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ABOUT COVER

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ORIGINAL ARTICLE

Retrospective Study

Effects of acute kidney injury on acute pancreatitis patients' survival rate in intensive care unit: A retrospective study

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Abstract

BACKGROUND

Acute kidney injury (AKI) is one of the most common acute pancreatitis (AP)-associated complications that has a significant effect on AP, but the factors affecting the AP patients' survival rate remains unclear.

AIM

To assess the influences of AKI on the survival rate in AP patients.

METHODS

A total of 139 AP patients were included in this retrospective study. Patients were divided into AKI group (n = 72) and non-AKI group (n = 67) according to the occurrence of AKI. Data were collected from medical records of hospitalized patients. Then, these data were compared between the two groups and further

GD, and Gao Y performed manuscript review; All authors have read and approved the content of the manuscript; and Shi N and Sun GD contributed equally to this work.

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analysis was performed.

RESULTS

AKI is more likely to occur in male AP patients (P = 0.009). AP patients in AKI group exhibited a significantly higher acute physiologic assessment and chronic health evaluation II score, higher Sequential Organ Failure Assessment score, lower Glasgow Coma Scale score, and higher demand for mechanical ventilation, infusion of vasopressors, and renal replacement therapy than AP patients in non-AKI group (P < 0.01, P < 0.01, P = 0.01, P = 0.001, P < 0.01, P < 0.01, respectively). Significant differences were noted in dose of norepinephrine and adrenaline, duration of mechanical ventilation, maximum and mean values of intra-peritoneal pressure (IPP), maximum and mean values of procalcitonin, maximum and mean serum levels of creatinine, minimum platelet count, and length of hospitalization. Among AP patients with AKI, the survival rate of surgical intensive care unit and in-hospital were only 23% and 21% of the corresponding rates in AP patients without AKI, respectively. The factors that influenced the AP patients' survival rate included body mass index (BMI), mean values of IPP, minimum platelet count, and hospital day, of which mean values of IPP showed the greatest impact.

CONCLUSION

AP patients with AKI had a lower survival rate and worse relevant clinical outcomes than AP patients without AKI, which necessitates further attention to AP patients with AKI in surgical intensive care unit.

Key Words: Acute kidney injury; Acute pancreatitis; Surgical intensive care unit; Survival rate; Risk factors; Intra-peritoneal pressure

Core Tip: Acute pancreatitis (AP) has become a common gastrointestinal disorder in surgical intensive care unit, and excessive secretion and/or poor drainage of pancreatic juice are the essence of AP onset. Acute kidney injury (AKI) is a common complication of AP, which is ordinarily associated with adverse outcomes. Among AP patients with AKI, the survival rate of surgical intensive care unit and in-hospital were only 23% and 21% of the corresponding rates in AP patients without AKI, respectively. The factors that influenced the AP patients' survival rate included body mass index (BMI), mean values of intra-peritoneal pressure, minimum platelet count, and hospital day, of which mean values of intra-peritoneal pressure showed the greatest impact.

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INTRODUCTION

Acute pancreatitis (AP) is an excessive inflammatory response caused by digestion of the pancreas itself, which can further lead to local and distant organ damage, or even single or multiple organ failure. In the wake of continuous in-depth understanding of pathophysiological mechanism of AP and improvement of treatment measures, AP-related mortality rate is annually declining, whereas AP-associated hospitalization rises year-by-year worldwide[1,2]. In clinical practice, about 80% of the common etiologies are attributed to gallstones and alcohol consumption[3], however, the proportion of different etiologies significantly varies among different countries. In addition, hypertriglyceridemia is a high-risk factor for AP, and may lead to direct damage to pancreas and pancreatic exocrine function[4,5]. Thus, identification of

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etiologies is highly essential to manage better AP patients. AP can be categorized into mild acute pancreatitis (MAP), moderately severe acute pancreatitis (MSAP), and severe acute pancreatitis (SAP) according to the presence and duration of organ failure presented in the revised Atlanta classification (2013)[6]. The mortality rate is high among SAP patients, reaching 15%-30% or even higher[7], due to persistent organ failure. Therefore, earlier identification and appropriate use of intensive care support can be conducive to prevent further disease progression, thereby improving AP patients' prognosis[8].

