



# Comparison of Scoring Systems in Predicting Severity and Prognosis of Hypertriglyceridemia-Induced Acute Pancreatitis

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## Abstract

**Background** In China, hyperlipidemia is the second major reason of acute pancreatitis.

**Aims** Comparison of Scoring Systems in identification patients at risk for severe acute pancreatitis (SAP), pancreatic necrosis (PNec), and infected pancreatic necrosis (IPN) early in the course of hypertriglyceridemia-induced acute pancreatitis (HTG-AP).

**Methods** Predictive accuracy of scoring systems was measured by the area under the receiver operating characteristic curve (AUC) in a retrospective study. Pairwise AUC comparisons were performed to calculate the difference between scoring systems.

**Results** A total of 238 patients diagnosed with HTG-AP were included. Sixty patients (25.2%) were classified as SAP. Twenty-nine patients (12.2%) had evidence of PNec. Nine patients (3.8%) were diagnosed with IPN. One patient (0.4%) died during hospitalization. In predicting SAP in HTG-AP, the AUCs of APACHE-II, SOFA, SIRS, Ranson's, BISAP, and MMS were 0.77, 0.83, 0.73, 0.88, 0.83, and 0.85, respectively; in predicting PNec, were 0.75, 0.77, 0.75, 0.86, 0.80, and 0.75, respectively; and in predicting IPN, were 0.92, 0.86, 0.76, 0.85, 0.84, and 0.87, respectively. Pairwise AUC comparisons revealed that Ranson's, MMS, BISAP, and SOFA had higher accuracy than SIRS, Ranson's and MMS had higher accuracy than APACHE-II in predicting SAP; Ranson's had the same accuracy with BISAP, but higher than other four criteria in predicting PNec; APACHE-II had higher accuracy than SIRS in predicting IPN.

**Conclusions** APACHE-II had high performance in predicting IPN, and all other score systems had medium performance in predicting SAP, PNec, and IPN in HTG-AP. Each score has its merit and weakness; BISAP may be the best criterion in predicting severity and prognosis of HTG-AP.

**Keywords** Hypertriglyceridemia · Severe acute pancreatitis · Pancreatic necrosis · Infected pancreatic necrosis

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## Introduction

Acute pancreatitis (AP) is a common disorder and is associated with several etiologies. In Western countries, biliary sludge and/or gallstones are the most prevalent

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(approximately 40–50%) cause, alcohol is the second most frequent (approximately 20%) cause [1, 2], and hypertriglyceridemia (HTG) is considered the third most common etiology and accounts for 7–10% of AP cases [3–5]. In China, the proportion of hypertriglyceridemia-induced AP (HTG-AP) is more than 10% [6–8], comes to as the second major reason of AP [9].

For most patients, AP has a mild course with a brief hospitalization [10]. Although the clinical course of HTG-AP is similar to other forms of AP, the complication rate and severity are significantly higher [5, 11]. Some patients (15–20%) develop severe AP (SAP), which is characterized by persistent organ failure, with a mortality reported to be as great as 36–50% [10, 12]. About 5–10% of patients develop necrosis of the pancreatic parenchyma, the peripancreatic tissue or both [10]. Necrotizing pancreatitis (PNec) is associated with significant morbidity, and mortality should undergo aggressive treatment at hospital [13]. The diagnosis of infected pancreatic necrosis (IPN) is also important because of the need for antibiotic treatment and likely intervention [14]. The presence of IPN indicates severe disease and relative high risk of mortality [15]. So, it is very important to recognize risk factors for SAP and detect PNec and IPN in early phase of HTG-AP, to triage patients appropriately to intensive care units (ICU) and deliver specific therapies.

So far, there are a large number of predictors to predict the severity and prognosis of AP, including clinical presentation, imaging, various scoring systems and laboratory tests [16]. There is research found that certain difference exists in etiologic distribution between difference score system [8]. The aim of this study is to compare several scoring systems, including acute physiology and chronic health examination (APACHE)-II, sequential organ failure assessment (SOFA), systemic inflammatory response syndrome (SIRS), Ranson's criteria, bedside index for severity in Acute Pancreatitis (BISAP), and modified Marshall scoring (MMS), in predicting SAP, PNec, and IPN in a retrospective cohort of patients with HTG-AP.

