Serum uric acid as a clinically useful nutritional marker and predictor of outcome in maintenance hemodialysis patients

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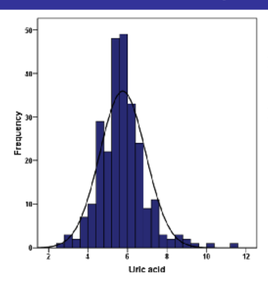
Objectives:

High circulating concentrations of UA have been shown to be associated with an increased risk of cardiovascular disease in the general population (1-2). The recently reported analysis of the DOPPS population (3), found higher uric acid levels associated with a lower risk of all-cause and cardiovascular mortality. We aimed to investigate the associations of UA levels with clinical and laboratory surrogates of nutrition and inflammation, muscle function, health-related quality of life, and all-cause and cardiovascular morbidity and mortality in maintenance HD (MHD) patients.

Methods:

A two-year prospective observational study, performed on 261 MHD outpatients (38.7% women) with a mean age of 68.6±13.6 years. We measured prospective all-cause and cardiovascular (CV) hospitalization and mortality, nutritional scores (malnutrition-inflammation score (MIS), and geriatric nutritional risk index (GNRI)), hand-grip strength (HGS), and short form 36 (SF-36) quality-of-life (QoL) scores.

Histogram showing the distribution of serum uric acid concentration in the study cohort (n=261)



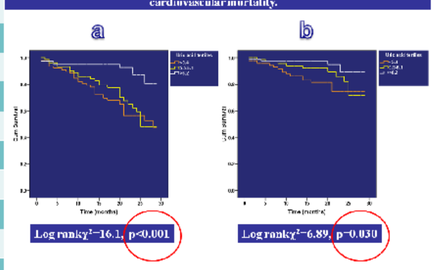
Mean±SD:
5.76±1.2 mg/dl

Median (IQR):
5.7 (5.1-6.3) mg/dl

Baseline demographic, clinical, and laboratory values in total and according to tertiles of uric acid (mg/dl) in 261 hemodialysis patients

Variable	Total (n=261)	Tertile1 (n=97)	Tertile 2 (n=81)	Tertile 3 (n=85)	P
Age (y)	68.6±13.6	72.6±12.4	69.4± 2.2	64.0±15.	<0.001
Gender (n/%)	38.7	11.3	38.3	32.5	<0.001
Vintage (mo)	20.0 (8.0-40.5)	16.0 (7.0-53.5)	27.0 (8.5-58.0)	21.0 (9.0-45.0)	0.40
DM (%)	39	54.6	64.2	59.0	<0.001
Co-morbidity index	4.0 (2.0-7.0)	7.0 (2.0-7.0)	5.0 (2.0-7.0)	3.0 (1.0-6.0)	0.02
Smoker (%)	13.8	17.7	13.6	9.6	<0.001
Systolic BP (mm Hg)	138.2±26.1	148.5±23.8	136.8±26.6	133.5±27.3	0.02
URR	54.0	57.3	56.0	53.5	<0.001
KDV	1.32±0.31	1.32±0.30	1.36±0.28	1.26±0.33	0.08

Kaplan-Meier survival analysis for tertiles of serum uric acid in 261 MHD patients followed for up to 2 years: (A) all-cause mortality, and (B) cardiovascular mortality.

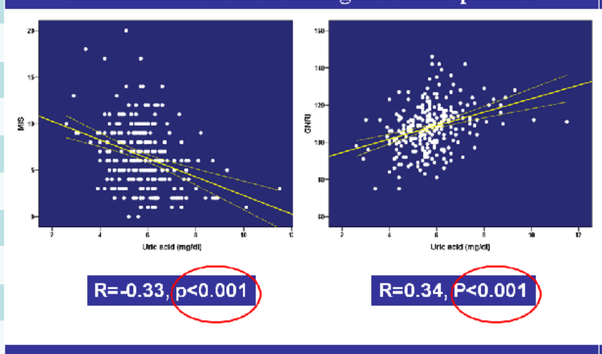


Graphs and tables

Raw and adjusted correlation coefficients of uric acid with the main nutritional and inflammatory markers in the study population (n=261)

