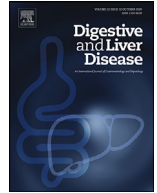




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Liver, Pancreas and Biliary Tract

## Dynamic nomogram for predicting infected pancreatic necrosis in female patients of childbearing age with hypertriglyceridemia-induced acute pancreatitis



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### ABSTRACT

**Background:** Hypertriglyceridemia is a common cause of acute pancreatitis. Pregnant women are at risk of developing hypertriglyceridemia-induced acute pancreatitis (HTG-AP); however, whether pregnancy increases the risk of infected pancreatic necrosis (IPN) is unknown.

**Aim:** We aimed to assess the association between pregnancy and IPN.

**Methods:** This 10-year retrospective cohort study was conducted at Jinling Hospital. Adult female patients of childbearing age with HTG-AP between January 2013 and September 2022 were screened. Logistic regression analyses were performed to assess the risk factors for IPN. Patients admitted within 7 days were assigned to the training and validation sets to develop a dynamic nomogram for IPN prediction.

**Results:** 489 patients were included, and 144 developed IPN. Logistic regression analyses revealed pregnancy (OR: 2.578 95% CI: 1.474–4.510) as an independent risk factor for IPN. Gestation weeks, ARDS, albumin level, and serum creatinine level were selected as the predictors of the dynamic nomogram for IPN prediction, with good discrimination in the training set (AUC 0.867 95% CI: 0.794–0.940) and validation set (AUC 0.957 95% CI: 0.885–1.000).

**Conclusion:** Pregnancy increases the risk of IPN in adult patients of childbearing age with HTG-AP, and the dynamic nomogram may help risk stratification for IPN.

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### 1. Introduction

Acute pancreatitis (AP) is a potentially lethal inflammatory disease with an annual morbidity of 5–30 per 100,000 persons in Western countries and an overall mortality rate of approximately 5% [1,2]. Moreover, a 20% of patients develop severe acute pancreatitis (SAP), a pathological type of necrotizing pancreatitis with a series of local and systemic complications and a much higher fatality rate of 20–40% [3–5]. The most common causes of AP are

gallstones and alcohol consumption, accounting for 80% in Western countries; however, hypertriglyceridemia-induced acute pancreatitis (HTG-AP) is the second most common type in China with a proportion of 14%–40% [6–8], becoming a non-negligible type of AP because of higher morbidity of complications and poorer outcomes [8].

The childbearing age is the period during which women get pregnant and bear children, typically defined as ages 15–49 by the World Health Organization (WHO) [9]. Pregnancy, a special physiological state, could cause various maternal physiological changes and partly disturb the pathophysiology of many diseases, often leading to deterioration [9,10]. Many studies have shown that acute pancreatitis in pregnancy contributes to high maternal and fetal mortality [11,12], which used to be as high as 35% and 60%, respectively, but has declined in recent years. To date, few studies have focused on the clinical characteristics of female patients of

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childbearing age with HTG-AP comprising the pregnant and non-pregnant populations, especially the effect of pregnancy on AP development, morbidity of complications, and eventual mortality.

Pancreatic/peripancreatic necrotic collection commonly occurs in necrotizing pancreatitis [3,13], with a diverse management strategy depending on whether it is infected or sterile. Avoiding intervention is recommended for sterile necrotic collections without obvious symptoms, whereas high-grade antibiotics therapy and a step-up treatment are used to treat infected pancreatic necrosis (IPN) [14]. IPN is one of the most troublesome complications of AP [15], with an extremely high mortality rate of 40% if complicated with organ failure [16]. Hence, identifying patients at high risk of IPN and predicting IPN may contribute to early clinical decisions and improve outcomes.

Here, we aimed to describe the clinical features of female patients of childbearing age with HTG-AP and investigate the relationship between pregnancy and IPN. In addition, we aimed to develop and validate a dynamic nomogram for predicting IPN in these patients to aid the risk stratification.

## 2. Materials and methods

### 2.1. Ethical statement

This study was approved by the Ethics Committee of Jinling Hospital (2021NZKY-042-01). Written informed consent was obtained from all the participants.

### 2.2. Study cohort

This 10-year, single-center retrospective cohort study was conducted at the Therapy Center for Severe Acute Pancreatitis, Jinling Hospital. According to the WHO, women of childbearing age are commonly defined as those aged 15–49, however, only adult patients were enrolled in this study considering ethical reasons and different pathophysiologies. All consecutive patients with AP admitted to our center between January 2013 and September 2022 were screened and only the adult female patients of childbearing age with HTG-AP were enrolled.

