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Risk Factors and Clinical Prognosis for the Development of Intra-Abdominal Hypertension in Patients with Acute Pancreatitis: An Observational Retrospective Analysis

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Abstract

Background: Intra-Abdominal Hypertension (IAH) is a pathological condition in which the Intra-Abdominal Pressure (IAP) rises above the standard range. IAH is very prevalent in patients with Acute Pancreatitis (AP), and it is an essential factor contributing to the high mortality rate in patients with AP. There are no validated tools to forecast the appearance of IAH. The purpose of this study was to identify risk factors for IAH in patients with AP and to establish a prediction model based on them that would help clinicians determine whether a patient has IAH.

Methods: We gathered the retrospective data of 383 patients with AP. By accumulating their statistical demographic characteristics, serologic indicators and in/out volume, we constructed a Nomogram prediction model based on associated risk elements screened using a binary logistic regression method. The accuracy of this prediction model was also assessed with the area under the subject's curve.

Results: In this study, we conclude that there was a remarkable discrepancy between the IAH and non-IAH groups and that mortality was substantially more in the IAH group (43.4% *vs.* 7.6%, (P<0.001)). By using logistic regression, we filtered out six risk factors for IAH, namely blood urea nitrogen (P<0.008, OR 1.197), C-reactive protein (P<0.001, OR 1. 008), serum calcium (P<0.007, OR 0.098), 24-h urine volume (P<0.009, OR 0.443), 24-h fluid volume (P<0.001, OR 2.348) and central venous pressure (P<0.001, OR 1.834). Based on these risk variables, a prediction model was constructed and its accuracy was to be evaluated with the calibration curve and the area under the receiver operating characteristic curve. The results showed that the model had excellent predictive performance (0.952 *vs.* 0.912).

Conclusion: This study identifies that IAH can impinge on the survival of AP patients and constructs a predictive model for IAH to help clinicians better diagnose the occurrence of IAH.

Keywords: Intra-abdominal hypertension; Acute pancreatitis; Risk factors; Mortality; Prediction model

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Abbreviations

HBV: Hepatitis B; COPD: Chronic Obstructive Pulmonary Disease; PCT: Procalcitonin; AST: Aspartate; BUN: Blood Urea Nitrogen; WBC: White Blood Cell Count; PH: Potential of Hydrogen; Lac: Lactic acid; CRP: C-Reactive Protein; HCT: Red Blood Cell Specific Volume; N: Neutral Particle Ratio; PT: Prothrombin Time; IAP: Intra-Abdominal Pressure; IAH: Intra-Abdominal Hypertension; ACS: Abdominal Compartment Syndrome; ICU: Intensive Care Unit; AP: Acute Pancreatitis; SAP: Severe Acute Pancreatitis; SD: Standard Deviation; CVP: Central Venous Pressure; AUROC: Area Under the Subject Operating Characteristic Curve; WSACS: the World Society for Inter-Abdominal Compartment Syndrome

Introduction

The incidence of IAH in patients hospitalized in the ICU with AP between 31 and 51%, with a mortality from 25% to 59% [1]. In a report published by the World Association for Inter-Abdominal Compartment Syndrome, it was noted that IAH can be conceptualized as a series of interrelated processes operating in a compartmentalized manner [1-4]. Failure to observe and manage intra-abdominal hypertension in a timely manner may lead to the development of inter-Abdominal Compartment Syndrome (ACS), multi-organ dysfunction syndrome, and eventually to death. The

definition of inter-abdominal compartment syndrome includes a rising Intra-Abdominal Pressure (IAP) of more than 20 mmHg and failure of at least one new organ system [1-4]. It is also a widespread and dangerous complication that can lead to death in a short period of time [5-7].

In patients lacking any underlying abdominal disease, it is clear that aggressive fluid resuscitation in the Intensive Care Unit (ICU) can lead to IAH. However, fluids are also ordinarily given in the early stages of resuscitation in patients with AP [1-4]. Although fluid resuscitation is an essential part of treating critically ill patients, it may cause IAH in patients with AP leading to a series of severity and even ACS, which may make their symptoms dramatically worse. IAH or ACS may make them more vulnerable to organ failure, all of which can increase the mortality risk [4,8].

If IAH is recognized in the initial stages of AP and treated expeditiously, it is possible to avoid its further progression in order to reduce the rate of severe illness and mortality in AP [4,6]. Additionally, this move can shorten the length of hospital stay and reduce medical costs. It is of great concern that many intensive care team members in medical ICUs have not paid sufficient attention to IAH and its untreated consequences, leading to frequent under-detection or treatment failure of IAH in such cases, and delayed diagnosis also leads to increasing mortality in patients with SAP [9].

Furthermore, at the moment, clinicians can only obtain the IAH of patients indirectly through Cystometry [4,6,7], and it is measured intermittently [1,2]. In addition to this, IAP cannot be measured directly in each patient in the general ward as it requires more medical resources, so we propose that a simpler and cheaper method should be worked out to predict the incurrence of IAH. In this study, we investigated the prevalence of IAH in patients with AP, the causes of risk and its impact on clinical outcomes in this group of patients. A predictive model was developed through risk parameters that relied on early clinical biochemical indicators and access to indirectly predict the occurrence probability of IAH. The model is expected to help clinicians more easily diagnose IAH and allow medical staff to intervene at an earlier stage if necessary.

