Association of Magnesium with Mortality in CKD and ESRD A Systematic Review and Meta-analysis of Cohort Studies

Jiachuan Xiong¹MD; Min Wang² MD; Ting He¹ MD; Jinghong Zhao¹ MD, Ph. D* ¹Department of Nephrology, Xinqiao Hospital, Third Military Medical University, Chongqing, 400037, P.R. China ²Department of Otorhinolaryngology and Head-Neck Surgery, Xinqiao Hospital, Third Military Medical University, Chongqing, 400037, P.R. China.



Magnesium has essential roles in a variety of physiological functions within human cells. Previous studies reported that

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Random, 95% CI	Hazard Ratio IV, Random, 95% CI		
1.1.1 Unadjusted							
Lacson 2014	0.47	0.1059	17.9%	1.60 [1.30, 1.97]	2014		
Sakaguchi 2014	0.7129	0.0363	20.2%	2.04 [1.90, 2.19]	2014		

magnesium deficiency is associated with vascular calcifications, atherosclerosis and cardiovascular disease. Additionally, magnesium deficiency is associated with cardiovascular disease and risk of death in CKD and ESRD patients. However, the results of these studies are controversial.

METHODS

We performed a systematic review and meta-analysis to evaluate the association between dysmagnesemia with mortality risk in CKD and dialysis patients. Literature were identified by searching MEDLINE, Embase, and PubMed database from date of inception to November 2016. The primary outcome was the all-cause and cardiovascular mortality. We pooled unadjusted and adjusted hazards ratios (HRs) with 95% confidence intervals (95%CIs).





Figure 1. The association between hypomagnesemia and all-cause mortality

		Hazard Ratio							
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI			
1.2.1 Unadjusted									
Ishimura 2007	-1.3432	0.307	14.3%	0.26 [0.14, 0.48]	2007				
Ortega 2013	0.4055	1.1748	1.9%	1.50 [0.15, 15.00]	2013				
Fein 2014	-1.9519	0.7087	4.6%	0.14 [0.04, 0.57]	2014				
Garagarza 2015	-0.7154	0.1563	22.4%	0.49 [0.36, 0.66]	2015				
Matias 2015	-0.1393	0.0659	26.6%	0.87 [0.76, 0.99]	2015	-			
de Roij van Zuijdewijn 2015	-0.1625	0.0504	27.1%	0.85 [0.77, 0.94]	2015	-			
Cai 2016	-3.1942	0.9019	3.1%	0.04 [0.01, 0.24]	2016				
Subtotal (95% CI)			100.0%	0.54 [0.39, 0.75]					
Heterogeneity: Tau ² = 0.10; Ch	ni² = 43.35, df = 6 (P	< 0.0000	01); l² = 86	%					
Test for overall effect: Z = 3.67	′ (P = 0.0002)								
1.2.2 Adjusted									
Ishimura 2007	-0.7236	0.3568	1.5%	0.49 [0.24, 0.98]	2007				
Laecke 2013	-0.0726	0.0242	22.8%	0.93 [0.89, 0.98]	2013	1			
Fein 2014	-0.0161	0.0082	24.1%	0.98 [0.97, 1.00]	2014				
Matias 2015	-0.1393	0.0659	16.2%	0.87 [0.76, 0.99]	2015				
de Roij van Zuijdewijn 2015	-0.1278	0.0615	16.9%	0.88 [0.78, 0.99]	2015				
Garagarza 2015	-0.7154	0.1563	6.4%	0.49 [0.36, 0.66]	2015				
Ye 2016	-0.1985	0.0955	11.8%	0.82 [0.68, 0.99]	2016				
Cai 2016	-2.5903	1.028	0.2%	0.07 [0.01, 0.56]	2016				
Subtotal (95% CI)			100.0%	0.86 [0.79, 0.94]					
Heterogeneity: Tau ² = 0.01; Chi ² = 43.53, df = 7 (P < 0.00001); l ² = 84%									
Test for overall effect: $Z = 3.27$ (P = 0.001)									
						· · · · · · · · · · · · · · · · · · ·			
						0.02 0.1 1 10 50			
		Hypomagnesemia worse Hypomagnesemia favor							

