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Clinical predictive value of control attenuation parameters in combination with miR-192-5p in patients with acute pancreatitis in nonalcoholic fatty liver disease

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Abstract

Introduction: Control attenuation parameters (CAP) can detect nonalcoholic fatty liver disease (NAFLD). Our previous study found that miR-192-5p could screen for acute pancreatitis (AP) in NAFLD patients. This study focused on the role of CAP and miR-192-5p in NAFLD of acute AP.

Material and methods: AP patients and controls were enrolled. Classification of AP patients into NAFLD/AP patients and non-NAFLD/AP was made based on the CAP value. CAP was measured by liver transient elastography. Serum miR-192-5p was measured by reverse transcription-quantitative polymerase chain reaction (RT-qPCR). Logistic regression analysis was conducted to examine the risk factors for the development of NAFLD. Receiver operating characteristic (ROC) was assessed for the predictive value of AP severity.

Results: NAFLD was more common in the AP group than in the controls (35.00% *vs*. 8.75%). The CAP value was higher in AP patients with NAFLD than in non-NAFLD, whereas miR-192-5p was significantly lower in AP patients with NAFLD. Additionally, AP patients with NALFD are more likely to experience respiratory failure, systemic inflammatory response syndrome (SIRS), and pancreatic necrosis with longer hospitalisation and exacerbate the incidence of moderate to severe AP. Both miR-192-5p and TG are potential risk factors for the development of NAFLD in patients with AP. Furthermore, the CAP value gradually increased with increasing AP severity, while miR-192-5p gradually decreased. Finally, the sensitivity and specificity of CAP combined with miR-192-5p for the prediction of moderate to severe AP were scored as 82.61% and 82.43%, respectively.

Conclusions: NAFLD exacerbated the progression of AP, and CAP combined with miR-192-5p could predict the severity of AP. Our study may provide more reference for AP disease progression and treatment. **(Endokrynol Pol 2024; 75 (2): 207–215)**

Key words: *CAP; miR-192-5p; AP; NAFLD*

Introduction

Acute pancreatitis (AP) is a sudden abdominal emergency with complex pathogenesis and diverse aetiology, often involving peripancreatic and distant tissues. Over 270,000 people are hospitalised for AP each year in the United States, with hospitalisation costs of 2.5 billion USD [1]. Mortality rates are up to 30% in patients with severe pancreatitis [2]. Previous studies have reported that fatty liver disease accelerates the severity of AP and leads to a worse prognosis [3]. Therefore, accurate assessment and timely suppression of abnormalities of hepatic lipid metabolism have become an important issues in mitigating the progression of AP.

Non-alcoholic fatty liver disease (NAFLD) is a metabolism-related liver disease that has recently been redefined as metabolic dysfunction-associated fatty liver disease (MAFLD) [4]. Recent studies have shown that the prevalence of NAFLD is significantly higher in patients with AP than in the normal population [5]. Liver biopsy is currently the gold standard for assessing hepatic steatosis in NAFLD. However, it is not only invasive, but also the biopsy specimen is only one-fifty-thousandth of the volume of the liver, which does not fully reflect the entirety of the liver [6]. Ultrasound is insensitive to mild fatty liver degeneration (up to 30% of degeneration can be detected) and is dependent on the skill and experience of the operator [7]. Controlled attenuation parameter (CAP) has recently been found to be a promising non-invasive assessment of hepatic steatosis, and its measurements can be obtained by liver transient elastography (TE) [8]. CAP measurements are noninvasive, easy to quantify, inexpensive, simple to perform, and highly sensitive to the degree of hepatic steatosis. However, it is unknown for fatty liver degeneration in AP patients.

With the increasing popularity of high-throughput sequencing technologies, the role of non-coding RNAs

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in disease is being investigated. MicroRNAs (miRNAs) are endogenous non-coding small RNA molecules. Su et al. identified 37 aberrantly expressed miRNAs in AP patients [9], and Luo et al. recognised 6 differentially expressed miRNAs in the serum of patients with AP [10]. Of note, miR-192-5p is dysregulated in NAFLD participates in lipid synthesis [11], and it regulates hyperlipidaemic pancreatitis [12]. Our preliminary study found that miR-192-5p can identify patients with AP combined with NAFLD and is a promising biomarker for AP [13].

