BMC Nephrology

RESEARCH

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Serum magnesium and risk of arteriovenous fistula thrombosis in hemodialysis: a retrospective cohort study

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Abstract

Background Arteriovenous fistula (AVF) thrombosis is a major cause of vascular access failure in patients undergoing maintenance hemodialysis (HD). Although magnesium has established vascular protective properties, its relationship with AVF thrombosis remains poorly characterized. This study aimed to examine the association between serum magnesium levels and the risk of AVF thrombosis in a retrospective cohort of HD patients.

Methods This bi-center retrospective cohort study included 408 HD patients treated between January 2020 and May 2025. Baseline serum magnesium was categorized into three thresholds based on the 25th and 75th percentiles of the cohort distribution: T1 (< 0.87 mmol/L), T2 (0.87–0.97 mmol/L), and T3 (≥0.98 mmol/L). The primary outcome was the first clinically confirmed episode of AVF thrombosis. Kaplan–Meier analysis and multivariable Cox proportional hazard model adjusted for demographic, clinical, and dialysis-related factors were used to assess associations. Sensitivity and subgroup analyses were performed to evaluate the robustness of findings.

Results Over a median follow-up of 33.5 months, 83 patients (20.3%) experienced AVF thrombosis. Compared to T1, patients in T2 and T3 groups had significantly lower thrombotic risk: HR 0.57 (95% CI: 0.40–0.82, $p = 0.002$) and HR 0.46 (0.28–0.77, $p = 0.003$), corresponding to a 1.75- and 2.17-fold higher risk for T1 versus T2 and T3, respectively. Independent predictors of increased AVF thrombosis risk included older age (HR 1.05 per year, 95% CI: 1.02–1.09), longer AVF duration (HR 1.02 per month, 95% CI: 1.007–1.08), higher serum phosphate (HR 1.11 per 0.1 mmol/L, 95% CI: 1.03–1.48), and use of calcium-based phosphate binders (HR 1.02, 95% CI: 1.003–1.27). Protective factors included male sex (HR 0.87, 95% CI: 0.54–0.98), higher dialysis adequacy (spKt/V; HR 0.16, 95% CI: 0.11–0.35) and statin therapy (HR 0.35, 95% CI: 0.14–0.86). The association between low magnesium and AVF thrombosis remained consistent in sensitivity and subgroup analyses.

Conclusions Low serum magnesium (< 0.87 mmol/L) was independently associated with a twofold increased risk of AVF thrombosis in HD patients. Magnesium may represent a modifiable target for improving vascular access outcomes, warranting further prospective investigation.

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Clinical trial number This was a retrospective observational cohort study and was not registered as a clinical trial because no interventions were performed for research purposes.

Keywords Hemodialysis, Arteriovenous fistula, Magnesium, Thrombosis, Risk factors

Introduction

Arteriovenous fistula (AVF) thrombosis is a major cause of vascular access failure among patients undergoing maintenance hemodialysis (HD), leading to increased morbidity, frequent hospitalizations, and higher healthcare costs [1, 2]. Despite advances in surgical technique and access surveillance, the annual incidence of AVF thrombosis remains high, with reported rates of 0.2–0.5 episodes per 1000 patient days [3]. Identifying modifiable risk factors for AVF thrombosis is, therefore, critical to improving outcomes in this vulnerable population.

Magnesium is a critical intracellular cation involved in various vascular functions, including endothelial protection, inhibition of vascular calcification, and suppression of platelet aggregation [4–6]. In patients with chronic kidney disease (CKD), and especially those on HD, disturbances in magnesium homeostasis are common due to impaired renal excretion, dietary restrictions, and variable dialysate magnesium concentrations [7, 8]. Currently, clinical interest in magnesium has increased, as low serum magnesium has been associated with greater cardiovascular risk and mortality in patients undergoing HD [9, 10]. Proposed mechanisms include its capacity to prevent calcium-phosphate precipitation, reduce oxidative stress and inflammation, and limit vascular smooth muscle cell transformation into pro-calcific phenotypes [11–13].

In this context, recent studies have begun to explore the association between serum magnesium and vascular access outcomes [14–16]. However, the prior investigations have focused on composite endpoints, combining thrombosis, stenosis, and access-related interventions, which may obscure the distinct pathophysiological mechanisms underlying each complication.

Therefore, we aimed to investigate the association between serum magnesium levels and the risk of AVF thrombosis in a retrospective cohort of maintenance HD patients. We hypothesized that lower serum magnesium concentrations would be independently associated with a higher risk of AVF thrombosis and may represent a modifiable factor influencing AVF survival in this population.

Methods

Study design and setting

This was a bicenter, retrospective observational cohort study analyzing data from patients undergoing HD between January 1, 2020, and May 31, 2025, at two affiliated dialysis units managed by Medical Center LLC "Nephrocenter" in Odesa and Zaporizhzhia, Ukraine. Both centers deliver HD care to patients with end-stage kidney disease following national and international guidelines. The study protocol received ethical approval from the Institutional Review Board of the Medical Center "Nephrocenter" (IRB No. 2/2025, June 16, 2025) and was carried out following the principles of the Declaration of Helsinki. Due to the retrospective design and use of de-identified data, the requirement for informed consent was waived.

Study population

All adult patients (aged ≥18 years) undergoing HD were screened for inclusion. Eligible patients met the following criteria:

- A functioning native AVF as the primary vascular access at baseline,
- A minimum of three months of continuous in-center HD,
- At least one recorded serum magnesium measurement during the baseline assessment period.

Patients were excluded if they:

- Used a central venous catheter or arteriovenous graft as the primary access,
- Had a documented history of AVF thrombosis before the baseline magnesium measurement,
- Had missing or incomplete data for key variables,
- Had a follow-up duration of less than 30 days, were transplanted, or lost to follow-up within the same period.

All patients received conventional high-volume hemodiafiltration using Fresenius 5008S dialysis machines (Fresenius Medical Care, Germany). High-flux synthetic dialyzers with polysulfone membranes were employed following standard clinical protocols. Dialysis treatment was prescribed as three sessions per week, each lasting approximately 4 hours. Standard parameters included a blood flow rate of 250–350 mL/min, a dialysate flow rate of 500 mL/min, and a dialysate composition containing magnesium at 0.5 mmol/L, sodium at 138–140 mmol/L, and bicarbonate at 32–35 mmol/L. Systemic anticoagulation was provided using unfractionated heparin, administered according to local protocol, with dosing individualized based on patient weight, bleeding risk, and prior clotting history.

Exposure, outcome, and follow-up

The primary exposure was serum magnesium concentration, assessed as part of routine laboratory monitoring. The index date was defined as the date of the baseline serum magnesium measurement, which marked the start of follow-up. Because laboratory testing schedules differed slightly between the two participating centers, baseline serum magnesium assessments were performed within a 30-day window around study entry. For the main analysis, serum magnesium levels were categorized into three thresholds based on the 25th and 75th percentiles of the distribution in the full cohort: T1 (low) < 0.87 mmol/L (< 2.12 mg/dL), T2 (intermediate) 0.87–0.97 mmol/L (2.12–2.36 mg/dL), and T3 (high) ≥ 0.98 mmol/L (≥2.38 mg/dL). This categorization strategy was selected to contrast patients with clearly low or high magnesium levels against a normative reference group representing the central 50% of the cohort. Importantly, no patients in the cohort received oral or intravenous magnesium supplementation during the observation period.

The primary outcome was AVF thrombosis, defined as a documented clinical event requiring intervention for thrombotic occlusion, confirmed by physical examination, imaging, or surgical findings. The diagnosis was based on standard clinical evaluation (absence of bruit or thrill), confirmatory imaging (Doppler ultrasound), or operative findings. Only the first incident of AVF thrombosis after the index date was considered in the primary analysis.

Patients were followed from the index date until the first occurrence of AVF thrombosis or until the end of follow-up (May 31, 2025). Those who underwent kidney transplantation, died, or experienced permanent AVF abandonment (due to severe unreconstructable/recurrent stenosis or infection without thrombosis) were censored at the date of these events.

Covariates

All data were retrospectively extracted from electronic medical records of the participating dialysis centers. Collected data included: demographics (age, sex), comorbidities (diabetes mellitus, hypertension, cardiovascular disease, hepatitis B and C status), dialysis-related factors (dialysis vintage, Kt/V, ultrafiltration volume), AVF age, and medications used, including antiplatelet agents and anticoagulants.

