Serum potassium levels and mortality in hemodialysis patients

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Introduction

- Hyperkalemia is associated with risk of ventricular arrhythmias and sudden cardiac arrest.[1]
- It is highly prevalent in dialysis patients due to imbalance in potassium (K) homeostasis.[2]
  - 5%-10% of hemodialysis (HD) patients have high K in any given month.[3]
  - 24% of ESRD patients require emergency HD at some time for treatment of high K.[3]
- Mortality due to high K among HD patients has been estimated at 3.1 per 1000 patient-years.[4]
- While there is no universal clinical definition for hyperkalemia, high K has been variously defined as serum K ≥ 5.0, ≥ 5.5, and ≥ 6.0 mEq/L.[5-7]
- We examined the association between high K, defined by varying thresholds of serum K, and mortality in HD patients.

Methods

DATA AND STUDY COHORT

- This retrospective cohort study used the linked USRDS/DaVita Clinical Data Warehouse database.
- Included patients met the following criteria:
  - Prevalent HD patients aged ≥ 18 years on a thrice-weekly schedule.
  - Alive and continuously enrolled in fee-for-service Medicare Parts A and B with no participation in an HMO from July 1, 2009, through January 31, 2010.
  - Received ≥ 6 dialysis sessions in December 2009.
  - No missing K dialysate bath records for dialysis treatments received in December 2009.
  - Serum K records in January 2010.

STUDY MEASURES

- For each patient, a time-varying exposure variable with 2 levels of K (high vs. normal) was ascertained.
- High K was successively defined by serum K levels 5.5–6.0 mEq/L at 0.1 mEq/L intervals.
- HD schedule was defined as Monday-Wednesday-Friday or Tuesday-Thursday-Saturday.
- Comorbid conditions were defined from the Medicare Medical Evidence Report (form CMS-2728) and from claims during the pre-index period; we required ≥ 1 inpatient or ≥ 2 outpatient claims with relevant diagnosis codes.
- The outcome variable was all-cause and cardiovascular-specific mortality.
  - Cause of death was defined from the ESRD Death Notification.

STATISTICAL ANALYSES

- Each patient was followed from first serum K measurement until the earlier of death or a censoring event.
- We created multiple records for each patient, corresponding to the distinct time intervals between consecutive hyperkalemia event ascertainment.
- Unadjusted and adjusted time-dependent Cox proportional hazards regression (employing the counting process method) was used to assess the association between high K and mortality.

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Figure 1. Construction of the study cohort

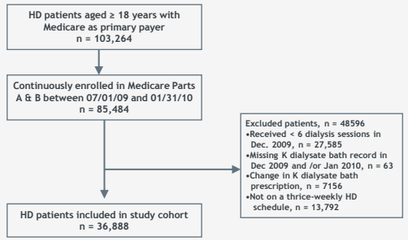


Table 1. Characteristics of patients included in the study cohort

	N	Percent	Mean (SD)
Cohort size , N	36888	100.0	
Age,[a] mean (SD), years			62.9 (14.6)
Female, %	16229	44.0	
Race, %			
White	19053	51.7	
Black	15574	42.2	
Other races	2261	6.1	
Dialysis duration,[a] mean (SD), years			5.2 (4.7)
Primary cause of ESRD, %			
Diabetes	16399	44.5	
Hypertension	11133	30.2	
Glomerulonephritis	3630	9.8	
Other cause	5726	15.5	
Access type, %			
Arteriovenous fistula	3744	10.1	
Graft	991	2.7	
Catheter	16440	44.6	
Other/unknown	15713	42.6	
Body mass index, mean (SD)			28.2 (7.1)
Hospitalized,[b] %	13070	35.4	
Cumulative hospital days,[c] mean (SD)			
Comorbid conditions,[d] %			
Atherosclerotic heart disease	11201	30.4	
Congestive Heart failure	14005	38.0	
Cerebrovascular accident	4521	12.3	
Peripheral vascular disease	8159	22.1	
Other cardiac disease	5403	14.6	
Chronic obstructive pulmonary disease	5294	14.4	
Gastrointestinal disorders	910	2.5	
Liver disease	452	1.2	
Dysrhythmia	5385	14.6	
Cancer	2530	6.9	
Diabetes	22248	60.3	
Weekly dialysis schedule,[e] %			
Tue-Thur-Sat	12849	34.8	
Mon-Wed-Fri	24039	65.2	
Dialysate potassium bath,[f] %			
< 2	3942	10.7	
2-<3	28648	77.7	
≥ 3	4298	11.7	

ESRD, end-stage renal disease; SD, standard deviation. [a]On index date. [b] Accessed during the 180 days before index date. [c] For those hospitalized. [d] Accessed from claims during the 6 months preceding the index date. [e] Accessed from claims during the 6 months preceding the index date. [f] Accessed from claims during the 6 months preceding the index date.