The present research focused on the levels of CAP and miR-192-5p in patients with AP combined with NAFLD and explores the predictive value of CAP combined with miR-192-5p in predicting the severity of AP disease to provide a new approach for the management and treatment of AP patients with fatty liver degeneration.

Material and methods

Study population

The research was conducted in accordance with the Declaration of The First Affiliated Hospital of Nanchang University Medical Ethics Committee. Subjects signed an informed consent form.

Patients with AP admitted to The First Affiliated Hospital of Nanchang University from June 2020 to July 2022 were included in the study.

Inclusion criteria: 1) meeting the diagnostic criteria for AP, i.e. abdominal pain (sudden, persistent, and severe), serum lipase or amylase more than three times the normal value, abdominal ultrasound, magnetic resonance, enhanced CT showing significant AP imaging changes; 2) age > 18 years; and 3) admission within 24 h of onset of disease.

Exclusion criteria: 1) combined chronic pancreatitis; 2) suffering from acute abdomen such as intestinal obstruction, acute appendicitis; 3) combined autoimmune system disease; 4) with severe cardiac, hepatic, renal, and other organ function abnormalities; 5) chronic liver diseases such as alcoholic fatty liver disease, viral hepatitis, drug-induced liver disease, and hereditary metabolic liver disease; and 6) history of taking hepatoprotective drugs or drugs affecting glucose and lipid metabolism within the last 3 months. A total of 120 patients with AP were finally included. They were categorised into mild acute pancreatitis (MAP), moderate severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP) according to the severity of the disease using the 2012 revised Atlanta classification criteria [14]. Eighty individuals with non-AP matched for age and body mass index (BMI) were consecutively selected as controls during the same period. Blood samples were collected from subjects within 24 h of admission. A portion of blood was then centrifuged at 12,000 rpm for 10 min, and the upper portion of the serum was collected and reversed for use.

Study variables and laboratory investigations

Biochemical parameters including triglyceride (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), C-reactive protein (CRP), blood urea ammonia (BUN), and creatinine (Cr) were discovered using an automatic biochemical analyser. The length of the patient's hospitalisation was also recorded, as well as the occurrence of complications such as respiratory failure, renal failure, pancreatic necrosis, and pancreatic necrosis infection.

Measurement of CAP

All subjects were tested by transient elastography (FibroScan 502, Echosens, Paris, France) by 2 professionally trained and experienced operators using a blinded method for detecting CAP, in patients with AP and controls. Briefly, the patients were placed in the supine position with their hands behind their head, the intercostal space of the right lobe of the liver was exposed, and the 7^{th}, 8^{th}, and 9^{th} intercostal spaces between the anterior axillary line of the right armpit and the mid-axillary line of the right armpit were selected as the detection area. At least 10 valid measurements were performed on the same point for each patient, and the median was taken as the final CAP value. According to the previous studies, NAFLD was defined as CAP ≥ 263 dB/m [15–19].

RNA extraction and reverse transcription-quantitative polymerase chain reaction (RT-qPCR)

The miRNeasy serum/plasma miRNA isolation Kit was designed to isolate and extract RNA from serum. RNA purity and concentration were examined by spectrophotometry at 260 and 280 nm. Complementary DNA (cDNA) of miRNA was synthesised using a Mir-X™ miRNA qRT-PCR SYBR kit (Takara, Japan). The cDNA, primers, and miRcute Plus miRNA qPCR Kit (SYBR Green) were then mixed and amplified on a 7500 Fast real-time PCR system (Applied Biosystems, USA). U6 was conducted as an internal reference and the relative expression of miR-192-5p was calculated by the $2^{-\Delta\Delta Ct}$ method.

Statistical analysis

SPSS 23.0 and GraphPad prism 9.0 were adopted for statistical analysis and visualisation of data. Each measurement was repeated at least 3 times and expressed as mean ± standard deviation (SD), or n (%). Comparisons between the 2 groups were made using Student's t-test or the Mann-Whitney U-test. Count data were analysed using the chi-squared test. The Pearson coeffect correlation was conducted to verify correlations. Logistic regression was conducted to explore the risk factors. $P < 0.05$ indicated that the difference was statistically significant.

Results

Demographic and clinical baseline characteristics of the subjects

A total of 200 subjects were enrolled, comprising 80 non-SAP subjects (Control) and 120 patients with AP. Patients with AP had significantly higher TG, ALT, BUN, CRP, lipase, and amylase than the controls ($p < 0.05$, Supplementary File — Tab. S1). No statistically significant differences were observed in age, BMI, male sex, smoking, alcohol drinking, diabetes, white blood cells (WBC), AST, and TBIL in the 2 groups ($p > 0.05$, Supplementary File — Tab. S1).

