Combination of Body Mass Index and Fasting Blood Glucose Improved Predictive Value of New-Onset Prediabetes or Diabetes After Acute Pancreatitis

A Retrospective Cohort Study

Shao-Yan Guo, MD, Hai-Yun Yang, MD, Xiao-Yan Ning, MD, Wan-Wei Guo, MS,
Xiao-Wu Chen, MS, and Man Xiong, MD

Objectives: We sought to evaluate whether combining body mass index (BMI) and fasting blood glucose (FBG) can refine the predictive value of new-onset prediabetes/diabetes after acute pancreatitis (NODAP).

Methods: In this retrospective cohort study, we used Kaplan–Meier analysis to compare differences in the NODAP rate among 492 patients with different BMI or FBG levels, or with the combination of these 2 factors mentioned above.

Results: In all, 153 of 492 (31.1%) eligible patients finally developed NODAP. According to univariate and multivariate analyses, BMI (hazard ratio, 2.075; 95% confidence interval, 1.408–3.060; $P < 0.001$) and FBG (hazard ratio, 2.544; 95% confidence interval, 1.748–3.710; $P < 0.001$) were important predictors of the incidence of NODAP. Subsequently, we divided 492 eligible patients into 3 groups according to the median BMI and FBG values, and found that the NODAP rate in the high-risk group was significantly higher than that in the medium-risk group ($P = 0.018$) or the low-risk group ($P < 0.001$).

Conclusions: Body mass index and FBG are independent predictors of NODAP. The combination of BMI and FBG can refine the prediction of NODAP and identify candidates for clinical prevention.

Key Words: body mass index, fasting blood glucose, diabetes, acute pancreatitis, predictive value

Endocrine disorder is a common phenomenon after acute pancreatitis (AP) because of the destruction of normal pancreatic tissues.[1,2] However, the reported data on the incidence of new-onset prediabetes or diabetes after AP (NODAP) are controversial, ranging from several cases to more than half of the patients.[3–6] According to some studies, NODAP increases the hospitalization

and mortality rates among patients compared with type 2 diabetes mellitus, contributing to a heavy burden on both family and society.[7] Therefore, discussing the risk factors of NODAP and then putting early intervention strategies into practice may lower the risk for NODAP, thus improving the clinical prognosis.

Body mass index (BMI) is an indicator in the assessment of obesity, and normally found to be associated with the occurrence of AP in clinical practice. In a previous study, Ma et al[8] revealed that BMI was an independent predictor of new-onset diabetes mellitus after the first attack of AP. This result was also confirmed by several other studies.[9–11] In addition, fasting blood glucose (FBG) is usually found to be elevated during the acute phase in many AP patients and has also been considered an independent risk factor for predicting new-onset prediabetes or diabetes after an episode of AP.[8,10,11] However, studies considering BMI or FBG as a risk factor of NODAP are still limited in number, which needs to be further discussed.

Given that both BMI and FBG are independent predictive factors for NODAP, whether combining BMI and FBG will improve the prediction of the incidence of NODAP remains unknown. Therefore, this retrospective cohort study sought to evaluate whether combining BMI and FBG can refine the prediction of NODAP and guide individual prevention measures for these patients to decrease the incidence of NODAP in clinical practice.

MATERIALS AND METHODS

Patients

In all, 492 patients who had an episode of AP were retrospectively enrolled between January 2016 and December 2020. The eligibility criteria (which 963 patients met) were as follows: (1) diagnosed with AP and (2) no history of diabetes or prediabetes. The exclusion criteria were as follows: (1) had a history of chronic pancreatitis, pancreatic carcinoma, or recent operation history of the pancreas, including endoscopic retrograde cholangiography (106 patients; 11.0%); (2) lactation or pregnancy (0 patients; 0%); (3) loss of follow-up data (27 patients; 2.8%); (4) follow-up time, less than 3 months (249 patients; 25.9%); and (5) fasting or random blood glucose did not reduce to the normal level during hospitalization (89 patients; 9.2%).

Definition of AP and Severity Classification

Acute pancreatitis was diagnosed by a gastroenterologist when 2 of the 3 following criteria were fulfilled: (1) typical abdominal pain; (2) serum amylase and/or lipase more than 3 times the upper limit of normal; and (3) typical characteristic findings from abdominal imaging.

