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ORIGINAL RESEARCH

The Significance of RUNX3 Expression Levels in the Prognosis of Severe Acute Pancreatitis

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Objective: To analyze the expression levels of RUNX3 in patients with severe acute pancreatitis (SAP) and its impact on disease progression.

Methods: Healthy individuals undergoing physical examinations during the same period were selected as a control group. General patient data were analyzed and compared. Enzyme-linked immunosorbent assay (ELISA) was used to detect the expression levels of RUNX3, and differences in RUNX3 levels between the groups were compared.

Results: Comparison of general characteristics showed no statistically significant differences in sex, age, body mass index (BMI), history of diabetes, hypertension, coronary artery disease, etiology, or prevalence of fatty liver among the groups ($P > 0.05$). The time from onset to admission and the length of hospital stay were significantly higher in the severe group compared to the mild group ($P = 0.001$). The severe group also exhibited significantly higher white blood cell counts (WBC), procalcitonin (PCT), C-reactive protein (CRP), lipase (LPS), and APACHE II scores ($P = 0.001$). RUNX3 levels were 97.67 ± 31.03 in the SAP group, significantly lower than 137.22 ± 53.07 in the mild group and 217.55 ± 76.59 in the control group ($P < 0.05$). Pearson correlation analysis revealed a negative correlation between RUNX3 levels and APACHE II scores in patients with acute pancreatitis ($r = -0.613$, $P < 0.0152$). RUNX3 levels in the poor prognosis group were significantly lower than those in the good prognosis group ($P < 0.05$). ROC curve analysis indicated that the area under the curve for RUNX3 levels in predicting the prognosis of acute pancreatitis was 0.835, with an optimal cutoff value of 162.31 pg/mL, a sensitivity of 90.00%.

Conclusion: RUNX3 expression levels are significantly reduced in patients with SAP and are negatively correlated with disease severity, making them a potential biomarker for assessing and predicting the prognosis of acute pancreatitis.

Keywords: severe acute pancreatitis, RUNX3, disease progression

Introduction

Acute pancreatitis (AP) is an acute abdominal condition caused by the autodigestion of the pancreas and surrounding organs by abnormally activated pancreatic enzymes. It is a common gastrointestinal disease with an increasing incidence rate.[1,2] The clinical course of AP can range from mild and transient episodes to severe forms often accompanied by necrosis, potentially leading to multi-organ failure, with mortality rates ranging from 20% to 40%.[3,4] Mild acute pancreatitis is the most common form, characterized by the absence of organ failure, local or systemic complications, and typically resolves spontaneously within a week.[5] Moderate AP is defined by transient organ failure, local complications, or the exacerbation of comorbid conditions. About 15–20% of AP patients progress to severe disease, characterized by persistent organ failure lasting more than 48 hours.[6,7]

The progression of severe acute pancreatitis (SAP) can be divided into two phases. The first 10–14 days are marked by systemic inflammatory response syndrome (SIRS) caused by the release of various inflammatory mediators.[8] The second phase, which begins after 10–14 days, is dominated by infection-related complications, primarily due to infected pancreatic or peripancreatic necrosis. This stage is often accompanied by sepsis-induced multi-organ failure, leading to mortality.[9,10] The clinical prognosis of SAP is not only related to the severity of the disease but also critically depends on the early identification of patients to enable timely intensive therapy during the initial stages of the disease.

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RUNX3 (Runt-related transcription factor 3) is a member of the RUNT family. The human RUNX family comprises three members: RUNX1, RUNX2, and RUNX3, which act as crucial transcription factors in cellular signaling and are associated with the onset and progression of various diseases.[11,12] RUNX3 plays a pivotal role in numerous biological processes, including cell differentiation, proliferation, apoptosis, and immune regulation. Its critical position in the TGF-β signaling pathway has made it a focus of extensive research.[13] RUNX3 expression is frequently downregulated in multiple cancers, such as gastric, lung, and colorectal cancers, and is closely associated with tumor initiation, progression, and poor prognosis. Additionally, RUNX3 has been widely studied in autoimmune diseases (eg, multiple sclerosis and rheumatoid arthritis) and neurodegenerative disorders (eg, Alzheimer's disease), highlighting its potential in regulating T-cell function and neuronal survival.[14] Although research on its role in cardiovascular diseases is limited, preliminary evidence suggests that RUNX3 may influence cardiomyocyte proliferation and apoptosis. Investigating the biological functions of RUNX3 and its roles in various diseases may provide new diagnostic and therapeutic targets.[15]

This study focuses on AP patients, comparing RUNX3 expression levels between mild and severe cases. It aims to explore the application of RUNX3 in predicting the progression of SAP, providing reference data for identifying prognostic biomarkers in SAP.

