Value of Systemic Inflammatory Response Index in Evaluating Severity in Patients with Acute Pancreatitis (Postprint)

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Abstract

Background Acute pancreatitis (AP) is a common acute condition of the digestive system. Moderately severe and severe AP progress rapidly, and early accurate identification is crucial for its management and prognostic assessment. However, effective and convenient predictive indicators remain lacking.

Objective To investigate the early dynamic changes of the systemic inflammatory response index (SIRI) in AP patients and its predictive value for AP severity.

Methods A total of 221 AP patients admitted to the Department of Gastroenterology, Beijing Tiantan Hospital, Capital Medical University between August 2020 and March 2023 and meeting the inclusion and exclusion criteria were enrolled. According to the 2012 revised Atlanta classification criteria, patients were divided into a mild group (MAP group, mild acute pancreatitis) and a non-mild group (non-MAP group, including moderately severe and severe acute pancreatitis). SIRI values (SIRI 0 h, SIRI 48 h) and C-reactive protein (CRP) (CRP 0 h, CRP 48 h) at admission and within 48 h after admission were retrieved from medical records. ROC analysis was performed, and the AUC was calculated to evaluate the value of SIRI in predicting non-MAP and compare it with the clinically commonly used inflammatory indicator CRP.

Results A total of 221 AP patients were included, including 102 in the MAP group and 119 in the non-MAP group. SIRI 0 h and SIRI 48 h were significantly higher in the non-MAP group than in the MAP group ($P<0.001$). ROC curves showed that the AUCs of SIRI 0 h and SIRI 48 h for predicting non-MAP were 0.685 (95%CI=0.615~0.756) and 0.753 (95%CI=0.689~0.816), respectively. Comparison with CRP at the same time points [0.607 (95%CI=0.533~0.681), 0.752 (95%CI=0.687~0.817)] revealed no statistically significant differences ($Z=1.67$, $P=0.095$; $Z=0.02$, $P=0.981$). The optimal cutoff value of SIRI 48 h for

predicting non-MAP was 2.49, with sensitivity, specificity, positive predictive value, and negative predictive value of 81.51%, 58.82%, 69.78%, and 73.17%, respectively.

Conclusion SIRI is an inexpensive and easily accessible detection method that can serve as an indicator for early assessment of AP severity.

Full Text

The Assessment Value of Systemic Inflammation Response Index in Evaluating the Severity of Acute Pancreatitis

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Abstract

Background: Acute pancreatitis (AP) is one of the common gastrointestinal emergencies, and the disease progression of moderately severe and severe AP is rapid. Early and accurate identification is crucial for effective intervention and prognosis assessment, yet there remains a lack of effective and simple predictive indicators. **Objective:** To investigate the early dynamic changes and predictive value of the systemic inflammation response index (SIRI) in patients with AP. **Methods:** A total of 221 AP patients who met the inclusion and exclusion criteria were enrolled from the Department of Gastroenterology, Beijing Tian Tan Hospital, Capital Medical University, between August 2020 and March 2023. According to the revised 2012 Atlanta criteria, patients were categorized into a mild group (MAP group, mild acute pancreatitis) and a non-mild group (non-MAP group, including moderately severe and severe acute pancreatitis). SIRI values (SIRI 0 h, SIRI 48 h) and C-reactive protein (CRP) levels (CRP 0 h, CRP 48 h) during admission and within 48 hours of admission were collected by reviewing medical records. Receiver operating characteristic (ROC) curves were plotted, and the area under the curve (AUC) was calculated to analyze the predictive value of SIRI for non-MAP and compare it with CRP as a common clinical inflammatory indicator. **Results:** A total of 221 AP patients were finally included, with 102 in the MAP group and 119 in the non-MAP group. SIRI 0 h and SIRI 48 h were significantly higher in the non-MAP group than in the MAP group ($P<0.001$). ROC curve analysis showed that the AUCs for SIRI 0 h and SIRI 48 h in predicting non-MAP were 0.685 (95%CI=0.615–0.756) and 0.753 (95%CI=0.689–0.816), respectively, with no significant difference compared with CRP [0.607 (95%CI=0.533–0.681) and 0.752 (95%CI=0.687–0.817)] during the corresponding time intervals ($Z=1.67$, $P=0.095$; $Z=0.02$, $P=0.981$). The optimal cut-off value for SIRI 48 h to predict non-MAP was 2.49, with

sensitivity, specificity, positive predictive value, and negative predictive value of 81.51%, 58.82%, 69.78%, and 73.17%, respectively. **Conclusion:** SIRI is an affordable and readily available test that can be used as an indicator for assessing the severity of early-stage AP.