## Materials and Methods

### Study Design and Patients

We identified potential patients using the discharge diagnoses of HTG-AP and AP with HTG. The diagnosis and severity of AP were determined based on the 2012 Atlanta criteria, which require at least two of the following three criteria to be fulfilled: (1) abdominal pain consistent with AP; (2) serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal; and (3) characteristic findings of AP on contrast-enhanced computed tomography (CECT), magnetic resonance imaging (MRI) or

transabdominal ultrasonography [10]. According to Atlanta's criteria, AP is divided into three degrees of severity: mild (MAP), moderately severe (MSAP), and severe (SAP). MAP is characterized by the absence of organ failure and the absence of local or systemic complications, whereas SAP is defined by the presence of persistent organ failure ( $\geq 48$  h); MSAP includes the presence of transient organ failure ( $< 48$  h) or local or systemic complications without persistent organ failure [10]. Three organ systems should be assessed to define organ failure: respiratory, cardiovascular, and renal. Organ failure is defined as a score of two or more for one of these three organ systems using the MMS [10]. CECT scans were reviewed by radiologists who dedicated to abdominal imaging and were blinded to clinical course and laboratory data, to categorize PNec according to the 2012 revision of the Atlanta Classification [10]. The diagnosis of IPN is presumed when the patient's clinical manifestations combined with extraluminal gas in the pancreatic and/or peripancreatic tissues on CECT or when the first aspiration of image-guided percutaneous drainage is positive for bacteria and/or fungi on Gram stain and/or culture.

Inclusion criteria include patients who was admitted to our hospital within three days after symptom onset, and serum triglyceridemic (TG) level reaches 11.3 mmol/L (or 1000 mg/dl) after excluding other known risk factors of AP [3]. Exclusion criteria included patients  $< 18$  years old, discharged without medical advice and duration of hospitalization less than 48 h, transferred from other hospitals, chronic pancreatitis, and concomitant with other serious conditions, such as severe infectious or immunosuppressive conditions, active malignancy, multiple organ dysfunction due to other diseases. The electronic medical records of 348 HTG-AP patients from Sir Run Run Shaw Hospital affiliated to medical college of Zhejiang University from January 1, 2016 to December 31, 2018 were retrospectively analyzed. Some patients met at least one exclusion criteria; the total number of eligible for this study was 238 patients. This retrospective study was approval by the Ethics Committee of Sir Run Run Shaw Hospital (Approval number: scientific research 20180611-6). The registration number was Chi-CRT1900020828 on Chinese Clinical Trial Register.

Extensive demographic such as age, height, weight, smoking habit, alcohol consumption, preexisting comorbidity such as diabetes mellitus, hypertension, hyperlipidemia, and pre-existing organ dysfunction (including chronic respiratory disease, chronic renal disease and cardiovascular disease), and the previous history of HTG-AP, radiographic, and laboratory data were collected. The APACHE-II, SOFA, SIRS and BISAP scores were calculated using data from the first 24 h after admission, the MMS, Ranson's score using data from the first 48 h after admission. All scoring systems calculated the worst laboratory indicators and vital signs during the evaluation period. Electronic medical records and paper charts were

reviewed by two independent physicians to calculate scores, inconsistent scores needed to be recalculated until came to the same score. No points were added to the scoring systems for missing values.

## Statistical Analysis

Statistical analysis was performed using SPSS 20.0 software (Statistical Package for Social Sciences, Chicago, IL, USA). Continuous dates were presented as mean  $\pm$  standard deviation (SD). Categorical data were described by frequencies and percentages (%). The predictive accuracy was measured by the area under the receiver operating curve (AUC). If AUC values between 0.5 and 0.7, the predictive value is low, between 0.7 and 0.9 is medium, and more than 0.9 is high [17]. Pairwise AUC comparisons were performed using MedCalc for Windows, version 16.8.4 (MedCalc Software, Ostend, Belgium), between different scoring systems at a time to determine whether the difference was statistically significant.  $P < 0.05$  was accepted as statistically significant. The optimal cutoff values of scoring systems were determined by ROC curve analysis and were used to calculate sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

## Results

### Patient Characteristics

A total of 238 patients with HTG-AP were retrospectively analyzed. All patients were admitted within 3 days after symptom onset. The median age was  $39.76 \pm 9.83$  years old (range 19–65), with 71 females (29.8%) and 167 males (70.2%), and all were Chinese. Sixty patients (25.2%) were diagnosed as SAP, and 101 (42.4%) were MAP and 77 (32.4%) were MSAP. Fifty-nine patients (24.8%) developed persistent respiratory failure, eight patients (3.4%) developed persistent renal failure, and only one patient with persistent cardiovascular failure. Twenty-nine patients (12.2%) had evidence of PNec on CECT. IPN occurred in 9 patients (3.8%). The average length of hospital stays was  $11.79 \pm 11.22$  days (range 3–117). One hundred and one patients (42.4%) admitted to ICU, and only 1 patient (0.4%) died during hospitalization. Seventy-eight patients (32.8%) underwent double filtration plasmapheresis (DFPP) after admission. One hundred and thirty-one patients (55%) had recurrent HTG-AP.

