CLINICAL RESEARCH STUDY

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Association of Serum Magnesium on Mortality in Patients Admitted to the Intensive Cardiac Care Unit

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ABSTRACT

BACKGROUND: Although electrolyte disturbances may affect cardiac action potential, little is known about the association between serum magnesium and corrected QT (QTc) interval as well as clinical outcomes.
METHODS: A consecutive 8498 patients admitted to the Mayo Clinic Hospital—Rochester cardiac care unit (CCU) from January 1, 2004 through December 31, 2013 with 2 or more documented serum magnesium levels, were studied to test the hypothesis that serum magnesium levels are associated with in-hospital mortality, sudden cardiac death, and QTc interval.
RESULTS: Patients were 67 ± 15 years; 62.2% were male. The primary diagnoses for CCU admissions were acute myocardial infarction (50.7%) and acute decompensated heart failure (42.5%), respectively. Patients with higher magnesium levels were older, more likely male, and had lower glomerular filtration rates. After multivariate analyses adjusted for clinical characteristics including kidney disease and serum potassium, admission serum magnesium levels were not associated with QTc interval or sudden cardiac death. However, the admission magnesium levels ≥2.4 mg/dL were independently associated with an increase in mortality when compared with the reference level (2.0 to <2.2 mg/dL), having an adjusted odds ratio of 1.80 and a 95% confidence interval of 1.25-2.59. The sensitivity analysis examining the association between postadmission magnesium and analysis that excluded patients with kidney failure and those with abnormal serum potassium yielded similar results.
CONCLUSION: This retrospective study unexpectedly observed no association between serum magnesium levels and QTc interval or sudden cardiac death. However, serum magnesium ≥2.4 mg/dL was an independent predictor of increased hospital morality among CCU patients.
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KEYWORDS: Acquired long-QT syndrome; Hypermagnesemia; Hypomagnesemia; Magnesium; Mortality; Ventricular arrhythmias; Sudden cardiac death; QTc interval

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Electrolyte disturbance, particularly hypokalemia and hypocalcemia, affects cardiac repolarization. Several studies in an early era have proposed that low serum magnesium may increase the risk of an acquired QT prolongation and torsade de pointes.[1-6] However, these studies were conducted in the setting of concomitant hypokalemia and the administration of antiarrhythmic drugs. Subsequent studies in isolated extracellular magnesium depletion were not able to reproduce the direct link between magnesium and the corrected QT (QTc) interval. Furthermore, population-based studies of patients with chronic renal disease and congestive heart failure found that both lowest and highest magnesium ranges were independently associated with greater mortality, after adjusting for other comorbidities.[7,8]

CLINICAL SIGNIFICANCE

- Serum magnesium levels are frequently obtained in patients admitted to the hospital.
- Admission and postadmission serum magnesium levels of ≥2.4 mg/dL are an independent marker of in-hospital mortality among cardiac care unit patients.
- Caution may be warranted to not overcorrect magnesium levels among hospitalized patients.

Although the effects of serum magnesium on clinical outcomes remain controversial, surveillance of serum magnesium levels is a common practice considering that it is a modifiable factor.[2,9-11] Consensus among various experts recommends maintaining serum magnesium levels >2 mg/dL among patients at risk for arrhythmias.[6] However, an optimal range of serum magnesium cannot be recommended with certainty. In addition, patients admitted to the cardiac care unit (CCU) may be at a greater risk for cardiovascular adverse effects from electrolyte disturbances, given their additional risks of QTc prolongation and ventricular arrhythmias. To fill this knowledge gap, this study utilized the CCU database to examine the level-dependent effects of the serum magnesium on 3 outcomes including hospital mortality; sudden cardiac death, defined as death secondary to sustained ventricular tachycardia or ventricular fibrillation; and QTc intervals.

