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Predictive value of different inflammatory combined indicators on early severity and prognosis of acute biliary pancreatitis

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Abstract: Objective To investigate the predictive efficacy of six inflammatory combined indicators mainly derived from complete blood count, including neutrophil-lymphocyte ratio (NLR), systemic inflammatory response index (SIRI), systemic immune inflammation index (SII), inflammatory burden index (IBI), pan-immunoinflammatory value (PIV), and C-reactive protein to albumin ratio (CAR), for early severity and complicated organ failure in acute biliary pancreatitis (ABP). **Methods** The clinical data of 544 ABP patients admitted to the Northern Jiangsu People's Hospital from January 2017 to December 2020 were retrospectively analyzed. The patients were divided into MAP group (mild acute pancreatitis, n=274), and non-MAP group (moderately severe/severe acute pancreatitis, n=270). Baseline data and laboratory indicators were collected and compared between groups. The receiver operating characteristics (ROC) curve was used to assess the predictive value of each inflammation indicator on the severity of early ABP and the occurrence of organ failure. **Results** Compared to the MAP group, non-MAP patients exhibited higher body weight, greater proportion of alcohol consumption history, longer hospital stays, and higher hospitalization costs, as well as higher levels of six inflammatory combined indicators (P<0.05). ROC curve analysis revealed that the area under the curve (AUC) of SII, PIV, SIRI, NLR, IBI, and CAR for predicting early moderately severe/severe ABP within 24 hours of admission were 0.635, 0.632, 0.624, 0.616, 0.592 and 0.582, with SII showing the highest AUC; among the six inflammatory combined indicators, procalcitonin and C-reactive protein, CAR had the largest AUC for predicting concurrent organ failure (AUC=0.772). **Conclusion** ABP patients with higher body weight and more alcohol consumption were more likely to progress to moderately severe/severe ABP. SII and CAR showed superior predictive value for disease severity and the occurrence of organ failure, respectively, and may serve as early warning indicators for disease progression and clinical outcomes in ABP patients.

Keywords: Acute biliary pancreatitis; Inflammatory combined indicators; Systemic immune inflammation index; C- reactive protein to albumin ratio; Disease severity; Organ failure

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Acute pancreatitis (AP) isa type of chemical inflammation caused by the self-digestion of the pancreas and surrounding tissues by pancreatic enzymes due to multiple etiologies. It is one of the common acute and critical diseases encountered in clinical practice. Among these, acute biliary pancreatitis (ABP) is the leading cause of AP, accounting for more than 50% of all AP cases. It is usually triggered by diseases of the biliary system into mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP) based on disease severity (according to the 2012 revised version of the Atlanta standard [1]). Among all AP patients, approximately 10%–20% progress to SAP. SAP usually develops rapidly, with the massive release of inflammatory mediators causing an inflammatory cascade reaction, which subsequently induces systemic inflammatory response syndrome. This often results in multiple organ dysfunction and may even become life-threatening, and the mortality rate is as high as 30% to 40% [2-3]. With a commonly used single inflammatory markers in clinical practice, such as procalcitonin (PCT), C-reactive protein (CRP), lymphocyte count (LYM), and neutrophil count (NEU), can reflect the inflammatory status of AP patients to a certain extent. Considering the complex changes involving various inflammatory cells during the development of AP, the inflammatory composite index, which includes different immune-inflammation components, may be more advantageous than single markers in assessing the condition of ABP [4].

In recent years, various inflammatory composite markers derived from complete blood cell counts [including systemic inflammatory response index (SIRI), systemic immune-inflammation index (SII), neutrophil-to-lymphocyte ratio (NLR), inflammatory burden index (IBI), pan-immunoinflammatory value (PIV), and C-reactive protein to albumin ratio (CAR)] have begun to be applied in the assessment of disease progression and outcome changes in AP [5].

For the time being, the value of combined inflammatory markers in predicting the severity and prognosis of ABP. This study focused on patients with ABP and investigated the value of SIRI, SII, NLR, CAR, IBI, and PIV in predicting disease severity and prognosis in ABP, with a comparative analysis among these indicators. The findings are reported as follows.

1 Subjects sand Methods

1.1 Study Subjects

A retrospective analysis was conducted on the clinical data of 544 hospitalized patients with ABP who were consecutively admitted to Northern Jiangsu People's Hospital Affiliated from January 1, 2017 to December 31, 2020.

Inclusion criteria:

(1) Age ≥18 years;
(2) Fulfillment of the diagnostic criteria for ABP;
(3) Length of hospital stay ≥2 days;
(4) Time from disease onset to hospital admission ≤7 days;
(5) Routine blood examination performed within 24 hours after admission.

Exclusion criteria:

(1) History of malignant tumors or hematological diseases;
(2) Recent use of corticosteroids and/or medications affecting white blood cells or platelets;
(3) Presence of severe cardio-cerebral dysfunction and/or hepatic or renal insufficiency;
(4) Pregnant or lactating women;
(5) Incomplete essential clinical information.

The screening process for ABP patients is shown in **Figure 1.** This study was approved by the Medical Ethics Committee of Northern Jiangsu People's Hospital on August 31, 2023 (Approval No.: 2023ky186).

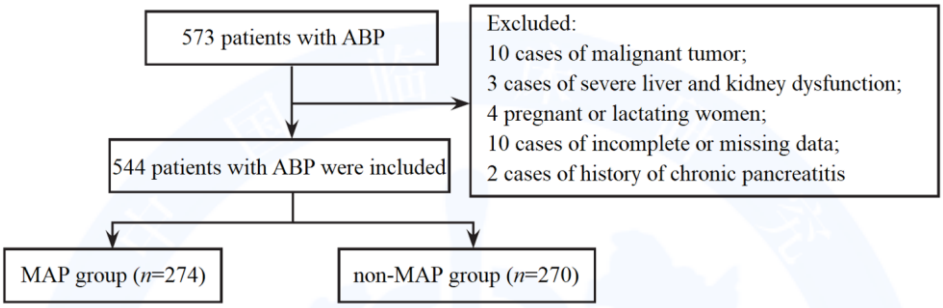

Fig.1 The flow chart of the selection of ABP patients

1.2 Grouping

According to disease severity, the patients were divided into: MAP group (n=274) and non-MAP group (MSAP+SAP, n=270).