We identified 18 cohort studies involving 200,443 participants that met our inclusion criteria and were included in the metaanalysis. The results show that there is a strong association between hypomagnesemia and the risk of all-cause mortality in CKD and ESRD patients (HR, 1.71; 95%CI, 1.34-2.19; *p*<0.001) (dichotomous variables). Multivariate analysis also showed there was a strong association between hypomagnesemia and all-cause mortality in CKD and ESRD patients (HR, 1.35; 95% CI, 1.19-1.54; *p*<0.001) (dichotomous variables). We found that hypermagnesemia was inversely associated with all-cause mortality in CKD and ESRD patients, and the HR was 0.54 (95%CI, 0.39-0.75; p<0.001) (continuous) variable) and 0.86 (95% CI, 0.79-0.94; p=0.001) (continuous variable) for unadjusted and multivariate adjusted data, respectively. We also found a significant association between hypermagnesemia and a decreased risk of cardiovascular mortality (HR, 0.71; 95%CI, 053-0.97, *p*=0.03) after multivariate analysis. In addition, we performed a subgroup analysis and found that hypomagnesemia was strongly associated with increased mortality (HR, 1.34; 95%CI, 1.10-1.62; *p*=0.003) (dichotomous variables) in hemodialysis patients.

Figure 2. The association between hypermagnesemia and all-cause mortality

				Hazard Ratio	Hazard Ratio				
Study or Subgroup	log[Hazard Ratio]	SE	Weight	IV, Random, 95% CI Year	IV, Random, 95% CI				
1.3.1 Unadjusted									
Ortega 2013	-0.6931	0.935	5.5%	0.50 [0.08, 3.13] 2013					
Matias 2015	-0.1985	0.0664	45.2%	0.82 [0.72, 0.93] 2015					
de Roij van Zuijdewijn 2015	-0.3147	0.0833	44.3%	0.73 [0.62, 0.86] 2015					
Cai 2016	-4.9618	0.9928	5.0%	0.01 [0.00, 0.05] 2016					
Subtotal (95% CI)			100.0%	0.60 [0.38, 0.95]					
Heterogeneity: Tau ² = 0.12; Chi ² = 23.93, df = 3 (P < 0.0001); l ² = 87%									
Test for overall effect: Z = 2.20 (P = 0.03)									
1.3.2 Adjusted									
Ishimura 2007	-0.0171	0.5839	5.9%	0.98 [0.31, 3.09] 2007					
Broek 2013	-0.4463	0.2527	19.3%	0.64 [0.39, 1.05] 2013					
Matias 2015	-0.1985	0.0664	37.6%	0.82 [0.72, 0.93] 2015					
de Roij van Zuijdewijn 2015	-0.3147	0.0833	36.1%	0.73 [0.62, 0.86] 2015					
Cai 2016	-5.8091	1.4841	1.0%	0.00 [0.00, 0.06] 2016					
Subtotal (95% CI)			100.0%	0.71 [0.53, 0.97]					
Heterogeneity: $T_{AU^2} = 0.06$; $C_{Di^2} = 15.98$, $df = 4.(P = 0.003)$; $l^2 = 75\%$									

Heterogeneity: Tau ² = 0.06; Chi ² = 15.98, df = 4 (P = 0.003); l ² = 75%					
Test for overall effect: Z = 2.19 (P = 0.03)					
				 	
	0.001	0.	1	1 10	1000
	Hypomagnesemia worse Hy			Hypomagnesemia favor	

Figure 3. The association between magnesium and cardiovascular mortality

CONCLUSIONS

Magnesium disturbance is significantly associated with risk of cardiovascular and all-cause mortality in CKD and ESRD patients. It is currently unclear if patients can benefit from magnesium correction, and additional prospective studies are needed to confirm our conclusions.







DOI: 10.3252/pso.eu.54ERA.2017