Laboratory parameters included hematology (hemoglobin, hematocrit, platelet count), biochemistry (serum creatinine, urea, sodium, potassium, calcium, phosphate, magnesium), intact parathyroid hormone (iPTH), serum albumin, total protein, ferritin, transferrin saturation (TSAT), C-reactive protein (CRP), fasting glucose, and lipid profile markers such as total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides.

All laboratory analyses were performed in ISO-certified external laboratories (Sinevo and/or Dila) using standardized and validated procedures. Hematologic parameters were measured using automated hematology analyzers based on flow cytometry and impedance methods. Serum creatinine, urea, sodium, potassium, calcium, phosphate, and magnesium were analyzed via photometric and ion-selective electrode methods on automated chemistry analyzers. Serum albumin, total protein, and CRP were determined using colorimetric or immunoturbidimetric assays.

Lipid profile markers and fasting glucose were measured enzymatically using spectrophotometric methods. iPTH and ferritin were quantified via chemiluminescent immunoassays, and TSAT was calculated as the ratio of serum iron to total iron-binding capacity, both measured spectrophotometrically. The value closest to the index date within a 30-day window was used for each parameter.

Bias minimization

To minimize potential selection bias, all consecutive patients meeting the inclusion criteria during the study period were considered for inclusion. Exclusion criteria were predefined and applied uniformly across both centers. Exposure and outcome variables were derived from standardized, routinely collected clinical and laboratory data. The primary outcome was objectively confirmed through clinical examination, imaging, or operative findings. To address potential confounding, we applied multivariable adjustments and conducted sensitivity and subgroup analyses.

Sample size justification

Although no formal a priori sample size calculation was performed, a post hoc approximation was informed by the study by Yao et al. [15]. That study included 263 HD patients and reported 95 AVF dysfunction events (36%) over a median follow-up of 32 months, with a hazard ratio (HR) of 4.53 (95% CI: 2.63–7.81) for low serum magnesium. For our analysis, assuming a more conservative HR of 2.0 for AVF thrombosis between low and high magnesium categories, with a two-sided α of 0.05, 80% power, and an expected event rate of 20%, the estimated required sample size was approximately 360 patients with 72 events. Our final cohort included 408 patients and 83 thrombosis events, exceeding this threshold and thus providing adequate power to detect moderate associations.

Statistical analysis

Continuous variables were summarized as means with standard deviations (M ± SD) or median (Me) and interquartile range (Q25–Q75), depending on the distribution assessed by the Shapiro–Wilk test. Categorical variables were summarized as frequencies and percentages. For comparison of baseline characteristics across serum magnesium quartiles, we used one-way ANOVA for normally distributed continuous variables, the Kruskal–Wallis test for non-normally distributed continuous variables, and the chi-squared (χ^2) test for categorical variables.

Because the exact date of AVF maturation was not available in the clinical records, follow-up for the time-to-event was defined as the duration from baseline serum magnesium measurement to the first documented AVF thrombosis or censoring. Survival curves were estimated using the Kaplan–Meier method, with comparisons between thresholds made using the log-rank test. Univariable Cox proportional hazards regression was used to identify potential predictors of AVF thrombosis. Variables with $p < 0.05$ and clinical relevance were entered into the multivariable model. Multivariable Cox regression was used to estimate adjusted hazard ratios (HRs) for AVF thrombosis. Covariates with significant associations in the univariable analysis ($p < 0.01$) and variables that did not reach statistical significance in our cohort but are considered clinically relevant based on prior studies (sex, diabetes status, and hemoglobin level) [17–19] were included in the final model. Multicollinearity among covariates was assessed using variance inflation factors (VIF); values > 5 indicated significant collinearity. Results are reported as HRs with 95% confidence intervals (CIs).

To test the robustness of our findings, we performed both sensitivity and subgroup analyses. In sensitivity analyses, serum magnesium was also modeled as a continuous variable to assess the linearity of its association with AVF thrombosis in the Cox regression model. In a separate analysis, a Fine–Gray subdistribution hazards model was applied, treating death, kidney transplantation, and vascular access conversion as competing events to account for their potential impact on the risk of AVF thrombosis. Subgroup analyses were stratified by age (< 70 vs. ≥70 years), diabetes status, serum albumin level (< 35 vs. ≥35 g/L), and vascular access age (< 1 year vs. ≥1 year), with separate Cox models fitted within each subgroup.

Results

Study cohort

A total of 480 patients undergoing HD were screened for eligibility. After applying exclusion criteria, 408 patients were included in the final analysis (Fig. 1).

Serum magnesium levels ranged from 0.66 to 1.36 mmol/L, with a median of 0.93 (0.87–0.98) mmol/L. Baseline characteristics of the study population, stratified by serum magnesium categories, are summarized in Table 1.

As shown in Table 1, patients in the lowest magnesium tertile (T1) exhibited several unfavorable clinical and biochemical characteristics. They were significantly older, had higher systolic blood pressure, and demonstrated lower hemoglobin and hematocrit levels compared to those in the highest tertile (T3). Serum calcium, phosphate, total protein, and albumin concentrations were also significantly lower in T1 than in the higher T categories. Furthermore, serum creatinine and urea levels were significantly lower in T1, with a progressive increase observed across magnesium categories.

A higher proportion of patients with AVF age < 1 year was observed in T2 compared to T1 and T3, although the clinical relevance of this distribution remains uncertain. The use of statins, antihypertensive agents, and calcium-based phosphate binders was more common in T1 than in the higher T categories.

Inflammatory and iron-related biomarkers, including CRP, ferritin, and TSAT, did not significantly differ among groups. However, there was a non-significant trend toward lower dialysis adequacy and a higher prevalence of CVD in the lowest magnesium tertile. Similarly, patients in T1 tended to exhibit a more atherogenic lipid profile, characterized by lower HDL cholesterol and higher triglyceride levels, though these differences did not reach statistical significance.

Association between serum magnesium and AVF thrombosis

During a median follow-up of 33.5 (16.2–55.6) months, 83 patients (20.3%) developed AVF thrombosis, corresponding to an incidence rate of 0.2 events per 1000 patient days. In addition, 10 (2.5%) patients developed AVF stenosis, and 7 (1.72%) experienced AVF infections requiring catheter conversion and permanent abandonment. Other censoring events included kidney transplantation ($n = 13$, 3.2%) and death ($n = 32$, 7.8%).

Across serum magnesium categories, the proportion of patients who experienced AVF thrombosis differed significantly (T1: $n = 42$, 40.8%, T2: $n = 29$, 13.6%, T3: $n = 12$, 13.2%; $\chi^2 = 35.5$, $p < 0.0001$), indicating an inverse relationship between baseline serum magnesium levels and thrombosis occurrence.

Kaplan-Meier analysis demonstrated a significantly lower thrombosis-free survival in patients within the lowest serum magnesium category (T1) compared to those in higher categories (T2–T3) (log-rank test 23.6, $p < 0.0001$) (Fig. 2).

Univariable Cox regression analysis identified several factors significantly associated with AVF thrombosis (Fig. 3, Supplementary Table S1).

