## Title page

**Title: INFLAMMATION-BASED PROGNOSTIC SCORES PREDICT DISEASE SEVERITY IN PATIENTS WITH ACUTE CHOLECYSTITIS.**

**Short Title: INFLAMMATION SCORES IN CHOLECYSTITIS**

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## Abstract

**Background:** Although several investigators have reported that inflammation-based prognostic scores are able to predict disease severity in patients with various inflammatory diseases, whether or not these scores are associated with disease severity in patients with acute cholecystitis (AC) has not yet been fully clarified.

**Materials and Methods:** Two-hundred and sixty-two patients with acute cholecystitis were retrospectively reviewed. We evaluated the correlations between demographic or clinical variables, including the neutrophil-to-lymphocyte ratio (NLR), Glasgow Prognostic Score (GPS), modified Glasgow Prognostic Score (mGPS), and CRP/albumin (CRP/Alb) ratio, as well as the disease severity grade based on the revised Tokyo guidelines (TG 13). Multivariate analyses were performed to identify the clinical parameters associated with disease severity grade.

**Results:** The NLR (P<0.0001), GPS (P<0.0001), mGPS (P<0.0001), and CRP/Alb ratio (P<0.0001), were all elevated according to the severity grade. **Multivariate analyses revealed that the NLR (odds ratio (OR) 3.41-4.77; P<0.005), GPS (OR 2.49; P=0.012), mGPS (OR 2.79; P=0.005), and CRP/Alb ratio (OR 12.53; P<0.0001) were independently associated with Grade II / Grade III AC.** The value of the area under the curve of the CRP/Alb ratio (continuous 0.759) or NLR (continuous 0.753)

was higher than that of other inflammation-based prognostic scores for diagnosing ≥ Grade II AC, Grade III AC, respectively.

**Conclusion:** Inflammation-based prognostic scores were able to predict the severity grade independently in patients with AC. **These scores may have a complementary role in predicting disease severity in patients with AC in conjunction with the TG 13 severity grade.**

**Keywords: acute cholecystitis; severity grade; neutrophil-to-lymphocyte ratio; Glasgow Prognostic Score; modified Glasgow Prognostic Score; CRP/albumin ratio**

# Text

## Introduction

Acute cholecystitis (AC) is the sixth-most common gastrointestinal disease seen in the emergency department and the second-most common cause of hospital admission in the United States, accounting for 0.2%-0.5% of mortality rates [1].

The accurate assessment of severity in patients with AC is clinically important for optimizing the treatment and achieving a better prognosis [2]. The revised Tokyo guidelines (TG 13) for the diagnosis and management of AC propose the following severity grades for AC based on clinical, laboratory, and imaging findings [3]. Grade I shows mild inflammatory changes in the gallbladder, Grade II shows moderate inflammatory changes without organ dysfunction, while Grade III shown to severe gallbladder inflammation in association with organ dysfunction. Regarding the severity grade, urgent/early gallbladder drainage is recommended for patients with Grade II, if the initial treatment is unsuccessful. For patients with Grade III severity, urgent/early gallbladder drainage is essential in addition to the initial medical treatment and organ support [4]. Therefore, accurately determining the severity grade in patients with AC, particularly those with Grade II and III who require advanced medical care, is clinically relevant.

Investigators have already shown that the presence of a systemic inflammatory response is associated with a poor outcome in patients with many types of cancer [5]. In the last few years, inflammation-based prognostic scores, including the neutrophil-to-lymphocyte ratio (NLR) [6], Glasgow Prognostic Score (GPS) [7], modified Glasgow Prognostic Score (mGPS) [8], and CRP/albumin (CRP/Alb) ratio [9], have been reported to have prognostic value in patients with various types of cancer.

Furthermore, these inflammation-based prognostic scores have been shown to correlate with the outcomes or disease severity in patients with acute appendicitis [10], acute heart failure [11], sepsis [12], and Crohn’ s disease [13].

However, whether or not these inflammation-based prognostic scores are associated with the disease severity in patients with AC has not yet been fully clarified. Therefore, we evaluated whether the inflammation-based prognostic scores can predict the disease severity in patients with AC.

## Materials and methods

### *Patients*

A total of 270 patients with acute cholecystitis who had been treated at our department between January 2008 and December 2016 were enrolled in this study. All medical

records were reviewed retrospectively for patients' demographic and clinical data, radiological findings and treatment modalities. Eight patients who had been lost to follow up or who had incomplete data or other inflammatory conditions were excluded. The remaining 262 patients were ultimately evaluated.

The diagnosis of AC was confirmed based on imaging findings obtained by ultrasound (US), or computed tomography (CT). The severity assessment of AC was based on the revised Tokyo guidelines [3]. Patients were divided into three groups according to the severity grade.