Keywords: Acute pancreatitis; Systemic Inflammation Response Index; Predictive score; Severity; Inflammation

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Acute pancreatitis (AP) is an inflammatory disease of the digestive system caused by abnormal activation of pancreatic enzymes that digest the pancreas itself and surrounding organs. According to the revised Atlanta classification, approximately 20% of patients progress to moderately severe or severe AP due to exacerbated inflammatory responses. Severe acute pancreatitis (SAP) has been reported to have a mortality rate as high as 15%–20%. Therefore, early assessment of AP severity and timely intensive monitoring and active treatment of high-risk patients are crucial for improving prognosis and overall survival.

Although several scoring systems currently exist for evaluating AP severity, such as the Ranson score, APACHE II score, and BISAP score, they have limitations in clinical application due to their complexity, time-consuming nature, and poor timeliness. Simplified serum biomarkers like C-reactive protein (CRP) and interleukin-6 (IL-6) have been used to predict AP prognosis, but they are expensive, not readily available, and have limited predictive capacity. The systemic inflammation response index (SIRI) is a novel inflammatory index first proposed by Qi et al. in 2016 for predicting prognosis in pancreatic cancer patients undergoing chemotherapy, demonstrating good predictive efficacy. Recent studies have shown that SIRI can also predict outcomes in various severe diseases, including colorectal cancer, gallbladder cancer, hypertension, and heart failure. However, the clinical value of SIRI in AP patients has rarely been reported. Therefore, this study aimed to investigate the early dynamic changes of SIRI after admission in AP patients and its predictive value for severity compared with CRP.

Methods

Study Subjects A total of 221 AP patients admitted to the Department of Gastroenterology, Beijing Tian Tan Hospital, Capital Medical University between August 2020 and March 2023 who met the inclusion and exclusion criteria were enrolled. Inclusion criteria were: (1) diagnosis of AP according to the Chinese Guidelines for the Diagnosis and Treatment of Acute Pancreatitis (2019, Shenyang); (2) age 18–80 years; and (3) availability of detailed laboratory results and medical records. Exclusion criteria included: (1) admission more than 72 hours after symptom onset; (2) transfer from another institution; (3) acute exacerbation of chronic pancreatitis; (4) history of severe organ dysfunction such as renal failure, heart disease (NYHA $\geq$ class 3), or liver disease; (5) concurrent infection or inflammation at admission; (6) autoimmune disease, malignancy, or

hematologic disorder; (7) steroid or antibiotic use within 2 weeks before admission; (8) pregnancy or lactation; and (9) pancreatitis following trauma, surgery, tumor, or ERCP. For patients with multiple admissions, only the first admission was included. According to the hospital's treatment protocol, all patients routinely received intravenous broad-spectrum antibiotics within 24 hours of admission. This study was approved by the Ethics Committee of Beijing Tian Tan Hospital, Capital Medical University (approval number: KY2020-089-02), and all patients provided informed consent.

Data Collection General Information: Patient demographics including sex, age, BMI, medical history, and etiology were collected by reviewing medical records.

Serum Biochemical Indicators: Aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin (Alb), blood urea nitrogen (BUN), creatinine (Cr), and serum calcium were collected.

SIRI Calculation: SIRI was calculated as neutrophil count (N) × monocyte count (M) / lymphocyte count (L). SIRI values at admission (SIRI 0 h) and within 48 hours of admission (SIRI 48 h) were collected.

CRP Measurement: CRP levels at admission (CRP 0 h) and within 48 hours of admission (CRP 48 h) were collected.

