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Hypokalemia is a risk factor for all-cause mortality in incident hemodialysis patients

Necosad

Aim

To investigate the relation between serum potassium level and all-cause mortality in incident hemodialysis patients and whether there is an optimum serum potassium level to pursue.

Background

Both hypo- and hyperkalemia can potentially induce fatal cardiac arrhythmias in the general population.[1]

Since hemodialysis patients chronically experience dyskalemia,[2,3] the effect of serum potassium on survival and the optimum serum potassium level might differ in these patients.

Methods

- 1114 incident hemodialysis patients (>18 y) from the Netherlands Cooperative Study on the Adequacy of Dialysis, a prospective multi-center cohort study
- Followed from 3 months after start of first dialysis treatment until death, transplantation or a maximum of 5 years
- Serum potassium levels obtained every 6 months and divided into 6 categories: ≤4.0, >4.0 - ≤4.5, >4.5 - ≤5.0, >5.0 - ≤5.5, >5.5 - ≤6.0 and >6.0 mmol/L
- Serum potassium category with lowest adjusted mortality risk set as reference category: >5.0 - ≤5.5 mmol/L
- Hazard ratios for all-cause mortality calculated using a Cox proportional-hazards model with serum potassium category as a time-dependent variable
- Continuous relation between time-dependent serum potassium and all-cause mortality modeled in a 4-knot restricted cubic spline
- Knots chosen at the 5th, 35th, 65th and 95th percentile of the potassium distribution
- All analyses adjusted for age, sex, current smoking, diabetes, cardiovascular disease, subjective global assessment (SGA) and residual kidney function

Results

The prevalence of the six serum potassium categories at baseline (3 months after start of dialysis) was: 11%, 18%, 26%, 22%, 15% and 8%, respectively. During 5 years of follow-up, 438 (39%) deaths were observed.

Baseline characteristics
N = 1114 hemodialysis patients

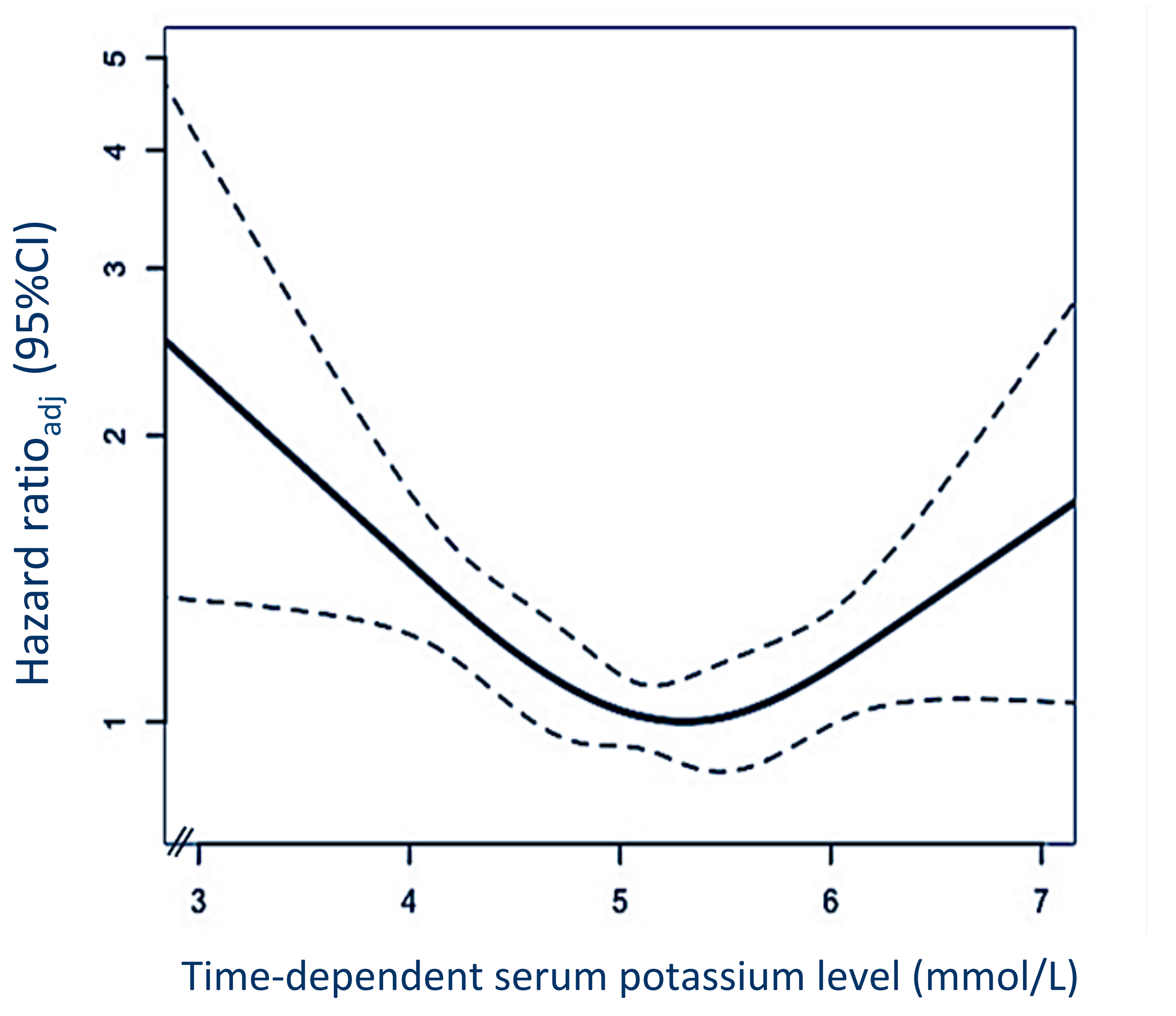
Age, mean (± SD)	63 (±14)
Men, *n* (%)	648 (58)
Potassium, mean (± SD)	5.0 (±0.8)
Current smoker, *n* (%)	287 (26)
Residual eGFR, median (IQR)	3.5 (1.4-4.8)
History of diabetes, *n* (%)	260 (24)
History of CVD, *n* (%)	353 (32)
SGA score	
1-3 (severe PEW)	70 (7)
4-5 (moderate PEW)	275 (26)
6-7 (normal PEW)	690 (67)