Levels of CAP and miR-192-5p in patients with AP

As illustrated in Figure 1A, patients with AP had significantly higher CAP values than the controls (219.77 ± 23.22 dB/m *vs*. 247.4 ± 41.67 dB/m; $p < 0.001$). However, miR-192-5p was poorly expressed in patients with AP ($p < 0.001$, Fig. 1B). Furthermore, Pearson

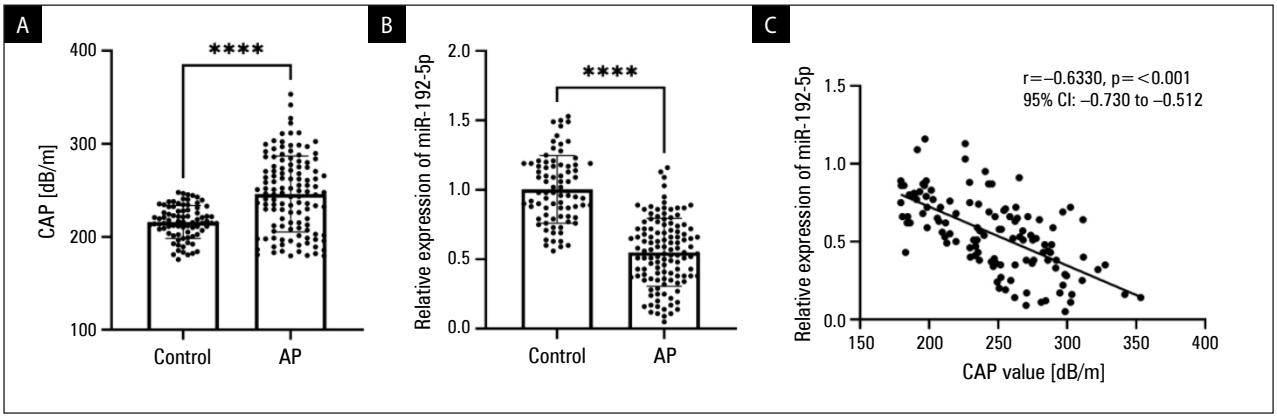

Figure 1. *The levels of control attenuation parameters (CAP) and miR-192-5p in subjects.* **A**. *The CAP value in the patients with acute pancreatitis (AP) and controls;* **B**. *Reverse transcription-quantitative polymerase chain reaction (RT-qPCR) was conducted to examine the mRNA levels of miR-192-5p;* **C**. *Pearson coefficient correlation was used to estimate the correlation between miR-192-5p expression and CAP value in patients with AP. ***p < 0.001 vs. control*

coefficients revealed that the CAP value was negatively correlated with miR-192-5p in patients with AP (r = –0.6330, p < 0.001, Fig. 1C).

Risk factors for the development of NAFLD in patients with AP

Based on previous studies, CAP ≥ 263 dB/m was employed to identify NAFLD in the subjects [17, 18]. In our study, the prevalence of NAFLD in AP patients was significantly higher at 35.0% (42/120), compared to controls, who had a prevalence of 8.75% (7/80, p < 0.001). Comparison of clinical baseline characteristics of AP patients with and without NAFLD. AP patients with NAFLD exhibited a higher prevalence of diabetes and hypertriglyceridaemia, and greater BMI (p < 0.05, Tab. 1). Additionally, TG, TBIL, CRP, lipase, and amylase were generally higher in NAFLD patients than in non-NAFLD subjects (p < 0.05, Tab. 1). The BISAP scores, which are associated with AP severity, were also significantly higher in NAFLD patients (p = 0.020, Tab. 1). More notably, the mean CAP value was markedly elevated in AP patients with NAFLD, whereas miR-192-5p was significantly lower (p < 0.05, Fig. 2A–B). Factors affecting the occurrence of NAFLD in patients with AP were explored. The occurrence of NAFLD in AP patients was the dependent variable, and miR-192-5p and clinical information were selected as independent variables. Univariate logistic regression analysis showed that BMI, diabetes, hypertriglyceridaemia, TG, amylase, BISAP score, and miR-192-5p were risk factors for NAFLD in patients with AP (p < 0.05, Tab. 2). Multivariate logistics regression analysis was carried out, showing that miR-192-5p [odds ratio (OR): 7.115, 95% confidence interval (CI): 2.680–18.891,