Materials and Methods

Study population

On the basis of patient classification criteria, this was a retrospective study focusing on a cohort of patients with AP treated in the ICU of the XXX between January 2019 and January 2023, involving only a single center. Enrolled patients were required to meet the filter criteria of age ≥ 18 years and admission within 72 h of the first episode of AP, while excluding lack of IAP records, chronic pancreatitis, pregnancy, abdominal tumors, intestinal obstruction, and history of abdominal surgery. All patients were managed by a standard protocol [1-4,9], and all clinical decisions were performed by clinicians. Data were obtained from a medical records database and the names and addresses of participants were treated confidentially. Because this study is retrospective, patients' informed consent is not required. Because the study did not involve the personal information of patients (such as name, telephone number and address), it was impossible to trace individuals, and we could not possibly cause psychological harm to them, so the study did not conduct ethical review.

Independent variable

The variables recorded within 24 h of ICU admission included demographics, comorbidities, etiology, glutamate transaminase, creatinine, urea nitrogen, potassium ion, calcium ion, pH, lactate, oxygenation index, CRP, PCT, white blood cell count, neutrophil ratio, red blood cell pressure, prothrombin time, INR, 24-h fluid volume, 24-h urine volume, and CVP. Whether vital organ support such as vasopressors and mechanical ventilation were also utilized, the duration of ICU stays, total length of stay, and whether organ failure and death occurred were recorded. All patients used Cystometry [4,6] to measure IAP as soon as they were admitted to the ICU. Based on the measured results, when there was one measurement above 12 mmHg, the measurement was repeated after an interval of 15 min, and if it still exceeded 12 mmHg, the patient was considered to have IAH.

Definition

The diagnosis of acute pancreatitis requires two of the following three features [8]: (1) abdominal pain consistent with acute pancreatitis (acute onset of persistent, severe epigastric pain, usually radiating to the back); (2) serum lipase activity (or amylase activity) at least three times higher than the upper limit of normal; and (3) characteristic findings on Contrast-Enhanced Computed Tomography (CECT) or Magnetic Resonance Imaging (MRI) or transabdominal ultrasonography indicating acute pancreatitis.

SAP [8]: Acute pancreatitis with persistent organ failure (>48 h) was defined as severe acute pancreatitis according to the revised Atlanta criteria definition.

The presence of organ failure was determined by the modified Marshall score [10]. Organ failure was determined when (PaO_2/FiO_2) was less than 300, or when systolic blood pressure was less than 90 mmHg and did not respond to fluid replacement, or when creatinine was elevated >1.9 mg/dL.

Measurement method of intra-abdominal pressure [6]: Bladder manometry was used according to the 2006 World Association for Abdominal Septal Chamber Syndrome recommendations: The patient was in a zero-degree supine position. After introduction of the bladder catheter under aseptic technique, ensure that the bladder has been completely emptied. Clamp the collector immediately after connection to the catheter. Inject 25 mL of saline, wait 25 sec to 30 sec to equalize the fluid in the closed system, and begin measurement at the end of expiration.

Statistical analysis

Analysis methods were selected based on whether the data complied with normality. Consecutive variables were expressed as the median and range (P25-P75) or as the mean and Standard Deviation (SD), while classified variables were expressed as the frequencies and percentages. U-test or t-test was used to compare continuous variables, while the chi-square test or Fisher's exact test was used to compare categorical variables. Univariate and multivariate logistic regression analyses were used to screen the Training Set for risk factors. Analyses were performed using IBM SPSS Statistics 26. Variables with P values less than 0.10 in univariate analysis were included in multivariate logistic regression (backward: condition). A nomogram was constructed from the results of the multivariate logistic regression analysis using R statistical software at $P<0.05$. Calibration curves were used to assess the consistency of the model, i.e., the discrepancy between predicted and actual values. To discern the accuracy of using the model to predict the diagnosis of IAH, ROC curves were used. models with an AUROC above 0.7 were considered

useful in terms of diagnostic accuracy.

Results

A total of 383 individuals met our study standards and were selected for inclusion in the ongoing study. The population characteristics and clinical indicators for the overall dataset, training set and validation set are shown in Table 1. The entire dataset was divided into two categories by a random sample, and the demographic characteristics and clinical indicators in both data sets were not known to be in a statistically significant manner. In the whole dataset, there were 71% of patients who were male. The medium age of the patients at the time of initial episode of AP with hospital admission was 45 (IQR 35-56) years. Among the etiologies of AP, hyperlipidemia is responsible in 58%, cholestatic for 34%, alcoholic by 5%, and other unknown causes at 3%. Of this group of 383 patients, 21% were diabetic, 23% suffered from hypertension, 2% had Hepatitis B, 2% developed

Table 1: General characteristics of the patients in all data, training data and validation data.