This study was conducted in compliance with the Declaration of Helsinki and the current ethical guidelines and was approved by the institutional ethics board. Written informed consent for participation was not obtained from the patients, because this study did not report on a clinical trial and the data were retrospective in nature and analyzed anonymously.

***Data collection***

Demographic and clinical data, including age, gender, pretreatment comorbidities [15], and treatment modalities, were extracted from patients' medical records. Blood samples were obtained on admission for the measurement of the levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, lactate

dehydrogenase (LDH), gamma-glutamyl transpeptidase ( $\gamma$ -GTP), alkaline phosphatase (ALP), total bilirubin (T.Bil), creatinine (Cr), C-reactive protein (CRP), albumin (Alb) as well as the white blood cell count (WBC), neutrophil count, lymphocyte count, platelet count (Plt), international normalized ratio of prothrombin time (PT-INR), and hemoglobin (Hb).

Regarding inflammation-based prognostic scores, the NLR was calculated by dividing the neutrophil count by the lymphocyte count [6]. Patients with both an elevated CRP level (>1.0 mg/dl) and hypoalbuminemia (<3.5 g/dl) were allocated a GPS 2, those with only one of these biochemical abnormalities were allocated a GPS 1, and those with neither of these abnormalities were allocated a GPS 0 [7]. Patients with both an elevated CRP level (>1.0 mg/dl) and hypoalbuminemia (<3.5 g/dl) were allocated a mGPS 2, those with an elevated CRP level (>1.0 mg/dl) only were allocated a mGPS 1, and those with a normal CRP level (≤1.0 mg/dl) and any albumin concentration were allocated a mGPS 0 [8]. The CRP/Alb ratio was calculated by dividing the serum CRP level by the serum albumin level [15].

***Treatment and patient follow-up***

A treatment decision was made based on the TG 13 [4] and patients' general condition and comorbidities. All patients received the initial treatment including the

administration of antibiotics. If the initial treatment was unsuccessful, urgent/early gallbladder drainage or emergent cholecystectomy was performed. For patients who showed clinical improvements, early or elective laparoscopic cholecystectomy was carried out, unless the patient's refusal or contraindications were noted.

***Statistical analyses***

All statistical analyses were performed using the IBM SPSS Statistics software program version 19.0 (IBM SPSS, Chicago, IL, USA). Continuous variables were presented as the median and range. Categorical variables were presented as numbers and percentages. Comparisons between groups were performed using the Kruskal-Wallis test for continuous and ordinal variables and the $\chi^2$-test for categorical variables. The optimum cut-off for the NLR or CRP/Alb ratio was determined by a receiver operating characteristics (ROC) analysis.

To assess of the association between demographic and clinical data and the severity of AC, logistic regression analyses were performed to calculate the odds ratio (OR) with a 95% confidence interval (CI).

To compare each predictive ability of inflammation-based prognostic scores for the severity of AC, ROC curves were generated, and the area under the curve (AUC) was measured. A $P<0.05$ was considered statistically significant.

## Results

### *Patients' characteristics*

The median age of patients was 73 (range 18-98) years. One hundred and fifty-three (58.4%) patients were men, and 109 (41.6%) were women. One hundred and sixty-seven (63.7%) patients underwent percutaneous transhepatic gallbladder aspiration (PTGBA) (24.0%) or percutaneous transhepatic gallbladder drainage (PTGBD) (39.7%), and the remaining 95 (36.3%) underwent initial medical treatment including intravenous fluids and antibiotics. Five patients (1.9%) died during hospitalization.

Based on the TG 13 severity grade, 199 patients (76.0%) were classified as Grade I, 46 (17.6%) as Grade II, and 17 (6.5%) as Grade III. Demographic and clinical data of the patients stratified according to the severity grade are shown in Table 1. Significant differences among the grade were observed in age ($P<0.0001$), pretreatment comorbidities ($P<0.0001$), WBC ($P<0.0001$), neutrophil count ($P<0.0001$), NLR ($P<0.0001$, Fig. 1a), Plt ($P<0.0001$), the PT-INR ($P<0.0001$), Hb ($P=0.001$), T.Bil ($P=0.006$), Cr ($P<0.0001$), Albumin ($P<0.0001$), CRP level ($P<0.0001$), the CRP/Alb ratio ($P<0.0001$, Fig. 1b), the presence of GB drainage as an initial treatment ($P<0.0001$), and in-hospital mortality ($P=0.008$).

An elevated GPS and mGPS were significantly associated with a higher severity grade

(P<0.0001, Fig. 2a, P<0.0001, Fig. 2b).

The optimum cut-off for the NLR to distinguish Grade I from Grade II / Grade III using the ROC analysis was 10.25. The sensitivity and specificity at the cut-off point were 81.5% and 57.0%, respectively. The optimum cut-off for the NLR to distinguish Grade I / II from Grade III was 11.26. The sensitivity and specificity at the cut-off point were 93.3% and 56.9%, respectively.

