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ORIGINAL RESEARCH

The Combined Diagnostic Value of Serum Trefoil Factor 2 and microRNA-186-5p for Evaluating Disease Severity in Patients with Acute Pancreatitis

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Objective: This study investigated the association of serum Trefoil Factor 2 (TFF2) and microRNA-186-5p (miR-186-5p) levels with the severity and prognosis of acute pancreatitis (AP).

Methods: A retrospective analysis was conducted on 380 AP patients, classified into mild to moderately severe (mild acute pancreatitis (MAP) and moderately severe acute pancreatitis (MSAP), n=205) and severe (SAP, n=175) groups. Serum TFF2 levels were measured by enzyme-linked immunosorbent assay (ELISA), and miR-186-5p expression was quantified via reverse transcription quantitative polymerase chain reaction (RT-qPCR). Correlations with inflammatory markers (high-sensitivity C-reactive protein (hs-CRP), interleukin-18 (IL-18), and tumor necrosis factor-α (TNF-α)) and Acute Physiology and Chronic Health Evaluation II (APACHE II) scores were assessed using Pearson analysis. Diagnostic performance was evaluated using receiver operating characteristic (ROC) curves, and logistic regression was used to identify risk factors for SAP.

Results: Compared with the MAP&MSAP group, the SAP group showed significantly elevated TFF2, hs-CRP, IL-18, TNF-α levels, and APACHE II scores, while miR-186-5p levels were significantly reduced ($P < 0.05$). TFF2 levels were positively correlated with inflammatory markers and APACHE II scores ($r = 0.427–0.546$), whereas miR-186-5p levels showed negative correlations ($r = –0.431$ to $–0.570$; all $P < 0.05$). TFF2 and miR-186-5p levels were inversely correlated ($r = –0.483$, $P < 0.05$). ROC analysis yielded AUCs of 0.804 for TFF2, 0.832 for miR-186-5p, and 0.895 for their combination in predicting SAP. Logistic regression identified TFF2 as an independent risk factor and miR-186-5p as a protective factor for SAP ($P < 0.05$).

Conclusion: Elevated serum TFF2 level and reduced miR-186-5p level were found to be associated with increased AP severity. These biomarkers may serve as useful indicators for assessing disease severity and prognosis in AP.

Keywords: acute pancreatitis, serum TFF2, miR-186-5p, disease severity, prognosis, relationship

Acute pancreatitis (AP) is a common acute digestive disorder characterized by pancreatic autodigestion, systemic inflammatory responses, and, in severe cases, multiple organ dysfunction syndrome (MODS), which can lead to significant mortality.[1] Based on clinical severity, AP is categorized into mild AP (MAP), moderately severe AP (MSAP), and severe AP (SAP) using the revised Atlanta Classification.[2] Scoring systems such as BISAP, which incorporates clinical parameters including BUN, SIRS, and pleural effusion, are also utilized to assess disease severity and predict outcomes.

Recent advances in molecular biology have facilitated the identification of novel biomarkers for early diagnosis and prognosis of AP.[3,4] Among these, Trefoil Factor 2 (TFF2) and microRNA-186-5p (miR-186-5p) have drawn increasing attention due to their roles in modulating inflammation and tissue homeostasis. TFF2, a secretory peptide belonging to the trefoil factor family, is mainly expressed in the gastrointestinal tract and plays a critical role in mucosal protection and epithelial restitution.[5] In addition to its barrier-maintaining functions, TFF2 has been implicated in a range of inflammatory and neoplastic diseases, such as gastritis, inflammatory bowel disease (IBD), and gastric cancer, where it has been

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shown to mediate anti-inflammatory responses and promote mucosal healing.[6,7] In inflammatory contexts, TFF2 may influence leukocyte infiltration and cytokine expression, thereby modulating the severity of tissue damage.

Notably, miR-186-5p is a small, non-coding RNA involved in post-transcriptional gene regulation. It has been reported to be dysregulated in various inflammatory and neoplastic conditions, including sepsis, rheumatoid arthritis, and colorectal cancer.[8,9] Functionally, miR-186-5p has been shown to regulate apoptosis, inflammatory cytokine production, and immune cell activation by targeting genes, such as FOXO1, MAPK1, and ZEB1.[10,11] These findings suggest that miR-186-5p may serve as a key regulator in inflammatory networks. However, its role in AP remains poorly defined.

