

LOWER SERUM MAGNESIUM IS ASSOCIATED WITH CARDIOVASCULAR RISK FACTORS AND MORTALITY IN HEMODIALYSIS PATIENTS

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Introduction and Aim

- Magnesium (Mg) is the second most abundant intracellular cation. In hemodialysis (HD) patients, its balance depends on the intake and most importantly on its dialysate concentration¹.
- Hypomagnesemia seems to play a role in the pathogenesis of arterial hypertension, endothelial dysfunction and inflammation in the general population, but few studies have been done in the dialysis population^{1,2}.
- The aim of this study was to evaluate the relationship between pre dialysis Mg levels and cardiovascular risk markers, including pulse pressure (PP), left ventricular mass index (LVMI) and vascular calcifications (VC), and mortality in chronic HD patients.

Patients and Methods

- This was a 48-month prospective study performed in 206 prevalent HD patients.
- Clinical data included etiology of renal failure, presence of diabetes mellitus, hypertension and coronary artery disease. Laboratory data considered were pre dialysis Mg, hemoglobin, C-reactive protein (CRP), albumin, serum calcium, serum phosphorus and total intact parathyroid hormone (iPTH).
- PP was evaluated in the beginning of the HD session in which serum Mg was collected. LVMI was calculated through the Devereux formula and indexed to body surface area. VC were evaluated by using a simple vascular calcification score (SVCS) based on plain radiographic films of pelvis and hands³.
- None of the patients was under oral Mg carbonate treatment.
- To perform the statistical analysis we used: Mann Whitney U or χ^2 for comparison between groups, Spearman correlation for univariate analysis and linear regression for multivariate analysis. Survival curves were estimated by Kaplan-Meier analysis and a Cox regression model was used to identify predictors of mortality. A $p < 0.05$ was considered significant.

Results

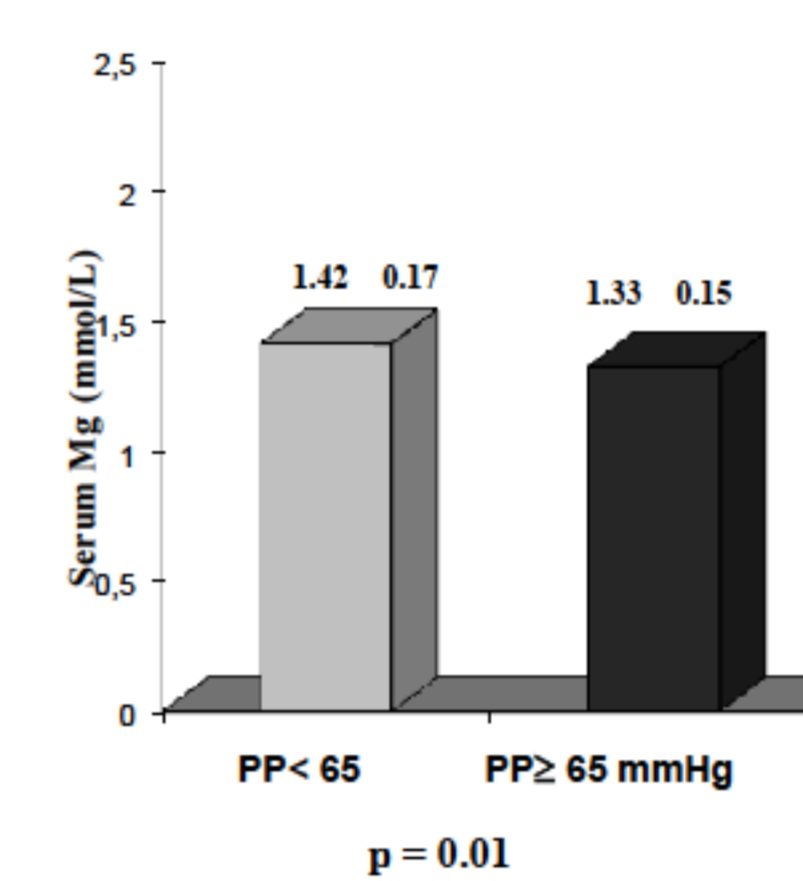
- Population data:**
 - 206 chronic HD patients
 - All submitted to pre-dilution on-line hemodiafiltration, with a dialysate Mg concentration of 1 mmol/L.
 - Ultrapure water dialysate and high flux helixone filter (Fresenius®) were used.
 - Mean age (\pm SD): 63.6 \pm 14.3 years, 45% female
 - Mean HD time: 42.3 \pm 38.6 months
 - 26% diabetics, 34% with hypertension and 28% with coronary artery disease.

