Increased circulating total bile acid levels were associated with organ failure in patients with acute pancreatitis

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Abstract

Background: Recent studies have shown that bile acids (BAs) are closely related to metabolic and inflammatory diseases. Our study aimed to investigate whether circulating total bile acid (TBA) levels were associated with the severity of acute pancreatitis (AP).

Methods: We retrospectively collected data on patients diagnosed with AP in a tertiary center from 01 January 2014 to 31 December 2016. Patients were divided into the high TBA (HTBA) group and the normal TBA (NTBA) group according to whether the highest TBA value (TBA_{max}) within 7 days after admission was ≥10μmol/L. The prognosis and complications, including death, organ failure (OF) and pancreatic necrosis, were compared between the two groups. Univariate and multivariate logistic regression analysis were used to evaluate the relationship between circulating TBA and organ failure in AP patients.

Results: 293 patients were included in this study, of whom 18.43% (54/293) were in the HTBA group. The incidence of OF in the HTBA group was significantly higher than that in the NTBA group (59.3% vs 17.2%; $P < 0.001$), and the AP severity classification in the HTBA group was more serious than that in the NTBA group. The pancreatic necrosis rate, percutaneous catheter drainage (PCD) rate, open surgery rate and mortality rate in the HTBA group were higher than those in the NTBA group. Multivariate regression analysis showed that HTBA (odds ratio (OR), 4.894; $P = 0.002$) was an independent risk factor for AP complicated with OF.

Conclusions: The increase of circulating TBA in early stage of AP is independently related to organ failure, which indicates the adverse prognosis of AP patients.

Background

Acute pancreatitis refers to an acute inflammation occurred in the pancreas, the annual incidence rate of which is about 13–45 cases / 100,000 worldwide and it is one of the most common digestive diseases requiring hospitalization[1, 2]. About 15% -20% of AP patients whose inflammation is not limited to the pancreas, but also involving the peripancreatic tissue and other distant organs, secondary to the local or systemic complications, developed into severe acute pancreatitis (SAP)[3, 4]. The mortality of SAP is reported as high as 40% -70%[5].The most common systemic complication is organ failure including acute respiratory distress syndrome (ARDS), acute kidney injury (AKI) and shock[6]. Therefore, it is important to identify the risk factors for OF, so that severe patients can be recognized in the early course of AP and receive appropriate and effective interventions.

Bile acids (BAs) are steroidal molecules generated in the liver by cholesterol oxidation, which have multiple physiological functions including stimulation of bile flow, intestinal absorption of lipophilic nutrients, maintenance of cholesterol homeostasis and regulation the metabolism of lipid, glucose and energy[7–9]. In addition, some studies have demonstrated that BAs can also regulate the inflammatory response of organs[9–11] and alleviate endoplasmic stress[10, 12, 13] through dedicated BAs receptors

such as the farnesoid X receptor (FXR) and the G-protein coupled receptor TGR5. Dysregulation of BAs transport and impaired BAs receptor signaling may contribute to the pathogenesis of some metabolic diseases such as non-alcoholic fatty liver disease, obesity, type 2 diabetes, and atherosclerosis[14]. The circulating TBA levels are maintained within a certain range under physiological conditions, generally 2–10 μmol/L[15], but in some states of diseases, the levels of circulating TBA will exceed the threshold. An increase in circulating TBA is predominately detected in several hepatobiliary diseases. For example, portasystemic shunting or damaged hepatocytes which are unable to extract the bile acids from the portal blood and extrahepatic obstruction in which bile acids leak directly from the liver to the systemic circulation may contribute to the elevated circulating TBA. Thus, circulating TBA is often used as an effective biomarker for the diagnosis of hepatobiliary diseases[16]. Additionally, some studies illuminated that the levels of circulating TBA were elevated in patients with metabolic diseases such as obesity and type 2 diabetes [17–20].

The studies about the relationship between BAs and AP are currently limited to the damage and inflammation of pancreatic acinar cells in experimental acute pancreatitis induced by retrograde injection of BA into biliopancreatic duct. There have been few clinical studies on the correlation between circulating TBA and AP so far. Maleszka A et al. found that the circulating TBA on the first day of AP in patients with biliary etiology is significantly higher compared to those with alcoholic and other etiologies. Therefore, the authors indicated that circulating TBA can be used as an aid to the diagnosis of AP etiology [15]. In this retrospective study, we analyzed clinical data of AP patients in a tertiary referral center. The results showed that elevated levels of circulating TBA in the early stages of AP were closely related to the development of organ failure.