CVD = cardiovascular disease, defined as cerebral vascular accident, myocardial infarction or peripheral vascular disease
PEW = protein energy wasting

	Hazard Ratio (95% CI)	
	All-cause mortality	
Time-dependent serum potassium category	Crude	Adjusted*
K ≤ 4.0	1.73 (1.18-2.54)	1.52 (1.03-2.24)
K > 4.0 - ≤ 4.5	1.38 (1.00-1.91)	1.24 (0.89-1.73)
K > 4.5 - ≤ 5.0	1.22 (0.91-1.64)	1.22 (0.91-1.64)
K > 5.0 - ≤ 5.5	1 [reference]	1 [reference]
K > 5.5 - ≤ 6.0	1.07 (0.76-1.49)	1.07 (0.76-1.50)
K > 6.0	1.49 (1.04-2.12)	1.53 (1.07-2.18)

*Adjusted for age, sex, current smoking, history of diabetes mellitus, history of cardiovascular disease, SGA score and residual kidney function
K = serum potassium level

Relation between potassium and 5-year mortality



Conclusion

- We found a U-shaped relation between serum potassium and all-cause mortality in incident hemodialysis patients.
- Low serum potassium was a 1.5-fold stronger risk factor for all-cause mortality compared to the reference category.

Implications

- Our results indicate an optimum serum potassium level between 5.0 and 5.5 mmol/L, emphasizing that potassium lowering therapy should be used with caution in hemodialysis patients.

Strengths

- Only incident hemodialysis patients were included in our study, which is therefore not susceptible to survivor bias, in contrast to studies that included maintenance dialysis patients.
- Serum potassium measurements were executed following study protocol and are therefore less affected to information bias.

Limitations

- As serum potassium fluctuates in hemodialysis patients, we updated it every 6 months. However, shorter intervals between serum potassium measurements would have allowed for a more precise estimation and less 'dilution' of the effect due to phenomena like regression to the mean.
- We used all-cause mortality as outcome, as dyskalemia related cardiac arrhythmias resulting in sudden death are more likely to be misclassified.

References
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3. Torlen K, Kalantar-Zadeh K, Molnar MZ et al. Serum potassium and cause-specific mortality in a large peritoneal dialysis cohort. Clin J Am Soc Nephrol CJASN. 2012;7(8):1272–84.

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