Research Square

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Association between Serum Magnesium and all-cause mortality in patients with Sepsis-associated liver injury: A Cohort Study

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Abstract

Background

Serum magnesium is critical for cellular function and impaired magnesium homeostasis is associated with increased mortality in critically ill patients. However, its role in sepsis-associated liver injury (SALI) remains unclear. This study aims to elucidate the association between serum magnesium and all-cause mortality in patients with SALI.

Methods

Data for this retrospective cohort study were obtained from the Medical Information Mart in Intensive Care IV (MIMIC-IV), which included the initial serum magnesium levels of patients diagnosed with SALI admitted to the ICU. Multivariable Cox regression analysis, Kaplan-Meier survival curves, and restricted cubic spline (RCS) were used to assess the association between serum magnesium levels on admission to the ICU and in-hospital mortality in patients with SALI.

Results

A total of 1367 patients were enrolled in the study with an in-hospital mortality rate of 34.97%. Multivariate Cox regression analysis showed that in-hospital mortality in patients with SALI increased with increasing serum magnesium levels at ICU admission, HR 1.28 (1.06–1.53, p 0.009). RCS suggests a nonlinear association between serum magnesium levels and in-hospital mortality in patients with SALI.

Conclusions

This study found that high serum magnesium levels were independently associated with in-hospital mortality in patients with SALI, showing a nonlinear association. Nevertheless, confirmation of this association requires further validation through large-scale prospective cohort studies.

Introduction

Sepsis is a complex and uncontrolled response of the body to infection that can ultimately lead to multiple organ dysfunction (MODS)[1–3]. It has become a global public health problem as it can be the cause of nearly one-sixth to one-third of all deaths in the world each year[4,5]. Given its role in metabolism, synthesis, and immune regulation, the liver undergoes some changes in the context of sepsis, such as altered immune responses, disruption of metabolic pathways, impaired microvascular dynamics, and coagulation abnormalities, which together lead to hepatic dysfunction and ultimately to sepsis-associated liver injury (SALI)[6]. Patients with SALI have a higher mortality rate, so the severity of SALI has become widely accepted. Therefore, there have been international guidelines and studies to diagnose SALI in patients based on total bilirubin and INR[7]. Overall, the early recognition and appropriate management of SALI are essential for the

prevention of deaths associated with this condition. Therefore, a comprehensive understanding of the liver's involvement in sepsis may be helpful in the mitigation of SALI and the improvement of patient prognosis. In addition, patient prognosis and clinical outcomes can be significantly affected by pre-existing conditions at the time of SALI diagnosis, such as electrolyte imbalances.

Magnesium is the second most abundant intracellular cation besides potassium ions and plays an important role in various pathophysiological processes (enzymatic reactions such as protein synthesis, energy metabolism, and DNA synthesis)[8]. Imbalances in magnesium homeostasis are prevalent in many patients. Hypomagnesemia increases risk and adverse outcomes in patients with cardiovascular disease[9], diabetes[10], stroke[11], and depression[12]. In addition, patients with hypomagnesemia in the intensive care unit had a significantly longer duration of invasive mechanical ventilation and a higher mortality rate[13]. Moreover, hypomagnesemia has been associated with a higher risk of hepatocellular carcinoma in patients with cirrhosis[14]. It is important to note that hypermagnesemia is not only associated with the severity of COVID-19 and a poor prognosis[15], but it is also significantly correlated with an increase in in-hospital mortality in critically ill children[16]. However, there is a paucity of studies on the association between serum magnesium levels at the onset of SALI and patient mortality.

Therefore, the primary aim of this study was to assess the association between serum magnesium levels and hospital mortality in patients undergoing SALI. A secondary objective was to investigate a potential non-linear dose-response relationship between serum magnesium exposure and the outcome of SALI mortality.

Methods

Study population

This retrospective cohort study was designed and reported in strict adherence to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines, ensuring methodological rigor and transparency[17]. Study data were extracted from the MIMICIV (v2.2) database, a publicly available database of more than 50,000 intensive care unit admissions at Beth Israel Deaconess Medical Center, Boston, from 2008 to 2019. The Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center institutional review boards waived the requirement for patient informed consent because the data were from a public database and de-identified. This study was conducted under the tenets of the Declaration of Helsinki (as revised in 2013).

Only data from their initial ICU admission were included in the analysis for patients with multiple hospital admissions to ensure independent observations and minimize potential bias[18]. The diagnostic criteria for SALI in this study were based on the guidelines of the Save Lives from Sepsis campaign[19]: total bilirubin level > 2 mg/dL (34.2 μ mol/L) and INR > 1.5 in patients with sepsis. This diagnostic criterion was mentioned in several publications. Exclusion criteria for the study were as follows: (1) admission for chronic liver disease, cirrhosis, alcoholic liver disease, autoimmune hepatitis, and hepatic malignancy; (2) lack of blood magnesium measurements on admission; (3) ICU length of stay < 24 hours; and (4) total length of stay < 24 hours.

Variable extraction

This study used PostgresSQL software (version 13.7.2) and Navicat Premium software (version 16) to extract information through the execution of structured query language (SQL). The initial baseline parameters were the data from the first day after the patient's admission to the ICU. These parameters included demographics (gender, age, height, weight), vital signs, comorbidities, and data related to the Severity of Functional Assessment (SOFA, Sequential Organ Failure Assessment; SAPS II, Simplified Acute Physiology Score II) scales. Furthermore, the use of related medications, vasoactive medications, continuous renal replacement therapy (CRRT), and mechanical ventilation were also extracted.

Statistical analysis

Serum magnesium levels were categorized into four groups(Mg Q1-Q4) based on quartiles[20,21]. Statistical analyses for categorical variables were conducted using Fisher's exact test or the Chi-square test, with results presented as counts (percentages) [22]. For continuous variables, the Wilcoxon rank-sum test, Student's t-test, or one-way analysis of variance (ANOVA) was employed. Continuous variables are expressed as mean and standard deviation (SD) or median with interquartile range (IQR). Multiple imputation was performed using five replications and a chained equation approach method to enhance statistical power and address potential bias resulting from missing data (*Supplementary Table 1*). The results of multiple imputations were consistent with the results of the main analysis (*Supplementary Table 2*). Statistical significance was defined as $p < 0.05$.

The selection of covariates was guided by clinical expertise, previous literature, and variables whose initial regression coefficients changed by more than 10% when added or removed from the basic and full models[23]. A variance spreading factor (VIF) greater than 2 indicated the presence of multicollinearity. Model 1 was unadjusted, while Model 2 adjusted for Age, Sex, and Ethnicity. Model 3 included other covariates including BMI, Care Unit, Heart Rate, RR, Hemoglobin, Albumin, PTT, INR, Total bilirubin, ALT, Lactate, Potassium, Calcium, VIS, Vaso agent, CRRT, Mechanical ventilation, Magnesium Sulfate, Diabetic, Myocardial infarct, Congestive Heart Failure, Renal Disease, Charlson Comorbidity Index.

To explore potential nonlinear relationships between serum magnesium levels and in-hospital mortality rates, restricted cubic spline (RCS) analysis was performed. The association between serum magnesium and in-hospital mortality was assessed using Cox multivariable logistic regression analysis, calculating hazard ratios (HR) and their corresponding 95% confidence intervals (CI) to quantify the impact of serum magnesium on these outcomes[24]. Kaplan-Meier survival analysis was used to compare the incidence of the primary outcome event between different blood magnesium level groups, and the difference between groups was assessed by the log-rank test to evaluate the association between blood magnesium levels and the primary outcome. The subgroup analysis was performed according to the different groupings, and the interaction between serum magnesium levels and in-hospital mortality in patients with SALI was evaluated using a likelihood ratio test, the results of which are presented using a forest plot.

The data analysis process was performed using packages R4.2.2 (The R Foundation) software and Free Statistics software version 1.9. Statistical significance was defined as $p < 0.05$.