Materials And Methods

Study design and data collecting

This study was a retrospective cohort study of AP patients admitted to the Acute Pancreatitis Treatment Center of Jinling Hospital from 01 January 2014 to 31 December 2016. The study was approved by the ethics committee of the Jinling Hospital, Medical School of Nanjing University. We included patients who met the following criteria: (1) within 7 days after onset of AP; (2) TBA values available within 7 days after admission; (3) 18 years ≤ age ≤ 75 years; (4) exclusion of tumor, pregnancy pancreatitis; (5) no renal replacement therapy (RRT) before admission. Because pregnancy and the use of RRT would greatly affect circulating TBA levels. We selected the highest TBA value (TBA_{max}) within 7 days after admission and other laboratory test results on the same day for further analysis. And then we divided all patients into the HTBA group and the NTBA group according to whether the circulating TBA_{max} value was ≥ 10 μmol/L. All data on patients were collected from the database of Pancreatitis Treatment Center including demographics, etiology, comorbidities, laboratory test results, diagnosis, and clinical outcomes.

Study outcomes

The primary outcome was organ failure, which is a very important factor that have a causal association with the severity of AP patients. In our study, organ failure was defined for 3 organ systems (cardiovascular, renal, and respiratory) on the basis of the worst measurement over a 24-hour period. In patients without preexisting organ dysfunction, organ failure was defined as either a score of 2 or more in the assessed organ system using the SOFA (Sepsis-related Organ Failure Assessment) score or when the relevant threshold was breached, as shown: 1. (Shock) Cardiovascular: need for inotropic agent; 2. (AKI) Renal: creatinine ≥ 171 μmol/L (≥ 2.0 mg/dL); 3. (ARDS) Respiratory: PaO2/FiO2 ≤ 300 mmHg (40 kPa). Persistent organ failure is the evidence of organ failure in the same organ system for 48 hours or more, while transient organ failure is less than 48 hours [21]. The secondary outcomes included AP classification, pancreatic or peripancreatic necrosis, percutaneous catheter drainage, laparotomy and death. AP classification was divided into mild, moderate, severe and critical according to the DBC classification [21]. Mild AP is characterized by the absence of both (peri)pancreatic necrosis and organ failure, whereas moderate AP is defined by the presence of sterile (peri)pancreatic necrosis and/or transient organ failure. Severe AP refers to the existence of either infected (peri)pancreatic necrosis or persistent organ failure. Finally, patients with critical AP are those who have both infected (peri)pancreatic necrosis and persistent organ failure.

Statistical analysis

Data involving demographics, AP etiology, comorbidities, smoking and drinking, and clinical outcomes were compared between patients in the HTBA and the NTBA groups. The categorical variables were described using frequency and percentage. Continuous variables were described using mean ± standard deviation (SD) or median ± interquartile range (IQR), depending on the distribution of the variables. We used the t test to compare the continuous variables of the normal distribution, and the Wilcoxon signed-rank tests compare the non-normally distributed variables. For categorical variables, a chi-square test was used.

Univariate logistic regression was used to explore the potential association between several factors and OF. Then, we introduced potential confounders ($P < 0.1$ in univariate analysis) and several related variables (age, gender, body mass index (BMI), etiology, biliary disease, fatty liver, etc.) that potentially affect the severity of AP to adjust the multivariate logistic regression models to determine whether TBA was independently associated with OF. All analyses were performed using SPSS, version 20 (SPSS, Chicago, IL, USA). A bilateral p-value less than 0.05 was considered to be a statistically significant.