### 2.3. Data collection

Laboratory tests such as the blood routine examination, blood biochemistry tests and so on were conducted for all patients with AP at admission to our center as general. All data analyzed in this study were extracted from an electronic database, including demographic information (i.e., age and body mass index (BMI)), pregnancy status (i.e., gestation weeks and previous childbearing history), medical history (i.e., history of AP, hypertriglyceridemia (HTG), hypertension, diabetes mellitus (DM), and fatty liver), clinical characteristics (i.e., severity, mortality, length of stay (LOS) and intensive care unit (ICU) stay, and occurrence of complications), and laboratory tests parameters (i.e., the levels/contents of white blood cell count (WBC), hemoglobin (Hb), procalcitonin (PCT), triglyceride (TG), total cholesterol (TC), total bilirubin (TBL), total protein (TP), albumin (ALB), serum creatinine (SCr), blood urea nitrogen (BUN), alanine aminotransferase (ALT) and so on).

### 2.4. Diagnoses and definitions

AP was diagnosed according to the revised Atlanta 2012 classification (RAC) [17]. HTG-AP was diagnosed based on the AP diagnosis and these two features: (1) serum triglyceride (TG) levels at onset  $\geq 1000$  mg/dL (11.3 mmol/L) or between 500 and 1000 mg/dL (5.65–11.3 mmol/L) with the presence of emulsion plasma and (2)

presence of no other obvious causes of AP [18,19]. IPN was defined as follows: (1) typical imaging findings on contrast-enhanced computed tomography (CECT) (the presence of extraluminal gas in the pancreatic and/or peripancreatic tissues) and (2) positive bacterial and/or fungal culture or positive Gram staining of pancreatic and/or peripancreatic necrosis, sampled from aspiration, drainage or the necrosectomy procedure [20]. Local and systemic complications were according to the RAC [17].

### 2.5. Statistical analysis

Continuous variables were reported as median with interquartile ranges or means and standard deviations and evaluated using the Mann–Whitney *U* test or Student's *t*-test, where appropriate. Categorical variables were expressed as frequencies and percentages and analyzed using Pearson's chi-square or Fisher's exact tests. Univariate logistic regression analysis was performed to evaluate the relationship between pregnancy status and IPN. Only variables with  $p < 0.10$  in the univariate analysis were included in the multivariable logistic regression.

The best predictors of IPN risk were determined using the least absolute shrinkage and selection operator (LASSO) method. A dynamic nomogram was developed to visually represent this model. Discrimination, calibration, and clinical utility of the IPN prediction model were evaluated using the area under the receiver operating characteristic curve (AUC), calibration plots, and decision curve analysis (DCA), respectively. The missing data were all less than 30%; assuming variables were missing at random, multiple imputations by chained equations were applied, as shown in Supplemental Fig. 3. Statistical significance was defined as a probability (*p*-value) of less than 0.05. All data were analyzed using SPSS version 25.0 software (IBM Analytics, Armonk, NY, USA) and R version 4.1.1 (R Foundation for Statistical Computing).