### Comparison of Scoring Systems in Predicting SAP, PNec, and IPN in HTG-AP

The AUC value, 95%CI, p value, cutoff value, sensitivity, specificity, PPV and NPV of six scoring systems in

predicting SAP, PNec, and IPN in HTG-AP are shown in Table 1. AUCs of all the criteria are statistically significant ( $P < 0.05$ ). In predicting SAP, the AUCs of APACHE-II, SOFA, SIRS, Ranson's, BISAP, and MMS were 0.77(0.70–0.84), 0.83(0.76–0.89), 0.73(0.66–0.80), 0.88(0.83–0.93), 0.83(0.77–0.90), and 0.85(0.80–0.91), respectively (Table 1). Pairwise comparisons of the AUCs between the six scoring systems revealed that Ranson's, MMS, BISAP, and SOFA had higher accuracy than SIRS, Ranson's and MMS had higher accuracy than APACHE-II ( $P < 0.05$ ), and Ranson's, MMS, BISAP, and SOFA had the same performance ( $P > 0.05$ ) (Fig. 1). The sensitivity and NPV of Ranson's score were the highest, and the specificity and PPV of BISAP were the highest.

In predicting PNec, the AUCs of APACHE-II, SOFA, SIRS, Ranson's, BISAP, and MMS were 0.75(0.65–0.85), 0.77(0.68–0.86), 0.75(0.66–0.84), 0.86(0.80–0.93), 0.80(0.72–0.89), and 0.75(0.65–0.84), respectively (Table 1). Pairwise comparisons of the AUCs between the six scoring systems revealed that Ranson's had the same accuracy as BISAP, but higher than other four criteria (Fig. 2). Therefore, Ranson's and BISAP had a better performance in predicting PNec. Ranson's score had the highest sensitivity and NPV, APACHE-II had the highest specificity, and BISAP had the highest PPV.

In predicting IPN, the AUCs of APACHE-II, SOFA, SIRS, Ranson's, BISAP, and MMS were 0.92(0.85–0.99), 0.86(0.74–0.98), 0.76(0.61–0.91), 0.85(0.71–1.00), 0.84(0.68–1.00), and 0.87(0.77–0.97), respectively (Table 1). Pairwise comparisons of the AUCs between the six scoring systems revealed that APACHE-II had higher accuracy than SIRS ( $P < 0.05$ ), and all other criteria difference were not statistically significant ( $P > 0.05$ ) (Fig. 3). The cutoffs of APACHE-II, SOFA, SIRS, Ranson's, BISAP, and MMS were 10, 2, 3, 6, 2, and 2, respectively. APACHE-II, SOFA, BISAP and MMS scores had the same sensitivity, BISAP had the highest NPV, and Ranson's had the highest specificity and PPV.

## Discussion

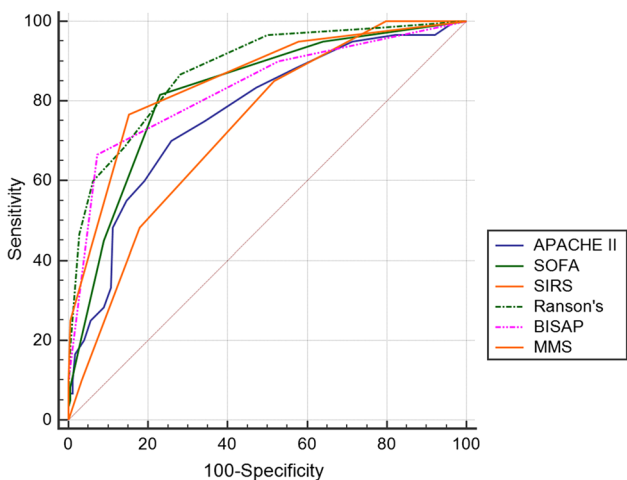
In this retrospective study, we compared the accuracy of APACHE-II, SOFA, SIRS, Ranson's, BISAP, and MMS six scoring systems in predicting severity, PNec and IPN in HTG-AP. In our cohort, sixty HTG-AP patients (25.2%) were classified as SAP. Twenty-nine patients (12.2%) had evidence of PNec on CECT. IPN occurred in nine patients (3.8%). only one patient (0.4%) died during hospitalization, so we just assessed PNec and IPN as prognostic indicators.

