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ORIGINAL ARTICLE

Retrospective Study

# Serum magnesium level as a predictor of acute kidney injury in patients with acute pancreatitis

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## Abstract

***BACKGROUND***

Decreased serum magnesium ($Mg^{2+}$) is commonly seen in critically ill patients. Hypomagnesemia is significantly more frequent in patients with severe acute pancreatitis. Acute kidney injury (AKI) in patients with acute pancreatitis (AP) is associated with an extremely high mortality. The association underlying serum $Mg^{2+}$ and AKI in AP has not been elucidated.

***AIM***

To explore the association between serum $Mg^{2+}$ on admission and AKI in patients with AP.

***METHODS***

A retrospective observational study was conducted in a cohort of patients ($n$ = 233) with AP without any renal injury before admission to our center from August 2015 to February 2019. Demographic characteristics on admission, severity score, laboratory values and in-hospital mortality were compared between patients with and without AKI.

***RESULTS***

A total of 233 patients were included for analysis, including 85 with AKI. Compared to patients without AKI, serum $Mg^{2+}$ level was significantly lower in

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patients with AKI at admission [OR = 6.070, 95%CI: 3.374-10.921, $P < 0.001$]. Multivariate logistic analysis showed that lower serum $Mg^{2+}$ was an independent risk factor for AKI [OR = 8.47, 95%CI: 3.02-23.72, $P < 0.001$].

*CONCLUSION*

Our analysis indicates that serum $Mg^{2+}$ level at admission is independently associated with the development of AKI in patients with AP and may be a potential prognostic factor.

**Key Words:** Acute pancreatitis; Acute kidney injury; Magnesium ($Mg^{2+}$); Kidney; Predictor of acute kidney injury



**Core Tip:** Acute kidney injury (AKI) is a serious complication of acute pancreatitis (AP) and is often difficult to predict at an early stage. However, our clinical analysis found that serum $Mg^{2+}$ on admission is a good predictor of the occurrence of AKI in AP patients. Therefore, this may provide a new method for the early prediction of AKI after AP.

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## INTRODUCTION

Acute pancreatitis (AP) is an autodigestive disease triggered by acinar cells, and about 20% of the patients progress to fatal severe acute pancreatitis (SAP)[1-4]. Acinar cell injury accompanied by intracellular electrolyte imbalance, further aggravating cell damage and even death is the recognized pathogenesis of AP[5,6]. In particular, organelle damage caused by intracellular calcium ($Ca^{2+}$) influx into mitochondria is the main risk factor for AP[7]. An *in vitro* AP model showed that $Ca^{2+}$ channel antagonists could effectively reduce $Ca^{2+}$ influx and increase mitochondrial membrane potential, thereby protecting acinar cells[8,9]. As an important cation in cells, magnesium ($Mg^{2+}$) is a coenzyme involved in a variety of enzymatic reactions and plays a role in maintaining membrane potential and physiological function[10-12]. In addition, $Mg^{2+}$ plays a protective role in AP acinar cells by antagonizing $Ca^{2+}$ signals[13]. On the contrary, abnormal regulation of $Mg^{2+}$ acts as a pivotal trigger in the pathogenesis of AP[14].

Acute kidney injury (AKI) is a common complication of SAP with poor prognosis, especially when patients require renal replacement therapy, the mortality rate is > 75% [15,16]. SAP-associated AKI is related to systemic inflammatory response syndrome (SIRS), hypoxemia, renal microcirculation injury after trypsin release, renal perfusion pressure reduction caused by intraperitoneal high pressure or low blood volume, endotoxins and reactive oxides[17]. Therefore, early prediction of AKI in AP is very important to improve the course and prognosis of the disease.

AKI is often accompanied by complex electrolyte disturbances[18]. However, the relationship between $Mg^{2+}$ and the occurrence of AP-associated AKI in AP pathophysiology has not been fully elucidated. Based on the beneficial role of $Mg^{2+}$ in acinar cells of AP, we therefore sought to assess the value of serum $Mg^{2+}$ on admission in correlation with the incidence of AKI in AP.

## MATERIALS AND METHODS

### Patient selection

We conducted a retrospective study of patients with AP admitted to the Center of Severe Acute Pancreatitis of Jinling Hospital between August 2015 and February 2019. All the data were extracted from an electronic database, which stored prospectively collected clinical data of all AP patients admitted to our center. We obtained the approval of the Acute Pancreatitis Database Management Committee (2018 JLAPDMC-009), and all the analyses were performed in accordance with the committee's regulations. Informed consent involving data storage and academic use of data was obtained from each patient during their hospitalization. Patients who met the following criteria were included: (1) Diagnosis of AP (ICD-10, K85) under the 2012 revision of the Atlanta classification; and (2) Admission to our department within one week after the disease onset. The exclusion criteria included any of the following: (1) The time from abdominal pain onset to hospital admission ≥ 7 d; (2) Age younger than 18 years; and (3) Suspected chronic pancreatitis, cancer, and chronic liver diseases such as cirrhosis or viral hepatitis, chronic kidney diseases such as nephritis, or renal failure. AKI (ICD-10: N17) was diagnosed according to the kidney disease: Improving Global Outcomes criteria based on serum/plasma creatinine and urine output. Patients meeting the diagnostic criteria for AP during hospitalization were included in the AKI group. The diagnosis of low serum $Mg^{2+}$ was made by laboratory measurements on the day of admission.