Results

Study population and baseline characteristics

The 1367 patients with SALI who were admitted to the intensive care unit between 2008 and 2019 and who were collected in the MIMIC IV database were included in this study. The inclusion and exclusion processes are illustrated in Fig. 1. Among the enrolled patients, 58.7% were male, with a median age of 65.0 years (interquartile range [IQR], 52.0–77.0 years). The overall in-hospital mortality rate was 35% (478 of 1367 patients). Based on quartiles of serum magnesium levels, the study population was divided into four groups(Q1-Q4). The baseline characteristics of this study are shown in **Table 1**. Significant differences were observed across groups (Q1-Q4) in multiple clinical and demographic variables. Sex distribution differed significantly ($p = 0.005$), with male predominance (63.4–63.5%) in the higher Mg groups (Q3, Q4) compared to lower groups (53.2–54.3%; Q1, Q2). Ethnicity composition also varied ($p = 0.013$). Clinical outcomes, including 28-day mortality, 90-day mortality, ICU mortality, and in-hospital mortality, demonstrated progressively higher rates with increasing Mg levels ($p < 0.001$). In different care units, significant differences were observed among the various groups of serum magnesium levels. Additionally, vital signs, including heart rate, blood pressure, temperature, and SpO_2, also exhibited significant differences. In the laboratory parameters, compared to the Q1 group, the Q4 group exhibited higher levels of albumin, BUN, creatinine, PT, PTT, INR, lactate, potassium, calcium, and phosphate, while hemoglobin levels were lower. Comorbidities, including MI, congestive heart failure and renal disease, were more prevalent in the Q4 group. Treatment modalities, such as vasoactive agent use, MV, and CRRT, also differed significantly ($p < 0.001$). In a similar vein, the mean scores for SOFA, SAPS II, CCI, and VIS in the Q4 group were found to be significantly higher compared to the Q1 group ($P < 0.001$).

Table 1 Baseline characteristics.

Variables	Total (n = 1367)	Serum Magnesium (mg/dL)				*p*
		Q1 (n = 308)	Q2 (n = 370)	Q3 (n = 323)	Q4 (n = 366)	
Male, n (%)	802 (58.7)	164 (53.2)	201 (54.3)	205 (63.5)	232 (63.4)	0.005
Age (year)	65.0 (52.0, 77.0)	64.0 (47.0, 76.0)	62.0 (50.0, 76.0)	66.0 (53.0, 78.0)	66.0 (54.0, 77.0)	0.05
Ethnicity, n (%)						0.013
Black	111 (8.1)	20 (6.5)	37 (10)	28 (8.7)	26 (7.1)	
White	841 (61.5)	213 (69.2)	228 (61.6)	179 (55.4)	221 (60.4)	
Other	415 (30.4)	75 (24.4)	105 (28.4)	116 (35.9)	119 (32.5)	
BMI (kg/m^2)	28.1 (24.2, 32.6)	27.6 (23.8, 32.0)	28.6 (24.6, 33.8)	27.2 (24.0, 32.6)	28.4 (24.3, 32.5)	0.224
28-day mortality, n (%)	476 (34.8)	87 (28.2)	111 (30)	129 (39.9)	149 (40.7)	< 0.001
90-day mortality, n (%)	583 (42.6)	103 (33.4)	139 (37.6)	156 (48.3)	185 (50.5)	< 0.001
In-hospital mortality, n (%)	478 (35.0)	84 (27.3)	112 (30.3)	130 (40.2)	152 (41.5)	< 0.001
ICU Mortality, n (%)	384 (28.1)	68 (22.1)	82 (22.2)	102 (31.6)	132 (36.1)	< 0.001
Los ICU (day)	4.4 (2.2, 10.0)	4.3 (2.3, 10.1)	3.9 (2.1, 8.5)	3.9 (2.0, 9.2)	5.6 (2.7, 11.7)	< 0.001
Los Hospital (day)	12.3 (6.9, 22.0)	11.7 (6.7, 21.2)	12.3 (6.8, 20.8)	12.0 (6.9, 19.8)	13.9 (7.0, 24.8)	0.247
Anchor Year Group, n (%)						0.731
2008-2010	395 (28.9)	102 (33.1)	98 (26.5)	96 (29.7)	99 (27)	
2011-2013	333 (24.4)	76 (24.7)	86 (23.2)	78 (24.1)	93 (25.4)	
2014-2016	348 (25.5)	72 (23.4)	100 (27)	80 (24.8)	96 (26.2)	
2017-2019	291 (21.3)	58 (18.8)	86 (23.2)	69 (21.4)	78 (21.3)	
Care Unit, n (%)						< 0.001
CVICU/CCU	299 (21.9)	35 (11.4)	62 (16.8)	68 (21.1)	134 (36.6)	
MICU	615 (45.0)	161 (52.3)	163 (44.1)	156 (48.3)	135 (36.9)	
SICU	335 (24.5)	93 (30.2)	110 (29.7)	68 (21.1)	64 (17.5)	
Other ICU	118 (8.6)	19 (6.2)	35 (9.5)	31 (9.6)	33 (9)	

Vital signs						
HR (bpm)	112.0 (97.0, 127.0)	118.0 (103.0, 131.0)	113.0 (99.8, 127.0)	111.0 (95.0, 125.0)	105.0 (92.0, 123.0)	< 0.001
SBP (mmHg)	84.0 (74.0, 93.0)	82.0 (70.0, 91.2)	87.0 (75.0, 96.0)	85.0 (76.2, 96.5)	83.0 (74.0, 92.0)	< 0.001
DBP (mmHg)	44.0 (37.0, 51.0)	43.0 (36.0, 49.0)	45.0 (37.0, 52.0)	45.0 (38.0, 51.0)	42.0 (37.0, 49.0)	0.011
MAP (mmHg)	56.0 (48.0, 62.0)	54.0 (45.2, 61.2)	57.0 (49.0, 64.0)	57.0 (49.0, 64.0)	54.0 (47.6, 60.0)	< 0.001
RR (bpm)	29.0 (25.0, 34.0)	29.0 (25.0, 33.2)	30.0 (25.0, 34.0)	29.0 (26.0, 34.0)	28.5 (24.0, 34.8)	0.413
Temperature (°C)	37.3 (36.9, 38.0)	37.4 (37.0, 38.2)	37.4 (37.0, 38.2)	37.3 (37.0, 37.9)	37.2 (36.8, 37.7)	< 0.001
SPO_2 (%)	92.0 (89.0, 94.0)	92.0 (89.0, 94.0)	93.0 (90.0, 95.0)	91.0 (88.5, 94.0)	92.0 (89.0, 94.0)	0.001
Laboratory tests						
Hemoglobin (g/dL)	9.2 (7.7, 11.0)	9.3 (7.8, 10.9)	9.3 (7.7, 11.3)	9.4 (8.0, 11.2)	8.7 (7.4, 10.5)	< 0.001
Platelets (10^9)	115.0 (66.0, 175.0)	109.0 (60.5, 176.0)	124.0 (72.0, 179.5)	124.0 (66.0, 186.5)	107.5 (64.5, 160.8)	0.085
WBC (10^9)	14.9 (10.1, 21.0)	15.8 (9.9, 22.4)	14.9 (9.7, 20.0)	13.6 (10.1, 19.5)	15.7 (10.4, 22.4)	0.07
Albumin (g/dL)	2.8 (2.3, 3.4)	2.7 (2.2, 3.2)	2.8 (2.4, 3.3)	2.9 (2.4, 3.5)	2.9 (2.4, 3.5)	0.008
BUN (mg/dL)	30.0 (18.0, 48.0)	22.0 (15.0, 33.0)	27.0 (16.0, 40.0)	33.0 (22.0, 53.5)	42.0 (24.0, 67.0)	< 0.001
Creatinine (u mol/L)	1.5 (1.0, 2.5)	1.3 (0.9, 1.9)	1.4 (0.9, 2.2)	1.6 (1.1, 2.5)	2.0 (1.3, 3.1)	< 0.001
PT (s)	20.6 (17.4, 28.9)	19.6 (17.5, 24.3)	21.5 (17.8, 31.8)	20.8 (17.0, 30.6)	21.1 (17.5, 29.7)	0.004
PTT (s)	43.6 (34.4, 65.4)	41.7 (34.4, 55.9)	42.3 (33.9, 63.6)	42.9 (34.6, 68.2)	48.8 (35.4, 74.7)	0.005
INR	2.5 (1.9, 3.7)	2.1 (1.7, 2.9)	2.4 (1.9, 3.6)	2.6 (1.9, 3.8)	2.9 (2.1, 4.3)	< 0.001
T-bil (u mol/L)	4.4 (2.8, 9.1)	4.3 (2.9, 7.2)	4.3 (2.8, 8.4)	4.4 (2.7, 8.4)	4.6 (2.9, 12.2)	0.096
ALT (U/L)	103.0 (32.5, 546.5)	99.0 (30.8, 429.2)	118.0 (35.0, 628.5)	100.0 (33.0, 677.0)	97.0 (31.5, 560.5)	0.379

