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Original Article

Predicting the clinical manifestations in necrotizing acute pancreatitis patients with splanchnic vein thrombosis

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ABSTRACT

Background: Splanchnic venous thrombosis (SVT) is a relatively rare but important complication of necrotizing acute pancreatitis (NAP). Clinical manifestations and severity of this complication in different patients vary greatly, ranging from mild abdominal discomfort even asymptomatic to lethal gastrorrhagia or hepatic failure. The aim of the present study was to develop a model to predict the clinical manifestations of SVT in NAP patients.

Methods: This retrospective cohort study was conducted in the surgical intensive care unit (SICU) of Jinling Hospital. Patients with the presence of both pancreatic necrosis and SVT were selected for possible inclusion. Both univariate and multivariate logistic regression analyses were applied using 12 indices including age, gender, Acute Physiology and Chronic Health Evaluation II scores (APACHE II), CRP(C - reactive protein) levels, etc to assess potential predictors for symptomatic pancreatic splanchnic venous thrombosis (PSVT) in this cohort. A prognostic nomogram was also applied to develop an easy-to-use prediction model.

Results: A total of 104 patients with necrotizing acute pancreatitis (NAP) and splanchnic vein thrombosis (SVT) from January 2012 to December 2013 were enrolled for analysis. A quarter of study subjects (26 of 104, 25%) developed variable symptomatic manifestations including variceal bleeding, persistent ascites and enteral nutrition (EN) intolerance during the disease course. In the multivariable regression model, the following factors were found to be associated with the occurrence of symptomatic SVT: Balthazar's computed tomography (CT) score (OR = 1.818; 95% CI: 1.251–2.641; P = 0.002), intra-abdominal pressure (IAP) (OR = 1.172; 95% CI: 1.001–1.251; P = 0.043 and presence of SMVT (OR = 6.946; 95% CI: 2.290 –21.074; P = 0.001). A prediction model incorporating these factors demonstrated an area under the receiver operating characteristic curve of 0.842.

Conclusions: Balthazar's CT score, IAP and SMVT are predictors of symptomatic SVT in NAP patients. The nomogram we conducted can be used as an easy-to-use risk stratification tool in either clinical practice or future studies.

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1. Introduction

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Nearly 16.4–36.4% of patients with necrotizing acute pancreatitis (NAP) develop splanchnic vein thrombosis (SVT) during disease courses, which may involve the portal vein (PV), splenic vein (SplV), and superior mesenteric vein (SMV), either in combination or separately [1–3]. Since the first description of SVT in pancreatitis in 1977, multiple attempts have been made to figure out the mechanism, pathophysiology, diagnosis and management of SVT. Its serious consequences such as gastrointestinal (GI) variceal bleeding, hepatic failure, significant ascites and poorly tolerated

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enteral nutrition have been reported in several studies [4-6].

Clinical manifestations and severity of SVT differ a lot, ranging from mild abdominal discomfort even asymptomatic to lethal gastrorrhagia or hepatic failure [7,8]. Therefore predicting whether SVT would be symptomatic or even life-threatening in each patient is of great importance, because aggressive anticoagulation therapy is of potential bleeding risk in NAP and clinical decisions may be altered accordingly. For instance, in patients who would probably develop clinical consequences mentioned above, prolonged anticoagulation or additional thrombolytic therapy should be considered to avoid lethal complications [9,10]. Conversely, for patients who are at low risk of developing clinical symptoms, expectant management is more appropriate [11].

However, no study regarding early prediction of SVT related symptoms was published by now as its clinical significance was still not well recognized. In the present study, we aimed to assess a series of potential predictors for symptomatic SVT in patients suffering NAP and develop an easy-to-use predictive tool for clinical work if possible. The study parameters included patient demographic characteristics (gender, age, etc.), disease severity (APACHE II score, SOFA score etc.), morphology on CT (Balthazar's CT score), and clinical complications (thrombosis occurrence and IAH).

2. Materials and methods

2.1. Patients

Between January 2012 and December 2013, 465 patients with a primary diagnosis of AP admitted to the surgical intensive care unit (SICU) of Jinling Hospital underwent CTV and only 104 patients with the presence of both pancreatic necrosis and SVT were selected for possible inclusion. The diagnostic details were described below. Patients who met the following criteria were excluded: (1) younger than 18 years old; (2) older than 70 years old; (3) pregnancy or severe immune system disorders; (4) end-stage chronic disease; (5) All cases of chronic pancreatitis. This study protocol was approved by the institutional review board of Jinling hospital. Besides, written informed consents for this study were obtained from each patient or his next of kin.