### Data collection

Demographic and baseline characteristics on admission included the following: Age, gender, body mass index (BMI), disease severity score (APACHE II), sequential organ failure assessment (SOFA), computed tomography severity index (CTSI), the Atlanta classification, comorbidities (diabetes, hypertension, hyperlipidemia), white blood cells, lymphocytes%, interleukin-6 (IL-6), procalcitonin (PCT), platelets, blood urea nitrogen (BUN), creatinine, $HCO^{3-}$, and $Cl^{-}$.

### Statistical analysis

Statistical analysis was performed using R software, version 3.6.2 (R Foundation for Statistical Computing). The Kolmogorov-Smirnov test was used to test the normality. Continuous variables are presented as means and standard derivations or medians and interquartile ranges. Categorical variables are presented as number (frequency). The Mann-Whitney *U* test was used to evaluate the differences in baseline characteristics between the two groups. The Chi-square test or Fisher's exact test was used to analyze categorical variables for group comparisons. All variables with statistically significant prognostic value in univariate analysis were selected for further multivariate analysis. Odds ratio (OR) and 95% confidence intervals (CIs) are presented. Receiver operating characteristic curves were constructed to evaluate the sensitivity and specificity of serum $Mg^{2+}$ in predicting AKI. $P$ value < 0.05 was considered statistically significant.

## RESULTS

### Baseline characteristics

A total of 233 patients were included for analysis. The participant selection process is shown in Figure 1. The serum $Mg^{2+}$ level of 0.755 mg/dL was identified as an effective cut-off point for in-hospital AKI occurrence (area under curve = 0.704; 95%CI: 0.640-0.775, $P$ < 0.001), with a sensitivity of 77.7%, and specificity of 63.5% (Figure 2). Baseline characteristics of these patients are shown in Table 1. Compared with the non-low serum $Mg^{2+}$ group, the group with low serum $Mg^{2+}$ had higher BMI ($P$ = 0.028) and APACHE II ($P$ = 0.002). With regard to laboratory parameters, patients in the low serum $Mg^{2+}$ group had higher admission IL-6 ($P$ < 0.001), PCT ($P$ < 0.001), and lower $HCO^{3-}$ ($P$ < 0.001).

### Clinical outcomes

The in-hospital clinical outcomes are shown in Table 2, divided according to admission serum $Mg^{2+}$ level. The serum $Mg^{2+}$ < 0.755 mg/dL group consisted of 87 patients (54 cases in the AKI group and 33 cases in the non-AKI group), and the serum $Mg^{2+}$ ≥ 0.755 mg/dL group consisted of 146 patients (31 cases in the AKI group and

