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Relationship between blood malondialdehyde, endotoxin, MPV/PLT ratio and early kidney injury in patients with severe acute pancreatitis

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Abstract: **Objective** To investigate the relationship between serum malondialdehyde (MDA), endotoxin, peripheral blood mean platelet volume (MPV) to platelet count (PLT) ratio and early acute kidney injury in patients with severe acute pancreatitis (SAP), and to provide a reference for predicting kidney injury in patients with SAP. **Methods** A total of 90 patients with SAP admitted to Jiamusi Central Hospital from February 2021 to March 2024 were enrolled. According to the occurrence of early acute kidney injury, patients were divided into a kidney injury group and a non-kidney injury group. Serum MDA, endotoxin, and peripheral blood MPV/PLT ratio were compared between the two groups. Multivariate logistic regression was used to analyze independent risk factors for early acute kidney injury in SAP patients. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive efficacy of the three indicators. **Results** Of the 90 patients, 37 (41.11%) developed early acute kidney injury (kidney injury group), and the remaining 53 (58.89%) did not (non-kidney injury group). Acute Physiology and Chronic Health Evaluation Ⅱ (APACHE Ⅱ)score, CRP, MDA, endotoxin, and MPV/PLT ratio were significantly higher, while urine volume and serum calcium (Ca^{2+}) were significantly lower in the kidney injury group compared to in the non-kidney injury group (P<0.05). Multivariate logistic regression analysis showed that high levels of MDA (OR=7.870, 95%CI:1.669-37.108), endotoxin (OR=1.260, 95%CI:4.814-34.034), and MPV/PLT ratio (OR=4.424, 95%CI:1.408-13.897) were independent risk factors for early acute kidney injury in SAP patients (P<0.05). ROC curve analysis showed that the area under the ROC curve (AUC) of endotoxin was 0.884, with a sensitivity of 78.38% and a specificity of 90.57%; the AUC of MDA was 0.874, with a sensitivity of 91.89% and a specificity of 69.81%; the AUC of MPV/PLT ratio was 0.875, with a sensitivity of 78.38% and a specificity of 92.45%. **Conclusion** MDA, endotoxin, and MPV/PLT ratio are closely related to the occurrence of early kidney injury in patients with SAP. These three all have high predictive efficacy for early kidney injury in patients with SAP.

Keywords: Severe acute pancreatitis; Kidney injury, early; Malondialdehyde; Endotoxin; Mean platelet volume; Platelet count

Fund program: Scientific Research Project of the Health Commission of Heilongjiang Province

Surveillance data shows that the global incidence rate of acute pancreatitis (AP) ranges from 5 to 74 cases per 100,000 population. Prolonged hospital stays and high treatment costs impose a heavy burden on patients and their families[1]. AP is classified into three severity categories: mild acute pancreatitis, moderately severe acute pancreatitis, and severe acute pancreatitis. Most patients with AP have mild disease, which typically resolves within 7 to 14 days of treatment with a low mortality rate. In contrast, patients with severe acute pancreatitis (SAP) present with severe clinical conditions and poor prognosis, with a mortality rate ranging from 20% to 30%[2]. Renal injury is a common complication of SAP. For patients requiring dialysis, the mortality rate can increase up to 75%. Therefore, to improve the prognosis of SAP patients, it is necessary to evaluate and predict the occurrence of early renal injury in these patients[3]. Studies have demonstrated that the level of malondialdehyde (MDA) is closely correlated with the degree of pancreatic tissue damage, and detection of MDA levels is helpful for assessing the prognosis and occurrence of complications in AP patients[4]. During the onset of SAP, affected by pancreatic enzymes, intestinal paralysis and other factors, substances such as 5-hydroxytryptamine and histamine are released, which affect the vascular permeability of the intestinal wall. Meanwhile, the level of endotoxin increases, causing impairment to systemic organ function[5]. Previous studies have indicated that platelets are associated with the occurrence of renal injury in patients with sepsis, and the value of the mean platelet volume (MPV)/platelet (PLT) ratio in evaluating the severity of sepsis has also been confirmed[6]. At present, there are relatively few research reports on the relationship between the above three indicators and early renal injury in SAP patients. Whether MDA, endotoxin, and MPV/PLT ratio can be used as indicators for predicting early renal injury in SAP patients remains to be further studied. This paper explores this issue to provide new insights for improving the prognosis of SAP patients.