Grouping According to the 2012 revised Atlanta classification criteria, patients were divided into: (1) mild acute pancreatitis (MAP): without organ failure or local/systemic complications; (2) moderately severe acute pancreatitis (MSAP): with transient organ failure (within 48 hours) or local/systemic complications; and (3) severe acute pancreatitis (SAP): with persistent organ failure (>48 hours). Organ failure was defined as a modified Marshall score $ $2 for any of the respiratory, circulatory, or renal systems. For analysis, MSAP and SAP were combined into the non-mild group (non-MAP group), while MAP patients constituted the MAP group.

Statistical Analysis Statistical analysis was performed using SPSS 26.0 and MedCalc 22.016 software, with graphs generated using GraphPad Prism 8.3.0. All data were tested for normality using the Shapiro-Wilk test. Normally distributed quantitative data were expressed as mean ± standard deviation and compared between groups using independent samples t-test. Non-normally distributed quantitative data were expressed as median (interquartile range) and compared using Mann-Whitney U test. Categorical data were analyzed using ^{2} test. ROC curves were plotted to evaluate AP severity, and AUCs were calculated. The optimal cut-off values and corresponding sensitivity, specificity, positive predictive value, and negative predictive value were determined based on the Youden index. Comparisons between different AUCs were performed using Delong's test. $P<0.05$ was considered statistically significant.

Results

Among the 221 patients, 102 were classified as MAP and 119 as non-MAP. Hypertriglyceridemia (36.2%) and gallstones (33.0%) were the most common etiologies of AP. There were no significant differences between the two groups in age, sex, BMI, medical history, etiology composition, or common biochemical indicators (P>0.05) .

Both groups showed peak SIRI values at admission (SIRI 0 h), which gradually decreased within 48 hours of admission (SIRI 48 h). In contrast, CRP levels were low at admission (CRP 0 h) and increased rapidly within 48 hours (CRP 48 h) in both groups. SIRI 0 h, SIRI 48 h, CRP 0 h, and CRP 48 h were all significantly higher in the non-MAP group compared with the MAP group (P<0.05) .

Predictive Value of SIRI and CRP for non-MAP At admission, the AUCs for CRP and SIRI in evaluating AP severity were 0.607 (95%CI=0.533–0.681, P=0.006) and 0.685 (95%CI=0.615–0.756, P<0.001), respectively, with optimal cut-off values of 18.59 mg/L and 3.77. Within 48 hours of admission, the AUCs for CRP and SIRI were 0.752 (95%CI=0.687–0.817, P<0.001) and 0.753 (95%CI=0.689–0.816, P<0.001), respectively, with optimal cut-off values of 104.12 mg/L and 2.49. Delong's test showed no significant difference between the AUCs of CRP and SIRI at either admission or within 48 hours (Z=1.67, P=0.095; Z=0.02, P=0.981). The sensitivity, specificity, positive predictive value, and negative predictive value of each indicator at different time points are shown in and [Figure 1: see original paper].

Discussion

AP is a common digestive system disease with a global incidence increasing at approximately 3.07% annually, imposing a substantial burden on healthcare systems. Moderately severe and severe patients experience rapid disease progression that may lead to severe complications and life-threatening conditions. Early and accurate identification of patients at risk for severe disease is essential for providing timely intensive care, improving prognosis, and preventing adverse outcomes. Currently, various indicators and scoring systems are used clinically to assess AP severity. However, these methods have limitations. For example, although CRP is widely studied and considered a "gold standard" for evaluating disease severity, it requires 48–72 hours to become accurate, with a sensitivity of only 53% for predicting SAP when using a cut-off of 15 mg/dL at 24 hours. The Ranson score, as one of the earliest assessment tools, requires 48 hours for completion, potentially missing the optimal treatment window. While the APACHE II score can be performed daily to monitor treatment effects, its complexity limits clinical application. The BISAP score is simple and can predict organ failure and pancreatic necrosis well, but its accuracy requires further validation through additional clinical studies. Therefore, early, rapid, and accurate assessment of disease severity remains a key focus and challenge in AP

clinical management.