**Table 1 Baseline characteristics**

| | $Mg^{2+}$ (mg/dL) | | | | | |
|---|---|---|---|---|---|---|
| | < 0.755 mg/dL, *n* = 87 | ≥ 0.755 mg/dL, *n* = 146 | *P* value | AKI, *n* = 85 | Non-AKI, *n* = 148 | *P* value |
| Age, yr | 39 (32, 52) | 44 (34, 58) | 0.063 | 38 (30, 50) | 44.5 (35.5, 54.5) | 0.011 |
| Gender, male, *n* (%) | 59 (67.8) | 98 (67.1) | 0.913 | 59 (69.4) | 98 (66.2) | 0.913 |
| BMI | 27.1 (24.7, 30.1) | 25.6 (23.9, 28.1) | 0.028 | 27.6 (24.8, 30.7) | 25.4 (23.4, 27.7) | < 0.001 |
| APACHE II | 9 (7, 12) | 7 (5, 9) | 0.002 | 11 (8, 14) | 7 (4, 9) | < 0.001 |
| SOFA | 3 (3, 4) | 3 (2, 4) | 0.075 | 4 (3, 5) | 3 (2, 4) | < 0.001 |
| CTSI | 6 (3, 6) | 5 (3, 6) | 0.122 | 6 (6, 6) | 4 (2, 6) | < 0.001 |
| Severity classification, *n* (%) | | | 0.064 | | | < 0.001 |
| MAP | 21 (24.1) | 50 (34.2) | | 7 (8.2) | 64 (43.2) | |
| MSAP | 47 (54.0) | 79 (54.1) | | 45 (53.0) | 81 (54.7) | |
| SAP | 19 (21.8) | 17 (11.6) | | 33 (38.8) | 3 (2.1) | |
| Comorbidities | | | | | | |
| Diabetes | 23 (26.4) | 24 (16.4) | 0.066 | 20 (23.5) | 27 (18.2) | 0.066 |
| Hypertension | 22 (25.3) | 36 (24.7) | 0.914 | 22 (25.9) | 36 (24.3) | 0.914 |
| Hyperlipidemia | 25 (28.7) | 36 (24.7) | 0.493 | 21 (24.7) | 40 (27.0) | 0.493 |
| Laboratory data | | | | | | |
| WBC | 13.4 (10.6, 16.6) | 12.8 (10.1, 15.7) | 0.336 | 12.9 (10.9, 16.6) | 12.9 (10.3, 16.1) | 0.685 |
| Ly% | 8.1 (5.1, 11.2) | 6.7 (4.7, 10.6) | 0.297 | 6.9 (4.9, 10.5) | 7.2 (5, 11.2) | 0.769 |
| IL-6 | 199.6 (104.8, 366.4) | 115.4 (45.4, 201.5) | < 0.001 | 222.8 (130.4, 370) | 104.8 (45.4, 178.4) | < 0.001 |
| PCT | 1.2 (0.4, 3.3) | 0.4 (0.1, 1.6) | < 0.001 | 2.1 (1.1, 7.7) | 0.3 (0.1, 0.8) | < 0.001 |
| Platelets | 193 (142, 238) | 174 (134, 224) | 0.215 | 199 (132, 236) | 176.5 (142, 218) | 0.248 |
| BUN | 5.4 (3.7, 6.3) | 5.1 (4, 6.9) | 0.576 | 6 (4, 8.3) | 4.8 (3.8, 5.9) | < 0.001 |
| Creatinine | 61 (49, 8) | 63 (53, 8) | 0.924 | 50 (41, 57.3) | 51 (46, 59) | 0.184 |
| $HCO^{3-}$ | 18.9 (15.1, 23.5) | 22 (18.7, 24.2) | < 0.001 | 17.8 (13.7, 21.3) | 22.6 (19.8, 24.7) | < 0.001 |
| $Cl^-$ | 103 (99, 105) | 102 (100, 105) | 0.825 | 103.7 (101, 107) | 102 (99, 104) | < 0.001 |
| $Mg^{2-}$ | | | | 0.7 (0.6, 0.7) | 0.885 (0.8, 0.9) | < 0.001 |

$Mg^{2+}$: Magnesium; BMI: Body mass index; AKI: Acute kidney injury; SOFA: Sequential organ failure assessment; CTSI: CT severity index; MAP: Mild acute pancreatitis; MSAP: Mild severe acute pancreatitis; SAP: Severe acute pancreatitis; WBC: White blood cells; Ly%: Lymphocytes%; IL-6: Interleukin-6; PCT: Procalcitonin; BUN: Blood urea nitrogen.

115 cases in the non-AKI group). Lower serum $Mg^{2+}$ was correlated with the occurrence of AKI (62.1% *vs* 21.2%, $P < 0.001$). The length of intensive care unit (ICU) stay ($P < 0.001$) and hospital stay ($P < 0.001$) of patients with low serum $Mg^{2+}$ level was longer.

### *Association of admission serum $Mg^{2+}$ level with AKI occurrence*

As shown in Figure 3, compared with the non-AKI group, the AKI group had significantly lower serum $Mg^{2+}$ level ($P < 0.001$). Following univariate logistic regression analysis, BMI (OR = 1.155, $P < 0.001$), APACHE II (OR=1.385, $P < 0.001$), SOFA (OR = 1.589, $P < 0.001$), CTSI (OR = 1.479, $P < 0.001$), severity classification ($P < 0.001$), IL-6 (OR = 1.006, $P < 0.001$), PCT (OR = 1.350, $P < 0.001$), BUN (OR = 1.368, $P < 0.001$), creatinine (OR = 1.051, $P < 0.001$), HCO3- (OR = 0.843, $P < 0.001$), and $Cl^-$ (OR = 1.100, $P = 0.003$) were important indicators of AKI in AP patients (Table 3). Multivariate logistic analysis showed that lower serum $Mg^{2+}$ (OR = 5.525, $P < 0.001$) was an independent risk factor for AKI (Table 3).

**Table 2 Influence of low serum magnesium on clinical course**

| | $Mg^{2+}$ (mg/dL) | | *P* value |
|---|---|---|---|
| | < 0.755 mg/dL, *n* = 87 | ≥ 0.755 mg/dL, *n* = 146 | |
| Primary outcome, *n* (%) | | | |
| AKI | 54 (62.1) | 31 (21.2) | < 0.001 |
| Clinical course, days median | | | |
| ICU days | 3 (2, 6) | 2 (1, 4) | < 0.001 |
| Hospital days | 6 (4, 10) | 4 (3, 7) | < 0.001 |
| Severe outcome, *n* (%) | | | |
| ICU mortality | 1 (1.15) | 3 (2.05) | 0.999 |
| 30 d mortality | 1 (1.15) | 3 (2.05) | 0.999 |

$Mg^{2+}$: Magnesium; AKI: Acute kidney injury; ICU: Intensive care unit.