1 Materials and Methods

1.1 General Information

A total of 90 patients with SAP admitted to Jiamusi Central Hospital from February 2021 to March 2024 were selected as the research subjects. **Inclusion criteria:** (1) Meet the diagnostic criteria for SAP specified in the

Guidelines for the Diagnosis and Treatment of Acute Pancreatitis (2021 Edition)[7]; (2) Aged 18 years or older; (3) Time from onset to admission ≤ 48 h, and no relevant treatment was received before admission. **Exclusion criteria:** (1) Complicated with renal interstitial or renal parenchymal injury caused by other etiologies; (2) Complicated with acute or chronic infection; (3) Non-AP patients, such as those with chronic pancreatitis (or acute exacerbation), traumatic pancreatitis, etc. Among the 90 patients, 58 were male and 32 were female; the age ranged from 28 to 74 years, with an average age of (51.10 ± 11.10) years. This study was approved by the Ethics Committee of Jiamusi Central Hospital (Approval number: JZ20200619).

1.2 Methods

1.2.1 Determination of Early Renal Injury and Grouping

The occurrence of early renal injury in patients was determined according to relevant guidelines[8]: (1) Serum creatinine (Scr) increase exceeding 26.5 μmol/L (or 0.3 mg/dL) within 48 h; (2) Scr increase exceeding 1.5 times the baseline level within 7 days (known or presumed); (3) Urine volume less than 0.5 mL/(kg·h) persisting for 6 h.

Diagnosis is confirmed if any one of the three criteria is met. Patients were divided into the renal injury group and the non-renal injury group according to the occurrence of early renal injury.

1.2.2 Detection of Serum MDA, Endotoxin and MPV/PLT Ratio

Serum MDA and endotoxin: Fasting venous blood samples were collected from patients, centrifuged at 3,000 r/min for 10 min (centrifugation radius: 13.5 cm), and the supernatant was obtained for detection. MDA level was determined by the thiobarbituric acid method (MDA detection kit purchased from Wuhan AmyJet Scientific). Endotoxin level was determined by the matrix colorimetric micro-quantitative method (endotoxin detection kit purchased from Wuhan Boster Biological Technology). The operation process was strictly carried out in accordance with the kit instructions. MPV/PLT ratio: Venous blood samples were collected from patients at admission, anticoagulated with dipotassium ethylenediaminetetraacetate (EDTA-K2). The mean platelet volume (MPV) and platelet count (PLT) were detected using the BC-11 automatic cell analyzer (Shenzhen Mindray Bio-Medical Electronics), and the MPV/PLT ratio was calculated.

1.2.3 Clinical Data Collection

By reviewing electronic medical records and hospital database records, the general data of patients were collected and statistically analyzed, including gender, age, etiology of onset, body mass index (BMI), urine volume, and Acute Physiology and Chronic Health Evaluation II (APACHE II) score. Laboratory indicators were also collected, including C-reactive protein (CRP), serum amylase (AMY), lipase (LPS), serum calcium, etc.

1.3 Statistical Methods

SPSS 28.0 statistical software was used for data analysis. Measurement data were described as $\bar{x}\pm s$, and independent samples *t*-test was used for comparison between two groups. Count data were expressed as case (%), and chi-square test was used for comparison between groups. Multivariate logistic regression analysis was used to analyze the influencing factors of early renal injury in SAP. Receiver operating characteristic (ROC) curves were plotted to analyze the predictive efficacy of the three indicators for the occurrence of early renal injury in SAP. The test level was set as $\alpha = 0.05$.

2 Results

2.1 Incidence of Early Renal Injury in SAP Patients

Among the 90 SAP patients, 37 patients (41.11%) developed early renal injury (renal injury group), while the remaining 53 patients (58.89%) did not develop renal injury (non-renal injury group).

2.2 Univariate Analysis of Early Renal Injury in SAP Patients

The APACHE II score, CRP level, MDA level, endotoxin level, and MPV/PLT ratio in the renal injury group were significantly higher than those in the non-renal injury group, while urine volume and serum calcium level were significantly lower than those in the non-renal injury group ($P < 0.05$). There were no statistically significant differences in gender, age, etiology of onset, BMI, and serum AMY level between the two groups ($P > 0.05$). The results are shown in **Table 1**.

