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Efficacy of resistin and leptin in predicting persistent organ failure in patients with acute pancreatitis

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ABSTRACT

Background: To investigate the accuracy of resistin, leptin and adiponectin levels in predicting persistent organ failure in patients with acute pancreatitis (AP).
Methods: Data from 90 consecutive patients admitted to our hospital for AP were retrospectively collected from an ongoing prospective cohort study. The levels of adiponectin, leptin and resistin were measured and compared between patients with and without persistent organ failure. The accuracy of the adipokines in predicting persistent organ failure were compared with the patients' Acute Physiology and Chronic Health Evaluation II (APACHE-II) score, and were separately investigated in overweight and non-overweight groups.
Results: Persistent organ failure occurred in 26.7% of the patients. The levels of resistin were significantly increased in AP patients with persistent organ failure, in both the overweight and the non-overweight subgroups. Resistin and APACHE-II score predicted persistent organ failure with comparable areas under the curve (AUC) of 0.72 and 0.75, respectively ($p = 0.66$). Resistin demonstrated similar accuracy with the APACHE-II score in predicting persistent organ failure in the overweight (0.69 vs. 0.66, $p = 0.82$) and non-overweight (0.76 vs. 0.87, $p = 0.39$) subgroups. There was no correlation between adiponectin and persistent organ failure, but a weak correlation between leptin and persistent organ failure was demonstrated.
Conclusions: Resistin and leptin levels, rather than adiponectin, correlate with persistent organ failure in patients with AP.

1. Introduction

Organ failure is the leading cause of early mortality in patients with AP. Organ failure during AP is categorised as either transient or persistent depending on whether the duration is less than or longer than 48 h, this classification can lead to distinct prognoses. The mortality rate in patients with persistent organ failure is up to 50%, which is approximately 8-fold higher than that of the patients with transient organ failure [1–3]. Accordingly, patients with persistent organ failure are the target population in the management of AP [4]. In treating such patients, a timely transfer to a tertiary medical center or intensive care unit is necessary [5]. Nevertheless, persistent organ failure cannot be confirmed until the organ failure has been documented for over 48 h. The general treatment for patients with organ failure is an urgent transfer to an intensive care unit (ICU). Accordingly, it may be unnecessary to transfer patients with transient organ failure to either a tertiary medical center or an ICU. However, differentiating between persistent and transient organ failure is difficult.

After over 30 years of efforts to assess the disease severity, it is

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still challenging to accurately predict persistent organ failure in patients with AP. Current scoring systems, including the APACHE-II score, BISAP score, and Ranson's score, only predict persistent organ failure with moderate accuracy, with areas under the curve (AUC) ranging from 0.57 to 0.74 [6]. The difficulty stems from a subgroup of patients who have developed organ failure [7]. It is thought that the existing scoring systems have reached their maximal efficacy in predicting persistent organ failure in AP [6]. One possible reason for the inaccuracies may be that the parameters involved in the scoring systems only reflect the passive clinical condition rather than the mechanisms underlying the increased severity.

AP is an inflammatory process in which many mediators are involved. Recently, it has been demonstrated that adipokines are closely involved in the process of AP [8], and the level of adipokines such as adiponectin, leptin and resistin, correlate well with the severity of AP [9–11]. For example, resistin was shown to predict the severity of AP (Schröder score >3) with a higher AUC (0.9) and sensitivity (93.3%) [9]. However, it is unclear whether adipokines measurement could to be applied to predict persistent organ failure. In the present study, the accuracy of using adipokines levels, such as those of resistin, leptin and adiponectin, to predict persistent organ failure in AP were investigated.

2. Methods

The present study was conducted according to the Declaration of Helsinki principles and was approved by the local ethics committee (First Affiliated Hospital of Fourth Military Medical University). All of the patients gave informed consent.

2.1. Patients

Data from 90 consecutive patients admitted to our hospital with AP between 2013/03/23 and 2014/07/18 were retrospectively collected from an ongoing prospective cohort study (registration no. ChiCTR-OCH-12002669). The registered study is an observational study and has no influence on the level of adipokines.