Accumulating evidence indicates that early and persistent activation of inflammation is the primary cause of severe local and systemic complications in AP patients. Consequently, monitoring inflammatory markers during the early disease stage is important for prognosis assessment. As a novel inflammatory index, SIRI integrates changes in neutrophils, lymphocytes, and monocytes, making it more economical, comprehensive, and accessible than previous inflammatory biomarkers. SIRI can reflect the body's inflammatory and immune status, and its role in predicting adverse outcomes in various malignancies and diseases such as hypertension, heart failure, and idiopathic pulmonary fibrosis has been confirmed. In AP, only one study has evaluated SIRI's clinical value, showing high predictive ability for SAP at 48 hours after onset (AUC 0.906), with sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 82%, 87%, 53%, 96%, and 85%, respectively, when SIRI>7.14.

The exact mechanism by which SIRI assesses AP severity remains unclear but can be attributed to the pathophysiological role of peripheral blood in systemic inflammatory response and disease progression. Studies have shown that in early SAP, abnormal activation of trypsinogen causes pancreatic injury, which induces sterile inflammatory signals that chemoattract neutrophils to the injury site, releasing numerous inflammatory factors and cytotoxic substances that trigger an inflammatory cascade, leading to progressive pancreatic damage and rapid progression from local inflammation to systemic inflammatory response syndrome and multiple organ dysfunction. Conversely, significant lymphocyte reduction may cause immune dysfunction, with immunosuppression potentially involved in the complex process of inflammation and infection caused by impaired intestinal mucosal barrier function in AP patients. Reduced total peripheral blood lymphocyte count at admission has been closely associated with poor AP prognosis. Additionally, after pancreatic injury, monocytes derived from bone marrow are recruited to the inflamed pancreas and activated into M1 macrophages, driving inflammation and acinar cell death. Thus, in AP, rising neutrophil and monocyte counts and declining lymphocyte numbers all reflect disease severity. Therefore, SIRI may more accurately reflect the level of inflammatory response and predict disease severity than absolute counts of individual cell types.

Based on the 2012 revised Atlanta classification, this study aimed to investigate SIRI's ability to differentiate mild from non-mild AP during the initial stage. To further assess its clinical value, we simultaneously collected CRP data for comparison. We found that SIRI values peaked at admission in both groups and gradually decreased within 48 hours, whereas CRP levels were low at admission and increased rapidly within 48 hours, consistent with previous observations. Throughout the study, SIRI and CRP levels in the non-MAP group remained significantly higher than in the MAP group, indicating more pronounced inflammatory responses in non-MAP patients. ROC curve analysis demonstrated that at admission, SIRI had a higher AUC than CRP for diagnosing non-mild AP

(0.685 vs. 0.607), with sensitivity of 63.86% compared to only 36.13% for CRP, possibly because CRP had not yet peaked in the early disease stage. Within 48 hours of admission, both SIRI and CRP showed improved diagnostic performance for non-MAP (AUC 0.753 vs. 0.752), but SIRI demonstrated higher sensitivity (81.51% vs. 68.91%), suggesting its superiority in early diagnosis of non-MAP. Delong's test revealed no statistically significant differences between AUCs at different time points, likely influenced by sample size and other unconsidered clinical variables. We also calculated optimal cut-off values based on the Youden index to provide benchmarks for early qualitative assessment of AP severity. In this study, the SIRI cut-off values for predicting non-MAP at admission and within 48 hours were 3.77 and 2.49, respectively. In contrast, Pedro et al. reported a cut-off of 7.14 for predicting SAP at 48 hours after onset. The substantial difference may be attributed to their study including only patients with biliary pancreatitis, who are prone to concurrent infection, as well as differences in antibiotic use and severity assessment criteria.

This study has several limitations. First, as a retrospective single-center study, prospective multicenter studies are needed to validate the accuracy and generalizability of our findings. Second, we did not compare SIRI with commonly used clinical scoring systems such as BISAP and APACHE II. Third, due to the hospital's treatment protocol, all confirmed AP patients received broad-spectrum antibiotics at admission, and further research is needed to explore whether antibiotics affect SIRI.