2.3 Multivariate Logistic Regression Analysis of Early Renal Injury in SAP Patients

Taking the occurrence of early renal injury in SAP patients as the dependent variable, variables with statistically significant differences in univariate analysis (urine volume, APACHE II score, CRP, serum calcium, MDA, endotoxin, and MPV/PLT ratio, all of which were continuous variables and included in the analysis at their original values) were included in the multivariate logistic regression analysis. MDA (*OR* = 7.870, 95% *CI*: 1.669–37.108), endotoxin (*OR* = 1.260, 95% *CI*: 4.814–34.034), and MPV/PLT ratio (*OR* = 4.424, 95% *CI*: 1.408–13.897) were independent risk factors for early renal injury in SAP patients ($P < 0.05$). The results are shown in **Table 2**.

2.4 Predictive Efficacy of Serum MDA, Endotoxin, MPV/PLT Ratio for Early Renal Injury in SAP Patients

ROC curve analysis showed that the area under the curve (AUC) of endotoxin, MDA, and MPV/PLT ratio were 0.884, 0.874, and 0.875, respectively. All three indicators had good predictive efficacy for the occurrence of early renal injury in SAP patients. Their sensitivity and specificity are shown in **Table 3** & **Figure 1**.

Tab.1 Univariate analysis of early kidney injury in patients with SAP（$\bar{x}\pm s$）

Item	Renal injury group (*n*=37)	Non-renal injury group (*n*=53)	χ^2/t value	*P* value
Gender [*n* (%)]				
Male	22（59.46）	36（67.92）	0.681	0.409
Female	15（40.54）	17（32.08）		
Age (years)	51.27±11.04	50.96±11.24	0.130	0.897
Etiology [*n* (%)]			0.060	0.970
Hyperlipidemic pancreatitis	16（43.24）	23（43.40）		
Biliary pancreatitis	14（37.84）	19（35.85）		
Others	7（18.92）	11（20.75）		
BMI (kg/m²)	23.15±1.09	22.83±1.24	1.265	0.209
Urine output [mL/(kg·h)]	1.41±0.22	1.53±0.15	3.079	0.003
APACHE II score	18.91±4.83	16.55±4.06	2.509	0.014
CRP (mg/L)	169.85±50.26	140.03±41.67	3.067	0.003
AMY (U/L)	1308.68±269.46	1299.34±236.12	0.174	0.862
Ca^{2+} (mmol/L)	1.81±0.32	1.95±0.30	2.119	0.037
MDA (μmol/L)	7.59±1.33	5.39±1.41	7.453	＜0.001
Endotoxin (EU/mL)	1.13±0.16	0.82±0.20	7.835	＜0.001
MPV/PLT ratio	0.09±0.02	0.06±0.01	8.419	＜0.001

Tab.2 Multivariate logistic regression analysis of early kidney injury in patients with SAP

Item	*β*	*SE*	Wald χ^2	*OR* value	95%*CI*	*P* value
Urine output	-8.755	4.710	3.455	<0.001	0.000-1.610	0.063
APACHE II score	-0.297	0.181	2.684	0.743	0.521-1.060	0.101
CRP	0.016	0.013	1.701	1.016	0.992-1.042	0.192
Ca^{2+}	-7.901	4.016	3.869	＜0.001	0.000-0.972	0.049
MDA	2.063	0.791	6.799	7.870	1.669-37.108	0.009
Endotoxin	12.911	4.788	7.272	1.260	4.814-34.034	0.007
MPV/PLT ratio	224.487	91.084	6.074	3.114	1.058-9.171	0.014

Tab.3 The predictive efficacy of serum MDA, endotoxin, and MPV/PLT ratio for early kidney injury in patients with SAP

Item	AUC (95%CI)	*Z*/*P* value	Youden index	Cut-off value	Sensitivity (%)	Specificity (%)
MDA	0.874（0.788-0.935）	10.304/＜0.001	0.617	6.26 μ mol/L	91.89	69.81
Endotoxin	0.884（0.799-0.942）	10.131/＜0.001	0.689	1.01 EU/mL	78.38	90.57
MPV/PLT ratio	0.875（0.788-0.935）	9.128/＜0.001	0.708	0.07	78.38	92.45

