Original Article

Predictive value of the ratio of venoarterial PCO_2 to arteriovenous O_2 content difference for organ injury in patients with severe acute pancreatitis

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Background: Severe acute pancreatitis (SAP) is a common but severe disease with high mortality. Organ injury is the primary risk factor for death in SAP patients. The purpose of this study was to explore the predictive value of the ratio of venoarterial PCO_2 to arteriovenous O_2 content difference [$P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$] for organ injury in patients with SAP to provide evidence for further clinical intervention.

Methods: We retrospectively collected data from 108 patients with SAP admitted to Huzhou Central Hospital between January 2018 and January 2021. Forty-five patients who experienced organ injury were defined as the organ injury group, and 63 patients without organ injury were defined as the control group. The differences in $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$, lactate, hematocrit (HCT), Acute Physiology and Chronic Health Evaluation (APACHE II) scores, and Ranson scores between the two groups were analyzed, and a receiver operating characteristic curve (ROC) was used to analyze the value of $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ in the prediction of organ injury in SAP patients.

Results: At admission, the organ injury group demonstrated significantly higher Ranson scores and APACHE II scores than the control group (Ranson scores: 6.09±1.35 *vs.* 3.97±2.02, respectively, P=0.000; APACHE II scores: 11.64±2.91 *vs.* 10.08±2.91, respectively, P=0.007). The value of $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ was also elevated compared to the control group (1.47±0.41 *vs.* 1.09±0.33, respectively, P=0.000) as was the level of lactate (3.33±0.86 *vs.* 2.56±0.70 mmol/L, respectively, P=0.000). There was no significant difference in HCT between the two groups at admission (44.47%±6.29% *vs.* 44.53%±5.75%, respectively, P=0.957). The Ranson score, APACHE II score, $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ and lactate levels were all significant predictors of organ injury in patients with SAP. The area under the curve of $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ was 0.733 (0.637–0.829), P=0.000.

Conclusions: $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ is a potential predictor of organ injury in patients with SAP.

Keywords: Severe acute pancreatitis (SAP); ratio of venoarterial PCO_2 to arteriovenous O_2 content difference; prognosis

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Introduction

Mortality in severe acute pancreatitis (SAP) is as high as 10–20%. Early low blood volume is an important factor in the death of patients with SAP (1-3). The causes of low blood volume are multifaceted, including vomiting, reduced oral intake, third space losses, and sweating, resulting in tissue hypoperfusion and organ failure (4). Organ failure is the most important determinant of outcome in acute pancreatitis. In the early stage, uncontrolled inflammatory response and tissue hypoperfusion caused by severe acute pancreatitis lead to organ failure. In the later stage, infected pancreatic necrosis will result in organ failure. In the natural course of SAP, 25–59.5% of patients experience acute renal injury (5). Early fluid resuscitation is the key to the treatment of SAP. Appropriate fluid resuscitation strategies help lower the severity of the systemic inflammatory response and maintain tissue perfusion (6-8). However, early fluid resuscitation is a double-edged sword because excessive fluid will aggravate tissue edema and reduce oxygen delivery due to the reduction of hematocrit (HCT) caused by hemodilution. At present, lactate, HCT, and urine volume are used to guide patients' early fluid resuscitation. These indicators can reflect the patient's tissue perfusion and the severity of the disease (9-11). In general, the worse the tissue hypoperfusion is, the more serious the disease. The Ranson score specifically evaluates the severity of SAP and is an important prognostic predictor (12). However, all the above indicators have poor real-time performance; for instance, the Ranson score can only be fully evaluated 48 hours after admission. In recent years, some researchers have used the ratio of venoarterial PCO_2 to arteriovenous O_2 content difference [$P(cv\text{-}a)CO_2$ /$C(a\text{-}cv)O_2$] to evaluate the perfusion and oxygen uptake in SAP patients' tissues (13). The $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ has the advantages of real-time performance and fast detection. We have added this in the introduction. Patients with SAP have also demonstrated tissue hypoperfusion and oxygen uptake disorder in the early stage. Therefore, $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ may be of value in predicting organ injury, but there is currently a lack of relevant research. The purpose of this study was to investigate the predictive value of $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ for organ injury in patients with SAP.

We present the following article in accordance with the STARD reporting checklist (available at https://dx.doi.org/10.21037/apm-21-2557).