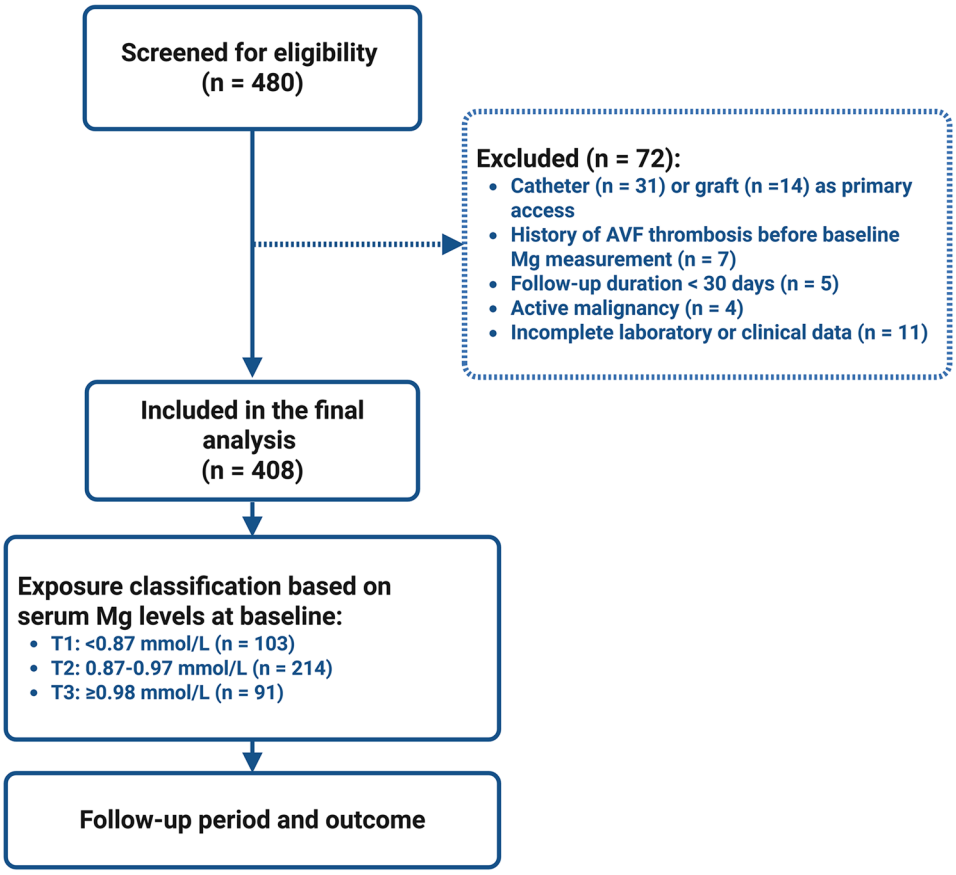

Fig. 1 Flow chart of patient selection. *abbreviations: AVF, arteriovenous fistula; Mg, magnesium*

As illustrated in Fig. 3, low serum magnesium (< 0.87 mmol/L) was associated with a twofold increased risk of AVF thrombosis. Similarly, advancing age, higher phosphate and calcium levels, use of calcium-based phosphate binders, and higher ultrafiltration volume also increased thrombotic risk. In contrast, higher serum magnesium levels, greater dialysis adequacy measured by spKt/V, higher albumin, shorter AVF age, and statin use were significantly associated with reduced risk of AVF thrombosis. Platelet count showed a borderline association with increased risk.

We further assessed multicollinearity among variables considered for inclusion in the multivariable Cox regression model. All candidate variables demonstrated acceptable levels of collinearity, with VIF values ranging from 1.052 to 1.603 (Supplementary Table S2). Variables were selected based on statistical significance in univariable analyses ($p < 0.01$). The final model included the primary exposure (serum magnesium categories), age, sex, diabetes status, hemoglobin, AVF age, spKt/V, total ultrafiltration volume, serum albumin, serum phosphate, statin use, and calcium-based phosphate binder use.

In the multivariable Cox regression model, low serum magnesium levels remained independently associated with the risk of AVF thrombosis after adjustment for relevant covariates. Compared to patients in the T1 group, those in the T2 and T3 groups had a 43 and 54% lower risk of AVF thrombosis, respectively. These results correspond to a 1.75-fold increased risk for T1 versus T2, and a 2.17-fold increased risk for T1 versus T3 (Table 2).

Other independent predictors included older age, female sex, longer AVF age, higher serum phosphate, and calcium-based phosphate binder use, all associated with increased risk of AVF thrombosis. Conversely, greater dialysis adequacy and statin use were independently associated with reduced risk of AVF thrombosis. Total ultrafiltration volume and serum albumin did not retain independent significance after multivariable adjustment.

Sensitivity and subgroup analyses

To assess the robustness of our findings, we conducted two sensitivity analyses. First, serum magnesium was modeled as a continuous variable in the multivariable Cox regression model to evaluate the linearity of its association with AVF thrombosis. The inverse relationship remained statistically significant, with each 0.1 mmol/L increase in serum magnesium associated with a lower risk of AVF thrombosis (adjusted HR 0.36, 95% CI:

Table 1 Baseline characteristics of the patients stratified by serum magnesium categories

Variable	All patients (*n* = 408)	T1: < 0.87 mmol/L (*n* = 103)	T2: 0.87–0.97 mmol/L (*n* = 214)	T3: ≥ 0.98 mmol/L (*n* = 91)	*p*-value
Demographics					
Age, years	59 (49–67)	63 (51–69)^{T3}	59 (49–67)^{T3}	56 (47.2–61)^{T1,2}	0.005
Male sex, n (%)	233 (57.1%)	64 (62.1%)	119 (55.6%)	50 (54.9%)	0.48
Smoking status, n (%)	52 (12.7%)	10 (9.7%)	30 (14.05%)	12 (13.2%)	0.58
Alcohol use, n (%)	22 (5.4%)	3 (2.9%)	11 (5.1%)	8 (8.8%)	0.19
Clinical characteristics					
Diabetes, n (%)	79 (19,4%)	22 (21.4%)	40 (18.7%)	17 (18.7%)	0.84
SBP (mmHg)	130 (125–140)	140 (130–145)^{T3}	130 (125–140)^{T3}	130 (120–140)^{T1,2}	0.05
DBP (mmHg)	80 (80–90)	80 (80–90)	80 (80–90)	80 (70–83.7)	0.24
CVD history, n (%)	66 (16.2%)	21 (20.4%)	29 (13.6%)	16 (17.6%)	0.13
Positive HBV or HCV status, n (%)	55 (13.5%)	17 (16.5%)	22 (10.3%)	16 (17.6%)	0.34
Dialysis vintage (months)	65.0 (33.0–87.0)	73 (31,7–96.7)	57.5 (31.0–80.0)	63.0 (38.0–99.0)	0.09
Blood flow rate, mL/min	302.5 ± 17.4	300.6 ± 18.2	302.7 ± 17.1	304.5 ± 17.1	0.31
spKt/V	1.34 (1.24–1.45)	1.30 (1.19–1.43)	1.30 (1.25–1.40)	1.35 (1.25–1.48)	0.06
Total volume UF, mL	2500 (2000–3000)	2500 (2200–3000)	2800 (2250–2900)	2500 (1800–3000)	0.57
AVF age < 1 year, n (%)	42 (10.3%)	6 (5.8%)^{T2}	30 (14.0%)^{T1,3}	6 (6.6%)^{T2}	0.03
Laboratory values					
Magnesium, mmol/L	0.93 (0.87–0.97)	0.83 (0.79–0.85)^{T2,3}	0.93 (0.91–0.95)^{T1,3}	1.03 (0.99–1.07)^{T12}	< 0.0001
Creatinine, µmol/L	839 (695–972)	782 (594–891)^{T2,3}	819 (673–941)^{T1,3}	938 (869–1026)^{T1,2}	< 0.0001
Urea, mmol/L	20.6 (17.1–25.2)	19.8 (15.8–24.2)^{T1,3}	20/3 (16.9–24.4)^{T1,3}	22.9 (19.4–27.4)^{T2,3}	0.001
Hemoglobin, g/L	101 (92–110.5)	98 (90–108)^{T3}	101 (92–111)^{T3}	107 (96–118)^{T1,2}	0.003
Ht, %	29.6 ± 4.8	28.4 ± 4.9^{T3}	29.4 ± 4.1^{T3}	31.2 ± 5.3^{T1,2}	0.001
PLT, *10^9/L	179.5 (142.5–221.0)	179.0 (137.5–220)	174.5 (141.0–221.0)	184.0 (145.5–222.5)	0.79
TSAT, %	22.7 (15.6–31.02)	22.9 (14.7–28.8)	21.6 (14.9–31.2)	25.5 (15.0–14.3)	0.29
Ferritin, ng/mL	261.1 (103.0–205.5)	301.4 (88.2–529.0)	276 (104.0–505.5)	243 (98.9–487.7)	0.69
Total protein, g/L	67.6 ± 5.6	66.4 ± 6.8^{T3}	67.6 ± 4.9	68.8 ± 4.9^{T1}	0.002
Albumin, g/L	40 (38–42)	39 (36–42)^{T2,3}	40 (39–42)^{T1}	41 (39.2–42)^{T1}	0.0002
CRP, mg/L	4.4 (3.3–9.5)	7.9 (4.5–11.6)	4.8 (2.7–6.9)	3.3 (2.9–13.9)	0.54
Glucose, mmol/L	4.9 (4.4–6.12)	4.8 (4.2–5.9)	4.9 (4.4–6.1)	4.9 (4.6–5.8)	0.78
Calcium, mmol/L	2.24 (2.15–2.33)	2.17 (2.11–2.29)^{T2,3}	2.24 (2.16–2.34)^{T1}	2.28 (2.17–2.37)^{T1}	0.0001
Phosphate, mmol/L	1.63 (1.35–1.98)	1.37 (1.19–1.72)^{T2,3}	1.67 (1.32–1.93)^{T1,3}	1.95 (1.46–2.22)^{T1,2}	< 0.0001
iPTH, pg/mL	302.6 (173.7–531.1)	321.8 (171.5–605.9)	294.8 (187.6–5015.7)	312.5 (130.1–55.4)	0.95
Total cholesterol, mmol/L	4.6 (4.0–5.5)	4.9 (4.3–5.7)	4.5 (3.9–5.4)	4.3 (3.9–5.2)	0.052
HDL, mmol/L	1.1 (0.32–1.32)	1.05 (0.8–1.3)	1.12 (0.9–1.35)	1.19 (1.0–1.35)	0.13
LDL, (mmol/L)	2.8 (2.2–3.5)	3.1 (2.6–3.5)	2.7 (2.2–3.3)	2.7 (2.1–3.3)	0.18
Triglycerides (mmol/L)	1.45 (1.1–2.2)	1.54 (1.14–2.22)	1.51 (1.04–2.33)	1.35 (1.11–2.08)	0.16
Medications					
Erythropoiesis-stimulating agents, n (%)	245 (52.7%)	65 (63.1%)	127 (59.3%)	56 (61.5%)	0.19
Iron therapy, n (%)	237 (58.1%)	65 (63.1%)	127 (58.9%)	45 (49.4%)	0.73
Statins, n (%)	124 (30.4%)	31 (30.1%)^{T3}	75 (35.0%)^{T3}	18 (19.8%)	0.04
Antihypertensives, n (%)	347 (85.1%)	95 (92.2%)^{T2}	177 (82.7%)	76 (83.5%)	0.02
Anticoagulants, n (%)	41 (10.1%)	9 (8.7%)	20 (9.3%)	12 (132%)	0.75
Antiaggregants, n (%)	122 (29.9%)	25 (24.3%)	66 (30.8%)	31 (34.0%)	0.14
Calcium-based phosphate binders, n (%)	183 (44.8%)	59 (57.3%)^{T2,3}	92 (43.0%)^{T1}	32 (35.24%)^{T1}	0.01