The optimum cutoff for the CRP/Alb ratio to distinguish Grade I from Grade II / Grade III using the ROC analysis was 2.11. The sensitivity and specificity at the cut-off point were 77.4% and 65.8%, respectively. The optimum cut-off for the CRP/Alb ratio to distinguish Grade I / II from Grade III was 4.41. The sensitivity and specificity at the cut-off point were 93.3% and 76.2%, respectively.

***Predictive factors for diagnosing of ≥Grade II AC***

The results of the univariate analysis to determine the predictive factors for diagnosing ≥ Grade II (Grade II / Grade III) AC are shown in Table 2. Given the correlations among the CRP, albumin, CRP/Alb ratio, GPS, and mGPS, or the WBC, neutrophil, lymphocyte, and NLR, we built three multivariate models: **model 1 included the variables of age, pretreatment comorbidities, Cr, GPS, NLR, Plt, and Hb; model 2 included the variables of age, pretreatment comorbidities, Cr, mGPS, NLR, Plt,**

**and Hb; and model 3 included the variables of age, pretreatment comorbidities, Cr, CRP/Alb ratio, NLR, Plt, and Hb. A multivariate analysis showed that the NLR (OR 4.77; P=0.001), GPS (OR 2.49; P =0.012), Cr (OR 4.66; P =0.042), and Hb (OR 24.07; P =0.012) in model 1; the NLR (OR 4.48; P=0.002), mGPS (OR 2.79; P=0.005), and Hb (OR 23.99; P =0.011) in model 2; and the NLR (OR 3.41; P=0.014), CRP/Alb ratio (OR 12.53; P<0.0001), and Hb (OR 67.95; P =0.001) in model 3 were independently associated with ≥ Grade II (Grade II / Grade III) AC (Table 2).**

***Comparison for assessing the discriminative ability of each inflammation-based prognostic score***

ROC curves were generated for diagnosing ≥ Grade II (Grade II / Grade III) and Grade III AC, and the AUC values were compared to assess the predictive ability of each inflammation-based prognostic score **(Table 3).**

The AUC value of the CRP/Alb ratio (continuous 0.759) was higher than that of the WBC alone (0.755), CRP alone (0.744), GPS (0.704), mGPS (0.737), and NLR (continuous 0.729, dichotomized 0.691) for diagnosing ≥ Grade II (Grade II or Grade III) AC.

The AUC value of the NLR (continuous 0.753) was higher than that of the WBC alone

(0.665), CRP alone (0.659), GPS (0.680), mGPS (0.703), and CRP/Alb ratio (continuous 0.693, dichotomized 0.683) for diagnosing Grade III AC **(Table 3)**.

## Discussion

In the current study, we demonstrated that the values of inflammation-based prognostic scores, namely the NLR, the GPS, the mGPS, and the CRP/Alb ratio, are significantly elevated in patients with AC according to the severity grade. Furthermore, multivariate analyses revealed that these inflammation-based prognostic scores could independently predict **≥ Grade II (Grade II / Grade III) AC**.

The assessment of severity grade in patients with AC is clinically important for choosing treatment strategies. The TG 13 has proposed the severity grades in patients with AC based on clinical, laboratory, and imaging findings as follows [3]: Grade I (mild), Grade II (moderate), and Grade III (severe). Based on this severity grade, urgent/early GB drainage is required in patients with Grade II and III severity following the initial treatment (only if initial treatment is unsuccessful in Grade II patients). In our study, the proportion of patients undergoing urgent/early GB drainage was significantly higher among Grade II and III patients than in those with Grade I severity, which is consistent with the proposal by the TG 13.

The assessment of severity grade in patients with AC is also relevant for determining the patients' prognosis. A recent report from Spain showed that the severity grade based on the TG 13 was an independent predictor for mortality in patients with AC [16]. More recently, a large-scale multicenter study from Japan and Taiwan also showed that the severity grade based on the TG 13 was significantly associated with the 30-day overall mortality [2]. The rate of organ dysfunction in patients with Grade III severity was also significantly correlated with the 30-day overall mortality in that study [2]. These findings are consistent with our results, with a significant difference in the in-hospital mortality rate among severity grades.

Many investigators have shown that inflammation-based prognostic scores have prognostic value in patients with various types of cancer, including gallbladder cancer [5-9,17]. In addition to cancer, several investigators have reported that these inflammation-based prognostic scores can also predict outcomes or disease severity in patients with inflammatory diseases, such as acute appendicitis, sepsis, and Crohn's disease. Reports from Japan and Ireland have indicated that an elevated NLR is associated with gangrenous appendicitis, longer hospital stay, and more postoperative complications in patients with acute appendicitis [10,18,19].The CRP/Alb ratio at admission has also been reported to be an independent predictor of 90- and 180-day

mortality in patients with sepsis [12,20]. Furthermore, a study from China showed that the CRP/Alb ratio was useful for identifying disease activity in patients with Crohn's disease [13].