## 3. Results

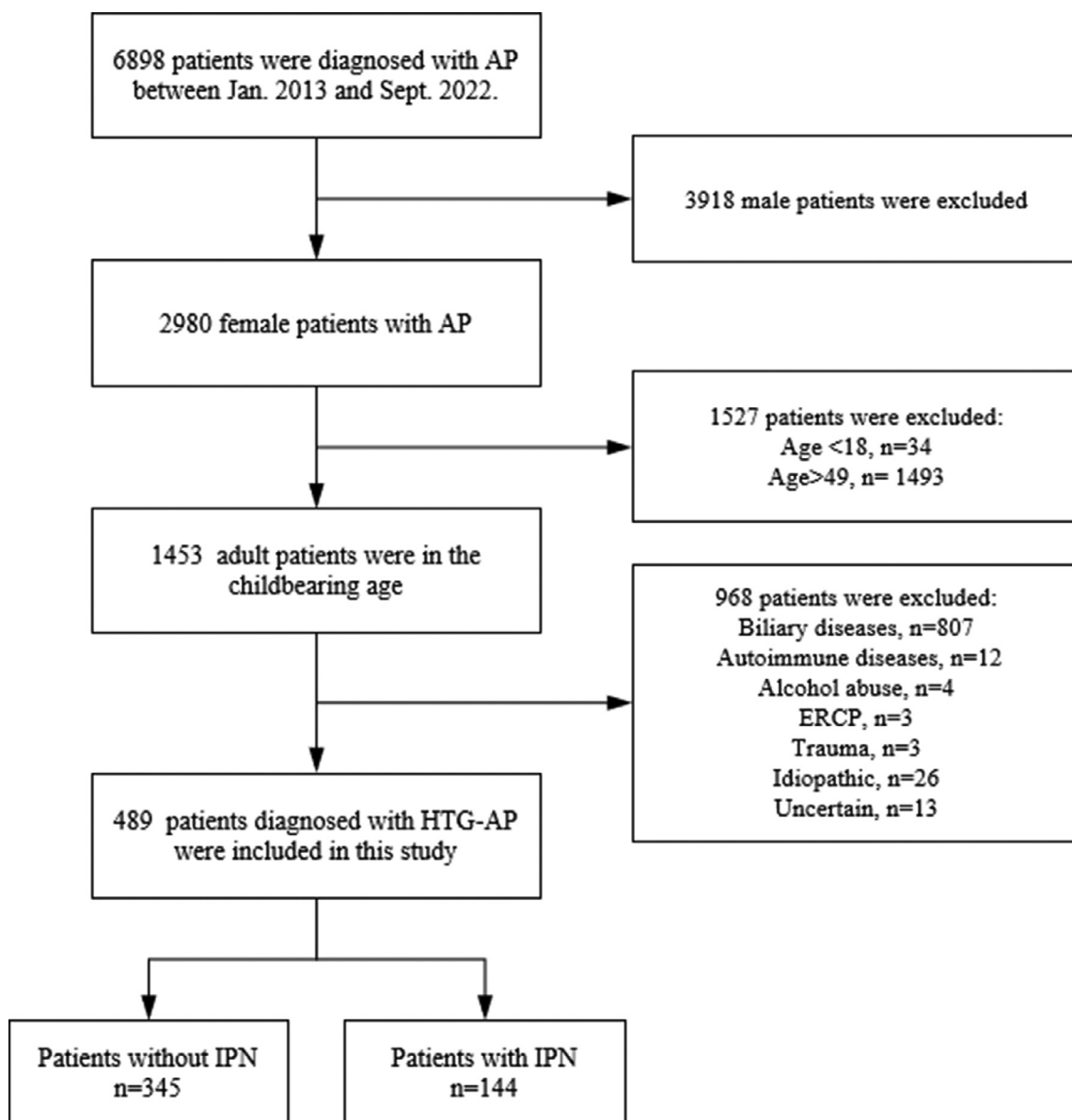
### 3.1. Patients and grouping

A total of 6898 patients were screened and all the male patients were excluded. Among the 2980 female patients, 1527 patients were further excluded based on age (i.e., age  $< 18$  years or  $> 49$  years). Of the 1453 adult patients of childbearing age with AP, 489 were diagnosed with HTG-AP and ultimately enrolled for analysis while the remaining 968 patients were excluded because of other etiologies including biliary diseases and so on. Finally, 144 patients were diagnosed with IPN, and 345 patients were non-IPN (Fig. 1).

Among the 489 patients, 300 patients who were transferred to our center within 7 days of AP onset were enrolled for further analyses for IPN prediction. A total of 251 patients were assigned to the training set (2013–2019) and 49 patients were assigned to the validation set (2020–2022) (Supplemental Fig. 1).

### 3.2. Baseline characteristics

The baseline characteristics of the IPN and non-IPN groups at admission to our center were compared, and the results are presented in Table 1. The percentage of pregnant women was significantly higher (30.55% vs. 11.30%,  $p < 0.001$ ) in the IPN group, whereas age and BMI had no statistical differences. Patients in the non-IPN group had a higher proportion of previous AP history than those in the IPN group (31.59% and 12.50%, respectively,  $p < 0.001$ ). Conversely, patients in the IPN group had lower hemoglobin (Hb) ( $p < 0.001$ ) and albumin (ALB) ( $p < 0.001$ ) levels, higher TG levels at onset ( $p = 0.009$ ), and higher alanine aminotransferase (ALT) ( $p = 0.002$ ), aspartate aminotransferase (AST) ( $p < 0.001$ ) and



**Fig. 1.** Flowchart of the enrollment of adult HTG-AP patients of childbearing age. HTG-AP, Hypertriglyceridemia-induced acute pancreatitis; IPN, infected pancreatic necrosis.

blood urea nitrogen (BUN) ( $p < 0.001$ ) levels. However, the other laboratory test parameters were comparable with that of the non-IPN group.

As shown in Table 1, the proportion of patients with SAP in the IPN group was 65.28%, higher than the non-IPN group. In addition, patients in the IPN group had a more than four times longer length of stay and an almost six times longer ICU stay than patients in the non-IPN group. They also had a higher morbidity rate due to local and systemic complications and an extremely high mortality rate of 18.06%, almost eight times higher than that of the non-IPN group (2.32%;  $p < 0.001$ ).

### 3.3. Association of pregnancy with IPN

Univariate logistic regression analysis revealed a potential association between pregnancy and IPN (Supplemental Table 1) In model 1 (Table 2), which included only the pregnancy status variable, pregnancy was significantly associated with an increased risk of IPN (odds ratio (OR): 3.452, 95% confidence interval (CI): 2.122–5.616). In model 2, after adjusting for AP, HTG, and DM history,

pregnancy (OR: 3.129, 95% CI: 1.901–5.151) and AP history (OR: 0.348, 95% CI: 0.198–0.614) were independently associated with IPN. Finally, after adjusting for all potential confounding factors in the multivariate regression analysis, the results of model 3 suggested that pregnancy (OR: 2.578, 95% CI: 1.474–4.510), AP history (OR: 0.367, 95%CI: 0.192–0.701), and Hb (OR: 0.969, 95% CI: 0.959–0.978) and BUN (OR: 1.113, 95%CI: 1.040–1.119) levels were independently associated with IPN.