Methods

General data

We retrospectively collected the data from 108 patients with SAP consecutively admitted to Huzhou Central Hospital from January 2018 to January 2021. The inclusion criteria were as follows: (I) the diagnostic criteria for SAP were met when the patient had pancreatic aseptic necrosis, organ failure, or pancreatic necrotic infection in addition to two of the following three symptoms of acute pancreatitis: acute epigastric pain, a serum amylase level three times above the upper limit of normal, or an abdominal CT scan showing acute pancreatitis; (II) onset within 72 hours after admission; (III) aged 18–65 years; (IV) the patient had received treatment in our hospital; and (V) complete clinical medical records were available. Patients were excluded if they displayed any of the following: (I) degenerative disease; (II) cancer; (III) primary hepatic or renal insufficiency; (IV) primary cardiac, cerebral, or pulmonary insufficiency; (V) pregnancy; (VI) serious adverse events unrelated to treatment that could affect the results; (VII) failure to cooperate with treatment. Patients were divided into either the organ injury group (n=45) or the control group (n=63) according to whether they experienced organ injury or not. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). As this study was a retrospective analysis of patients' imaging and clinical data only and did not use the patient's serum or tissue for additional testing, the ethical approval is waived by the Ethics committee of Huzhou Central Hospital (Affiliated Hospital of Huzhou Normal University). Individual consent for this retrospective analysis was waived.

Treatment

According to the latest treatment guidelines, all patients received standardized treatments, including continuous hemodynamic monitoring, fluid resuscitation, early enteral nutrition, and prophylactic use of antibiotics for patients with pancreatic necrosis. The step-up drainage mode was used to treat patients with pancreatic necrotic tissue infections, including percutaneous drainage, continuous double-cannula negative-pressure irrigation and drainage, endoscopic removal of pancreatic necrotic tissue, and open drainage.

Definition criteria

Table 1 Comparison of general data between the two groups

Category	n	Age (years), mean ± SD	Gender (male), n (%)	Course of disease (hours), mean ± SD	Etiology, n (%)		
					Hyperlipidemia	Cholelithiasis	Alcoholic
Organ injury group	45	43.87±8.12	28 (62.22)	28.48±8.46	12 (26.67)	28 (62.22)	5 (11.11)
Control group	63	44.26±8.65	39 (61.90)	29.04±9.12	18 (28.57)	38 (60.32)	7 (11.11)
t/χ^2 value		0.237	0.001	0.324		0.050	
P value		0.813	0.973	0.746		0.975	

SD, standard deviation.

Table 2 Comparison of main complications between the two groups

Category	n	Pancreatic necrosis infection, n (%)	Pancreatic pseudocyst, n (%)
Organ injury group	45	34 (75.56)	3 (6.67)
Control group	63	12 (19.05)	2 (3.17)
χ^2 value		34.280	0.725
P value		0.000	0.395

The diagnosis of pancreatic necrosis was based on an enhanced CT scan taken at least 48 hours after onset. The diagnosis of pancreatic necrotic tissue infection was based on a positive bacterial culture result from peritoneal drainage fluid and a persistent fever. In the Sequential Organ Failure Assessment (SOFA), a score of two or more for an individual organ was considered organ failure. Multiple organ failure was diagnosed if two or more organs failed.

Observed indicators

The observed indicators included age, gender, etiology, Ranson score, Acute Physiology and Chronic Health Evaluation (APACHE II) score, [P(cv-a)CO_2/C(a-cv)O_2], lactate, and HCT.

Calculation method

The patients' radial artery and elbow vein blood samples were taken at admission for blood gas analysis, and the ratio of [P(cv-a)CO_2/C(a-cv)O_2] was calculated according to the blood gas analysis results.

Statistical analysis

All statistical analyses were conducted with SPSS 26.0 software (IBM, Chicago, USA). All tests were two-tailed, and a P value <0.05 was considered statistically significant. A receiver operating characteristic (ROC) curve was used to analyze the predictive value of the different indexes for organ injury in patients with SAP. The measurement and count data of the two groups were analyzed by *t*-tests and chi-square tests, respectively.

Results

Comparison of general data between the two groups

There was no significant difference in age, gender, course of disease, or etiology between the two groups (P>0.05) (*Table 1*).