Table 1. ***Clinical baseline characteristics of patients with acute pancreatitis with nonalcoholic fatty liver disease (NAFLD) versus non-NAFLD***

Parameters	non-NAFLD (n = 78)	NAFLD (n = 42)	p-value
General situation			
Age [year]	56.77 ± 10.10	58.29 ± 10.74	0.444
BMI	24.30 ± 2.83	26.55 ± 2.73	0.000
Male, n (%)	40 (51.28)	27 (64.29)	0.184
Smoking, n (%)	43 (55.13)	20 (47.62)	0.450
Alcohol drinking, n (%)	45 (57.69)	28 (66.67)	0.433
Diabetes, n (%)	10 (12.82)	12 (28.57)	0.047
Aetiology, n (%)			
Gallstone	43 (55.13)	20 (47.62)	0.450
Hypertriglyceridaemia	9 (11.54)	14 (33.33)	0.007
Other	27 (36.62)	8 (19.05)	0.093

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Table 1. *Clinical baseline characteristics of patients with acute pancreatitis with nonalcoholic fatty liver disease (NAFLD) versus non-NAFLD*

Parameters	non-NAFLD (n = 78)	NAFLD (n = 42)	p-value
Laboratory indicators			
WBC [×10⁹/L]	10.13 ± 5.24	11.93 ± 5.43	0.079
BPC [×10⁹/L]	200.71 ± 72.64	209.83 ± 74.31	0.517
TG [mmol/L]	1.67 ± 0.60	3.22 ± 0.99	0.000
AST [U/L]	25.34 ± 6.62	26.18 ± 6.86	0.514
ALT [U/L]	33.05 ± 33.05	36.07 ± 10.35	0.072
TBIL [μmol/L]	13.29 ± 6.17	16.36 ± 6.51	0.012
Alb [g/L]	37.09 ± 4.14	35.88 ± 4.74	0.149
BUN [mmol/L]	5.54 ± 2.82	4.94 ± 0.85	0.632
Cr [μmol/L]	71.61 ± 11.16	68.55 ± 8.94	0.129
CRP [mg/L]	75.67 ± 23.13	87.65 ± 26.55	0.016
Lipase [U/L]	639.91 ± 328.99	770.26 ± 285.46	0.032
Amylase [U/L]	419.48 ± 181.22	488.16 ± 173.20	0.047
BISAP score	2.08 ± 0.88	2.48 ± 0.89	0.020

Variables are expressed as the mean ± standard deviation or n (%). BMI — body mass index; WBC — white blood cells; BPC — blood platelet count; ASL — aspartate aminotransferase; ALT — alanine aminotransferase; Alb — albumin; TBIL — total bilirubin; BUN — blood urea ammonia; Cr — creatinine; CRP — C-reactive protein; BISAP — Bedside index for severity in acute pancreatitis