Variable	ALL (n=383)	Training data (n=268)	Validation data (n=115)	P-value
Age (years)	45 (35, 56)	44 (34, 56)	47 (35, 56)	0.483
Weight (Kg)	72 (65, 80)	72 (64, 82)	72 (65, 80)	0.437
Sex (male: female)	273:110	193:75	80:35:00	0.627
Etiologic factor				0.64
Biliary	129 (34%)	94 (35%)	35 (30%)	
Hyperlipidemia	224 (58%)	153 (57%)	71 (62%)	
Alcohol	10 (3%)	6 (2%)	4 (3%)	
Others	20 (5%)	15 (6%)	5 (4%)	
Diabetes	79 (21%)	53 (20%)	26 (23%)	0.53
Hypertension	88 (23%)	57 (21%)	31 (27%)	0.225
HBV	9 (2%)	8 (3%)	1 (1%)	0.376
Chronic renal insufficiency	5 (1%)	4 (1%)	1 (1%)	0.999
Cardiac insufficiency	8 (2%)	7 (3%)	1 (1%)	0.482
COPD	9 (2%)	8 (3%)	1 (1%)	0.376
AST (U/L)	39 (23, 75)	42 (24, 79)	33 (22, 55)	0.037
BUN (mmol/L)	6 (4, 10)	6 (4, 10)	6 (4, 10)	0.736
Creatinine (umol/L)	79 (59, 134)	81 (59, 133)	78 (59, 140)	0.766
Serum potassium (mmol/L)	4.0 (3.7, 4.4)	4.0 (3.7, 4.4)	4.0 (3.6, 4.4)	0.447
Serum calcium (mmol/L)	2.0 (1.8, 2.2)	2.0 (1.8, 2.2)	2.0 (1.8, 2.2)	0.456
PH	7.38 (7.33, 7.42)	7.38 (7.33, 7.42)	7.37 (7.33, 7.41)	0.528
Lac (mmol/L)	1.9 (1.2, 3.0)	1.9 (1.2, 3.0)	1.9 (1.3, 2.8)	0.975
PaO_2/FiO_2	317 (243, 405)	320 (238, 405)	310 (248, 412)	0.695
CRP (mg/L)	179 (82, 279)	182 (83, 275)	174 (79, 280)	0.862
PCT (ng/mL)	1.39 (0.34, 5.18)	1.38 (0.36, 5.12)	1.39 (0.28, 5.39)	0.923
WBC count (10^9/L)	12 (9, 16)	12 (9, 16)	12 (9, 15)	0.531
HCT (L/L)	(0.42 ± 0.08)	(0.42 ± 0.08)	(0.41 ± 0.08)	0.079
Neutral particle ratio (%)	86.5 (81.3, 89.8)	87.0 (81.3, 90.0)	85.8 (81.3, 89.2)	0.142
PT (S)	12.2 (10.9, 13.4)	12.2 (10.9, 13.4)	12.1 (11.0, 13.3)	0.8
24-hour-urine volume (L)	1.7 (1.1, 2.2)	1.7 (1.1, 2.3)	1.7 (1.0, 2.1)	0.502
24-hour-fiuid volume (L)	3.2 (2.5, 4.4)	3.2 (2.5, 4.5)	3.2 (2.4, 4.3)	0.65
CVP (mmHg)	6 (4, 9)	6 (4, 9)	6 (5, 10)	0.996
endotracheal intubation	93 (24%)	65 (24%)	28 (24%)	0.984
vasopressors	60 (16%)	41 (15%)	19 (17%)	0.763
hospital duration (days)	14 (9, 23)	14 (9, 25)	12 (8, 21)	0.141
ICU duration (days)	6 (3, 14)	6 (3, 14)	7 (3, 14)	0.99
Respiratory failure	165 (43%)	36 (13%)	72 (63%)	0.093
Circulatory failure	57 (15%)	10 (4%)	28 (24%)	0.555
renal failure	76 (20%)	17 (6%)	39 (34%)	0.431
SAP	263 (69%)	72 (27%)	109 (95%)	0.466
Non-survivor	91 (24%)	11 (4%)	51 (44%)	0.661

Table 2: Clinical course of SAP patients with or without IAH.

Outcome	ALL (n=383)	Non-IAH (210)	IAH (173)	P-value
Hospital duration (days)	14 (9, 23)	11 (8, 15)	21 (12, 33)	<0.001
ICU duration (days)	6 (3, 14)	4 (2, 7)	14 (7, 23)	<0.001
Respiratory failure (%)	165 (43.1%)	58 (27.6%)	107 (61.8%)	<0.001
Circulatory failure (%)	57 (14.9%)	13 (6.2%)	44 (25.4%)	<0.001
Renal failure (%)	76 (19.8%)	21 (10%)	55 (31.8%)	<0.001
SAP (%)	263 (68.7%)	105 (50%)	158 (91.3%)	<0.001
Non-survivor (%)	91 (23.8%)	16 (7.6%)	75 (43.4%)	<0.001