Simply, patients who developed organ failure lasting for longer than 48 hours were classified as "severe," whereas other patients were considered as "mild" cases in our study.

Definition of NODAP and non-NODAP

Diabetes was diagnosed by an endocrinologist when the FBG was 7.0 mmol/L or greater (≥126 mg/dL), or 2-hour oral glucose tolerance test was 11.1 mmol/L or higher (≥200 mg/dL), or random blood glucose was 11.1 mmol/L or higher (≥200 mg/dL), or hemoglobin A1c (HbA1c) was 6.5% (48 mmol/mol) or higher. For patients without typical manifestations, such as polydipsia, polyphagia, polyuria, or weight loss, the abovementioned indicators needed to be confirmed once again. Prediabetes was diagnosed when the FBG was 6.1 mmol/L or greater (≥110 mg/dL) and less than 7.0 mmol/L (<126 mg/dL), and/or 2-hour oral glucose tolerance test was 7.8 mmol/L or higher (≥140 mg/dL) and less than 11.1 mmol/L (<200 mg/dL), and/or the HbA1c was 5.6% or higher (39 mmol/mol) and less than 6.5% (48 mmol/mol). In our study, NODAP included both new-onset prediabetes and diabetes. On the contrary, patients who did not develop prediabetes or diabetes after AP were considered the non-NODAP group.

Measurement of BMI and FBG

Body mass index (kg/m^2) was calculated using the weight (kg) and height (m) of patients. For weight measurement, patients were asked to remove their shoes, coat, belt, and other carry-on items. For height measurement, patients were asked to remove any head attire and their shoes. For patients who could not get up and/or stand upright on admission, weight and height were measured when they felt able to cooperate.

For FBG measurement, patients were asked to fast for 8 hours or longer before blood collection. Blood samples in our study were tested within 2 hours using enzymatic colorimetric assay (F. Hoffman-La Roche Ltd.; Basel, Switzerland).

In our study, FBG refers to the FBG on admission. Patients whose fasting or random blood glucose did not reduce to the normal level during hospitalization were excluded, as mentioned previously.

Data Collection

We viewed the medical records of each enrolled patient from a hospital-based electronic database. The following baseline clinical data were collected: (1) general characteristics, including age, sex, identical number, admission time, concurrent diseases (high blood pressure [HBP], coronary heart disease, liver cirrhosis), weight, and height; and (2) laboratory data, including white blood cell (WBC), platelet (PLT), hematocrit (HCT), thrombocytocrit, aspartate aminotransferase, alanine aminotransferase, glutamyl transpeptidase (GGT), total bilirubin (TBIL), lactate dehydrogenase, triglyceride (TG), blood urea nitrogen, creatinine, serum sodium (Na), serum potassium, serum calcium, serum amylase, serum lipase, FBG, C-reactive protein (CRP), prothrombin time (PT), activated partial thromboplastin time, fibrinogen, and D-dimer.