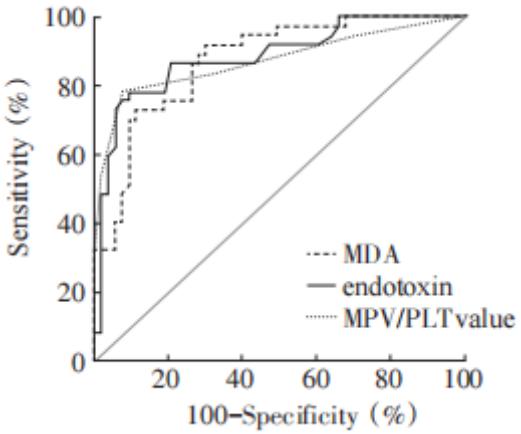

Fig.1 ROC curve of MDA, endotoxin, and MPV/PLT ratio for predicting early kidney injury in patients with SAP

3 Discussion

SAP is characterized by rapid disease progression, poor prognosis, and frequent complications. Without timely treatment, it may lead to multiple organ failure, with a mortality rate as high as 20%. More than 70% of patients develop renal injury during disease progression, which increases the risk of poor prognosis and death[9-10]. The pathophysiological mechanism of renal injury in SAP patients has not been fully elucidated, but relevant studies have shown that pancreatic enzymes are activated in pancreatic acinar cells, leading to autodigestion of the pancreas and surrounding tissues, triggering the release of toxic substances, insufficient circulating blood volume, and systemic inflammatory response, which further contribute to the occurrence of renal injury[11-12]. In this study, 41.11% of the 90 SAP patients developed early renal injury, indicating a high incidence of renal injury in SAP patients, which should receive clinical attention. To improve the prognosis and reduce the mortality of SAP patients, effective indicators should be explored to predict the occurrence of early renal injury.

MDA is a product of lipid peroxidation. Clinical detection of its serum level can reflect the level of free radicals in the body, thereby determining the degree of cell damage[4]. The body is extremely sensitive to endotoxin content. When the endotoxin level increases abnormally, microcirculation dysfunction occurs[5]. Endotoxin induces renal injury mainly through two pathways: inducing endothelin and mediating nuclear factor (NF)-κB. The mechanism of the former pathway is that endotoxin stimulates endothelin to significantly increase its level in the human body, which binds to its receptors and reduces renal blood flow, leading to renal injury[13]. For the latter

pathway, endotoxin binds to Toll-like receptors and activates NF-κB under the action of related accessory molecules, increasing the expression level of inflammatory factors in the body and subsequently causing renal injury[14]. Relevant studies have shown that the release of toxic substances from necrotic pancreatic tissue can lead to renal injury in SAP patients, and endotoxin is one of these relevant toxic substances[15]. MPV can reflect platelet activation, function, and morphological changes. Studies have shown that the MPV/PLT ratio has good efficacy in the condition assessment of patients with sepsis[16]. The results of univariate analysis showed that urine volume, APACHE II score, CRP, serum calcium, MDA, endotoxin, and MPV/PLT ratio were all influencing factors for early renal injury in SAP. The results of multivariate logistic regression analysis showed that MDA, endotoxin, and MPV/PLT ratio were independent influencing factors for early renal injury in SAP. The results of ROC curve analysis showed that the AUC values of endotoxin, MDA, and MPV/PLT ratio were 0.884, 0.874, and 0.875, respectively, with high sensitivity and specificity, indicating that all three indicators have high predictive efficacy for early renal injury in SAP.

In conclusion, MDA, endotoxin, and MPV/PLT ratio are influencing factors for the occurrence of early renal injury in SAP patients, and all three indicators have high predictive efficacy for early renal injury in SAP patients. However, this study is a single-center study with a limited number of cases, and further multi-center, large-sample studies are needed to validate the results of this study.