1.3 Data Collection

After admission, all patients received treatment according to the guidelines for the diagnosis and management of AP [6]. Patients in the MAP group received supportive treatments including fluid replacement, analgesia, anti-inflammatory therapy, and pancreatic enzyme inhibition. Patients in the non-MAP group received intensive fluid resuscitation, maintenance of organ function, early nutritional intervention, and infection prevention and control.

The clinical data of all ABP patients were collected through the hospital information system. The main clinical data included the following:

(1) General data: age, gender, height, body weight, body mass index (BMI), length of hospitalization, hospitalization costs, etc.

(2) Medical history data: history of hypertension, diabetes mellitus, coronary heart disease, fatty liver disease, cerebrovascular disease, smoking history, alcohol consumption history, previous history of AP episodes, etc.

(3) Laboratory indicators: the first complete blood count and biochemical test results obtained within 24 hours after admission were collected [including white blood cell count (WBC), NEU, platelet count (PLT), LYM, monocyte count (MONO), CRP, PCT, total bilirubin (TB), alanine aminotransferase (ALT), albumin (ALB), Ca^{2+}, serum amylase (AMY)]

(4) Imaging data: abdominal ultrasonography, CT or MRI.

1.4 Calculation of Study Indicators

The composite inflammatory indicators included in this study were: SII, SIRI, NLR, CAR, IBI and PIV.

The formulas for each indicator were as follows:

SII = PLT × NEU /LYM
SIRI = MONO × NEU / LYM
NLR =NEU / LYM
CAR = CRP / ALB
IBI = CRP × NEU / LYM
PIV = NEU × PLT × MONO /LYM

1.5 Statistical Methods

Statistical analysis was performed using IBM SPSS 27.0 software. Measurement data conforming to a normal distribution were expressed $\bar{x}\pm s$, and comparisons between groups were performed using the independent samples t-test. Measurement data not conforming toa normal distribution were expressed as $M(P_{25},P_{75})$, and comparisons between groups were performed using the Mann-Whitney U test. Categorical data were expressed as cases (%), and comparisons between groups were performed using the chi-square test. Receiver operating characteristic (ROC) curves and area under the curve (AUC) analyses were used to evaluate the predictive value of each inflammatory indicator for the early severity and prognosis of ABP. All tests were two-sided, and P<0.05 was considered statistically significant.

2 Results

2.1 Comparison of general data between the MAP group and the non-MAP group

Compared with the MAP group, the non-MAP group had significantly higher body weight, proportion of patients with Alcohol consumption history, hospitalization costs, and length of hospital stay (P<0.05). There was no statistically significant difference between the two groups in terms of age, gender, history of hypertension, history of coronary heart disease, history of diabetes, history of fatty liver, history of smoking, or history of previous AP (P>0.05). See **Table 1**.

Tab.1 Comparison of general data between ABP patients with different disease degrees

Indicator	MAP group (n=274)	non-MAP group (n=270)	$t/\chi^2/z$ value	P value
Age(case)[a]	62.00 (49.00,70.00)	59.00 (47.00,70.00)	1.471	0.141
Gender [case(%)]				
Female	149(54.4)	132(48.9)	1.642	0.200
Male	125(45.6)	138(51.1)		
Weight (kg)[a]	65.00 (57.00,72.00)	66.00 (60.00,75.00)	2.741	0.006
Medical history [case(%)]				
Hypertension	87(31.8)	97(35.9)	1.059	0.304
Coronary heart disease	9(3.3)	8(3.0)	0.046	0.829
Diabetes	35(12.8)	39(14.4)	0.323	0.570
Fatty liver	11(4.0)	18(6.7)	1.895	0.169
Smoking history	29(10.6)	41(15.2)	2.568	0.109
Alcohol consumption history	26(9.5)	46(17.0)	6.747	0.009
History of AP	62(22.6)	65(24.1)	0.159	0.690
Length of hospital stay (d)[a]	8(6,11)	10(7,14)	5.560	<0.001
Hospitalization costs (ten thousand yuan)[a]	1.36 (0.96,2.46)	17.51 (11.51,27.53)	3.761	<0.001

Note: [a], data was expressed as $M(P_{25}, P_{75})$.

2.2 Comparison of laboratory indicators between MAP group and non-MAP group

The levels of ALB, ALT, and Ca^{2+} in the non-MAP group were lower than those in the MAP group (P<0.05). There was no significant difference in LYM or TB levels between the two groups (P>0.05). The levels of WBC, NEU, MONO, PLT, AMY, PCT, CRP, SII, SIRI, NLR, PIV, CAR, and IBI in the non-MAP group were higher than those in the MAP group (P<0.05). See **Table 2.**

2.3 Predictive value of inflammatory markers for MSAP and SAP

ROC analysis showed that CRP, PCT, SII, SIRI, NLR, PIV, CAR, and IBI were all statistically significant predictors of early MSAP and SAP (P<0.05). Among the combined inflammatory markers, SII had the largest AUC value for predicting early MSAP and SAP, which was 0.635, with an optimal cut-off value of 2170.00. See **Table 3** and **Figure 2.**

2.4 Predictive value of inflammatory markers for organ failure in patients with ABP

Among the 544 patients with ABP, 56 developed organ failure. ROC curve analysis showed that CRP, PCT, SII, SIRI, NLR, PIV, CAR, and IBI could be used to predict organ failure (P<0.05). CAR had the largest AUC value for predicting organ failure, which was 0.772, with an optimal cut-off value of 3.29. See **Table 4** and **Figure 3**.