TABLE 1. Patient Characteristics

	NODAP (n = 153)	Non-NODAP (n = 339)	U/χ^2	*P*
Sex, male	111 (72.5)	206 (60.8)	6.386	**0.012**
Age, y	44.0 (35.0–54.0)	52.0 (39.0–63.0)	20,020.0	**<0.001**
Concurrent with HBP, yes	43 (28.1)	65 (19.2)	4.907	**0.027**
Concurrent with CHD, yes	10 (6.5)	14 (4.1)	1.315	0.251
Concurrent with LC, yes	2 (1.3)	7 (2.1)	0.337	0.727
BMI, kg/m^2	26.3 (24.3–28.5)	22.9 (20.3–25.9)	13,573.0	**<0.001**
WBC, $\times 10^9$/L	12.9 (9.8–15.9)	11.1 (8.4–14.1)	20,591.5	**<0.001**
PLT, $\times 10^9$/L	236.0 (187.5–298.0)	229.0 (188.0–288.0)	24,283.5	0.258
HCT	0.42 (0.39–0.46)	0.41 (0.37–0.44)	21,458.5	**0.002**
PCT, %	0.25 (0.20–0.30)	0.24 (0.19–0.29)	24,274.5	0.255
AST/ALT	0.79 (0.58–1.21)	0.85 (0.59–1.25)	24,875.5	0.469
GGT, U/L	120.0 (36.0–320.0)	64.0 (32.0–210.0)	22,084.0	**0.008**
TBIL, μmol/L	25.4 (16.0–55.7)	21.6 (14.6–32.9)	22,357.5	**0.014**
LDH, U/L	207.5 (168.3–315.3)	214.5 (169.3–305.5)	4466.0	0.932
TG, mmol/L	3.04 (1.29–11.78)	1.23 (0.73–2.31)	14,790.5	**<0.001**
BUN, mmol/L	4.63 (3.96–5.56)	4.92 (3.84–6.16)	24,030.0	0.192
Cr, μmol/L	69.0 (59.0–85.0)	71.0 (58.0–87.0)	25,334.5	0.682
Na, mmol/L	139.0 (137.0–142.0)	140.0 (138.0–143.0)	21,202.0	**0.001**
K, mmol/L	3.82 (3.55–4.19)	3.84 (3.52–4.08)	24,509.0	0.329
Ca, mmol/L	2.22 (2.10–2.34)	2.20 (2.10–2.31)	25,491.0	0.762
Amylase, U/L	490.0 (198.0–1289.0)	317.0 (149.0–914.0)	21,394.5	**0.002**
Lipase, U/L	1231.0 (548.0–2392.0)	1239.0 (643.0–2413.0)	24,550.5	0.343
CRP, mg/L	27.9 (11.2–69.4)	20.0 (7.1–56.6)	22,192.0	**0.010**
FBG, mmol/L	9.07 (7.00–13.15)	6.10 (5.32–7.37)	9897.5	**<0.001**
PT, s	13.4 (12.7–14.2)	12.9 (12.5–13.8)	20,671.0	**<0.001**
APTT, s	36.8 (33.8–39.7)	37.0 (34.1–40.9)	24,654.5	0.381
Fib, g/L	4.09 (3.36–5.71)	3.97 (3.08–5.19)	23,338.0	0.075
D-dimer, ug/mL	1.11 (0.50–2.58)	1.10 (0.60–2.30)	25,707.0	0.877

Data are shown as n (%) or median (IQR). Bold values are statistically significant.

CHD indicates coronary heart disease; LC, liver cirrhosis; PLT, platelet; PCT, thrombocytocrit; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; Cr, creatinine; K, serum potassium; Ca, serum calcium; APTT, activated partial thromboplastin time.

Statistics

In our study, categorical variables were described by frequency and their corresponding percentages, whereas continuous variables were described by median values and their corresponding 25th to 75th percentiles (interquartile range [IQR]) because of nonnormal distribution. Differences in categorical variables between the NODAP and non-NODAP groups were analyzed by Pearson χ^2 test, and differences in continuous variables between these 2 groups were analyzed by a nonparametric test. The risk predictors of NODAP were evaluated by univariate and multivariate Cox proportional hazards analyses. Variables with a P value less than 0.1 in the univariate analysis were tested in the multivariate analysis. Hazard ratios (HRs), as well as their corresponding 95% confidence intervals (CIs), were estimated by means of the Cox proportional hazards regression model. Finally, the cumulative rates of NODAP were calculated using the Kaplan-Meier method, and the differences among the 3 subgroups divided according to the BMI and FBG values (details as follows) were evaluated by the log-rank test. Statistical analyses were performed using SPSS 26.0 (International Business Machines Corporation; Armonk, NY). All P values in our study were 2-sided, and those less than 0.05 were considered statistically significant.