Notes: Values are presented as Me (Q25–Q75) or M ± SD as appropriate. Superscript letters denote statistically significant differences between categories based on pairwise comparisons using ANOVA or Kruskal–Wallis with post hoc testing

Abbreviations: CRP, C-reactive protein; CVD, cardiovascular disease; DBP, diastolic blood pressure; Hb, hemoglobin; HDL, high-density lipoprotein cholesterol; Ht, hematocrit; iPTH, intact parathyroid hormone; LDL, low-density lipoprotein cholesterol; PLT, platelet count; SBP, systolic blood pressure; spKt/V, single-pool Kt/V; TSAT, transferrin saturation; UF, ultrafiltration

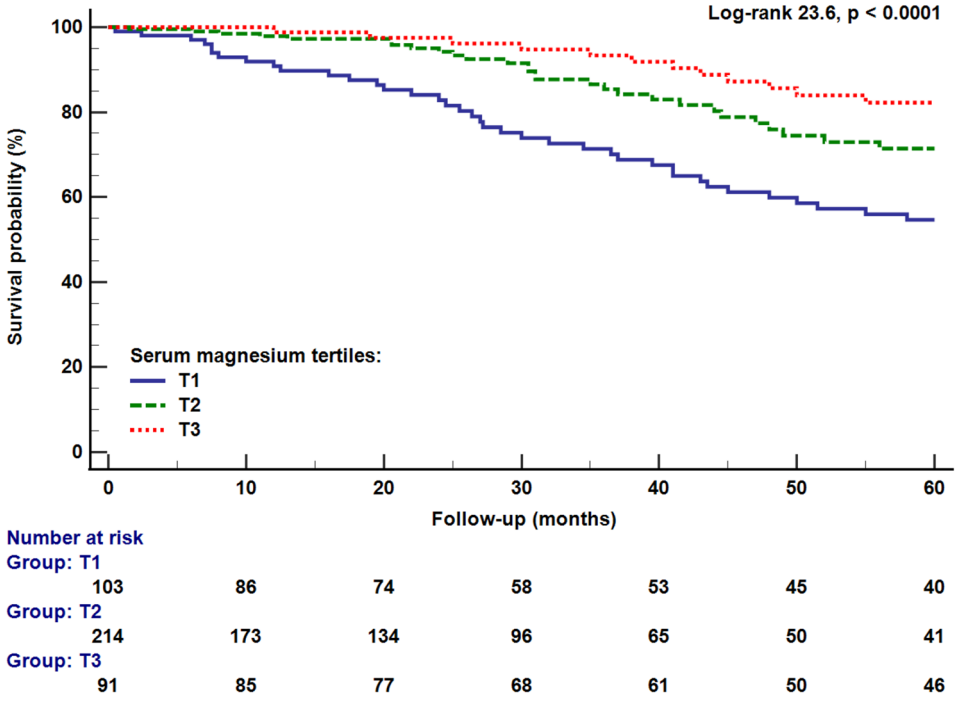

Fig. 2 Kaplan-meier curves for AVF thrombosis-free survival stratified by serum magnesium categories in patients undergoing HD. Abbreviations: T1, T2, T3 – serum magnesium categories (T1 = lowest, T3 = highest)

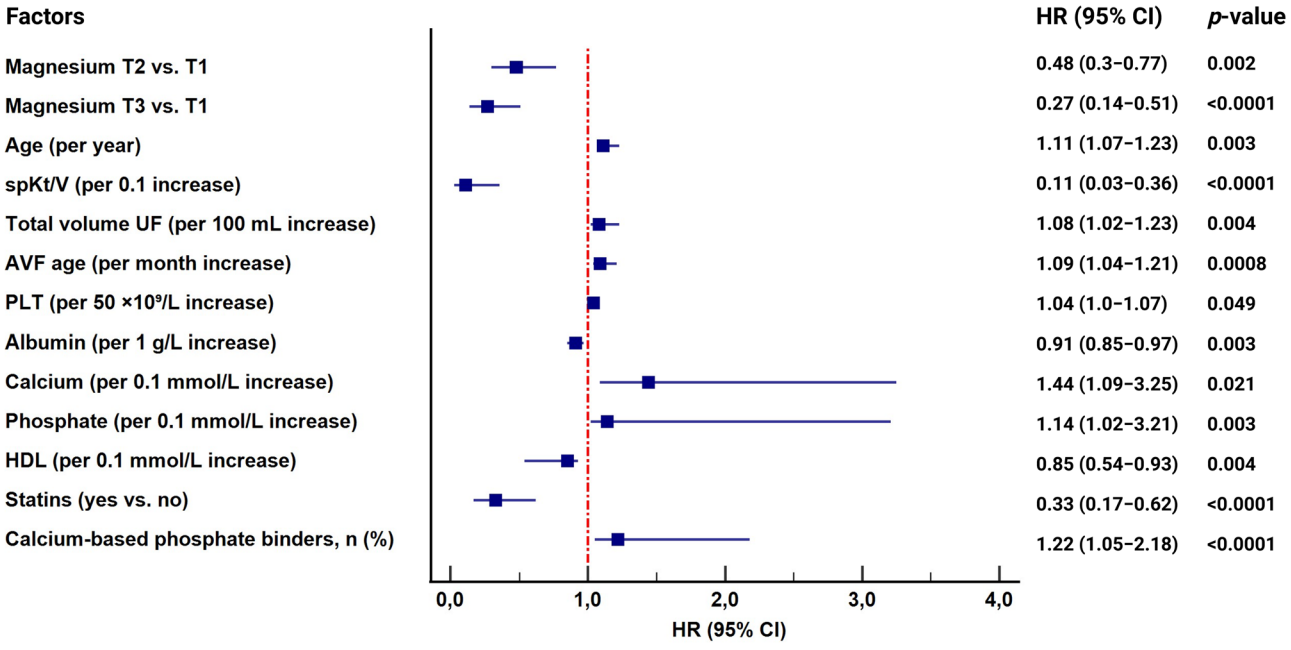

Fig. 3 Forest plot of HRs and 95% CIs for factors associated with AVF thrombosis in univariable cox regression analysis. the reference category for serum magnesium is T1 (< 0.87 mmol/L, hr = 1.00). Abbreviations: AVF, arteriovenous fistula; HDL, high-density lipoprotein cholesterol; hr (95% ci), hazard ratio (95% confidence Interval); PLT, platelet count; spKt/V, single-pool Kt/V; T1, T2, T3, categories of serum magnesium concentration (T1 = lowest, T3 = highest)

0.22–0.62, $p = 0.021$). Second, a Fine–Gray subdistribution hazards model yielded consistent estimates (sHR for T2 vs T1 = 0.61, 95% CI 0.42–0.89, $p = 0.011$; sHR for T3 vs T1 = 0.48, 95% CI 0.26–0.81, $p = 0.010$). These results confirmed the robustness of the association between serum magnesium levels and AVF thrombosis risk.