ALP (U/L)	107.0 (68.0, 190.0)	107.0 (64.0, 202.0)	107.0 (70.5, 179.5)	112.0 (75.0, 204.5)	99.0 (63.5, 174.0)	0.072
AST (U/L)	166.0 (59.8, 889.0)	156.0 (60.0, 578.0)	189.5 (61.0, 1072.5)	148.0 (54.0, 918.0)	172.5 (65.5, 947.5)	0.15
Lactate (mmol/L)	4.2 (2.3, 7.4)	4.6 (2.6, 7.1)	3.5 (2.0, 6.8)	3.8 (2.2, 6.9)	4.6 (2.6, 8.3)	0.003
pH	7.3 (7.2, 7.4)	7.3 (7.2, 7.3)	7.3 (7.2, 7.4)	7.3 (7.2, 7.4)	7.3 (7.2, 7.4)	< 0.001
PO_2 (mmHg)	78.0 (61.0, 100.0)	79.0 (61.0, 99.0)	79.0 (65.0, 99.5)	76.0 (57.5, 95.0)	77.0 (61.0, 100.0)	0.309
PCO_2 (mmHg)	44.0 (38.0, 53.0)	45.0 (38.0, 53.0)	43.0 (37.0, 51.0)	43.0 (36.0, 53.0)	45.5 (39.0, 54.0)	0.012
Sodium (m Eq/L)	137.0 (134.0, 141.0)	138.0 (134.8, 141.0)	138.0 (135.0, 141.0)	137.0 (134.0, 141.0)	137.0 (133.0, 140.0)	0.072
Potassium (m Eq/L)	4.1 (3.7, 4.8)	3.9 (3.5, 4.4)	4.0 (3.6, 4.6)	4.2 (3.7, 4.7)	4.6 (4.0, 5.1)	< 0.001
Calcium (mg/dL)	7.7 (7.2, 8.3)	7.5 (6.9, 8.0)	7.7 (7.1, 8.2)	7.8 (7.3, 8.4)	8.0 (7.3, 8.6)	< 0.001
Phosphate (m Eq/L)	3.8 (2.8, 5.1)	3.6 (2.7, 4.5)	3.6 (2.5, 4.8)	3.8 (2.9, 5.1)	4.4 (3.3, 6.1)	< 0.001
Glucose (mg/dL)	130.0 (103.0, 178.0)	128.0 (101.8, 171.8)	130.5 (102.0, 180.0)	130.0 (104.0, 167.0)	131.0 (106.0, 185.0)	0.606
Comorbidities						
Diabetic, n (%)	402 (29.4)	80 (26)	98 (26.5)	101 (31.3)	123 (33.6)	0.075
MI, n (%)	241 (17.6)	42 (13.6)	54 (14.6)	66 (20.4)	79 (21.6)	0.01
CHF n (%)	483 (35.3)	75 (24.4)	116 (31.4)	121 (37.5)	171 (46.7)	< 0.001
CPD, n (%)	318 (23.3)	70 (22.7)	88 (23.8)	69 (21.4)	91 (24.9)	0.733
RD, n (%)	294 (21.5)	46 (14.9)	64 (17.3)	78 (24.1)	106 (29)	< 0.001
CCI	6.0 (4.0, 8.0)	5.0 (3.0, 7.0)	6.0 (4.0, 7.0)	6.0 (4.0, 8.0)	6.0 (5.0, 8.0)	< 0.001
Scoring systems						
SAPS II	46.0 (35.0, 57.0)	44.0 (35.0, 55.0)	44.0 (33.0, 54.0)	46.0 (35.0, 57.0)	50.0 (39.0, 61.0)	< 0.001

Sofa	10.0 (6.5, 13.0)	9.0 (6.0, 13.0)	9.0 (6.0, 13.0)	9.0 (6.0, 13.0)	11.0 (8.0, 14.0)	< 0.001
VIS	6.5 (0.0, 22.2)	5.5 (0.0, 21.7)	5.0 (0.0, 18.4)	4.6 (0.0, 23.3)	11.4 (0.0, 25.5)	< 0.001
Infection site, n (%)						
Bacteremia, n (%)	99 (7.2)	30 (9.7)	20 (5.4)	21 (6.5)	28 (7.7)	0.166
AI, n (%)	126 (9.2)	33 (10.7)	35 (9.5)	22 (6.8)	36 (9.8)	0.354
Pneumonia, n (%)	464 (33.9)	89 (28.9)	119 (32.2)	123 (38.1)	133 (36.3)	0.06
SSTI, n (%)	38 (2.8)	4 (1.3)	11 (3)	12 (3.7)	11 (3)	0.3
UTI, n (%)	311 (22.8)	68 (22.1)	86 (23.2)	72 (22.3)	85 (23.2)	0.975
Interventions						
Vaso agent, n (%)	807 (59.0)	174 (56.5)	202 (54.6)	176 (54.5)	255 (69.7)	< 0.001
CRRT, n (%)	308 (22.5)	54 (17.5)	68 (18.4)	62 (19.2)	124 (33.9)	< 0.001
MV n (%)	690 (50.5)	154 (50)	187 (50.5)	128 (39.6)	221 (60.4)	< 0.001
Calcium Supplement, n (%)	350 (25.6)	84 (27.3)	91 (24.6)	81 (25.1)	94 (25.7)	0.874
Magnesium Sulfate, n (%)	522 (38.2)	119 (38.6)	115 (31.1)	109 (33.7)	179 (48.9)	< 0.001

Abbreviations: Q1 <0.8 (n = 308); Q2 0.8,1.8 (n = 370); Q3 1.8,2.1(n = 323); Q4 >=2.1 (n = 366)

BMI Body mass index; HR heart rate; SBP systolic blood pressure; DBP Diastolic blood pressure; MAP mean arterial pressure; RR Respiratory rate; SpO2 Peripheral capillary oxygen saturation; WBC white blood cell counts; BUN blood urine nitrogen; PT Prothrombin time; PTT Activated partial thromboplastin time; INR International normalized ratio; T-bil Bilirubin total; ALT Alanine transaminase; AST Aspartate Transaminase; ALP Alkaline phosphatase; MI Myocardial infarct; CHF Congestive heart failure; CPD Chronic pulmonary disease; RD renal disease; CCI charlson comorbidity index; SAPS II Simplified Acute Physiology Score II; SOFA Sequential Organ Failure Assessment, AI Abdominal Infection; UTI Urinary tract infection; SSTI Skin and soft tissues infection CRRT Continuous renal replacement therapy; MV Mechanical ventilation; VIS The vasoactive-inotropic score was calculated as follows: dopamine dose (in micrograms per kilogram per minute) + dobutamine dose (in micrograms per kilogram per minute) + 100 × epinephrine dose (in micrograms per kilogram per minute) + 10 × milrinone dose (in micrograms per kilogram per minute) + 10000 × vasopressin dose (in international units per kilogram per minute) + 100 × norepinephrine dose (in micrograms per kilogram per minute).