Table 2. Association between elevated serum levels and all-cause mortality in hemodialysis patients

Serum K cut-offs for high K definition	Unadjusted analyses HR[1]	95% CI	P	Adjusted analyses HR[1]	95% CI	P
K ≥ 5.5 mEq/L	1.00	0.91-1.11	0.94	0.99	0.89-1.09	0.78
K ≥ 5.6 mEq/L	1.05	0.94-1.16	0.42	1.03	0.92-1.15	0.62
K ≥ 5.7 mEq/L	1.14	1.01-1.28	0.03	1.13	1.01-1.28	0.04
K ≥ 5.8 mEq/L	1.18	1.03-1.34	0.01	1.18	1.03-1.35	0.01
K ≥ 5.9 mEq/L	1.27	1.10-1.46	< 0.001	1.29	1.12-1.50	< 0.001
K ≥ 6.0 mEq/L	1.34	1.14-1.58	< 0.001	1.37	1.16-1.62	< 0.001

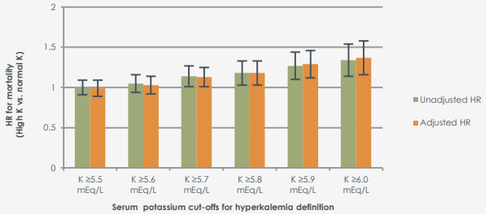
[1]Hazard ratio for High K vs. normal K

Table 3. Association between elevated serum potassium levels and cardiovascular mortality in hemodialysis patients

Serum K cut-offs for high K definition	Unadjusted analyses HR[1]	95% CI	P	Adjusted analyses HR[1]	95% CI	P
K ≥5.5 mEq/L	1.05	0.91-1.21	0.94	1.00	0.86-1.17	0.97
K ≥5.6 mEq/L	1.10	0.94-1.29	0.42	1.06	0.90-1.25	0.49
K ≥5.7 mEq/L	1.12	0.94-1.34	0.03	1.09	0.91-1.31	0.36
K ≥5.8 mEq/L	1.17	0.96-1.42	0.01	1.13	0.93-1.39	0.22
K ≥5.9 mEq/L	1.22	0.98-1.52	<0.001	1.20	0.95-1.50	0.12
K ≥6.0 mEq/L	1.29	1.01-1.66	<0.001	1.28	0.99-1.64	0.06

[1]Hazard ratio for High K vs. normal K

Figure 2. Hazard ratios and 95% CI for risk of all-cause mortality due to hyperkalemia using varying serum potassium cut-offs for the definition of hyperkalemia



Results

COHORT CHARACTERISTICS

- Figure 1 shows the inclusion criteria flowchart.
- Patient demographics and baseline disease characteristics are shown in Table 1.
- A total of 36,888 HD patients with Medicare as primary payer were included (mean age 62.9 ± 14.6 years; 51.7% white; 44.0% female).
- Dialysis K bath was between 2 and 3 mEq/L (inclusive) for 77.7%.

MORTALITY OUTCOMES

- During follow-up, 10.2 % of patients (n = 3753) died of any cause; 4.4% (n = 1604, 42.7%) died of cardiovascular causes.
- Hyperkalemia, defined as serum K ≥ 5.7 mEq/L, was associated with all-cause mortality (adjusted hazard ratio [HR] 1.1, 95% CI 1.01-1.28, P = 0.037, Table 2).
- After adjustment for demographic and clinical factors in time-dependent models, the adjusted HRs increased progressively as the threshold for hyperkalemia rose (adjusted HRs 1.18, P = 0.014, for K ≥ 5.8 mEq/L; 1.29, P = 0.001, for K ≥ 5.9 mEq/L; 1.37, P = 0.0002, for K ≥ 6.0 mEq/L).
- The pattern of the point estimates was similar for cardiovascular mortality, although the results did not reach statistical significance (adjusted HRs 1.09 for K ≥ 5.7 mEq/L, 1.13 for K ≥ 5.8 mEq/L, 1.20 for K ≥ 5.9 mEq/L, 1.28 for K ≥ 6.0 mEq/L).

Conclusions

- This analysis showed that, relative to normal serum K concentrations, elevated serum K is associated with increased risk of death.
- Risk of adverse events increased with increasing degree ("severity") of hyperkalemia.
- A serum K of 5.7 mEq/L may be the threshold at which hyperkalemia becomes overtly dangerous, suggesting a clinically-relevant value that may warrant focused intervention.

1.Weiner ID et al, 1998; 2. Putcha N et al, 2007; 3. Mount DB et al, 2004; 4. USRDS ADR, Reference Tables, 2006; 5. Nyirenda MF et al, 2009; 6. Ahee PP et al, 2000; 7. Kovesdy C et al, 2014.