Comparison of main complications between the two groups

There was no significant difference in the incidence of pancreatic pseudocysts between the two groups (P>0.05). The incidence of pancreatic necrosis infection in the organ injury group was significantly higher than that in the control group (75.56% *vs.* 19.05%, respectively, P=0.000) (*Table 2*).

Comparison of observation indexes between the two groups at admission

At admission, the organ injury group demonstrated significantly higher Ranson scores and APACHE II

Table 3 Comparison of observation indexes between the two groups at admission

Category	n	Ranson score, mean ± SD	APACHE II score, mean ± SD	$P(cv-a)CO_2/C(a-cv)O_2$, mean ± SD	Lactate (mmol/L), mean ± SD	HCT (%), mean ± SD
organ injury group	45	6.09±1.35	11.64±2.91	1.47±0.41	3.33±0.86	44.47±6.29
control group	63	3.97±2.02	10.08±2.91	1.09±0.33	2.56±0.70	44.53±5.75
t value		6.143	2.757	5.289	5.183	0.054
P value		0.000	0.007	0.000	0.000	0.957

APACHE II score, Acute Physiology and Chronic Health Evaluation; $P(cv-a)CO_2/C(a-cv)O_2$, ratio of venoarterial PCO_2 to arteriovenous O_2 content difference; HCT, hematocrit; SD, standard deviation.

Table 4 The predictive value of $P(cv-a)CO_2/C(a-cv)O_2$ for organ injury in patients with SAP

Category	Ranson score	APACHE II score	$P(cv-a)CO_2/C(a-cv)O_2$	Lactate (mmol/L)	HCT (%)
The area under the curve	0.789	0.642	0.733	0.747	0.489
95% CI	0.707–0.871	0.537–0.748	0.637–0.829	0.653–0.841	0.376–0.602
P value	0.000	0.012	0.000	0.000	0.847
Optimal cut-off value of diagnosis	5.50	10.50	1.15	3.06	43.89
Specificity	0.667	0.711	0.711	0.644	0.556
Sensitivity	0.714	0.556	0.571	0.730	0.492

APACHE II score, Acute Physiology and Chronic Health Evaluation; $P(cv-a)CO_2/C(a-cv)O_2$, ratio of venoarterial PCO_2 to arteriovenous O_2 content difference; HCT, hematocrit; CI, confidence interval; SAP, severe acute pancreatitis.

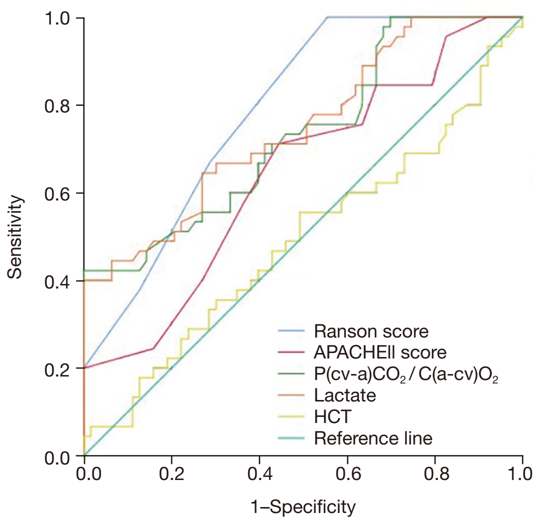

Figure 1 The predictive value of $P(cv-a)CO_2/C(a-cv)O_2$ for organ injury in patients with SAP. $P(cv-a)CO_2/C(a-cv)O_2$, ratio of venoarterial PCO_2 to arteriovenous O_2 content difference. SAP, severe acute pancreatitis.

scores than the control group (Ranson scores: 6.09±1.35 *vs.* 3.97±2.02, respectively, P=0.000; APACHE II scores: 11.64±2.91 *vs.* 10.08±2.91, respectively, P=0.007). The value of $P(cv-a)CO_2/C(a-cv)O_2$ was also elevated compared to the control group (1.47±0.41 *vs.* 1.09±0.33, respectively, P=0.000) as was the level of lactate (3.33±0.86 *vs.* 2.56±0.70 mmol/L, respectively, P=0.000). There was no significant difference in HCT between the two groups at admission (44.47%±6.29% *vs.* 44.53%±5.75%, respectively, P=0.957) (*Table 3*).