In conclusion, there is currently no universally accepted indicator for early, rapid, and simple assessment of AP severity. This study is the first to systematically evaluate the early dynamic changes of SIRI in AP patients and explore its predictive value for non-MAP compared with CRP. The results demonstrate that SIRI exhibits more stable and earlier diagnostic capability for non-mild AP than the traditional inflammatory indicator CRP and can serve as a simpler and more widely available reference index for assessing AP prognosis and improving patient management, though further validation studies are warranted.

References

[1] BANKS P A, BOLLEN T L, DERVENIS C, et al. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus[J]. Gut, 2013, 62(1): 102-111. DOI: 10.1136/gutjnl-2012-302779.

[2] BOXHOORN L, VOERMANS R P, BOUWENSE S A, et al. Acute pancreatitis[J]. Lancet, 2020, 396(10252): 726-734. DOI: 10.1016/s0140-6736(20)31310-6.

[3] LEEPPÄNIEMI A, TOLONEN M, TARASCONI A, et al. 2019 WSES guidelines for the management of severe acute pancreatitis[J]. World J Emerg Surg, 2019, 14: 27. DOI: 10.1186/s13017-019-0247-0.

[4] MEDEROS M A, REBER H A, GIRGIS M D. Acute pancreatitis[J]. JAMA,

2021, 325(4): 382. DOI: 10.1001/jama.2020.20317.

[5] KNAUS W A, DRAPER E A, WAGNER D P, et al. APACHE II: a severity of disease classification system[J]. Crit Care Med, 1985, 13(10): 818-829.

[6] RANSON J H, RIFKIND K M, ROSES D F, et al. Prognostic signs and the role of operative management in acute pancreatitis[J]. Surg Gynecol Obstet, 1974, 139(1): 69-81.

[7] WU B U, JOHANNES R S, SUN X, et al. The early prediction of mortality in acute pancreatitis: a large population-based study[J]. Gut, 2008, 57(12): 1698-1703. DOI: 10.1136/gut.2008.152702.

[8] CHO S K, JUNG S, LEE K J, et al. Neutrophil to lymphocyte ratio and platelet to lymphocyte ratio can predict the severity of gallstone pancreatitis[J]. BMC Gastroenterol, 2018, 18(1): 18. DOI: 10.1186/s12876-018-0748-4.

[9] QI Q, ZHUANG L P, SHEN Y H, et al. A novel systemic inflammation response index (SIRI) for predicting the survival of patients with pancreatic cancer after chemotherapy[J]. Cancer, 2016, 122(14): 2158-2167. DOI: 10.1002/cncr.30057.

[10] CAO Y H, ZHENG X, HU Y G, et al. Levels of systemic inflammation response index are correlated with tumor-associated bacteria in colorectal cancer[J]. Cell Death Dis, 2023, 14(1): 69. DOI: 10.1038/s41419-023-05602-9.

[11] SUN L J, HU W M, LIU M X, et al. High systemic inflammation response index (SIRI) indicates poor outcome in gallbladder cancer patients with surgical resection: a single institution experience in China[J]. Cancer Res Treat, 2020, 52(4): 1199-1210. DOI: 10.4143/crt.2020.303.

[12] ZHAO S F, DONG S Y, QIN Y K, et al. Inflammation index SIRI is associated with increased all-cause and cardiovascular mortality among patients with hypertension[J]. Front Cardiovasc Med, 2022, 9: 1066219. DOI: 10.3389/fcvm.2022.1066219.

[13] WANG X, NI Q W, WANG J, et al. Systemic inflammation response index is a promising prognostic marker in elderly patients with heart failure: a retrospective cohort study[J]. Front Cardiovasc Med, 2022, 9: 871031. DOI: 10.3389/fcvm.2022.871031.

[14] DU Y Q, CHEN Q K, LI H Y, et al. Chinese guidelines for the diagnosis and treatment of acute pancreatitis (2019, Shenyang)[J]. J Clin Hepatol, 2019, 35(12): 2706-2711.

[15] MARSHALL J C, COOK D J, CHRISTOU N V, et al. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome[J]. Crit Care Med, 1995, 23(10): 1638-1652. DOI: 10.1097/00003246-199510000-00007.

[16] IANNUZZI J P, KING J A, LEONG J H, et al. Global incidence of acute pancreatitis is increasing over time: a systematic review and meta-analysis[J]. Gastroenterology, 2022, 162(1): 122-134. DOI: 10.1053/j.gastro.2021.09.043.

