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Neutrophil percentage-to-albumin ratio as a predictor of conservative treatment failure in acute cholecystitis: a retrospective cohort study

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Abstract

Background While early laparoscopic cholecystectomy is the standard treatment for acute cholecystitis, conservative management remains necessary in specific scenarios such as high-risk patients or resource-limited settings. This study evaluated the predictive value of neutrophil percentage-to-albumin ratio (NPAR), a biomarker derived from routine laboratory tests, alongside established inflammatory markers and clinical parameters in identifying patients at risk of conservative treatment failure.

Methods In this retrospective cohort study at 2 tertiary centers (2020–2023), we analyzed 508 patients with acute cholecystitis who received conservative management. The study period coincided with the COVID-19 pandemic when healthcare resource constraints led to increased utilization of conservative management. Using admission laboratory data, we calculated NPAR, neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and assessed Charlson Comorbidity Index (CCI) and American Society of Anesthesiologists Physical Status (ASA-PS) classification. Receiver operating characteristic analysis and logistic regression were performed to evaluate their predictive value.

Results Conservative treatment failed in 107 patients (21.1%). Risk assessment showed higher proportions of CCI ≥ 6 (32.7% vs. 22.9%; $P=.008$) and ASA-PS class III-IV (16.8% vs. 8.0%; $P=.002$) in the failed treatment group. NPAR demonstrated superior predictive performance (area under curve, 0.906 [95% CI, 0.867–0.944]) compared with NLR (0.810 [0.765–0.855]) and PLR (0.614 [0.554–0.673]). The optimal NPAR cutoff value of 21.5 showed sensitivity of 88.8% and specificity of 84.8%. In multivariable analysis, NPAR > 21.5 emerged as the strongest independent predictor (adjusted odds ratio, 19.876 [95% CI, 8.934–42.651]; $P<.001$), followed by fever > 37.8 °C (2.845 [1.476–5.483]; $P=.002$) and leukocytosis (2.234 [1.112–4.485]; $P=.024$). Most treatment failures (77.6%) occurred within 48 h, requiring emergency surgery (57.9%), percutaneous drainage (37.4%), or endoscopic interventions (4.7%).

Conclusions NPAR, combined with fever and leukocytosis, provides a practical and cost-effective framework for predicting conservative treatment failure in acute cholecystitis using routine laboratory tests. Although our study was

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conducted during the COVID-19 pandemic, these findings remain valuable for any clinical setting where conservative treatment is considered. The 48-hour window for most treatment failures provides a practical timeframe for clinical monitoring and intervention decisions.

Keywords Neutrophil percentage-to-albumin ratio, NPAR, Acute cholecystitis, Early laparoscopic cholecystectomy, Conservative treatment, Risk stratification, Treatment failure, Predictive biomarkers

Background

Acute cholecystitis is a common surgical emergency, with significant impact on healthcare resources and patient outcomes. Studies show it accounts for approximately 3–10% of all cases of abdominal pain presenting to emergency departments, with increasing incidence globally [1, 2]. The current standard of care according to both the Tokyo Guidelines 2018 (TG18) and the World Society of Emergency Surgery (WSES) Guidelines 2020 is early laparoscopic cholecystectomy [3, 4].

However, there are situations where conservative management becomes necessary. These include high-risk patients with significant comorbidities, those who refuse surgery, or settings with limited surgical resources [3, 5, 6]. The decision between early surgery and conservative management requires careful consideration of patient factors, institutional capabilities, and potential outcomes. Both TG18 and WSES guidelines recommend using objective measures such as the Charlson Comorbidity Index (CCI) and American Society of Anesthesiologists Physical Status (ASA-PS) classification for risk stratification [3, 7].

The challenge lies in predicting which patients will respond successfully to conservative treatment. A systematic review by Loozen et al. found that 15–30% of patients fail conservative management and ultimately require urgent surgical intervention [5]. This treatment failure not only leads to increased morbidity but also results in longer hospital stays and higher healthcare costs. Despite this significant clinical problem, reliable predictors of conservative treatment failure remain limited [8, 9].

In recent years, inflammation-based markers have gained attention for their potential prognostic value in acute inflammatory conditions. The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have shown promise in predicting outcomes in various inflammatory and surgical conditions [10–12]. Lee et al. demonstrated the utility of preoperative NLR in predicting severe cholecystitis, while other studies have found both NLR and PLR to be effective in predicting complicated cases [13, 14].

The neutrophil percentage-to-albumin ratio (NPAR) is a novel marker that combines both inflammatory and nutritional status assessment. This ratio has shown promise in predicting outcomes in several acute conditions, including sepsis and inflammatory diseases [15, 16]. Unlike traditional inflammatory markers, NPAR incorporates albumin levels, which may reflect both the acute phase response and the patient's nutritional status. However, its utility in predicting conservative treatment failure in acute cholecystitis remains unexplored [17].

