

HYPERKALEMIA IN ADVANCED CHRONIC KIDNEY DISEASE NOT YET ON DIALYSIS: CLINICAL SIGNIFICANCE AND ASSOCIATION WITH SUDDEN DEATH

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Introduction and Aims

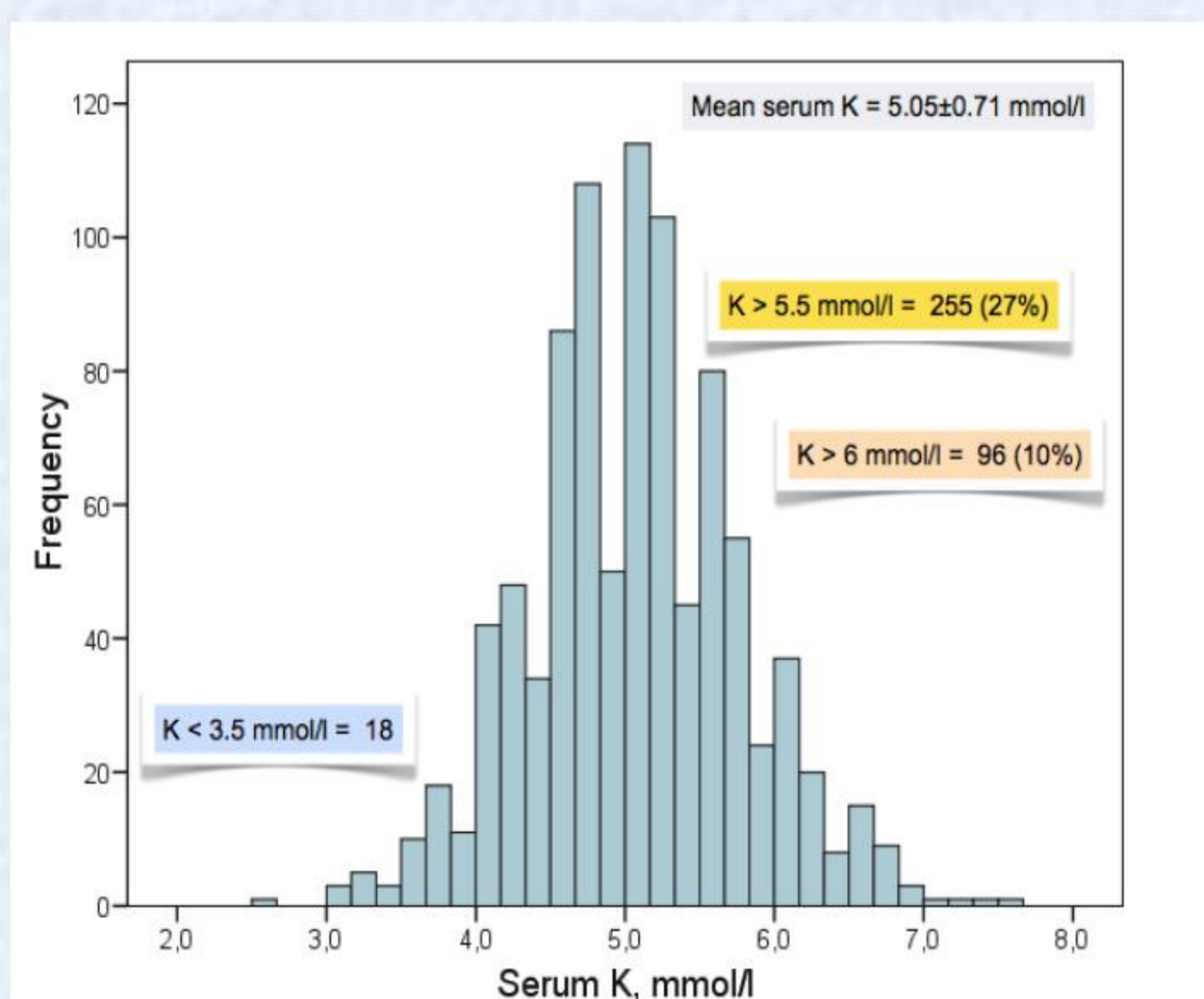
- Hyperkalemia is a common electrolytic disorder in advanced chronic kidney disease (CKD). The potential deadly effect of hyperkalemia has been well established in patients on dialysis. However, the clinical significance of hyperkalemia in pre-dialysis advanced CKD has not yet been addressed.
- Aims: to determine the prevalence and determinants of hyperkalemia in advanced CKD patients not on dialysis and to analyze whether hyperkalemia is associated with increased mortality or sudden death