In subgroup analyses, the association between serum magnesium and AVF thrombosis was generally consistent. For the subgroup Cox models, magnesium category

Table 2 Multivariable cox proportional hazards regression for risk of AVF thrombosis

Variable	HR (95% CI)	*p*-value
Serum magnesium T1: < 0.87 mmol/L (reference)	1.00	—
Serum magnesium T2 vs. T1: 0.87–0.97 mmol/L	0.57 (0.40–0.82)	0.002
Serum magnesium T3 vs. T1: ≥0.98 mmol/L	0.46 (0.28–0.77)	0.003
Age (per year)	1.05 (1.02–1.09)	0.021
Sex (male vs female)	0.87 (0.54–0.98)	0.044
Diabetes (yes vs no)	1.2 (0.52–2.77)	0.661
Hemoglobin (per g/L)	1.01 (0.95–1.24)	0.327
AVF age (per month increase)	1.02 (1.007–1.08)	0.003
spKt/V (per 0.1 increase)	0.16 (0.11–0.35)	0.002
Total volume UF (per 100 mL increase)	1.00 (0.97–1.02)	0.233
Albumin (per 1 g/L increase)	0.95 (0.88–1.05)	0.142
Phosphate (per 0.1 mmol/L increase)	1.11 (1.03–1.48)	0.004
Statins (yes vs. no)	0.35 (0.14–0.86)	0.022
Calcium-based phosphate binders (yes vs. no)	1.02 (1.003–1.27)	0.047

Abbreviations: HR (95% CI), Hazard ratio (95% Confidence Interval); spKt/V, single-pool Kt/V; T1, T2, T3, magnesium category

Table 3 Subgroup analysis of the association between serum magnesium categories and AVF thrombosis (adjusted Cox regression)

Subgroup	Serum magnesium			
	T1 (< 0.87 mmol/L)		T3 (≥0.98 mmol/L)	
	HR (95% CI_	*p*-value	HR, 95% CI	*p*-value
Age ≥ 70 years	5.21 (1.44–8.18)	0.022	0.56 (0.11–5.62)	0.621
Age < 70 years	3.64 (1.44–8.18)	< 0.0001	0.43 (0.32–0.57)	< 0.0001
Diabetes – Yes	2.36 (1.02–5.47)	0.045	0.47 (0.13–1.74)	0.74
Diabetes – No	4.09 (2.77–6.02)	< 0.0001	0.37 (0.28–0.490	< 0.0001
Albumin ≤ 35 g/L	7.41 (1.62–11.6)	0.014	0.58 (0.08–4.14)	0.582
Albumin > 35 g/L	3.95 (2.68–5.82)	< 0.0001	0.43 (0.31–0.58)	< 0.0001
AVF age < 1 year	4.46 (1.43–7.32)	0.019	0.11 (0.02–1.00)	0.050
AVF age ≥ 1 year	2.47 (1.62–3.77)	< 0.0001	0.51 (0.26–0.96)	0.039

Notes: Multivariable Cox regressions were repeated within each subgroup, adjusting for age, spKt/V, phosphate, albumin, ultrafiltration volume, statin use, and calcium-phosphate binder use (excluding the stratifying variable). T2 (0.87–0.97 mmol/L) was used as the reference in all models

T2 (0.87–0.97 mmol/L) was set as the reference group. Patients in the lowest magnesium tertile showed significantly increased risk of thrombosis across all subgroups, with HRs ranging from 2.36 to 7.41 (Table 3).

In contrast, the protective effect associated with the highest magnesium tertile was significant in younger patients, non-diabetics, well-nourished, and patients with AVF age ≥1 year. However, in older subjects (≥70 years), diabetics, and patients with hypoalbuminemia (≤35 g/L), the association with T3 was not statistically significant.

Discussion

This study is the first to investigate the association between serum magnesium levels and the risk of AVF thrombosis as an isolated clinical endpoint in patients undergoing HD. Unlike previous studies that examined AVF dysfunction using composite outcomes, we focused specifically on thrombotic events confirmed by clinical, imaging, or surgical criteria. This approach allowed for a more precise evaluation of risk factors specifically associated with thrombosis, rather than broader or overlapping vascular access complications.

In our cohort of 408 HD patients, lower serum magnesium was independently associated with an increased risk of AVF thrombosis. Patients in the lowest magnesium category (< 0.87 mmol/L) had a 1.75- to 2.17-fold higher risk of thrombosis compared to those in the middle and highest categories, even after adjustment for demographic, clinical, and dialysis-related covariates. The observed association remained consistent across sensitivity analyses. When serum magnesium was modeled as a continuous variable, higher levels were associated with a significantly lower risk of thrombosis. A Fine–Gray competing risks model, which accounted for death, kidney transplantation, and vascular access conversion as competing events, yielded similar effect estimates.

Although magnesium levels in the lowest category fall within the normal range for the general population, such concentrations may represent a relative magnesium deficiency in HD patients [9, 20]. During HD, magnesium is continuously removed from the circulation, and the net balance depends on the dialysate magnesium concentration, treatment duration, and residual kidney function [20–22]. As a result, serum magnesium levels in HD patients are influenced by both dialytic losses and impaired renal excretion, and may fluctuate around or even below the general population range. Several studies have shown that serum magnesium concentrations below approximately 0.9–1.0 mmol/L are associated with adverse vascular and cardiovascular outcomes in HD cohorts [9, 10, 23]. However, these concentrations may not necessarily reflect true magnesium sufficiency, as functional or intracellular deficits can still occur [24]. Therefore, the magnesium levels represented by our lowest category (< 0.87 mmol/L) likely reflect a state of subclinical deficiency in this population, consistent with emerging evidence suggesting that the lower limit of the reference range should be raised to approximately 0.85 mmol/L even in the general population [25].

Subgroup analyses further supported the robustness of this relationship. The elevated thrombotic risk linked to low magnesium remained significant across all examined subgroups. However, the protective effect of higher magnesium was attenuated and no longer statistically significant in older individuals, patients with diabetes, and those with hypoalbuminemia, suggesting that magnesium's vascular benefits may be less pronounced in patients with higher baseline cardiovascular or inflammatory risk.

Our findings are consistent with and extend previous research examining the relationship between serum magnesium and vascular access outcomes. To date, only two studies have specifically addressed this topic, encompassing a combined cohort of 352 HD patients [15, 16]. In line with our results, Stolić et al. reported significantly lower serum magnesium concentrations in patients with AVF complications compared to those without [16]. Similarly, Yao et al. observed a 4.5-fold higher risk of AVF dysfunction in patients with serum magnesium levels below 0.88 mmol/L compared to those in the highest magnesium group [15]. However, both studies relied on composite endpoints, limiting the ability to isolate thrombosis-specific mechanisms.

Several biological mechanisms may explain this relationship. Magnesium modulates vascular tone, inhibits platelet aggregation, stabilizes endothelial function, and reduces inflammation [4, 12]. Experimental studies have shown that low extracellular magnesium can promote vascular smooth muscle cell calcification and endothelial injury, both of which predispose to thrombosis [11, 26, 27]. Additionally, magnesium inhibits platelet activation by modulating intracellular calcium handling and interfering with thromboxane synthesis, both of which are critical steps in thrombus formation [28, 29].

These mechanisms provide a compelling rationale for the inverse association observed in our cohort. However, we also observed an attenuation of the protective effect of higher serum magnesium levels among older patients, individuals with diabetes, and those with hypoalbuminemia. In older patients, age-related alterations in magnesium handling, a higher prevalence of vascular calcification, and the burden of comorbidities may reduce the vascular and antithrombotic benefits typically conferred by elevated magnesium levels [30]. The presence of advanced vascular disease and frailty in this population may overshadow magnesium's protective effects, including the inhibition of vascular smooth muscle cell calcification and the preservation of endothelial function.