Tab.2 Comparison of biochemical indicators between ABP patients with different disease degrees [$M(P_{25},P_{75})$]

Indicator	MAP group (n=274)	non-MAP group (n=270)	Z value	P value
WBC($\times10^9$/L)	11.63 (8.09,14.96)	13.36 (11.51,17.87)	8.038	<0.001
NEU($\times10^9$/L)	9.43 (6.52,13.16)	12.05 (9.38,15.51)	8.269	<0.001
LYM($\times10^9$/L)	1.37 (1.09,1.88)	1.41 (1.13,1.81)	1.701	0.089
MONO($\times10^9$/L)	0.58 (0.43,0.81)	0.70 (0.55,0.99)	6.436	<0.001
PLT($\times10^9$/L)	200.00 (142.00,249.00)	222.00 (186.00,270.00)	2.377	0.017
TB(μmol/L)	29.51 (16.83,62.51)	36.20 (20.94,59.82)	0.986	0.324
ALB(g/L)	37.00 (33.00,39.00)	35.00 (31.00,38.00)	7.598	<0.001
ALT(u/L)	160.00 (76.00,330.00)	119.00 (47.00,334.00)	2.173	0.030
Ca^{2+}(mmol/L)	2.12 (2.05,2.23)	2.06 (1.96,2.17)	7.525	<0.001
AMY(u/L)	613.00 (199.00,1349.00)	912.00 (173.00,1531.00)	2.457	<0.001
PCT(ng/mL)	0.14 (0.07,0.71)	0.28 (0.09,1.96)	2.593	0.010
CRP(mg/L)	60.13 (8.68,128.03)	130.93 (60.19,193.51)	7.793	<0.001
SII	1,426.13 (799.96, 2585.44)	2,571.48 (1544.91, 4386.65)	5.444	<0.001
SIRI	4.69 (2.15,9.37)	7.93 (4.59,12.30)	4.990	<0.001
NLR	9.73 (5.40,16.22)	14.2 (7.85,21.67)	4.674	<0.001
PIV	764.26 (312.06,1641.39)	1502.51 (852.91,2303.41)	5.326	<0.001
CAR	0.70 (0.12,2.68)	1.67 (0.26,3.84)	2.477	0.013
IBI	284.95 (33.96,1384.91)	624.22 (104.52,1793.79)	2.736	0.006

Tab.3 Predictive value of inflammatory indicaters for MSAP and SBP

Indicator	AUC (95%CI)	Sensitivity	Specificity	Cut-off value	P value
CRP	0.716(0.668-0.763)	0.584	0.762	98.11 mg/L	<0.001
PCT	0.589(0.523-0.656)	0.460	0.718	0.375 ng/mL	0.010
SII	0.635(0.588-0.681)	0.522	0.701	2,170.00	<0.001
SIRI	0.624(0.577-0.670)	0.652	0.558	4.57	<0.001
NLR	0.616(0.569-0.662)	0.756	0.453	7.39	<0.001
PIV	0.632(0.585-0.678)	0.667	0.555	768.20	<0.001
CAR	0.582(0.518-0.645)	0.296	0.876	3.50	0.013
IBI	0.592(0.527-0.656)	0.589	0.574	285.50	0.006

Tab.4 Predictive value of inflammatory indicators for predicting organ failure in ABP

Indicator	AUC (95%CI)	Sensitivity	Specificity	Cut-off value	P value
CRP	0.750(0.585-0.915)	0.667	0.816	134.4 mg/L	0.004
PCT	0.734(0.644-0.825)	0.613	0.821	1.640 ng/mL	<0.001
SII	0.676(0.611-0.742)	0.804	0.545	1 818	<0.001
SIRI	0.697(0.624-0.770)	0.696	0.635	6.635	<0.001
NLR	0.680(0.608-0.751)	0.643	0.641	13.63	<0.001
PIV	0.681(0.605-0.757)	0.482	0.846	2 283	<0.001
CAR	0.772(0.671-0.873)	0.714	0.806	3.291	<0.001
IBI	0.770(0.669-0.871)	0.857	0.657	642.8	<0.001

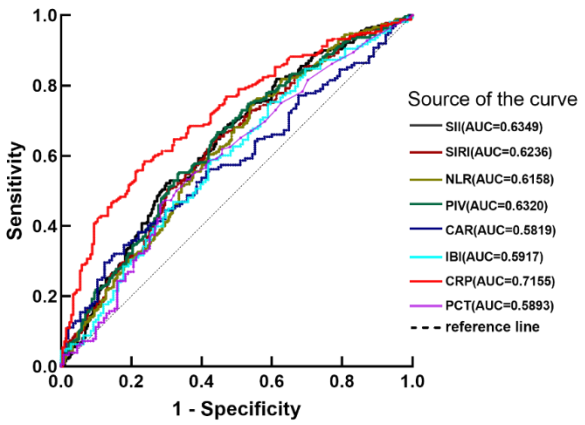

Fig.2 ROC curve of inflammatory indexes for predicting MSAP and SAP

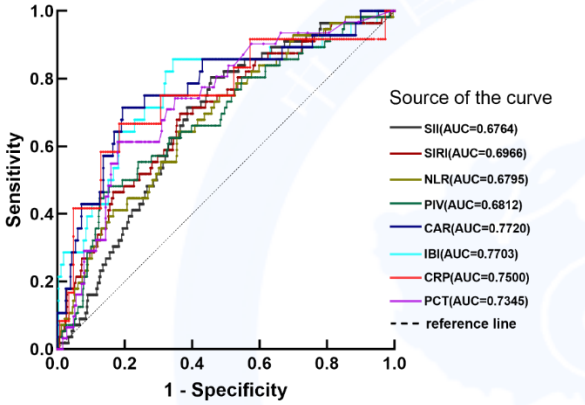

Fig.3 ROC curve of inflammatory indicators for predicting organ failure in ABP

3 Discussion

The pathogenesis of AP is closely associated with inflammatory factors in the body [7]; therefore, relevant inflammatory markers may be considered as reference indicators for disease assessment. Currently, in the clinical diagnosis and treatment of AP, traditional markers reflecting infection and inflammation remain mainly CRP and PCT, which have high sensitivity but relatively low specificity, resulting in suboptimal overall diagnostic performance. SIRI, SII, NLR, PIV, IBI, and CAR are composite markers used to assess immune, nutritional, and infection status, playing important roles in disease evaluation and prognosis prediction for tumours, cardiovascular diseases, and metabolic diseases [8-10]. These combined inflammatory indices are derived from complete blood cell counts and are readily available. In recent years, studies have suggested that systemic inflammatory composite markers are also helpful in predicting the severity of AP [11-14]; however, reports on the predictive value of the above markers for early ABP severity and comparisons between them are still limited, requiring further clinical investigation.