Conflict of interest None

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·急性胰腺炎专题·论著·

重症急性胰腺炎患者血丙二醛、内毒素、MPV/PLT比值与早期肾损伤的关系

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摘要：目的　探讨重症急性胰腺炎（SAP）患者血清丙二醛（MDA）、内毒素、外周血平均血小板体积（MPV）/血小板计数（PLT）比值与早期肾损伤发生的关系，为SAP患者肾损伤的预测提供参考。**方法**　选取2021年2月至2024年3月佳木斯市中心医院收治的90例SAP患者为研究对象，根据早期肾损伤发生情况将患者分为肾损伤组与非肾损伤组，比较两组血清MDA、内毒素和外周血MPV/PLT比值，采用多因素logistic回归分析SAP患者早期肾损伤的危险因素。绘制受试者工作特征（ROC）曲线分析3种指标对患者早期肾损伤的预测效能。**结果**　90例患者中有37例（41.11%）发生早期肾损伤（肾损伤组），其余53例（58.89%）患者未发生肾损伤（非肾损伤组）。肾损伤组急性生理学与慢性健康状况评分系统Ⅱ（APACHE Ⅱ）评分、CRP、MDA、内毒素水平、MPV/PLT比值均显著高于非肾损伤组（P<0.05），尿量、血钙水平显著低于非肾损伤组（P<0.05）。多因素logistic回归分析显示，高水平的MDA（OR=7.870，95%CI：1.669~37.108）、内毒素（OR=1.260，95%CI：4.814~34.034）、MPV/PLT比值（OR=4.424，95%CI：1.408~13.897）为SAP患者早期肾损伤的独立危险因素（P<0.05）；ROC曲线分析结果显示，内毒素预测早期急性肾损伤的ROC曲线下面积（AUC）为0.884，敏感度、特异度分别为78.38%、90.57%；MDA预测的AUC为0.874，敏感度、特异度分别为91.89%、69.81%；MPV/PLT比值预测的AUC为0.875，敏感度、特异度分别为78.38%、92.45%。**结论**　MDA、内毒素及MPV/PLT比值与SAP患者早期肾损伤发生存在密切关联，三者对SAP患者早期肾损伤发生具有较高的预测效能。

关键词：重症急性胰腺炎；肾损伤，早期；丙二醛；内毒素；平均血小板体积；血小板计数

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Relationship between blood malondialdehyde, endotoxin, MPV/PLT ratio and early kidney injury in patients with severe acute pancreatitis

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Abstract: Objective　To investigate the relationship between serum malondialdehyde (MDA), endotoxin, peripheral blood mean platelet volume (MPV) to platelet count (PLT) ratio and early acute kidney injury in patients with severe acute pancreatitis (SAP), and to provide a reference for predicting kidney injury in patients with SAP. **Methods**　A total of 90 patients with SAP admitted to Jiamusi Central Hospital from February 2021 to March 2024 were enrolled. According to the occurrence of early acute kidney injury, patients were divided into a kidney injury group and a non-kidney injury group. Serum MDA, endotoxin, and peripheral blood MPV/PLT ratio were compared between the two groups. Multivariate logistic regression was used to analyze independent risk factors for early acute kidney injury in SAP patients. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive efficacy of the three indicators. **Results**　Of the 90 patients, 37 (41.11%) developed early acute kidney injury (kidney injury group),

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and the remaining 53 (58.89%) did not (non-kidney injury group). Acute Physiology and Chronic Health Evaluation Ⅱ (APACHE Ⅱ) score, CRP, MDA, endotoxin, and MPV/PLT ratio were significantly higher, while urine volume and serum calcium (Ca^{2+}) were significantly lower in the kidney injury group compared to in the non-kidney injury group (P<0.05). Multivariate logistic regression analysis showed that high levels of MDA (OR=7.870, 95%CI: 1.669-37.108), endotoxin (OR=1.260, 95%CI: 4.814-34.034), and MPV/PLT ratio (OR=4.424, 95%CI: 1.408-13.897) were independent risk factors for early acute kidney injury in SAP patients (P<0.05). ROC curve analysis showed that the area under the ROC curve (AUC) of endotoxin was 0.884, with a sensitivity of 78.38% and a specificity of 90.57%; the AUC of MDA was 0.874, with a sensitivity of 91.89% and a specificity of 69.81%; the AUC of MPV/PLT ratio was 0.875, with a sensitivity of 78.38% and a specificity of 92.45%. **Conclusion** MDA, endotoxin, and MPV/PLT ratio are closely related to the occurrence of early kidney injury in patients with SAP. These three all have high predictive efficacy for early kidney injury in patients with SAP.