The period from 2020 to 2023 saw a significant shift in acute cholecystitis management due to the COVID-19 pandemic, with many centers reporting increased utilization of conservative treatment [18–21]. While this shift was primarily driven by pandemic-related healthcare constraints, it provided an opportunity to study conservative treatment outcomes in a larger patient cohort. Martinez Caballero et al. noted that findings regarding predictive factors for treatment failure during this period remain relevant for patient assessment in any setting where conservative management is necessary [18].

Given the potential complications and increased healthcare costs associated with failed conservative treatment [22], identifying reliable predictors of treatment failure could significantly improve patient management. This study aims to evaluate the novel use of NPAR, alongside established markers like NLR and PLR, in predicting conservative treatment failure in patients with acute cholecystitis. Understanding these predictive factors could help optimize patient selection for conservative management and improve clinical outcomes, regardless of the circumstances necessitating non-operative treatment [23, 24].

Methods

A retrospective study was conducted at H.R.H Maha Chakri Sirindhorn Medical Center and Samutprakarn Hospital, Thailand, from January 1, 2020, to December 31, 2023. The study protocol was approved by the Institutional Review Boards of both participating hospitals, and informed consent was waived due to the retrospective nature.

We included adult patients (aged ≥ 18 years) with acute cholecystitis who received conservative management. The study period (2020–2023) coincidentally overlapped with the COVID-19 pandemic, during which healthcare resources were significantly constrained [18]. Acute cholecystitis was diagnosed according to Tokyo Guidelines 2018 criteria [4]. While early laparoscopic cholecystectomy remains the standard treatment [3], resource limitations during this period led to increased utilization of conservative management [18].

Patient allocation was based on systematic evaluation of hospital resources (operating room capacity, critical care bed availability), disease severity (Tokyo Guidelines 2018 grading), and patient risk factors (assessed by CCI and ASA-PS classification) [7]. We excluded patients who required immediate intervention (comprising all Grade III cases per guidelines and selected Grade I/II cases based on institutional protocols), those with incomplete medical records, and those with concurrent conditions including acute pancreatitis, cholangitis, other acute infections, active malignancy, or hematological disorders.

Conservative management consisted of standardized treatment including nil per oral status, intravenous fluid resuscitation, empiric antibiotics following TG18 recommendations [25], appropriate analgesics, and nasogastric decompression when indicated. Treatment decisions were based on physician judgment considering patient factors, surgical risk (assessed by CCI and ASA-PS scores), and institutional resources during the COVID-19 pandemic period.

Conservative treatment failure was defined as: (1) no improvement or worsening symptoms after 48–72 h of treatment, including persistent/increasing abdominal pain, worsening tenderness, or new/persistent fever > 38 °C; (2) deteriorating laboratory parameters; (3) development of complications; (4) progression to sepsis/septic shock; or (5) need for emergency surgical intervention. Severity grading followed the TG18 criteria, incorporating clinical findings, inflammatory markers, and imaging results [4].

Three key inflammatory markers were calculated using admission laboratory values:

- NPAR: neutrophil percentage divided by serum albumin level
- NLR: absolute neutrophil count divided by absolute lymphocyte count
- PLR: platelet count divided by absolute lymphocyte count.

Two independent investigators extracted data using standardized electronic forms. Variables included demographics, comorbidities (CCI), ASA-PS classification, clinical presentation, admission laboratory values, imaging findings, treatment course, and outcomes. Discrepancies were resolved through consensus.

Sample size calculation was based on an estimated conservative treatment failure rate of 15–30% [5], with 95% confidence level and 5% margin of error. For statistical analysis, continuous variables were assessed for normality using Shapiro-Wilk test and expressed as mean (SD) or median [interquartile range] accordingly. Categorical variables were reported as number (percentage).

Between-group comparisons utilized t test or Mann-Whitney U test for continuous variables and χ^2 test or Fisher exact test for categorical variables, as appropriate. Receiver operating characteristic curves assessed the discriminative ability of inflammatory markers, with areas under the curve (AUCs) calculated with 95% CIs. Optimal cutoff values were determined using the Youden index.

Univariable and multivariable logistic regression identified independent predictors of treatment failure, with results presented as odds ratios (95% CIs). The multivariable model included variables with $P<.10$ in univariable analysis. Time-to-event analysis employed Kaplan-Meier method with log-rank test for group comparisons. Model performance was evaluated using accuracy, sensitivity, specificity, and Hosmer-Lemeshow test. Statistical significance was set at two-sided $P<.05$, using SPSS version 26.0 (IBM Corp).