Magnesium and all-cause mortality

The Cox multivariate regression analysis examined the association between serum magnesium levels and in-hospital mortality among patients with SALI (**Table 2**). A total of 1,367 patients were included, with 478 (35%) experiencing in-hospital mortality during a follow-up period of approximately 322,104 days. Model 1 indicates a significant hazard ratio (HR) of 1.41 (95% CI: 1.20–1.66, P < 0.001) for serum magnesium levels, suggesting that higher magnesium levels are associated with increased mortality risk. Subsequent models (Model 2 and Model 3) show a consistent trend, with HRs of 1.38 (95% CI: 1.17–1.62, P < 0.001) and 1.28 (95% CI: 1.06–1.53, P = 0.009), respectively, indicating a robust association. Additionally, the analysis of magnesium quartiles reveals that patients in the lowest quartile (MgQ1) serve as the reference group, while those in the highest quartile (MgQ4) exhibit a significantly elevated risk of mortality (HR: 1.70, 95% CI: 1.30–2.22, P < 0.001). The trend test across quartiles is statistically significant (P < 0.001), reinforcing the conclusion that high serum magnesium levels are associated with increased in-hospital mortality risk in this patient population. The Kaplan–Meier survival curve indicates that patients of Q4 have a higher risk of in-hospital mortality than the other group, and there are significant differences in all-cause mortality among the four groups (**Figure 2**). It is noteworthy that the 28-day, and 90-day mortality rates were comparable to the in-hospital mortality results (*Supplementary Figure 1*).

Table 2 Multivariate COX analysis between serum Magnesium level and in-hospital mortality.

Variable	Total	Event %	Model 1		Model 2		Model 3	
			HR (95%CI)	P value	HR (95%CI)	P value	HR (95%CI)	P value
Magnesium	1367	478 (35)	1.41 (1.2~1.66)	<0.001	1.38 (1.17~1.62)	<0.001	1.28 (1.06~1.53)	0.009
Mg Q								
Q1	308	84 (27.3)	1(Ref)		1(Ref)		1(Ref)	
Q2	370	112 (30.3)	1.14 (0.86~1.51)	0.362	1.13 (0.85~1.5)	0.397	1.24 (0.93~1.66)	0.144
Q3	323	130 (40.2)	1.62 (1.23~2.14)	0.001	1.53 (1.16~2.02)	0.002	1.62 (1.22~2.17)	0.001
Q4	366	152 (41.5)	1.7 (1.3~2.22)	<0.001	1.63 (1.25~2.14)	<0.001	1.51 (1.12~2.04)	0.007
P for trend				<0.001		<0.001		0.002

Abbreviations: Q1 <0.8 mg/dL; Q2 (0.8,1.8) mg/dL; Q3 (1.8,2.1) mg/dL; Q4 >=2.1 mg/dL

Model 1: unadjusted

Model 2: Gender, Age, and Ethnicity

Model 3: Gender, Age, Ethnicity, BMI, Care Unit, Heart Rate, Resp Rate, Hemoglobin, Albumin, PTT, INR, T-bil, ALT, Lactate, Potassium, Calcium, VIS, Vaso agent, CRRT, MV, Magnesium Sulfate, Diabetic, Myocardial

infarct, Congestive Heart Failure, Renal Disease, and Charlson Comorbidity Index

The nonlinear relationship between blood magnesium and in-hospital mortality

Restricted cubic spline curves showed a nonlinear relationship between blood magnesium and in-hospital mortality (p for overall 0.007, nonlinear p of 0.047). The critical value in this study was 1.838 mg/dL, and when serum magnesium levels were less than 1.838 mg/dL, the hazard ratio (HR) was 1.691 (0.742-3.853), p was 0.2109, while when serum magnesium levels were greater than or equal to 1.838, HR was 1.215 (0.924-1.597), p 0.1635 (**Figure 3,** *Supplementary Table 4*). Furthermore, the study found that magnesium levels also showed a similar correlation with 28-day and 90-day mortality (*Supplementary Figure 2*).

Subgroup analysis of Serum Magnesium and In-hospital mortality

Subgroup analyses revealed significant heterogeneity in the association between serum magnesium levels and in-hospital mortality. In the overall cohort, elevated magnesium levels were associated with increased mortality risk (adjusted HR = 1.28, 95% CI: 1.06–1.53). Significant interaction effects were observed for sex (P = 0.002) and care unit (P < 0.001). Males exhibited higher mortality risk (HR = 1.53, 95% CI: 1.19–1.97), whereas no association was found in females (HR = 0.97, 95% CI: 0.73–1.28). No interactions were detected for age, ethnicity, BMI, or comorbidities (all P > 0.05). Subgroup analyses confirmed the robustness of the findings through interaction tests and calculation of 95% confidence intervals (**Figure 4**).

Discussion

The objective of this retrospective cohort study was to examine the association between serum magnesium levels and in-hospital mortality in patients with SALI who were admitted to the intensive care unit. The findings indicate a substantial correlation between hypermagnesemia and increased in-hospital mortality, which is consistent with previous findings that elevated magnesium levels may be associated with severe disease and poor prognosis in SALI. Specifically, patients with hypermagnesemia exhibited a higher mortality rate in comparison with patients exhibiting normal or low magnesium levels. This association remained significant even after adjusting for other confounders, suggesting that magnesium levels may serve as an independent risk factor for in-hospital mortality in SALI. Furthermore, this study revealed a non-linear association between serum magnesium levels and hospital mortality, with a cutoff value of 1.838 mg/dL.

This study found a notable association between serum magnesium levels and SALI mortality. This result is consistent with the findings of Cheungpasitporn et al., who showed that variations in serum magnesium levels were statistically correlated with increased in-hospital mortality rates among hospitalized patients[25]. In a similar vein, Cidade-Rodrigues et al. found that higher magnesium levels correlated with increased hospital mortality in patients with acute heart failure, reinforcing that elevated magnesium levels may possibly be associated with adverse outcomes[26]. Recent studies have demonstrated a significant association between high serum magnesium levels and increased in-hospital mortality in patients with various conditions, including COVID-19[15], sepsis[16], and severe acute myocardial infarction[27] patients. Consistent with these findings, our study found a marked association between elevated serum magnesium levels and ICU admission and mortality in patients with SALI. However, it should not be overlooked that our investigation found an in-hospital mortality rate of 31.9% in patients with SALI, which is comparable to other

findings in the literature[28–30] that reported the high mortality associated with SALI. Consequently, SALI emerges as a critical health domain that warrants heightened attention from the medical research community. Notably, the role of serum magnesium levels in SALI has not been thoroughly investigated in previous studies. By examining this relationship, our study broadens the understanding of serum magnesium levels in the context of SALI, providing novel insights that may inform future research and clinical practice.

Magnesium is a crucial electrolyte involved in numerous physiological processes, including nerve conduction, muscle contraction, and enzymatic reactions. Its levels can be influenced by various factors, such as renal function, gastrointestinal absorption, and inflammatory states. In critically ill patients, hypermagnesemia may result from reduced renal excretion or increased gastrointestinal absorption due to decreased motility. Additionally, conditions like acidosis, rhabdomyolysis, and tumor lysis syndrome can cause a shift of magnesium from intracellular to extracellular spaces, leading to hypermagnesemia[31]. This understanding is supported by Zafar et al., who emphasized that magnesium deficiency in critical illness correlates with higher morbidity and mortality, highlighting the importance of monitoring magnesium levels in this patient population[32]. Furthermore, Wang et al. noted that hypermagnesemia developed during ICU hospitalizations was an independent risk factor for mortality, suggesting that the dynamics of magnesium levels during critical illness are crucial for patient outcomes[16]. Our study's results are consistent with those of Guerin et al., who found that hypermagnesemia was associated with higher ICU mortality in a general ICU population[33].