RESULTS

Patient Characteristics

The characteristics of the 492 eligible patients with AP episodes are listed in Table 1. Among these 492 AP patients, 153 (31.1%) patients finally developed NODAP, whereas 339 (68.9%) were placed in the non-NODAP group. The proportions of men in the NODAP and non-NODAP groups were 72.5% (111/153) and 60.8% (206/339), respectively ($P = 0.012$). The median age of the NODAP group was 44.0 years (IQR, 35.0–54.0 years), and that of the non-NODAP group was 52.0 years (IQR, 39.0–63.0 years) ($P < 0.001$). When comparing concurrent diseases, we found that the proportions of patients with concurrent HBP in the NODAP and non-NODAP groups were 28.1% (43/153) and 19.2% (65/339), respectively ($P = 0.027$), whereas there were no significant differences in the proportions of patients with concurrent coronary heart disease (6.5% vs 4.1%, $P = 0.251$) or liver

cirrhosis (1.3% vs 2.1%, $P = 0.727$) between the 2 groups. By calculating BMI based on the height and weight of the AP patients, the median value of BMI in the NODAP group (26.3 kg/m²; IQR, 24.3–28.5 kg/m²) was found to be significantly higher than that in the non-NODAP group (22.9 kg/m²; IQR, 20.3–25.9 kg/m²; $P < 0.001$).

For laboratory tests, the median values of WBC in the NODAP and non-NODAP groups were 12.9 (IQR, 9.8–15.9) × 10⁹/L and 11.1 (IQR, 8.4–14.1) × 10⁹/L, respectively ($P < 0.001$), which were consistent with those of HCT. When comparing indexes of biochemistry, we found that both the median values of GGT (120 U/L vs 64 U/L, $P = 0.008$) and TBIL (25.4 μmol/L vs 21.6 μmol/L, $P = 0.014$) in the NODAP group were significantly higher than those in the non-NODAP group. Moreover, the median value of TG in the NODAP group (3.04 mmol/L; IQR, 1.29–11.78 mmol/L) was significantly higher than that in the non-NODAP group (1.23 mmol/L; IQR, 0.73–2.31 mmol/L; $P < 0.001$), whereas the median value of Na in the NODAP group (139 mmol/L; IQR, 137–142 mmol/L) was significantly lower than that in the non-NODAP group (140 mmol/L; IQR, 138–143 mmol/L; $P = 0.001$). For amylase, the median values were 490 U/L (IQR, 198–1289 U/L) in the NODAP group and 317 U/L (IQR, 149–914 U/L) in the non-NODAP group ($P = 0.002$). For CRP, the median values were 27.9 mg/L (IQR, 11.2–69.4 mg/L) in the NODAP group and 20.0 mg/L (IQR, 7.1–56.6 mg/L) in the non-NODAP group ($P = 0.010$). For FBG, the median values were 9.07 mmol/L (IQR, 7.00–13.15 mmol/L) in the NODAP group and 6.10 mmol/L (IQR, 5.32–7.37 mmol/L) in the non-NODAP group ($P < 0.001$). Finally, for PT, the median values were 13.4 s (IQR, 12.7–14.2 s) in the NODAP group and 12.9 (IQR, 12.5–13.8) s in the non-NODAP group ($P < 0.001$). The other indexes of laboratory tests showed no significant differences between these 2 groups.

Risk Factors of NODAP by Univariate and Multivariate Analyses

By comparing patient characteristics, the following indexes showing significant differences between the NODAP and non-NODAP groups were identified: sex, age, concurrency with HBP, BMI, WBC, HCT, GGT, TBIL, TG, Na, amylase, CRP,

TABLE 2. Univariate and Multivariate Cox Proportional Hazards Analyses

Variables	Univariate Analysis		Multivariate Analysis	
	HR (95% CI)	*P*	HR (95% CI)	*P*
Sex, male vs female)	1.248 (0.872–1.787)	0.226		
Age, ≥49 vs <49 y	0.762 (0.550–1.054)	**0.091**	0.760 (0.542–1.065)	0.111
Concurrent with HBP, yes vs no	0.993 (0.697–1.416)	0.971		
Severity of AP, severe vs mild	1.270 (0.954–1.691)	0.102		
BMI, ≥24 vs <24 kg/m²	2.053 (1.390–3.031)	**<0.001**	2.075 (1.408–3.060)	**<0.001**
WBC, ≥11.7 vs <11.7 × 10⁹/L	1.177 (0.849–1.632)	0.327		
HCT, ≥0.41 vs <0.41	0.965 (0.692–1.345)	0.833		
GGT, ≥94.5 vs <94.5 U/L	0.897 (0.645–1.248)	0.519		
TBIL, ≥23.2 vs <23.2 μmol/L	0.703 (0.507–0.974)	**0.034**	0.913 (0.659–1.265)	0.585
TG, ≥1.5 vs <1.5 mmol/L	1.223 (0.869–1.721)	0.248		
Na, ≥140 vs <140 mmol/L	0.764 (0.553–1.057)	0.104		
Amylase, ≥444 vs <444 U/L	1.022 (0.740–1.411)	0.897		
CRP, ≥22.8 vs <22.8 mg/L	0.817 (0.589–1.132)	0.224		
FBG, ≥7 vs <7 mmol/L	2.074 (1.426–3.014)	**<0.001**	2.544 (1.748–3.710)	**<0.001**
PT, ≥13.4 vs <13.4 s	1.106 (0.794–1.540)	0.551		