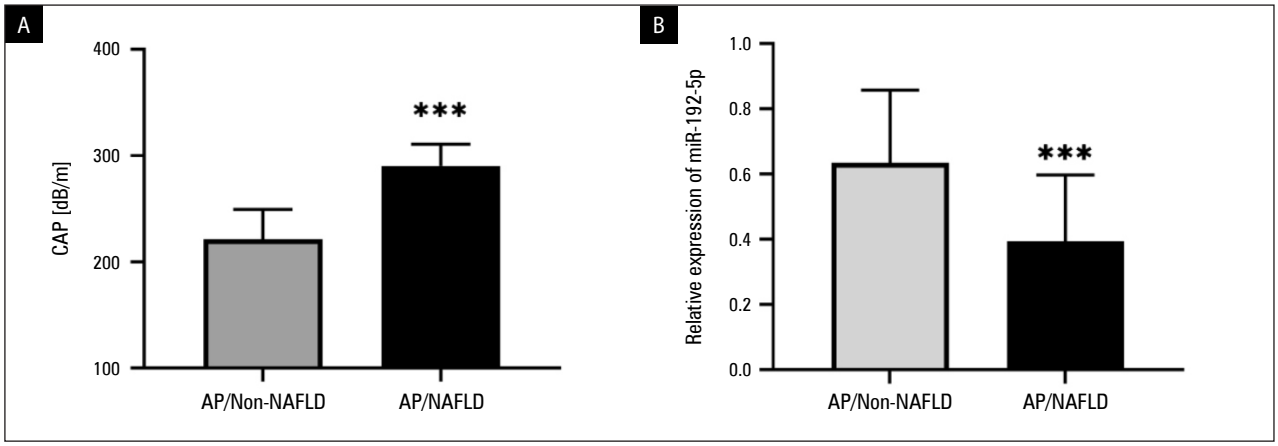

Figure 2. *The levels of control attenuation parameters (CAP) and miR-192-5p in acute pancreatitis (AP) patients with nonalcoholic fatty liver disease (NAFLD) and without NAFLD.* **A**. *The CAP value was higher in AP patients with NAFLD than the AP/non-NAFLD;* **B**. *The miR-192-5p levels in AP patients with NAFLD were lower than in the AP patients without NAFLD. ***p < 0.001 vs. AP/Non-NAFLD group*

p = 0.001, Tab. 2] and TG were independent risk factors for NAFLD in AP patients.

The effect of NAFLD on the condition and prognosis of patients with AP

To compare the condition and prognosis of AP patients with and without NAFLD. As shown in Table 3, AP patients with NAFLD had longer hospitalisation as well as higher rates of concomitant systemic inflammatory response syndrome (SIRS), disseminated intravascular coagulation (DIC), respiratory failure, pancreatic necrosis, and pancreatic necrosis infection compared with the non-NAFLD group (p < 0.05). Patients with AP are categorised into MAP, MASP, and ASP according to severity based on the 2012 revised Atlanta classification criteria. The percentage of patients with MASP and SAP was significantly higher in the NAFLD group than in non-NAFLD groups (p < 0.05, Tab. 3).

The association between the severity of hepatic steatosis and the severity of AP

As illustrated in Figure 3A–B, the measure of the CAP value, which represents the degree of hepatic fat accumulation, increased progressively with increas-

Table 2. *Analysis of risk factors for nonalcoholic fatty liver disease (NAFLD) in patients with acute pancreatitis (AP)*

Parameters	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	p-value	OR	95% CI	p value
BMI	2.485	1.152–5.358	0.020	2.530	0.992–6.455	0.052
Diabetes	2.720	1.060–6.982	0.038	3.013	0.914–9.928	0.070
Hypertriglyceridemia	3.833	1.489–9.868	0.005	2.745	0.850–8.868	0.091
TG	2.729	1.255–5.937	0.011	3.043	1.175–7.879	0.022
TBIL	1.630	0.762–3.483	0.208			
CRP	2.103	0.977–4.528	0.057			
Lipase	1.544	0.718–3.317	0.266			
Amylase	2.230	1.037–4.792	0.040	1.819	0.720–4.592	0.206
BISAP score	2.120	0.982–4.576	0.056			
miR-192-5p	6.926	2.895–16.569	0.000	7.115	2.680–18.891	0.000

OR — odds ratio; CI — confidence interval; BMI — body mass index; TG — triglycerides; TBIL — total bilirubin; CRP — C-reactive protein; BISAP — Bedside index for severity in acute pancreatitis

Table 3. *Condition and prognosis analysis of acute pancreatitis patients with and without nonalcoholic fatty liver disease (NAFLD)*

Parameters	NAFLD (n = 42)	non-NAFLD (n = 78)	p-value
Length of hospitalisation (d)	12.8 ± 2.9	8.8 ± 2.1	0.000
MSAP+SAP, n (%)	32 (76.19)	14 (33.33)	0.000
SIRS, n (%)	22 (52.38)	10 (23.81)	0.000
DIC, n (%)	3 (7.14)	4 (9.52)	0.694
Renal failure, n (%)	11 (26.19)	6 (14.29)	0.011
Respiratory failure, n (%)	6 (14.29)	9 (21.43)	0.774
Circulatory failure, n (%)	3 (7.14)	2 (4.76)	0.342
Pancreatic necrosis, n (%)	7 (16.67)	3 (7.14)	0.032
Pancreatic necrosis infection, n (%)	4 (9.52)	1 (2.38)	0.050

Variables are expressed as the mean ± standard deviation or n (%). BISAP — Bedside index for severity in acute pancreatitis; SIRS — systemic inflammatory response syndrome; DIC — disseminated intravascular coagulation

ing severity of AP, whereas serum miR-192-5p was significantly lower ($p < 0.05$). The occurrence of MSAP and SAP was a dependent variable; miR-192-5p and clinical information were selected as independent variables. Univariate logistic regression analysis showed that hypertriglyceridaemia, amylase, BISAP score, CAP, and miR-192-5p were risk factors for MSAP and SAP ($p < 0.05$, Tab. 4). Multivariate logistics regression analysis found that CAP (OR: 11.775, 95% CI: 3.719–37.280, $p < 0.0001$,) and miR-192-5p (OR: 14.722, 95% CI: 4.723–45.888, $p < 0.0001$, Tab. 4) were independent risk factors for more severe AP.