Given the established roles of TFF2 and miR-186-5p in inflammation and tissue repair in other disease contexts, this study aimed to explore their potential as biomarkers for assessing the severity of AP. We hypothesized that their serum levels may correlate with disease progression and prognosis, and that their combined evaluation may offer novel insights into the molecular pathogenesis of AP.

Subjects and Methods

This study was approved by the ethics committee of Liupanshui People's Hospital. Informed consent was obtained from all study participants. All the methods were carried out in accordance with the Declaration of Helsinki.

Study Subjects and Inclusion Criteria

A retrospective analysis was conducted on the clinical data of 380 patients diagnosed with AP and admitted to our hospital over a 23-month period (July 2022 to May 2024), which provided an adequate timeframe for observing clinical outcomes, including disease progression and in-hospital mortality (Figure 1). Inclusion criteria: ① Patients met the clinical diagnostic criteria for AP;[10] ② Patients were aged ≥18 years, with no gender restrictions; ③ Patients had no other infectious diseases; ④ Patients had not taken or received any medications or interventions that could affect the study results within the past 30 days; ⑤ All subjects had complete and authentic clinical data available for analysis. Exclusion criteria: ① Presence of pre-existing severe dysfunction in organs, such as the heart, liver, or kidneys unrelated to AP; ② Concurrent pancreatic diseases; ③ Presence of malignant tumors and/or diseases of the immune or hematologic systems; ④ Coexisting cardiovascular and cerebrovascular diseases; ⑤ Presence of cognitive, communication, or psychiatric disorders; ⑥ Inability to fully participate in the study and/or incomplete clinical data. Patients were

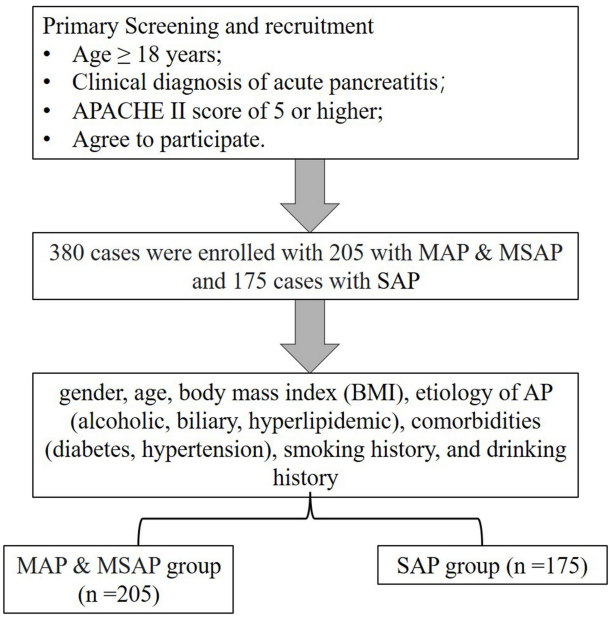

Figure 1 Flowchart illustrating the patient inclusion process.

divided into mild acute pancreatitis group (MAP & MSAP group, n = 205) and severe acute pancreatitis group (SAP group, n = 175) based on the revised Atlanta classification criteria (2012). According to this classification:

- Mild acute pancreatitis (MAP) is characterized by the absence of organ failure and local or systemic complications.
- Moderately severe acute pancreatitis (MSAP) involves transient organ failure (resolving within 48 h) and/or local or systemic complications without persistent organ failure.
- SAP is defined by persistent organ failure lasting more than 48 h.

This classification system was used to ensure consistent and clinically validated stratification of disease severity.[11,12]

Diagnostic Methods:[13–15] Acute pancreatitis was diagnosed based on clinical findings, elevated serum levels of amylase or lipase, and imaging studies. Imaging modalities included abdominal ultrasound and computed tomography (CT) scans to assess the extent of pancreatic inflammation and complications.