This study found that compared with the MAP group, the non-MAP group had a higher proportion of patients with a history of alcohol consumption and a higher body weight. Previous studies have indicated that age >69 years, BMI ≥30 kg/m², and alcohol consumption are independent risk factors for AP, and such patients are also more likely to develop SAP [2,15]. Therefore, it is necessary to pay attention to patients' past medical history or clinical data to assist in assessing disease severity, in addition to hematological findings and/or imaging examinations.

The results of this study showed that CRP, PCT, SII, SIRI, NLR, CAR, IBI, and PIV were higher in patients with MSAP/SAP than in those with mild AP, whereas ALB, ALT, and Ca^{2+} were lower. ROC curve analysis revealed that SII had good efficacy in predicting ABP severity, and CAR had good efficacy in predicting organ failure, outperforming other combined inflammatory markers.

SII consists of NEU, LYM, and PLT. NEU are the core effector cells of the innate immune system and the first responders to acute inflammation. LYM are central to the adaptive immune system, responsible for specific immune responses and immunomodulation. PLT are involved not only in coagulation but also in inflammation and innate immunity. SII was first used to predict disease progression in patients with hepatocellular carcinoma [16]; subsequently, SII was found to be closely associated with hyperlipidemia, fatty liver disease, and severe sepsis [17-19]. Studies have shown that SII can be used to assess and predict disease severity and clinical outcomes in AP patients and is associated with multiple AP outcome indicators [20]. In this study, the AUC value of SII for predicting early ABP severity was superior to that of other combined inflammatory markers. Liu *et al*. [21] demonstrated that SII is a powerful indicator for predicting AP severity, with patients having SII ≥2207.53 being more likely to develop SAP (AUC = 0.920). Zhang *et al*. [22] and Araiza-Rodríguez *et al*. [23] confirmed the important clinical value of SII for early stratification of AP severity, and continuous monitoring of dynamic changes in SII may help identify patients requiring intensive care or intensified treatment. Incorporating SII into clinical practice may optimize decision-making processes; early identification of high-risk patients and timely intervention can help reduce the occurrence of SAP and secondary infections, thereby improving clinical outcomes.

CAR is a composite marker that includes CRP and ALB, reflecting both infection status and nutritional status. Khanna *et al*. [24] showed that CRP has high sensitivity and accuracy in predicting AP severity, pancreatic necrosis, and mortality. Some studies suggest that a CRP level >150 mg/L within 48 hours of onset can be used for early diagnosis of SAP and also has good sensitivity for predicting pancreatic necrosis [25]. ALB levels reflect hepatic synthetic function and nutritional status. In this study, the ALB level in the non-MAP group was significantly lower than that in the MAP group. Studies have shown that low serum ALB levels in AP patients are significantly associated with poor prognosis and can serve as an important tool for predicting adverse outcomes, especially persistent organ failure and death [26]. In this study, CAR demonstrated good predictive efficacy for assessing organ failure in ABP, outperforming CRP, PCT, and other combined inflammatory markers. This is

primarily because, compared with other composite inflammatory indices, CAR consists of markers related to both inflammation and nutritional depletion. Ghaffar *et al*. [27] showed that compared with traditional imaging, CAR only requires blood tests for CRP and ALB, offering advantages of time saving and cost-effectiveness. A prospective study supported that CAR is an independent predictor of hospitalization >7 days in AP patients, with an AUC superior to the Glasgow Outcome Scale (GOS) and modified GOS (0.677, 0.637, 0.671), suggesting that CAR can serve as a reliable indicator for assessing disease severity via length of hospital stay [28]. Other studies have noted that CAR is significantly associated with SAP, but its predictive efficacy is limited; it can be used as a supplementary indicator to existing AP prognostic scoring systems [29]. Additional research has suggested that CAR combined with PCT/ALB may predict AP severity more accurately [30].

Currently, the main clinical challenge in AP management is the early assessment of disease severity and prognostic risk, which has important implications for patient outcomes, healthcare resource consumption, and socioeconomic burden. From a clinical perspective, SII and CAR, as simple composite inflammatory markers, facilitate early risk stratification in AP, particularly in emergency settings or resource-limited environments. Therefore, early identification and assessment of at-risk patients using reliable composite inflammatory markers are crucial for selecting appropriate treatment strategies and optimizing patient management.

By monitoring various hematological parameters and calculating systemic composite inflammatory markers, this study helps to assess inflammatory status, disease severity, and prognostic risk in ABP, which has important clinical significance for early individualized treatment and prognostic prediction. This study is a retrospective analysis with potential selection bias, and further prospective studies are necessary for validation. As a single-center study, the sample size is limited. All enrolled subjects were of Chinese ethnicity; whether the results are applicable to other nationalities and races requires further validation.