APACHE-II is a frequently used scoring system to assess severity of patients in ICU and is used for assessment and monitoring AP since 1989 [18]. Though it used

**Table 1** Comparison of six scoring systems in predicting SAP, PNec, and IPN

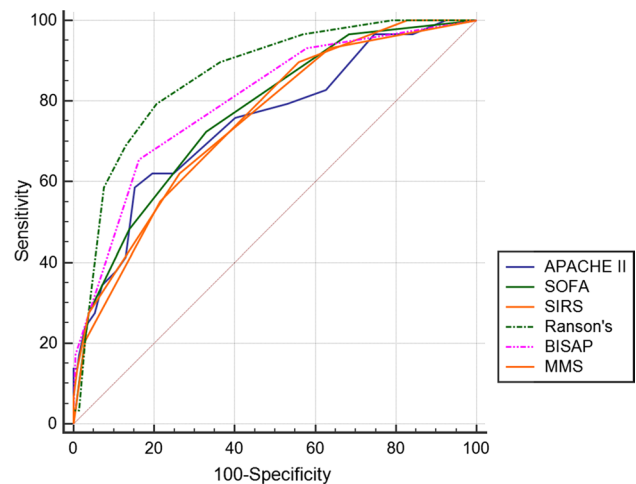
Score	AUC	95% CI	P	Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
<b>SAP</b>								
APACHE-II	0.77	0.70–0.84	0.000	8	70.0	74.2	47.7	88.0
SOFA	0.83	0.76–0.89	0.000	2	81.7	77.0	54.4	92.6
SIRS	0.73	0.66–0.80	0.000	2	85.0	48.3	35.6	90.5
Ranson’s	0.88	0.83–0.93	0.000	3	86.7	71.9	51.0	94.1
BISAP	0.83	0.77–0.90	0.000	2	66.7	92.7	75.5	89.2
MMS	0.85	0.80–0.91	0.000	2	76.7	84.8	63.0	91.5
<b>PNec</b>								
APACHE-II	0.75	0.65–0.85	0.000	11	58.6	84.7	34.7	93.7
SOFA	0.77	0.68–0.86	0.000	2	72.4	67.0	23.3	94.6
SIRS	0.75	0.66–0.84	0.000	3	55.2	78.5	26.2	92.7
Ranson’s	0.86	0.80–0.93	0.000	4	79.3	79.4	34.8	96.5
BISAP	0.80	0.72–0.89	0.000	2	65.5	83.7	35.8	94.6
MMS	0.75	0.65–0.84	0.000	2	62.1	73.7	24.7	93.3
<b>IPN</b>								
APACHE-II	0.92	0.85–0.99	0.000	10	88.9	77.7	13.6	99.4
SOFA	0.86	0.74–0.98	0.000	2	88.9	64.2	8.9	99.3
SIRS	0.76	0.61–0.91	0.008	3	66.7	76.0	9.8	98.3
Ranson’s	0.85	0.71–1.00	0.000	6	77.8	88.6	21.2	99.0
BISAP	0.84	0.68–1.00	0.001	2	88.9	80.3	15.1	99.5
MMS	0.87	0.77–0.97	0.000	2	88.9	71.6	11.0	99.4

SAP severe acute pancreatitis, PNec pancreatic necrosis, IPN infected pancreatic necrosis, PPV positive predictive value, NPV negative predictive value, APACHE-II acute physiology, and chronic health examination-II, SOFA sequential organ failure assessment, SIRS systemic inflammatory response syndrome, BISAP bedside index for severity in acute pancreatitis, MMS modified Marshall scoring