In this study, serum magnesium included the admission levels that were measured at the time of the CCU admission. These were less likely to have been confounded by events occurring during the CCU course. We also included mean postadmission levels, which were the potentially modifiable subjects and possible targets for treatment.[12]

METHODS

The Mayo Clinic Institutional Review Board approved this study and waived the requirement for individual consent. This retrospective study utilized data from the Multidisciplinary Epidemiology and Translational Research in Intensive Care Data Mart, and interrogated using an automated query-building tool called Data Discovery and Query Builder. The Translational Research in Intensive Care Data Mart is an exhaustive research database that stores patient health information gathered from patients' electronic health records for both inpatients and outpatients at the Mayo Clinic Hospital in Rochester, Minn.[13]

Eligibility criteria encompassed all consecutive patients who were ≥18 years of age at the time of CCU admission from January 1, 2004 through December 31, 2013. All patients had at least 2 serum magnesium and potassium measurements during their hospitalizations. Patients with recurrent admissions and those who declined authorization of their records were excluded (n = 1077). The final cohort comprised 8498 consecutive patients admitted to the CCU at Mayo Clinic Hospital − Rochester.

Data Collection

The following was abstracted from the electronic health record using the Data Discovery and Query Builder: clinical characteristics, preexisting comorbidities, and laboratory data. This method of abstraction was previously validated with a sensitivity of ≥92% and a specificity of ≥98%.[14] Antiarrhythmic drugs including nondihydropyridine calcium channel blockers, beta-blockers, medications known to cause a prolonged QT interval (Appendix, Supplementary Table 1, available online),[15,16] diuretics, and electrolyte replacements given during the CCU admission were reviewed from the Electronic Medication Administration Record by 2 authors (CK and CT) blinded to the analysis of the study. Causes of death in patients who had died during their hospitalizations were reviewed from many resources, including the telemetry, when available, the autopsy report, and the physician's last medical note by SS, JYP, and ANR, blinded to other analysis. Sudden cardiac death was defined as death primarily due to ventricular fibrillation or tachycardia.

Serum Electrolytes

Our primary interest was the admission serum magnesium levels, which were defined as the first level obtained upon admission to the CCU. The rationale was that these levels were less likely to be affected by potential confounders occurring during hospitalization. We also reported the mean of postadmission magnesium levels, which were defined as the mean of serum electrolytes after excluding the first measurement. These postadmission electrolyte levels were likely modifiable subjects.[12] The reference for serum magnesium levels of 2.0 to <2.2 mg/dL were selected on the basis of reviewing relevant literature, as well as an acceptable normal range from our laboratory.[6,17]

Corrected QT Interval

The measurements of QT intervals and QRS complexes were obtained from the automated standard 12-lead electrocardiogram (GE, Marquette Medical Systems, Milwaukee, Wis). The QT intervals were calculated by the stepwise approach. First, to account for an abnormal depolarization, in patients with QRS complexes wider than 120 ms, the additional QRS width was subtracted from the QT interval.[18] We then applied the Bazett formula to calculate the QTc interval.[18]

Statistical Analysis

Continuous variables are presented as mean ± standard deviation or median (interquartile range [IQR]) and compared using the analysis of variance test. Categorical variables were reported as counts with percentages and compared using the chi-squared test.

The association between the admission magnesium levels and in-hospital mortality as well as sudden cardiac death was determined using a multivariate logistic regression and reported as the adjusted odds ratio (AOR) with a 95% confidence interval (CI). Variables included in the multivariate model were age, male, white, acute myocardial infarction, cardiac arrest, cardiogenic shock, heart failure, stroke, baseline QRS complex, baseline glomerular filtration rate (GFR), admission serum potassium, and admission serum ionized calcium. The association between the admission magnesium levels and admission QTc intervals was assessed using a multivariate linear regression. Linear regression coefficients (B) with 95% CI were reported. This represents the differences in the QTc intervals at the respective serum electrolyte strata.

Using a similar method to the main analysis, we performed a sensitivity analysis to examine the associations between the postadmission magnesium levels and the following: in-hospital mortality, sudden cardiac death, and postadmission QTc intervals. In this model, postadmission serum electrolyte levels, postadmission QRS complex, left ventricular ejection fraction, and medications given during the CCU stay (antiarrhythmic drugs, nondihydropyridine calcium channel blockers, beta-blockers, potential medications known to cause QT interval prolongation, and electrolyte supplements) were also included. All comparisons were 2-sided, and a P value $<.05$ was considered statistically significant. Statistical analyses were performed using JMP statistical software version 9.0 (SAS, Cary, NC) and MedCalc version 12.5 (Ostend, Belgium).