Conflict of Interest None

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·急性胰腺炎专题·论著·

不同炎症联合指标对急性胆源性胰腺炎早期严重程度及预后的预测价值

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摘要：目的 探讨主要由全血细胞计数衍生的6项炎症联合指标[中性粒细胞-淋巴细胞比值(NLR)、全身炎症反应指数(SIRI)、全身免疫炎症指数(SII)、炎症负荷指数(IBI)、泛免疫炎症值(PIV)及C反应蛋白与白蛋白比值(CAR)]对急性胆源性胰腺炎(ABP)早期严重程度及并存器官衰竭的预测效能。**方法** 回顾性分析2017年1月至2020年12月苏北人民医院收治的544例ABP患者的临床资料，将患者分为轻症急性胰腺炎(MAP)组274例，非MAP(中度重症/重症，non-MAP)组270例。收集各项基线资料及实验室指标并进行组间比较，采用受试者工作特征(ROC)曲线分析各炎症指标对ABP早期病情严重程度及并发器官衰竭的预测价值。**结果** 相较于MAP组，non-MAP组患者体质量更高、饮酒史占比更高、住院时间更长、住院费用更高、6项联合炎症指标水平更高($P<0.05$)；ROC曲线分析显示，入院24 h内SII、PIV、SIRI、NLR、IBI、CAR预测早期中度重症/重症ABP的曲线下面积(AUC)依次为0.635、0.632、0.624、0.616、0.592和0.582，以SII最大；在6项炎症联合指标及降钙素原、C反应蛋白中，CAR预测合并器官衰竭的AUC最大(AUC=0.772)。**结论** 体质量较高且饮酒多的ABP患者更易进展为中度重症/重症ABP；相较于其他联合炎症指标，SII对预测ABP严重程度、CAR对并发器官衰竭方面具有更优的预测价值，可作为ABP患者疾病进展与临床结局的早期预警指标。

关键词： 急性胆源性胰腺炎；炎症联合指标；全身免疫炎症指数；C反应蛋白与白蛋白比值；疾病严重程度；器官衰竭
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Predictive value of different inflammatory combined indicators on early severity and prognosis of acute biliary pancreatitis

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Abstract: Objective To investigate the predictive efficacy of six inflammatory combined indicators mainly derived from complete blood count, including neutrophil-lymphocyte ratio (NLR), systemic inflammatory response index (SIRI), systemic immune inflammation index (SII), inflammatory burden index (IBI), pan-immunoinflammatory value (PIV), and C-reactive protein to albumin ratio (CAR), for early severity and complicated organ failure (OF) in acute biliary pancreatitis (ABP). **Methods** The clinical data of 544 ABP patients admitted to the Northern Jiangsu People's Hospital from January 2017 to December 2020 were retrospectively analyzed. The patients were divided into MAP group (mild acute pancreatitis, n=274), and non-MAP group (moderately severe/severe acute pancreatitis, n=270). Baseline data and laboratory indicators were collected and compared between groups. The receiver operating characteristics (ROC) curve was used to assess the predictive value of each inflammation indicator on the severity of early ABP and the

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occurrence of OF. **Results** Compared to the MAP group, non-MAP patients exhibited higher body weight, greater proportion of alcohol consumption history, longer hospital stays, and higher hospitalization costs, as well as higher levels of six inflammatory combined indicators (P<0.05). ROC curve analysis revealed that the areas under the curve (AUCs) of SII, PIV, SIRI, NLR, IBI, and CAR for predicting early moderately severe/severe ABP within 24 hours of admission were 0.635, 0.632, 0.624, 0.616, 0.592 and 0.582, with SII showing the highest AUC; among the six inflammatory combined indicators, procalcitonin and C-reactive protein, CAR had the largest AUC for predicting concurrent organ failure (AUC=0.772). **Conclusion** ABP patients with higher body weight and more alcohol consumption were more likely to progress to moderately severe/severe ABP. SII and CAR showed superior predictive value for disease severity and the occurrence of OF, respectively, and may serve as early warning indicators for disease progression and clinical outcomes in ABP patients.

Keywords: Acute biliary pancreatitis; Inflammatory combined indicators; Systemic immune inflammation index; C-reactive protein to albumin ratio; Disease severity; Organ failure

Fund program: Jiangsu Province Chinese Medicine Science and Technology Development Plan Project(MS2023138)

急性胰腺炎(acute pancreatitis,AP)是多种病因引起的胰腺及周围组织被胰酶自身消化的一类化学性炎症,是临床常见的急危重症之一。其中,急性胆源性胰腺炎(acute biliary pancreatitis,ABP)是 AP 第一大病因,约占 AP 发病总数的 50%以上,通常以胆道系统疾病为诱因,患者常出现腹痛、发热、黄疸等症状[1-3]。根据 2012 年修订版的亚特兰大标准[1],目前临床上根据严重程度将 AP 分为轻症 AP(mild acute pancreatitis,MAP)、中度重症 AP(moderately severe acute pancreatitis,MSAP)和重症 AP(severe acute pancreatitis,SAP)。其中 10%~20%的 AP 患者会发展为 SAP。SAP 通常病情发展迅猛,大量炎症因子释放引起炎症级联反应,继而诱发全身炎症反应综合征,常导致多器官功能障碍,甚至危及生命,死亡率高达 30%~40%[2-3]。临床常见的单一炎症相关标志物如降钙素原(procalcitonin,PCT)、C 反应蛋白(C-reactive protein,CRP)、淋巴细胞计数(lymphocyte count,LYM)、中性粒细胞计数(neutrophil count,NEU)等可以在一定程度上反映 AP 患者的炎症水平。考虑到 AP 发生发展中涉及多种炎症细胞的复杂变化,而炎症联合指数包含不同免疫炎症成分,可能在 ABP 病情评估方面相较于单一标志物更具优势[4]。

近年来,多种由全血细胞计数衍生的炎症联合标志物[全身炎症反应指数(systemic inflammatory response index,SIRI)、全身免疫炎症指数(systemic immune-inflammation index,SII)、中性粒细胞与淋巴细胞比值(neutrophil-lymphocyte ratio,NLR)、炎症负荷指数(inflammatory burden index,IBI)和泛免疫炎症值(pan-immunoinflammatory value,PIV)及 CRP 与白蛋白比值(C-reactive protein to albumin ratio,CAR)等]开始应用于 AP 病情发展及结局变化评估中[5]。目前,关于以上炎症联合指标预测 ABP 病情及预后的价值仍需进一步探讨。本研究以 ABP 患者为研究对象,探讨 SIRI、SII、NLR、CAR、IBI 和 PIV 预测 ABP 病情严重程度及预后的价值并进行对比,现报道如下。