2.2. Inclusion criteria

The primary criteria were a diagnosis of AP and admission to our hospital within 72 h after symptom onset.

2.3. Exclusion criteria

The exclusion criteria were as follows: recurrent pancreatitis; chronic pancreatitis; history of pancreas, liver or spleen surgery; pregnancy; malignancy related pancreatitis; and chronic liver diseases.

2.4. Data and sample collection

Demographic characteristics such as age, sex, and aetiology were recorded on admission. Blood samples were collected upon admission and stored at −80 °C until further testing. Computed tomography was performed within 24 h of admission. The APACHE-II and the modified Marshall scores were calculated by the clinicians based on the clinical parameters collected within 24 h of admission. Once organ failure was detected, the organ function was monitored until it recovered. The duration of organ failure, length of hospital stay, incidence of infection, need for intervention and in-hospital mortality were recorded during the course of AP.

2.5. Diagnostic criteria

AP was diagnosed when two or more of the following were present: 1) abdominal pain characteristic of AP, 2) serum amylase and/or lipase ≥3 times the normal upper limit and 3) characteristic findings of AP on a CT scan. Organ failure was defined as a score of 2 or more for respiratory, cardiovascular and renal systems using the modified Marshall scoring system [4]. Persistent organ failure was defined as organ failure that lasts for over 48 h [4].

Pancreatic necrosis infection was diagnosed by a positive culture result for pancreatic necrosis obtained either during open surgery or from drainage fluid collected by a retro-peritoneal percutaneous catheter. Obvious gas bubbles observed at the (peri)-pancreatic location on the CT image were also considered pancreatic necrosis infection. Bacteraemia was diagnosed when the blood culture results were positive. Pneumonia was diagnosed by either chest X-ray or the sputum culture. Overweight was defined as a body mass index ≥25 kg/m^2.

2.6. Grouping

Patients were divided into two groups: with and without persistent organ failure. The clinical outcomes (including the incidence of ICU transfer, infectious complications, dialysis, percutaneous catheter drainage, hospital stay and mortality), APACHE-II score, and the levels of leptin, resistin and adiponectin were compared among patients with and without persistent organ failure. The predictive accuracy of the APACHE-II score may be amplified as persistent organ failure commonly occurs more frequently in patients who have a history of organ failure. Accordingly, adipokines levels were investigated exclusively in patients admitted without organ failure. To exclude the interference of adipose tissue on adipokines levels, patients were further divided into overweight and non-overweight subgroups. The levels of the three adipokines and the APACHE-II score were compared between patients with and without persistent organ failure in the two BMI-classified subgroup.

2.7. Measurement of adipokines

The serum leptin levels were measured in duplicate using an enzyme-linked immunosorbent assay (ELISA), whereas the levels of resistin and adiponectin were measured in duplicate using MILLIPLEX® MAP. Serum leptin concentrations were measured using a human leptin ELISA kit (Millipore, Boston, USA; sensitivity: 0.2 ng/ml; intra-assay coefficient of variation: 2.6–4.6%, and interassay coefficient of variation: 2.6–6.2%). The serum resistin and adiponectin concentrations were measured using the human adipokine magnetic bead panel 1 (Millipore, Boston, USA; sensitivity: 2.2 pg/ml, 11 pg/ml, respectively; intra-assay coefficient of variation: 3% and 4%, respectively, and interassay coefficient of variation: 14% and 10%, respectively).

2.8. Statistics

The statistical analysis was conducted using Medcalc 9.2.0.1 (MedCalc Software, Mariakerke, Belgium). Unless particularly noted, the categorical data were reported as numbers with proportions, and the quantitative data were reported as either medians with interquartile ranges (IQRs) or means with standard deviation. The categorical data were compared using the Chi-squared or Fisher's exact tests where appropriate. For the continuous data, the Mann–Whitney *U* test or Student's t-test were used for the group comparisons as appropriate. A two-sided p value of <0.05 was considered to be statistically significant. ROCs were constructed for

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