CAP combined with miR-192-5p has a high diagnostic value in moderate to severe AP

Receiver operating characteristic (ROC) curves were plotted based on the level of CAP in patients with MAP and in MSAP + SAP patients. As shown in Figure 3C, the area under the curve (AUC) of the ROC was 0.778, and the sensitivity and specificity of CAP values in identifying SAP and MASP patients from MAP were 69.57% and 86.49%, respectively. Additionally, the AUC of the ROC curve based on miR-192-5p expression was 0.828, and the sensitivity and specificity were 76.09% and 75.68, respectively (Fig. 3D). Notably, when combining CAP and miR-192-5p, the AUC was 0.911, and the sensitivity and specificity were 82.61% and 82.43%, respectively (Fig. 3E). The results suggest that combining CAP and miR-192-5p significantly predicts the severity of patients with AP.

Discussion

NAFLD has become the most common metabolic disease of the liver, and its incidence is increasing. Previous studies have found that the development of

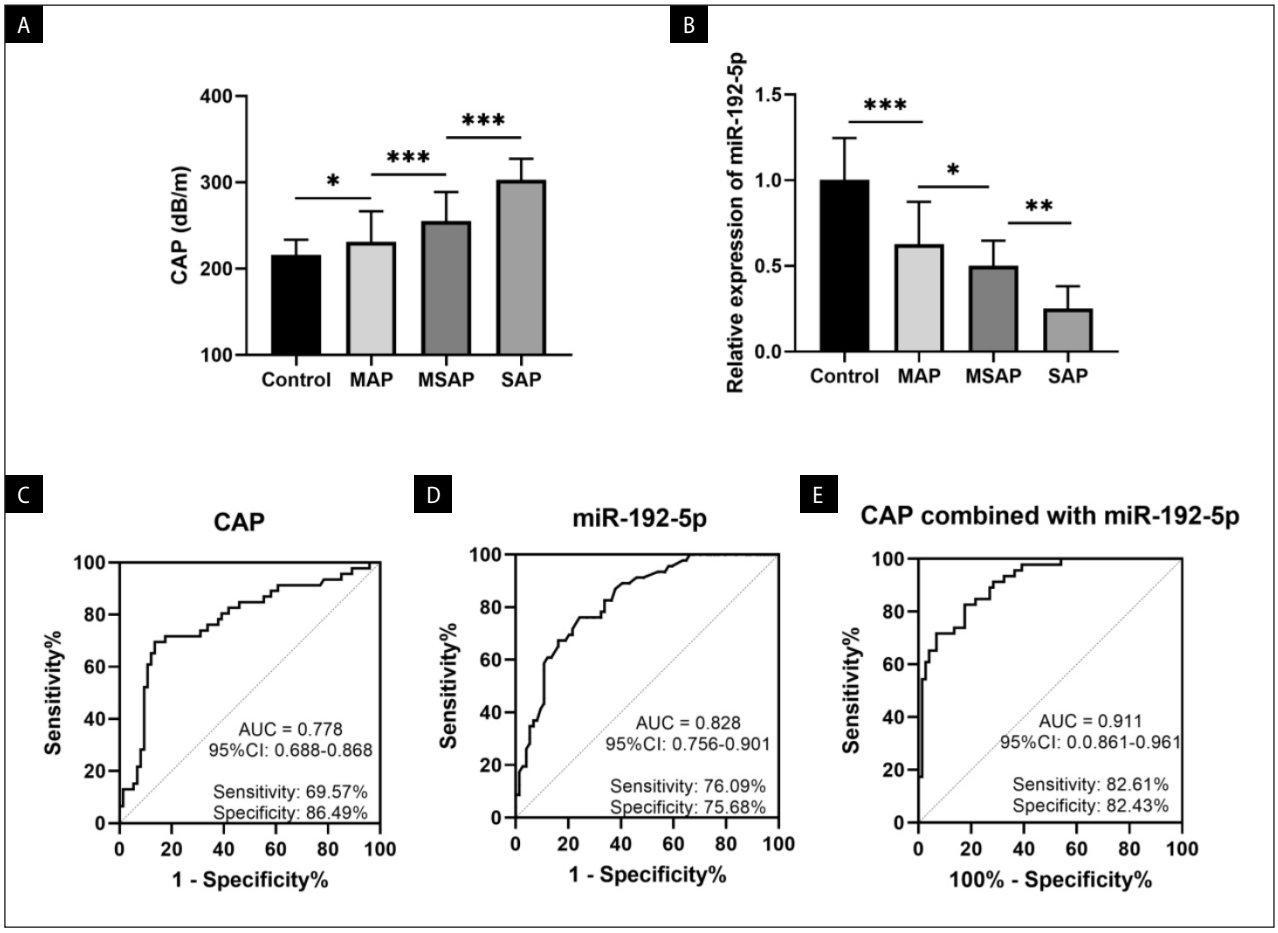

Figure 3. *Control attenuation parameters (CAP) combined with miR-192-5p can predict acute pancreatitis (AP) severity. As the severity of AP increased, the CAP value (***A***) gradually elevated, whereas serum miR-192-5p (***B***) significantly decreased. The receiver operating characteristic (ROC) curves based on CAP value (***C***), miR-192-5p (***D***), and CAP combined with miR-192-5p (***E***) to predict severe acute pancreatitis (SAP) and moderate severe acute pancreatitis (MSAP) patients from mild acute pancreatitis patients (MAP). *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$*

Table 4. *Logistic regression analysis affecting the occurrence of moderate to severe pancreatitis*

Parameters	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	p-value	OR	95% CI	p-value
BMI	1.562	0.745–3.276	0.237			
Diabetes	1.500	0.713–3.154	0.285			
Hypertriglyceridaemia	2.729	1.112–6.694	0.028	3.046	0.906–10.235	0.072
TG	1.091	0.522–2.278	0.817			
TBIL	1.033	0.495–2.159	0.930			
CRP	1.327	0.634–2.775	0.453			
Lipase	1.706	0.804–3.620	0.164			
Amylase	2.205	1.042–4.667	0.039	2.316	0.826–6.491	0.110