1　对象与方法

1.1　*研究对象*　回顾性收集 2017 年 1 月 1 日至 2020 年 12 月 31 日苏北人民医院连续收治的 544 例 ABP 住院患者的临床资料。纳入标准:(1)年龄≥18 岁;(2)满足 ABP 的诊断标准;(3)住院时间≥2 d;(4)发病至入院时间≤7 d;(5)入院后 24 h 内检测血常规。排除标准:(1)有恶性肿瘤、血液系统疾病史;(2)近期使用过皮质类固醇及(或)影响白细胞、血小板的相关药物;(3)合并严重心脑功能障碍及(或)肝肾功能不全;(4)妊娠期或哺乳期妇女;(5)重要信息不全。ABP 患者筛选流程见图 1。本研究于 2023 年 8 月 31 日获得苏北人民医院医学伦理委员会的批准(审查号:2023ky186)。

1.2　*分组*　根据严重程度将患者分为 MAP 组 274 例,非 MAP 组(MSAP+SAP,non-MAP 组)270 例。

1.3　*资料收集*　所有患者入院后均按照 AP 诊疗指南进行治疗[6],MAP 组予以补液、止痛、抗炎、抑酶等支持治疗;non-MAP 组患者强化液体复苏、器官功能维持、早期营养干预以及感染防控。所有 ABP 患者的临床资料通过医院信息系统收集。主要的临床资料如下,(1)一般资料:年龄、性别、身高、体质量、身体质量指数(body mass index, BMI)、住院时间、住院费用等。(2)病史资料:高血压史、糖尿病史、冠心病史、脂肪肝病史、脑血管病史、吸烟史、饮酒史、既往 AP 发病史等。(3)实验室指标:收集患者入院 24 h 内的首次血常规和生化检查结果,主要包括白细胞计

数(white blood cell count, WBC)、NEU、血小板计数(platelet count, PLT)、LYM、单核细胞计数(monocyte count, MONO)、CRP、PCT、总胆红素(total bilirubin, TB)、丙氨酸氨基转移酶(alanine aminotransferase, ALT)、白蛋白(albumin, ALB)、血清钙离子(calcium, Ca^{2+})、血清淀粉酶(amylase, AMY)等。(4)影像学资料:腹部B超、CT、MRI等。

1.4　*研究指标计算*　本研究中纳入的联合炎症指标为SII、SIRI、NLR、CAR、IBI和PIV。各指标计算公式如下:SII=PLT×NEU/LYM;SIRI= MONO×NEU/LYM;NLR=NEU/LYM; CAR=CRP/ALB; IBI=CRP × NEU/LYM;PIV=NEU×PLT×MONO/LYM。

1.5　*统计学方法*　应用IBM SPSS 27.0软件进行统计分析。符合正态分布的计量资料采用$\bar{x}\pm s$描述,使用独立样本t检验进行组间比较;不符合正态分布的计量资料采用$M(P_{25}, P_{75})$描述,使用Mann-Whitney U检验进行组间比较。计数资料采用例(%)表示,组间比较采用χ^2检验。使用受试者工作特征(receiver operating characteristic, ROC)曲线及曲线下面积(area under the curve, AUC)分析各项炎症指标对ABP早期病情严重程度及预后的预测价值。双侧检验,P<0.05为差异有统计学意义。

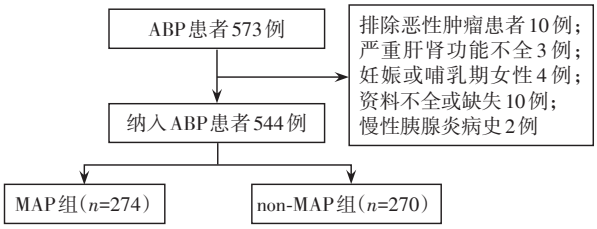

图1　ABP患者筛选流程图

Fig.1　The flow chart of the selection of ABP patients

2　结　果

2.1　MAP组和non-MAP组患者的一般资料比较　与MAP组比较,non-MAP组患者的体质量、饮酒史占比、住院费用更高,住院时间更长,差异有统计学意义(P<0.05)。两组年龄、性别、高血压病史、冠心病史、糖尿病史、脂肪肝史、吸烟史、既往AP史等方面差异无统计学意义(P>0.05)。见表1。

2.2　MAP组和non-MAP组患者的实验室指标比较　non-MAP组ALB、ALT、Ca^{2+}水平低于MAP组(P<0.05);LYM、TB水平两组间差异无统计学意义(P>0.05); non-MAP组WBC、NEU、MONO、PLT、AMY、PCT、CRP、SII、SIRI、NLR、PIV、CAR、IBI水平均高于MAP组(P<0.05)。见表2。

表1　两组ABP患者的一般资料比较

Tab.1　Comparison of general data between two groups of ABP patients

项目	MAP组(n=274)	non-MAP组(n=270)	$t/\chi^2/z$值	P值
年龄(岁)[a]	62.00(49.00,70.00)	59.00(47.00,70.00)	1.471	0.141
性别[例(%)]				
女	149(54.4)	132(48.9)	1.642	0.200
男	125(45.6)	138(51.1)		
体质量(kg)[a]	65.00(57.00,72.00)	66.00(60.00,75.00)	2.741	0.006
既往史[例(%)]				
高血压	87(31.8)	97(35.9)	1.059	0.304
冠心病	9(3.3)	8(3.0)	0.046	0.829
糖尿病	35(12.8)	39(14.4)	0.323	0.570
脂肪肝	11(4.0)	18(6.7)	1.895	0.169
吸烟史	29(10.6)	41(15.2)	2.568	0.109
饮酒史	26(9.5)	46(17.0)	6.747	0.009
AP史	62(22.6)	65(24.1)	0.159	0.690
住院天数(d)[a]	8(6,11)	10(7,14)	5.560	<0.001
住院费用(万元)[a]	1.36(0.96,2.46)	17.51(11.51,27.53)	3.761	<0.001