Acute kidney injury (AKI) is one of the most common AP-associated complications, resulting from uncontrolled inflammatory response, release of pancreatic amylase, hypovolemia, insufficient renal perfusion, micro-circulatory disturbance, intra-abdominal hypertension, and reactive oxygen species[9]. At present, AKI is mainly diagnosed based on the criteria presented by the Kidney Disease Improving Global Outcomes (KIDGO) guidelines[10,11]. The incidence of AKI has gradually, while steadily, increased year-by-year worldwide[12]. AKI can deteriorate AP patient's medical status and is an independent risk factor for increased mortality and development of chronic kidney disease (CKD). When AKI and AP occur simultaneously, a worse clinical prognosis is expected[13,14], involving longer period of hospitalization and higher mortality rate. However, in clinical practice, there is no an effective therapeutic approach for AKI except for renal replacement therapy (RRT)[15]. AKI has imposed a huge medical burden in China as well as in the world. Therefore, development of early detection and prevention measures is highly significant to avoid adverse outcomes associated with AKI[16].

Although previous studies have confirmed that concurrent AKI is associated with a poor prognosis[17], there is no reliable research assessing the influences of AKI on Chinese AP patients' survival rate who were hospitalized at surgical intensive care unit (SICU). Hence, to address this scientific gap, the current retrospective study was conducted.

MATERIALS AND METHODS

Study design

This retrospective study enrolled 139 AP patients who were admitted to the SICU of The Second Affiliated Hospital of Harbin Medical University (Harbin, Heilongjiang Province, China) between January 2014 and March 2019. Baseline and clinical data were collected during hospitalization. The enrolled AP patients were divided into AKI group (n = 72) and non-AKI group (n = 67) according to occurrence of AKI. This study was approved by the Ethics Committee of The Second Affiliated Hospital of Harbin Medical University.

Study population

The inclusion criteria for this retrospective study were as follows: Patients who were admitted to the SICU of The Second Affiliated Hospital of Harbin Medical University; patients who were diagnosed with AP; patients' age > 18-years-old. The exclusion criteria were as follows: Pregnant or breastfeeding women; patients with CKD; patients with recurrent pancreatitis; patients who received renal transplantation; incomplete medical data.

Diagnosis of AP

A combination of medical history, symptoms and physical examinations, laboratory tests, and radiographic examinations (*e.g.*, abdominal ultrasound, contrast-enhanced computed tomography, or magnetic resonance imaging) was applied to confirm the diagnosis of AP. A limited number of diagnosed AP patients were eventually confirmed by undergoing exploratory laparotomy.

Diagnosis and classification of AKI

Diagnosis and classification of AKI were conducted based on the criteria presented by the KIDGO guidelines (2012)[18], in which serum creatinine criteria was defined as an increased absolute value in serum creatinine level of ≥ 0.3 mg/dL (≥ 26.4 μmol/L) or a percentage increase in serum creatinine level of ≥ 50% within 48 h. Baseline serum creatinine level was defined as the lowest serum creatinine level measured within 2 d prior to admission to SICU. If no serum creatinine level was measured, the serum creatinine level recorded in the first measurement within 2 d after admission to SICU

was considered as baseline serum creatinine level.

RRT

In the present study, all AP patients who needed to undergo RRT were managed with continuous veno-venous hemofiltration (CVVH), anti-coagulation with heparin, and fixed pre- and post-dilution strategies. Blood flow rates, amount of substitute fluid, and dehydration volume were individually adjusted according to each patient's medical status.

Measurement of serum procalcitonin level and intra-peritoneal pressure

Serum procalcitonin (PCT) level was intermittently measured after AP patients' admission to SICU through Mini-VIDAS (Hain Lifescience GmbH; Nehren, Germany). Intra-peritoneal pressure (IPP) was indirectly reflected *via* measuring intravesical pressure with Freund's catheter.

Data collection

Baseline and clinical data, including patients' age, gender, body mass index (BMI), Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, Glasgow Coma Scale (GCS) score, duration of mechanical ventilation (MV), abdominal puncture drainage, gallbladder puncture drainage, infusion of vasopressors, demand of RRT, IPP, body temperature, PCT, creatinine, platelet count, hospital day, and prognosis were collected from medical records of hospitalized patients. APACHE II score and SOFA score were calculated by the first 24 h clinical data after SICU admission.