The value of $P(cv-a)CO_2/C(a-cv)O_2$ in predicting organ injury in patients with SAP

The Ranson score, APACHE II score, $P(cv-a)CO_2/C(a-cv)O_2$, and lactate were all significant predictors of organ injury in patients with SAP. The area under the curve for $P(cv-a)CO_2/C(a-cv)O_2$ was 0.733 (0.637–0.829), P=0.000 (*Table 4* and *Figure 1*).

Discussion

Pancreatitis is a common fatal disease with a high incidence rate. In China, acute pancreatitis is mainly caused by kidney stones, whereas alcoholic pancreatitis is more common in patients from Western countries. When acute pancreatitis patient had pancreatic aseptic necrosis, organ failure, or pancreatic necrotic infection, severe acute pancreatitis were diagnosed. Approximately 20% of patients with acute pancreatitis will develop SAP. The early treatment of severe acute pancreatitis is mainly to maintain the patient's organ function and restore tissue perfusion. The mortality rate of SAP is reported to be 20%, but for patients with pancreatic necrosis infection or sustained organ failure, the mortality rate can be as high as 50% (14).

The early stage of SAP is mainly characterized by insufficient volume and systemic inflammation. Evaluating the insufficient volume of patients can simultaneously provide evidence for early fluid resuscitation and predict the prognosis of patients. For critically ill patients, aggressive interventions and treatments are needed to improve their prognosis. SAP is often accompanied by low blood volume and the "cytokine storm" in the early stage, leading to tissue hypoperfusion, oxygen uptake dysfunction, and even organ failure (15-17). The $P(cv\text{-}a)CO_2$ is a sensitive index to reflect whether the tissue has sufficient blood flow to clear CO_2. It also has great guiding value for judging the degree of tissue hypoxia damage. When the oxygen supply is insufficient, anaerobic metabolism occurs, in contrast to aerobic metabolism when the oxygen supply is sufficient. The metabolites produced by aerobic and anaerobic metabolism are different, so it is possible to identify anaerobic metabolism in the patient. When the same amount of O_2 is consumed, the amount of CO_2 produced by anaerobic metabolism and aerobic metabolism differs and reflects the body's oxygen metabolism. An increased ratio of $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ indicates that anaerobic metabolism is enhanced, the body is hypoxic, the blood volume is insufficient, or the oxygen uptake is impaired, showing that the patient's condition is serious. A normal $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ ratio represents normal aerobic metabolism, sufficient blood volume, and a relatively mild condition. The $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ ratio directly reflects metabolism and is not affected by other factors (including lung function) and changes more rapidly than lactic acid levels. The linear map of the $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ ratio can reflect the oxygen supply dependence of patients and has diagnostic value for the presence of oxygen uptake disorders (such as microcirculation deposition and mitochondrial dysfunction). Studies have shown that $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ has high sensitivity and specificity in the diagnosis of hyperlactatemia, with a ratio higher than 1.4 indicating a poor prognosis (18). Our results show that $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$, Ranson scores and APACHE II scores are all good predictors of organ injury in patients with SAP, but $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ has the advantages of real-time performance and fast detection. Moreover, we compared the predictive values of $P(cv\text{-}a)\ CO_2/C(a\text{-}cv)\ O_2$, lactate and HCT. We found that the predictive values of $P(cv\text{-}a)\ CO_2/C(a\text{-}cv)\ O_2$ and lactate were equivalent, and the predictive value of HCT was poor.

Taken together, our findings suggest that $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ may be valuable in predicting organ injury in patients with SAP. It has distinct advantages, such as a simple measurement method, real-time performance, repeated monitoring, and few influencing factors. Furthermore, it could be used to guide the early fluid therapy of SAP patients. Currently, there is a lack of relevant research on the role of $P(cv\text{-}a)CO_2/C(a\text{-}cv)O_2$ as a predictor of organ injury in SAP, so further clinical studies are urgently needed.

Limitations

The main limitation of this study is that it is a retrospective clinical study, so the number of cases is relatively small, which is likely to cause some deviations in the results. It needs to be further confirmed by multi-center clinical trials.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://dx.doi.org/10.21037/apm-21-2557

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki (as revised in 2013). As this study was a retrospective analysis of patients' imaging and clinical data only and did not use the patient's serum or tissue for additional testing, the ethical approval is waived by the Ethics committee of Huzhou Central Hospital (Affiliated Hospital of Huzhou Normal University). Individual consent for this retrospective analysis was waived.

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