Results

Of 980 patients diagnosed with acute cholecystitis during the study period, 472 (48.2%) were excluded: 390 required immediate intervention (82 Grade III cases and 308 selected Grade I and II cases), 19 had incomplete medical records, and 63 had concurrent conditions. The remaining 508 patients (51.8%) who received conservative management were included in the final analysis (Fig. 1). The higher proportion of conservative management during this period reflected modified treatment protocols during the COVID-19 pandemic. Conservative treatment was successful in 401 patients (78.9%) and failed in 107 patients (21.1%).

The study population had a mean age of 57.9 ± 17.8 years, with female predominance (55.5%). Risk assessment revealed higher proportions of elevated risk factors in the failed treatment group, including CCI ≥ 6 (32.7% vs. 22.9%; $P=.008$) and ASA-PS class III-IV (16.8% vs. 8.0%; $P=.002$). Clinical parameters also differed significantly between groups, with failed treatment patients showing higher body temperature (37.92 ± 0.67 °C vs. 37.44 ± 0.82 °C; $P<.001$), more frequent fever (72.0% vs. 30.4%; $P<.001$), and elevated white blood cell count (18,444 ± 12,091 vs. 13,631 ± 4,718 cells/mm^3; $P<.001$). Mean albumin levels were lower in the failed treatment group (3.69 ± 0.27 vs. 4.06 ± 0.20 g/L; $P<.001$). The failed treatment group also had a higher proportion of Grade II cases (54.2% vs. 29.9%; $P<.001$) (Table 1).

Regarding inflammatory markers (Table 1), all inflammatory markers showed significant elevation in the failed treatment group: NPAR (23.63 ± 2.64 vs. 19.65 ± 2.06; $P<.001$), NLR (14.43 ± 7.59 vs. 7.98 ± 5.44; $P<.001$), and PLR (241.47 ± 128.66 vs. 201.36 ± 118.43; $P=.002$). ROC analysis demonstrated superior predictive performance for NPAR (AUC 0.906 [95% CI, 0.867–0.944]), compared