Statistical analysis

Variables conforming to normal distribution were described as mean ± SD, while those abnormally distributed variables were expressed as median (range). Normality analysis was applied to continuous data. SPSS 22.0 software (IBM, Armonk, NY, United Sates) was used to carry out statistical analyses. Independent-samples *t*-test was used to perform inter-group comparison for normally distributed data, while Mann-Whitney *U* test was employed for inter-group comparison for abnormally distributed data. Classification data were expressed by the number of samples, and χ^2 test was adopted. The prognosis of AP patients who were admitted to SICU was analyzed by binary logistic regression analysis, while the remaining indicators were analyzed by the *t*-test or Mann-Whitney *U* test. P value < 0.05 was considered statistically significant.

RESULTS

Patients' baseline and clinical data

A total of 139 AP patients were enrolled in this retrospective study. The enrolled AP patients were divided into AKI group (n = 72) and non-AKI group (n = 67) according to occurrence of AKI. As shown in Table 1, AKI was more likely to occur in male AP patients (P = 0.009). AP patients with AKI exhibited a significantly higher APACHE II score, higher SOFA score, lower GCS score, and higher demand for MV, infusion of vasopressors, and RRT than non-AKI AP patients (P < 0.01, P < 0.01, P = 0.01, P = 0.001, P < 0.01, P < 0.01, respectively). No significant difference was observed in the remaining baseline and clinical data, including patients' age, BMI, proportion of abdominal puncture drainage, and gallbladder puncture drainage.

Vasopressor infusion

There were significant differences in types of vasopressors and proportion of norepinephrine, adrenaline, and vasopressor infusion between the two groups (Table 2).

Analysis of prognostic indicators

Significant differences were noted in dose of norepinephrine and adrenaline, duration of MV, maximum and mean values of IPP, maximum and mean values of PCT, maximum and mean serum levels of creatinine, minimum platelet count, prognosis of AP patients admitted to SICU, and hospital day between the two groups (Table 3). Among AP patients with AKI, the survival rates of SICU and in-hospital were only 23% and 21% of the corresponding rates in AP patients without AKI, respectively.

Table 1 Baseline and clinical data of patients

	AKI (*n* = 72)	Non-AKI (*n* = 67)	Z/χ^2	*P* value
Age	45.00 (17.50)	44.00 (21.00)	-0.07	0.94
Gender			6.745	0.009
Male	50	32		
Female	22	35		
BMI	24.45 (2.38)	23.80 (2.60)	-1.20	0.23
APACHE II Score	18.00 (7.75)	9.00 (7.00)	-7.47	< 0.01
SOFA Score	9.00 (6.00)	4.00 (4.00)	-6.50	< 0.01
GCS Score	15.00 (3.00)	15.00 (0.00)	-2.71	0.01
MV			10.94	0.001
Yes	46	24		
No	26	43		
Abdominal puncture drainage			0.19	0.66
Yes	36	36		
No	36	31		
Gallbladder puncture drainage			2.36	0.12
Yes	17	9		
No	55	58		
Vasopressor infusion			26.84	< 0.01
Yes	21	18		
No	51	49		
RRT				
Yes	44	20	13.651	< 0.01
No	28	47		

AKI: Acute kidney injury; APACHE II: Acute Physiology and Chronic Health Evaluation II; BMI: Body mass index; GCS: Glasgow Coma Scale; MV: Mechanical ventilation; RRT: Renal replacement therapy; SOFA: Sequential Organ Failure Assessment.

Analysis of the related factors influencing AP patients' survival rate

The factors influencing the AP patients' survival rate who were hospitalized at SICU included BMI, mean values of IPP, minimum platelet count, and hospital day. Among these factors, mean values of IPP showed the greatest effect (Table 4). The values of area under the receiver operating characteristic (ROC) curve for the four factors related to patients with or without AKI were calculated to predict the AP patients' survival rate, and were 0.896 and 0.891, respectively (Figure 1 and Table 5; $P > 0.5$). However, there was no significant different in values of the area under the two ROC curves. The sensitivity and specificity of the two ROC curves were approximately the same [sensitivity (80.6%) *vs* specificity (88.0%)].

Risk thresholds of the related factors

Risk thresholds of BMI, mean values of IPP, minimum platelet count, and hospital day were ≥ 24, ≥ 23, ≤ 77, and ≤ 4, respectively, which indicated that BMI ≥ 24, mean values of IPP ≥ 23, minimum platelet count ≤ 77, and hospital day ≤ 4 were risk factors for AP patients' survival rate who were hospitalized at SICU.