Results

Patient demographics and clinical characteristics

In our study, 1097 AP patients admitted to the Pancreatitis Treatment Center of Jinling Hospital from 01 January 2014 to 31 December 2016 were screened. Of these patients a total of 659 (60.07%) patients developing AP for more than 7 days were excluded. Among the 438 patients within 7 days after onset, 39 patients whose TBA did not measured within 7 days after admission, 17 patients with age less than 18 or

older than 75 years, 1 patient with tumor, 11 patients with pregnancy, and 77 patients receiving RRT before admission were exclude. A total of 293 patients were eligible for further study. Among these patients, 54 (18.43%) patients had a $TBA_{max} \geq 10$ μmol/L, and 239 (81.57%) patients had a $TBA_{max} < 10$ μmol/L (Fig. 1). Demographics and baseline characteristics of patients between the HTBA group and the NTBA group are presented in Table 1. These 54 patients in the HTBA group were more commonly male (88.9% vs. 59.8%; $p < 0.001$) when compared with patients in the NTBA group. Notably, patients with HTBA were more likely to be smoking (59.3% vs. 38.5%; $p = 0.006$) and drinking (59.3% vs. 28.9%; $p < 0.001$). Whereas, we observed no significant difference in demographics including age and the proportion of BMI ≥ 28 between the HTBA group and the NTBA group. Similarly, etiology of AP and comorbidities including hypertension, diabetes mellitus (DM), biliary tract disease and fatty liver between both groups did not differ (Table 1).

Table 1

Comparison of demographics and clinical characteristics between the HTBA group and the NTBA group

Variable	NTBA n = 239	HTBA n = 54	P value
Demographics			
Age, yr, mean ± SD	46 ± 12.6	48 ± 12.2	0.382
Male, n(%)	143(59.8)	48(88.9)	0.001
BMI, n(%) 28 ≥28	158(78.2) 44(21.8)	32(68.1) 15(31.9)	0.181
Etiology of SAP, n(%) Biliary Hyperlipidemia Alcoholic Idiopathic Comorbidities, n(%)	116(48.5) 100(41.8) 8(3.3) 15(6.3)	31(57.4) 18(33.3) 2(3.7) 3(5.6)	0.674
Hypertension	62(25.9)	21(38.9)	0.066
DM	58(24.3)	11(20.4)	0.599
Biliary tract disease	120(50.2)	25(46.3)	0.653
Fatty liver	106(44.4)	23(42.6)	0.880
Smoking, n(%)	92(38.5)	32(59.3)	0.006
Drinking, n(%)	69(28.9)	32(59.3)	0.001

HTBA, the high TBA group; NTBA, the normal TBA group; SD, standard deviation; BMI, body mass index; SAP, severe acute pancreatitis; DM, diabetes mellitus.

Clinical outcomes

Classified by DBC classification there was a significant difference between the two groups in the severity of AP ($P < 0.001$). Most of the patients in the HTBA group suffered from severe or critical AP (55.6%), while in the NTBA groups mild and moderate AP were in the majority (89.1%). Overall, organ failure developed in 73(24.9%) out of 293 patients whose early TBA values were available. In these 73 patients, ARDS was the most common organ failure (76.7%), followed by AKI (68.5%) and Shock (28.8%). The incidence of organ failure was higher in the HTBA group than in the NTBA group (59.3% vs. 17.2%; $p < 0.001$). Pancreatic or peripancreatic necrosis was identified in 160 (54.6%) of 293 patients according to the CT scan results. In the HTBA group more patients developed pancreatic or peripancreatic necrosis compared with the NTBA group (72.2% vs. 50.6; $p = 0.004$). Twelve of 54 patients in the HTBA group vs. 13 of 239 patients in the NTBA group received PCD (22.2% vs. 5.4%; $p < 0.001$). On the contrary, no significant difference was observed in the proportion of laparotomy between the two groups (5.6% vs. 2.1%; $p = 0.343$). A total of 12 patients died, including 8 (14.8%) in the HTBA group and 4 (1.7%) in the NTBA group with $p < 0.001$(Table 2). In summary, the clinical prognosis of AP patients in the HTBA group was worse than those in the NTBA group.