Mean values of the studied variables:

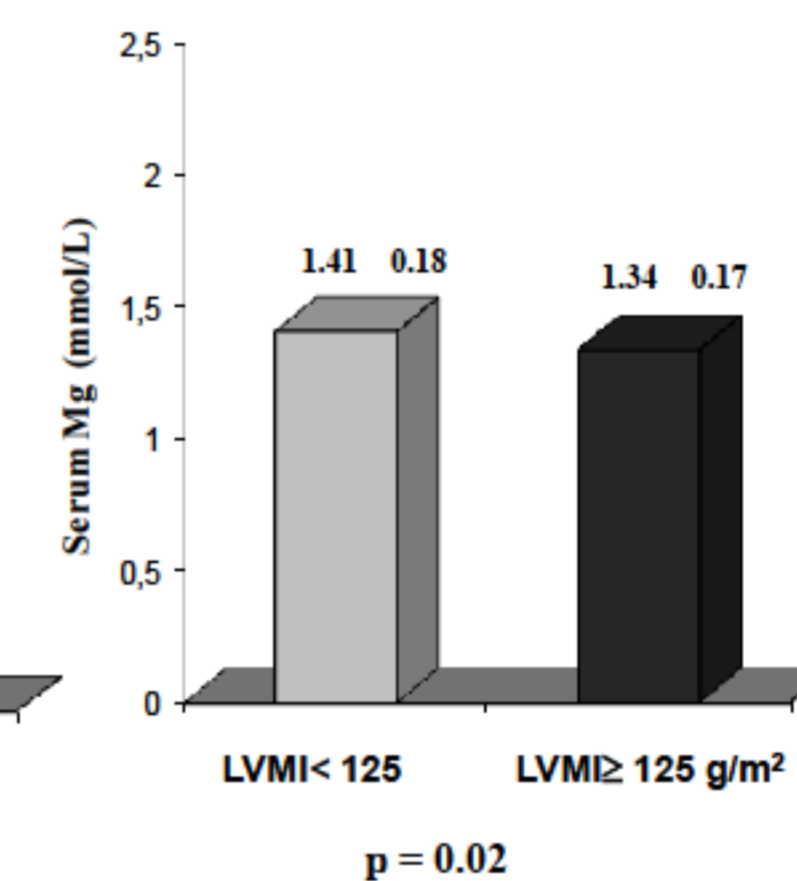
Hemoglobin (g/dL)	12.4	1.3 (8.6-15.2)
Albumin (g/dL)	4.0	0.3 (3.1-5.1)
CRP (mg/dL)	0.8	1.6 (0.1-16.2)
Calcium (mg/dL)	8.5	0.6 (6.9-10.5)
Phosphorus (mg/dL)	4.6	1.5 (1.8-9.7)
iPTH (pg/mL)	288.5	247.8 (3-1873)
Mg (mmol/L)	1.36	0.18 (0.82-1.81)
PP (mmHg)	69.2	19.1 (38-114)
LVMI (g/m ²)	129.2	33.6 (62.7-213.0)
SVCS	2.1	2.4 (0-8)

None of the patients presented hypo (< 0.6 mmol/L) or severe hypermagnesemia (> 2 mmol/L).