[17] TENNER S, BAILLIE J, DEWITT J, et al. American College of Gastroenterology guideline: management of acute pancreatitis[J]. Am J Gastroenterol, 2013, 108(9): 1400-1415; 1416. DOI: 10.1038/ajg.2013.218.

[18] VAN DEN BERG F F, DE BRUIJN A C, VAN SANTVOORT H C, et al. Early laboratory biomarkers for severity in acute pancreatitis; a systematic review and meta-analysis[J]. Pancreatology, 2020, 20(7): 1302-1311. DOI: 10.1016/j.pan.2020.09.007.

[19] STAUBLI S M, OERTLI D, NEBIKER C A. Laboratory markers predicting severity of acute pancreatitis[J]. Crit Rev Clin Lab Sci, 2015, 52(6): 273-283. DOI: 10.3109/10408363.2015.1051659.

[20] SAH R P, DAWRA R K, SALUJA A K. New insights into the pathogenesis of pancreatitis[J]. Curr Opin Gastroenterol, 2013, 29(5): 523-530. DOI: 10.1097/MOG.0b013e328363e399.

[21] YANG Z W, MENG X X, XU P. Central role of neutrophil in the pathogenesis of severe acute pancreatitis[J]. J Cell Mol Med, 2015, 19(11): 2513-2520. DOI: 10.1111/jcmm.12639.

[22] BAILEY-WHYTE M, MINAS T Z, DORSEY T H, et al. Systemic inflammation indices and association with prostate cancer survival in a diverse patient cohort[J]. Cancers, 2023, 15(6): 1869. DOI: 10.3390/cancers15061869.

[23] ACHAIAH A, RATHNAPALA A, PEREIRA A, et al. Neutrophil lymphocyte ratio as an indicator for disease progression in Idiopathic Pulmonary Fibrosis[J]. BMJ Open Respir Res, 2022, 9(1): e001202. DOI: 10.1136/bmjresp-2022-001202.

[24] SILVA-VAZ P, ABRANTES A M, MORGADO-NUNES S, et al. Evaluation of prognostic factors of severity in acute biliary pancreatitis[J]. Int J Mol Sci, 2020, 21(12): 4300. DOI: 10.3390/ijms21124300.

[25] LI J P, YANG J, HUANG J R, et al. Immunosuppression and the infection caused by gut mucosal barrier dysfunction in patients with early severe acute pancreatitis[J]. Front Biosci, 2013, 18(3): 892-900. DOI: 10.2741/4150.

[26] SHEN X, SUN J, KE L, et al. Reduced lymphocyte count as an early marker for predicting infected pancreatic necrosis[J]. BMC Gastroenterol, 2015, 15: 147. DOI: 10.1186/s12876-015-0381-7.

[27] WU J H, ZHANG L, SHI J J, et al. Macrophage phenotypic switch orchestrates the inflammation and repair/regeneration following acute pancreatitis injury[J]. EBioMedicine, 2020, 58: 102920. DOI: 10.1016/j.ebiom.2020.102920.

[28] CARDOSO F S, RICARDO L B, OLIVEIRA A M, et al. C-reactive protein prognostic accuracy in acute pancreatitis: timing of measurement and cutoff points[J]. Eur J Gastroenterol Hepatol, 2013, 25(6): 784-789. DOI: 10.1097/MEG.0b013e32835fd3f0.

Author Contributions: LI Sisi was responsible for study conception and design, data collection and analysis, and manuscript writing. HE Qiang developed the writing framework and revised the manuscript. XU Youqing was responsible for final version revision and overall accountability for the article.

Conflict of Interest: The authors declare no conflict of interest.

Tables and Figures

Table 1 Comparison of baseline data between the two groups of patients at admission

Table 2 Comparison of SIRI and CRP between the two groups of patients at different time periods

Table 3 Comparison of serum CRP and SIRI for predicting the severity of AP

Figure 1 [Figure 1: see original paper] ROC curves of CRP and SIRI for predicting AP severity at different time periods

Note: Figure translations are in progress. See original paper for figures.