In the setting of AC, previous studies have shown that an elevated CRP level is a useful predictor for the presence of gangrenous cholecystitis [21,22], conversion from laparoscopic cholecystectomy to open cholecystectomy [23], and disease severity [24,25]. Nikfarjam et al. reported that patients with gangrenous cholecystitis had a greater elevated CRP value (9.4 mg/dl) than those with non-gangrenous AC (1.7 mg/dl) [21]. Mok et al. also found that an elevated CRP value of more than 200 mg/dl had a 50% positive predictive value and 100% negative predictive value for predicting gangrenous cholecystitis with 100% sensitivity and 87.9% specificity [22]. Wevers et al. showed that an elevated CRP value with a cut-off value of 16.5 mg/dl was an independent predictor for conversion to open cholecystectomy [23]. With regard to the severity grade, investigators from Turkey and New Zealand evaluated the predictive ability of serum CRP in determining the severity grade of AC [24,25]. Gurbulak et al. showed that the serum CRP level at admission was a predictor in classifying different severity grades of AC defined by the TG 13 severity grade and found the cut-off values of CRP as 7.065 mg/dl with 75.5% sensitivity and 96.5% specificity in patients with

Grade 2, 19.895 mg/dl with a 73.9% sensitivity and 75.5% specificity in patients with Grade 3, respectively [24]. In a large-scale cohort study of 1843 patients, Beliaev et al. demonstrated that the serum CRP value was a useful marker for the diagnosis of AC and stratifying severity of AC defined pathologically. They also found that the discriminative power of the serum CRP value was superior to that of the WBC [25].

In the current study, we demonstrated that inflammation-based prognostic scores were independently associated with the severity grade based on the TG 13. These findings extend those of Beliaev et al, confirming that the NLR is a potential biomarker predictive of the severity grade of AC and is superior to WBC and similar to CRP in discriminative ability [26]. However, the definition of the severity grade differed between their study and the present study, as the severity grade of Beliaev et al. was based on the histological findings, while ours was based on the TG 13.

In our study, multivariate analyses revealed that the NLR, GPS, mGPS, and CRP/Alb ratio were independently associated with ≥ Grade II (Grade II or Grade III) AC. These findings may be partly reasonable **because an elevated WBC count (>18000/ml) is included as a variable in the Grade II AC criteria according to the TG 13** [3]. In contrast, the serum CRP value and albumin level were not incorporated into the severity grade based on the TG 13, although elevated CRP levels are included in the diagnostic

criteria for AC under the TG 13 [3]. These results suggest that CRP-based prognostic scores, such as the GPS, mGPS, and CRP/Alb ratio, have a complementary role in predicting disease severity in patients with AC in conjunction with the TG 13 severity grade.

**Moreover, the ROC analyses in our study showed that the areas under the curve of the CRP/Alb ratio and NLR were higher than those values of other inflammation-based prognostic scores for diagnosing ≥ Grade II and III AC, respectively. These findings suggest that the CRP/Alb ratio and NLR are the factors most useful for predicting ≥ Grade II AC and III AC, respectively.**

Several limitations associated with the present study warrant mention. First, this was a retrospective study with a relatively small sample; in particular, the number of patients stratified into the Grade III AC is too small to affect the statistical analyses. Second, this was a single-center study. Therefore, the possibility of unintentional selection bias could not be fully excluded. Third, the definition of AC in our study was not based on histological findings but imaging findings. However, the histological findings can be influenced by the administration of antibiotics or gallbladder drainage. Therefore, a large-scale, prospective study is needed to confirm our findings.

## 5. Conclusions

We showed that inflammation-based prognostic scores, such as the NLR, GPS, mGPS, and CRP/Alb ratio, were able to predict the severity grade independently in patients with AC. These scores may have a complementary role in predicting disease severity in patients with AC in conjunction with the TG 13 severity grade.

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## Figure legends

**Fig. 1. Box plots indicating the distribution of the NLR (a) and CRP/Alb ratio (b) according to the severity grade of acute cholecystitis. The asterisk in the box indicates the median value, and the box indicates the 1st (25%) and 3rd (75%) quartiles. Significant differences among the severity grade are observed in both NLR (all P<0.0001) and CRP/Alb ratio (all P<0.0001).**

**Fig. 2. The distribution of patients stratifiedby the GPS (a) and mGPS (b) according to the severity grade of acute cholecystitis. Higher GPS and mGPS are associated with higher severity grade (all P<0.0001, all P<0.0001).**