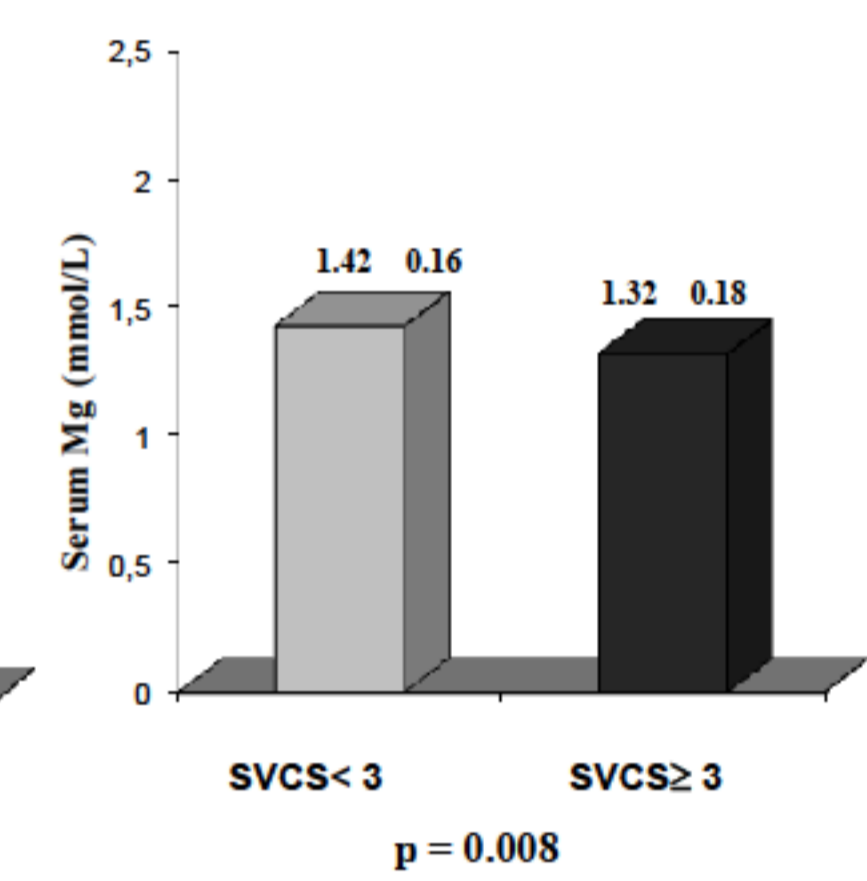
Pulse pressure



LVMI



SVCS



Patients with higher pulse pressure, left ventricular hypertrophy and more vascular calcifications had significantly lower serum Mg concentrations.

Univariate analysis:

	Serum Mg	
	r	p
Age	-0.44	0.006
Time on HD	-0.42	0.007
Albumin	0.57	< 0.001
iPTH	-0.33	0.02
PP	-0.36	0.01
LVMI	-0.37	0.01
SVCS	-0.40	0.008