RESULTS

Study Cohort

Patients were 67 ± 15 years, and 62.2% were male. The primary diagnoses for CCU admission were acute myocardial infarction (50.7%) and acute decompensated heart failure (42.5%). A total of 27,657 serum magnesium measurements were included in this analysis, with a median of 3 (IQR 2, 5) times per each patient. The mean of the admission magnesium levels and postadmission levels was 2.0 ± 0.3 mg/dL and 2.0 ± 0.7 mg/dL, respectively.

Table 1 displays the complex relationships between baseline characteristics of the study patients according to different magnesium strata. Patients with higher magnesium levels were older, more likely to be male, and tended to have lower baseline GFRs, compared with patients with lower magnesium levels (P <.001 for all comparisons). Moreover, the patients with higher serum magnesium tended to have lower left ventricular ejection fraction and were more likely to be on antiarrhythmic drugs, with P <.001 for comparisons. However, the prevalence of potentially QT-prolonging medications was similar across each group. The proportion of acute myocardial infarction was lower in those with higher magnesium strata. The relationship between the mean serum magnesium levels and baseline variables was U-shaped for cardiac arrest, cardiogenic shock, and heart failure. Other characteristics including race, baseline serum potassium, and serum ionized calcium were relatively flat across different magnesium levels.

Serum Electrolyte Levels and Hospital Mortality

Of the total cohort, the hospital mortality was 7.0%. There was a relatively flat curved relation between serum magnesium and the hospital mortality, as shown in Figure 1. In the univariate analysis, an increase in each unit of serum magnesium was associated with a 1.74-fold increased hospital mortality (95% CI, 1.39-2.18; P <.0001). In the multivariate analysis, only magnesium level ≥2.4 mg/dL was an independent predictor of mortality, with AOR 1.80; 95% CI, 1.25-2.59 (Table 2).

To exclude renal disease or renal hypoperfusion as a potential link for the relationship between hypermagnesemia and increased mortality, subgroup analysis was performed among patients without chronic kidney disease. Serum magnesium of ≥2.4 mg/dL remained an independent risk of hospital mortality after excluding renal disease. Hypermagnesemia was again an independent risk factor in subgroup analysis of patients with acute myocardial infarction and acute decompensated heart failure. However, magnesium ≥2.4 mg/dL was not independently associated with mortality in patients with cardiac arrest or cardiogenic shock, as seen in Figure 2 and Supplementary Table 2, available online.

Sensitivity analysis for postadmission potassium and hospital mortality yielded consistent results with an AOR of 2.20 (95% CI, 1.42-3.40), as shown in Table 2. In addition, the hospital mortality was greater among patients with both admission and postadmission magnesium at the highest level, compared with patients with serum magnesium levels <2.4 mg/dL at all times, 12% vs 6% (AOR 1.63; 95% CI, 1.15-2.30).

Table 1 Characteristics of the Study Patients According to Admission Magnesium Levels

