IL-8 and TNF-alpha, which are involved in systemic inflammation.[15] In their study with 632 patients, Lee et al. showed that NLR over three was significantly associated with severe cholecystitis.[16] Similarly, in another study of only laparoscopic cholecystectomy cases, an NLR value above 4.18 was mainly related to severe cholecystitis.[17] In the retrospective analysis of Ahmed et al., NLR over 5 was significantly correlated with early-period surgery difficulty.[18] Another retrospective study included emergency abdominal surgeries (appendicectomy, inguinal and femoral hernia repairs) in elderly patients over 80. It was shown that NLR is a simple method for predicting morbidity.[7] In the present study, unlike the literature, NLR did not affect morbidity in patients aged 85 years and older who underwent surgery for acute cholecystitis.

PLR, also based on complete blood count values, is another inflammatory marker that can be used as a prognostic marker in inflammatory diseases and malignancies. Turhan et al.'s study, a PLR value over 146.90, is a predictive marker of complicated cholecystitis. In addition, PLR had a 66.7% sensitivity and a 66.2% specificity.[19] Bedel showed that PLR could be a potential biomarker for acute cholecystitis.[20] A study evaluating 156 acute cholecystitis patients over 65 showed that the computed tomography parameters of increased pericholecystic fat envelopment and pericholecystic fluid collection helped predict the severity of AC in elderly patients with an NLR threshold of 9.9.[8] There are few studies examining the relationship between PLR and acute cholecystitis. No morbidity relationship between PLR and acute cholecystitis was found in our study.

Serum albumin is an inflammatory marker and a negative acute-phase protein that can be used as a marker for all inflammatory diseases. Regardless of the localised or generalised nature of the disease, the acute phase response is a general host reaction. As inflammation increases, negative acute-phase proteins decrease. Therefore, serum albumin levels decrease in progressive inflammation.[21] The relationship between serum albumin level and morbidity in acute cholecystitis cases in elderly patients has not been evaluated yet. According to the results of our study, albumin level was found to be lower in morbidity-positive cases. The present study found that the AUC for albumin was 0.894 ([95% CI: 0.770–1.000]; P=0.002), and at the cut-off value of 3.05 g/dL, albumin's sensitivity was 91.3% and its specificity was 71.4%.

The concept of a PNI was proposed by Smale et al. in 1981.[22] PNI is an effective parameter and a new research topic in evaluating preoperative nutritional conditions and surgical risk.[23] Recently, PNI has been associated with outcomes in various inflammatory diseases and malignancies. PNI is calculated using only two parameters: lymphocyte count and serum albumin concentration. In cases of infectious diseases, the serum albumin concentration is lower. In addition, since acute cholecystitis is a bacterial infection, the neutrophil count increases, and the lymphocyte count decreases. Therefore, PNI is expected to be low in infectious diseases. The lower the PNI value, the more severe the infection. The study of Guven et al. showed that PNI, which was lower in severe disease than in mild/moderate disease, was a determiner of ulcerative colitis clinical severity.[24] The PNI index has also been used to evaluate disease activity in inflammatory conditions such as systemic lupus erythematosus and rheumatoid arthritis.[25] On the other hand, Cakcak and Kula study showed that PNI was a negative predictive factor for the clinical severity of acute cholecystitis.[26] The relationship between PNI and

cholecystitis in super-elderly patients is a subject that has just been evaluated in studies. A PNI lower than 45.88 has been associated with a poor prognosis in patients with gallbladder cancer.[27] In the present study, the AUC for PNI was 0.780 ([95% CI: 0.568–0.991]; P=0.027), and at the cut-off value of 41.70, PNI's sensitivity was 82.6%, and its specificity was 71.4%.

Limitations

This study is retrospective, and the limited data obtained prevented the examination of more parameters. In addition, the number of patients included in the study was also limited, as a particular age group (85 years old and above) was examined. This is a significant obstacle to reaching a large number of patients. Therefore, more accurate results should be obtained by conducting more patient studies.