Keywords: Severe acute pancreatitis; Kidney injury, early; Malondialdehyde; Endotoxin; Mean platelet volume; Platelet count

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调查数据显示,在全球范围内急性胰腺炎(acute pancreatitis,AP)的发病率为(5~74)/10万,长时间住院、高昂的治疗费用给患者及家属带来沉重负担[1]。AP按照严重程度分为轻症、中度重症以及重症3种类型,多数AP患者为轻症,治疗7~14 d即可恢复,死亡率较低。而重症急性胰腺炎(severe acute pancreatitis,SAP)患者病情严重、预后差,死亡率为20%~30%[2]。肾损伤为SAP常见并发症,特别对于需要透析的患者来说,其死亡率可上升至75%。因此,为改善SAP患者预后,需对患者早期肾损伤发生情况进行评估与预测[3]。研究表明,丙二醛(malondialdehyde,MDA)水平与胰腺组织损害程度密切相关,MDA水平检测有助于对AP患者的预后及并发症发生情况进行判断[4]。SAP发生时,受到胰酶、肠麻痹等影响,5-羟色胺、组胺等物质释放,影响肠壁血管通透性,且内毒素水平增加,对全身器官功能造成损害[5]。有研究表明,血小板与脓毒症患者肾损伤的发生有关,平均血小板体积(mean platelet volume,MPV)/血小板计数(platelet,PLT)比值在脓毒症病情中的评估价值也已得到证实[6]。目前,关于以上3种指标与SAP患者早期肾损伤关系的研究报道较少,MDA、内毒素、MPV/PLT比值可否作为预测SAP患者早期肾损伤的指标仍有待研究。本文对此进行探讨,为改善SAP患者预后提供新思路。

1 资料与方法

1.1 一般资料 选取2021年2月至2024年3月佳木斯市中心医院收治的90例SAP患者作为研究对象。纳入标准:(1)符合《急性胰腺炎诊治指南(2021版)》[7]中SAP的诊断标准;(2)年满18周岁;(3)发病至入院时间≤48 h,且入院前未进行相关治疗。排除标准:(1)合并其他原因导致的肾间质或肾实质损伤疾病;(2)合并急慢性感染;(3)非AP患者,如慢性胰腺炎(或急性发作)、创伤性胰腺炎等。90例患者中男58例,女32例;年龄28~74(51.10±11.10)岁。该研究已获佳木斯市中心医院伦理委员会批准(批准文号:JZ20200619)。

1.2 方法

1.2.1 早期肾损伤发生情况判定与分组 根据相关指南对患者早期肾损伤发生情况进行判定[8]:(1)48 h内血肌酐(serum creatinine,Scr)升高超过26.5 μmol/L(或0.3 mg/dL);(2)已知或假定7 d内发生的Scr升高超过基线的1.5倍;(3)持续6 h尿量小于0.5 mL/(kg·h)。符合3项中的一项即可确诊。根据早期肾损伤发生情况将患者分为肾损伤组与非肾损伤组。

1.2.2 血MDA、内毒素、MPV/PLT比值检测 血清MDA、内毒素:抽取患者空腹静脉血,3 000 r/min离心10 min(离心半径为13.5 cm)后,取上清采用硫代巴比妥酸法测定MDA水平(MDA检测试剂盒购自武汉艾美捷科技);采用基质显色微量定量法测定内毒素水平(内毒素检测试剂盒购自武汉博士德生物科技)。操作过程严格按照试剂盒说明书进行。MPV/PLT比值:入院时抽取患者静脉血,乙二胺四乙酸二钾抗凝,采用BC-11全自动细胞分析仪(深圳迈瑞生物医疗)检测患者MPV、PLT,并计算MPV/PLT比值。

1.2.3 临床资料收集 查阅电子病历及医院数据库记录,收集并统计患者一般资料,包括性别、年龄、发病原因、身体质量指数(body mass index,BMI)、尿量、急性生理学与慢性健康状况评分系统Ⅱ(Acute Physiology and Chronic Health Evaluation Ⅱ,APACHE Ⅱ)评