BISAP score	2.217	1.038–4.738	0.040	2.996	1.059–8.473	0.039
CAP	5.914	2.544–13.748	0.000	11.775	3.719–37.280	0.000
miR-192-5p	8.565	3.566–20.568	0.000	14.722	4.723–45.888	0.000

OR — odds ratio; CI — confidence interval; BMI — body mass index; TG — triglycerides; TBIL — total bilirubin; CRP — C-reactive protein; BISAP — Bedside index for severity in acute pancreatitis; CAP — control attenuation parameters

fatty liver accelerates the severity of AP and leads to a worsening of prognosis. In this preliminary study, AP patients with NAFLD were found to have worse disease and prognosis than non-NAFLD patients, which is similar to previous studies. We further explored and found that this state was associated with the level of TG and miR-192-5p. What is more, CAP was significantly higher in AP patients with NAFLD, whereas miR-192-5p was significantly lower. The results suggest that CAP and miR-192-5p are associated with the status of NAFLD in patients with AP. Finally, both CAP and miR-192-5p are risk factors for AP progression to severe AP, and combined they have some sensitivity and specificity to predict AP severity.

NAFLD is a manifestation of hepatic metabolic syndrome. Xu et al. conducted a retrospective evaluation of 2671 patients with AP, of whom 480 had NAFLD, and aggravated the progression of AP [20]. Our study analysed AP patients with NAFLD and non-NAFLD, and compared their clinical baseline characteristics. Significant differences were found between lipid indicators and CRP, lipase, amylase, and BISAP scores in AP patients with NAFLD. In addition, our study agrees with the study by Wu et al., who found that hyperlipidaemic pancreatitis has the highest prevalence in NAFLD and is associated with a higher severity of AP and a higher incidence of SIRS in patients with NAFLD [5]. Furthermore, similarly to our study, Jia et al. found that TG levels were higher in AP patients than in chronic pancreatitis and controls [21]. Previous investigation established that dyslipidaemia, especially TG, relates to AP. The pathophysiology may be pancreatic cell damage and ischaemia resulting from the metabolism of excess TG to non-esterified fatty acids by pancreatic lipase.