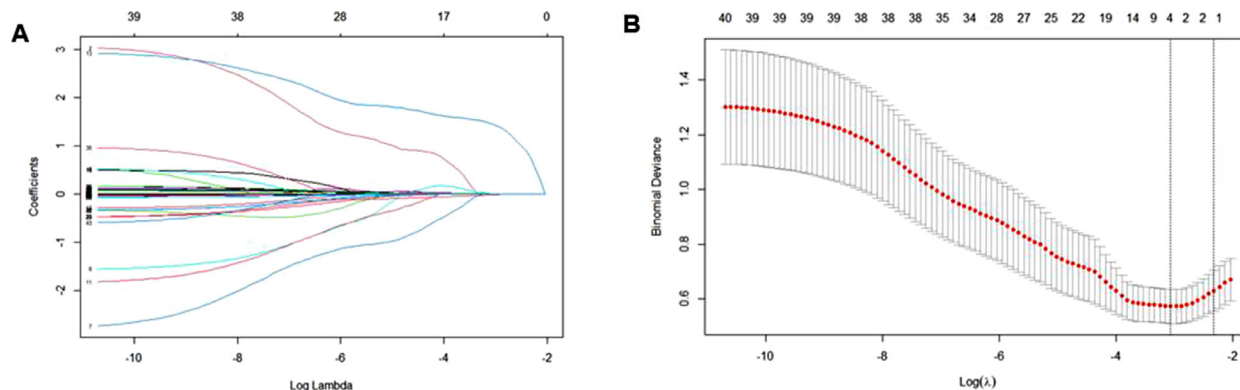
### 3.4. Nomogram development and the dynamic nomogram application

Candidate variables were selected as four potential predictors based on the 251 patients in the training cohort using the LASSO method, including the gestation weeks, acute respiratory distress syndrome (ARDS), the ALB and serum creatinine (SCr) levels (Fig. 2). A nomogram was established to demonstrate the weights of these four predictors of IPN (Fig. 3A). The instructions for this nomogram and dynamic nomogram application (Fig. 3B) are briefly described as follows: all variables were assigned a score based on the actual situation, from which the total score was calculated. The

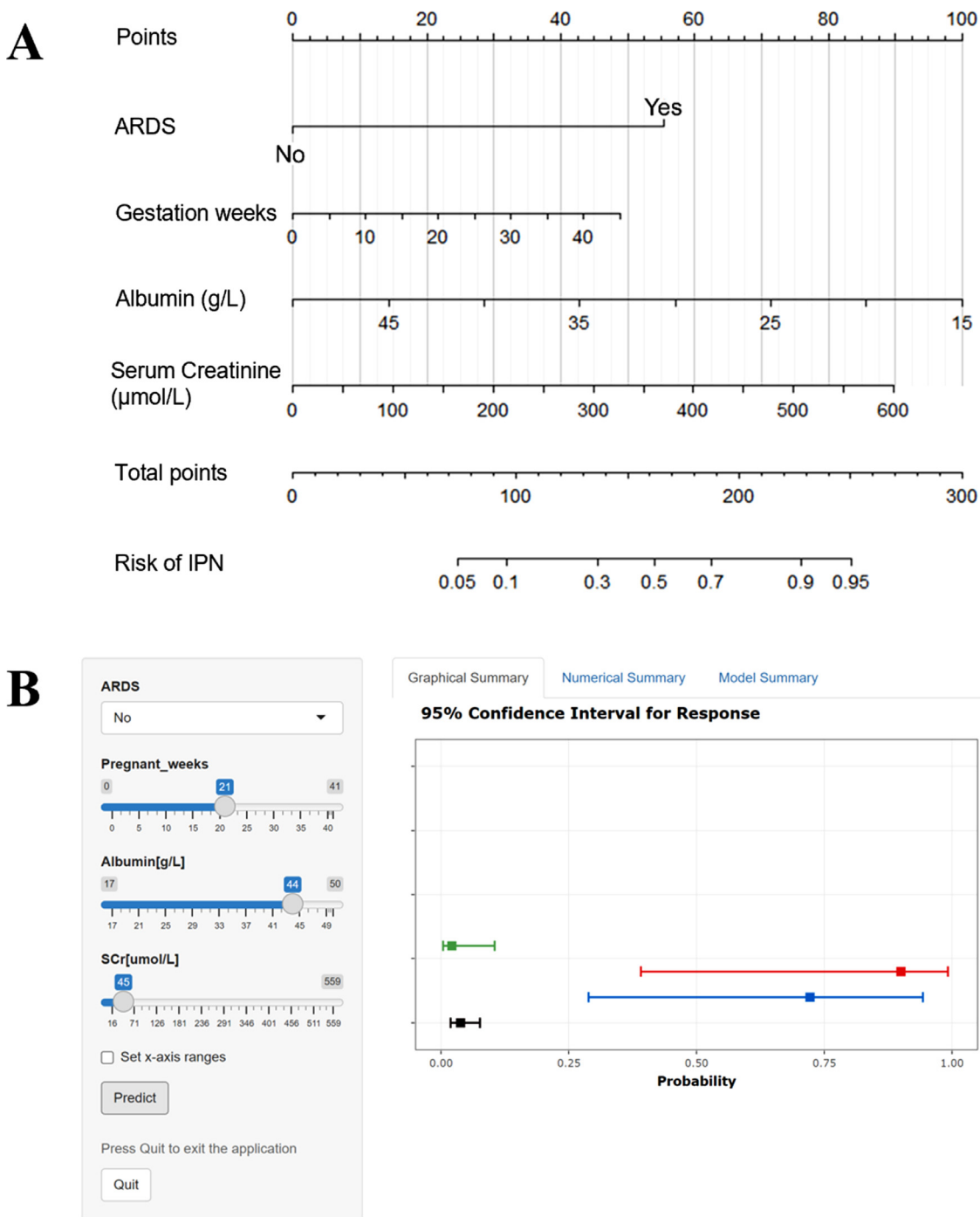
**Table 1**  
Baseline characteristics and clinical outcomes of the HTG-AP patients of childbearing age with or without IPN.