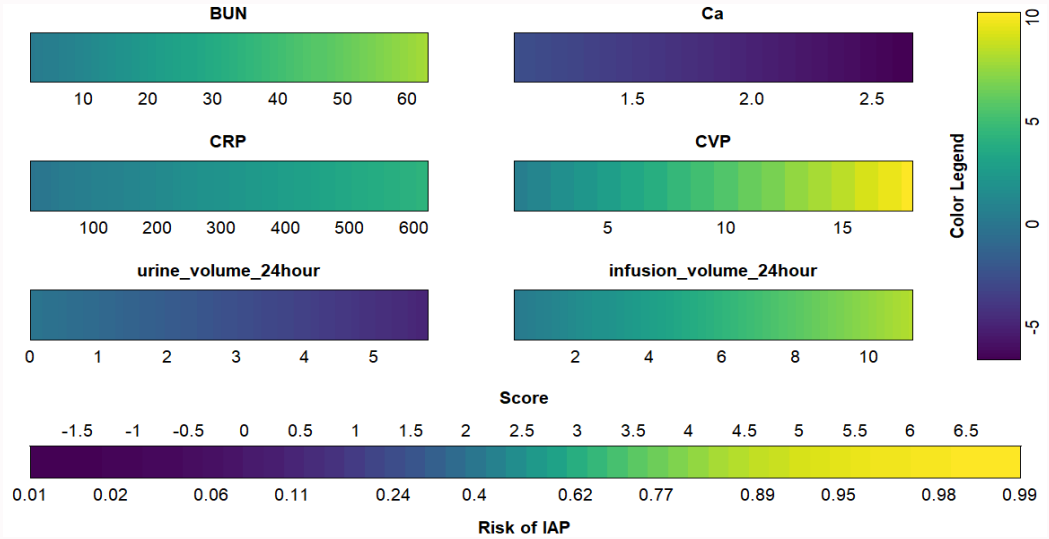

Figure 1: The Nomogram for intra-abdominal hypertension of acute pancreatitis.

chronic obstructive pulmonary disease, 1% kidney insufficiency, and 2% suffering from cardiac insufficiency. 24% of the patients were intubated; 16% were on vasopressors; and 43% of them developed acute respiratory failure; of all 383 patients with acute pancreatitis, 15% presented with acute circulatory failure, 20% experienced acute renal failure; of the 69% affected with SAP, and 24% had a death during their hospitalization. The duration of ICU was a median of 6 days (IQR 3-14). The hospitalization duration was a mean of 14 days (IQR 9-23). The first day of infusion had a median volume of 3.2 (IQR 2.5-4.4) L, the first 24-h urine volume had a median of 1.7 (IQR 1.1-2.2) L, and the CVP was 6 mmHg (IQR 4-9).

The mortality

On the basis of the statistics shown in Table 3, there were a grand total of 383 patients with AP at the admission to the ICU, of which there were 292 in the survival group (76% of the overall population) and 91 in the non-survival group (24% of the overall population). In the non-survival group, the major etiology was biliary (51%), while in the survival group, the majority of causes were hyperlipidemia (63%). Among the non-survivor group, ICU hospital stays were lengthier with a 12-day median (IQR 4-27 days) compared with a 5-day median (IQR 3-10 days) in the survivor group, based on the data; organ failure occurred at a greater rate in the non-survivor group, with 66% respiratory failure *vs.* 36% in the survivor group, 45% circulatory failure *vs.* 5% in the survivor group, and 48% renal failure *vs.* 1% in the survivor group. In addition, the non-survivor group had more 24-h infusion volume with a median of 3.74 (IQR 2.66-5.94L) compared to 3.09 (IQR 2.50-4.17L) in the survivor group. However, there were no meaningful differences in these differences. Up to 82% of patients with IAH in the non-survival group were statistically different compared to 34% in the survival group (OR 0.308 (95% CI 0.139-0.682)). Meanwhile, a high 98% of the non-survival group had SAP, which was statistically meaningful compared to 59% of the survival group (OR 4.862 (95% CI 1.747-13.530)). Older age in the death group (54 (IQR42-68) years *vs.* 41 (IQR34-53) years, OR 1.042 (95% CI 1.027-1.057)), high PCT (OR 1.014 (95% CI 1.001-1.028)), high rate of vasopressor use (46% *vs.* 6%, OR 0.166 (95% CI 0.068-0.409)) and endotracheal intubation use (59% *vs.* 42%, OR 0.245 (95% CI 0.080-0.750)), low 24-h urine output (0.86 (IQR0.42-1.60)L *vs.* 1.75 (IQR1.36-2.35)L, OR 0.519 (95% CI 0.362-0.746)). Associations were also found between mortality and Renal failure new onset after admission (48% *vs.* 1%, OR 0.046 (95% CI 0.006-0.363)).

Clinical course

From the data in Table 4, we can draw a significant discrepancy between the IAH and non-IAH groups in terms of organ failure ratio (61.8% *vs.* 27.6% for respiratory failure, 61.8% *vs.* 27.6% for circulatory failure, and 31.8% *vs.* 10% for renal failure) (p<0.001) and with a longer total hospital stay (21 (IQR 12-33) days *vs.* 11 (IQR 8-15) days) (P<0.001). The duration of ICU stay was lengthier in IAH patients (14 (IQR7-23) days *vs.* 4 (IQR2-7) days) compared to the non-IAP group (P<0.001). The occurrence of SAP was markedly more frequent in the IAH group (91.3% *vs.* 50%, respectively) (P<0.001). There was also a mortality rate found to be noticeably superior, with 43.4% within the

Table 3: Univariate regression analysis and multivariate regression analysis of mortality.