General Information and Methods

General Information

This study included 90 patients diagnosed with severe acute pancreatitis (SAP) who were admitted to the ICU of our hospital between January 2022 and January 2024. Inclusion criteria: (1) Admission within 48 hours of disease onset, meeting the diagnostic criteria for SAP according to the 2012 Atlanta Classification for Acute Pancreatitis.[16] The diagnostic criteria included the following: (1) acute persistent upper abdominal pain, which can radiate to the back, shoulder, or waist; (2) serum amylase or lipase levels elevated to more than three times the normal limit; (3) abdominal ultrasound or contrast-enhanced CT revealing characteristic pancreatic changes, such as pancreatic edema, necrosis, or peripancreatic fluid collection. A diagnosis of SAP was confirmed if two of the above criteria were met, and imaging studies, such as CT or MRI, were essential for evaluating the extent of pancreatic injury and related complications. Additionally, the severity of pancreatitis was classified as mild, moderately severe, or severe according to the Atlanta Classification. APACHE II score ≥8 points. (2) Admitted between January 2022 and January 2024. (3) Aged ≥18 years, with no gender restrictions. (4) Complete clinical data and signed informed consent to participate in the study. Exclusion criteria: (1) Combined with other severe diseases (eg, malignancies, severe cardiovascular diseases, chronic renal failure). (2) Previous history of chronic or idiopathic pancreatic disease. (3) Pancreatic mass lesions. (4) Pregnant or lactating women. (5) Prior targeted treatment for pancreatitis before admission. (6) Incomplete clinical data or refusal to participate.

Patients were further divided into two groups based on APACHE II scores: a mild group (68 cases, APACHE II score <20) and a severe group (22 cases, APACHE II score ≥20). Additionally, 20 healthy individuals undergoing physical examinations during the same period were selected as the control group. Data on the following general characteristics were collected and compared: age, gender, body mass index (BMI), disease duration, diabetes, hypertension, fatty liver, length of hospital stay, white blood cell count (WBC), procalcitonin (PCT), C-reactive protein (CRP), lipase (LPS), and APACHE II scores. Baseline characteristics between the study and control groups showed no significant differences (P>0.05), ensuring comparability. Informed consent was obtained from all patients upon admission, and the study was approved by the Zhoukou Central Hospital ethics committee. All the methods were carried out in accordance with the Declaration of Helsinki.

Methods

Grading of Disease Severity[16]

(1) Mild: No local complications and no organ dysfunction. (2) Moderately severe: Presence of local complications and/or transient (≤48h) organ dysfunction. (3) Severe: Persistent (>48h) organ dysfunction. Organ dysfunction was assessed using the modified Marshall scoring system, with any organ score ≥2 indicating organ dysfunction.

Treatment Methods

Treatment was administered following the Chinese Guidelines for the Diagnosis and Treatment of Acute Pancreatitis (2021), including pain management, fluid therapy, nutritional support, etiology-targeted treatment, reduction of intra-abdominal pressure, and active prevention of local and systemic complications as symptomatic management.

Specimen Collection

On the second morning after admission, 5 mL of fasting peripheral venous blood was collected from each study subject and placed in EDTA anticoagulation tubes. The samples were centrifuged at 3000 r/min for 15 minutes at 20°C, and the supernatant was stored at −80°C for later use. RUNX3 expression levels in serum were measured using enzyme-linked immunosorbent assay (ELISA).

Observational Indicators and Evaluation Criteria

Primary Endpoint

The relationship between changes in RUNX3 expression levels and the progression of Severe Acute Pancreatitis (SAP) was analyzed. Mortality among patients with hospital stays exceeding 48 hours was recorded, and RUNX3 detection values were compared between the favorable prognosis group (survivors) and the unfavorable prognosis group (deceased).