It is worth noting that while hypomagnesemia has been extensively studied and is known to be associated with adverse outcomes, including prolonged mechanical ventilation and increased ICU stay, our study did not find a significant relationship between hypomagnesemia and in-hospital mortality. This discrepancy could be due to the specific patient population studied or the timing of magnesium level measurements. Previous studies have indicated that hypomagnesemia can prolong ventilator support and hospital stay, but the relationship with mortality remains less clear. Further research is needed to elucidate the precise mechanisms underlying the association between magnesium levels and mortality and to determine the optimal timing and frequency of magnesium monitoring in critically ill patients.

The mechanisms underlying the observed associations between elevated magnesium levels and increased mortality remain unclear. The relationship between elevated magnesium levels and increased mortality remains to be elucidated. The potential underlying mechanisms contributing to this phenomenon include several potential pathways. 1) One significant mechanism involves magnesium-induced vasodilation, which may exacerbate hepatic hypoperfusion. Magnesium acts as a potent vasodilator by activating potassium channels, leading to smooth muscle relaxation and subsequent vasodilation of hepatic vessels. This vasodilation can reduce hepatic perfusion pressure, impairing the liver's ability to function effectively during sepsis. Murata et al. investigated the signaling mechanisms of magnesium-induced vasodilation, highlighting magnesium's role in vascular tone regulation[34]. Additionally, Elevated magnesium levels are associated with severe cardiovascular complications, such as hypotension and bradycardia, which are particularly critical in the context of sepsis. These complications can further impair organ perfusion, including hepatic perfusion, leading to ischemia and subsequent liver injury[35,36]. 2) A second potential mechanism may be that hypermagnesemia is associated with an exacerbated inflammatory response during

sepsis. The liver is particularly vulnerable during sepsis due to its central role in immune regulation and metabolic processes. The liver's ability to clear pathogens and produce acute-phase proteins is impaired in the presence of elevated magnesium levels, which may exacerbate the systemic inflammatory response[37]. Moreover, the inflammatory milieu in sepsis is characterized by the overproduction of pro-inflammatory cytokines, such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6). These cytokines are known to induce liver injury by promoting oxidative stress and apoptosis in hepatocytes[38,39]. Elevated magnesium levels may further amplify this inflammatory cascade, leading to a detrimental cycle of liver damage and systemic inflammation[40]. The mechanisms underlying sepsis-induced liver injury include oxidative stress and mitochondrial dysfunction, which are exacerbated by hypermagnesemia. Studies have shown that magnesium can influence mitochondrial function and reactive oxygen species (ROS) production, which are critical in the pathogenesis of liver injury during sepsis[41,42]. The accumulation of ROS leads to cellular damage and apoptosis, further impairing liver function and contributing to the high mortality associated with sepsis[43]. 3) There is also a potential mechanism involving the relationship between elevated magnesium levels and the severity of coagulopathy, sepsis can lead to endothelial dysfunction and increased vascular permeability, which, when coupled with elevated magnesium levels, may further predispose patients to bleeding events[44,45]. In critically ill patients, particularly those with pre-existing conditions such as liver cirrhosis or acute coronary syndrome, the risk of gastrointestinal bleeding is notably increased during septic episodes, highlighting the need for careful monitoring of magnesium levels in these populations[44,46,47]. In summary, the mechanism of association between elevated magnesium levels and increased in-hospital mortality in patients with SALI is not very clear, emphasizing the importance of monitoring and managing magnesium levels. The interaction between their physiological mechanisms requires further well-designed large prospective studies to clarify mechanisms and develop effective treatment strategies aimed at mitigating the risk of mortality in these patients.

This study also found a non-linear relationship between serum magnesium levels and in-hospital mortality in patients with SALI, suggesting that serum magnesium levels may be significant for patient outcomes. This is particularly concerning because it implies that serum magnesium levels should be closely monitored and managed in patients with SALI.

Limitation

This study has several limitations. First, it is a retrospective cohort study, and the inherent design makes causality determination impossible. Second, this study only included the initial serum magnesium level at ICU admission and cannot prove the relationship between its dynamic changes and all-cause mortality of SALI. Perhaps, subsequent studies can include dynamic changes in blood magnesium levels. Third, because this study does not include intracellular magnesium levels, it cannot fully represent the total magnesium level in the body. Finally, because this study was observational, it was impossible to explain the exact mechanism of the relationship between serum magnesium levels and mortality, which needs to be confirmed in future prospective cohort studies with large samples and rigorous designs.

Conclusion

The present study found that elevated serum magnesium levels were independently associated with in-hospital mortality in patients with SALI, exhibiting a non-linear association. These findings suggest that serum magnesium levels should be closely monitored and managed in patients diagnosed with SALI. However, these results require confirmation by large-scale prospective cohort studies.

Declarations

Acknowledgment

We would like to express our gratitude to all the participants for their valuable contributions to this study.

Ethical Statement

The study was approved by Massachusetts Institute of Technology Affiliates. (ID: 52390976). The study conformed to the provisions of the Declaration of Helsinki (revised in 2013). The studies involving human participants were reviewed and approved by the Institutional Review Board of the Massachusetts Institute of Technology and Beth Israel Deaconess Medical Center. The Medical Ethics Committee agreed to waive the ethics review because anonymous data was used in this study (ID: KY2024ML079).

Declaration of Interest Statement

The authors declare no competing interests.

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Data availability statement

The datasets generated and analyzed during the current study are available in the Medical Information Mart for Intensive Care IV (https://mimic.physionet.org/).

Author Contributions

Concept and design: Yuhong Jin, Xiaona Yi, Meixia Zheng, Junjie Yang, Shanshan Huang. Acquisition, analysis, or interpretation of data: Xiaona Yi, Xingkai Shen, Dongkai Li. Drafting of the manuscript: Xiaona Yi, Xiaoya Yang. Critical revision of the manuscript for important intellectual content: Xiaona Yi, Bingyang Liu. Statistical analysis: Xiaona Yi, Dongkai Li. Supervision: Yuhong Jin, Xiaona Yi.

References

1. Singer M, Deutschman CS, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA. 2016;315(8):801. 10.1001/jama.2016.0287.
2. Evans L. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Intensive Care Med* 2021 471181–1247. Published online 2021. 10.1007/s00134-021-06506-y