## DISCUSSION

In this research, we examined the involvement of serum $Mg^{2+}$ and AKI in AP patients. Our results suggest that serum $Mg^{2+}$ levels detected at admission were significantly lower in AP patients with AKI than in non-AKI patients. Moreover, the low serum $Mg^{2+}$ group had a longer ICU and hospital stay than the non-low serum $Mg^{2+}$ group. Furthermore, serum $Mg^{2+}$ was revealed as an independent risk factor for the development of AKI. Therefore, serum $Mg^{2+}$ is an effective predictor of AKI after AP.

$Mg^{2+}$ is a well-known divalent cation abundant in human cells and is concentrated in mitochondria. It mainly plays the role of a cofactor in enzyme reactions and a second messenger in cellular signaling pathways[19-21]. In the physiological state of acinar cells, $Mg^{2+}$ plays an antagonistic role in the influx of $Ca^{2+}$ channel ions and inhibits the secretion of intracellular enzymes[9,22]. In the acinar cell model of AP, the addition of $Mg^{2+}$ mitigates the effects of AP by inhibiting $Ca^{2+}$ influx into the mitochondria, thereby reducing the secretion of digestive enzymes and promoting ATP generation[14]. In conclusion, $Mg^{2+}$ plays an important regulatory role in the pathophysiological state of acinar cells. Mitochondria are the key organelles for the energy supply in acinar cells. It is obvious that $Mg^{2+}$ plays an important role in maintaining mitochondrial homeostasis and ATP generation from this perspective.

The persistent influx of $Ca^{2+}$ into the mitochondria of acinar cells in AP leads to increased oxygen radicals further triggering cell necrosis, which in turn induces SIRS [23-25]. This imbalance leads to further inflammatory response and oxygen radical production, resulting in multiple organ dysfunction including AKI[26]. Therefore, it is important to prevent the continuous influx of $Ca^{2+}$ into mitochondria to reduce acinar cell necrosis and inhibit trypsin activation in AP. This is consistent with research in animal experiments[8,9]. In a murine model, the risk of triggering AP was decreased by inhibiting $Ca^{2+}$ release-activated $Ca^{2+}$ channels[27]. To the best of our knowledge, hypomagnesemia is commonly seen in severely ill patients including those with SAP [28]. In our SAP patients, there was a significant negative correlation between the incidence of AKI and adjusted serum $Mg^{2+}$ on admission.

AKI as a complication, which is associated with increased mortality, occurs in approximately 15%-70% of SAP patients[18,29]. Therefore, early prediction of AKI in hospitalized patients with AP is imperative, especially for screening graded treatment strategies[30]. Currently, there are various clinical methods to predict the occurrence of AKI in patients with AP. On the whole, current studies on biomarkers for AP-associated AKI are insufficient, and the number of patients included in the analysis was limited. In addition, from the latest clinical evidence on the markers of AKI in AP, PCT showed relatively better clinical predictive value than neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C[31-33]. At present, serum or urine NGAL and serum cystatin C are recognized as the best laboratory indicators for predicting AKI in AP with good diagnostic accuracy. However, these single-center clinical data are not convincing enough. Large multicenter clinical studies on biomarkers are of great clinical value in identifying AKI in AP.

**Table 3 Univariate predictors and multivariate model for acute kidney injury occurrence**

| Univariate analysis | OR | 95%CI | *P* value | Multivariate model | OR | 95%CI | *P* value |
|---|---|---|---|---|---|---|---|
| $Mg^{2+}$ < 0.755, mg/dL | 6.070 | (3.374, 10.921) | < 0.001 | $Mg^{2+}$ < 0.755, mg/dL | 5.525 | (2.074, 14.718) | < 0.001 |
| Age | 0.981 | (0.963, 1.000) | 0.052 | Age | 0.966 | (0.926, 1.007) | 0.104 |
| Gender | 1.158 | (0.652, 2.054) | 0.617 | | | | |
| BMI | 1.155 | (1.073, 1.244) | < 0.001 | BMI | 1.081 | (0.946, 1.236) | 0.251 |
| APACHE II | 1.385 | (1.256, 1.527) | < 0.001 | APACHE II | 1.130 | (0.976, 1.310) | 0.103 |
| SOFA | 1.589 | (1.307, 1.931) | < 0.001 | SOFA | 0.896 | (0.604, 1.330) | 0.585 |
| CTSI | 1.479 | (1.279, 1.711) | < 0.001 | CTSI | 1.107 | (0.815, 1.505) | 0.516 |
| Severity classification (MAP as reference) | | | | Severity classification (MAP as reference) | | | |
| MSAP | 4.870 | (2.071, 11.450) | < 0.001 | MSAP | 1.126 | (0.240, 5.289) | 0.880 |
| SAP | 84.857 | (23.269, 309.458) | < 0.001 | SAP | 15.260 | (1.817, 128.189) | 0.012 |
| Diabetes | 1.379 | (0.718, 2.647) | 0.334 | | | | |
| Hypertension | 1.086 | (0.588, 2.007) | 0.791 | | | | |
| Hyperlipidemia | 0.886 | (0.480, 1.634) | 0.698 | | | | |
| WBC | 1.026 | (0.970, 1.086) | 0.910 | | | | |
| Ly | 0.734 | (0.938, 1.046) | 0.734 | | | | |
| IL-6 | 1.006 | (1.004, 1.009) | < 0.001 | IL-6 | 1.003 | (0.999, 1.006) | 0.113 |
| PCT | 1.350 | (1.166, 1.562) | < 0.001 | PCT | 1.109 | (0.959, 1.283) | 0.163 |
| Platelets | 1.003 | (0.999, 1.007) | 0.139 | | | | |
| BUN | 1.368 | (1.196, 1.565) | < 0.001 | BUN | 1.102 | (0.826, 1.470) | 0.508 |
| Creatinine | 1.051 | (1.034, 1.069) | < 0.001 | Creatinine | 1.052 | (1.014, 1.091) | 0.006 |
| $HCO^{3-}$ | 0.843 | (0.794, 0.896) | < 0.001 | $HCO^{3-}$ | 0.993 | (0.894, 1.103) | 0.892 |
| $Cl^-$ | 1.100 | (1.032, 1.172) | 0.003 | $Cl^-$ | 1.042 | (0.936, 1.160) | 0.453 |