	Mg <1.8 mg/dL n = 1484	Mg 1.8-<2.0 mg/dL n = 2150	Mg 2.0-<2.2 mg/dL n = 2428	Mg 2.2-<2.4 mg/dL n = 1416	Mg ≥2.4 mg/dL n = 1020	*P*-Value
Age, mean ± SD, years	66.2 ± 15.7	67.3 ± 14.8	67.3 ± 14.9	67.5 ± 14.8	69.5 ± 15.4	<.001
Male, n (%)	777 (52.4)	1294 (60.2)	1599 (65.9)	926 (65.4)	689 (67.6)	<.001
White, n (%)	1245 (83.9)	1813 (84.3)	2061 (84.9)	1199 (84.7)	849 (83.2)	.77
AMI, n (%)	788 (53.1)	1185 (55.1)	1300 (53.5)	679 (48.0)	360 (35.3)	<.001
Cardiac arrest, n (%)	165 (11.1)	185 (8.6)	184 (7.6)	100 (7.1)	107 (10.5)	<.001
Cardiogenic shock, n (%)	181 (12.2)	176 (8.2)	153 (6.3)	108 (7.6)	124 (12.2)	<.001
Heart failure, n (%)	619 (41.7)	835 (38.8)	926 (38.1)	615 (43.4)	615 (60.3)	<.001
Stroke, n (%)	102 (6.9)	133 (6.2)	162 (6.4)	91 (6.4)	67 (6.6)	.91
First QRS complex, ms	107.5 ± 31.1	108.6 ± 30.2	112.5 ± 32.5	113.4 ± 33.5	123.9 ± 37.3	<.001
GFR, mL/min	71.3 ± 40.1	72.6 ± 30.6	71.3 ± 30.3	66.8 ± 44.0	50.3 ± 29.4	<.001
Admission potassium, mEq/L	4.0 ± 0.6	4.2 ± 0.6	4.2 ± 0.6	4.3 ± 0.6	4.6 ± 0.8	<.001
Admission ionized calcium, mg/dL	4.6 ± 0.4	4.7 ± 0.4	4.8 ± 0.4	4.8 ± 0.3	4.7 ± 0.4	<.001
Left ventricular ejection fraction, %	49.6 ± 0.5	48.0 ± 0.4	47.4 ± 0.4	46.6 ± 0.6	43.8 ± 0.9	<.001
Postadmission potassium, mEq/L	4.0 ± 0.6	4.2 ± 0.6	4.2 ± 0.6	4.3 ± 0.6	4.6 ± 0.8	<.001
Postadmission calcium, mg/dL	4.6 ± 0.4	4.7 ± 0.4	4.8 ± 0.4	4.8 ± 0.3	4.7 ± 0.4	<.001
Medications						
Antiarrhythmic drugs,* n (%)	337 (21.6)	759 (26.7)	746 (29.5)	300 (29.3)	174 (32.6)	<.001
Beta-blockers, n (%)	1073 (68.8)	2113 (74.2)	1822 (71.9)	715 (69.9)	332 (62.2)	<.001
Other at risk medications,† n (%)	795 (51.0)	1419 (49.8)	1231 (48.6)	487 (47.6)	267 (50.0)	.44
Potassium repletion, n (%)	676 (42.5)	1199 (41.4)	963 (37.4)	373 (35.8)	183 (33.5)	<.001
Calcium repletion, n (%)	340 (21.4)	621 (21.4)	533 (20.7)	232 (22.3)	124 (22.7)	<.001
Magnesium repletion, n (%)	634 (39.8)	834 (28.8)	474 (18.4)	141 (13.5)	65 (11.9)	<.001

AMI = acute myocardial infarction; GFR = glomerular filtration rate (mL/min).

*Medications known to cause QT prolongation including amiodarone, digoxin, diltiazem, disopyramide, flecainide, lidocaine, mexiletine, procainamide, propafenone, quinidine, ranolazine, sotalol, verapamil.

†See Supplementary Table 1, available online.

Serum Electrolyte Levels and Sudden Cardiac Death

There were 113 patients (1.5%) whose causes of death were primarily due to ventricular arrhythmias. The prevalence of sudden cardiac death in different magnesium strata was relatively flat, but highest in the patients with serum magnesium >2.4 mg/dL, with P <.0001 (**Figure 1**). However, in the multivariate analysis, sudden cardiac death occurred equally in patients with different magnesium levels, as shown in **Table 2**.

Serum Magnesium Levels and the QTc Intervals

There were 43,381 standard electrocardiograms obtained during CCU admission per patient (4 IQR [3, 7] per patient). **Figure 3** presents the likelihood of longer QTc intervals and QRS complexes among patients with higher magnesium levels. However, in the multivariate analysis, there was no direct association between serum magnesium levels and QTc intervals, as shown in **Table 2**.