**Table 1. Demographic and clinical data of the patients stratified according to the severity grade**

| Variable | Grade I (n=199 ) | Grade II (n=46) | Grade III (n=17) | P-value |
|---|---|---|---|---|
| Age (years) | 71 (18-98) | 74 (21-96) | 83 (65-98) | <0.0001 |
| Sex (men/women) | 117/82 | 26/20 | 10/7 | 0.96 |
| Comorbidities (mild/moderate/severe) | 194/2/3 | 45/1/0 | 12/4/1 | <0.0001 |
| GB draingae (present/absent) | 110/89 | 42/4 | 15/2 | <0.0001 |
| AST (IU/l) | 31 (10-1747) | 34 (13-620) | 58 (13-541) | 0.771 |
| ALT (IU/l) | 32 (5-1122) | 37 (10-396) | 78 (8-157) | 0.784 |
| LDH (IU/l) | 218 (18-15212) | 220 (134-965) | 62 (5-308) | 0.088 |
| ɤ-GTP (IU/l) | 71 (11-1324) | 78 (11-584) | 194 (10-741) | 0.729 |
| ALP (IU/l) | 303 (91-3056) | 393 (167-1273) | 416 (192-1485) | 0.357 |
| Total bilirubin (mg/dl) | 1.1 (0.2-17.9) | 1.3 (0.3-4.8) | 2.2 (0.6-9.0) | 0.006 |
| Creatinine (m/dl) | 0.8 (0.3-4.8) | 0.8 (0.5-6.0) | 2.0 (0.4-4.3) | <0.0001 |
| Albumin (g/dl) | 3.8 (1.6-4.9) | 3.4 (1.9-5.0) | 2.9 (1.9-4.4) | <0.0001 |
| CRP (mg/dl) | 3.1 (0.1-37.8) | 15.1 (0.4-28.3) | 14.2 (0.1-39.2) | <0.0001 |
| GPS (1/2/3) | 56/90/53 | 1/23/22 | 2/3/12 | <0.0001 |
| mGPS (1/2/3) | 63/83/53 | 0/22/24 | 2/2/13 | <0.0001 |
| CRP/Albumin ratio | 0.8 (0.02-10.6) | 4.4 (0.09-10.2) | 4.6 (0.02-13.5) | <0.0001 |
| WBC (cells/$mm^3$ ) | 10900 (200-18700) | 16650 (5200-33200) | 14300 (1100-47000) | <0.0001 |
| neutrophil count (cells/$mm^3$ ) | 8900 (1800-17300) | 14300 (4100-31100) | 13300 (2000-44900) | <0.0001 |
| lymphocyte count (cells/$mm^3$ ) | 1000 (100-5900) | 900 (100-2200) | 600 (100-1600) | 0.093 |
| NLR | 9.4 (0.7-73) | 15.2 (3.6-165) | 19.7 (7.5-74.8) | <0.0001 |
| Platelet count ($10^4/mm^3$ ) | 20.6 (3.8-194) | 21.2 (7.9-69.8) | 9.7 (2.3-39.1) | <0.0001 |
| PT-INR | 1.1 (0.8-3.0) | 1.2 (1.0-1.8) | 1.3 (1.0-1.9) | <0.0001 |
| Hb | 13.5 (6.7-17.5) | 13.7 (8.9-17.6) | 11.2 (7.2-17.5) | 0.001 |
| in-hospital mortality (n, %) | 2/199, 1% | 1/46, 2.2% | 2/17, 11.8% | 0.0079 |

GB, gallbladder; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; gamma-glutamyl transpeptidase; ALP, alkaline phosphatase
CRP, C-reactive protein; GPS, Glasgow Prognostic Score; mGPS, modified Glasgow Prognostic Score; WBC = white blood cell count; NLR, Neutrophil Lymphocyte ra
PT-INR, international normalized ratio of prothrombin time; Hb, hemoglob