Variable	Non-IPN (n = 345)	IPN (n = 144)	p-value
<b>Baselines</b>			
Age, years	37.00(30.00–44.00)	35.83(30.00–44.00)	0.839
BMI, kg/m <sup>2</sup>	25.63(23.05–27.34)	25.90(23.47–26.48)	0.790
Pregnancy (%)	39(11.30)	44(30.55)	<0.001
<b>Medical histories (%)</b>			
AP history	109(31.59)	18(12.50)	<0.001
Fatty liver	138(40.00)	53(36.81)	0.509
DM history	99(28.70)	30(20.83)	0.091
HTG history	115(33.33)	37(25.69)	0.096
Hypertension history	54(15.65)	20(13.89)	0.620
<b>Laboratory tests</b>			
TG of onset, mmol/L	21.00(12.69–30.00)	27.00(16.95–30.03)	0.009
WBC, × 10 <sup>9</sup> /L	11.60(7.94–15.35)	10.64(7.56–15.50)	0.376
Hb, g/L	111.00(94.00–128.00)	84.00(75.03–97.08)	<0.001
PLT, × 10 <sup>9</sup> /L	218.00(169.00–279.00)	241.00(145.50–333.50)	0.333
PCT, µg/L	0.42(0.19–1.14)	0.56(0.17–1.64)	0.171
CRP, mg/L	143.00(84.00–202.00)	128.60(55.10–185.00)	0.055
TBL, µmol/L	15.10(10.70–21.60)	17.55(10.13–29.60)	0.052
TP, g/L	31.40(28.00–35.10)	57.90(52.20–64.00)	0.241
ALB, g/L	31.50(28.00–35.10)	30.00(19.00–33.00)	<0.001
ALT, U/L	22.00(16.00–31.00)	26.00(18.00–45.00)	0.002
AST, U/L	24.00(18.00–37.00)	33.00(19.00–56.00)	<0.001
BUN, mmol/L	3.40(2.25–4.80)	5.00(3.00–10.30)	<0.001
SCr, µmol/L	42.00(35.15–52.25)	44.50(31.18–108.23)	0.145
D-dimer, mg/L	4.50(1.77–7.72)	3.56(1.49–8.00)	0.343
<b>Outcomes (%)</b>			
Mortality	8(2.32)	26(18.06)	<0.001
SAP	58(16.81)	94(65.28)	<0.001
LOS, days	8.00(5.00–13.00)	33.0(15.25–57.75)	<0.001
Length of ICU stay, days	3.00(0.00–6.50)	17.0(6.00–36.75)	<0.001
<b>Complications (%)</b>			
ARDS	67(19.42)	81(56.25)	<0.001
AKI	44(12.75)	62(43.06)	<0.001
ALI	3(0.87)	13(9.03)	<0.001*
ACS	11(3.19)	10(6.94)	0.062
Digestive tract fistula	2(0.58)	47(32.64)	<0.001*
Abdominal hemorrhage	4(1.16)	28(19.44)	<0.001*
Portal vein thrombosis	3(0.87)	10(6.94)	<0.001*
Sepsis	7(2.03)	43(29.86)	<0.001
Intestinal obstruction	1(0.29)	14(9.72)	<0.001*
DKA	12(3.48)	5(3.47)	1.000*

HTG-AP, hypertriglyceridemia-induced acute pancreatitis; IPN, infected pancreatic necrosis; BMI, body mass index; AP, acute pancreatitis; DM, diabetes mellitus; HTG, hypertriglyceridemia; WBC, white blood cell; Hb, hemoglobin; PCT, procalcitonin; CRP, C-reactive protein; PLT, platelet; TBL, total bilirubin level; TP, total protein; ALB, albumin; ALT, Alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; SCr, serum creatinine; HTG-AP, hypertriglyceridemia-induced acute pancreatitis; IPN, infected pancreatic necrosis; SAP, severe acute pancreatitis; LOS, length of stay; ICU, intensive care unit; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury; ALI, acute liver injury; ACS, abdominal compartment syndrome; DKA, diabetic ketoacidosis. \* Fisher's exact test.