Variable	Non-survivor (n=91)	survivor (n=292)	P-value	OR (95%CI)
Age (years)	54 (42, 68)	41 (34, 53)	<0.001	1.042 (1.027, 1.057)
Weight (Kg)	70 (60, 80)	73 (65, 82)		
Sex (male: female)	60:31:00	213:79		
Etiologic factor				
Biliary	46 (51%)	83 (28%)		
Hyperlipidemia	39 (43%)	185 (63%)		
Alcohol	4 (4%)	6 (2%)		
Others	2 (2%)	18 (6%)		
Diabetes	16 (18%)	63 (22%)		
Hypertension	33 (36%)	55 (19%)		
HBV	2 (2%)	7 (2%)		
Chronic renal insufficiency	2 (2%)	3 (1%)		
Cardiac insufficiency	2 (2%)	6 (2%)		
COPD	5 (6%)	4 (1%)		
AST (U/L)	75 (47, 160)	33 (21, 56)		
BUN (mmol/L)	11 (6, 17)	5 (4, 8)		
Creatinine (umol/L)	163 (87, 261)	71 (56, 101)		
Serum potassium (mmol/L)	4.2 (3.7, 4.8)	4.0 (3.7, 4.3)		
Serum calcium (mmol/L)	1.8 (1.5, 2.1)	2.1 (1.9, 2.2)		
PH	7.35 (7.28, 7.41)	7.38 (7.34, 7.42)		
Lac (mmol/L)	2.6 (1.6, 4.2)	1.7 (1.1, 2.7)		
PaO_2/FiO_2	259 (201, 335)	333 (271, 413)		
CRP (mg/L)	237 (162, 320)	157 (57, 266)		
PCT (ng/mL)	7.10 (1.81, 24.99)	0.83 (0.25, 2.45)	0.037	1.014 (1.001, 1.028)
WBC count (10^9/L)	11 (8, 16)	12 (10, 16)		
HCT (L/L)	0.40 ± 0.09	0.42 ± 0.08		
Neutral particle ratio (%)	87.4 (1.8, 90.3)	86.2 (81.3, 89.7)		
PT (S)	13.8 (11.9, 15.3)	11.9 (10.8, 13.0)		
24-hour-urine volume (L)	0.86 (0.42, 1.60)	1.75 (1.36, 2.35)	<0.001	0.519 (0.362, 0.746)
24-hour-fulid volume (L)	3.74 (2.66, 5.94)	3.09 (2.50, 4.17)		
CVP (mmHg)	8 (5,12)	5 (4, 8)		
endotracheal intubation	54 (59%)	39 (42%)	0.014	0.245 (0.080, 0.750)
vasopressors	42 (46%)	18 (6%)	<0.001	0.166 (0.068, 0.409)
hospital duration(days)	15 (5, 27)	14 (9, 22)		
ICU duration(days)	12 (4, 27)	5 (3, 10)		
Respiratory failure (%)	60 (66%)	105 (36%)		
Circulatory failure (%)	41 (45%)	16 (5%)		
Renal failure (%)	44 (48%)	32 (1%)	0.003	0.046 (0.006, 0.363)
SAP (%)	90 (98%)	173 (59%)	0.002	4.862 (1.747, 13.530)
IAP: Non-IAP (%)	75:16 (82%)	98:194 (34%)	0.004	0.308 (0.139, 0.682)

IAH group versus 7.6% in the non-IAH group (P<0.001).

The risk factors of IAH

In accordance with univariate logistic analysis of the demographic and clinical indicators of the training set, Table 4 shows that the following variables were associated for significant reasons with the prevalence of IAH: AST, BUN, Cr, K, Ca, PH, Lac, oxygenation index, CRP, PCT, HCT, PT, 24-h urine volume, 24-h fluid volume, CVP, the use of endotracheal intubation, and the use of blood pressure-raising drugs. And age, gender, weight, etiology, comorbidities, white blood cell count and neutrophil ratio were not correlated with IAH. From the results of multivariate analysis gained from variables with P<0.1, six variables were identified after backward conditional stepwise regression screening. They were BUN (P<0.008, OR 1.197 (95% CI 1.048-1.369)), CRP (P<0.001, OR 1.008 (95% CI 1.004-1.013)), Ca (P<0.007, OR 0.098 (95% CI 0.018-0.523)), 24-h urine

Table 4: Univariate analysis and Multivariate analysis of possible predictors of risk of IAH based on training data.