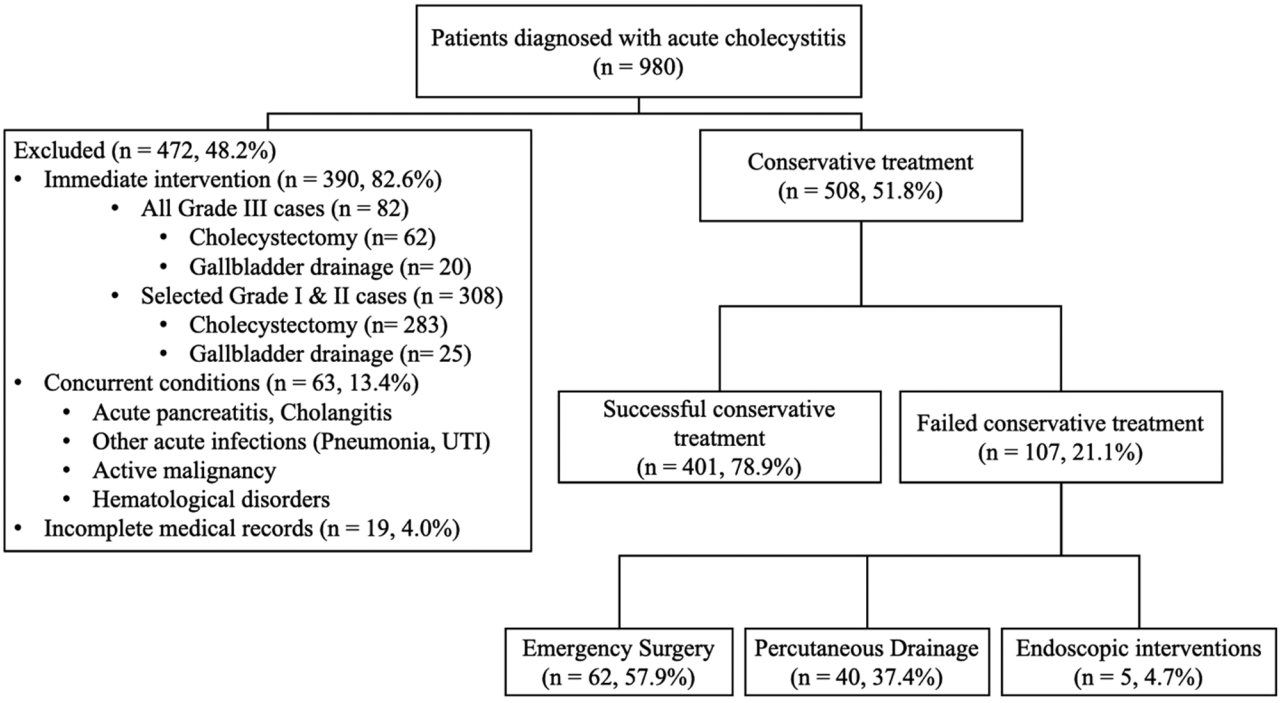

Fig. 1 Flow diagram of patient selection and study outcomes. Flow diagram showing patient selection process from January 2020 through December 2023. During the COVID-19 pandemic, selection of Grade I and II patients for immediate intervention was based on hospital resources availability, operating room capacity, critical care bed availability, disease severity, and patient factors, reflecting modified treatment protocols during the pandemic period

with NLR (0.810 [0.765–0.855]) and PLR (0.614 [0.554–0.673]) (Fig. 2).

Optimal cutoff values with corresponding diagnostic performance were determined for each marker: NPAR at 21.5 (sensitivity 88.8%, specificity 84.8%), NLR at 8.3 (sensitivity 84.1%, specificity 72.0%), and PLR at 179.9 (sensitivity 63.6%, specificity 52.5%) (Table 2).

Multivariable analysis identified NPAR > 21.5 as the strongest independent predictor of treatment failure (adjusted OR 19.876 [95% CI: 8.934–42.651]; $P < .001$), followed by fever > 37.8 °C (2.845 [1.476–5.483]; $P = .002$) and leukocytosis > 15,000/μL (2.234 [1.112–4.485]; $P = .024$). While CCI ≥ 6 and ASA-PS III-IV showed significant associations in univariable analysis, these relationships did not persist in the multivariable model (Table 3).

Time-to-failure analysis revealed a mean time to treatment failure of 46.41 h (95% CI, 43.33–49.49), with most failures (77.6%) occurring within 48 h (Table 4). Kaplan-Meier analysis demonstrated significantly earlier treatment failure in patients with NPAR > 21.5 compared to those with NPAR ≤ 21.5 (median time to failure 44.0 vs. 72.0 h; log-rank $P < .001$) (Fig. 3).

Among failed treatments, subsequent management included emergency surgery in 62 patients (57.9%), percutaneous drainage in 40 (37.4%), and endoscopic interventions in 5 (4.7%) (Table 5). The failed treatment group experienced longer hospital stays (7.8 ± 2.4 vs. 5.3 ± 1.6 days; $P < .001$).

Surgery-related complications among patients who underwent emergency surgery included bile duct injury (1.6%, 1/62) and wound infection (6.5%, 4/62). Intra-abdominal collection occurred more frequently in the failed treatment group (3.7% vs. 0.2%; $P = .004$). One patient (0.9%) in the failed treatment group died within 30 days.

Discussion

This study demonstrates that NPAR is a robust predictor of conservative treatment failure in acute cholecystitis, outperforming traditional inflammatory markers. The optimal NPAR cutoff value of 21.5 showed excellent predictive performance (AUC 0.906), with high sensitivity (88.8%) and specificity (84.8%). Notably, in our multivariable analysis, NPAR remained the strongest independent predictor (adjusted OR: 19.876, $P < .001$), followed by fever (OR: 2.845, $P = .002$) and leukocytosis (OR: 2.234, $P = .024$).

Early laparoscopic cholecystectomy remains the standard treatment for acute cholecystitis according to both Tokyo Guidelines 2018 and WSES Guidelines 2020 [3, 4]. However, conservative management may be necessary in specific situations, including high-risk patients or resource-limited settings [5, 6]. Our study was conducted during the COVID-19 pandemic (2020–2023), which led to increased utilization of conservative management due to healthcare resource constraints [18]. While this

Table 1 Baseline characteristics, risk assessment, and inflammatory markers of patients with acute cholecystitis