3. Fleischmann C, Scherag A, Adhikari NKJ, et al. Assessment of global incidence and mortality of hospital-treated sepsis. current estimates and limitations. Am J Respir Crit Care Med. 2016;193(3):259–72. 10.1164/rccm.201504-0781OC.
4. Rhee C, Dantes R, Epstein L, et al. Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009–2014. JAMA. 2017;318(13):1241. 10.1001/jama.2017.13836.
5. Fleischmann-Struzek C, Mellhammar L, Rose N, et al. Incidence and mortality of hospital- and ICU-treated sepsis: results from an updated and expanded systematic review and meta-analysis. Intensive Care Med. 2020;46(8):1552–62. 10.1007/s00134-020-06151-x.
6. Beyer D, Hoff J, Sommerfeld O, Zipprich A, Gaßler N, Press AT. The liver in sepsis: molecular mechanism of liver failure and their potential for clinical translation. Mol Med. 2022;28(1):84. 10.1186/s10020-022-00510-8.
7. Anderko RR, Gómez H, Canna SW, et al. Sepsis with liver dysfunction and coagulopathy predicts an inflammatory pattern of macrophage activation. Intensive Care Med Exp. 2022;10(1):6. 10.1186/s40635-022-00433-y.
8. De Baaij JHF, Hoenderop JGJ, Bindels RJM. Magnesium in man: Implications for health and disease. Physiol Rev. 2015;95(1):1–46. 10.1152/physrev.00012.2014.
9. Ye L, Zhang C, Duan Q, Shao Y, Zhou J. Association of magnesium depletion score with cardiovascular disease and its association with longitudinal mortality in patients with cardiovascular disease. J Am Heart Assoc. 2023;12(18):e030077. 10.1161/JAHA.123.030077.
10. Li W, Jiao Y, Wang L, et al. Association of serum magnesium with insulin resistance and type 2 diabetes among adults in China. Nutrients. 2022;14(9):1799. 10.3390/nu14091799.
11. Adebamowo SN, Jiménez MC, Chiuve SE, Spiegelman D, Willett WC, Rexrode KM. Plasma magnesium and risk of ischemic stroke among women. Stroke. 2014;45(10):2881–6. 10.1161/STROKEAHA.114.005917.
12. Tarleton EK, Kennedy AG, Rose GL, Crocker A, Littenberg B. The association between serum magnesium levels and depression in an adult primary care population. Nutrients. 2019;11(7):1475. 10.3390/nu11071475.
13. Santosh Raju K, BhaskaraRao JV, Naidu BTK, Sunil Kumar N. A study of hypomagnesemia in patients admitted to the ICU. Cureus. 2023;15(7):e41949. 10.7759/cureus.41949.
14. Zhang X, Zhao L, Dai Q, et al. Blood magnesium level and risk of hepatocellular carcinoma in a prospective liver cirrhosis cohort. Cancer Epidemiol Biomark Prev Publ Am Assoc Cancer Res Cosponsored Am Soc Prev Oncol. 2024;33(10):1368–74. 10.1158/1055-9965.EPI-24-0327.
15. Sharma R, Heidari A, Johnson RH, Advani S, Petersen G. Serum magnesium levels in hospitalized patients with SARS-CoV-2. J Investig Med. 2022;70(2):409–14. 10.1136/jim-2021-001948.
16. Wang H, Huang J, Jin X, et al. Hypermagnesaemia, but not hypomagnesaemia, is a predictor of inpatient mortality in critically ill children with sepsis. Dis Markers. 2022;2022:3893653. 10.1155/2022/3893653.
17. Elm EV, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. BMJ. 2007;335(7624):806–8. 10.1136/bmj.39335.541782.AD.

18. Feng M, McSparron JI, Kien DT, et al. Transthoracic echocardiography and mortality in sepsis: analysis of the MIMIC-III database. Intensive Care Med. 2018;44(6):884–92. 10.1007/s00134-018-5208-7.
19. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165–228. 10.1007/s00134-012-2769-8.
20. Liao Y, Zhang R, Shi S, et al. Triglyceride-glucose index linked to all-cause mortality in critically ill patients: a cohort of 3026 patients. Cardiovasc Diabetol. 2022;21(1):128. 10.1186/s12933-022-01563-z.
21. Li L. High serum magnesium level is associated with increased mortality in patients with sepsis: An international, multicenter retrospective study. Medcomm. 2024;5(10). 10.1002/mco2.713.
22. Franke T, Ho T, Christie CA. The chi-square test. Am J Eval. 2011;33(3):448–58. 10.1177/1098214011426594.
23. Kim JH. Multicollinearity and misleading statistical results. Korean J Anesthesiol. 2019;72(6):558–69. 10.4097/kja.19087.
24. Hellwege JN, Keaton JM, Giri A, Gao X, Edwards DRV, Edwards TL. Population stratification in genetic association studies. Curr Protoc Hum Genet. 2017;95(1). 10.1002/cphg.48.
25. Cheungpasitporn W, Hansrivijit P, Thirunavukkarasu S, et al. Association of serum magnesium level change with in-hospital mortality. BMJ Evid-Based Med. 2020;25(6):206–12. 10.1136/bmjebm-2019-111322.
26. Cidade-Rodrigues C, Cunha F, Elias C, et al. The prognostic impact of magnesium in acute heart failure is different according to the presence of diabetes mellitus. Porto Biomed J. 2022;7(6):e197. 10.1097/j.pbj.0000000000000197.
27. Tan L, Xu Q, Li C, Liu J, Shi R. High-normal serum magnesium and hypermagnesemia are associated with increased 30-day in-hospital mortality: A retrospective cohort study. Front Cardiovasc Med. 2021;8:625133. 10.3389/fcvm.2021.625133.
28. Yi X, Jin D, Huang S, et al. Association between lactate-to-albumin ratio and 28-days all-cause mortality in patients with sepsis-associated liver injury: a retrospective cohort study. BMC Infect Dis. 2024;24(1):65. 10.1186/s12879-024-08978-x.
29. Cui L, Bao J, Yu C, et al. Development of a nomogram for predicting 90-day mortality in patients with sepsis-associated liver injury. Sci Rep. 2023;13:3662. 10.1038/s41598-023-30235-5.
30. Liu Y, Sun R, Jiang H, et al. Development and validation of a predictive model for in-hospital mortality in patients with sepsis-associated liver injury. Ann Transl Med. 2022;10(18):997–997. 10.21037/atm-22-4319.
31. Nasser R, Naffaa ME, Mashiach T, Azzam ZS, Braun E. The association between serum magnesium levels and community-acquired pneumonia 30-day mortality. BMC Infect Dis. 2018;18(1). 10.1186/s12879-018-3627-2.
32. Zafar MSH, Wani JI, Karim R, Mir MM, Koul PA. Significance of serum magnesium levels in critically ill-patients. Int J Appl Basic Med Res. 2014;4(1):34. 10.4103/2229-516x.125690.
33. Pannem RB, Munamala CSR. An observational study on effects of hypomagnesemia among critically ill patients at a tertiary care hospital. Int J Adv Med. 2018;5(6):1347. 10.18203/2349-3933.ijam20184254.

34. Murata T, Dietrich HH, Horiuchi T, Hongo K, Dacey RG. Mechanisms of magnesium-induced vasodilation in cerebral penetrating arterioles. Neurosci Res. 2016;107:57–62. 10.1016/j.neures.2015.12.005.
35. Li □. – 2021 - Active supplementation with magnesium sulfate may be associated with worse prognosis in sepsis A re.pdf. Accessed January 28, 2025. https://www.researchsquare.com/article/rs-331143/v1.pdf
36. Li L, Li L, Zhao Q, et al. High serum magnesium level is associated with increased mortality in patients with sepsis: An international, multicenter retrospective study. MedComm. 2024;5(10):e713. 10.1002/mco2.713.
37. Strnad P, Tacke F, Koch A, Trautwein C. Liver — guardian, modifier and target of sepsis. Nat Rev Gastroenterol Hepatol. 2016;14(1):55–66. 10.1038/nrgastro.2016.168.
38. Song Y, Miao S, Li Y, Fu H. Ulinastatin attenuates liver injury and inflammation in a cecal ligation and puncture induced sepsis mouse model. J Cell Biochem. 2018;120(1):417–24. 10.1002/jcb.27396.
39. Aydın S, Şahin TT, Bacanlı M, et al. Resveratrol protects sepsis-induced oxidative DNA damage in liver and kidney of rats. Balk Med J. 2016;33(6):594–601. 10.5152/balkanmedj.2016.15516.
40. Hadi NR. Rebastinib attenuates liver injury following cecal ligation and puncture in male mice. J Med Life. 2023;16(11):1678–84. 10.25122/jml-2023-0089.
41. Xu S, Xu J, Hao T, et al. Paeonol alleviates lipopolysaccharide–induced hepatocytes injury through alteration of mitochondrial function and NF–κB translocation. Mol Med Rep. 2021;24(5). 10.3892/mmr.2021.12419.
42. Song Z, Meng L, He Z, et al. LBP protects hepatocyte mitochondrial function via the PPAR-CYP4A2 signaling pathway in a rat sepsis model. Shock. 2021;56(6):1066–79. 10.1097/shk.0000000000001808.
43. Cerrah S, Cadirci E, OKÇU N, Deveci Ö. The determination of the protective role of sildenafil administration in rats with sepsis-induced liver injury. Turk J Trauma Emerg Surg. Published online 2023. 10.14744/tjtes.2022.45605
44. Yang Q, Ouyang J, Yang J. Sepsis as an important risk factor for gastrointestinal bleeding in acute coronary syndrome patients. Med (Baltim). 2018;97(36):e12273. 10.1097/md.0000000000012273.
45. Cho JY, Choi SM, Yu SJ, et al. Bleeding complications in critically ill patients with liver cirrhosis. Korean J Intern Med. 2016;31(2):288–95. 10.3904/kjim.2014.152.
46. Søgaard M, Skjøth F, Kjældgaard JN, Lip GY, Larsen TB. Bleeding complications in anticoagulated patients with atrial fibrillation and sepsis: A propensity-weighted cohort study. J Am Heart Assoc. 2017;6(11). 10.1161/jaha.117.007453.
47. Barletta JF. Histamine-2-receptor antagonist administration and gastrointestinal bleeding when used for stress ulcer prophylaxis in patients with severe sepsis or septic shock. Ann Pharmacother. 2014;48(10):1276–81. 10.1177/1060028014540513.