**Fig. 2.** Texture feature selection for IPN prediction using the LASSO generalized linear models. (A) LASSO coefficient profiles of the 40 candidate predictors. A coefficient profile plot was produced against the log ( $\lambda$ ) sequence. (B) Selection of the optimal penalization coefficient in the LASSO regression. Based on the minimum value criterion, dotted vertical lines were drawn at the optimal values to obtain four features with non-zero coefficients as the optimal predictors. A  $\lambda$  value of 0.04672, with log ( $\lambda$ ),  $-3.063$  was chosen (minimum criteria) according to 10-fold cross-validation. LASSO: least absolute shrinkage and selection operator.



**Fig. 3.** The nomogram for IPN prediction in adult HTG-AP patients of childbearing age. (A)Development of the nomogram. (B)The online application of this dynamic nomogram. IPN, infected pancreatic necrosis; HTG-AP, hypertriglyceridemia-induced acute pancreatitis; ARDS, acute respiratory distress syndrome.

total score was used to predict IPN risk in adult patients of childbearing age with HTG-AP admitted within 7 days of onset.

The dynamic nomogram can be accessed at [https://htgap.shinyapps.io/HTGAP\\_DN/](https://htgap.shinyapps.io/HTGAP_DN/) or by scanning the QR code in Supplemental Fig. 2. The association of the variables with IPN was presented in Supplemental Table 2.

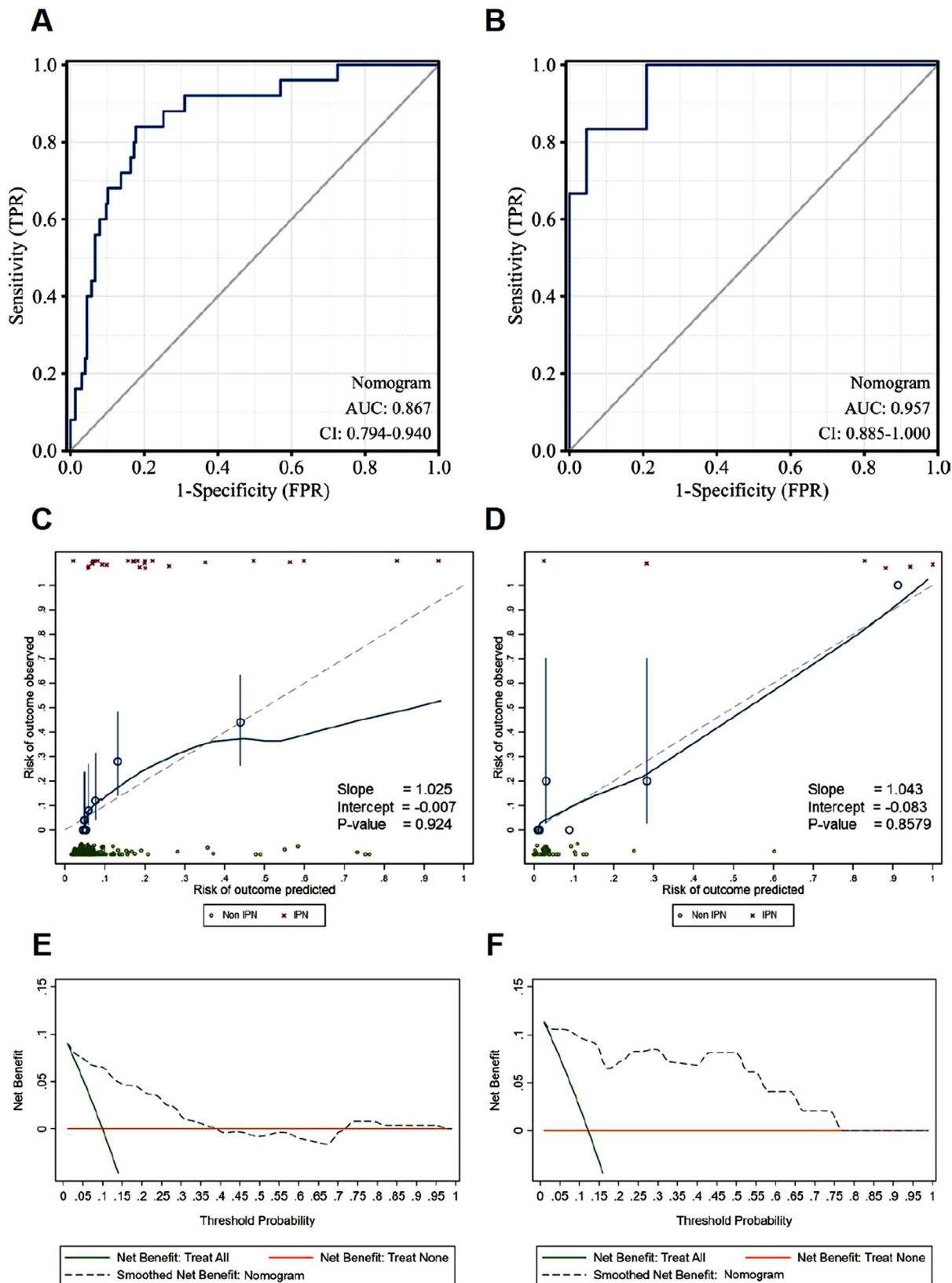
### 3.5. Evaluation of the model prediction performance and clinical application