2.2. Imaging protocols

All patients with predicted severe pancreatitis or with ongoing unexplained pain underwent Computed tomography venography (CTV) soon after admission if no contraindications were cited. The diagnoses of SVT was based on the results of CTV, which is a quick, safe, noninvasive and widely-available procedure. The technical details were described in our previous study [3]. CT scans for patients with positive findings were reviewed by two expert radiologists with rich experience in abdominal imaging. The radiologists were blinded to the clinical history and the patients. Thrombosis was defined as a filling defect within the lumen of the vessel or the vein appeared compressed or was not visualized with the presence of collaterals. During hospitalization, consecutive imaging was performed every two weeks to evaluate progression or regression of thrombus in patients with positive findings. In those with negative CT results, addition examination was applied depending on the physician's decision.

2.3. Diagnosis and definitions

Pancreatic necrosis was defined according to the Determinant-Based Classification of Acute Pancreatitis and the revision of the Atlanta classification [12,13]. We defined SVT-caused persistent ascites as the volume of transudative ascites drained >1000 ml/ d without other possible causes such as serum ascites albumin fluid gradient, duct disruption and chylous ascites. Enteral nutrition (EN) intolerance was defined as sudden reappearance of failure to EN after achieving full-calorie feeding target. GI bleeding was confirmed via emergent gastroscopy operation.

2.4. Treatment

All the study patients initially received standard medical treatment according to the recent international guidelines including intensive care management; fluid therapy; nutritional support; preventing infectious complications and biliary tract management [14]. Infected pancreatic necrosis (IPN) was managed in a step-up fashion using percutaneous drainage as the primary choice of treatment. Patients underwent open surgery when minimallyinvasive drainage failed. Anticoagulation therapy (subcutaneous low molecular weight heparin) was performed after SVT was diagnosed and catheter directed thrombolysis via transjugular or transhepatic approach would be considered when necessary. Diuretics were used after albumin infusion to reduce the volume of ascites. The treatment of varices was according to the AASLD guidelines and the Baveno V consensus for detailed management issues [15].

2.5. Data collection

As previously described, data collection in this study included demographic characteristics like age, gender, cause of illness, smoking and drinking habits and clinical parameters such as BMI levels, APACHE II score, hematocrit, C-reactive protein (CRP) level, IAP, D-dimer, AT-III and platelet at admission, Balthazar's CT score and occurrence of IPN. The time interval between blood sample collection and admission ranges from 30 to 45 min in our center. All the laboratory results were obtained at the Central Laboratory of Jinling Hospital according to the standard protocols. IAP was measured with a catheter inserted into the bladder, according to the standard technique established by WSACS in 2006 [16]: 25 ml of 0.9% NaCl was instilled, and the midaxillary line was considered as level 0. For every patients, IAP was recorded every 6 h during the first 24 h after admission and intra-abdominal hypertension (IAH) was defined according to the WSACS recommendations as a sustained or repeated pathological elevation in IAP \geq 12 mmHg. Moreover, the management strategies (e.g. endoscopic and surgical), hospital and ICU length of stay, rate of systemic and local complications including organ failure (OF), multiple organ dysfunction syndrome (MODS), pancreatic infection, and mortality-were recorded to compare the prognosis of patients with or without symptomatic manifestations mentioned above.

2.6. Statistical analysis

Results are expressed as the median (interquartile range) unless mentioned otherwise. Categorical variables were described in absolute numbers and in percentages. Continuous variables were compared using the Mann–Whitney *U* test, and categorical data were analyzed with the chi-squared test. The association between the predictive factors and SVT clinical manifestations was first evaluated by univariable logistic regression. Factors potentially associated with development of SVT clinical manifestations in the univariable regression analysis were included in multivariable regression analysis. All statistical tests were two-tailed, and the significance level was set at P < 0.05. A nomogram was constructed on the basis of the outcome of the final multivariable regression analysis. Data were analyzed with SPSS 19.0 for Windows (Chicago, IL).

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