DISCUSSION

Excessive secretion and/or poor drainage of pancreatic juice are the essence of AP onset. With the increasing incidence of gallstones and alcohol abuse, AP had become a

Table 2 Vasopressor infusion

	AKI, *n* = 72	Non-AKI, *n* = 67	χ^2	*P* value
Types of vasopressors			27.44	< 0.01
No	21	49		
1	34	14		
≥ 2	17	4		
Norepinephrine infusion			35.35	< 0.01
Yes	49	17		
No	23	50		
Adrenaline infusion			12.75	< 0.01
Yes	15	1		
No	57	66		
Vasopressor infusion			26.84	< 0.01
Yes	51	18		
No	21	49		

AKI: Acute kidney injury.

common gastrointestinal disorder. The majority of cases with AP are MAP characterized by no new onset of organ dysfunction, whereas SAP not only leads to new onset of organ dysfunction, but also lasts for more than 48 h[6]. With aggravation of the condition from MAP to SAP, the length of stay at SICU and mortality rate significantly increased. Hence, SAP patients should be managed in SICU for multiple organ support therapy and surgical interventions to avoid further disease progression [19]. When AP happens, hemodynamic status should be assessed immediately to avoid hypovolemia or volume overload caused by excessive fluid resuscitation[20], which might cause detrimental influences[21]. Routine use of prophylactic antibiotics in SAP or necrotizing pancreatitis was not clinically recommended in the guidelines [22], because of no mortality benefit or reduction in the incidence of infected necrosis [23]. The ability to penetrate pancreatic necrotic tissue is of great significance in the selection of antibiotics. Less than 50% of necrotizing pancreatitis patients need surgical interventions, in which step-up approach and minimally invasive strategies were advocated[24-27], involving endoscopic nasobiliary drainage, percutaneous transhepatic gallbladder drainage, percutaneous transhepatic biliary drainage, endoscopic retrograde cholangiopancreatography, endoscopic transgastric/transduodenal drainage, and video-assisted retroperitoneal debridement.

During AP, kidney is the most vulnerable organ and is typically sacrificed to protect other important organs, such as heart, lung, brain, and liver. As a consequence, AKI is a common complication of AP, which is ordinarily associated with adverse outcomes, including risk of subsequent CKD, end-stage renal disease, RRT dependence, in-hospital and post-discharge mortality, and even healthcare cost-containment concerns [28-30]. It was generally believed that the incidence of AKI was about 20% in critically ill adult patients[31]. More than 50% of SAP patients would develop into AKI according to previous literature[3,17,32]. Different organs interact with each other in the whole body, and the deteriorated kidney function can inevitably cause or aggravate damage to other organs without early intervention. Diuretics had been demonstrated to be an independent risk factor for AKI[33], and thus, were no longer recommended for routine use in clinical practice. When RRT is required, the mortality rate may even exceed 75%[34]. Compared with developed countries, AKI is typically substantial underdiagnoses and undertreatment in developing countries[35], especially in African countries, which may be partially explained as seriously inadequate repeated serum creatinine assay[36].

At present, about 20% of AKI patients require to undergo RRT[37], and this rate continues to increase worldwide. Some eligible patients for RRT may decline to undergo this intervention because of resource constraints, high costs of therapy, or severe comorbidities[38], which significantly increase mortality rate compared with those cases who received it[39]. RRT involves different treatment modalities, such as

Table 3 Analysis of prognostic indicators

	AKI, *n* = 72	Non-AKI, *n* = 67	*Z/t/Wald*	*P* value	OR
Prognosis of SICU			9.54	0.002	0.23
cure	48	60			
other	24	7			
Prognosis of in-hospital			11.33	0.001	0.21
cure	46	60			
other	26	7			
Duration of MV	34.00 (87.75)	0.00 (18.00)	-3.92	< 0.01	
Maximum values of IPP	24.50 (10.00)	18.00 (10.00)	-5.39	< 0.01	
Mean values of IPP	21.40 (6.82)	15.29 (4.73)	6.175	< 0.01	
Maximum values of body temperature	37.80 (1.20)	37.50 (1.00)	-2.00	0.05	
Mean values of body temperature	37.00 (0.50)	37.00 (0.30)	-0.59	0.56	
Maximum values of PCT	16.28 (21.12)	2.87 (9.28)	-5.96	< 0.01	
Mean values of PCT	8.52 (11.52)	1.58 (4.20)	-6.42	< 0.01	
Maximum serum levels of creatinine	284.35 (215.73)	87.60 (47.80)	-9.94	< 0.01	
Mean serum levels of creatinine	197.45 (172.10)	65.60 (29.60)	-9.48	< 0.01	
Minimum platelet count	93.00 (87.75)	137.00 (73.00)	-3.18	< 0.01	
Mean platelet count	174.40 (112.15)	198.00 (103.60)	-1.64	0.10	
Hospital day	9.00 (12.75)	8.00 (11.00)	-0.07	0.94	
Dose of norepinephrine	16.00 (52.00)	0.00 (4.00)	-5.11	< 0.01	
Dose of adrenaline	0.00 (0.00)	0.00 (0.00)	-3.58	< 0.01	