It should be noted that, in this retrospective study design, patients were stratified into SAP and MAP/MSAP groups based on established clinical criteria prior to biomarker assessment. This pre-classification may limit the ability to independently evaluate whether serum TFF2 and miR-186-5p levels alone can distinguish disease severity in a blinded or prospective manner. Although this approach may reduce the objectivity of evaluating these biomarkers as standalone predictive tools, it reflects real-world clinical decision-making processes. Moreover, while AP severity is typically assessed using validated scoring systems, such as APACHE II or BISAP, these tools require comprehensive clinical and laboratory data. In contrast, serum biomarkers, including TFF2 and miR-186-5p may offer more rapid, objective, and potentially automated assessment options. Future prospective, blinded studies are warranted to evaluate the independent diagnostic power of these biomarkers and their potential utility in early triage, particularly in resource-limited settings or for real-time monitoring.

Methods

Basic Information

Basic information was collected for all study subjects, including gender, age, body mass index (BMI), etiology of AP (alcoholic, biliary, hyperlipidemic), comorbidities (diabetes, hypertension), smoking history, and drinking history.

Inflammatory Factor Level Detection

Fasting venous blood (5 mL) was collected from all study subjects on the day of admission and left at room temperature for 30 minutes before being centrifuged (3,000 r/min) for 15 minutes to obtain the upper layer of serum. The level of high-sensitivity C-reactive protein (CRP) was measured using the turbidimetric method, and the levels of interleukin-18 (IL-18) and tumor necrosis factor-α (TNF-α) were measured using enzyme-linked immunosorbent assay (ELISA), following the kit instructions strictly.

The study duration and inpatient observation period were sufficient to capture meaningful clinical outcomes and biomarker fluctuations, ensuring the reliability of the associations examined between molecular markers and disease severity.

Acute Physiology and Chronic Health Evaluation II (APACHE II) Score Measurement

The Acute Physiology and Chronic Health Evaluation II (APACHE II) score[11] was calculated for all patients upon admission to assess the overall severity of illness. This scoring system incorporates acute physiological measurements, age, and chronic health status to generate a score ranging from 0 to 71, where higher scores indicate more severe illness. In this study, the APACHE II score was used as a clinical severity index to correlate with serum levels of TFF2 and miR-186-5p, allowing for a comprehensive evaluation of their prognostic relevance in acute pancreatitis. This approach complemented the classification of disease severity based on the Revised Atlanta Classification and the BISAP score.

Detection of Serum TFF2 and miR-186-5p Levels

Serum samples collected in Inflammatory Factor Level Detection were used to detect serum TFF2 levels via ELISA, with all procedures strictly following the kit instructions to ensure accuracy and reproducibility. Total RNA was extracted from

Table 1 Primer Sequences

Gene	Primer Sequences
miR-186-5p	F: GCGCTAAGGCACGCGGT
	R: CAGTGCAGGGTCCGAGGT
U6	F: AGCCTAAGGAACTAGCATTCACTAT
	R: GTTCGCTTCATTACGACGTAGTC

the serum using TRIzol reagent, following steps for lysis, separation, and purification to ensure RNA integrity and purity. To further confirm RNA quality, the purity (OD260/OD280 ratio) and concentration of RNA were measured using a Nanodrop 2000 spectrophotometer. RNA samples meeting the standards were reverse transcribed into cDNA using a reverse transcription kit, and cDNA samples were stored at −20°C. For quantitative detection of miR-186-5p, U6 snRNA was used as the internal reference control. The design and synthesis of primers were completed by Shanghai Biotechnology Corporation (specific primer sequences are shown in Table 1). The reaction conditions were set as follows: pre-denaturation at 95°C for 10 minutes, followed by 40 cycles of 95°C for 15 seconds, 58°C for 30 seconds for annealing, and 72°C for 30 seconds for extension. After the PCR reaction, the relative expression of miR-186-5p was calculated using the $2^{-\Delta\Delta Ct}$ method. Each sample was tested in triplicate to eliminate experimental errors and ensure data reliability.

Patients were followed up throughout their hospitalization, either in the intensive care unit (ICU) or general wards, according to the severity of their condition. This hospital-based observation allowed for comprehensive monitoring of disease progression and outcome assessment, including complications, recovery, or in-hospital mortality. The primary outcomes of the study included the rates of mortality and recovery among the patients. Specifically, we recorded the number of patients who died during hospitalization and those who fully recovered, defined as the absence of complications and return to baseline health.

The secondary outcomes consisted of the assessment of serum TFF2 and miR-186-5p levels in relation to APACHE II, BISAP, and Atlanta scores, providing a comprehensive evaluation of the prognostic indicators in acute pancreatitis.