Characteristic	Total (*n* = 508)	Successful treatment (*n* = 401)	Failed treatment (*n* = 107)	*p*-value
Patient Demographics				
Age (years), mean ± SD	57.9 ± 17.80	57.44 ± 17.96	59.57 ± 17.44	0.274
Gender, n (%)				0.726
Male	226 (44.5%)	180 (44.9%)	46 (43.0%)	
Female	282 (55.5%)	221 (55.1%)	61 (57.0%)	
Diabetes Mellitus, n (%)	112 (22.0%)	84 (20.9%)	28 (26.2%)	0.247
Risk Assessment				
CCI score, n (%)				0.008
0–5	381 (75.0%)	309 (77.1%)	72 (67.3%)	
≥6	127 (25.0%)	92 (22.9%)	35 (32.7%)	
ASA-PS class, n (%)				0.002
Class I-II	458 (90.2%)	369 (92.0%)	89 (83.2%)	
Class III-IV	50 (9.8%)	32 (8.0%)	18 (16.8%)	
Clinical Parameters				
Duration of symptoms (days), mean ± SD	1.65 ± 0.82	1.64 ± 0.84	1.68 ± 0.75	0.623
Body temperature (°C), mean ± SD	37.54 ± 0.80	37.44 ± 0.82	37.92 ± 0.67	< 0.001
Fever (BT > 37.8 °C), n (%)	199 (39.2%)	122 (30.4%)	77 (72.0%)	< 0.001
Laboratory Values				
WBC count (cells/mm^3), mean ± SD	14,663 ± 7,188	13,631 ± 4,718	18,444 ± 12,091	< 0.001
Leukocytosis (WBC ≥ 15,000), n (%)	211 (41.6%)	131 (32.7%)	80 (75.5%)	< 0.001
Albumin (g/L), mean ± SD	3.97 ± 0.22	4.06 ± 0.20	3.69 ± 0.27	< 0.001
Inflammatory Markers, mean ± SD				
NPAR	20.48 ± 2.73	19.65 ± 2.06	23.63 ± 2.64	< 0.001
NLR	9.12 ± 6.53	7.98 ± 5.44	14.43 ± 7.59	< 0.001
PLR	210.17 ± 121.44	201.36 ± 118.43	241.47 ± 128.66	0.002
Severity Grade, n (%)				< 0.001
Grade I (Mild)	330 (65.0%)	281 (70.1%)	49 (45.8%)	
Grade II (Moderate)	178 (35.0%)	120 (29.9%)	58 (54.2%)	

Data are presented as mean ± SD for continuous variables and number (percentage) for categorical variables. NPAR indicates neutrophil percentage-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CCI, Charlson Comorbidity Index; ASA-PS, American Society of Anesthesiologists Physical Status; WBC, white blood cell count; BT, body temperature

resulted in a higher proportion of conservative treatment cases than typically recommended, it provided a unique opportunity to study predictive factors in a larger cohort.

The superior performance of NPAR compared to NLR and PLR may be explained by its unique combination of inflammatory and nutritional parameters [15, 16]. While NLR has shown utility in predicting severe cholecystitis [13], and both NLR and PLR have demonstrated value in predicting complicated cases [10, 14], NPAR incorporates albumin levels, which reflect both acute phase response and nutritional status. This finding aligns with recent studies showing the value of combined inflammatory-nutritional markers in acute conditions [15, 17, 26].

A significant advantage of NPAR is its simplicity and cost-effectiveness. NPAR is derived from routine Complete Blood Count (CBC) and Liver Function Test (LFT) results, which are standard investigations in the diagnosis and management of acute cholecystitis [5, 6]. This predictive tool can be readily implemented in clinical practice without incurring additional costs or requiring extra blood tests [3, 27]. The accessibility of these laboratory parameters makes NPAR particularly valuable in various clinical settings, from resource-limited environments to advanced healthcare facilities [24].

In our analysis of established risk assessment tools, CCI and ASA-PS scores showed significant associations with treatment failure in univariable analysis but lost significance in the multivariable model when adjusted for NPAR and other factors [28]. This finding does not diminish the importance of these tools, which remain crucial for overall patient evaluation as recommended by Tokyo Guidelines 2018 [7]. Rather, it suggests that NPAR provides complementary information specifically about the likelihood of conservative treatment success. The integration of NPAR with these established risk assessment tools could enhance clinical decision-making,