Among individuals with diabetes, persistent hyperglycemia and insulin resistance promote chronic vascular injury and inflammation, which may not be fully mitigated by elevated serum magnesium concentrations [31]. Additionally, diabetes is associated with increased magnesium loss and impaired cellular uptake [32, 33], potentially limiting the intracellular actions of magnesium that are critical for inhibiting platelet activation and maintaining endothelial health. In our cohort, diabetes was significant in subgroup analyses but not in the overall multivariable model. This discrepancy likely reflects confounding by related clinical factors such as age, phosphate, and albumin, which may have attenuated its independent effect. Consequently, the influence of diabetes on AVF thrombosis in our study appears to be indirect and largely mediated through other metabolic and vascular pathways.

In patients with hypoalbuminemia, the interpretation of serum magnesium is further complicated, as a significant portion of circulating magnesium is albumin-bound [34]. Low albumin levels can reduce total serum magnesium even when the physiologically active ionized fraction remains normal [34]. Moreover, hypoalbuminemia reflects underlying malnutrition and inflammation, both of which are strong risk factors for vascular complications [35] and may blunt the protective effects of magnesium. In line with this hypothesis, Streja et al. have demonstrated that HD patients with both low albumin and low magnesium had a 17% higher risk of death compared to those with low albumin and high magnesium [36]. However, when albumin levels were adequate, the relationship between magnesium and mortality was attenuated, suggesting that serum albumin may modify the clinical impact of magnesium levels [36]. Consistent with these observations, our subgroup analyses showed that the association between low magnesium and AVF thrombosis was strongest among patients with albumin ≤ 35 g/L and weaker among those with albumin > 35 g/L, indicating that albumin status influences the clinical relevance of magnesium concentrations.

Beyond magnesium, our study identified several other independent factors associated with the risk of AVF thrombosis, highlighting the multifactorial nature of vascular access failure in HD patients. Older age, female sex, longer AVF age, elevated serum phosphate levels, and the use of calcium-based phosphate binders were all associated with a higher risk of AVF thrombosis.

The increased risk observed in women aligns with prior evidence suggesting sex-related differences in vessel caliber, hormonal influences on endothelial function, and a higher rate of AVF non-maturation or early failure in females [19, 37]. Similarly, longer AVF age likely reflects progressive vascular remodeling, neointimal hyperplasia, and cumulative hemodynamic stress, all of which may predispose to late thrombotic failure [38, 39].

Elevated serum phosphate levels were significantly associated with an increased risk of thrombosis, aligning with previous reports that have linked hyperphosphatemia to endothelial dysfunction, vascular smooth muscle

cell calcification, and heightened platelet activation [40]. Excess phosphate can promote the transformation of vascular smooth muscle cells into osteoblast-like phenotypes, contributing to medial calcification and reduced vascular compliance, factors that may impair AVF integrity and predispose to thrombosis [41].

Additionally, the use of calcium-based phosphate binders was independently associated with a higher risk of AVF thrombosis. This finding is consistent with prior studies suggesting that calcium-based binders may contribute to arterial and arteriolar calcification through increased calcium loading and deposition in the vessel wall [42, 43].

In contrast, high dialysis adequacy, measured by spKt/V, and statin use were associated with a reduced risk of AVF thrombosis. It is well-proven that better uremic toxin clearance may improve endothelial function and reduce systemic inflammation, both of which are critical in maintaining vascular access patency [44]. Rodrigues et al. have also reported higher access failure rates in patients with low delivered dialysis doses [45], although studies are limited in this area.

Statins use emerged as another protective factor in our analysis. Beyond their lipid-lowering properties, statins exert a wide range of pleiotropic effects, including enhancement of endothelial function, attenuation of oxidative stress, inhibition of pro-inflammatory cytokines, and suppression of thrombotic pathways such as tissue factor expression and platelet aggregation [46–48]. These mechanisms are particularly pertinent in the HD population, where chronic inflammation and a prothrombotic state are prevalent. Our findings are consistent with previous observational studies reporting a lower risk of AVF thrombosis among HD patients treated with statins [47, 48]. Although a meta-analysis by Wan et al. did not demonstrate a statistically significant association between statin use and AVF patency [49], our recent report has suggested a dose-dependent protective effect of statins on the risk of AVF thrombosis, highlighting the potential influence of treatment intensity [50].

Taken together, these findings underscore the multifactorial nature of AVF thrombosis and point toward several modifiable targets, including serum magnesium, phosphate balance, HD adequacy, and statin use, that may inform preventive strategies. Furthermore, combining these modifiable factors with previously proposed complementary biomarkers and vascular access monitoring strategies may improve the prediction and early identification of AVF failure in HD patients [19, 51–53].

Several limitations of this study should be acknowledged. First, the retrospective design precludes causal inference. Although we performed multivariable adjustments and sensitivity analyses, the possibility of residual confounding from unmeasured variables cannot be excluded. Second, because the exact date of AVF maturation was not recorded in the clinical data, follow-up was anchored to the baseline serum magnesium assessment. Although patients with prior AVF thrombosis were excluded, some degree of residual immortal time bias cannot be fully ruled out. Patients maintained a functioning AVF until the baseline magnesium measurement was obtained, which created a period during which thrombosis could not occur by definition. Third, serum magnesium was assessed at a single time point, which may not capture longitudinal variability or reflect cumulative exposure. Fourth, only total serum magnesium concentrations were available; ionized magnesium was not measured and may have provided a more accurate reflection of magnesium status, particularly in hypoalbuminemic patients. Fifth, although thrombotic AVF events were rigorously defined, we did not account for the timing of these events in relation to changes in medications or dialysis prescriptions, which could have influenced thrombosis risk. In addition, the relatively low number of outcome events constrained the number of covariates that could be included in the multivariable models. Finally, while subgroup analyses offered insights into potential effect modifiers, these analyses were exploratory in nature and not adequately powered for formal interaction testing.

Conclusions

The present study demonstrated that lower serum magnesium levels (< 0.87 mmol/L) were independently associated with a twofold increased risk of AVF thrombosis in patients undergoing HD. This association remained robust across sensitivity analyses and was consistent across most clinically relevant subgroups. The findings underscore the potential importance of magnesium homeostasis in preserving vascular access patency and suggest that hypomagnesemia may represent a modifiable risk factor for AVF thrombosis. In addition to magnesium, other modifiable factors, such as elevated serum phosphate, use of calcium-based phosphate binders, suboptimal dialysis adequacy, and absence of statin therapy, were independently associated with increased risk of AVF thrombosis. Prospective studies are warranted to confirm these associations and to determine whether magnesium-targeted interventions can reduce AVF thrombosis and improve long-term vascular access outcomes in the HD population.

Abbreviations

AVF	Arteriovenous fistula
CRP	C-reactive protein
CKD	Chronic kidney disease
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
ESA	Erythropoiesis-stimulating agents
Hb	Hemoglobin
HDL	High-density lipoprotein cholesterol

HR	Hazard ratio
Ht	Hematocrit
HCV	Hepatitis C virus
HBV	Hepatitis B virus
HD	Hemodialysis
iPTH	Intact parathyroid hormone
LDL	Low-density lipoprotein cholesterol
Mg	Magnesium
Me	Median
M ± SD	Mean ± standard deviation
PLT	Platelet count
SBP	Systolic blood pressure
spKt/V	Single-pool Kt/V
T1, T2, T3	Categories of serum magnesium concentration
TSAT	Transferrin saturation
UF	Ultrafiltration

Supplementary information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-025-04679-y.

Supplementary Material 1

Acknowledgements
Not applicable.

Author contributions
NS: Conceptualization; Formal analysis; Visualization; Writing – review & editing. TO and AR: Writing – original draft. IP and AH: Formal analysis. AS, VM, and MD: Data curation. All authors contributed to data interpretation, reviewed and edited the manuscript for important intellectual content, approved the final version for publication, and agree to be accountable for all aspects of the work.

Funding
This study received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data availability
The data used in the study are available upon reasonable request to the corresponding author.