**Table 2. An analysis of the predictive factors in diagnosing ≥ Grade II (Grade II/Grade III) AC**

| | Univariate analysis | Multivariate analysis | | |
|---|---|---|---|---|
| | | Model 1 | Model 2 | Model 3 |
| Variable | P-value | OR (95% CI) P-value | OR (95% CI) P-value | OR (95% CI) P-value |
| Age 80 ≥ years | 0.05 | | | |
| Sex (men/women) | 0.817 | | | |
| Comorbidities (mild/moderate/severe) | 0.042 | | | |
| AST ≥ 2×normal limit (IU/l) | 0.862 | | | |
| ALT ≥ 2×normal limit (IU/l) | 0.932 | | | |
| LDH ≥ 2×normal limit (IU/l) | 0.909 | | | |
| ɤ-GTP ≥ 2×normal limit (IU/l) | 0.43 | | | |
| ALP ≥ 2×normal limit (IU/l) | 0.307 | | | |
| Total bilirubin ≥ 2.0 (mg/dl) | 0.201 | | | |
| Creatinine ≥ 2.0 (m/dl) | ＜0.0001 | 4.66 (1.05-20.59) 0.042 | | |
| Albumin ≥ 3.5 (g/dl) | ＜0.0001 | | | |
| CRP ≥ 1.0 (mg/dl) | ＜0.0001 | | | |
| GPS (1/2/3) | ＜0.0001 | 2.49 (1.22-5.07) 0.012 | | |
| mGPS (1/2/3) | ＜0.0001 | | 2.79 (1.36-5.72) 0.005 | |
| CRP/Albumin ratio ≥ 2.11 | ＜0.0001 | | | 12.53 (4.00-39.37) ＜0.0001 |
| WBC ≥ 18000 (cells/$mm^3$) | ＜0.0001 | | | |
| neutrophil count ≥ 9700 (cells/m | 0.023 | | | |
| lymphocyte count ≥ 900 (cells/mı | 0.237 | | | |
| NLR ≥ 10.25 | ＜0.0001 | 4.77 (1.85-12.33) 0.001 | 4.48 (1.73-11.63) 0.002 | 3.41 (1.29-9.02) 0.014 |
| Platelet count ≤ 10 (×$10^4$/$mm^3$) | ＜0.0001 | | | |
| PT-INR ≥ 1.5 | 0.11 | | | |
| Hb ≤ 10 (g/dl) | ＜0.0001 | 24.07 (2.00-289.88) 0.012 | 23.99 (2.05-280.95) 0.011 | 67.95 (6.04-764.82) 0.001 |

AC, acute cholecystitis; OR, odds ratio; CI, confidence interval ; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase
ɤ-GTP, gamma-glutamyl transpeptidase; ALP, alkaline phosphatase; CRP, C-reactive protein; GPS, Glasgow Prognostic Score; mGPS, modified Glasgow Prognostic Score
WBC, white blood cell count; NLR, Neutrophil Lymphocyte ratio PT-INR, international normalized ratio of prothrombin time; Hb, hemoglobin

Table 3. A comparison of the area under the curve to assess the discriminative ability

| Severity grade | AUC | 95% CI | P-value |
|---|---|---|---|
| ≥ Grade II (Grade II/Grade III) AC | | | |
| WBC alone | 0.755 | 0.673-0.836 | <0.0001 |
| CRP alone | 0.744 | 0.675-0.814 | <0.0001 |
| NLR (continuous) | 0.729 | 0.657-0.801 | <0.0001 |
| (dichotomized) | 0.691 | 0.613-0.768 | <0.0001 |
| GPS | 0.704 | 0.628-0.780 | <0.0001 |
| mGPS | 0.737 | 0.666-0.808 | <0.0001 |
| CRP/Alb ratio (continuous) | 0.759 | 0.690-0.829 | <0.0001 |
| (dichotomized) | 0.723 | 0.645-0.802 | <0.0001 |
| Grade III AC | | | |
| WBC alone | 0.665 | 0.512-0.818 | 0.032 |
| CRP alone | 0.659 | 0.521-0.796 | 0.04 |
| NLR (continuous) | 0.753 | 0.661-0.845 | 0.001 |
| (dichotomized) | 0.752 | 0.653-0.852 | 0.001 |
| GPS | 0.68 | 0.534-0.825 | 0.02 |
| mGPS | 0.703 | 0.563-0.844 | 0.009 |
| CRP/Alb ratio (continuous) | 0.693 | 0.552-0.835 | 0.012 |
| (dichotomized) | 0.683 | 0.534-0.833 | 0.018 |

AUC, area under the receiver operating curve; CI, confidence interval; AC, acute cholecystitis; WBC, white blood cell count; CRP, C-reactive protein NLR, Neutrophil Lymphocyte ratio; GPS, Glasgow Prognostic Score; mGPS, modified Glasgow Prognostic Score; Alb, albumin