Figures

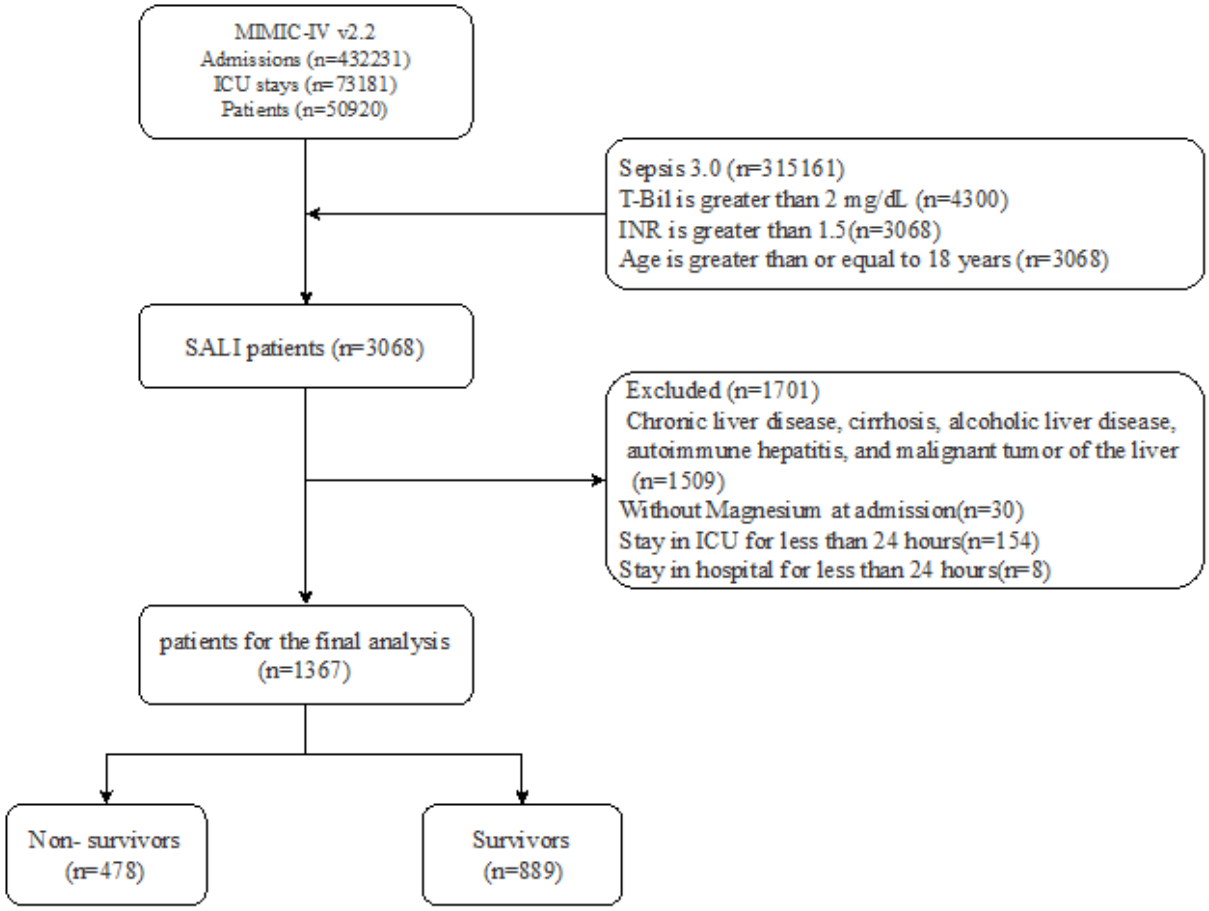


Figure 1

Study flowchart.

MIMIC, Medical Information Mart for Intensive Care; SALI, Sepsis-associated liver injury

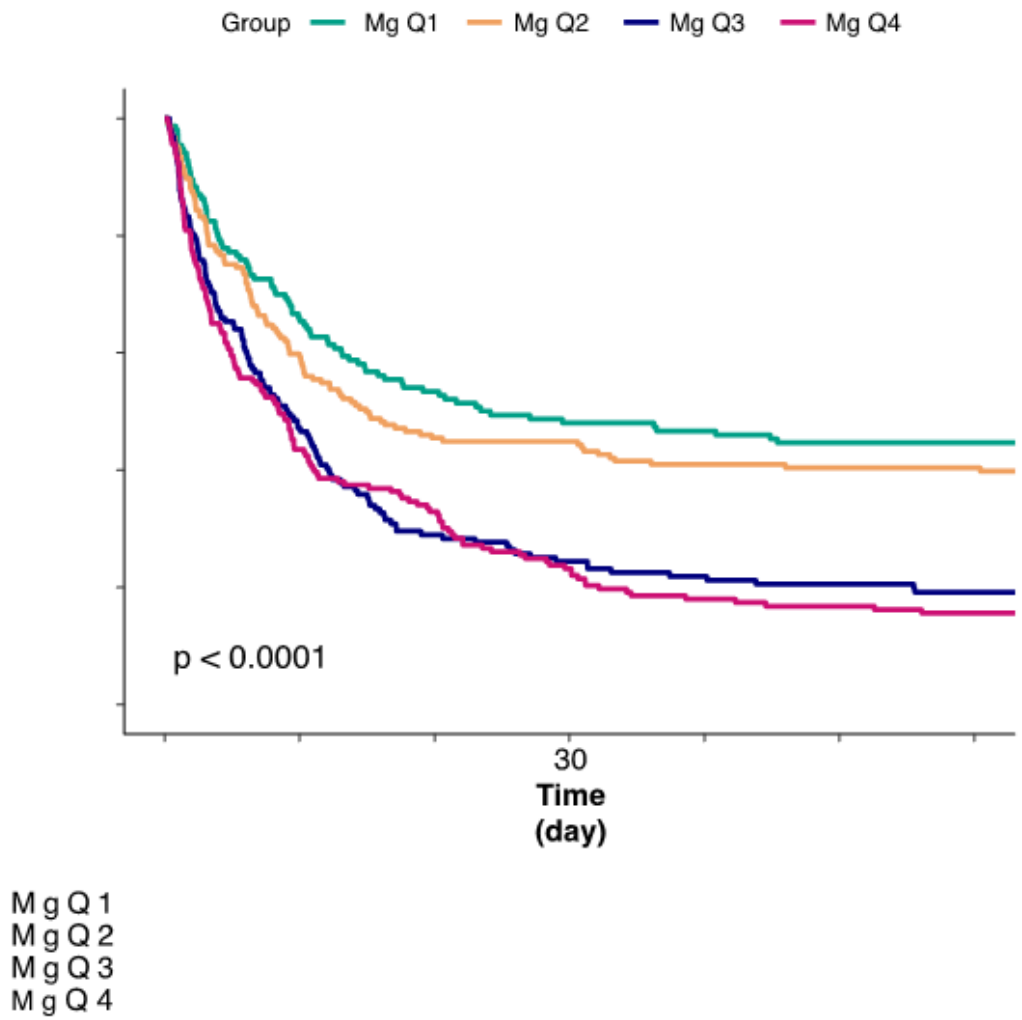


Figure 2

Kaplan-Meier survival analysis curve for in-hospital mortality.