Statistical Analysis

GraphPad Prism 8 software was used for plotting, and SPSS 22.0 software was used for data processing. Categorical data were expressed as [n(%)] and analyzed using the chi-square test; measurement data following normal distribution were expressed as ($\bar{x} \pm s$), and independent sample t-tests were used for intergroup comparisons. Pearson's method was used to analyze the correlation between serum TFF2, miR-186-5p levels, and hs-CRP, IL-18, TNF-α levels, and APACHE II scores. To determine the cut-off points for serum TFF2 and miR-186-5p levels used in the multivariate logistic regression analysis, we performed receiver operating characteristic (ROC) curve analysis. We collected serum levels of both biomarkers from all patients and constructed ROC curves using SPSS software. The optimal cut-off point for each biomarker was identified by maximizing the sum of sensitivity and specificity, known as Youden's J statistic. This point was selected as the threshold that best discriminated between patients with severe acute pancreatitis (SAP) and those with milder forms of the disease. The selected cut-off points were validated by assessing their diagnostic performance, including sensitivity and specificity. These thresholds were then applied to categorize TFF2 and miR-186-5p levels into binary variables for the logistic regression analysis, allowing for a robust evaluation of their roles as risk factors for SAP. The diagnostic value of serum TFF2 and miR-186-5p levels for SAP was analyzed using ROC curves. Multivariate logistic regression was used to analyze factors influencing SAP. A P-value of <0.05 was considered statistically significant.

Results

Comparison of Basic Information

As shown in Table 2, patients were classified into MAP & MSAP group (n = 205) and SAP group (n = 175) based on the revised Atlanta classification. The SAP group included patients with complications such as persistent organ failure, in

Table 2 Comparison of Basic Information [$\bar{x} \pm s$, n(%)]

Characteristic	MAP &MSAP Group (n=205)	SAP Group (n=175)	t/x²	P
Gender				
Male	109 (53.17)	87 (49.71)	0.522	0.47
Female	96 (46.83)	88 (50.29)		
Age (years)	50.76 ± 12.43	51.27 ± 11.94	0.224	0.822
BMI (kg/m²)	23.51 ± 2.39	23.32 ± 2.67	0.405	0.685
AP Etiology			0.163	0.683
Alcoholic	70 (34.15)	69 (39.43)		
Biliary	93 (45.37)	86 (49.14)		
Hyperlipidemic	42 (20.49)	20 (11.43)		
Comorbidities				
Diabetes	35 (17.07)	26 (14.86)	0.093	0.759
Hypertension	55 (26.83)	49 (28.00)	0.044	0.833
Smoking History	70 (34.15)	63 (36.00)	0.027	0.867
Drinking History	51 (24.88)	46 (26.29)	0.03	0.861

Abbreviations: BMI, body mass index; MAP, mild acute pancreatitis; SAP, severe acute pancreatitis.

accordance with definitions of complicated acute pancreatitis. The basic information of the two groups, including gender, age, BMI, etiology, comorbid diabetes, comorbid hypertension, smoking history, and drinking history, were comparable, with no statistically significant differences (P > 0.05).

Comparison of Serum TFF2 and miR-186-5p Levels

As shown in Figure 2, the TFF2 level in the SAP group was higher than that in the MAP& MSAP group, while the miR-186-5p level in the SAP group was lower than that in the MAP& MSAP group (P < 0.05).

Comparison of Inflammatory Factor Levels and APACHE II Scores

As shown in Figure 3, the levels of hs-CRP, TNF-α, IL-18, and APACHE II scores in the SAP group were higher than those in the MAP& MSAP group (P < 0.05).