DISCUSSION

This hospital database analysis, which examined the associations between serum magnesium levels and clinical outcomes in patients admitted to the CCU observes some unexpected results. There is no level-dependent relationship between serum magnesium and QTc interval or the prevalence of sudden cardiac death. Although there is a trend of serum magnesium >2.4 mg/dL relating to a prolonged QTc interval, this is not statistically significant after adjusting for QRS width. Further, serum magnesium levels of ≥2.4 mg/dL are independently associated with an increase in hospital mortality. Importantly, this finding is consistent even after excluding renal disease, thus making low GFR and resulting

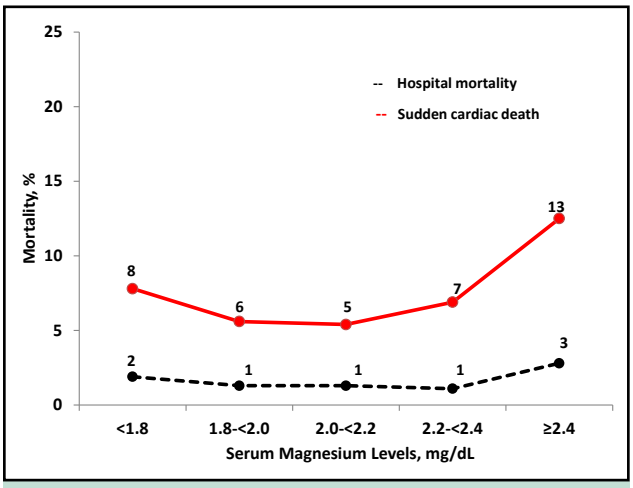

Figure 1 Hospital mortality and sudden cardiac death by admission serum magnesium levels.

renal hypoperfusion an unlikely link between hypermagnesemia and increased mortality. Our findings suggest that serum magnesium >2.4 mg/dL may have an inhibitory effect on cardiac function (as suggested by an observed trend of widened QRS complexes) and is a marker of adverse outcomes among a variety of patients admitted to the CCU.

Hypomagnesemia is a hypothetical cause of an acquired prolonged QTc syndrome. But in contrast to this conventional knowledge, this study found no association between serum magnesium levels and QTc intervals, as well as sudden cardiac death. In the absence of previous systemic study, the explanation for our findings remains plausible. First, the general concept of hypomagnesemia related to the arrhythmogenic tendency has stemmed from early case series in the setting of concomitant hypokalemia and administration of high-risk antiarrhythmic drugs including digitalis, quinidine, disopyramide, procainamide, and amiodarone.[2,9-11,19] Our analysis, which has adjusted for these factors, perhaps has disclosed the null relationship between serum magnesium and the QT interval. In fact, our findings are in line with subsequent studies conducted in the setting of normal other electrolytes and an absence of antiarrhythmic drugs, which showed that low serum magnesium levels did not alter the repolarization.[9,20,21]

Secondly, magnesium is mostly stored intracellularly and not well correlated with the serum level.[21] As a result, the effect of serum measurements on cardiac action potential may not link. This may be an explanation of inconsistent reports on the relationship between serum magnesium and the QTc interval.

The only prospective study in a human setting found the paradoxical result that lower serum magnesium levels were related to a less pronounced increase in the QTc interval among patients with subarachnoid hemorrhage, which is similar to our observation.[22] This may be explained by a complex, yet unclear, interaction between magnesium and the cardiac action potential.[23] Magnesium is an important

Table 2 Association Between Admission and Postadmission Serum Magnesium Levels and Hospital Mortality, Sudden Cardiac Death, and QTc intervals

	Serum Magnesium Levels (mg/dL)									
	<1.8 n = 1484		1.8-<2.0 n = 2150		2.0-<2.2 n = 2428		2.2-<2.4 n = 1416		≥2.4 n = 1020	
	Admission	Postadmission	Admission	Postadmission	Admission/ Postadmission	Admission	Postadmission	Admission	Postadmission	
Hospital mortality: AOR (95% CI)	1.04 (0.74-1.45)	0.81 (0.55-1.19)	0.85 (0.64-1.14)	0.75 (0.56-1.02)	Reference	1.24 (0.88-1.74)	1.37 (0.96-1.94)	1.80 (1.25-2.59)	2.20 (1.42-3.40)	
SCD: AOR (95% CI)	0.92 (0.46-1.81)	0.57 (0.24-1.32)	1.06 (0.54-2.07)	0.76 (0.38-1.53)	Reference	0.64 (0.30-1.32)	0.82 (0.34-1.90)	1.10 (0.57-2.14)	1.39 (0.55-3.48)	
QTc interval: Adjusted LRC* (95% CI)	−2.1 (−6.3-2.1)	0.2 (−2.1-2.4)	−2.3 (−5.6-1.0)	0.6 (−0.9-2.0)	Reference	1.9 (−1.7-5.5)	1.1 (−1.0-3.2)	2.1 (−1.8-6.1)	0.1 (−2.9-3.1)	

AOR = adjusted odds ratio; CI = confidence interval; LRC = linear regression coefficient (B); Mg = magnesium; OR = odds ratio; SCD = sudden cardiac death.
*Change in QT interval per a change in serum electrolyte strata.