**Fig. 1** Comparisons of the AUCs between scoring systems in prediction of SAP

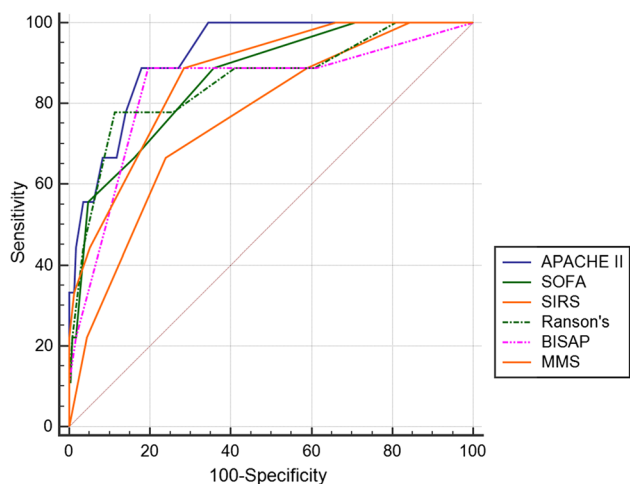
to be recognized as the most useful scoring system in AP and recommended by several guidelines [19, 20]. In our study, it had medium value in predicting SAP and PNec and AUCs value were 0.77 and 0.75, respectively. As for predicting IPN, it had high performance with the highest



**Fig. 2** Comparisons of the AUCs between scoring systems in prediction of PNec

AUC and AUC was 0.92. It can be completed within 24 h, but the operation is cumbersome with many indicators.

Organ failure is a marker of the severity of pancreatitis. There are several scoring systems assessing for organ failure but do not directly measure the severity of AP. SOFA is developed to describe organ dysfunction/failure in sepsis



**Fig. 3** Comparisons of the AUCs between scoring systems in prediction of IPN

[21]. It also has been used to predict mortality after organ failure for other reasons. These include acute liver failure after acetaminophen overdose [22], and cancer patients [23]. In our cohort, SOFA had medium value in predicting SAP, PNec, and IPN. The AUCs were 0.83, 0.77, and 0.86, respectively. It was simpler but had the same performance as APACHE-II in predicting SAP, PNec, and IPN.

SIRS score is simple and widely used in clinic. Several studies shown that SIRS score can predict the severity of AP [24, 25]. In this study, it had medium performance with the lowest AUC in predicting SAP, PNec, and IPN. The AUCs were 0.73, 0.75, and 0.76, respectively. The cutoffs of them were 2, 3, and 3, respectively. It is not a priority score in predicting SAP, PNec, and IPN.

Ranson's criteria are one of the earliest scoring systems to predict the severity of AP [26]. It consists of eleven parameters; five factors are assessed at admission and six are assessed during the next 48 h. In our HTG-AP cohort, it had medium and the same performance as BISAP though its AUC was higher in predicting SAP, PNec, and IPN and the difference in AUC was not statistically significant. In predicting SAP and PNec, it had the highest AUC, sensitivity and NPV. In predicting IPN, the AUCs of Ranson's criteria were 0.85, and the cutoff was 6. The specificity and PPV were the highest among all the criteria.

BISAP score is a simple scoring system initially proposed by Wu et al. [27] and can be assessed during the first 24 h. In this study, it had a moderate value in predicting SAP, PNec, and IPN. The AUCs were 0.83, 0.80, and 0.84, respectively. All cutoffs were two. It had the highest specificity and PPV for SAP, and highest sensitivity and NPV for IPN. Its performance was the same as Ranson's criteria, but it is simpler and can be completed within 24 h after admission.

The MMS has the merit of simplicity, universal applicability across international centers and is preferred to the SOFA scoring system [10]. It has the advantage of being used on presentation and repeated daily. The 2012 Atlanta criterion defined organ failure as a score of two or more for one of three organ systems using the MMS criterion. In our study, MMS had medium value in predicting SAP, PNec, and IPN. The AUCs were 0.85, 0.75, and 0.87, respectively. It had similar performance in predicting SAP, PNec, and IPN as SOFA score, and it is simpler but it takes 48 h to complete.

In conclusion, all score systems had medium performance in predicting SAP and PNec in HTG-AP. Among them, Ranson's score had the highest AUC value, sensitivity and NPV. In predicting IPN, APACHE-II had high performance and the highest AUC value, but the difference in AUC between APACHE-II and other criteria was not statistically significant except SIRS. Considering that only nine patients in this study had IPN, the results may be inaccurate. In our study, though different values of scoring system in predicting SAP, PNec, and IPN but the difference is marginal. The difference in AUC between Ranson's and BISAP was not statistically significant in predicting SAP, PNec, and IPN. BISAP score was simpler and can be completed within 24 h after admission. MMS had similar performance as SOFA score, and MMS is simpler but SOFA can be completed within 24 h. SIRS is not a priority score in HTG-AP. Combined with the characteristics of each score, BISAP may be the best criterion in predicting severity and prognosis of HTG-AP. This was a single-center retrospective study; further studies are needed to confirm the results.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required.

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**Compliance with Ethical Standards**

**Conflicts of interest** All authors declare no conflicts of interest.

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