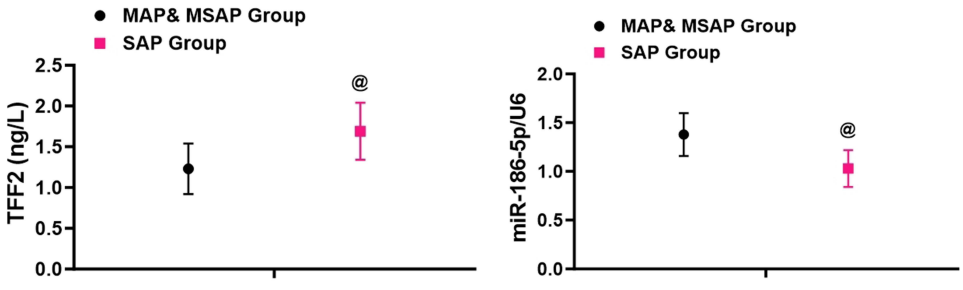

Figure 2 TFF2 and miR-186-5p expression levels in the MAP&MSAP group (black circles) and SAP group (magenta squares). Error bars represent the standard error of the mean (SEM). Statistical significance was assessed using Student's *t*-test. *P* < 0.05 was considered significant, as indicated by @.
Note: Comparison between groups, @P < 0.05.

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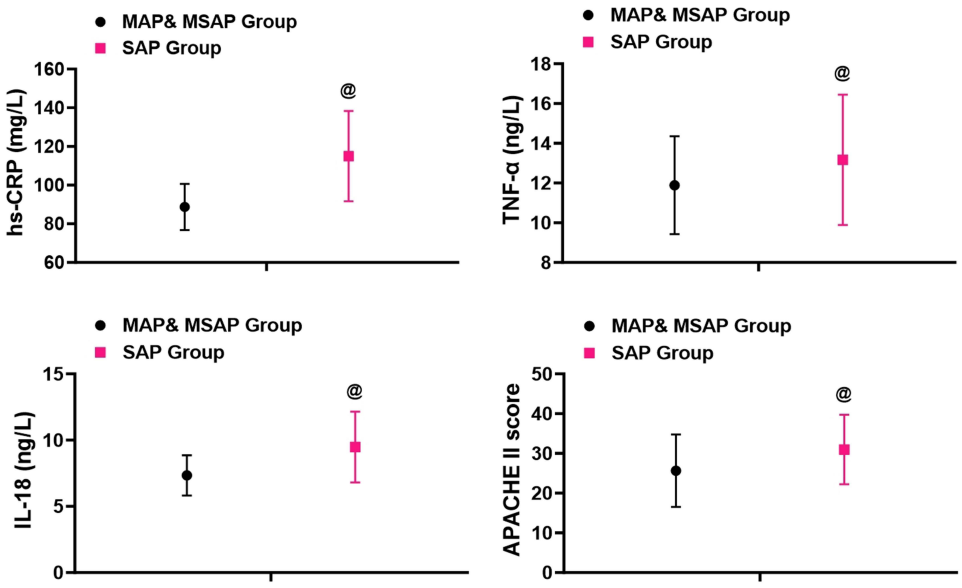

Figure 3 Levels of hs-CRP, TNF-α, IL-18, and APACHE II scores in the MAP&MSAP group (black circles) and SAP group (magenta squares). Error bars represent the standard error of the mean (SEM). Statistical comparisons between groups were performed using Student's *t*-test. *P* < 0.05 was considered statistically significant, as indicated by @.
Note: Comparison between groups, @P < 0.05.

Correlation Between miR-186-5p and TFF2

As shown in Figure 4, Pearson correlation analysis indicated that miR-186-5p expression was negatively correlated with TFF2 expression (r = −0.483, P < 0.05).

Correlation of Serum TFF2, miR-186-5p Levels with Inflammatory Factor Levels and APACHE II Scores

As shown in Table 3, Spearman analysis results indicated that serum TFF2 was positively correlated with hs-CRP, TNF-α, IL-18, and APACHE II scores (P < 0.05); miR-186-5p was negatively correlated with hs-CRP, TNF-α, IL-18, and APACHE II scores (P < 0.05).

Diagnostic Value of Serum TFF2 and miR-186-5p Levels for SAP

Taking TFF2 and miR-186-5p as test variables, and the occurrence of SAP (No = 0, Yes = 1) as the state variable, ROC curves were drawn. As shown in Table 4 and Figure 5, the AUC of TFF2 and miR-186-5p in predicting the occurrence of SAP were 0.804 and 0.832, respectively, and the AUC of the combined detection was 0.895. To ensure the robustness of our

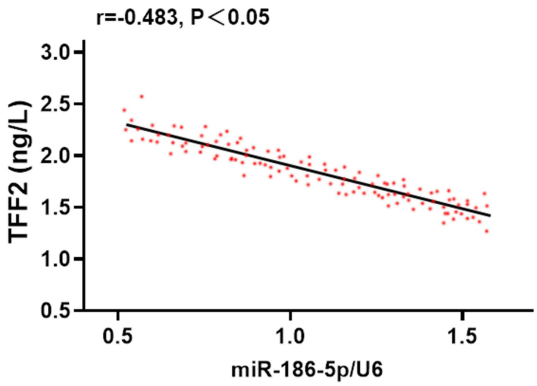

Figure 4 Correlation Between miR-186-5p and TFF2.