Secondary Endpoints

General characteristics, including age, gender, body mass index (BMI), disease duration, history of diabetes, hypertension, coronary heart disease, etiology, fatty liver, length of hospital stay, white blood cell count (WBC), procalcitonin (PCT), C-reactive protein (CRP), lipopolysaccharide (LPS), and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores, were compared among study subjects.

Statistical Analysis

Data were analyzed using SPSS 25.0 statistical software. Measurement data were expressed as mean ± standard deviation. Independent sample tests were used for comparisons between two groups, one-way analysis of variance (ANOVA) for comparisons among multiple groups, and SNK-q tests for multiple comparisons between groups. Count data were expressed as frequency (percentage), with group comparisons conducted using the chi-square test. Pearson correlation analysis was performed to explore the relationship between RUNX3 and disease severity, and receiver operating characteristic (ROC) curve analysis was used to assess the prognostic value of RUNX3 levels in patients. The optimal cut-off point was determined using the Youden's index, which is the point that maximizes the sum of sensitivity and specificity. A value of $P<0.05$ was considered statistically significant.

Results

Comparison of General Information

There were no statistically significant differences among the groups in terms of gender, age, body mass index (BMI), history of diabetes, hypertension, coronary heart disease, etiology, or proportion of fatty liver ($P > 0.05$). However, the time from onset to admission and length of hospital stay in the severe group were significantly higher than those in the mild group ($P = 0.001$). The severe group also exhibited significantly higher levels of white blood cell count (WBC), procalcitonin (PCT), C-reactive protein (CRP), lipase (LPS), and APACHE II scores compared to the mild group ($P = 0.001$). See Table 1.

Comparison of RUNX3 Levels

The RUNX3 levels in the severe acute pancreatitis group were 97.67 ± 31.03, significantly lower than those in the mild acute pancreatitis group (137.22 ± 53.07) and the control group (217.55 ± 76.59). The differences were statistically significant ($P < 0.05$). See Figure 1.

Table 1 Comparison of General Information

Variable	Control Group (n=20)	Mild Group (n=68)	Severe Group (n=22)	F/x^2	p
Age (years)	45.2 ± 12.3	50.39 ± 14.13	51.66 ± 13.53	1.461	0.147
Gender (Male/Female)	14/6	35/33	12/10	2.150	0.143
BMI (kg/m²)	22.5 ± 2.1	24.38 ± 3.29	24.18 ± 4.02	2.459	0.128
Time from onset to admission (days)	–	5.24 ± 1.47	10.35 ± 2.64	11.454	0.001
Length of hospital stay (days)	–	7.51 ± 2.20	15.82 ± 3.55	13.096	0.001
History of diabetes (cases)	5	10	8	0.545	0.461
History of hypertension (cases)	8	15	10	2.577	0.108
History of coronary heart disease (cases)	3	5	4	0.364	0.546
Etiology	–			0.124	0.724
Biliary		40	12		
Alcoholic		20	6		
Others		8	4		
Fatty liver (cases)	3	25	15	3.375	0.066
WBC (10^9/L)	6.25 ± 1.27	9.81 ± 2.37	12.54 ± 3.17	38.332	0.001
PCT (ng/mL)	0.15 ± 0.01	0.52 ± 0.21	1.53 ± 0.54	136.596	0.014
CRP (mg/L)	62.31 ± 0.53	85.64± 12.36	105.42 ± 20.14	55.569	0.001
LPS (U/L)	0.82 ± 0.13	1.32 ± 0.27	1.64 ± 0.30	54.086	0.001
APACHE II score		15.32 ± 2.26	25.69 ± 3.41	16.378	0.001

Abbreviations: BMI, Body Mass Index; SAP, Severe Acute Pancreatitis; WBC, White Blood Cell count; PCT, Procalcitonin; CRP, C-reactive protein; LPS, Lipopolysaccharide; APACHE II, Acute Physiology and Chronic Health Evaluation II.

Correlation Analysis Between RUNX3 Levels and Severity of Acute Pancreatitis

Pearson correlation analysis showed that RUNX3 levels were negatively correlated with APACHE II scores in acute pancreatitis patients ($r = -0.613$, $P < 0.0152$). See Figure 2.