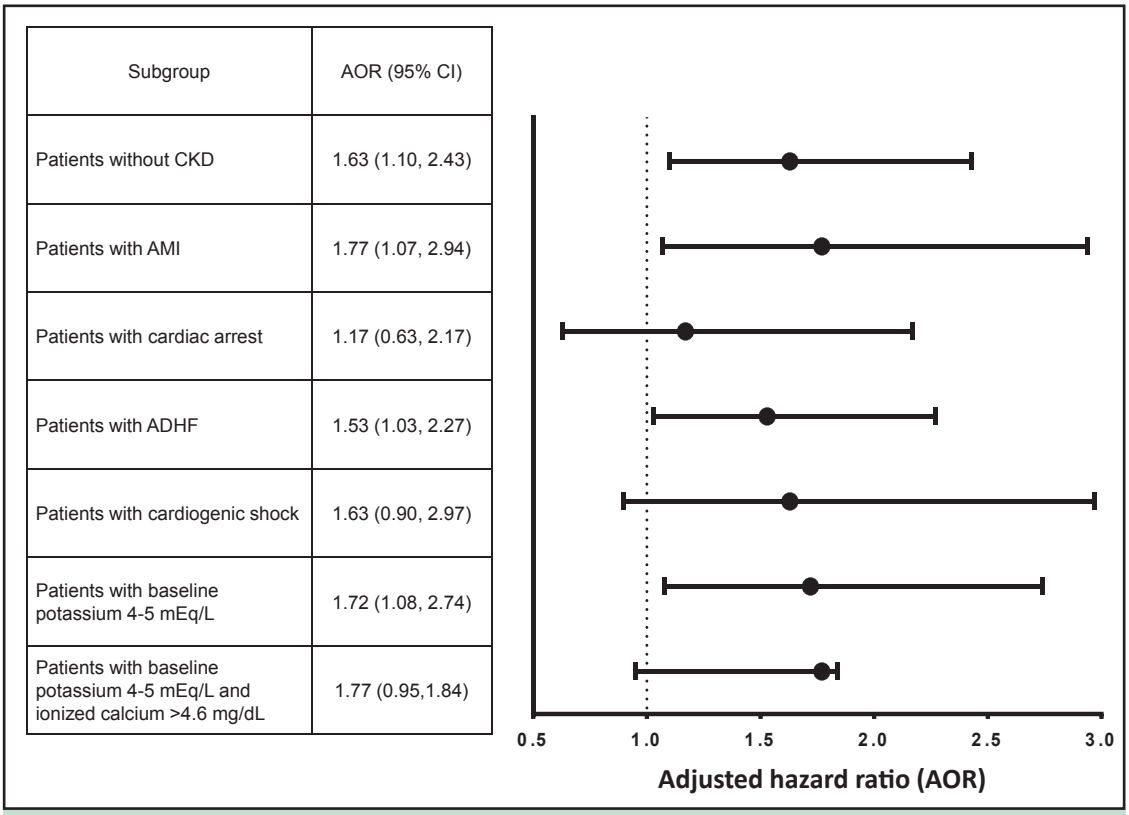

Figure 2 Adjusted odds ratio (AOR) for association between serum magnesium >2.4 g/dL and hospital mortality in subgroup analysis. ADHF = acute decompensated heart failure; AMI = acute myocardial infarction; CI = confidence interval; CKD = chronic kidney disease.

cofactor of the Na-K-ATPase pump; thus, its depletion may manifest as hyperpolarization and cause a wide QRS complex, as demonstrated in this current study.