$Mg^{2+}$: Magnesium; BMI: Body mass index; AKI: Acute kidney injury; SOFA: Sequential organ failure assessment; CTSI: CT severity index; MAP: Mild acute pancreatitis; MSAP: Mild severe acute pancreatitis; SAP: Severe acute pancreatitis; WBC: White blood cells; IL-6: Interleukin-6; PCT: Procalcitonin; BUN: Blood urea nitrogen; OR: Odds ratio; CI: Confidence interval.

However, the relationship between admission serum $Mg^{2+}$ level and AKI incidence in patients with AP has not been fully elucidated. Our results are the first to show that reduced serum $Mg^{2+}$ levels are significantly associated with an increased risk of AKI in patients with AP. We found that $Mg^{2+}$ level of 0.755 mg/dL was an effective cut-off point for in-hospital AKI occurrence, with a sensitivity of 77.7%, and specificity of 63.5%.

However, there are some limitations to our analysis. Firstly, our study did not consider the value of peripheral blood $Mg^{2+}$; thus, the reliability of the actual level of free $Mg^{2+}$ in peripheral blood may be significantly reduced from this perspective. Secondly, the causal relationship between $Mg^{2+}$ and AP-associated AKI still needs to be verified by a large number of prospective studies. Thirdly, our analysis included only one checkup at admission, and as serum $Mg^{2+}$ is a dynamic state, it may not fully reflect the true status of $Mg^{2+}$ in these patients. From this perspective, dynamic serum $Mg^{2+}$ measurement after admission is more objective in predicting AP-associated AKI. Finally, there may be methodological bias in our analysis, it is necessary to explore new machine models (such as train-validation models) to verify the current analysis results.

## CONCLUSION

Our analysis indicates that serum $Mg^{2+}$ level at admission is independently associated the development of AKI in patients with AP and may be a potential prognostic factor.

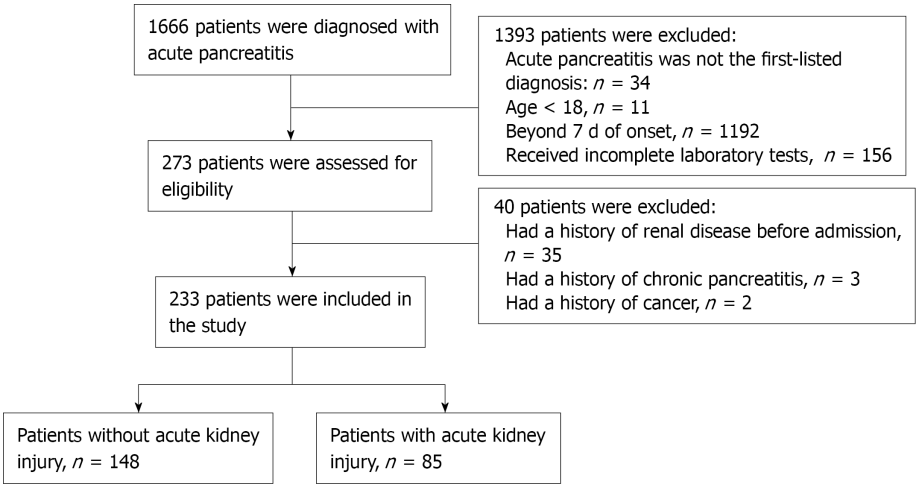


**Figure 1 The flow diagram of patients.** A total of 1666 patients were included in the analysis. AKI: Acute kidney injury.