注:[a]数据形式为$M(P_{25}, P_{75})$。

表2　两组ABP患者实验室指标比较　[$M(P_{25}, P_{75})$]

Tab.2　Comparison of laboratory indicators between two groups of ABP patients　[$M(P_{25}, P_{75})$]

项目	MAP组(n=274)	non-MAP组(n=270)	Z值	P值
WBC(×10⁹/L)	11.63(8.09,14.96)	13.36(11.51,17.87)	8.038	<0.001
NEU(×10⁹/L)	9.43(6.52,13.16)	12.05(9.38,15.51)	8.269	<0.001
LYM(×10⁹/L)	1.37(1.09,1.88)	1.41(1.13,1.81)	1.701	0.089
MONO(×10⁹/L)	0.58(0.43,0.81)	0.70(0.55,0.99)	6.436	<0.001
PLT(×10⁹/L)	200.00(142.00,249.00)	222.00(186.00,270.00)	2.377	0.017
TB(μmol/L)	29.51(16.83,62.51)	36.20(20.94,59.82)	0.986	0.324
ALB(g/L)	37.00(33.00,39.00)	35.00(31.00,38.00)	7.598	<0.001
ALT(u/L)	160.00(76.00,330.00)	119.00(47.00,334.00)	2.173	0.030
Ca^{2+}(mmol/L)	2.12(2.05,2.23)	2.06(1.96,2.17)	7.525	<0.001
AMY(u/L)	613.00(199.00,1 349.00)	912.00(173.00,1 531.00)	7.525	<0.001
PCT(ng/mL)	0.14(0.07,0.71)	0.28(0.09,1.96)	2.593	0.010
CRP(mg/L)	60.13(8.68,128.03)	130.93(60.19,193.51)	7.793	<0.001
SII	1 426.13(799.96,2 585.44)	2 571.48(1 544.91,4 386.65)	5.444	<0.001
SIRI	4.69(2.15,9.37)	7.93(4.59, 12.30)	4.990	<0.001
NLR	9.73(5.40,16.22)	14.20(7.85,21.67)	4.674	<0.001
PIV	764.26(312.06,1 641.39)	1 502.51(852.91,2 303.41)	5.326	<0.001
CAR	0.70(0.12,2.68)	1.67(0.26,3.84)	2.477	0.013
IBI	284.95(33.96,1 384.91)	624.22(104.52,1 793.79)	2.736	0.006

2.3　炎症指标对MSAP和SAP的预测价值　ROC分析显示，CRP、PCT、SII、SIRI、NLR、PIV、CAR、IBI对早期MSAP和SAP的预测均有统计学意义（P<0.05）。联合炎症指标中，SII预测早期MSAP和SAP的AUC值最大，为0.635，最佳截断值为2 170.00。见表3、图2。

2.4　炎症指标对ABP患者脏器功能衰竭的预测价值　544例ABP患者中，56例发生器官衰竭。ROC曲线分析显示，CRP、PCT、SII、SIRI、NLR、PIV、CAR、IBI可用于预测器官衰竭（P<0.05）。CAR预测器官衰竭的AUC值最大，为0.772，最佳截断值为3.29。见表4、图3。

表3　炎症指标对MSAP和SAP的预测价值

Tab.3　Predictive value of inflammatory indexes for MSAP and SAP

指标	AUC(95%*CI*)	敏感度	特异度	最佳截断值	*P*值
CRP	0.716(0.668~0.763)	0.584	0.762	98.11 mg/L	<0.001
PCT	0.589(0.523~0.656)	0.460	0.718	0.37 ng/mL	0.010
SII	0.635(0.588~0.681)	0.522	0.701	2 170.00	<0.001
SIRI	0.624(0.577~0.670)	0.652	0.558	4.57	<0.001
NLR	0.616(0.569~0.662)	0.756	0.453	7.39	<0.001
PIV	0.632(0.585~0.678)	0.667	0.555	768.20	<0.001
CAR	0.582(0.518~0.645)	0.296	0.876	3.50	0.013
IBI	0.592(0.527~0.656)	0.589	0.574	285.50	0.006

表4　炎症指标对ABP患者并发器官衰竭的预测价值

Tab.4　Predictive value of inflammatory indicators for predicting organ failure in ABP patients

指标	AUC(95%*CI*)	敏感度	特异度	最佳截断值	*P*值
CRP	0.750(0.585~0.915)	0.667	0.816	134.40 mg/L	0.004
PCT	0.734(0.644~0.825)	0.613	0.821	1.64 ng/mL	<0.001
SII	0.676(0.611~0.742)	0.804	0.545	1 818.00	<0.001
SIRI	0.697(0.624~0.770)	0.696	0.635	6.64	<0.001
NLR	0.680(0.608~0.751)	0.643	0.641	13.63	<0.001
PIV	0.681(0.605~0.757)	0.482	0.846	2 283.00	<0.001
CAR	0.772(0.671~0.873)	0.714	0.806	3.29	<0.001
IBI	0.770(0.669~0.871)	0.857	0.657	642.80	<0.001