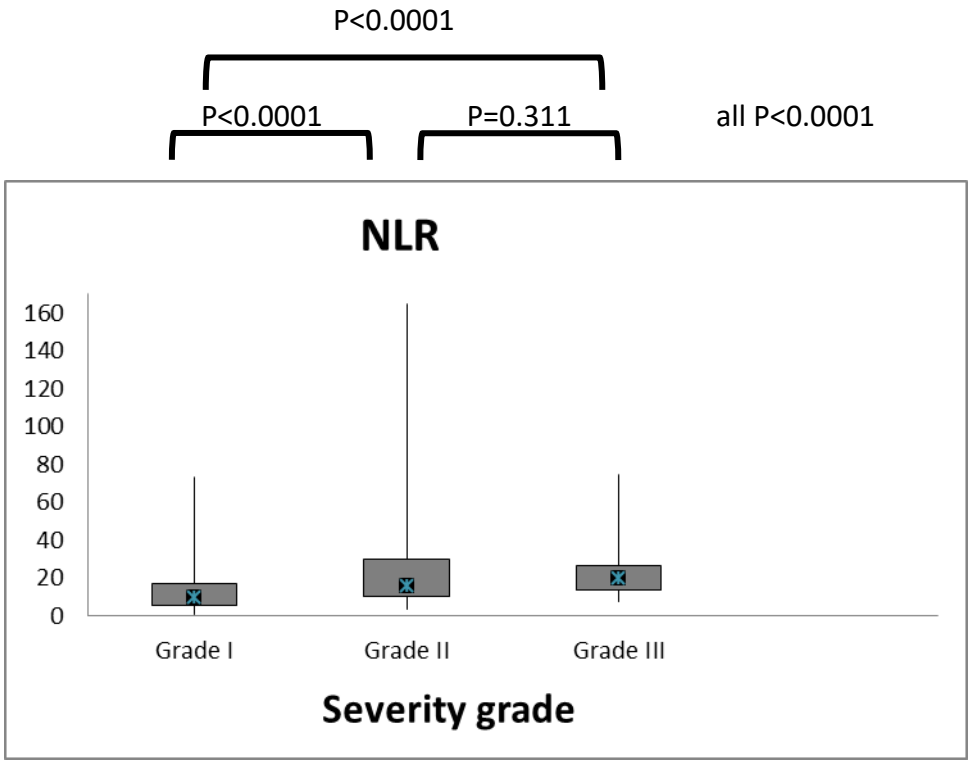
P<0.0001
P<0.0001
P=0.311
all P<0.0001
NLR
160
140
120
100
80
60
40
20
0
Grade I
Grade II
Grade III
Severity grade

Fig. 1a.

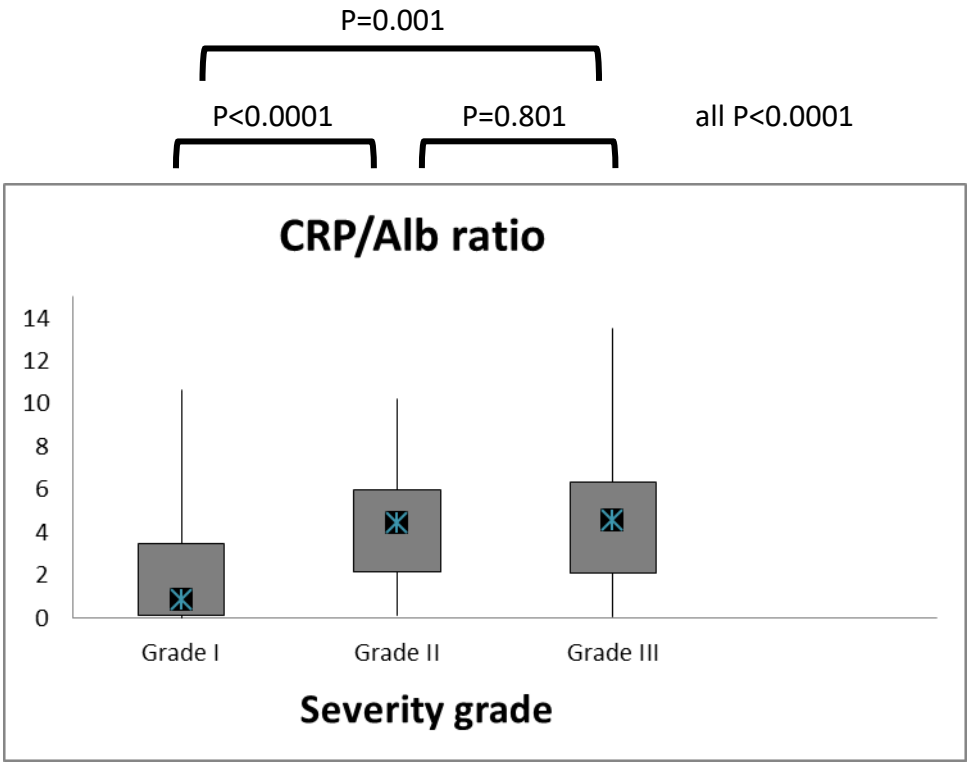
P=0.001
P<0.0001
P=0.801
all P<0.0001
CRP/Alb ratio
14
12
10
8
6
4
2
0
Grade I
Grade II
Grade III
Severity grade

Fig.1b.