Table 2
Clinical outcomes of patients classified by TBA_{max}

Variable	NTBA n = 239	HTBA n = 54	P value
DBC classification, n(%) mild moderate severe critical	108(45.2) 105(43.9) 20(8.4) 6(2.5)	11(20.4) 13(24.1) 19(35.2) 11(20.4)	<0.001
Organ failure, n(%)	41(17.2)	32(59.3)	<0.001
ARDS, n(%)	33(13.8)	23(42.6)	<0.001
AKI, n(%)	22(9.2)	28(51.9)	<0.001
Shock, n(%)	11(4.6)	10(18.5)	0.001
Pancreatic necrosis, n(%)	121(50.6)	39(72.2)	0.004
PCD, n(%) Laparotomy, n(%) Death, n(%)	13(5.4) 5(2.1) 4(1.7)	12(22.2) 3(5.6) 8(14.8)	<0.001 0.343 <0.001

HTBA, the high TBA group; NTBA, the normal TBA group; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; PCD, percutaneous catheter drainage.

Univariate and multivariate analysis

In order to determine the potential risk factors for OF we applied univariate analysis and the result are shown in Table 3. In the univariate analysis some clinical parameters involving inflammation (white blood cell count, WBC; neutrophil ratio, NEUT%; C-reactive protein, CRP), hepatobiliary diseases (total

bilirubin, TBIL; alanine aminotransferase, ALT; aspartate aminotransferase, AST; alkaline phosphatase, ALP; γ-glutamyl transpeptadase, γ-GT) and OF (blood urea nitrogen, BUN) were also included. To adjust for baseline differences we incorporated age, gender, BMI ≥ 28 and some potentially confounding variables($p < 0.1$ in the univariate analysis) (Table 3) such as etiology of AP, biliary tract disease, fatty liver, smoking, drinking and some clinical parameters(including TBIL, AST, WBC, NEUT%, CRP, BUN) into a multivariate model and found that HTBA (TBA_{max}≥10 μmol/L) was an independent risk factor for OF with an odds ratio of 4.89 (95% CI, 1.81–13.21; $p = 0.002$). Furthermore, BUN was also associated with the development of OF with an odds ratio of 1.19 (95% CI, 1.03–1.37; $p = 0.022$) lower than that of HTBA. Notably, other variables such as age, gender, etiology have no significant relationship with OF (Table 4).

Table 3

Univariate analysis showing the potential risk factors for organ failure in acute pancreatitis.

Univariate analysis	OR(95%CI)	P value
Age	0.997(0.976,1.018)	0.786
Male	1.887(1.038,3.431)	0.037
BMI ≥ 28	2.396(1.278,4.493)	0.006
Etiology		0.047
Biliary	2.138(0.466,9.799)	0.328
Hypertriglyceridemia	3.949(0.864,18.043)	0.076
Alcohol	0.889(0.070,11.221)	0.927
Hypertension	1.455(0.824,2.510)	0.197
DM	0.795(0.417,1.516)	0.486
Biliary tract disease	0.591(0.345,1.012)	0.055
Fatty liver	2.233(1.303,3.829)	0.003
Smoking	2.280(1.331,3.907)	0.003
Drinking	1.844(1.072,3.172)	0.027
TBA	7.024(3.709,13.302)	0.001
TBIL	1.018(1.008,1.027)	0.001
ALP	1.003(0.999,1.007)	0.138
r-GT	1.000(0.998,1.001)	0.986
ALT	1.001(0.999,1.003)	0.411
AST	1.006(1.002,1.011)	0.005
WBC	1.107(1.056,1.161)	0.001
NEUT%	1.113(1.065,1.163)	0.001
CRP	1.006(1.003,1.010)	0.001
PLT	0.997(0.993,1.001)	0.131
BUN	1.025(1.014,1.035)	0.001

OR, Odds ratio; CI, confidence interval; BMI, body mass index; DM, diabetes mellitus; TBA, total bile acid; TBIL, total bilirubin; ALP, alkaline phosphatase; γ-GT, γ-glutamyl transpeptadase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; WBC, white blood cell count; NEUT%, neutrophil ratio; CRP, C-reactive protein; PLT, platelet; BUN, blood urea nitrogen.