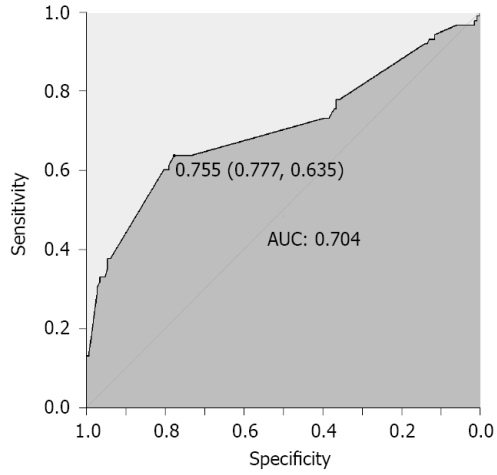


**Figure 2 Receiver operating characteristic curve for serum magnesium in predicting acute kidney injury.** AUC: Area under the curve.

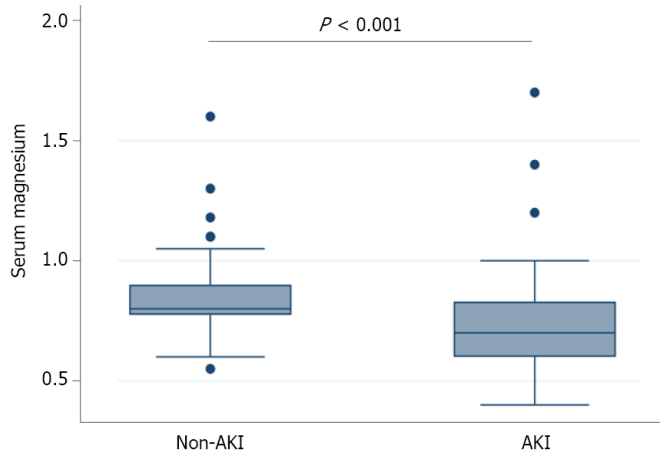


**Figure 3 Serum magnesium in the acute kidney injury group versus the non-acute kidney injury group.** AKI: Acute kidney injury.

## ARTICLE HIGHLIGHTS

### *Research background*

There is a lack of effective predictors of acute kidney injury (AKI) after acute pancreatitis (AP) in clinical practice.

### *Research motivation*

To investigate the association between serum $Mg^{2+}$ on admission and AKI after AP.

### *Research objectives*

To determine whether serum $Mg^{2+}$ is a valid predictor of AP-associated AKI using clinical data from our severe acute pancreatitis center.

### *Research methods*

Our center is one of the largest severe acute pancreatitis treatment centers in China. A total of 233 patients with AP from August 2015 to February 2019 were included in a retrospective analysis. Almost all clinical and laboratory indicators were included in the study.

### *Research results*

Lower serum $Mg^{2+}$ was correlated with the occurrence of AKI (62.1% *vs* 21.2%, $P < 0.001$). Patients in the low serum $Mg^{2+}$ level group had a longer intensive care unit ($P < 0.001$) and hospital stay ($P < 0.001$).

### *Research conclusions*

Serum $Mg^{2+}$ on admission can effectively predict AKI in AP patients.

### *Research perspectives*

This study provides ideas and a basis for prospective observation of AKI after AP, and provides early warning for effective intervention of the disease.

## REFERENCES


1 **Windsor JA**, Escott A, Brown L, Phillips AR. Novel strategies for the treatment of acute pancreatitis based on the determinants of severity. *J Gastroenterol Hepatol* 2017; **32**: 1796-1803 [PMID: 28294403 DOI: 10.1111/jgh.13784]

2 **Talukdar R**, Vege SS. Acute pancreatitis. *Curr Opin Gastroenterol* 2015; **31**: 374-379 [PMID: 26154427 DOI: 10.1097/MOG.0000000000000201]

3 **Forsmark CE**, Vege SS, Wilcox CM. Acute Pancreatitis. *N Engl J Med* 2016; **375**: 1972-1981 [PMID: 27959604 DOI: 10.1056/NEJMra1505202]

4 **Trikudanathan G**, Wolbrink DRJ, van Santvoort HC, Mallery S, Freeman M, Besselink MG. Current Concepts in Severe Acute and Necrotizing Pancreatitis: An Evidence-Based Approach. *Gastroenterology* 2019; **156**: 1994-2007.e3 [PMID: 30776347 DOI: 10.1053/j.gastro.2019.01.269]

5 **Krüger B**, Albrecht E, Lerch MM. The role of intracellular calcium signaling in premature protease activation and the onset of pancreatitis. *Am J Pathol* 2000; **157**: 43-50 [PMID: 10880374 DOI: 10.1016/S0002-9440(10)64515-4]

6 **Feng S**, Wei Q, Hu Q, Huang X, Zhou X, Luo G, Deng M, Lü M. Research Progress on the Relationship Between Acute Pancreatitis and Calcium Overload in Acinar Cells. *Dig Dis Sci* 2019; **64**: 25-38 [PMID: 30284136 DOI: 10.1007/s10620-018-5297-8]