Declarations

Ethics approval and consent to participate
The study was conducted following the principles of the Declaration of Helsinki. The protocol was approved by the Institutional Review Board of the Medical Center "Nephrocenter" (IRB No. 2/2025, June 16, 2025). Due to the retrospective design and use of de-identified data, the requirement for informed consent was waived.

Consent for publication
The waiver of consent for publication was granted by the Institutional Review Board as part of the ethics approval, as no identifiable personal data were included in the study.

Competing interests
The authors declare no competing interests.

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Received: 4 August 2025 / Accepted: 1 December 2025
Published online: 10 December 2025

References

1. Girerd S, Girerd N, Frimat L, Holdaas H, Jardine AG, Schmieder RE, et al. Arteriovenous fistula thrombosis is associated with increased all-cause and cardiovascular mortality in haemodialysis patients from the AURORA trial. Clin Kidney J. 2019;13(1):116–22. https://doi.org/10.1093/ckj/sfz048.
2. Jiménez-Almonacid P, Gruss E, Lasala M, Del Riego S, López G, Rueda JA, et al. Economic repercussions of implementing a protocol for urgent surgical repair of thrombosed arteriovenous fistulae. Nefrologia. 2014;34(3):377 - 82. English, Spanish. https://doi.org/10.3265/Nefrologia.pre2014.Feb.12347.
3. Al-Jaishi AA, Liu AR, Lok CE, Zhang JC, Moist LM. Complications of the arteriovenous fistula: a systematic review. J Am Soc Nephrol. 2017;28(6):1839–50. https://doi.org/10.1681/ASN.2016040412.
4. Fiorentini D, Cappadone C, Farruggia G, Prata C. Magnesium: biochemistry, nutrition, detection, and social Impact of diseases linked to its deficiency. Nutrients. 2021;13(4):1136. https://doi.org/10.3390/nu13041136.
5. DiNicolantonio JJ, O'Keefe JH, Wilson W. Subclinical magnesium deficiency: a principal driver of cardiovascular disease and a public health crisis. Open Heart. 2018;5(1):e000668. https://doi.org/10.1136/openhrt-2017-000668 . Erratum in: Open Heart. 2018 Apr 5;5(1):e000668corr1. https://doi.org/10.1136/openhrt-2017-000668corr1 .
6. Zaslow SJ, Oliveira-Paula GH, Chen W. Magnesium and vascular calcification in chronic kidney disease: current insights. Int J Mol Sci. 2024;25(2):1155. https://doi.org/10.3390/ijms25021155.
7. van de Wal-Visscher ER, Kooman JP, van der Sande FM. Magnesium in chronic kidney disease: should we care? Blood Purif. 2018;45(1–3):173–78. https://doi.org/10.1159/000485212.
8. Macías Ruiz MDC, Cuenca Bermejo L, Veronese N, Fernández Villalba E, González Cuello AM, Kublickiene K, Raparelli V, et al.; GOING-FWD Consortium. Magnesium in kidney function and disease-implications for aging and Sex-A narrative review. Nutrients. 2023;15(7):1710. https://doi.org/10.3390/nu15071710.
9. Pérez-García R, Jaldo MT, Puerta M, Ortega M, Corchete E, de Sequera P, et al. Hypomagnesaemia in haemodialysis is associated with increased mortality risk: its relationship with dialysis fluid. Nefrologia (Engl Ed). 2020;40(5):552 - 562. English, Spanish. https://doi.org/10.1016/j.nefro.2020.04.013.
10. Huang CY, Yang CC, Hung KC, Jiang MY, Huang YT, Hwang JC, et al. Association between hypomagnesemia and mortality among dialysis patients: a systematic review and meta-analysis. PeerJ. 2022;10:e14203. https://doi.org/10.7717/peerj.14203.
11. de Oca A M, Guerrero F, Martinez-Moreno JM, Madueño, Herencia C, Peralta A, Almaden Y, et al. Magnesium inhibits Wnt/β-catenin activity and reverses the osteogenic transformation of vascular smooth muscle cells. PLoS One. 2014;9(2):e89525. https://doi.org/10.1371/journal.pone.0089525.
12. Liu M, Dudley SC Jr. Magnesium, oxidative stress, inflammation, and cardiovascular disease. Antioxid (Basel). 2020;9(10):907. https://doi.org/10.3390/antiox9100907.
13. Ter Braake AD, Shanahan CM, de Baaij JHF. Magnesium counteracts vascular calcification: passive interference or active modulation? Arterioscler Thromb Vasc Biol. 2017;37(8):1431–45. https://doi.org/10.1161/ATVBAHA.117.309182.
14. Zaher MM, Abdel-Salam M, Abdel-Salam R, Sabour R, Morsy AA, Gamal D. Serum magnesium level and vascular stiffness in children with chronic kidney disease on regular hemodialysis. Saudi J Kidney Dis Transpl. 2016;27(2):233–40. https://doi.org/10.4103/1319-2442.178205.
15. Yao WB, Shen Y, Shen LL, Wang XH, Yang HL, Chen JJ, Ma LL, Huang HX. Effect of serum magnesium level on arteriovenous fistula dysfunction in patients on maintenance hemodialysis. Ann Ital Chir. 2025;96(4):478–87. https://doi.org/10.62713/aic.3869.
16. Stolic RV, Jovanovic AN, Trajkovic GZ, Kostic MM, Odalovic AM, Sovtic SR, Sipic MV, Pajovic SD, Sojevic-Timotijevic ZN. Is low magnesium a clue to arteriovenous fistula complications in hemodialysis? Int Urol Nephrol. 2016;48(5):773–79. https://doi.org/10.1007/s11255-015-1207-6.
17. Chen J, Zhou M, Zeng K, Zhang X, Yang X, He L, Pan X. The risk factors of autogenous arteriovenous fistula dysfunction in maintenance hemodialysis