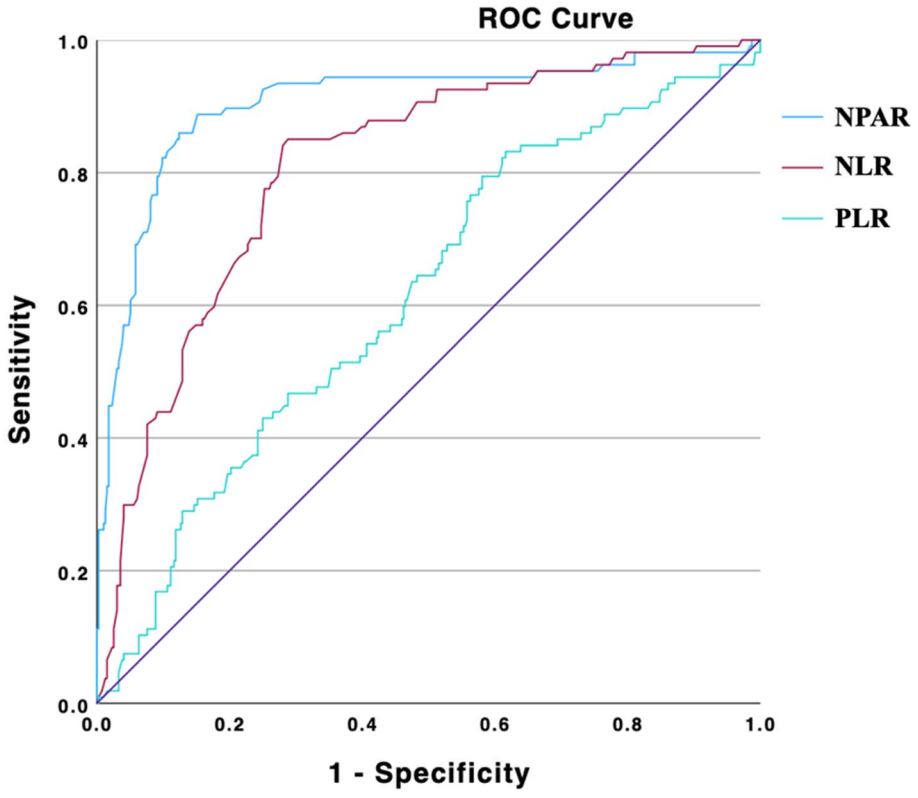

Fig. 2 Receiver operating characteristic curves for NPAR, NLR, and PLR in predicting conservative treatment failure. Receiver operating characteristic curves comparing the predictive performance of neutrophil percentage-to-albumin ratio (NPAR), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR). Area under the curve (AUC) values: NPAR, 0.906 (95% CI, 0.867–0.944); NLR, 0.810 (95% CI, 0.765–0.855); and PLR, 0.614 (95% CI, 0.554–0.673). Optimal cutoff values were determined using the Youden index

Table 2 Results of ROC curve analysis for inflammatory markers

Marker	AUC (95% CI)	Cut-off	*p*-value	Sensitivity	Specificity	Positive likelihood ratio
NPAR	0.906 (0.867–0.944)	21.5	< 0.001	88.8%	84.8%	5.84
NLR	0.810 (0.765–0.855)	8.3	< 0.001	84.1%	72.0%	3.00
PLR	0.614 (0.554–0.673)	179.9	< 0.001	63.6%	52.5%	1.34

AUC indicates area under the curve; CI, confidence interval. Optimal cutoff values were determined using the Youden index (sensitivity + specificity − 1). NPAR indicates neutrophil percentage-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio

Table 3 Univariable and multivariable logistic regression analysis for predictors of Conservative treatment failure

Variable	Univariate analysis			Multivariable analysis		
	Odds ratio	95% CI	*p*-value	Adjusted odds ratio	95% CI	*p*-value
NPAR > 21.5	44.993	23.250–87.069	< 0.001	19.876	(8.934–42.651)	< 0.001
NLR > 8.3	13.328	7.599–23.378	< 0.001	1.156	(0.487–2.744)	0.742
PLR > 179.9	1.929	1.242–2.996	0.003	1.624	(0.763–3.457)	0.208
CCI ≥ 6	2.384	1.526–3.442	< 0.001	1.512	0.825–2.774	0.182
ASA-PS III-IV	1.967	1.342–2.884	< 0.001	1.428	0.736–2.471	0.289
Fever (BT > 37.8 °C)	5.870	3.660–9.414	< 0.001	2.845	1.476–5.483	0.002
Leukocytosis (WBC > 15,000)	6.342	3.888–10.343	< 0.001	2.234	1.112–4.485	0.024

OR indicates odds ratio; CI, confidence interval. Multivariable model included all variables with *P* <.10 in univariable analysis. NPAR indicates neutrophil percentage-to-albumin ratio; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CCI, Charlson Comorbidity Index; ASA-PS, American Society of Anesthesiologists Physical Status; WBC, white blood cell count; BT, body temperature

Table 4 Time to treatment failure distribution

Time Period	Number of treatment failures	Percentage	Cumulative percentage
0–24 h	3	2.8%	2.8%
24–48 h	80	74.8%	77.6%
48–72 h	16	15.0%	92.5%
> 72 h	8	7.5%	100%

Time to treatment failure was calculated from initiation of conservative management to the time point when treatment failure was determined based on predefined criteria. Percentages are calculated from total number of treatment failures ($n = 107$)