Patients and Methods

- Observational prospective cohort study which included 936 patients (mean age 65±15 years, 435 women) with eGFR < 30 ml/min/1.73 m², followed at advanced chronic kidney disease hospital-based outpatient clinic (Hospital Infanta Cristina) from Jan 2000 to Jan 2012. Exclusion criteria: age < 18 years
- Hyperkalemia was defined as serum K levels > 5.5 mmol/l in the baseline sample. Hemolysis or other causes of artifactual elevation of serum K level were excluded
- Patients with hypokalemia (serum K < 3.5 mmol/l) were excluded for survival comparisons
- Patients were followed for a median of 402 days (pre-dialysis period), and they were treated according to standard CKD care. Correction of metabolic acidosis (with sodium bicarbonate) and anti-angiotensin drugs (ACEIs, ARB or DRI) were considered major therapeutic objectives, and none of patients was treated with potassium restriction diets, potassium-sparing diuretics, digital, or ion-exchange resins.
- Outcome variables: all-cause mortality and sudden death. Survival comparison test: Kaplan-Meier curves (log-rank test), Cox proportional hazard model (covariates of interest: age, gender, eGFR, comorbidity index, diabetes, BMI, hemoglobin, serum albumin, C reactive protein, serum bicarbonate, serum calcium, anti-angiotensin drugs, diuretics, beta-blockers, EPO)

Results

Frequency distribution of serum potassium levels



Clinical and biochemical characteristics according to basal serum potassium levels