Variable	Non-IAH (n=147)	IAH (n=121)	Univariate analysis		Multivariate analysis	
			P-value	OR (95% [CI])	P-value	OR (95% [CI])
Age (years)	43 (34, 56)	45 (34, 57)	0.834	0.998 (0.984, 1.013)		
Weight (Kg)	70 (62, 81)	75 (65, 84)	0.697	1.003 (0.989, 1.016)		
Sex (male: female)	101:46:00	92:29:00	1.185	0.692 (0.402, 0.192)		
Etiologic factor			0.664			
Biliary	55(37%)	39(32%)				
Hyperlipidemia	83(56%)	70(58%)				
Alcohol	1(1%)	5(4%)				
Others	8 (5%)	8 (7%)				
Diabetes	32 (22%)	21 (17%)	0.368	1.325 (0.718, 2.444)		
Hypertension	28 (19%)	29 (24%)	0.328	0.746 (0.415, 1.342)		
HBV	6 (4%)	2 (2%)	0.267	2.532 (0.502, 12.779)		
Chronic renal insufficiency	5 (3%)	2 (2%)	0.43	2.500 (0.257, 24.347)		
Cardiac insufficiency	3 (2%)	1 (1%)	0.382	2.095 (0.399, 10.995)		
COPD	4 (3%)	4 (3%)	0.78	0.818 (0.200, 3.342)		
AST (U/L)	31 (20, 69)	56 (37, 98)	0.007	1.004 (1.001, 1.007)		
BUN (mmol/L)	5 (4, 7)	9 (6, 14)	<0.001	1.225 (1.146, 1.310)	0.008	1.197 (1.048, 1.369)
Creatinine (umol/L)	66 (53, 82)	119 (83, 228)	<0.001	1.008 (1.005, 1.011)		
Serum potassium (mmol/L)	3.9 (3.7, 4.2)	4.2 (3.8, 4.8)	<0.001	2.384 (1.614, 3.521)		
Serum calcium (mmol/L)	2.1 (2.0, 2.3)	1.8 (1.5, 2.0)	<0.001	0.015 (0.005, 0.046)	0.007	0.098 (0.018, 0.523)
PH	7.38 (7.34, 743)	7.36 (7.31, 7.41)	0.047	0.040 (0.002, 0.965)		
Lac (mmol/L)	1.6 (1.1, 2.8)	2.1 (1.4, 3.5)	0.007	1.222 (1.055, 1.415)		
PaO_2/FiO_2	348 (305, 502)	258 (199, 353)	<0.001	0.992 (0.900, 0.995)		
CRP (mg/L)	110 (25, 212)	249 (175, 320)	<0.001	1.010 (1.007, 1.012)	<0.001	1.008 (1.004, 1.013)
PCT (ng/mL)	0.58 (0.25, 1.84)	3.75 (1.23, 14.07)	<0.001	1.066 (1.029, 1.105)		
WBC count(10^9/L)	12 (9, 16)	12 (9, 16)	0.493	1.015 (0.972, 1.061)		
HCT (L/L)	0.42 (0.38, 0.47)	0.44 (0.37, 0.51)	0.011	58.492 (2.516, 1360.058)		
Neutral particle ratio (%)	87.4 (81.9, 90.4)	86.1 (80.3, 89.7)	0.231	0.978 (0.943, 1.014)		
PT (S)	11.7 (10.6, 13.0)	12.9 (11.7, 14.0)	<0.001	1.334 (1.164, 1.528)		
24-hour-urine volume (L)	1.9 (1.5, 2.4)	1.3 (0.6, 1.9)	<0.001	0.412 (0.294, 0.577)	0.009	0.443 (0.240, 0.878)
24-hour-fiuid volume (L)	2.8 (2.4, 3.5)	4.3 (3.0, 6.0)	<0.001	1.981 (1.604, 2.448)	<0.001	2.348 (1.476, 3.734)
CVP (mmHg)	5 (4, 6)	9 (7, 120)	<0.001	1.953 (1.661, 2.298)	<0.001	1.834 (1.434, 2.345)
endotracheal intubation	12 (8%)	53 (44%)	<0.001	1.110 (0.057, 0.228)		
vasopressors	11 (7%)	30 (25%)	<0.001	0.245 (0.117, 0.514)		

volume (P<0.009, OR 0.443 (95% CI 0.240-0.878)), 24-h fluid volume (P<0.001, OR 2.348 (95% CI 1.476-3.734)) and CVP (P<0.001, OR 1.834 (95% CI 1.434-2.345)). Among them, serum calcium level and 24-h urine volume were to some extent protective factors for IAP in acute pancreatitis, while BUN, CVP, CRP and 24-h fluid volume were a part of risk factors.

In Figure 1, we use these risk elements to constrain a predictive model. To evaluate the possibility of intra-abdominal hypertension, the patient's values on each axis are labeled and the number of points is calculated for all variables. Next, the sum is marked on the total point axis and a line is drawn perpendicular to the likelihood axis to derive the probability that the patient suffers from IAH. In Figure 2, we use the calibration curve to estimate the model. Figure 2(1) demonstrates the calibration curve for the training set, while Figure 2(2) shows the calibration curve for the validation set. The Bias-corrected and Apparent lines are close to the ideal line on both the training and validation sets, which demonstrates a high agreement between the predicted and actual values. In Figure 3, we illustrate the receiver operating characteristic curves of the prediction model on both the training and validation data. The area under the curve for the prediction model is 0.952 on the training data and 0.912 on the validation data. the expected value is 1.00, and the reference line is the chance base case (0.50). Both are greater than 0.9, indicating that the model has good predictive power.

Discussion

IAH is one of the complications commonly seen in patients with SAP, and its morbidity has been reported differently in the literature, ranging from 14% to 42% [4,6,7]. Our study found the incidence of