Table 5 Management strategies after failed treatment and clinical outcomes

Parameter	Successful treatment ($n = 401$)	Failed treatment ($n = 107$)	*P* value
Management Strategy			
Emergency surgery	NA	62 (57.9%)	
Percutaneous drainage	NA	40 (37.4%)	
Endoscopic interventions	NA	5 (4.7%)	
Hospital Course			
Length of stay, mean ± SD, days	5.3 ± 1.6	7.8 ± 2.4	< 0.001
Surgery-related Complications*			
Bile duct injury	NA	1 (1.6%)	
Wound infection	NA	4 (6.5%)	
Other Complications			
Intra-abdominal collection	1 (0.2%)†	4 (3.7%)‡	0.004
Pneumonia	2 (0.5%)	3 (2.8%)	0.061
Mortality			
30-day mortality	0	1 (0.9%)	0.211

* Percentages calculated from patients who underwent emergency surgery ($n = 62$)

† Detected during follow-up after discharge

‡ Detected during admission and follow-up

Data are presented as number (percentage) or mean ± SD. NA indicates not applicable. Length of stay was calculated from admission to discharge. All outcomes were assessed within 30 days. P values shown only for comparable parameters between groups

particularly when conservative management is being considered [23].

The significant association of fever and leukocytosis with treatment failure, alongside NPAR, provides a practical clinical assessment framework [29]. Our finding that the combination of NPAR > 21.5, fever, and leukocytosis strongly predicts treatment failure aligns with previous studies emphasizing the importance of both clinical and laboratory parameters in risk assessment [9, 12, 29]. This multi-parameter approach is particularly relevant given the limitations of single markers in predicting outcomes in acute cholecystitis.

The timing of treatment failure in our study provides important clinical insights. The observation that 77.6% of failures occurred within 48 h is consistent with previous studies suggesting that the initial 48–72 h are crucial in determining the success of conservative management [5, 8]. This finding has practical implications for resource allocation and monitoring protocols, particularly in

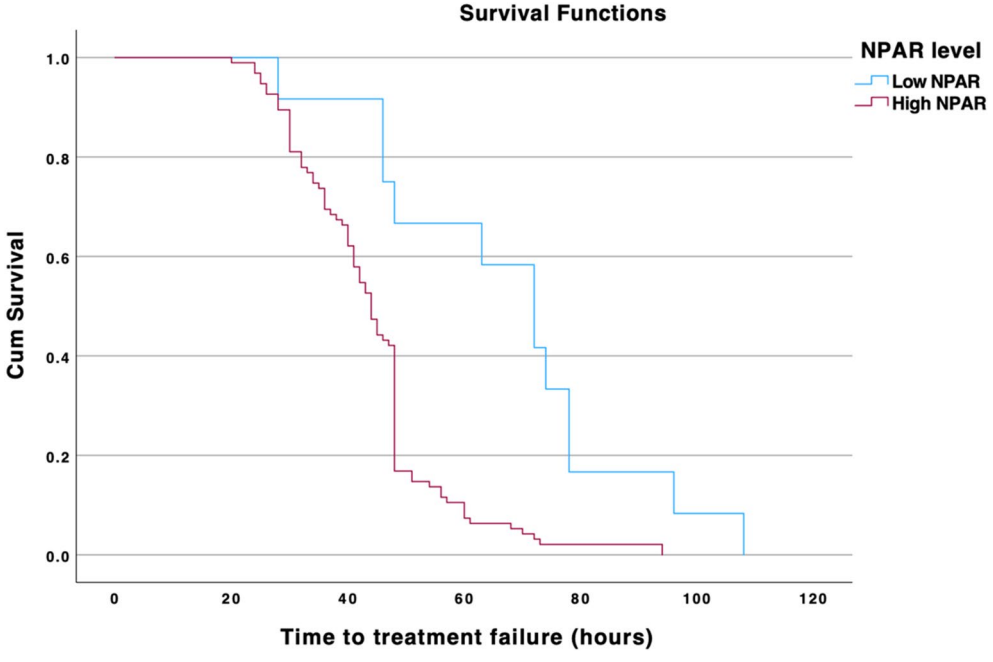

Fig. 3 Kaplan-Meier analysis of time to treatment failure stratified by NPAR. Kaplan-Meier curves showing the probability of successful conservative treatment over time, stratified by NPAR value (≤ 21.5 vs. > 21.5). Median time to failure was 72.0 h (95% CI, 56.937–87.063) for NPAR ≤ 21.5 and 44.0 h (95% CI, 41.065–46.935) for NPAR > 21.5 (log-rank *P* < .001). Vertical marks indicate censored observations

settings where immediate surgical intervention may not be available [6].