Table 4
Multivariate analysis showing association of proposed risk factors for organ failure in AP

Multivariate analysis	OR(95%CI)	P value
Age	1.009(0.974,1.044)	0.631
Male	0.967(0.321,2.913)	0.953
BMI ≥ 28	1.635(0.702,3.806)	0.254
Etiology		0.413
Biliary	2.022(0.298,13.716)	0.471
Hypertriglyceridemia	3.112(0.524,18.495)	0.212
Alcohol	0.550(0.016,18.537)	0.739
Biliary tract disease	0.481(0.170,1.361)	0.168
Fatty liver	1.588(0.693,3.638)	0.275
Smoking	1.474(0.567,3.834)	0.426
Drinking	0.728(0.305,1.740)	0.475
TBA_{max}≥10 μmol/L	4.894(1.813,13.208)	0.002
TBIL	0.996(0.982,1.010)	0.595
AST	1.002(0.995,1.008)	0.580
WBC	1.064(0.986,1.148)	0.113
NEUT%	1.063(0.993,1.138)	0.080
CRP	1.002(0.996,1.007)	0.539
BUN	1.185(1.025,1.371)	0.022

OR, Odds ratio; CI, confidence interval; BMI, body mass index; TBA_{max}, the highest TBA value within 7 days after admission; TBIL, total bilirubin; AST, aspartate aminotransferase; WBC, white blood cell count; NEUT%, neutrophil ratio; CRP, C-reactive protein; BUN, blood urea nitrogen.

Discussion

Organ failure and (peri)pancreatic necrosis are two key factors that are causally associated with the severity of AP[21]. A large number of investigations demonstrated a statistically significant association between a wide array of factors and the severity of acute pancreatitis, such as prolonged hospitalization and need for intervention, but the relationships are non-causal[22, 23]. Therefore, the early and accurate prediction of organ failure is particularly important in the treatment of SAP patients. The widely adopted

guidelines of the International Association of Pancreatology and the American Pancreatic Association recommend the persistent (lasting ≥ 48 h) SIRS as early markers to predict the development of organ failure [24]. However, despite a reasonably good sensitivity of 50–95%, SIRS has a lower specificity of 75% [25, 26]. Several clinical scores can also be exploited to predict the development of organ failure in AP, such as APACHE II, BISAP score and SOFA score[27], which are involved multiple parameters and are somewhat cumbersome to use. Single laboratory markers (including IL-6, CRP, and procalcitonin) can also be used as a sensitive marker, but the guidelines emphasize the need for a repeated clinical assessment [24, 28, 29]. At present, no single laboratory marker can be recommended for the early prediction of the development of OF in AP. Recent studies showed that angiopoietin-2(a marker of vascular leak syndrome)[30] or serum urokinase-type plasminogen activator receptor (uPAR)[31] can be applied as a marker in predicting persistent organ failure. Unfortunately, the detection of these indicators is not widely used so far and is difficult to obtain in clinical practice. It is necessary to find early and appropriate markers of organ failure, which can help doctors identify critically ill patients and allow for the proper allocation of intensive care resources in time.

BAs are physiological detergent molecules synthesized from cholesterol in the liver. Dietary intake stimulates Bile acids into the intestines and then they can facilitate the absorption of dietary lipids and vitamins in the intestines[32].Over the past few decades, many studies have suggested that bile acids are signaling molecules that regulate lipid, glucose and energy metabolism which are predominately mediated by bile acid-activated FXR and TGR5[8, 9, 14, 33]. When the homeostasis of BAs is broken or the signaling pathway is impaired, it can lead to a variety of metabolic disorders or inflammatory diseases [14, 33]. At present, circulating TBA can be used as a marker for diagnosing hepatobiliary diseases, and has been widely used in clinical work[16, 34], besides, some studies have reported that circulating TBA can predict the occurrence of colorectal cancer[35, 36] and pancreatic cancer[37]. However, there are few researches in the field of critical illness or AP involving BAs.

The results of our study shown that 54 (18.43%) patients with AP had a TBA_{max} ≥ 10 μmol/L within 7 days of admission, and the increase of circulating TBA was not only observed in biliary AP, but also in hyperlipidemia and alcohol AP. Further research revealed that the incidence of OF in the HTBA group was significantly higher than that in the NTBA group, and the AP severity classification in the HTBA group was more serious than that in the NTBA group. The pancreatic necrosis rate, PCD rate, open surgery rate and mortality rate in the HTBA group were higher than those in the NTBA group. All of the above results indicated that the increase in circulating TBA in AP patients was not related to the etiology, and the AP patients with HTBA had a worse prognosis.