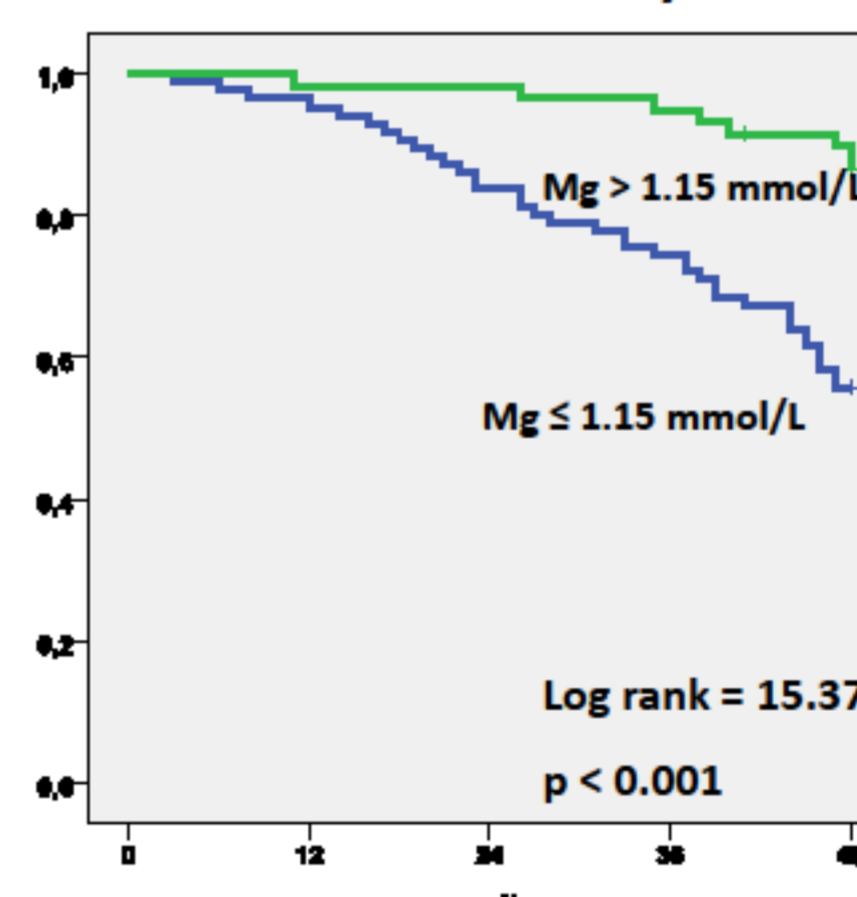
Multivariate analysis:

Dependent variable	Independent variables	OR	CI (95%)	p	R ²
Serum Mg	Age	0.19	0.05-0.33	<0.001	0.436
	Diabetes mellitus	0.16	0.09-0.29	0.006	
	Albumin	3.3	2.03-3.73	0.01	
	PP \geq 65 mmHg	0.18	0.07-0.29	0.002	
	LVMI \geq 140 g/m ²	0.15	0.10-0.24	0.03	
SVCS \geq 3	0.17	0.08-0.30	0.01		

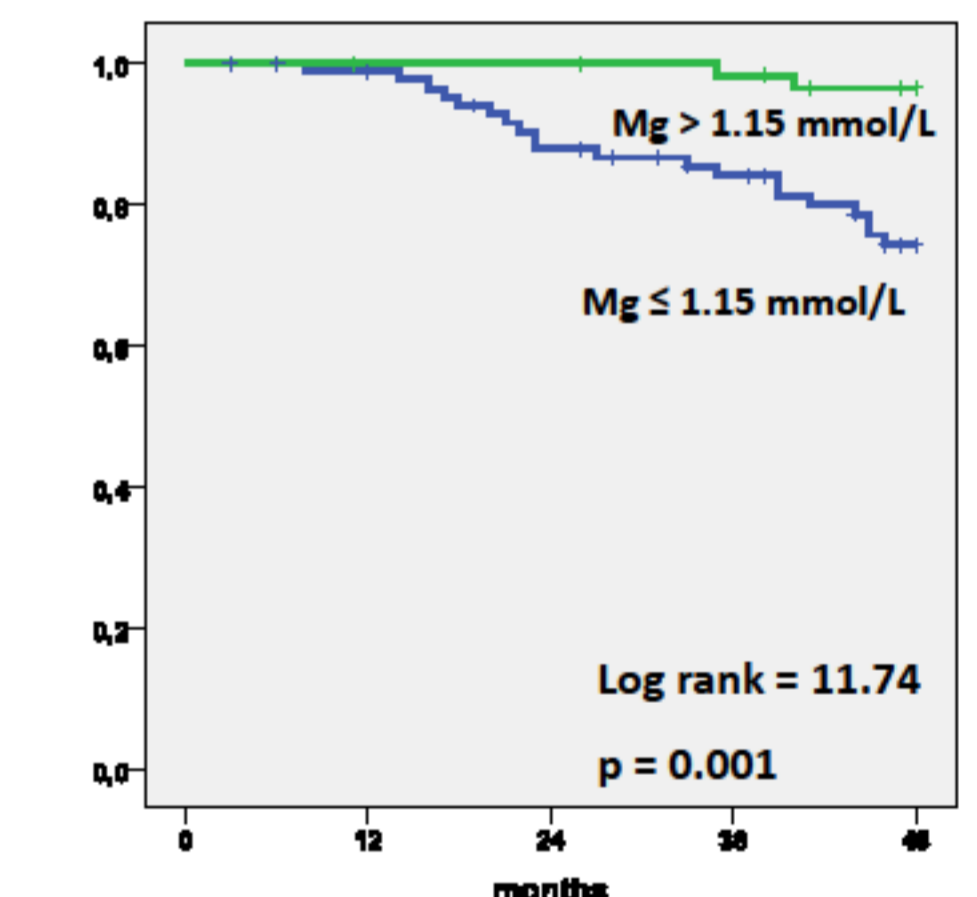
Lower serum Mg concentrations were predictors of an increased pulse pressure (≥ 65 mmHg) and left ventricular mass index (≥ 140 g/m²) and of a higher vascular calcification score (≥ 3).