Table 3 Correlation of Serum TFF2, miR-186-5p Levels with Inflammatory Factor Levels and APACHE II Scores

Indicator	TFF2		miR-186-5p	
	r	*P*	*r*	*P*
hs-CRP	0.501	<0.05	−0.432	<0.05
TNF-α	0.546	<0.05	−0.570	<0.05
IL-18	0.485	<0.05	−0.454	<0.05
APACHE II Score	0.427	<0.05	−0.431	<0.05

Table 4 Diagnostic Value of Serum TFF2 and miR-186-5p Levels for SAP

Indicator	Critical Value	AUC	95% CI	P	Sensitivity	Specificity
TFF2	1.47	0.804	0.709~0.876	<0.05	76.39	74.82
miR-186-5p	1.15	0.832	0.742~0.903	<0.05	74.27	73.15
Union	–	0.895	0.821~0.954	<0.05	80.36	84.43

findings, we excluded various confounding factors that could influence the levels of TFF2 and miR-186-5p. We established strict inclusion criteria, ensuring that patients had no other infectious diseases, severe dysfunction of vital organs (such as the heart, liver, or kidneys), or concurrent pancreatic diseases. Additionally, patients with malignant tumors, immune system disorders, and significant cardiovascular and cerebrovascular diseases were excluded. Furthermore, baseline comparability between groups was confirmed for lifestyle factors, including smoking and drinking history, as well as comorbidities, such as diabetes and hypertension (Table 2), thereby minimizing their potential confounding effects.

Multivariate Logistic Regression Analysis of Factors Influencing SAP

Taking SAP as the dependent variable (No = 0, Yes = 1), factors with statistical significance in univariate analysis, including TFF2, miR-186-5p, hs-CRP, TNF-α, IL-18, and APACHE II scores, were further analyzed using multivariate logistic regression analysis (variable assignments are shown in Table 5). Multivariate logistic regression analysis showed that TFF2 was a risk factor influencing SAP, while miR-186-5p was a protective factor ($P < 0.05$), as detailed in Table 6.

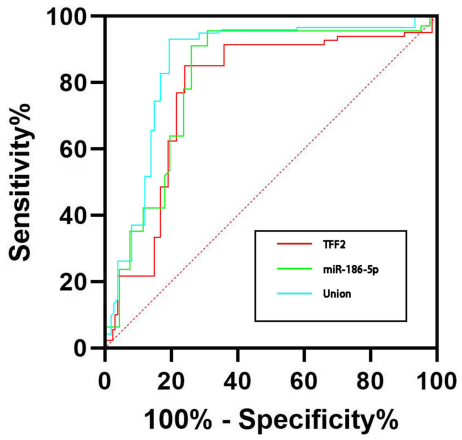

Figure 5 ROC Curve of Diagnostic Value of Serum TFF2 and miR-186-5p Levels for SAP.

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Table 5 Variable Assignments

Variable	Assignment
TFF2	<1.43 ng/L = 0, ≥1.43 ng/L = 1
miR-186-5p	≥1.12 = 0, <1.12 = 1
hs-CRP	Input the original value
IL-18	Input the original value
TNF-α	Input the original value
APACHE II Score	Input the original value

Table 6 Multivariate Logistic Regression Analysis of Factors Influencing SAP

Influencing Factor	*β*	*SE*	*Wald x²*	*P*	*OR (95% CI)*
TFF2	0.987	0.316	9.149	0.003	2.668 (1.409~5.062)
miR-186-5p	−0.172	0.068	6.451	0.012	0.854 (0.739~0.965)
hs-CRP	0.164	0.303	0.289	0.578	1.164 (0.672~2.107)
TNF-α	0.465	0.297	2.304	0.133	1.579 (0.867~2.854)
IL-18	0.241	0.292	0.685	0.406	1.273 (0.725~2.243)
APACHE II Score	0.296	0.314	0.867	0.342	1.329 (0.716~2.439)