Regarding management after failed conservative treatment, our distribution of interventions reflects current guideline recommendations [3, 4]. The majority of failed cases required emergency surgery (57.9%), while others underwent percutaneous drainage (37.4%) or endoscopic interventions (4.7%). This distribution aligns with recent evidence supporting various interventional approaches [30–32]. Among patients who underwent emergency surgery, complications included bile duct injury (1.6%) and wound infection (6.5%), which were comparable to previous reports of delayed interventions [5, 9, 24]. Intra-abdominal collections were detected at different time points: during follow-up in the successful group versus during admission and follow-up in the failed group.

The impact of the COVID-19 pandemic on our treatment selection warrants discussion. During this period, healthcare systems worldwide faced unprecedented challenges in resource allocation, leading to modifications in standard treatment protocols [18]. The increased utilization of conservative management in our study reflects similar trends reported in other centers during the pandemic [18–21, 23]. However, this circumstance provided an opportunity to evaluate predictive factors in a larger cohort than would typically be available, enhancing the statistical power of our analysis.

Our study has several important clinical implications. First, the combination of NPAR with fever and leukocytosis provides a practical risk assessment framework that can be readily implemented in various clinical settings. Second, the identification of a critical 48-hour window for treatment failure allows for more focused monitoring and timely intervention decisions. Third, our findings suggest potential modifications to current management algorithms for acute cholecystitis, particularly in situations where conservative management is being considered.

Several limitations of our study should be acknowledged. First, the retrospective design introduces potential selection bias, although we attempted to minimize this through strict inclusion criteria and comprehensive data collection. Second, our study was conducted at two tertiary care centers, potentially limiting the generalizability of our findings to other healthcare settings. Third, we were unable to include C-reactive protein (CRP) in our analysis, as it was not part of routine admission testing during the study period. Given that CRP has shown value in predicting acute cholecystitis severity [4, 9], future studies should evaluate the relationship between NPAR and CRP.

These limitations suggest several directions for future research. First, prospective, multicenter validation studies are needed to confirm the predictive value of NPAR across diverse healthcare settings. Second, studies evaluating the impact of NPAR-guided decision-making on clinical outcomes could help establish its role in routine clinical practice [4]. Third, economic analyses comparing NPAR-guided management strategies with current approaches could provide valuable insights for healthcare resource allocation [22].

Despite these limitations, our study provides valuable insights for the management of acute cholecystitis patients requiring conservative treatment. The strong predictive performance of NPAR, combined with readily available clinical parameters, offers a practical framework for risk stratification. While early laparoscopic cholecystectomy remains the standard of care when feasible [3], our findings are particularly relevant for situations where conservative management is necessary, whether due to patient factors, resource limitations, or other constraints on immediate surgical intervention.

Conclusion

In this retrospective cohort study, we found that NPAR is a robust predictor of conservative treatment failure in acute cholecystitis. While early laparoscopic cholecystectomy remains the standard treatment, our findings provide valuable insights for situations where conservative management is necessary. The optimal NPAR cutoff value of 21.5, combined with clinical parameters including fever and leukocytosis, offers a practical and cost-effective framework for risk assessment using routine laboratory tests. Although our study was conducted during the COVID-19 pandemic, which necessitated increased conservative management, these findings remain valuable for any clinical setting where conservative treatment is considered. The identification of a critical 48-hour window for treatment failure provides a practical timeframe for clinical monitoring and intervention decisions. While prospective multicenter validation studies are needed, NPAR shows promise as an accessible tool for optimizing the management of acute cholecystitis patients requiring conservative treatment.

Abbreviations

NPAR	Neutrophil Percentage-to-Albumin Ratio
NLR	Neutrophil-to-Lymphocyte Ratio
PLR	Platelet-to-Lymphocyte Ratio
CCI	Charlson Comorbidity Index
ASA-PS	American Society of Anesthesiologists Physical Status
ROC	Receiver Operating Characteristic
AUC	Area Under the Curve
CI	Confidence Interval
OR	Odds Ratio
WBC	White Blood Cell
CRP	C-Reactive Protein
LC	Laparoscopic Cholecystectomy
TG18	Tokyo Guidelines 2018
WSES	World Society of Emergency Surgery
CBC	Complete Blood Count
LFT	Liver Function Test

COVID-19 Coronavirus Disease 2019

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Author contributions
H. Y. conceived and designed the study. K. S. and K. T. collected the data. H. Y. and K. S. performed the statistical analysis. H. Y.drafted the manuscript. All authors read and approved the final manuscript.

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Data availability
"The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request."

Declarations

Ethics approval and consent to participate
This study was approved by the Institutional Review Board of Srinakharinwirot University (approval number: SWUEC-M-038/2565E) and conducted in accordance with the Declaration of Helsinki. The requirement for informed consent was waived due to the retrospective nature of the study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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