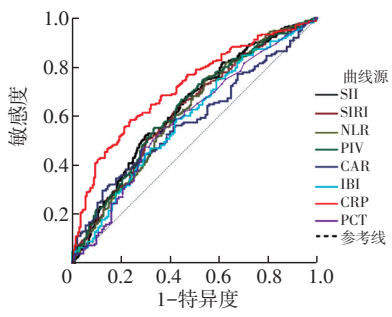

图2　炎症指标预测MSAP和SAP的ROC曲线

Fig.2　ROC curve of inflammatory indexes for predicting MSAP and SAP

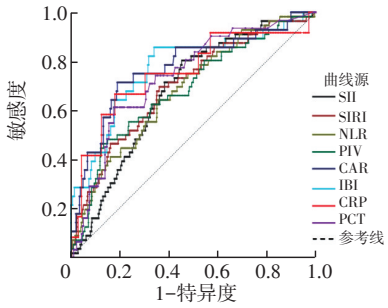

图3　炎症指标预测ABP患者发生脏器衰竭的ROC分析

Fig.3　ROC curve of inflammatory indicators for predicting organ failure in ABP patients

3　讨　论

AP发病过程与机体炎性因子存在紧密关联[7]，因而可考虑将相关炎症指标作为疾病评估的参考指标。目前针对AP的临床诊治，传统反映感染及炎症的指标仍以CRP、PCT等为主，具有较高敏感度，但特异度相对较低，整体诊断效果欠佳。SIRI、SII、NLR、PIV、IBI、CAR是用于评估机体免疫、营养、感染状态的复合指标，对肿瘤、心血管疾病和代谢疾病的病情评估和预后预测有重要作用[8-10]。这些炎症联合指标主要基于全血细胞计数衍生而来，获取方便快捷。近年来，已有研究提出全身性炎症联合指标对预测AP严重程度也有一定帮助[11-14]，但有关上述指标对早期ABP病情的预测价值及其对比的报道仍较少，临床上仍需进一步探讨。

本研究发现，相较于MAP组，non-MAP组患者饮酒史占比更多、体质量相对更高；此前，有研究提示年龄>69岁、BMI≥30 kg/m^{2}和饮酒是AP的独立危险因素，这些患者也更容易发生SAP[2,15]。因此，有必要在关注血液学结果和/或影像学检查的同时，留意患者的既往病史或临床资料来协助评估病情严重程度。

本研究结果显示，CRP、PCT、SII、SIRI、NLR、CAR、IBI、PIV在中度重症/重症患者均高于轻症患者，而ALB、ALT、Ca^{2+}低于轻症患者。ROC曲线分析发现，SII在预测ABP严重程度、CAR在预测器官衰竭方面具有较好的效能，优于其他炎症联合指标。

SII由NEU、LYM及PLT组成。NEU是先天免疫系统的核心效应细胞，是急性炎症反应的第一响应者；LYM是适应性免疫系统的核心，负责特异性免疫应答和免疫调节；PLT不仅参与凝血，也参与炎症反应和先天免疫。SII最早被用于预测肝细胞癌患者的病情[16]，后来发现SII与高脂血症、脂肪性肝病、重症脓毒症等密切相关[17-19]。有研究表明，SII可用于评估和预测AP患者的病情和临床转归，并与AP的多个结

局指标相关[20]。本研究中，SII预测ABP早期病情严重程度的AUC值优于其他联合炎症指标。Liu等[21]研究显示，SII是预测AP病情严重程度的有力指标，SII≥2 207.53的患者更容易发生SAP（AUC=0.920）。Zhang等[22]和Araiza-Rodríguez等[23]证明SII在AP严重程度早期分层中具有重要临床应用价值，持续监测SII的动态变化有助于及时识别需要重症监护或强化治疗的患者。将SII纳入临床实践可能优化决策流程，通过早期发现高风险患者并及时干预有助于减少SAP及其继发感染的出现，从而改善临床预后。

CAR是囊括了CRP与ALB的复合指标，能够反映机体感染状态和营养状况。Khanna等[24]研究表明CRP在预测AP严重程度、胰腺坏死和死亡率方面具有较高的敏感度和准确度。有研究提示，发病48 h内的CRP>150 mg/L可以用于早期诊断SAP，并且在预测胰腺坏死方面也有良好的敏感度[25]。ALB的水平可以反映肝脏的合成功能及身体的营养状况。本研究中non-MAP组的ALB水平显著低于MAP组。有研究表明，AP患者血清ALB水平低与预后不良显著相关，可作为预测不良结局的重要工具，尤其是预测持续性器官衰竭和死亡[26]。本研究中，CAR在评估ABP器官衰竭方面展现了良好的预测效能，优于CRP、PCT和其他炎症联合指标，这主要归因于与其他炎症联合指标相比，CAR同时由炎症和营养消耗相关的标志物构成。Ghaffar等[27]研究表明，相较于传统影像学检查，CAR只需通过抽血检测CRP和ALB水平，具有省时且经济高效的优点。一项前瞻性研究支持CAR是AP患者住院>7 d的独立预测因子，CAR预测的AUC优于格拉斯哥预后评分（Glasgow Outcome Scale，GOS）和改良GOS（0.677、0.637、0.671），提示CAR可作为通过住院时间评估疾病严重程度的可靠指标[28]。也有研究指出CAR与SAP显著相关，但其预测效能有限，可作为现有AP预后评分系统的补充指标[29]。还有研究提示，CAR与PCT/ALB可更准确地预测AP的严重程度[30]。

目前AP临床管理的主要挑战在于早期评估病情程度及预后风险，这对患者预后、医疗资源消耗及社会经济负担均有重要影响。从临床角度而言，SII、CAR作为简便的炎症联合指标，有助于AP的早期风险分层，尤其在急诊或医疗资源匮乏的环境中更具有实用价值。因此，通过可靠的炎症联合指标对风险患者进行早期识别和评估，对于选择恰当的治疗策略和优化患者管理至关重要。

本研究通过监测各项血液学指标，并计算全身性炎症联合指标，有助于评估ABP的炎症情况、病情严重程度和预后风险，对于早期个性化治疗和预后预测都具有重要的临床意义。本研究为回顾性分析，存在选择偏倚，有必要进一步开展前瞻性研究加以验证；作为单中心研究，样本量有限；纳入对象均为中国人群，研究结果是否适用于其他国家及种族还有待进一步验证。

利益冲突 无

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(上接第707页)

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