Discussion

Trefoil factor 2 (TFF2) is an important biological factor widely involved in mucosal repair and protection in both the digestive and respiratory systems.[16] As a major component of the gastric mucosa, TFF2 plays a key role in maintaining the integrity of the gastric mucosa and promoting tissue repair and remodeling.[17] Moreover, the expression of TFF2 is not limited to humans but is also present in various animals, indicating its evolutionary conservation and functional diversity. In this study, we found that serum levels of TFF2, hs-CRP, IL-18, TNF-α, and APACHE II scores were higher in the SAP group compared to the MAP group (P<0.05). This result is consistent with previous literature,[18,19] further supporting the potential role of TFF2 in the pathogenesis and progression of AP. A study by Zhou et al[20] showed that TFF2 levels increase with the severity of AP and are positively correlated with the grading of acute gastrointestinal injury, suggesting that TFF2 could serve as an important biomarker for assessing the extent of gastrointestinal injury in AP patients. In this study, we also observed a positive correlation between serum TFF2 and levels of hs-CRP, TNF-α, IL-18, and APACHE II scores in AP patients, indicating that TFF2 levels are not only associated with the intensity of the inflammatory response but may also reflect the severity of the patient's condition. This suggests that as TFF2 levels increase, the inflammatory response in the patient's body gradually intensifies, and the patient's condition worsens. It is worth noting that through further correlation analysis, we found a negative correlation between serum miR-186-5p and TFF2 in AP patients, suggesting that miR-186-5p may be involved in the occurrence and development of AP by targeting and negatively regulating TFF2 expression. However, the specific mechanisms by which miR-186-5p regulates TFF2 and its role in AP remain unclear and require further in-depth research. Additionally, through multivariate logistic regression analysis, we found that TFF2 is an independent risk factor for the development of severe AP. This finding suggests that abnormal changes in TFF2 levels may reflect dynamic changes in the patient's condition, providing a reference for clinical diagnosis and treatment decisions. A study by Valentini et al[21] further revealed the potential role of TFF2 in pancreatic cancer. They found that TFF2 can influence the maturation process of dendritic cells (DCs) by adsorbing immature DCs, thereby promoting tumor immune evasion and drug resistance, indicating that TFF2 may be a specific biomarker for pancreatic cancer. Similarly, in this study, we analyzed the diagnostic value of TFF2 in SAP, and the results showed that elevated TFF2 levels could serve as a potential assessment indicator for predicting SAP, providing important evidence for future clinical applications.

The importance of evaluating these biomarkers in tandem lies in their complementary roles in the pathophysiology of AP. TFF2, known for its protective function in maintaining the intestinal mucosal barrier, is significantly elevated in

inflammatory states, suggesting a systemic response to injury. Conversely, miR-186-5p, which regulates key inflammatory pathways, tends to decrease in response to dysregulated inflammation, potentially exacerbating tissue damage. Together, these markers provide a multifaceted view of the inflammatory process occurring in AP, which may enhance the ability to stratify patients based on disease severity.

The rationale for choosing TFF2 and miR-186-5p for our research analysis stems from their established involvement in gastrointestinal health and inflammatory responses. TFF2's elevation is indicative of an inflammatory response that extends beyond the pancreas, involving the gastrointestinal tract as a whole. This is particularly relevant in AP, where gastrointestinal dysfunction often accompanies pancreatic inflammation. By including TFF2 in our analysis, we aimed to capture the broader implications of inflammatory responses in AP.

Similarly, the selection of miR-186-5p was motivated by its role in modulating inflammation and apoptosis. Altered expression levels of miR-186-5p in various disease states suggest its potential as a biomarker for inflammatory conditions. In the context of AP, decreased levels of miR-186-5p may reflect an inability to properly regulate inflammatory pathways, leading to increased tissue damage and complications.

Importantly, the severity of AP is frequently associated with local and systemic complications, such as pancreatic necrosis, infection, and systemic inflammatory response syndrome (SIRS). These complications can significantly influence the levels of TFF2 and miR-186-5p, potentially confounding the interpretation of our results. For instance, the presence of pancreatic necrosis may elevate TFF2 levels due to widespread inflammation, while also affecting miR-186-5p expression. By not stratifying patients based on these complications, we may have overlooked critical factors that could alter the relationship between these biomarkers and disease severity.