The nomogram was reliable in terms of its prediction performance. As shown in Fig. 4, the AUC of the nomogram was 0.867 (95% CI: 0.794–0.940) in the training set and 0.957 (95% CI: 0.855–

1.000) in the validation set. Other discrimination parameters are listed in Supplemental Table 3. Calibration plots indicated that the predicted probability of the nomogram was consistent with the actual probability. Regarding clinical application, DCA was performed to determine the clinical applicability of the nomogram, which revealed that a net clinical benefit was attainable for patients with a predicted probability between the 2% and 78% thresholds.

### 4. Discussion

In this study, we described the clinical features of female patients of childbearing age with HTG-AP and revealed that pregnancy is an independent risk factor for IPN. Meanwhile, we also



**Fig. 4.** The predictive performance of the nomogram in the training and validation set. Receiver operating characteristic (ROC) curves of the nomogram in the training cohort(A) and validation cohort (B). Calibration curve of the nomogram in the training cohort(C) and validation cohort (D). Decision curve analysis in the training cohort (E) and validation cohort (F).

**Table 2**  
Association between pregnancy and IPN in different logistic regression models.

	Odds Ratio (95%CI)	p-value
<b>Model 1</b>		
Pregnancy	3.452 (2.122–5.616)	<0.001
<b>Model 2</b>		
Pregnancy	3.129(1.901–5.151)	<0.001
AP history	0.348(0.198–0.614)	<0.001
DM history	0.853(0.520–1.399)	0.530
HTG history	0.930(0.578–1.495)	0.764
<b>Model 3</b>		
Pregnancy	2.578(1.474–4.510)	<b>0.001</b>
AP history	0.367(0.192–0.701)	<b>0.002</b>
DM history	1.074(0.600–1.923)	0.810
HTG history	0.922(0.535–1.591)	0.772
Hb, g/L	0.969(0.959–0.979)	<0.001
TBL, $\mu\text{mol/L}$	1.012(0.997–1.026)	0.123
ALB, g/L	1.000(0.999–1.000)	0.190
BUN, mmol/L	1.113(1.040–1.190)	<b>0.002</b>
SCr, $\mu\text{mol/L}$	0.998(0.994–1.002)	0.372

IPN, infected pancreatic necrosis; AP, acute pancreatitis; DM, diabetes mellitus; HTG, hypertriglyceridemia; Hb, hemoglobin; PLT, platelet; TBL, total bilirubin level; ALB, albumin; BUN, blood urea nitrogen; SCr, serum creatinine.

developed a dynamic nomogram composed of factors such as gestation weeks, ARDS, ALB levels, and SCr level to predict IPN in patients admitted within 7 days of onset, providing a novel tool for early warning of IPN

Pregnancy is a special physiological period that may contribute to a potential deterioration of AP due to the additional burden on many organs caused by the fetus. IPN is one of the most troublesome and life-threatening complications of SAP [15,21] with an extremely high mortality rate of 40% if complicated with ongoing or new onset of organ dysfunction [15,18,22]. In this study, we focused on a special population of female patients of childbearing age with HTG-AP to investigate the potential relationship between pregnancy and the IPN risk. As shown in Table 1, the IPN group had a high proportion of pregnant women and patients with higher TG levels at onset, higher indicators of poor liver (ALT and AST) and renal functions (BUN), and lower Hb and ALB levels. Low Hb and ALB levels were strongly associated with poor situations in critically ill patients [23–26]; therefore, we included these two variables for further logistic regression analyses. Meanwhile, a multicenter cohort study has revealed that a higher TG level is associated with a severe course of AP [27], consistent with the findings of our study. Elevated levels of organ function indicators, including ALT, AST, BUN, and SCr, suggest a high incidence of organ dysfunctions, consistent with the observed conditions of our patients. However, the proportion of patients with previous AP history in the non-IPN group was double that of the IPN group. A possible explanation for this difference is that, to some extent, IPN development results in a much worse clinical outcome, leading to a higher possibility of mortality during the first episode of SAP. In other words, patients who suffered from IPN or other severe complications of SAP experienced a grievous and life-threatening episode and thus developed stronger health consciousness to avoid recurrence. As shown in Table 1, patients in the IPN group experienced a worse course of HTG-AP, with a higher mortality rate, a higher proportion of SAP, a longer hospital stay, a longer ICU stay, and higher morbidity due to organ dysfunctions and local complications, consistent with the previous reports [22,28].