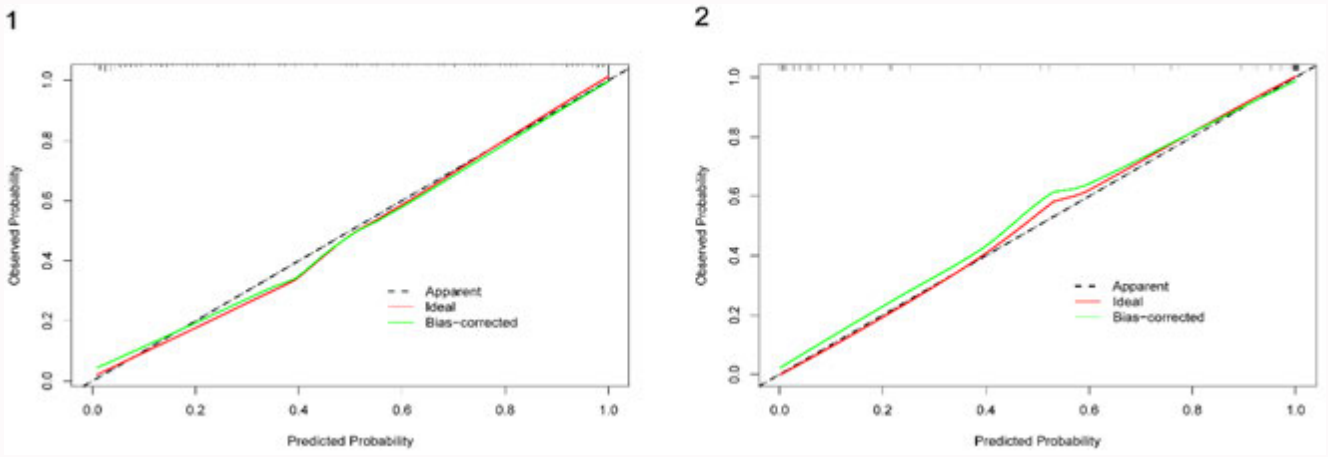

Figure 2: The Calibration curve of training data and validation data.
Evaluation of the model using the calibration curve. The calibration curve of the training set is shown in Figure 2(1), and the calibration curve of the verification set is shown in Figure 2(2).

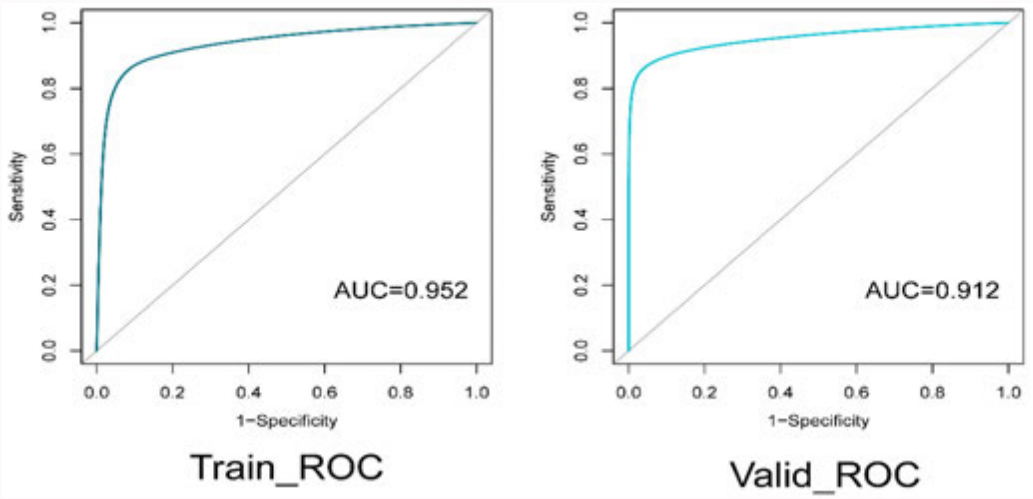

Figure 3: The Receiver operating characteristic curves of the predictive model on the training data and validation data.

IAH in patients with SAP to be 45.2%, which is in accordance with the literature data. The presence of IAH may be due to a variety of factors, but these factors are currently poorly described in the literature.

In the current study, we identified serum calcium levels as an essential role as a key risk factor for IAH. Calcium levels have long been seen as one of the predictors of poor prognosis in SAP and have been included in the RANSON criteria developed in 1974 [11,12]. SAP is exacerbated by cellular necrosis and inflammatory cell activation. It is known that the pathophysiology of AP is implicated in the imbalance of intracellular calcium homeostasis and elevated cytoplasmic calcium concentration in pancreatic alveolar cells [13,14]. Entrainment of calcium into other cells leads to cellular calcium overload, which activates inflammatory stimuli that are triggered by multiple cytokines mediated through pro-inflammatory immune responses. This inflammation can in turn be transmitted to organs *via* lymphatic vessels and the body circulation cascade [15]. A positive feedback loop between cytokine release and programmed immune cell death leads to the most extreme cytokine storm syndrome [13]. This process also contributes to the early clinical features of SIRS that endure in AP [16,17]. In extreme cases, cytokine storm syndrome is caused by a positive feedback loop that exacerbates multi-organ dysfunction [13,16-18]. Therefore, it needs to be considered that low serum calcium levels may enhance the incidence of IAH in patients with SAP.

Supportive treatment remains the foundation of AP, and early aggressive rehydration is extensively considered an important measure in the management of AP, as untreated inadequate perfusion of the pancreas may lead to adverse outcomes such as pancreatic necrosis and death [19]. However, there are no data from specific randomized controlled trials addressing the amount and rate of rehydration and the type of rehydration to support this view [20,21]. The investigators initiated a multicenter open-label RCT called WATERFALL that compared early massive fluid resuscitation with moderate fluid resuscitation. In that randomized trial involving patients with AP, early aggressive fluid resuscitation resulted in a higher incidence of fluid overload, but clinical outcomes were not ameliorated [22]. WATERFALL's findings suggest that excessive re-hydration may be correlated with poor prognosis in critical patients, and that aggressive fluid resuscitation is associated with an elevated risk of volume overload. The severity of AP is correlated with increased IAP, and

excessive intravenous fluid administration may contribute to higher IAP. These results emphasize the importance of avoiding excessive fluid rehydration in the treatment of acute pancreatitis to reduce volume overload and elevated IAP [19,22].