AKI: Acute kidney injury; MV: Mechanical ventilation; IPP: Intra-peritoneal pressure; OR: Odds ratio; PCT: Procalcitonin; SICU: Surgical intensive care unit.

Table 4 Analysis of the related factors influencing acute pancreatitis patients' survival rate

	B	SE	Wald	*df*	*P* value	Exp (B)
BMI	1.4904	0.6467	5.3105	1.0000	0.0212	4.4387
Mean values of IPP	2.6477	0.6217	18.1355	1.0000	0.0000	14.1211
Minimum platelet count	-1.2285	0.6125	4.0237	1.0000	0.0449	0.2927
Hospital day	-1.8571	0.5965	9.6913	1.0000	0.0019	0.1561
Constant	-0.9863	0.8689	1.2883	1.0000	0.2564	0.3730

BMI: Body mass index; IPP: Intra-peritoneal pressure; SE: Standard error.

hemodialysis, hemofiltration, hemodiafiltration, and peritoneal dialysis. It has been suggested that continuous RRT has several advantages over intermittent RRT, including better hemodynamic stability (blood pressure control and blood circulation), improved survival, and greater likelihood of renal recovery[38,40,41]. Thus, CVVH had occupied the mainstream of RRT, particularly for AP patients who were hospitalized at SICU, because of its outstanding effectiveness and safety. Although it has been suggested that early application of RRT in patients with severe sepsis, irrespective of the presence of renal failure, might be beneficial, CVVH did not limit further organ damage and even prolonged the need for organ support. RRT is a non-selective method, which can simultaneously remove detrimental and beneficial substances. In clinical practice, in spite of great advances in RRT development, there is still a lack of uniform standards for RRT-associated strategies, such as optimal timing

Table 5 Area under the receiver operating characteristic curve

Variables	Area	SE	Asymptotic, *P* value	Asymptotic 95%CI	
				Lower bound	Upper bound
With AKI	0.896	0.033	0	0.831	0.961
Without AKI	0.891	0.037	0	0.819	0.963

AKI: Acute kidney injury; CI: Confidence interval; SE: Standard error.

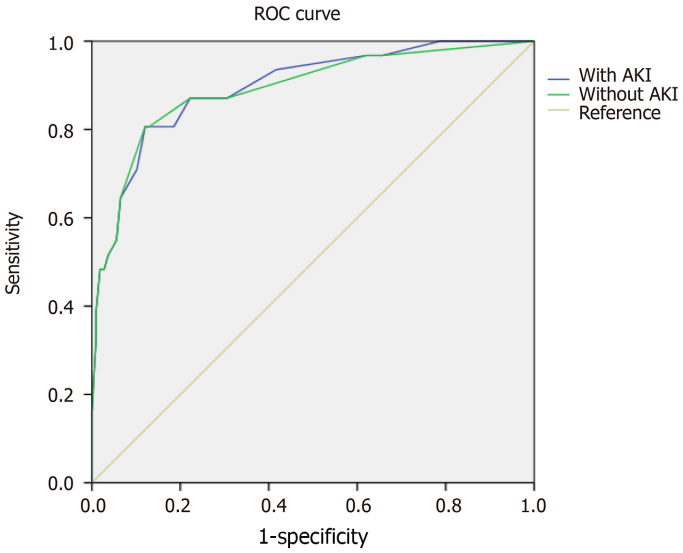

Figure 1 The receiver operating characteristic curve of these four factors related to acute pancreatitis patients without or with acute kidney injury. AKI: Acute kidney injury; ROC: Receiver operating characteristic.

for initiation of RRT, anti-coagulation, and optimal dosage[42,43].