分；收集实验室指标，包括C反应蛋白（C-reactive protein，CRP）、血淀粉酶（amylase，AMY）、脂肪酶（lipase，LPS）、血钙等。

1.3　统计学方法　采用SPSS 28.0统计软件分析数据。计量资料以$\bar{x}\pm s$描述，两组间比较采用独立样本t检验；计数资料以例（%）表示，组间比较采用χ^2检验。采用多因素logistic回归分析SAP早期肾损伤发生的影响因素。绘制受试者工作特征（receiver operating characteristic，ROC）曲线分析3种指标对SAP早期肾损伤发生的预测效能。检验水准α=0.05。

2　结　果

2.1　SAP患者早期肾损伤发生情况　90例SAP患者中共37例（41.11%）患者发生早期肾损伤（肾损伤组），其余53例（58.89%）未发生肾损伤（非肾损伤组）。

2.2　SAP患者早期肾损伤的单因素分析　肾损伤组APACHE Ⅱ评分、CRP、MDA、内毒素水平、MPV/PLT比值均显著高于非肾损伤组，尿量、血钙水平显著低于非肾损伤组（P<0.05）；两组患者性别、年龄、发病原因、BMI、血AMY水平比较，差异无统计学意义（P>0.05）。见表1。

2.3　SAP患者早期肾损伤的多因素logistic回归分析　以SAP患者早期肾损伤发生情况为因变量，将单因素分析差异有统计学意义的变量：尿量、APACHE Ⅱ评分、CRP、血钙、MDA、内毒素、MPV/PLT（均为连续变量，以原值代入）纳入多因素logistic回归分析。结果显示，MDA（OR=7.870，95%CI：1.669~37.108）、内毒素（OR=1.260，95%CI：4.814~34.034）、MPV/PLT比值（OR=4.424，95%CI：1.408~13.897）为SAP患者早期肾损伤的独立危险因素（P<0.05）。见表2。

2.4　血MDA、内毒素、MPV/PLT比值对SAP患者早期肾损伤发生的预测效能　ROC曲线分析结果显示，内毒素、MDA、MPV/PLT比值的曲线下面积（area under the curve，AUC）分别为0.884、0.874、0.875，3种指标对SAP患者早期肾损伤发生均有较好的预测效能，其敏感度、特异度见表3、图1。

表1　SAP患者早期肾损伤的单因素分析　（$\bar{x}\pm s$）

Tab.1　Univariate analysis of early kidney injury in patients with SAP　（$\bar{x}\pm s$）

项目	肾损伤组（n=37）	非肾损伤组（n=53）	χ^2/t值	P值
性别[例（%）]				
男	22（59.46）	36（67.92）	0.681	0.409
女	15（40.54）	17（32.08）		
年龄（岁）	51.28±11.04	50.97±11.25	0.130	0.897
发病原因[例（%）]				
高脂血症性	16（43.24）	23（43.40）		
胆源性	14（37.84）	19（35.85）	0.060	0.970
其他	7（18.92）	11（20.75）		
BMI（kg/m^2）	23.15±1.09	22.83±1.24	1.265	0.209
尿量[mL/（kg·h）]	1.41±0.22	1.53±0.15	3.079	0.003
APACHE Ⅱ评分	18.91±4.83	16.55±4.06	2.509	0.014
CRP（mg/L）	169.85±50.26	140.03±41.67	3.067	0.003
AMY（u/L）	1 308.69±269.46	1 299.34±236.12	0.174	0.862
血钙（mmol/L）	1.81±0.32	1.95±0.30	2.119	0.037
MDA（μmol/L）	7.59±1.33	5.39±1.41	7.453	<0.001
内毒素（EU/mL）	1.13±0.16	0.82±0.20	7.835	<0.001
MPV/PLT比值	0.09±0.02	0.06±0.01	8.419	<0.001

表2　SAP患者早期肾损伤的多因素logistic回归分析

Tab.2　Multivariate logistic regression analysis of early kidney injury in patients with SAP

项目	β	SE	Waldχ^2	OR值	95%CI	P值
尿量	−8.755	4.710	3.455	<0.001	0.000~1.610	0.063
APACHEⅡ评分	−0.297	0.181	2.684	0.743	0.521~1.060	0.101
CRP	0.016	0.013	1.701	1.016	0.992~1.042	0.192
血钙	−1.216	0.680	3.198	<0.001	0.890~12.792	0.074
MDA	2.063	0.791	6.799	7.870	1.669~37.108	0.009
内毒素	12.911	4.788	7.272	1.260	4.814~34.034	0.007
MPV/PLT比值	1.487	0.584	6.483	4.424	1.408~13.897	0.011