Survival analysis:

Overall mortality



Cardiovascular mortality



Patients with lower Mg serum levels (≤ 1.15 mmol/L) had a significantly lower overall and cardiovascular survival at the end of the 48-month studied period.

Serum Mg levels were negatively correlated with age, time on HD, iPTH, pulse pressure, left ventricular mass index and simple vascular calcification score. Serum Mg concentrations were positively correlated with albumin. In patients with CRP ≤ 5 mg/dL (n= 194), there was a negative correlation (r= -0.41, p= 0.007) between Mg and CRP serum levels.

Dependent variable	Independent variables	HR	95% CI	p	R ²
Overall mortality	Age	1.42	1.08 to 1.53	0.02	0.473
	Time on HD	5.21	1.70 to 13.52	<0.001	
	Diabetes mellitus	7.34	2.81 to 18.83	<0.001	
	Albumin	0.81	0.82 to 0.97	0.01	
	C-reactive protein	1.93	1.07 to 3.16	0.007	
	Magnesium	0.87	0.88 to 0.99	0.01	
	PP ≥ 65 mmHg	2.17	1.13 to 3.24	0.004	
	LVMI ≥ 140 g/m ²	1.98	1.09 to 3.20	0.003	
SVCS ≥ 3	3.26	2.11 to 5.08	0.001		
Cardiovascular mortality	Age	1.76	1.12 to 2.98	0.01	0.418
	Time on HD	5.77	1.94 to 14.37	0.005	
	Diabetes mellitus	2.93	1.29 to 7.37	0.008	
	Coronary disease	1.87	1.23 to 2.34	0.02	
	C-reactive protein	1.90	1.25 to 2.87	0.01	
	Magnesium	0.82	0.72 to 0.95	0.02	
	PP ≥ 65 mmHg	1.95	1.13 to 3.19	0.006	
	LVMI ≥ 140 g/m ²	2.19	1.16 to 3.22	0.004	
SVCS ≥ 3	3.12	2.17 to 6.14	0.002		

Lower Mg serum levels were predictors of overall and cardiovascular mortality.

Conclusions

- In our study, lower pre dialysis Mg serum levels were associated with increased cardiovascular risk markers, like pulse pressure, left ventricular mass index and vascular calcifications, and with higher mortality in prevalent HD patients.
- These results still need to be confirmed in large prospective studies.

Bibliography:
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 3 - Adragao T, Pires A, Lucas C, et al. A simple vascular calcification score predicts cardiovascular risk in haemodialysis patients. *Nephrol Dial Transplant* 2004; 19: 1480 - 1488

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