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Predicting and evaluation the severity in acute pancreatitis using a new modeling built on body mass index and intra-abdominal pressure

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ABSTRACT

Object: Acute pancreatitis (AP) keeps as severe medical diagnosis and treatment problem. Early evaluation for severity and risk stratification in patients with AP is very important. Some scoring system such as acute physiology and chronic health evaluation-II (APACHE-II), the computed tomography severity index (CTSI), Ranson's score and the bedside index of severity of AP (BISAP) have been used, nevertheless, there're a few shortcomings in these methods. The aim of this study was to construct a new modeling including intra-abdominal pressure (IAP) and body mass index (BMI) to evaluate the severity in AP.

Methods: The study comprised of two independent cohorts of patients with AP, one set was used to develop modeling from Jinling hospital in the period between January 2013 and October 2016, 1073 patients were included in it; another set was used to validate modeling from the 81st hospital in the period between January 2012 and December 2016, 326 patients were included in it. The association between risk factors and severity of AP were assessed by univariable analysis; multivariable modeling was explored through stepwise selection regression. The change in IAP and BMI were combined to generate a regression equation as the new modeling. Statistical indexes were used to evaluate the value of the prediction in the new modeling.

Results: Univariable analysis confirmed change in IAP and BMI to be significantly associated with severity of AP. The predict sensitivity, specificity, positive predictive value, negative predictive value and accuracy by the new modeling for severity of AP were 77.6%, 82.6%, 71.9%, 87.5% and 74.9% respectively in the developing dataset. There were significant differences between the new modeling and other scoring systems in these parameters ($P < 0.05$). In addition, a comparison of the area under receiver operating characteristic curves of them showed a statistically significant difference ($P < 0.05$). The same results could be found in the validating dataset.

Conclusions: A new modeling based on IAP and BMI is more likely to predict the severity of AP.

1. Introduction

Acute pancreatitis (AP) has gradually become one of the most serious acute digestive disorders all over the world.[1–3] Despite deeper understandings of pathogenesis of AP and rapid growth of multidisciplinary team (MDT), AP keeps as severe medical diagnosis and treatment problem. The mortality rate of mild AP is less than 1%, however up to 20% of it may develop a clinically serious proceeding and the mortality rate for severe acute pancreatitis (SAP) remains high from 10 to 30% due to pancreatic necrosis and organs failure.[4] It's very important to perform early evaluation for severity and risk stratification in patients with AP. Then the patients may receive more aggressive examination and treatment, such as computed tomography (CT) imaging, early fluid resuscitation and nutritional support.

Currently some scoring systems are capable of being used including the Acute Physiology and Chronic Health evaluation-II (APACHE-II), the computed tomography severity index (CTSI), Ranson's score and the bedside index of severity of AP (BISAP).[5–7] Nevertheless, there're a few shortcomings in these methods. Calculation method of APACHE-II scoring system is complex to clinicians. Balthazar CTSI is based on a CT examination, which may

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increase medical costs and is not recommended to all patients, Ranson and BISAP scoring system were often used to predict the mortality of AP rather than evaluate the severity; and some studies found the predicting accuracy of these scoring systems to SAP was not high. In view of the drawback of the scoring systems, there remains an unmet requirement for an accurate and convenient method to evaluate and predict severity of AP.

In recent years, some studies showed that high intra-abdominal pressure (IAP) can reduce cardiac output and venous return, lead to progressive hypoperfusion and ischemia of the abdominal viscera including pancreas.[8,9] When IAP is more than 20 mmHg, it may cause abdominal compartment syndrome and multiple organ failure. And many studies showed that obesity was associated with the severity of AP.[10,11]

In present study, we constructed and validated a modeling combining body mass index (BMI) with IAP to predict SAP by using retrospective data from our hospitals, furthermore to compare the modeling with other scoring systems.

2. Method

2.1. General information

Our study comprised of two independent cohorts of patients with AP, one set was used to develop modeling from Jinling hospital in the period between January 2013 and October 2016, the set included 1073 patients with AP. Another set was used to validate modeling from the 81st hospital in the period between January 2012 and December 2016, the set included 326 patients with AP.