CONCLUSION

Acute cholecystitis is a global problem that can occur at any age. In addition, morbidity and mortality are increased in super-elderly patients, and studies on acute cholecystitis in 85 and older patients are limited. This study found that PNI and albumin values can be used as prognostic factors and have high sensitivity and specificity. Therefore, this study is critical to determine the predictive factors for acute cholecystitis that can be used in super-elderly patients.

Ethics Committee Approval: This study was approved by the Erzurum Regional Training and Research Hospital Research Ethics Committee (Date: 05.07.2021, Decision No: KAEK 2021/13-225).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: T.K., M.K.; Design: T.K., M.K.; Supervision: T.K., M.K.; Resource: T.K., M.K.; Materials: T.K., M.K.; Data collection and/or processing: T.K., M.K.; Analysis and/or interpretation: T.K., M.K.; Literature search: T.K.; Writing: T.K.; Critical review: T.K., M.K.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

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ORİJİNAL ÇALIŞMA - *ÖZ*

Süper yaşlı hastalarda kolesistektomi morbiditesini tahmin etmek için nötrofil-lenfosit oranı, trombosit-lenfosit oranı, prognostik beslenme indeksi ve albümin kullanılabilir mi?

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AMAÇ: Bu çalışma, akut kolesistit nedeniyle kolesistektomi ameliyatı geçirmiş süper-yaşlı hastalarda (≥85 yaş) kolesistektomi morbiditesini öngörmede nötrofil lenfosit oranı (NLO), trombosit lenfosit oranı (TLO), prognostik beslenme indeksi (PBİ) ve serum albümin düzeyinin kullanılabilirliğini değerlendirmeyi amaçladı.
GEREÇ VE YÖNTEM: Bu retrospektif çalışmaya Ocak 2010 ile Ocak 2021 tarihleri arasında üçüncü basamak bir sağlık merkezinde akut kolesistit nedeniyle kolesistektomi uygulanan süper yaşlı hastalar alındı. Hastalar postoperatif komplikasyon (morbidite) varlığına göre iki gruba ayrıldı. İki grup arasındaki farklar değerlendirildi. Ek olarak, süper yaşlı hastalarda akut kolesistit için kolesistektomi morbiditesini öngörmede NLO, TLO, PBİ ve serum albümin düzeyinin rolü ROC analizi ile değerlendirildi.
BULGULAR: Çalışma kriterlerini karşılayan 30 hastanın 22'si (%73.3) kadındı ve tüm hastaların yaş ortalaması 87.43±2.66 (dağılım 85-94) yıl idi. Yedi (%23.3) hastanın ameliyat öncesi dönemde en az bir ek hastalığı vardı. Ortalama NLO, TLO, albümin ve PBİ sırasıyla 8.31, 153.76, 3.45 ve 48.37 idi. Çalışmanın morbidite oranı %23.3 idi. NLO için eğri altındaki alan (EAA) 0.466 ([95% CI: 0.259-0.672]; p=0.787) ve TLO için EAA 0.429 ([95% CI: 0.201-0.656]; p=0.573) idi. Bu iki faktör morbiditeyi öngörmek için uygun değildi. PBİ için EAA 0.780 ([%95 CI: 0.568-0.991]; p=0.027) ve albümin için EAA 0.894'tür ([95% CI: 0.770-1.000]; p=0.002). 3.05 g/dL kesme değerinde albüminin sensitivitesi %91.3 ve spesifitesi %71.4 iken, PBİ'nin 41.70 kesme değerinde sensitivitesi %82.6 ve spesifitesi %71.4 idi.
SONUÇ: Bu çalışma, süper yaşlı hastalarda akut kolesistit için kolesistektomi morbiditesini öngörmede PBİ ve albüminin yüksek duyarlılık ve özgüllük ile prediktif faktörler olarak kullanılabileceğini bulmuştur. Ancak NLO ve TLO'nun kolesistektomi morbiditesini öngörmede önemi yoktu.
Anahtar sözcükler: Akut kolesistit; albümin; morbidite; prognostik beslenme indeksi.

Ulus Travma Acil Cerrahi Derg 2023;29(8):890-896 DOI: 10.14744/tjtes.2023.31462