Pregnancy is associated with the deterioration of many diseases, such as inflammatory bowel disease [29]. However, few studies have explored the relationship between pregnancy and the complications of SAP, especially IPN. In our study, univariate logistic regression analysis indicated that pregnancy, previous AP history, and the levels of Hb, TBL, ALB, BUN, and SCr were associated with IPN (Supplemental Table 1). In addition, we performed multivariate

logistic regression analyses to identify independent risk factors for IPN (Table 2). We successively established three models to verify the sensitivity of pregnancy as an independent risk factor for IPN, including pregnancy alone, pregnancy and previous medical histories, and pregnancy, previous medical histories, and laboratory test parameters. Although the OR of pregnancy decreased from 3.452 to 2.578 after adjusting for all potential confounding factors, it was still statistically significant with a *p*-value of 0.002, confirming a high correlation between pregnancy and a high risk of IPN. In addition, no previous AP history, a lower Hb level, and higher TBL and BUN levels were associated with a higher risk of IPN. Sun et al. revealed that the level of hematocrit and BUN were independent risk factors with IPN [30], consistent with our findings. An increased TBL level indicates liver injury, such as biliary obstruction, which was possibly related to the compression of pancreatic necrosis and/or portal vein thrombosis.

In this study, we developed and validated a dynamic nomogram to predict IPN in adult patients of childbearing age with HTG-AP who were admitted within 7 days of onset. Organ dysfunction typically develops in the early course of SAP, determining the clinical process and contributing to outcomes [4,31]. In contrast, IPN is generally regarded as a late event during AP [32]. Padhan RK et al. revealed that primary organ failure that developed early because of pancreatitis was significantly associated with IPN [33]. Therefore, in our prediction, early ARDS occurrence (within 7 days of onset) was used as one of the parameters affecting late IPN occurrence. Four candidate variables were finally selected by the LASSO method, including gestation weeks, ARDS occurrence, the ALB level and the SCr level. The weights of these four parameters were presented by the nomogram (Figs. 2 and 3A).

Both ALB and SCr are well-established markers of more severe courses of AP [34–36], which may explain their potential predictive value for IPN. Moreover, Shi et al. revealed that gestation weeks and ARDS are risk factors for fetal death and SAP in patients with AP in pregnancy [37], which supports and explains our results considerably. In addition, we developed an online application of this dynamic nomogram for simplicity and utility avoiding the calculation difficulty of continuous variables for easy use (Fig. 3B). In summary, this is the first prediction model for IPN for female patients of childbearing age with HTG-AP, providing a novel tool for risk stratification.

However, this study had some limitations. (1) This study was retrospective. However, we unsured to minimize information bias by reassessing the medical records and rechecking imaging manifestation. (2) This study was conducted at one of the largest tertiary referral centers for SAP in China. Therefore, patients enrolled in this study suffered from more severe conditions and higher morbidity from complications, which may introduce selection bias and limit the generalizability of the findings to other populations or healthcare settings. (3) The interventions for the fetuses in the pregnant patients with HTG-AP were performed at local hospitals where they were first admitted; therefore, we had little information about the fetuses. (4) The sample size in our prediction model is still limited; therefore, further validations with a larger sample size are required.

In conclusion, we focused on the female patients of childbearing age with HTG-AP to develop a novel prediction for IPN in this study. We revealed that pregnancy is an independent risk factor for IPN. The web-based dynamic nomogram can provide early warning and risk stratification for IPN occurrence in patients admitted within 7 days of onset.

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### Data transparency statement

A request for access to the study data can be made by contacting the corresponding author.

### Conflict of Interest

The authors declare that they have no conflict of interest.

### Author contribution

**Yuepeng Hu:** Conceptualization, Methodology, Writing – review & editing, Validation. **Yang Liu:** Writing – review & editing, Validation. **Kaiwei Li:** Conceptualization, Data curation, Validation. **Kuikui Wei:** Data curation, Validation. **Kun Gao:** Data curation, Validation. **Yao Xu:** Data curation, Validation. **Guofu Zhang:** Data curation, Validation. **Na Pu:** Data curation, Validation. **Dadong Liu:** Data curation, Validation. **Shuai Li:** Data curation, Validation. **Gang Li:** Supervision, Validation. **Bo Ye:** Supervision, Validation. **Jing Zhou:** Supervision, Validation. **Baiqiang Li:** Supervision, Validation. **Yuxiu Liu:** Conceptualization, Resources, Validation. **Qi Yang:** Methodology, Validation. **Zhihui Tong:** Methodology, Validation. **Weiqin Li:** Methodology, Validation.

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### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.dld.2023.07.034](https://doi.org/10.1016/j.dld.2023.07.034).

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