Central venous pressure is commonly utilized in clinical settings to monitor rehydration therapy. When AP is in its early stages, fluid loss may lead to hypovolemic shock and systemic organ ischemia, and timely fluid resuscitation can help reduce the incidence of adverse events and mortality [23]. However, massive fluid resuscitation is a cause of IAH [3,4,24]. Complication rates and mortality are higher in patients with aggressive massive fluid resuscitation compared to moderate fluid resuscitation [19-22,25]. Therefore, after a patient's central venous pressure continues to increase, indicating a normal or unresponsive fluid balance, aggressive fluid resuscitation should be appropriately discontinued and monitoring of IAP should be considered.

Decreased 24-h urine output is considered another risk factor for the progression of IAH. When urine output decreases, metabolic wastes accumulate in the body, leading to altered serological indicators, such as BUN. In the pathogenesis of AP, premature activation of pancreatic enzymes in the alveoli leads to self-digestion of the pancreas and surrounding tissues, and the release of activated enzymes and proteases into the body circulation may lead to endothelial damage and fluid extravasation in the interstitial space of blood vessels [18]. Fluid extravasation contributes to the appearance of hypovolemia, which in turn causes acute pre-renal renal failure, decreased glomerular filtration rate, oliguria and anuria [26-30].

In conclusion, in clinical practice, changes in baseline such as BUN and creatinine are occasionally taken as evidence of inadequate vascular volume. When BUN or creatinine is increased, it is an indication of inadequate intravascular volume and the need for fluid resuscitation [31-33]. Restoration of urine output is generally regarded as a marker of successful fluid resuscitation. If BUN or creatinine continues to decrease, fluid resuscitation can be considered to be effective. However, after fluid resuscitation, if the patient still has low urine output, elevated BUN or high creatinine levels, the physician is required to consider that the patient is not responsive to fluids [34]. At this point, other solutions should be sought rather than excessive fluid resuscitation, which can lead to excess fluid, increased abdominal pressure, or even IAH. Consequently, when a patient is resuscitated with fluids, if there is still an elevated BUN level, increased creatinine or decreased 24-h urine output, it shows that the patient is not responding well to fluids and may lead to fluid excess. If the volume load is too high and vascular permeability increases, it may cause IAH, further aggravating renal impairment and creating a vicious cycle. Therefore, when patients are observed to have rising creatinine or reduced urine output despite fluid revitalization, the occurrence of IAH should be continuously monitored and interventions should be made at an early stage to avoid acute kidney injury [31].

CRP is an acute chronotropic protein, a non-specific protein to detect tissue damage and inflammatory response. Its levels in the blood increase over several hours with the onset of inflammation and sepsis and peak approximately 48 h to 72 h after onset [35]. CRP can be used for diagnosis, prognosis, treatment follow-up and mortality prediction, especially in inflammatory diseases [36-38]. Clinicians usually regard CRP as a reference standard for disease severity within 48 h [39]. This acute phase reactant has been widely applied as an independent predictor of AP severity and mortality and is considered to correlate well with severity and prognostic indicators of acute pancreatitis [36,40]. This was confirmed by the results of the present study.

Studies have demonstrated that approximately 20% of patients with AP progress to severe disease [41,42]. In contrast, SAP is a devastating disease with mortality rates ranging from less than 10% to as high as 85% [43-45]. In comparison with other studies, the cohort in this study had a severe disease rate of 68.7% and a mortality rate of 23.8%. High IAP was strongly correlated with high mortality. Multivariate analysis showed that respiratory failure, severity of AP, 24-h urine output, age, IAP, PCT level, and use of vasopressor or tracheal intubation were factors that enhanced the risk of in-hospital mortality.

Studies have suggested that 24-h urine output is one of the risk factors for the development of IAH in patients with AP, which increases the risk of death. Furthermore, PCT levels are higher during inflammation and sepsis [46]. The risk of AP is higher with age, but advanced age does not necessarily affect the severity of AP or mortality [47,48]. Additionally, this study found that PCT had a higher predictive value for mortality at the time of hospital admission in patients with AP. Respiratory failure is very frequent in the early stages of AP, and respiratory failure is one of the most common causes of death in patients with AP [49,50]. Therefore, physicians should pay more attention when patients with AP present with IAH or acute respiratory failure and take timely interventions to avoid further deterioration or even death.

There are some limitations of this study that require attention. First, because this study was a retrospective study conducted at a single center, it may suffer from sample selection bias and is not representative of the general population. Second, retrospective studies are also subject to inherent bias and other limitations. These shortcomings could be reduced by further use of larger multicenter samples or prospective studies. In the additional, the patients in this study were from provincial hospitals and most of them had more severe disease, so it may not be applicable to patients with mild pancreatitis. In conclusion, patients with AP with the above risk factors should be vigilant and undergo regular IAP testing. Also, this study developed and validated the IAH prediction model, which proved to be a strong predictor of visceral hypertension in patients with AP.

Conclusion

The presence of IAH is implicated in disease severity, high mortality and poor prognosis according to our study. The independent risk factors for IAH are BUN, Ca, CRP, CVP, 24-h urine volume and 24-h fluid volume. With these factors, a predictive model can be constructed by which clinicians can better identify whether IAH occurs in patients with AP. Patients with AP can benefit from early diagnosis and treatment.

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