The results of this study indicate that serum TFF2 and miR-186-5p levels have significant diagnostic and prognostic value for patients with acute pancreatitis, particularly in distinguishing severe AP from milder forms. From a clinical perspective, early identification of patients at risk of developing SAP is critical for timely initiation of intensive monitoring, organ support, and potential transfer to a higher-level care facility. The measurement of TFF2 and miR-186-5p upon hospital admission could provide clinicians with a rapid, non-invasive, and cost-effective tool to stratify disease severity. Elevated TFF2 levels, reflecting mucosal injury and systemic inflammation, may prompt more aggressive management, while decreased miR-186-5p levels may signal dysregulated inflammation and a need for closer observation. Furthermore, combined assessment of both markers enhances diagnostic accuracy and complements existing scoring systems, such as APACHE II, providing a more nuanced risk stratification model. This biomarker-based approach may ultimately contribute to improved clinical outcomes by enabling earlier intervention in high-risk patients.

In this study, we observed that as the severity of AP increased, the levels of miR-186-5p in the patient's serum significantly decreased, suggesting that miR-186-5p may to some extent reflect the severity of AP. Correlation analysis further indicated that miR-186-5p levels were negatively correlated with hs-CRP, TNF-α, IL-18, and APACHE II scores, implying that a decrease in miR-186-5p levels may predict an exacerbation of the inflammatory response and worsening of the patient's condition. Through multivariate logistic regression analysis, we further confirmed the role of miR-186-5p as a protective factor in AP patients. This result suggests that a decrease in serum miR-186-5p levels may indicate worsening of the condition, while its stability may be associated with a milder condition. Therefore, miR-186-5p has the potential to serve as a biomarker for evaluating SAP, providing clinical doctors with a basis for early intervention. Further analysis through ROC curves showed that the combined detection of serum TFF2 and miR-186-5p has higher accuracy in diagnosing SAP. The AUC for the combined detection was significantly higher than that for the detection of TFF2 or miR-186-5p alone, indicating that the combined detection of both has higher diagnostic efficiency in predicting and diagnosing SAP. This finding provides a new approach for more accurate assessment of AP patients' conditions in clinical practice, which is expected to improve the identification and treatment success rate of severe patients.

Conclusion and Limitations

This study indicates that TFF2 and miR-186-5p play important roles in the occurrence and development of AP. Both are closely related to the severity of the condition and may serve as molecular markers for evaluating and predicting the prognosis of AP patients. In particular, the combined detection of TFF2 and miR-186-5p can improve the diagnostic efficiency for severe AP, providing new reference bases for early clinical intervention. These findings suggest that

implementing the combined detection of TFF2 and miR-186-5p in clinical practice may facilitate early risk stratification and timely therapeutic decision-making for AP patients. Their potential as accessible and non-invasive biomarkers supports their value in guiding individualized treatment strategies and improving clinical outcomes.

However, it is important to note that despite the significant findings of this study, there are still some limitations: ① Relatively small sample size: This study included only 117 patients with SAP, which is a relatively small sample size and may affect the generalizability and robustness of the statistical results and conclusions; ② Single-center study: The data were obtained from a single medical center, which may be influenced by regional and institutional characteristics, thereby limiting the broader applicability of the findings; ③ Insufficient mechanistic exploration: Although a correlation between TFF2 and miR-186-5p levels and AP severity was identified, the underlying biological mechanisms through which these biomarkers influence disease progression remain unclear; ④ Lack of longitudinal follow-up data: The study did not include long-term patient follow-up, limiting the ability to assess the predictive value of TFF2 and miR-186-5p for long-term outcomes or recurrence; ⑤ Lack of external validation: The findings require validation in independent, multi-center cohorts to confirm their reliability and applicability across diverse patient populations; ⑥ No correlation analysis with complicated AP: This study did not evaluate the relationship between TFF2 and miR-186-5p levels and the development of complicated AP, such as pancreatic necrosis, infection, or organ failure, which limits the clinical scope of these biomarkers.

Disclosure

The authors report no conflicts of interest in this work.

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