The Serum Magnesium was grouped according to the quartile, the survival curve of the four groups is shown in the figure, and the shaded area represents the 95% confidence interval.

Serum Magnesium (mg/dL): Q1 (<0.8); Q2 (0.8,1.8); Q3 (1.8,2.1); Q4 (≧2.1)

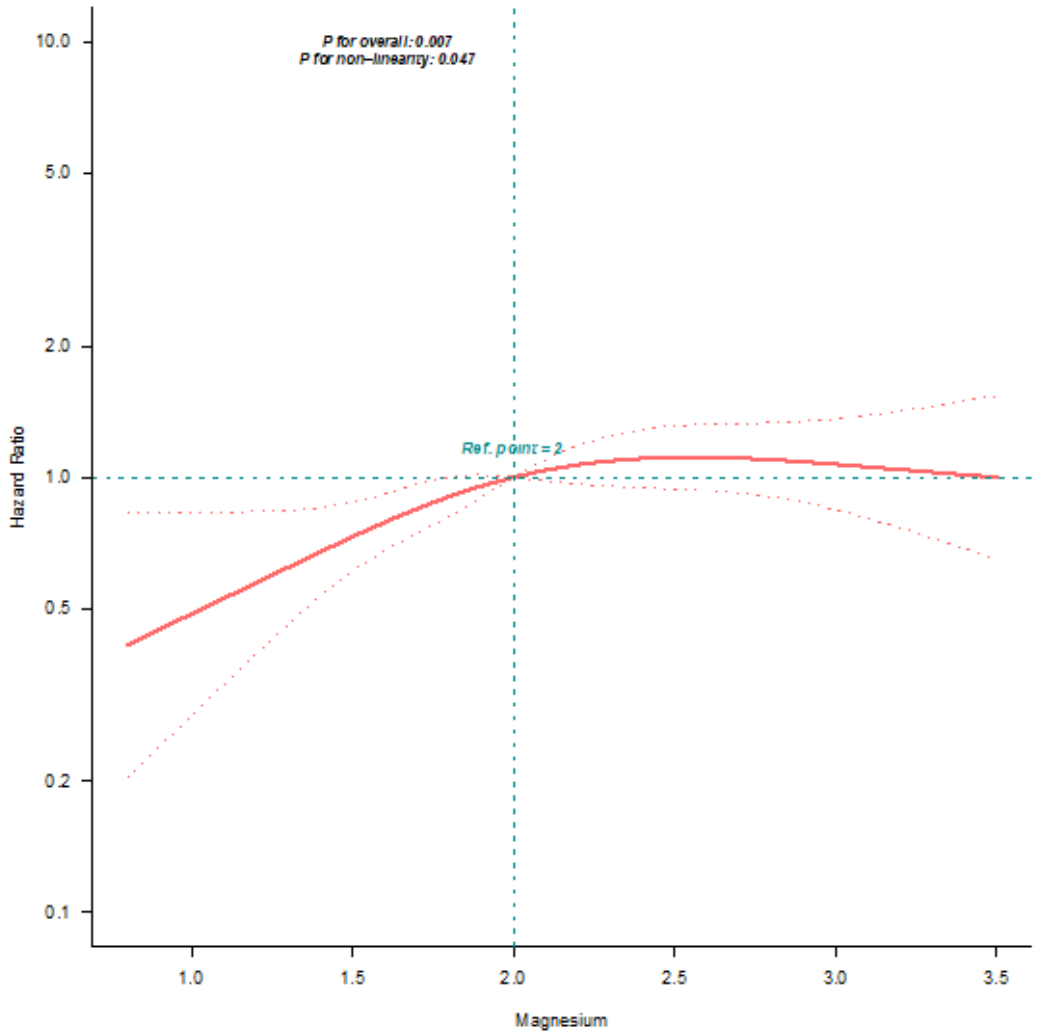


Figure 3

Restricted cubic spline regression analysis of Serum Magnesium in-hospital all-cause mortality.

The thick solid lines represent the estimated adjusted risk ratios, while the dashed bands illustrate the 95% confidence intervals.

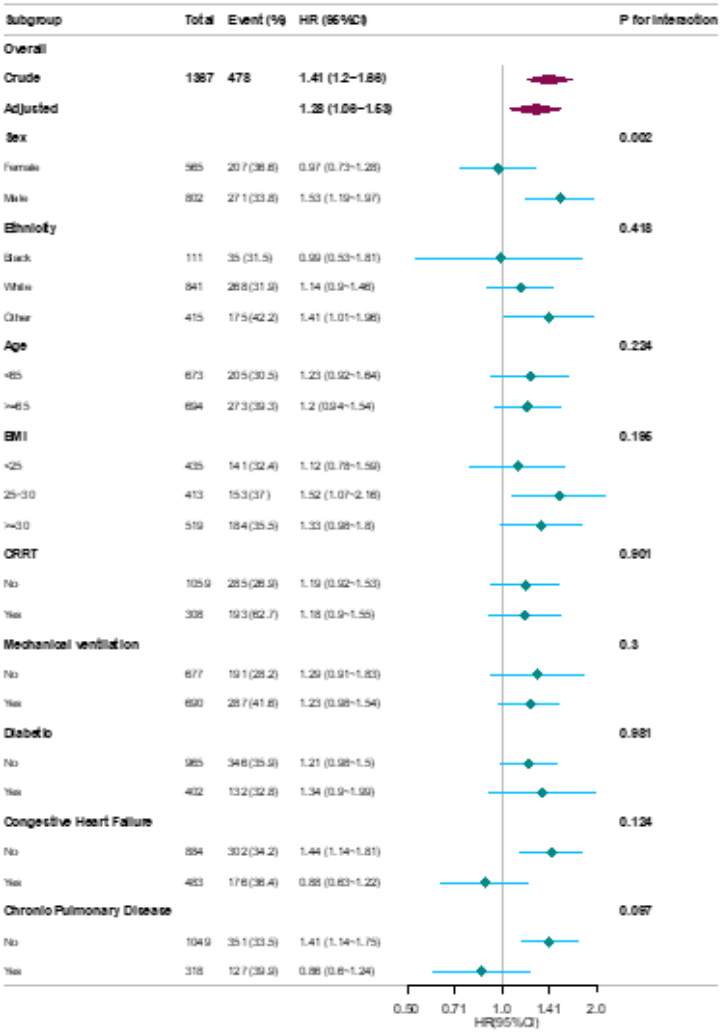


Figure 4

Subgroup Analyses and Interaction for in-hospital mortality.

The stratification factor was not used as an adjustment variable. The small diamonds represent hazard ratios, and the horizontal line represents the 95% confidence interval. The large diamonds represent the overall HRs, whereas the outer points of the diamonds represent a 95% confidence interval.

BMI body mass index, CRRT Continuous renal replacement therapy.

Supplementary Files

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- SupplementaryTable1Percentageofmissingdata.docx
- SupplementaryTable2Multipleimputation.docx
- Supplementarytable3Univariatecoxanalysis.docx

- SupplementaryTable4Coxinflectionpointanalysis.docx
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