Comparison of RUNX3 Levels in Acute Pancreatitis Patients with Different Outcomes

The RUNX3 levels were significantly lower in the poor prognosis group than in the good prognosis group ($P < 0.05$). See Table 2.

Predictive Value of RUNX3 for the Prognosis of Acute Pancreatitis Patients

ROC curve analysis revealed that the area under the curve (AUC) for RUNX3 levels in predicting the prognosis of acute pancreatitis patients was 0.835. The optimal cutoff value was 162.31 pg/mL, with a sensitivity and specificity of 90.00% and 82.50%, respectively. See Figure 3.

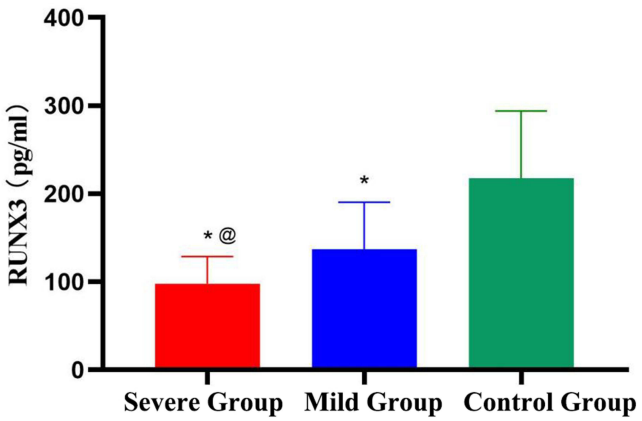

Figure 1 Comparison of RUNX3 Levels.
Note: *Indicates $P < 0.05$ compared to the control group, and @ indicates $P < 0.05$ compared to the mild group.

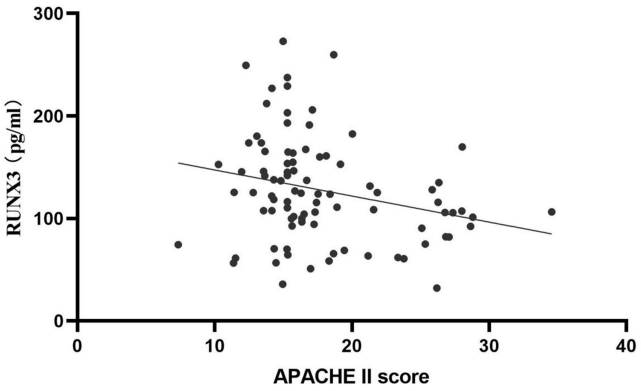

Figure 2 Correlation Between RUNX3 Levels and Severity of Acute Pancreatitis.

Discussion

The main finding of this study is that plasma RUNX3 levels are significantly reduced in patients with severe acute pancreatitis (SAP), and its expression levels are negatively correlated with disease severity, suggesting that RUNX3 may serve as a potential biomarker for predicting the progression of SAP. Our results showed that SAP patients had markedly lower plasma RUNX3 levels compared to the mild pancreatitis group and healthy controls, supporting the hypothesis that reduced RUNX3 expression could be linked to more severe disease outcomes.[17,18]

RUNX3, a critical regulator of immune responses and inflammation, plays a vital role in regulating T and B cell differentiation, apoptosis, and inflammatory responses. Previous studies have demonstrated its downregulation in diseases associated with inflammation, such as bronchiolitis and chronic gastritis.[19–21] In this study, we observed that RUNX3 expression was significantly reduced in SAP patients, which is consistent with the findings from other inflammatory conditions. This reduction could reflect the inflammatory cascade and acinar cell damage that are central to the pathogenesis of SAP.[22,23]

The APACHE II scoring system, which is commonly used to assess the severity of acute pancreatitis, was applied in this study to categorize patients into mild and severe groups. Our findings further show that plasma RUNX3 levels were negatively correlated with APACHE II scores, indicating that RUNX3 could help assess the severity of SAP. ROC curve analysis demonstrated that RUNX3 has excellent potential for predicting SAP, with an optimal cutoff value of 162.31 pg/mL, sensitivity of 90.00%, and specificity of 82.50%.