Bold values in the univariate analysis are further analyzed in the multivariate analysis and bold values in the multivariate analysis are statistically significant.
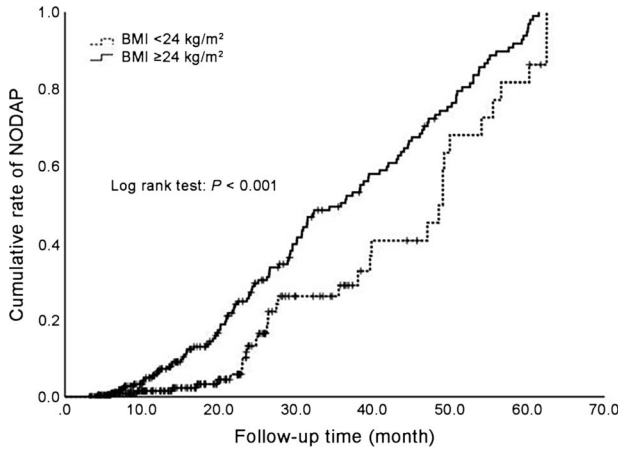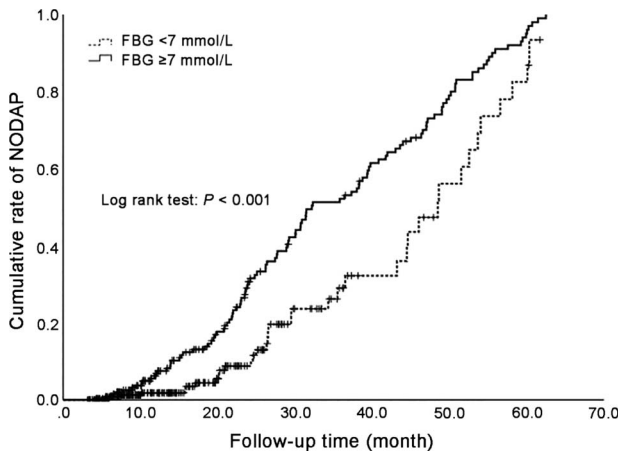
FIGURE 1. Survival curves by Kaplan-Meier analyses, comparing the cumulative rate of NODAP between patients with BMI ≥24 kg/m² and BMI <24 kg/m².

FBG, and PT. Then, these indexes were further put into univariate and multivariate Cox proportional hazards analyses to evaluate risk factors of NODAP. Moreover, an index, such as the severity of AP, which might have a correlation with the incidence of NODAP, was also put into the univariate and multivariate analyses. Before that, continuous variables were described as categorical variables according to their median values among 492 eligible AP patients. The results of univariate and multivariate analyses are listed in Table 2. In this study, we found that only BMI and FBG reached a *P* value less than 0.05, with corresponding HR values of 2.075 (95% CI, 1.408–3.060) and 2.544 (95% CI, 1.748–3.710), respectively. Body mass index and FBG are independent risk factors of NODAP. However, the severity of AP was not correlated with NODAP in the univariate analysis, with a corresponding HR value of 1.270 (95% CI, 0.954–1.691; *P* = 0.102). Similar results that show BMI and FBG are independent risk factors of NODAP can also be found in Supplemental Table 1 (http://links.lww.com/MPA/A944) when using BMI and FBG as continuous variables.