Finally, the null effect of serum magnesium levels on the QTc interval may simply reflect the study cohort's characteristics. In this real-world CCU population, patients already had a slightly prolonged QTc interval, which was likely due to an underlying cardiac disease, comorbidities, drug effects, activation of a neurohormonal system, and alteration of the ionic channels from acute illness.[24,25] As a result, the effect of other factors on the QTc interval may not be easily reproduced.

Our study also found that high serum magnesium was an independent factor of hospital mortality among CCU

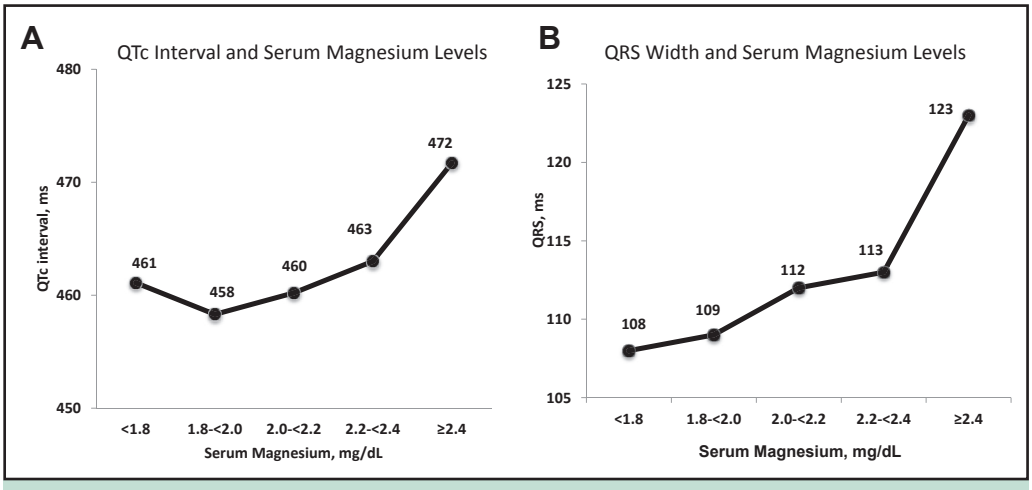

Figure 3 (**A** and **B**) Corrected QT (QTc) and QRS intervals by admission serum magnesium, respectively.

patients. Although this cannot be translated into a recommended serum magnesium level, it appears that high serum magnesium levels may not be preferable. Prior studies have reported an inconclusive association between serum magnesium and mortality. Higher serum magnesium reduced ventricular ectopy in studies of small numbers of patients with congestive heart failure on diuretics.[26,27] However, in a post hoc analysis of the Prospective Randomized Milrinone Survival Evaluation (PROMISE), which enrolled 1068 patients, only the magnesium levels of >2.3 mg/dL were associated with greater all-cause mortality.[28] We have extended the previous studies by examining the entire ranges of serum magnesium and their related hospital mortality in a CCU population with various cardiovascular diseases. Further, we were able to show the consistent findings that both first and postadmission serum magnesium levels ≥2.4 mg/dL were associated with increased hospital mortality. Our findings, therefore, suggest that hypermagnesemia may be a marker of adverse outcomes among CCU patients.

Limitations

Several limitations in this study merit comment. A retrospective cohort study design is vulnerable to confounders of which the causative relationships cannot be confirmed. Particularly, an increased risk of hospital mortality in patients with extremely high magnesium abnormalities may represent the severity of underlying illnesses rather than the causative effect. However, we performed several subgroup analyses with consistent results. Secondly, the perfect formula to correct the QT interval remains debatable. To minimize the effect of repolarization, we adjusted the QT intervals by correcting for the width of the QRS complex.[29] Although the Bazett equation is one of the most commonly used formulas, it has a tendency to overcorrect the QT interval when the heart rate is too slow or too fast.[30-32] Further, our study did not aim to investigate the benefit of administration of magnesium for treatment during cardiac arrest. The subgroup analysis of cardiac arrest showed no association between serum magnesium and hospital mortality. Indeed, experts have recommended intravenous magnesium for patients who have developed cardiac arrest secondary to torsade de pointes, regardless of their serum level, given its therapeutic effect on suppression of early depolarization and ventricular arrhythmias.[9,10] Finally, our findings may not be applicable to cohorts of a nonhospital setting. For instance, patients on chronic diuretic therapy are at risk for tissue magnesium depletion and concomitant hypokalemia; therefore, attention to maintenance of serum magnesium is reasonable.[33]