Although this study provides significant insights into the role of RUNX3 in SAP, it does have several limitations. The sample size is relatively small, and larger-scale studies are needed to confirm these results. Furthermore, this study only explored RUNX3 expression levels in SAP patients. Future studies should investigate the molecular mechanisms through which RUNX3 contributes to the pathogenesis of SAP, including its role in regulating inflammation and acinar cell apoptosis. Additionally, the role of RUNX3 in other related diseases warrants further exploration to provide a broader understanding of its regulatory functions.

Although this study provides significant insights into the role of RUNX3 in SAP, it does have several limitations. First, the sample size is relatively small, which may limit the generalizability of our findings. Larger-scale, multicenter

Table 2 Comparison of RUNX3 Levels in Acute Pancreatitis Patients With Different Outcomes

Group	n	RUNX3 (pg/mL)
Good prognosis	70	150.3 ± 44.1
Poor prognosis	20	85.6 ± 23.5
t		6.293
p		0.001

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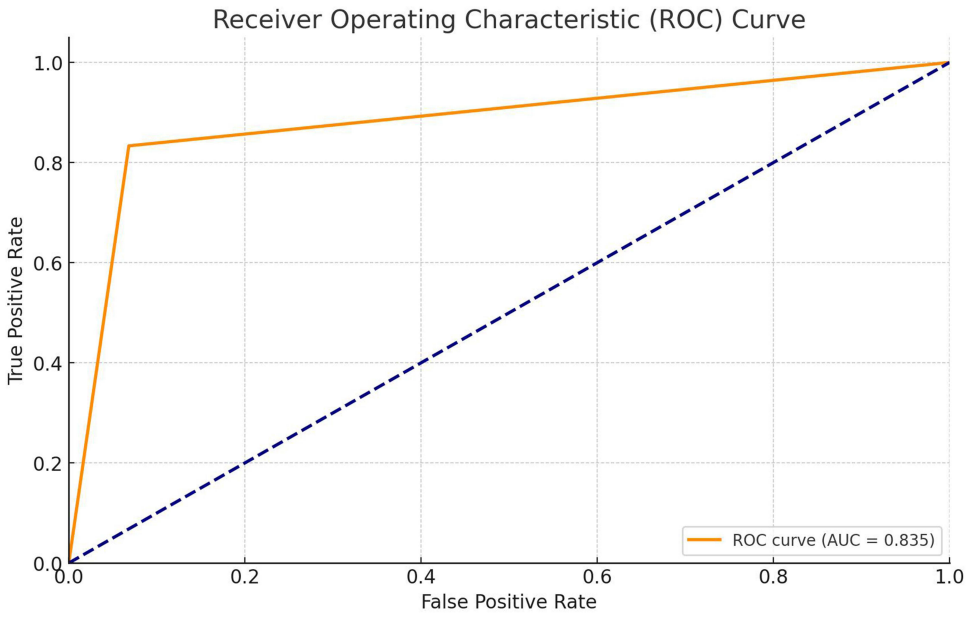

Figure 3 Predictive Value of RUNX3 for the Prognosis of Acute Pancreatitis Patients.

studies are needed to confirm these results and provide a more robust understanding of RUNX3 as a biomarker for SAP. Additionally, this study was conducted at a single center, and the patient population may not fully represent the diversity of SAP patients in different regions. Therefore, future research should consider the impact of regional and cultural differences on the results. Furthermore, this study only explored RUNX3 expression levels in SAP patients. Future studies should investigate the molecular mechanisms through which RUNX3 contributes to the pathogenesis of SAP, including its role in regulating inflammation and acinar cell apoptosis. Moreover, while plasma RUNX3 levels showed promise as a predictive marker, the method for measuring RUNX3 expression may not be widely available in all clinical settings, limiting its immediate applicability in routine practice. Finally, the role of RUNX3 in other related diseases warrants further exploration to provide a broader understanding of its regulatory functions.

Conclusion

In conclusion, our study highlights the potential role of RUNX3 as a biomarker for predicting the severity and progression of severe acute pancreatitis. The findings suggest that RUNX3 may be involved in the inflammatory processes associated with SAP and could be used as an early predictor of disease outcomes. Future research with larger sample sizes and a focus on the molecular mechanisms of RUNX3 will be necessary to validate its clinical applicability and further elucidate its role in the pathogenesis of SAP.

Disclosure

The authors report no conflicts of interest in this work.

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