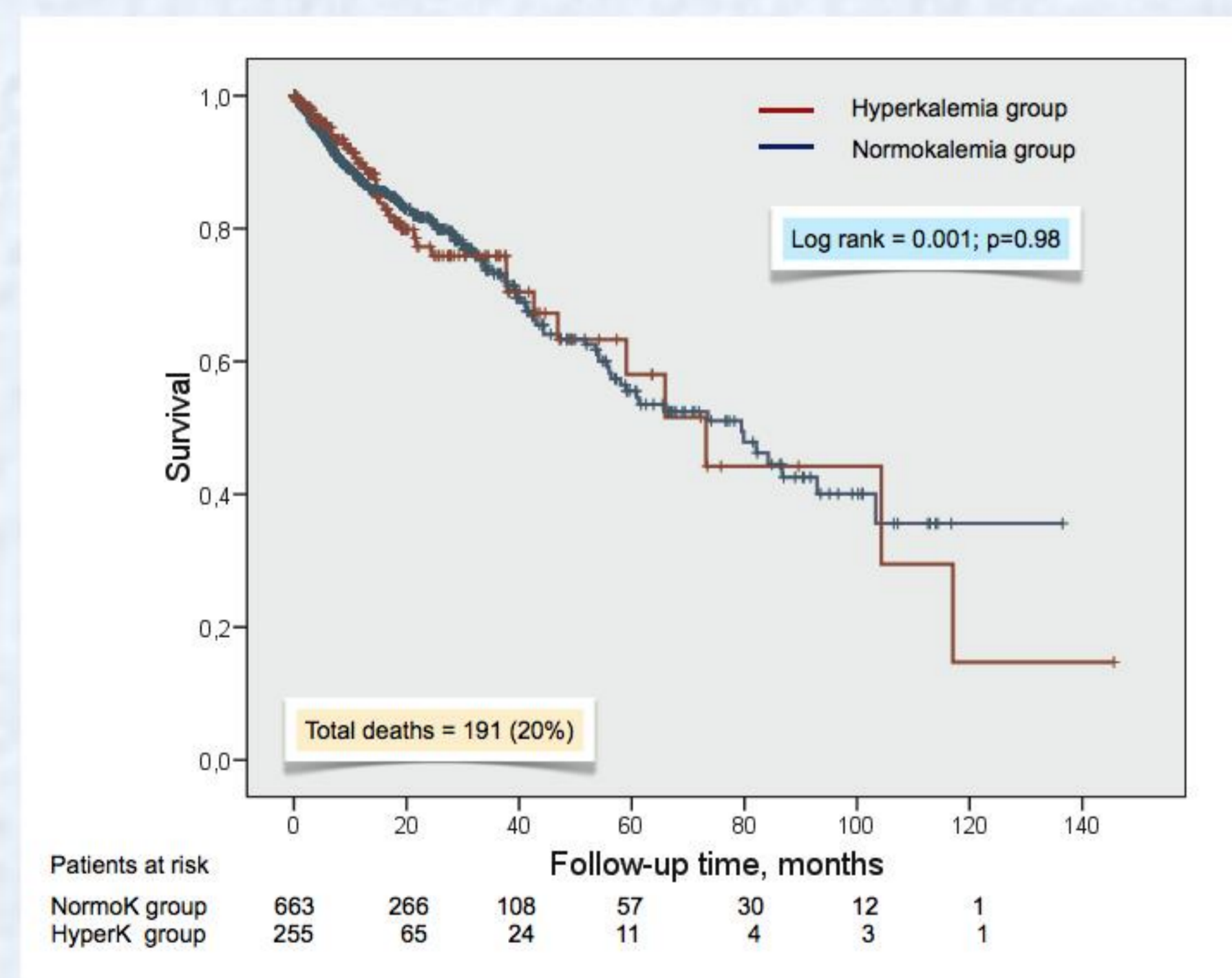
	Serum K > 5,5 mmol/l	Serum K ≤ 5,5 mmol/l	p
N patients	255	681	
Age, years	64±16	65±15	0.09
Gender, male / female	143 / 112	358 / 323	NS
eGFR, ml/min/1,73 m ²	13,3±4,3	14,7±5,1	<0.0001
Diabetes, %	40%	32%	0.016
Comorbidity Index Davies, absence/mild-moderate/severe	90/130/35	241/331/109	NS
Serum K, mmol/l	5.92±0.41	4.72±0.49	<0.0001
Hemoglobin, g/dl	11.1±1.7	11.4±1.7	0.004
Serum Bicarbonate, mmol/l	20.0±3.4	22.2±3.7	<0.0001
Serum Albumin, g/dl	3.86±0.50	3.85±0.48	NS
C-reactive protein, mg/l	8.36±15.16	10.25±17.62	NS
Serum total Calcium, mg/dl	9.10±0.79	9.25±0.86	0.018
Serum Phosphate, mg/dl	5.03±1.12	4.71±1.11	<0.0001
Serum Magnesium, mg/dl	2.00±0.35	2.07±0.33	NS
Protein Catabolic Rate, g/Kg/24h	1.04±0.32	1.02±0.30	NS
Diuretics, %	58%	62%	NS
IECAs/ARAs, %	83%	66%	<0.0001
Betablockers, %	20%	24%	NS
EPO, %	70%	65%	NS

Determinants of hyperkalemia (serum K > 5.5 mmol/l) by multiple logistic regression analysis

Variable	Odds Ratio	95% C.I. OR	p
Diabetes mellitus, 0,1	1.582	1.145 - 2.184	0,005
eGFR, ml/min/1.73 m ²	0.962	0.929 - 0.995	0.026
Serum Bicarbonate, mmol/l	0.856	0.817 - 0.898	<0.0001
Anti-angiotensin therapy (ACEi, ARB or DRI), 0,1	1.979	1.352 - 2.896	<0.0001

Variables which did not enter in the best prediction equation (backward elimination procedure): age, gender, comorbidity index, hemoglobin, serum albumin, protein catabolic rate, C-reactive protein, eGFR, diuretics, and betablockers