CAP is a good diagnostic instrument for the non-invasive measurement and quantification of fatty liver degeneration. It uses a Fibroscan device to quantify the level of hepatic steatosis by reducing the amplitude of the ultrasound as the sound waves pass through the liver fatty tissue using the same radio frequency [22]. CAP is recommended as a screening tool for NAFLD by the Asia Pacific Working Party on NAFLD [23]. Several recent studies have emphasised that a CAP greater than 263 dB/m for detecting the degree of fatty liver degeneration defines NAFLD [15–19]. We defined NAFLD in AP patients based on this. Wu et al. discovered that the presence of NAFLD on admission predicted both higher AP severity and a higher risk of SIRS and organ failure [24]. It has been reported that 50.9–76.3% of SAP cases die of MODS within 2 weeks of onset and 33.3%–49.1% of these are caused by co-infections [25]. Early prediction of poor prognosis in patients with AP allows for initial management of early SAP focusing on fluid resuscitation, pain control, and nutritional support to minimise systemic inflammatory response syndrome. In this study, it was found that AP patients with NAFLD experienced more SIRS and sustained organ failure as well as pancreatic necrosis and peripancreatic necrosis, and longer hospital stays. Importantly, we identified AP patients with NAFLD who had high levels of CAP and downregulation of miR-192-5p compared to non-NAFLD. They were both independent risk factors for the development of NAFLD in AP. Therefore, early promotion of miR-192-5p and inhibition of NAFLD in patients with AP in the presence of NAFLD may be a good therapeutic approach to suppress the poor prognosis of AP.

That AP severity correlates with NAFLD severity has been confirmed. We examined the level of CAP in patients with different severity of AP and found that CAP gradually increased with increasing AP severity. We speculate that CAP may be able to predict the severity of AP. MiR-192-5p negatively regulates lipid synthesis in NAFLD [11] and is present in hepatocyte-derived exosomes; it is associated with the progression of NAFLD [26]. MiR-192-5p was also identified by Tan et al. as a good diagnostic biomarker for NAFLD [27]. Our previous study demonstrated that serum miR-192-5p is typically reduced in patients with AP combined with NAFLD and is a potential diagnostic biomarker [13]. In the present research, we again identified that serum miR-192-5p distinctly decreased with increasing AP severity in patients with NAFLD. The levels of miR-192-5p and CAP were negatively correlated in patients with AP. Hence, we strongly believe that both miR-192-5p as well as CAP might be implicated in the severity of AP. Logistic regression analysis confirmed our speculation and found that CAP, miR-192-5p, and BSIAP scores were considered potential risk factors for the progression of AP into SAP. Yang et al. examined BISAP scores in predicting the severity of AP in hyperlipidaemia and found that BISAP scores were more specific in identifying severe AP but less sensitive [28]. However, for the first time, we discovered that CAP combined with miR-192-5p had high sensitivity and specificity to identify severe AP and could be considered a promising diagnostic biomarker for AP severity. Clinical scoring is relatively complex, involving multiple biological and clinical details gathered at different times from the time of admission, and it does not take into account underlying factors of AP, such as hyperlipidaemia or gallstones [29]. This study identified CAP combined with serum miR-192-5p as a non-invasive and highly accurate biomarker for early definition of SAP in patients with NAFLD, allowing for early attention and timely treatment of AP patients.

There are several limitations of the current study. First, the present study was carried out in a single centre, which may produce bias. Second, elastography using the M-probe produced invalid measurements in nearly 10% of patients, but this was within the allowable failure rate of 4–24%.

Conclusions

In summary, our study confirms that NAFLD promotes the progression of AP. CAP combined with miR-192-5p can predict the severity of AP disease and provide a more reference basis for clinical prediction of AP disease. This study may provide new ideas and direction for the disease progression in patients with NAFLD combined with AP.

Conflicts of interest

There is no conflict of interest in this study.

Funding

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Data availability statement

All data generated or analysed during this study are included in this article and its supplementary material files. Further enquiries can be directed to the corresponding author.

Ethics statement

The research was conducted in accordance with the Declaration of The First Affiliated Hospital of Nanchang University Medical Ethics Committee. All subjects signed an informed consent form.

Authors' contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Y H, L Z, and RL C. The first draft of the manuscript was written by Y H, L Z, and RL C. And all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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