Among several scoring systems, APACHE II score and SOFA score are commonly used to reflect timely and accurately illness severity and predict prognosis of AP patients[44]. It is well known that GCS score is a simple and valuable tool for indication of nervous system function and prediction of short- and long-term mortality [45], in which its discriminative power is similar to other more complex scoring systems[46]. Therefore, these three scoring systems were selected to assess the severity of AP in the present research. A number of scholars pointed out that demand for MV, infusion of vasopressors, and RRT could be risk factors for increased mortality in AP patients[47]. PCT level may contribute to earlier and better stratification of septic patients who are at risk of death and admitted to SICU[48]. To our knowledge, the increased IPP and decreased platelet count are closely associated with the severity and prognosis of AP in clinical practice[49]. Hence, the above-mentioned indicators were employed in the current study.

The present retrospective study provided a comprehensive description about the influences of AKI on AP patients' survival rate who were hospitalized at SICU in accordance with the criteria presented by the KIDGO guidelines. Our findings revealed that AP patients with AKI had more severe degree of illness than AP patients without AKI, as evidenced by higher APACHE II score, higher SOFA score, and lower GCS score, and the survival rates of SICU and in-hospital were only 23% and 21% of the corresponding rates in AP patients without AKI, respectively, which were roughly consistent with previously reported rates[10,31]. These gaps can be partially explained by the increased emphasis placed on AP and improvement of diagnostic methods and standardized therapeutic bundles. For AP patients with AKI, other influences were found to be associated with demand for MV, infusion of vasopressors and RRT, dosages of norepinephrine and adrenaline, duration of MV, maximum and mean values of IPP, maximum and mean values of PCT, maximum and mean serum levels of creatinine, and minimum platelet count. It was revealed that AKI negatively and seriously affected AP patients who were hospitalized at SICU.

The factors that influenced AP patients' survival rate who were hospitalized at SICU included BMI, mean values of IPP, minimum platelet count, and hospital day. With every unit change in BMI, mean values of IPP, minimum platelet count, and hospital day, the AP patients' survival rate was 4.4387, 14.1211, 0.1561, and 0.3730 of the original rates, respectively. Therefore, mean values of IPP had the greatest influence on the AP patients' survival rate who were hospitalized at SICU. Risk thresholds of BMI, mean values of IPP, minimum platelet count, and hospital day were ≥ 24, ≥ 23, ≤ 77, and ≤ 4, respectively, which indicated that BMI ≥ 24, mean values of IPP ≥ 23, minimum platelet count ≤ 77, and hospital day ≤ 4 were risk factors for the AP patients' survival rate who were hospitalized at SICU.

The present study contains a number of limitations. First, although significant differences were detected, this was only a small sample-size, single-center, retrospective study, which might reduce the reliability of our conclusion and its application to AP patients in clinical practice. Second, clinical data were obtained only on the basis of the medical records during hospitalization, which might lead to research bias. Last but not least, the etiology of AP had not been further differentiated. It is noteworthy that different etiologies may induce different clinical manifestations and prognosis, necessitating conducting further studies in the future.

CONCLUSION

In conclusion, this study attempted to clarify the influence of AKI on AP patients' survival rate who were hospitalized at SICU. Results showed that AP patients with AKI exhibited lower survival rate and worse relevant clinical outcomes than AP patients without AKI. Besides, BMI, mean values of IPP, minimum platelet count, and hospital day may play significant roles in predicting the AP patients' survival rate who were hospitalized at SICU. Our findings suggest that prevention of AKI is clinically important.

ARTICLE HIGHLIGHTS

Research background

Acute kidney injury (AKI) is common in acute pancreatitis (AP) patients, but the risk factors are not clear.

Research motivation

This study tried to explore the associated risk factors of AKI in AP patients.

Research objectives

This study aimed to assess the influences of AKI on the survival rate in AP patients.

Research methods

Patients were divided into two groups based on AKI status, and comparisons between the groups were calculated for diverse variables.

Research results

AKI is more likely to occur in male AP patients.

Research conclusions

AP patients with AKI exhibited lower survival rate and worse relevant clinical outcomes than AP patients without AKI in SICU.

Research perspectives

This study provided clinical evidence for prevention of AKI in AP patients.

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