7 **Ward JB**, Petersen OH, Jenkins SA, Sutton R. Is an elevated concentration of acinar cytosolic free ionised calcium the trigger for acute pancreatitis? *Lancet* 1995; **346**: 1016-1019 [PMID: 7475553 DOI: 10.1016/s0140-6736(95)91695-4]

8 **Saluja AK**, Bhagat L, Lee HS, Bhatia M, Frossard JL, Steer ML. Secretagogue-induced digestive enzyme activation and cell injury in rat pancreatic acini. *Am J Physiol* 1999; **276**: G835-G842 [PMID: 10198325 DOI: 10.1152/ajpgi.1999.276.4.G835]

9 **Mooren FCh**, Hlouschek V, Finkes T, Turi S, Weber IA, Singh J, Domschke W, Schnekenburger J, Krüger B, Lerch MM. Early changes in pancreatic acinar cell calcium signaling after pancreatic duct obstruction. *J Biol Chem* 2003; **278**: 9361-9369 [PMID: 12522141 DOI: 10.1074/jbc.M207454200]

10 **Song Y**, Manson JE, Buring JE, Liu S. Dietary magnesium intake in relation to plasma insulin levels and risk of type 2 diabetes in women. *Diabetes Care* 2004; **27**: 59-65 [PMID: 14693967 DOI: 10.2337/diacare.27.1.59]

11 **Kao WH**, Folsom AR, Nieto FJ, Mo JP, Watson RL, Brancati FL. Serum and dietary magnesium and the risk for type 2 diabetes mellitus: the Atherosclerosis Risk in Communities Study. *Arch Intern Med* 1999; **159**: 2151-2159 [PMID: 10527292 DOI: 10.1001/archinte.159.18.2151]

12 **Kim DJ**, Xun P, Liu K, Loria C, Yokota K, Jacobs DR Jr, He K. Magnesium intake in relation to systemic inflammation, insulin resistance, and the incidence of diabetes. *Diabetes Care* 2010; **33**: 2604-2610 [PMID: 20807870 DOI: 10.2337/dc10-0994]

13 **Mooren FC**, Turi S, Gunzel D, Schlue WR, Domschke W, Singh J, Lerch MM. Calcium-magnesium interactions in pancreatic acinar cells. *FASEB J* 2001; **15**: 659-672 [PMID: 11259384 DOI: 10.1096/fj.00-0172com]

14 **Schick V**, Scheiber JA, Mooren FC, Turi S, Ceyhan GO, Schnekenburger J, Sendler M, Schwaiger T, Omercevic A, Brandt Cv, Fluhr G, Domschke W, Krüger B, Mayerle J, Lerch MM. Effect of magnesium supplementation and depletion on the onset and course of acute experimental pancreatitis. *Gut* 2014; **63**: 1469-1480 [PMID: 24277728 DOI: 10.1136/gutjnl-2012-304274]

15 **Susantitaphong P**, Cruz DN, Cerda J, Abulfaraj M, Alqahtani F, Koulouridis I, Jaber BL; Acute Kidney Injury Advisory Group of the American Society of Nephrology. World incidence of AKI: a meta-analysis. *Clin J Am Soc Nephrol* 2013; **8**: 1482-1493 [PMID: 23744003 DOI: 10.2215/CJN.00710113]

16 **Hoste EA**, Bagshaw SM, Bellomo R, Cely CM, Colman R, Cruz DN, Edipidis K, Forni LG, Gomersall CD, Govil D, Honoré PM, Joannes-Boyau O, Joannidis M, Korhonen AM, Lavrentieva A, Mehta RL, Palevsky P, Roessler E, Ronco C, Uchino S, Vazquez JA, Vidal Andrade E, Webb S, Kellum JA. Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study. *Intensive Care Med* 2015; **41**: 1411-1423 [PMID: 26162677 DOI: 10.1007/s00134-015-3934-7]

17 **Beker BM**, Corleto MG, Fieiras C, Musso CG. Novel acute kidney injury biomarkers: their characteristics, utility and concerns. *Int Urol Nephrol* 2018; **50**: 705-713 [PMID: 29307055 DOI: 10.1007/s11255-017-1781-x]

18 **Zhou J**, Li Y, Tang Y, Liu F, Yu S, Zhang L, Zeng X, Zhao Y, Fu P. Effect of acute kidney injury on mortality and hospital stay in patient with severe acute pancreatitis. *Nephrology (Carlton)* 2015; **20**: 485-491 [PMID: 25726708 DOI: 10.1111/nep.12439]

19 **Edmondson HA**, BERNE CJ, HOMANN RE Jr, WERTMAN M. Calcium, potassium, magnesium and amylase disturbances in acute pancreatitis. *Am J Med* 1952; **12**: 34-42 [PMID: 14902852 DOI: 10.1016/0002-9343(52)90166-6]