The pathophysiological mechanism of AP complicated with OF is that pancreatitis per se (sterile inflammation) causes the release of a large number of inflammatory mediators leading to primary (early) OF or infected pancreatic necrosis leads to the secondary (late) OF [27]. Cholestasis is a common complication of sepsis. Hao et al. showed that the amplified plasma levels of BAs are important for the prediction of sepsis-associated mortality. They proved that bile acids activate the NLRP3 inflammasome via promoting calcium influx. Their research also depicted that the FXR-bile acid axis involves in the

regulation of cholestasis-associated sepsis, which can be mediated by the negative regulation of NLRP3 inflammasome via the direct binding of FXR to NLRP3 and caspase 1 in macrophages [38, 39]. Maleszka A et al. reported that circulating TBA on the first day of AP could be used to discriminate the biliary AP from the other etiology. The cut-off values of 4.7_mol/L, with a diagnostic accuracy of 85%. However, circulating TBA had nothing to do with the severity of AP in this study [15]. On the contrary, the levels of circulating TBA were closely related to the severity of AP, and logistic analysis suggested that circulating HTBA was an independent risk factor for AP complicated with organ failure. Our results are somewhat different from those of Aleksandra et al. The reasons for the differences may be in the following aspects: first, in their study, the values of circulating TBA were continuously monitored for three days after AP onset, while the time span of our test was longer; secondly, the sample size of their study was 66 patients which was relatively smaller; finally, our center is a SAP tertiary referral center in which our patients are more serious.

In recent years, the pathophysiological mechanisms of BAs and its receptors in diseases were elucidated in some researches. Iracheta-Vellve A et al. manifested that agonists of FXR and TGR5 (OCA, INT-767 and INT-777) can reduce the expression of inflammatory cytokine in animal models of alcoholic liver disease by inhibiting macrophage inflammation through activation of protein kinase A induced by cyclic adenosine monophosphate (cAMP)[40]. This mechanism was confirmed in TGR5 ligand ameliorating the immunity of intestinal mucosa in experimental colitis [41]. Moreover, in the pancreas, local accumulation of BAs molecules could inhibit autophagy of pancreatic acinar cells through FXR, leading to the increasing of apoptosis and necrotic apoptosis [42]. Our team previously found that the administration of INT-777 could protect AP in mice and improve pancreatic acinar cell necrosis [43]. Based on the above studies, we hypothesize that the imbalance of BAs, may cause organ failure in AP patients with increased circulating TBA levels, which may lead to the disorder in BAs metabolism and inflammatory response, thus affecting the organ function. However, the specific mechanism of circulating TBA elevation and AP complicated with OF is still unclear, which still needs further study.

Our study reports for the first time that circulating TBA levels in the early stage of AP patients are associated with the development of organ failure and can be used as a predictor for OF. This can help clinicians identify patients whom are at risk of organ failure in the early stage of AP (within 14 days), so as to treat them promptly and reduce the mortality rate. In addition, the detection of circulating TBA has been widely used, exerting multiple effects of the same indicator. However, our research also has some disadvantages. First, this is a single-center retrospective study. Moreover, our observation marker, TBA_{max}, was the highest value of circulating TBA within 7 days of admission. Long monitoring time span may cause some bias to the results.

Overall, the circulating TBA in the early stage of AP can be used as a predictive marker for AP complicated with OF, but its specific mechanism and the roles of components of BAs need further research.

Conclusions

Elevation of circulating TBA in the early stage of AP is independently associated with organ failure and can serve as a predictive marker for the development of organ failure.

Declarations

Ethics approval and consent to participate

The study was approved by the ethics committee of the Jinling Hospital, Medical School of Nanjing University. All participants agreed to participate in the study, and written informed consent was obtained from each subject.

Consent for publication

Not applicable.

Availability of data and materials

The datasets analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Xiaochun Xie and Guotao Lu: study design, Jie Dong and Kun Gao: acquisition of data and statistical analysis, Jie Dong, Xiaoyao Li, Wenjian Mao and Faxi Chen: analysis and interpretation of data, Xiaochun Xie: drafting of the manuscript, Guotao Lu and Weiqin Li: critical revision of the manuscript, Zhihui Tong, Baiqiang Li and Weiqin Li: study supervision and guidance. All authors have read and approved the final version of this manuscript, including the authorship.