CONCLUSIONS

This hospital-based cohort found that serum magnesium is not independently associated with a prolongation of QTc intervals or the risk of sudden cardiac death when adjusted for serum potassium and serum calcium abnormalities and antiarrhythmic drugs. Although it contradicts the conventional concept, this observation is in line with prior studies in the setting of low magnesium alone. Nonetheless, we do not suggest the ignorance of serum magnesium surveillance among patients admitted to the CCU given their potential exposure to other risks of acquired QTc prolongation. Our findings, however, have supplemented the common practice of monitoring serum magnesium; a level above 2.4 mg/dL is an independent marker of mortality, and thus caution may be warranted to not overcorrect magnesium levels.

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SUPPLEMENTARY DATA

Supplementary table accompanying this article can be found in the online version at http://dx.doi.org/10.1016/j.amjmed.2016.08.033.

APPENDIX

Supplementary Table 1 Medications Known to Cause QTc Prolongation[15,16]

Amitriptyline	Itraconazole	Ranitidine
Amoxapine	Ketoprofen	Saquinavir
Atazanavir	Levofloxacin	Sertraline
Azithromycin	Lithium	Sulfamethoxazole and trimethoprim
Baclofen	Lopinavir/Ritonavir	Sunitinib
Citalopram	Methadone	Tacrolimus
Clomipramine	Mirtazapine	Tamoxifen
Clozapine	Moxifloxacin	Telithromycin
Desipramine	Nortriptyline	Thioridazine
Doxepin	Ondansetron	Tizanidine
Escitalopram	Paliperidone	Trazodone
Famotidine	Paroxetine	Trimethoprim
Fluoxetine	Pentamidine	Venlafaxine
Fluphenazine	Pimozide	Voriconazole
Flurazepam	Posaconazole	Vorinostat
Imipramine	Promethazine	Zaleplon
Isradipine	Protriptyline	

QTc = corrected QT.

Supplementary Table 2 Association Between Initial Serum Magnesium Levels and Hospital Mortality in Subgroup Analysis*

	n	Mg <1.8 mg/dL†	Mg 1.8-<2.0 mg/dL†	Mg 2.0-<2.2 mg/dL†	Mg 2.2 <2.4 mg/dL†	Mg ≥2.4 mg/dL†
Patients without baseline CKD	4020	1.28 (0.88-1.87)	0.88 (0.60-1.28)	Reference	1.27 (0.86-1.87)	1.63 (1.10-2.43)
Patients with AMI	4312	1.00 (0.61-1.61)	0.82 (0.50-1.28)	Reference	0.94 (1.59-1.06)	1.77 (1.07-2.94)
Patients with cardiac arrest	616	1.01 (0.59-1.74)	0.65 (0.37-1.13)	Reference	1.17 (0.64-2.13)	1.17 (0.63-2.17)
Patients with ADHF	2446	1.23 (0.80-1.88)	1.00 (0.66-1.51)	Reference	1.20 (0.79-1.83)	1.53 (1.03-2.27)
Patients with cardiogenic shock	742	0.83 (0.45-1.52)	0.92 (0.51-1.67)	Reference	0.91 (1.76-1.10)	1.63 (0.90-2.97)
Patients with baseline potassium 4-5 mEq/L	4778	1.12 (0.68-1.81)	0.67 (0.41-1.09)	Reference	1.10 (0.69-1.75)	1.72 (1.08-2.74)
Patients with baseline potassium 4-5 mEq/L and ionized calcium >4.6 mg/dL	2189	1.59 (0.85-2.95)	0.74 (0.74-1.39)	Reference	1.26 (0.70=2.25)	1.77 (0.95-1.84)

ADHF = acute decompensated heart failure; Mg = magnesium; AMI = acute myocardial infarct; CKD = chronic kidney disease.

*Adjusted for age, male, White, acute myocardial infarction, cardiac arrest, cardiogenic shock, heart failure, stroke, baseline QRS complex, baseline glomerular filtration rate, initial serum potassium, and initial serum ionized calcium.

†Adjusted odds ratio (95% confidence interval).