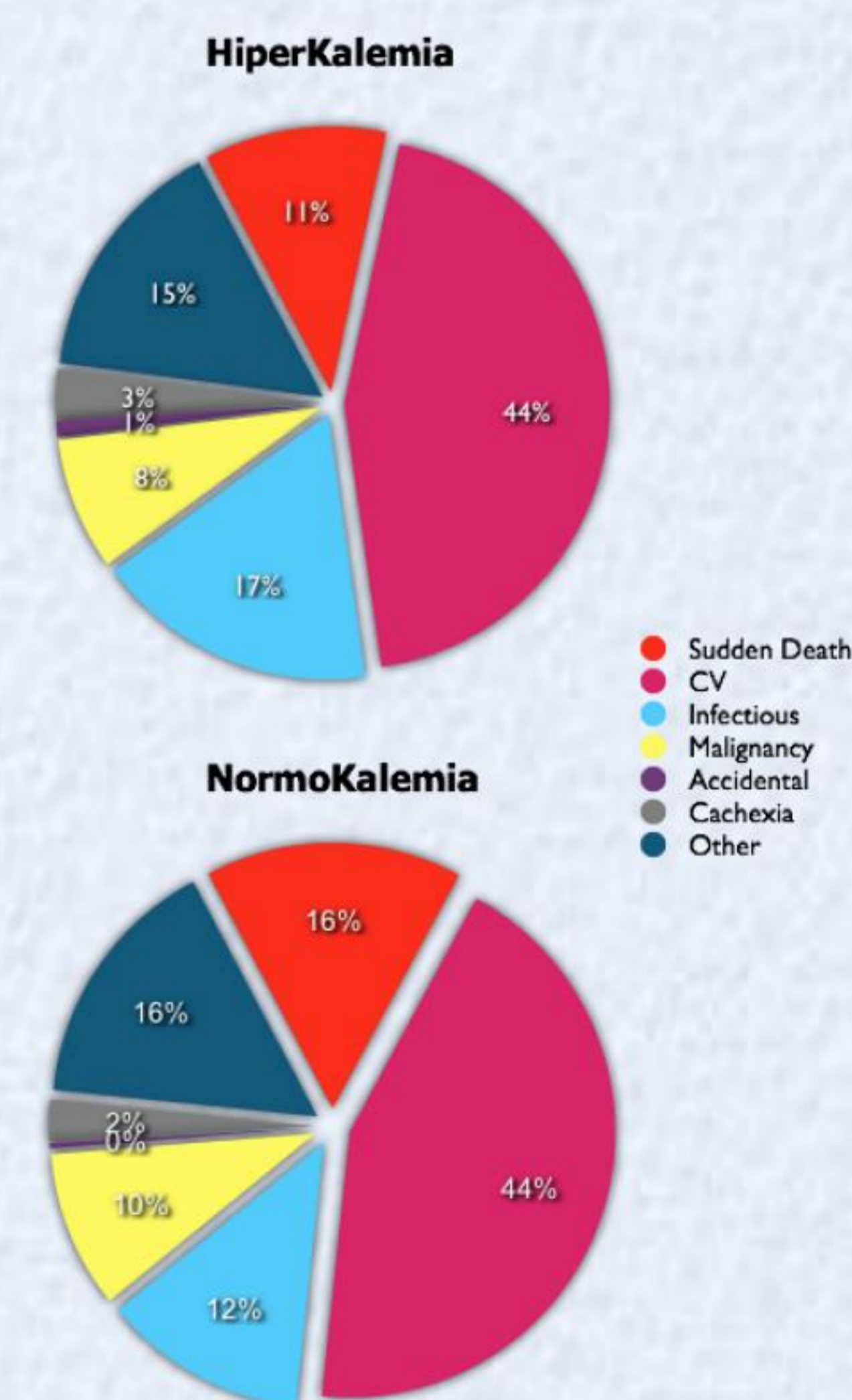
Kaplan-Meier survival analysis in patients with hyperkalemia and normokalemia



Cox regression analysis for mortality in the pre-dialysis study period

Variable	Hazard Ratio	95% C.I. HR	p
Age, years	1.060	1.040 - 1.080	<0.0001
Comorbidity Index (0,1,2)	2.511	1.985 - 3.177	<0.0001
Body Mass Index, Kg/m ²	0.971	0.944 - 1.000	0.046
Serum Albumin, g/dl	0.688	0.489 - 0.969	0.032
C-reactive protein, mg/l	1.014	1.007 - 1.021	<0.0001
Diuretics, (0,1)	1.514	1.097 - 2.090	0.012
Anti-angiotensin therapy (ACEi, ARB or DRI) (0,1)	0.638	0.468 - 0.870	0.005
Hyperkalemia (serum K > 5,5 mmol/l)	1.097	0.752 - 1.599	0.632
Serum K levels, mmol/l	1.020	0.804 - 1.627	0.868

Cause of death in patients with hyper- or normokalemia



Conclusions

- Hyperkalemia is highly prevalent in advanced CKD patients not yet on dialysis. Diabetes, anti-angiotensin drugs and acidosis increase its prevalence
- Hyperkalemia was not associated with worse overall survival or higher incidence of sudden death