Association of BMI and FBG With Cumulative Rates of NODAP

In this study, we found that the cumulative rate of NODAP in patients with BMIs of 24 kg/m² or greater was significantly higher

than that of patients with BMIs less than 24 kg/m² (*P* < 0.001, Fig. 1). Similarly, for patients with an FBG of 7 mmol/L or greater, the cumulative rate of NODAP was also significantly higher than that of those with an FBG less than 7 mmol/L (*P* < 0.001, Fig. 2).

Combination of BMI and FBG Improved the Prediction of NODAP

According to the results described above, both BMI and FBG are effective predictive factors for NODAP. Therefore, we divided the entire population of 492 eligible AP patients into 3 groups according to the median values of BMI and FBG, as follows: a low-risk group (with BMI <24 kg/m² and FBG <7 mmol/L), a medium-risk group (with BMI ≥24 kg/m² and FBG <7 mmol/L or with BMI <24 kg/m² and FBG ≥7 mmol/L), and a high-risk group (with BMI ≥24 kg/m² and FBG ≥7 mmol/L). After that, differences in the cumulative rate of NODAP among these 3 groups were compared by Kaplan–Meier analysis and a log-rank test (Fig. 3). The results of the analyses revealed that the cumulative rate of NODAP in the high-risk group was significantly higher than that in the medium-risk group (*P* = 0.018) or the low-risk group (*P* < 0.001). In addition, the cumulative rate of NODAP in the medium-risk group was found to be significantly higher than the cumulative rate of NODAP in the low-risk group (*P* = 0.002). Similar results showing that the cumulative rate of NODAP in the high-risk group was significantly higher than that in the low-risk group were also found in patients younger than 49 years (*P* = 0.008), patients 49 years or older (*P* < 0.001), and in male patients (*P* < 0.001). Differences in the NODAP cumulative rate between patients younger than 49 years (Supplemental Fig. 1, http://links.lww.com/MPA/A944) and those 49 years or older (Supplemental Fig. 2, http://links.lww.com/MPA/A944) and between male patients (Supplemental Fig. 3, http://links.lww.com/MPA/A944) and female patients (Supplemental Fig. 4, http://links.lww.com/MPA/A944) across the 3 groups were compared by Kaplan-Meier analysis and a log-rank test.

DISCUSSION

Findings from this retrospective cohort study suggest that prediabetes/diabetes is an important problem for patients who have an episode of AP. However, reported incidences of NODAP are diverse across different studies. In a previous investigation, Das et al[3] reported that the incidence of pancreatic endocrine dysfunction after the first attack of AP, including prediabetes and diabetes, was nearly 40%. However, in a recent systemic review and

FIGURE 2. Survival curves by Kaplan-Meier analyses, comparing the cumulative rate of NODAP between patients with FBG ≥7 mmol/L and FBG <7 mmol/L.
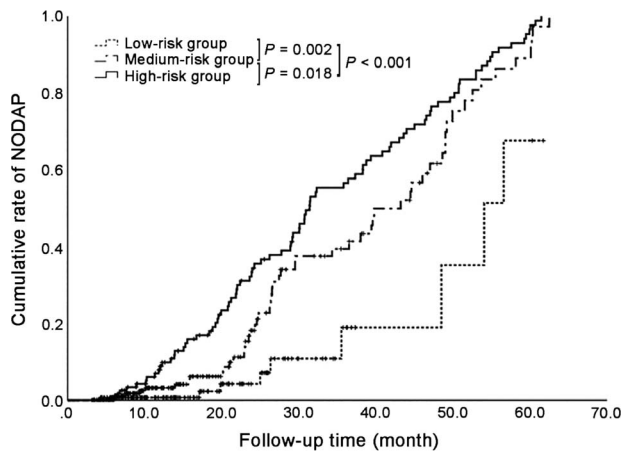

FIGURE 3. Survival curves by Kaplan-Meier analyses, comparing the cumulative rate of NODAP among the high-risk group, medium-risk group, and low-risk group.

meta-analysis published in 2019, the estimated incidence of prediabetes or diabetes after AP was reported to be about 23%.[12] According to our study, 153 of 492 eligible AP patients finally developed NODAP, representing a percentage of 31.1%. This means that approximately one-third of the patients with a first episode of AP suffered from prediabetes or diabetes. This result is similar to the incidence of NODAP that was reported before.