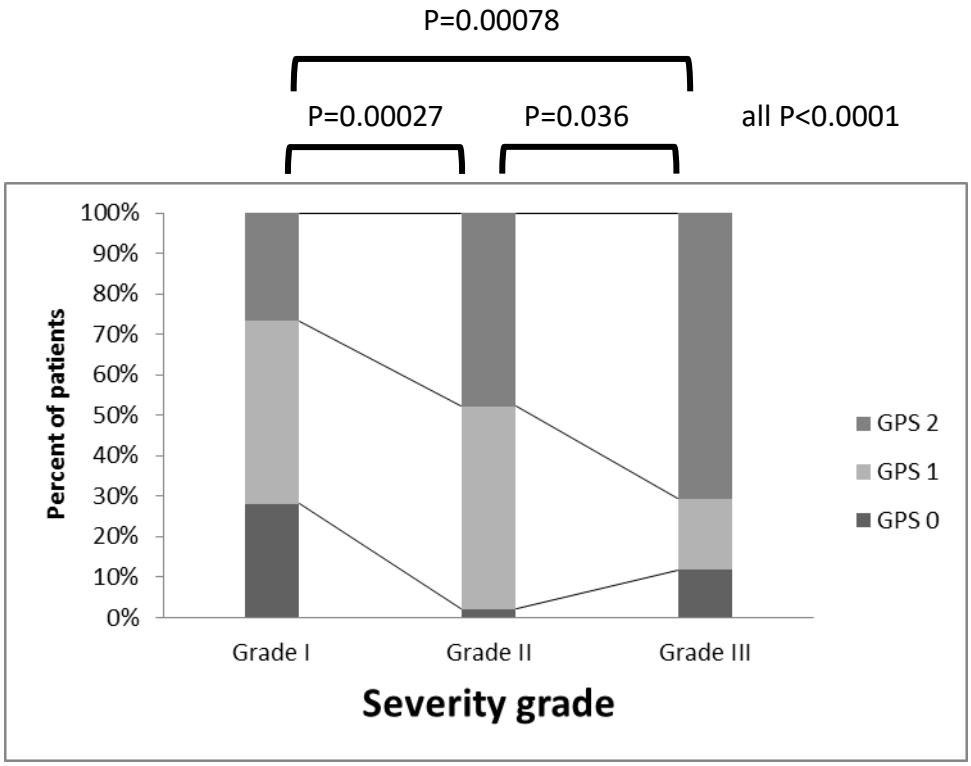
P=0.00078
P=0.00027
P=0.036
all P<0.0001
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Percent of patients
Grade I
Grade II
Grade III
Severity grade
GPS 2
GPS 1
GPS 0

Fig. 2a.

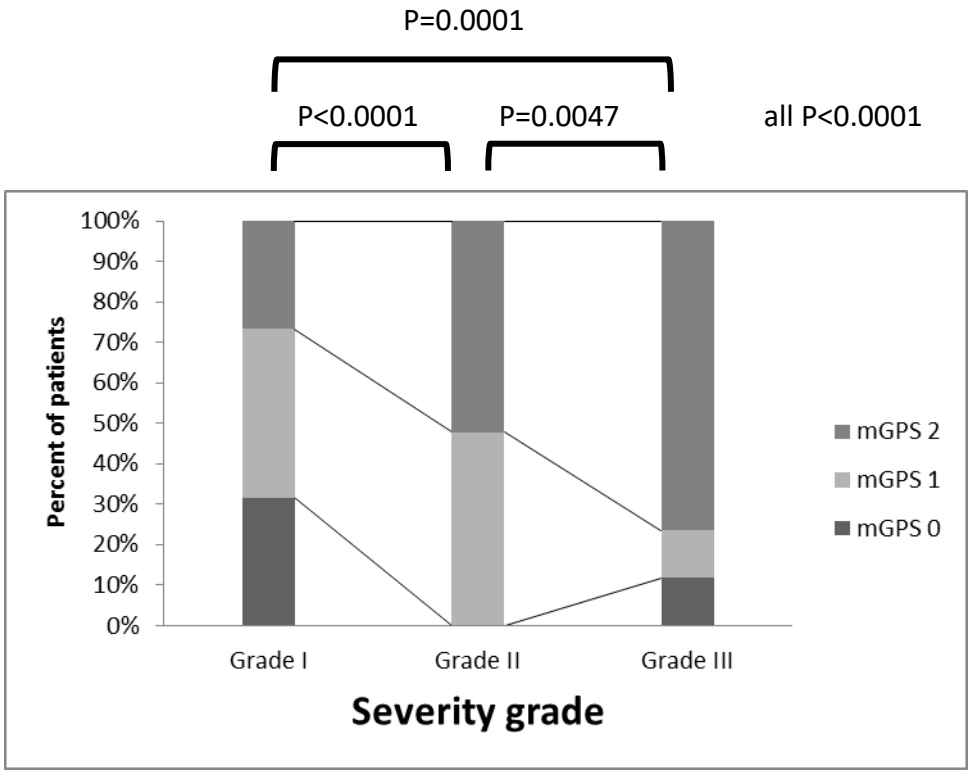
P=0.0001
P<0.0001
P=0.0047
all P<0.0001
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Percent of patients
Grade I
Grade II
Grade III
Severity grade
mGPS 2
mGPS 1
mGPS 0

Fig. 2b.