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Abbreviations

BAs: bile acids; TBA: total bile acid; AP: acute pancreatitis; HTBA: high TBA; NTBA: normal TBA; OF: organ failure; PCD: percutaneous catheter drainage; OR: odds ratio; SAP: severe acute pancreatitis; ARDS: acute respiratory distress syndrome; AKI: acute kidney injury; FXR: farnesoid X receptor; RRT: renal replacement therapy; SD: standard deviation; IQR: interquartile range; BMI: body mass index; DM: diabetes mellitus; CI: confidence interval; TBIL: total bilirubin; ALP: alkaline phosphatase; γ-GT: γ-glutamyl transpeptadase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; WBC: white blood cell count; NEUT%: neutrophil ratio; CRP: C-reactive protein; PLT: platelet; BUN: blood urea nitrogen.

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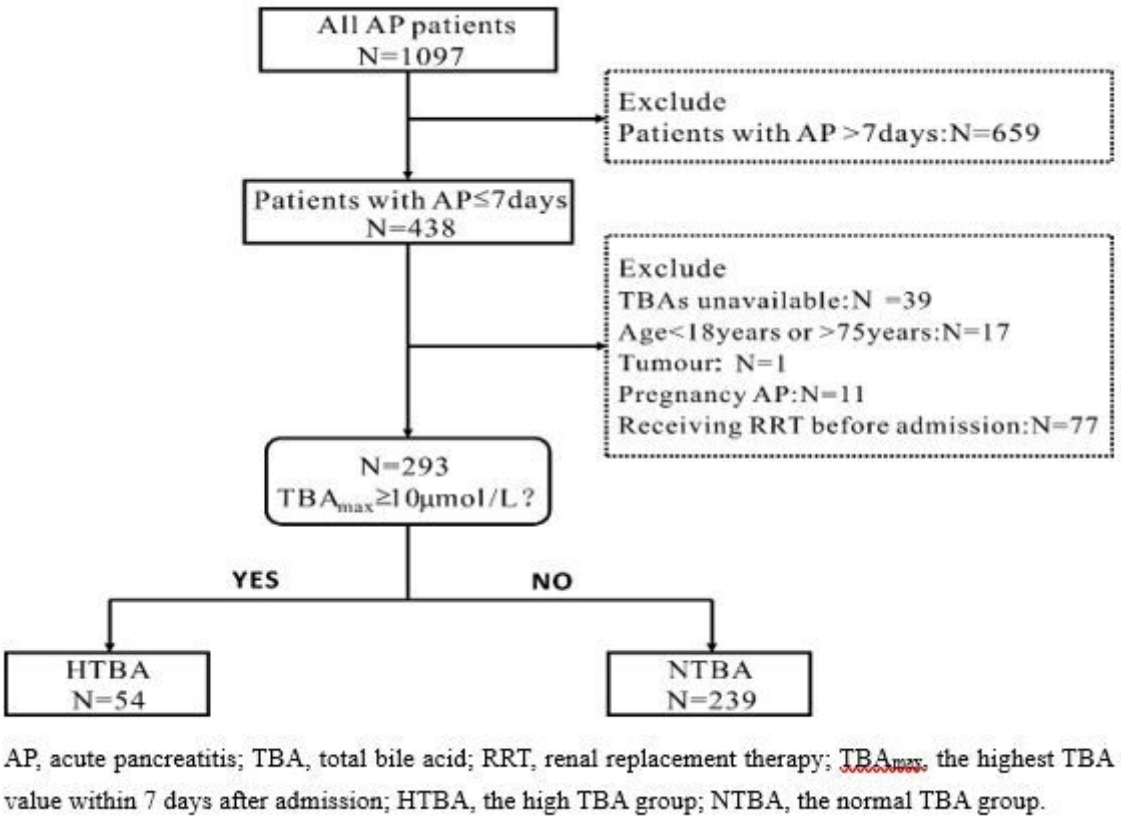
Figures



AP, acute pancreatitis; TBA, total bile acid; RRT, renal replacement therapy; TBA_{max}, the highest TBA value within 7 days after admission; HTBA, the high TBA group; NTBA, the normal TBA group.

Figure 1

Flow chart of the patients with AP in the study