patients and the curative effect of personalized nursing. Am J Transl Res. 2021;13(5):5107–16.
18. Ying J, Cai G, Zhang Y, Zhu M, Pan M, Zhang P. Development and validation of a risk prediction model for autologous arteriovenous fistula thrombosis in patients receiving maintenance hemodialysis. Ren Fail. 2025;47(1):2477832. https://doi.org/10.1080/0886022X.2025.2477832.
19. Zhang Y, Yi J, Zhang R, Peng Y, Dong J, Sha L. Risk factors for arteriovenous fistula thrombus development: a systematic review and meta-analysis. Kidney Blood Press Res. 2022;47(11):643–53. https://doi.org/10.1159/000526768.
20. Cunningham J, Rodríguez M, Messa P. Magnesium in chronic kidney disease Stages 3 and 4 and in dialysis patients. Clin Kidney J. 2012, Feb;5(Suppl 1):i39–51. https://doi.org/10.1093/ndtplus/sfr166.
21. Yamada S, Matsueda S, Arase H, Yamada K, Nishida H, Nakano T. Simultaneous conversion of dialysate magnesium concentration from 1.0 to 1.2 mEq/L and dialysate calcium concentration from 3.0 to 2.6 mEq/L and changes in serum mineral and bone metabolism markers in patients undergoing maintenance hemodialysis: a retrospective study. Renal Replacement Ther. 2024, Dec;10(1):75. https://doi.org/10.1186/s41100-024-00595-3.
22. Leenders NHJ, van Ittersum FJ, Hoekstra T, Hoenderop JGJ, Vervloet MG. Routine hemodialysis induces a decline in plasma magnesium concentration in most patients: a prospective observational cohort study. Sci Rep. 2018;8(1):10256. https://doi.org/10.1038/s41598-018-28629-x.
23. Matias PJ, Ávila G, Domingos D, Gil C, Ferreira A. Lower serum magnesium levels are associated with a higher risk of fractures and vascular calcifications in hemodialysis patients. Clin Kidney J. 2024;18(1):sfae381. https://doi.org/10.1093/ckj/sfae381.
24. Del Giorno R, Riva H, Donato G, Gabutti L. Ionized and total serum magnesium in hemodialysis: predictors and variability. A longitudinal cross-sectional study. Clin Exp Nephrol. 2018;22(3):620–28. https://doi.org/10.1007/s10157-017-1494-6.
25. Rosanoff A, West C, Elin RJ, Micke O, Baniasadi S, Barbagallo M, Campbell E, Cheng FC, Costello RB, Gamboa-Gomez C, Guerrero-Romero F, et al. MaGNet global magnesium project (MaGnet). Recommendation on an updated standardization of serum magnesium reference ranges. Eur J Nutr. 2022;61(7):3697–706. https://doi.org/10.1007/s00394-022-02916-w.
26. Ter Braake AD, Tinnemans PT, Shanahan CM, Hoenderop JGJ, de Baaij JHF. Magnesium prevents vascular calcification in vitro by inhibition of hydroxyapatite crystal formation. Sci Rep. 2018;8(1):2069. https://doi.org/10.1038/s41598-018-20241-3.
27. Kudryavtseva O, Lyngsø KS, Jensen BL, Dimke H. Nitric oxide, endothelium-derived hyperpolarizing factor, and smooth muscle-dependent mechanisms contribute to magnesium-dependent vascular relaxation in mouse arteries. Acta Physiol (oxf). 2024;240(3):e14096. https://doi.org/10.1111/apha.14096.
28. Sheu JR, Hsiao G, Shen MY, Fong TH, Chen YW, Lin CH, Chou DS. Mechanisms involved in the antiplatelet activity of magnesium in human platelets. Br J Haematol. 2002;119(4):1033–41. https://doi.org/10.1046/j.1365-2141.2002.03967.x.
29. Toaima DN, Abdel-Maksoud KS, Atef HM, Salah NY. Magnesium, fibrinolysis and clotting interplay among children and adolescents with type 1 diabetes mellitus; potential mediators of diabetic microangiopathy. Nutr Diabetes. 2025;15(1):13. https://doi.org/10.1038/s41387-025-00368-9.
30. Barbagallo M, Veronese N, Dominguez LJ. Magnesium in aging, health and diseases. Nutrients. 2021;13(2):463. https://doi.org/10.3390/nu13020463.
31. Barbagallo M, Dominguez LJ. Magnesium and type 2 diabetes. World J Diabetes. 2015;6(10):1152–57. https://doi.org/10.4239/wjd.v6.i10.1152.
32. Piuri G, Zocchi M, Della Porta M, Ficara V, Manoni M, Zuccotti GV, et al. Magnesium in obesity, metabolic syndrome, and type 2 diabetes. Nutrients. 2021;13(2):320. https://doi.org/10.3390/nu13020320.
33. Xu EJ, Steele DJR, Fenves AZ. Hypomagnesemia with metformin use in diabetes mellitus: a case and narrative review. Kidney Med. 2025;7(7):101030. https://doi.org/10.1016/j.xkme.2025.101030.
34. Scarpati G, Baldassarre D, Oliva F, Pascale G, Piazza O. Ionized or total magnesium levels, what should we measure in critical ill patients? Transl Med UniSa. 2020;23:68–76. https://doi.org/10.37825/2239-9747.1015.
35. Choi SR, Lee YK, Cho AJ, Park HC, Han CH, Choi MJ, et al. Malnutrition, inflammation, progression of vascular calcification and survival: inter-relationships in hemodialysis patients. PLoS One. 2019;14(5):e0216415. https://doi.org/10.1371/journal.pone.0216415.
36. Li L, Streja E, Rhee CM, Mehrotra R, Soohoo M, Brunelli SM, et al. Hypomagnesemia and mortality in incident hemodialysis patients. Am J Kidney Dis. 2015;66(6):1047–55. https://doi.org/10.1053/j.ajkd.2015.05.024.
37. Silpe J, Koleilat I, Yu J, Kim YH, Taubenfeld E, Talathi S, Coluccio M, Wang K, Woo K, Etkin Y. Sex disparities in hemodialysis access outcomes: a systematic review. Semin Vasc Surg. 2023;36(4):560–70. https://doi.org/10.1053/j.semvascsurg.2023.10.002.
38. Liu S, Wang Y, He X, Wang Y, Li X. Factors affecting suboptimal maturation of autogenous arteriovenous fistula in elderly patients with diabetes: a narrative review. Heliyon. 2024;10(15):e35766. https://doi.org/10.1016/j.heliyon.2024.e35766.
39. Soliveri L, Bozzetto M, Brambilla P, Caroli A, Remuzzi A. Hemodynamics in AVF over time: a protective role of vascular remodeling toward flow stabilization. Int J Artif Organs. 2023;46(10–11):547–54. https://doi.org/10.1177/03913988231191960.
40. Jung J, Jeon-Slaughter H, Nguyen H, Patel J, Sambandam KK, Shastri S, Van Buren PN. Hyperphosphatemia and its relationship with blood pressure, vasoconstriction, and endothelial cell dysfunction in hypertensive hemodialysis patients. BMC Nephrol. 2022;23(1):291. https://doi.org/10.1186/s12882-022-02918-0.
41. Cozzolino M, Ciceri P, Galassi A, Mangano M, Carugo S, Capelli I, Cianciolo G. The key role of phosphate on vascular calcification. Toxins (basel). 2019;11(4):213. https://doi.org/10.3390/toxins11040213.
42. Spoendlin J, Paik JM, Tsacogianis T, Kim SC, Schneeweiss S, Desai RJ. Cardiovascular outcomes of Calcium-Free vs Calcium-based phosphate binders in patients 65 years or Older with end-stage renal disease requiring hemodialysis. JAMA Intern Med. 2019;179(6):741–49. https://doi.org/10.1001/jamainternmed.2019.0045.
43. Tsai PH, Chung CH, Chien WC, Chu P. Effects of calcium-containing phosphate binders on cardiovascular events and mortality in predialysis CKD stage 5 patients. PLoS One. 2020;15(10):e0241435. https://doi.org/10.1371/journal.pone.0241435.
44. Cunha RSD, Santos AF, Barreto FC, Stinghen AEM. How do uremic toxins affect the endothelium? Toxins (Basel). 2020;12(6):412. https://doi.org/10.3390/toxins12060412.
45. Rodrigues N, Jorge A, Mendes P. 3179 predictors of vascular access thrombosis in maintenance hemodialysis patients - qa, KT/V and Convective volume. Nephrol Dialys Transpl. 2023;38(Suppl 1):gfad063c_3179. https://doi.org/10.1093/ndt/gfad063c_3179.
46. Wasim R, Ansari TM, Ahsan F, Siddiqui MH, Singh A, Shariq M, Parveen S. Pleiotropic benefits of statins in cardiovascular diseases. Drug Res (stuttg). 2022;72(9):477–86. https://doi.org/10.1055/a-1873-1978.
47. Martinez L, Duque JC, Escobar LA, Tabbara M, Asif A, Fayad F, Vazquez-Padron RI, Salman LH. Distinct impact of three different statins on arteriovenous fistula outcomes: a retrospective analysis. J Vasc Access. 2016;17(6):471–76. https://doi.org/10.5301/jva.5000612.
48. Suh D, Amendola MF, Reeves M, Wolfe L, Posner M, Davis R. Statins protect against thrombosis of cannulated Radiocephalic fistulas in diabetic patients. Ann Vasc Surg. 2021;75:280–86. https://doi.org/10.1016/j.avsg.2021.01.073.
49. Wan Q, Li L, Yang S, Chu F. Impact of statins on arteriovenous fistulas outcomes: a meta-analysis. Ther Apher Dial. 2018;22(1):67–72. https://doi.org/10.1111/1744-9987.12597.
50. Stepanova N, Ostapenko T, Marchenko V, Holovanova A, Lysii M, Kucher T, et al. Retrospective analysis of statin use and arteriovenous fistula thrombosis in hemodialysis: is there a dose-dependent effect? Ukr J Nephrol Dialys. 2025;2(86):24–34. https://doi.org/10.31450/ukrjnd.2(86).2025.03.
51. Roca-Tey R, Ramírez de Arellano M, González-Oliva JC, Roda A, Samon R, Ibrik O, Ugalde-Altamirano J, Viladoms J, Calls J. Is fetuin-A a biomarker of dialysis access dysfunction? J Vasc Access. 2023;24(3):458–64. https://doi.org/10.1177/11297298211035846.
52. Wei S, Liu N, Fu Y, Sun M. Novel insights into modifiable risk factors for arteriovenous fistula failure and the importance of CKD lipid profile: a meta-analysis. J Vasc Access. 2024;25(5):1416–31. https://doi.org/10.1177/11297298221115557.
53. Roca-Tey R, Samon R, Ibrik O, Roda E, González-Oliva JC, Martínez-Cercós R, Viladoms J. Five years of vascular access stenosis surveillance by blood flow rate measurements during hemodialysis using the Delta-H method. J Vasc Access. 2012;13(3):321–28. https://doi.org/10.5301/jva.5000053.

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