Diagnostic standard of AP was in accordance with the revision of the Atlanta classification consensus in 2012.[12] AP patients were diagnosed based on the presence of at least two of the following three criteria: (1) an initial serum amylase and/or lipase level at least three-fold above the normal upper limit; (2) typical abdominal pain consistent with AP; and (3) suggestive imaging evidence compatible with AP, such as CT, MRI and ultrasonography. SAP is defined as an episode of AP with persistent organ function failure, and/or local complications (abscess, necrosis, or pseudocyst). Organ function failure was defined as shock (systolic pressure less than 90 mm Hg), renal function failure (serum creatinine more than 2.0 mg/dL after hydration), pulmonary function insufficiency (PaO2 no more than 60 mm Hg), or gastrointestinal hemorrhage (more than 500ml/24 h).

Patients who met the following criteria were excluded: 1) accompanied with history of serious cardiopulmonary diseases, hepatic disease, renal disease or severe immune system disorders; 2) presence of pancreatic cancer or other organs of tumor; 3) the interval between onset of typical abdominal symptoms and admission of more than 48 h; 4) younger than 18 years old age; 5) pregnancy.

The characteristics of AP patients including age, gender, etiology of AP, BMI, biochemical tests, IAP, serum amylase, mortality, BISAP, APACHII score, Ranson score and CTSI, were picked up on admission and were summarized in Table 1.

IAP and BMI were the most important variables in our studies. When IAP was determined, a catheter were used and inserted into the bladder jointed to a pressure transducer,[13] and then 50 mL of normal saline was instilled into it. It was determined in the first three days after admission. The pubic symphysis was deemed to level 0. BMI was calculated as weight (kilograms) divided by height (meters) squared and measured on admission.

The study protocol conformed to the guidelines by the institutional ethical committee (both of the two hospitals) and was approved by the authors' institutional review board. All patients gave their informed consent to be included in the study. The research was carried out according to the principles of The Declaration of Helsinki.

2.2. Modeling

Different variables were evaluated by univariable analysis as the predictors of SAP. The change in IAP was calculated as: $\left[\mathrm{IAP}_{\mathrm{day1}} - \frac{(\mathrm{IAP}_{\mathrm{day2}}+\mathrm{IAP}_{\mathrm{day3}})}{2}\right]/\mathrm{IAP}_{\mathrm{day1}}*100$. Then multivariable modelings were inferred by stepwise selection regression. The IAP change and BMI were combined to the result. After constructing modeling, we validated it for predicting the severity and mortality of AP with database from the 81st hospital. The modeling was accessed for accuracy and compared with the CTSI, Ranson scoring, BISAP and APACHII scoring on admission for severity and mortality in AP.

2.3. Statistical analysis

Continuous data were expressed as mean values ± standard deviation. Significant differences between groups were determined by chi-squared analysis and unpaired Student t-test. Modeling was developed to predict the severity of AP. Statistical analyses were performed using SPSS 21.0 software. Dichotomous variables were created out of continuous variables by using clinically important cut off points. Receiver operating characteristic (ROC) curves for models were applied to measure the discrimination of the modelings, an automated stepwise variable selection method used with 1000 bootstrap samples was performed to decide the final modelings; variables with inclusion rates >20% were further evaluated and the combination with highest area under the curve was selected. In our study, P values < 0.05 were considered statistically significant.

3. Results

3.1. Patient characteristics

The dataset from Jinling hospital and 81st hospital of P.L.A. were used to build and validate modeling. Characteristics on admission of the developing and validating dataset are summarized in Table 1. The two datasets were not different significantly for any of the eleven variables (P > 0.05) except fasting blood glucose (FBG), the two datasets were well balanced in the distribution of clinical characteristics.

3.2. Developing dataset

In the developing dataset, 517 of them were SAP. Univariate regression analysis identified eleven relevant factors of AP (Table 2). In these factors, the change of IAP and BMI were the significant predictors for severity of AP(P < 0.05).

Multivariable models were explored through stepwise selection regression (Table 3). The ultimate model was composed of BMI and change of IAP, and it offered ideal prediction in SAP (AUC = 0.849). The ultimate logistic regression equation could be displayed as: $P = \frac{1}{1+e^{(37.195-0.613*\mathrm{IAP}-0.702*\mathrm{BMI})}}$. In the formula, P is forecast probability of logistic regression model, the unit of BMI was kg/m^2, IAP was calculated as: $\left[\frac{(\mathrm{IAP}_{\mathrm{day2}}+\mathrm{IAP}_{\mathrm{day3}})}{2} - \mathrm{IAP}_{\mathrm{day1}}\right]/\mathrm{IAP}_{\mathrm{day1}}*100$, Nagelkerke decision coefficient was 0.731 which showed the modeling fitting well. The cutoff point of our new modeling was set according to Youden index with the value of 0.263, when applied to the developing dataset, the logistic regression modeling had a sensitivity of

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