	Raw r	P	Adjusted* r	P
nPNA (g/kg/d)	0.16	0.06	0.16	0.08
Albumin (g/dL)	0.29	<0.001	0.21	0.01
Creat (mg/dL)	0.47	<0.001	0.43	<0.001
Trf (mg/dL)	0.19	0.04	0.04	0.67
IL-6 (pg/ml)	-0.13	0.04	-0.15	0.03
BMI (kg/m^2)	0.26	<0.001	0.29	<0.001
Waist–hip ratio	0.16	0.01	0.18	0.009
MAMC (cm)	0.23	<0.001	0.14	0.05
BIA FM (kg)	0.29	<0.001	0.32	<0.001
BIA LBM (kg)	0.20	0.001	0.15	0.03

Bivariate correlations between levels of serum uric acid and nutritional scores among 261 MHD patients

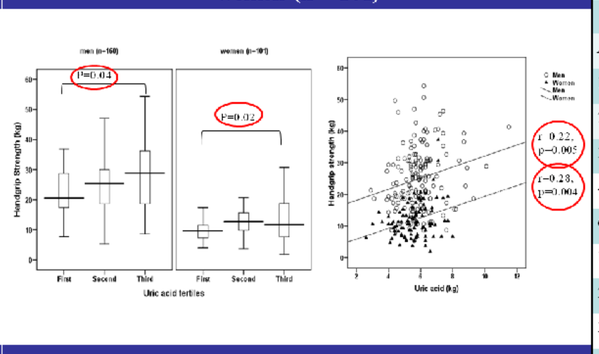


R=-0.33, p<0.001

R=0.34, P<0.001

Solid line represents regression line and dashed lines above and below solid line – 95% confidence interval

Comparison of handgrip strength in men (n = 160) and women (n = 101)



Crude and adjusted all-cause and CVD-related mortality according to uric acid levels in 261 MHD patients

	HR	95% CI	P
All-cause mortality			
1. Crude	0.55	(0.43-0.72)	<0.001
2. 1+age, gender, RRF and vintage	0.56	(0.43-0.74)	<0.001
3. 2+DM, CMI, WHR, Smoking and SBP	0.59	(0.44-0.80)	0.001
4. 3+MIS and IL-6	0.59	(0.41-0.85)	0.005
Cardio-vascular mortality			
1. Crude	0.55	(0.37-0.80)	0.002
2. 1+age, gender, RRF and vintage	0.55	(0.38-0.80)	0.002
3. 2+DM, CMI, WHR, Smoking and SBP	0.61	(0.41-0.91)	0.01
4. 3+MIS and IL-6	0.53	(0.33-0.86)	0.01

Results:

UA positively correlated with laboratory nutritional markers (albumin, creatinine), body composition parameters, HGS (r=0.26, p<0.001) and GNRI (r=0.34, p<0.001). UA negatively correlated with MIS (r=-0.33, p<0.001) and interleukin 6 (r=-0.13, p=0.04). Patients in the highest SUA tertile had higher total SF-36 scores (p=0.04), higher physical functioning (p=0.003) and role-physical (p=0.006) SF-36 scales. For each 1.0 mg/dL increase in baseline UA levels, the first hospitalization hazard ratio (HR) was 0.79 (95% confidence interval (CI), 0.68 to 0.91) and first CV event HR was 0.60 (95% CI, 0.44 to 0.82); all-cause death HR was 0.55 (95% CI, 0.43 to 0.72) and CV death HR was 0.55 (95% CI, 0.35-0.80). Associations between UA and mortality risk continued to be significant after adjustments for various confounders including MIS and interleukin 6. Cubic spline survival models confirmed the linear trends.

Conclusions:

We provide for the first time evidence that SUA is associated with most surrogates of body composition, muscle function, inflammation, and health-related quality of life in MHD patients, suggesting that SUA is a good nutritional marker. Furthermore, SUA is a good marker of upcoming hospitalizations (both all-cause and CVD), as well as an independent predictor of all-cause and cardiovascular death risk. These findings may have important clinical implications. UA is a simple, easily performed and inexpensive laboratory test that can be useful in conjunction with serum albumin in quickly identifying MHD patients with nutritional risks and those needing early nutritional interventions.

References:

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M) Dialysis. M9) Protein-energy wasting, inflammation and oxidative stress in CKD 5D.
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