To the best of our knowledge, this is the first study to combine BMI and the FBG level to evaluate the predictive value of the incidence of NODAP. In our study, we found that both BMI and FBG were independent factors for predicting NODAP. This result was also recorded in previous studies.[8–11] One possible mechanism for BMI as a predictor of NODAP is that a higher BMI may contribute to the accumulation of inflammatory factors, such as tumor necrosis factor and adiponectin, thus leading to microcirculatory disturbance of the pancreas and endogenous insulin deficiency.[13] Furthermore, BMI as an obesity index was found to be correlated with insulin resistance and contributed to the incidence of NODAP.[14,15] The other possible mechanism at play is that AP patients with higher BMIs usually exhibit worse destruction of the pancreas as well as pancreatic beta-cells, thus reducing the secretion of endogenous insulin.[16] In previous studies, FBG was also found to be closely associated with the incidence of NODAP because FBG is an indicator for pancreatic destruction and is usually elevated significantly in the acute phase of AP.[17–21] In addition, our study combined BMI and FBG to evaluate their prediction of NODAP and found that the combination of both could refine the prediction of NODAP, an approach that could be used to guide individual prevention measures to decrease the incidence of NODAP among eligible patients in clinical practice.

Until now, whether or not the severity of AP can predict the incidence of NODAP remains controversial. A study by Garip et al[22] in 2013 showed that endocrine dysfunction (including prediabetes and diabetes) was present in 56.4% of severe AP patients, whereas the incidence rate after mild AP was only 23.2%. However, there are several other studies holding opposite opinions that the incidence of NODAP did not differ significantly regardless of the severity of AP.[23–25] According to our study, NODAP was not significantly correlated with the severity of AP (HR, 1.270; $P = 0.102$), similar to the results mentioned above. The specific mechanisms at play are not clear yet. One speculation is that the severity of AP is defined by the presence of pancreatic necrosis and organ dysfunction, in which only the presence and extent of pancreatic necrosis contribute to the destruction of the pancreas.[26]

However, our study has several limitations. First, although we ruled out patients with prediabetes or diabetes on admission and those whose fasting or random blood glucose did not reduce to the normal level during hospitalization in our study, the measurement of HbA1c within the first 3 months after an episode of AP, which could definitely exclude prediabetes and diabetes, was not performed. As a result, the real incidence of NODAP might be slightly impacted. Second, because a portion of patients with acute pancreatitis were rather sick at admission in our study, for those who could not get up and stand upright, weight and height were measured only when the patients felt able to cooperate. Therefore, the measurements of weight and height were not unified in the strictest sense. Third, because this is a retrospective cohort study, risk factors, such as waist-to-hip ratio, smoking status, alcohol consumption status, and family history of diabetes, were not analyzed in our study because of the data being unavailable. Therefore, further studies are needed to confirm our study.

In summary, BMI and FBG are independent predictors of NODAP. The combination of BMI and FBG can refine the prediction of NODAP and guide individual prevention measures for these patients to decrease the incidence of NODAP in clinical practice.

REFERENCES

1. Petrov MS, Yadav D. Global epidemiology and holistic prevention of pancreatitis. *Nat Rev Gastroenterol Hepatol*. 2019;16:175–184.

2. Woodmansey C, McGovern AP, McCullough KA, et al. Incidence, demographics, and clinical characteristics of diabetes of the exocrine pancreas (Type 3c): A retrospective cohort study. *Diabetes Care*. 2017; 40:1486–1493.

3. Das SL, Singh PP, Phillips AR, et al. Newly diagnosed diabetes mellitus after acute pancreatitis: a systematic review and meta-analysis. *Gut*. 2014; 63:818–831.

4. Umapathy C, Raina A, Saligram S, et al. Natural history after acute necrotizing pancreatitis: a large US Tertiary care experience. *J Gastrointest Surg*. 2016;20:1844–1853.

5. Pelli H, Lappalainen-Lehto R, Piironen A, et al. Pancreatic damage after the first episode of acute alcoholic pancreatitis and its association with the later recurrence rate. *Pancreatology*. 2009;9:245–251.

6. Halonen KI, Pettilä V, Leppäniemi AK, et al. Long-term health-related quality of life in survivors of severe acute pancreatitis. *Intensive Care Med*. 2003;29:782–786.