20 **Ryzen E**, Rude RK. Low intracellular magnesium in patients with acute pancreatitis and hypocalcemia. *West J Med* 1990; **152**: 145-148 [PMID: 2407029]

21 **Krzewicki J**. Clinical study on magnesium and calcium level in the blood during the acute pancreatitis. *Magnes Res* 1998; **11**: 19-23 [PMID: 9595546]

22 **Wisdom DM**, Salido GM, Baldwin LM, Singh J. The role of magnesium in regulating CCK-8-evoked secretory responses in the exocrine rat pancreas. *Mol Cell Biochem* 1996; **154**: 123-132 [PMID: 8717426 DOI: 10.1007/BF00226780]

23 **Ammori BJ**, Barclay GR, Larvin M, McMahon MJ. Hypocalcemia in patients with acute pancreatitis: a putative role for systemic endotoxin exposure. *Pancreas* 2003; **26**: 213-217 [PMID: 12657944 DOI: 10.1097/00006676-200304000-00001]

24 **Huang W**, Cane MC, Mukherjee R, Szatmary P, Zhang X, Elliott V, Ouyang Y, Chvanov M, Latawiec D, Wen L, Booth DM, Haynes AC, Petersen OH, Tepikin AV, Criddle DN, Sutton R. Caffeine protects against experimental acute pancreatitis by inhibition of inositol 1,4,5-trisphosphate receptor-mediated $Ca^{2+}$ release. *Gut* 2017; **66**: 301-313 [PMID: 26642860 DOI: 10.1136/gutjnl-2015-309363]

25 **Frick TW**. The role of calcium in acute pancreatitis. *Surgery* 2012; **152**: S157-S163 [PMID: 22906890 DOI: 10.1016/j.surg.2012.05.013]

26 **Dumnicka P**, Maduzia D, Ceranowicz P, Olszanecki R, Drożdż R, Kuśnierz-Cabala B. The Interplay between Inflammation, Coagulation and Endothelial Injury in the Early Phase of Acute Pancreatitis: Clinical Implications. *Int J Mol Sci* 2017; **18** [PMID: 28208708 DOI: 10.3390/ijms18020354]

27 **Kim MS**, Hong JH, Li Q, Shin DM, Abramowitz J, Birnbaumer L, Muallem S. Deletion of TRPC3 in mice reduces store-operated $Ca^{2+}$ influx and the severity of acute pancreatitis. *Gastroenterology* 2009; **137**: 1509-1517 [PMID: 19622358 DOI: 10.1053/j.gastro.2009.07.042]

28 **Shahbaz AU**, Zhao T, Zhao W, Johnson PL, Ahokas RA, Bhattacharya SK, Sun Y, Gerling IC, Weber KT. Calcium and zinc dyshomeostasis during isoproterenol-induced acute stressor state. *Am J Physiol Heart Circ Physiol* 2011; **300**: H636-H644 [PMID: 21076021 DOI: 10.1152/ajpheart.00900.2010]

29 **Lin HY**, Lai JI, Lai YC, Lin PC, Chang SC, Tang GJ. Acute renal failure in severe pancreatitis: A population-based study. *Ups J Med Sci* 2011; **116**: 155-159 [PMID: 21250932 DOI: 10.3109/03009734.2010.547636]

30 **Kuśnierz-Cabala B**, Gala-Błądzińska A, Mazur-Laskowska M, Dumnicka P, Sporek M, Matuszyk A, Gil K, Ceranowicz P, Walocha J, Kucharz J, Pędziwiatr M, Bartuś K, Trąbka R, Kuźniewski M. Serum Uromodulin Levels in Prediction of Acute Kidney Injury in the Early Phase of Acute Pancreatitis. *Molecules* 2017; **22** [PMID: 28613246 DOI: 10.3390/molecules22060988]

31 **Chai X**, Huang HB, Feng G, Cao YH, Cheng QS, Li SH, He CY, Lu WH, Qin MM. Baseline Serum Cystatin C Is a Potential Predictor for Acute Kidney Injury in Patients with Acute Pancreatitis. *Dis Markers* 2018; **2018**: 8431219 [PMID: 30581500 DOI: 10.1155/2018/8431219]

32 **Siddappa PK**, Kochhar R, Sarotra P, Medhi B, Jha V, Gupta V. Neutrophil gelatinase-associated lipocalin: An early biomarker for predicting acute kidney injury and severity in patients with acute pancreatitis. *JGH Open* 2019; **3**: 105-110 [PMID: 31061884 DOI: 10.1002/jgh3.12112]

33 **Huang HL**, Nie X, Cai B, Tang JT, He Y, Miao Q, Song HL, Luo TX, Gao BX, Wang LL, Li GX. Procalcitonin levels predict acute kidney injury and prognosis in acute pancreatitis: a prospective study. *PLoS One* 2013; **8**: e82250 [PMID: 24349237 DOI: 10.1371/journal.pone.0082250]

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