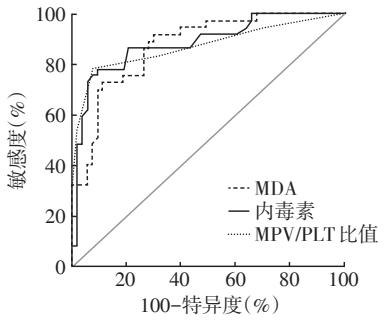

图1　MDA、内毒素、MPV/PLT比值预测SAP患者发生早期肾损伤的ROC曲线

Fig.1　ROC curve of MDA, endotoxin, and MPV/PLT ratio for predicting early kidney injury in patients with SAP

表3　MDA、内毒素、MPV/PLT比值对SAP患者早期肾损伤发生的预测效能

Tab.3　The predictive efficacy of MDA, endotoxin, and MPV/PLT ratio for early kidney injury in patients with SAP

项目	AUC（95%CI）	Z/P值	约登指数	截断值	敏感度（%）	特异度（%）
MDA	0.874（0.788~0.935）	10.304/<0.001	0.617	6.26 μmol/L	91.89	69.81
内毒素	0.884（0.799~0.942）	10.131/<0.001	0.689	1.01 EU/mL	78.38	90.57
MPV/PLT比值	0.875（0.788~0.935）	9.128/<0.001	0.708	0.07	78.38	92.45

3 讨 论

SAP具有疾病进展快、预后差、并发症多等特点，若未得到及时治疗将导致多器官衰竭，死亡率可高达20%，且超过70%的患者在疾病进展过程中并发肾损伤，增加患者预后不良与死亡风险[9-10]。SAP患者发生肾损伤的病理生理机制尚未完全明确，但相关研究表明，胰酶在胰腺腺泡细胞内被激活，造成胰腺及其周围组织自身消化，引发有毒物质释放、循环血量不足、全身炎症反应，进而导致肾损伤的发生[11-12]。本研究90例SAP患者有41.11%发生早期肾损伤，表明SAP患者发生肾损伤的概率较高，临床应引起重视。为改善SAP患者预后、降低死亡率，应寻求有效的指标对患者早期肾损伤发生情况进行预测。

脂质过氧化后可产生MDA，临床通过检测其血清水平能反映患者机体自由基水平，进而对细胞损伤程度进行判定[4]。机体对内毒素含量极为敏感，当内毒素水平异常升高时，机体微循环出现障碍[5]。内毒素引发肾损伤主要通过诱导内皮素以及介导核因子(nuclear factor，NF)-κB两种途径，前者主要作用机制为内毒素刺激内皮素导致其在人体中的水平显著上升，与其受体结合后导致肾脏血流量减少进而引发肾损伤[13]；后者则通过与Toll样受体结合，在相关辅助分子的作用下激活NF-κB，增加机体中炎症因子的表达水平进而导致肾损伤[14]。相关研究表明，坏死性胰腺有毒物质释放可导致SAP患者肾损伤，而内毒素则为相关有毒物质之一[15]。MPV可反映血小板活化情况、功能及形态变化，有研究表明，MPV/PLT比值在脓毒症患者病情评估中具有良好的效能[16]。单因素分析结果显示，尿量、APACHE Ⅱ、CRP、血钙、MDA、内毒素、MPV/PLT比值均是SAP发生早期肾损伤的影响因素。多因素logistic回归分析结果显示，MDA、内毒素、MPV/PLT比值是SAP发生早期肾损伤的独立影响因素。ROC曲线分析结果显示出内毒素、MDA、MPV/PLT比值的AUC值分别为0.884、0.874、0.875，且均具有较高的敏感度、特异度，表明3种指标对SAP早期肾损伤均具有较高的预测效能。

综上所述，MDA、内毒素及MPV/PLT比值为SAP患者早期肾损伤发生的影响因素，3种指标对SAP患者早期肾损伤发生均具有较高的预测效能。但本研究为单中心研究，病例数有限，需要多中心、大样本研究进一步验证本研究结果。

利益冲突 无

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