7. Cho J, Scragg R, Petrov MS. Risk of mortality and hospitalization after post-pancreatitis diabetes mellitus vs type 2 diabetes mellitus: a population-based matched cohort study. *Am J Gastroenterol*. 2019;114:804–812.

8. Ma JH, Yuan YJ, Lin SH, et al. Nomogram for predicting diabetes mellitus after the first attack of acute pancreatitis. *Eur J Gastroenterol Hepatol*. 2018;31:323–328.

9. Eriksson J, Doepel M, Widén E, et al. Pancreatic surgery, not pancreatitis, is the primary cause of diabetes after acute fulminant pancreatitis. *Gut*. 1992;33:843–847.

10. Yang YL, Li MX, Wang ZQ. Risk factors and predictive models of new-onset diabetes mellitus after severe acute pancreatitis. *J Chengdu Med*. 2020;15:232–237.

11. Xu SQ, Xu YH, Bian C, et al. Factors associated with impaired blood glucose or diabetes after the episode of acute pancreatitis. *Academy Med Qingdao*. 2018;54:291–295.

12. Zhi M, Zhu X, Lugea A, et al. Incidence of new onset diabetes mellitus secondary to acute pancreatitis: a systematic review and meta-analysis. *Front Psychol*. 2019;10:637.

13. Zvonic S, Lefevre M, Kilroy G, et al. Secretome of primary cultures of human adipose-derived stem cells: modulation of serpins by adipogenesis. *Mol Cell Proteomics*. 2007;6:18–28.

14. Johnson CD. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. *Gut*. 2004;53:1340–1344.

15. Mery CM, Rubio V, Duarte-Rojo A, et al. Android fat distribution as predictor of severity in acute pancreatitis. *Pancreatology*. 2002;2:543–549.

16. Dobszai D, Mátrai P, Gyöngyi Z, et al. Body-mass index correlates with severity and mortality in acute pancreatitis: a meta-analysis. *World J Gastroenterol*. 2019;25:729–743.

17. Kunutsor SK, Zaccardi F, Karppi J, et al. Is high serum LDL/HDL cholesterol ratio an emerging risk factor for sudden cardiac death? Findings from the KIHD Study. *J Atheroscler Thromb*. 2017;24:600–608.

18. Yasuda T, Ueda T, Takeyama Y, et al. Long-term outcome of severe acute pancreatitis. *J Hepatobiliary Pancreat Surg*. 2008;15:397–402.

19. Wang SH, Chou YC, Shangkuan WC, et al. Relationship between plasma triglyceride level and severity of hypertriglyceridemic pancreatitis. *PLoS One*. 2016;11:e0163984.

20. Petrov MS, Zagainov V. Influence of enteral versus parenteral nutrition on blood glucose control in acute pancreatitis: a systematic review. *Clin Nutr*. 2007;26:514–523.

21. Gornik I, Vujaklija A, Lukić E, et al. Hyperglycemia in sepsis is a risk factor for development of type II diabetes. *J Crit Care*. 2010;25:263–269.

22. Garip G, Sarandöl E, Kaya E. Effects of disease severity and necrosis on pancreatic dysfunction after acute pancreatitis. *World J Gastroenterol*. 2013;19:8065–8070.

23. Wu D, Xu Y, Zeng Y, et al. Endocrine pancreatic function changes after acute pancreatitis. *Pancreas*. 2011;40:1006–1011.

24. Ho TW, Wu JM, Kuo TC, et al. Change of both endocrine and exocrine insufficiencies after acute pancreatitis in non-diabetic patients: a nationwide population-based study. *Medicine (Baltimore)*. 2015;94:e1123.

25. Nikkola J, Laukkarinen J, Lahtela J, et al. The long-term prospective follow-up of pancreatic function after the first episode of acute alcoholic pancreatitis: recurrence predisposes one to pancreatic dysfunction and pancreatogenic diabetes. *J Clin Gastroenterol*. 2017;51:183–190.

26. Tu J, Zhang J, Ke L, et al. Endocrine and exocrine pancreatic insufficiency after acute pancreatitis: long-term follow-up study. *BMC Gastroenterol*. 2017;17:114.