Association between urinary sodium, creatinine, albumin and long term survival in chronic kidney disease

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Abstract

Dietary sodium intake is associated with hypertension and cardiovascular risk in the general population. In patients with chronic kidney disease, sodium intake has been associated with progressive renal disease, but not independently of proteinuria. We studied the relationship between urinary sodium excretion and urinary sodium:creatinine ratio and mortality or requirement for renal replacement therapy in chronic kidney disease. Adults attending a renal clinic who had at least one 24-hour urinary sodium measurement were identified. 24-hour urinary sodium measures were collected and urinary sodium:creatinine ratio calculated. Time to renal replacement therapy or death was recorded. 423 patients were identified with mean estimated glomerular filtration rate of 48ml/min/1.73m^2. 90 patients required renal replacement therapy and 102 patients died. Mean slope decline in estimated glomerular filtration rate was -2.8ml/min/1.73m^2/year. Median follow-up was 8.5 years. Patients who died or required renal replacement therapy had significantly higher urinary sodium excretion and urinary sodium:creatinine but the association with these parameters and poor outcome was not independent of renal function, age and albuminuria. When stratified by albuminuria, urinary sodium:creatinine was a significant cumulative additional risk for mortality, even in patients with low level albuminuria. There was no association between low urinary sodium and risk, as observed in some studies. This study demonstrates an association between urinary sodium excretion and mortality in chronic kidney disease, with a cumulative relationship between sodium excretion, albuminuria and reduced survival. These data support reducing dietary sodium intake in

chronic kidney disease but further study is required to determine the target sodium intake.

Key Words: Hypertension, mortality, sodium, progression, diet, urinary sodium, urinary creatinine, urinary albumin

Introduction

Experimental and population studies have established dietary sodium intake as a key mediator of blood pressure[1], with sodium reduction demonstrated to result in a fall in systolic blood pressure of 3 to 5 mmHg[2, 3]. The Trial of Hypertension Prevention (TOHP) demonstrated 25% cardiovascular risk reduction with a low sodium diet[4]. Population extrapolations suggest that salt-related blood pressure elevation accounts for 14% of strokes and 9% of myocardial infarctions[5]. Damaging effects of dietary sodium on end-organs have been shown in hypertension, including left ventricular hypertrophy (LVH) and albuminuria[6-8]. However, conflicting data exist, with a Cochrane review finding no definitive evidence that sodium intake directly impacted on cardiovascular risk[9].

Sodium intake is widely believed to influence progression of chronic kidney disease (CKD), independently of effects on blood pressure[10]. Experimental evidence suggests a direct pathogenic role for increased sodium intake in renal failure[11] and sodium reduction has been shown to reduce proteinuria in CKD[12, 13]. One Italian study[14] showed patients with low urinary sodium excretion to have lower baseline creatinine clearance but slower long-term progression of CKD. Long term follow-up from the Ramipril in non-diabetic

renal failure (REIN) cohort demonstrated that higher urinary sodium:creatinine ratio (UNa:Cr) was associated with progression to end stage renal failure[15].

Urinary sodium (UNa) excretion (mmol/24h) is a reliable method of measuring sodium intake, independent of dietary assessment, even in patients with reduced estimated glomerular filtration rate (eGFR), where 90% of ingested sodium is excreted in the urine[2]. UNa mirrors dietary sodium intake in patients with CKD[16]. The kidney adapts to reduced nephron mass by altering sodium handling and increasing fractional excretion of sodium. As overall GFR declines with falling nephron mass, there is an increase in single nephron GFR, decreased proximal tubular sodium reabsorption and altered capacity of the distal tubule to reabsorb sodium[17], increasing fractional excretion of sodium. Therefore, the kidneys maintain sodium homeostasis between intake and excretion.

Measuring urinary creatinine excretion takes account of muscle mass and calculating urinary sodium:creatinine ratio (UNa:Cr) may minimise inaccuracy associated with 24-hour collections. One caveat is that lower urinary creatinine has been associated with worse outcome[18]. In this study, we assessed whether urinary sodium excretion, corrected for urinary creatinine, as a method to maximise the utility of 24-hour urine collection, correlates with renal outcome or patient survival in CKD.

Patients

Adult patients attending renal clinics at Glasgow Royal Infirmary between 1992 and 2007 who had at least one 24-hour urinary sodium measurement (UNa) were identified using the electronic patient record. Patients were advised to collect urine for 24 hours after the first void. Urinary electrolytes were measured using flame photometry in a standard laboratory. The 24-hour urinary sodium:creatinine (UNa:Cr) ratio was calculated- as mmol per mmol, UNa:Cr has no units. Date of first urinary sodium measurement was deemed date of study entry. Trained nurses measured blood pressure manually 3 times, using standardized sphygmomanometers; the mean of the last 2 measurements was recorded. Height and weight were recorded. Baseline drug therapy, eGFR using the 4-variable MDRD formula, albuminuria as urinary albumin:creatinine ratio (uACR) were also recorded. The electronic patient record was updated prospectively. General advice was given regarding reducing sodium intake, but a dietician did not routinely assess patients. Patients receiving renal replacement therapy (RRT) at the time of measurement, patients without a weight recording, patients without eGFR recording at time of urinary sodium measurement and at least one further reading were excluded. Patients with decline in eGFR >10ml/min/1.73m^2/yr were excluded to provide a cohort with slowly progressive CKD. The West of Scotland Ethics committee granted a waiver to approve this study as analysis of routinely collected clinical data.

Outcomes and analysis

Dates of starting RRT or death were recorded. Each outcome was analyzed separately and together, censoring for death after starting RRT. Annual decline in eGFR was calculated. Baseline demographics were compared using Student's t-test, Mann-Whitney U test, Chi-square test or one-way analysis of variance (ANOVA) as appropriate with mean values and standard deviation (SD) presented for normally distributed data and median and inter-quartile range (IQR) for non-normally normally distributed data. Correlations between urinary sodium measures and other factors were ascertained using Spearman or Pearson correlation coefficients. Kaplan-Meier survival analysis was performed for time to RRT and or death for patients divided by quartiles of UNa:Cr or stratified by group of UNa:Cr and uACR based on the median value for each, with significance estimated by the log rank method. Cox survival analysis was performed to determine independent predictors of RRT and death, with variables identified as significantly influential on outcome by univariate analysis entered into a backward stepwise regression model[19]. Different measures of urinary sodium excretion were entered separately because of collinearity. Data were analyzed using SPSS version 21 (IBM, Armonk, New York), with Kaplan Meier curves drawn with KMWin[20] using R (R Foundation for Statistical Computing, Vienna, Austria) .

Results

Baseline demographics

Table 1 summarizes baseline demographics for the cohort. 423 patients were included. 50.1% were male with mean age of 51.1 (SD 16.8) years. Online data Figure S1 shows the overall cohort with excluded subjects. Mean baseline eGFR was 48 (SD 28) ml/min/1.73m^2. Mean UNa was 155.8 (SD 66.0) mmol/24h and mean UNa:Cr 16.4 (SD 5.9). 154 patients had repeat UNa available. Median time to repeat sampling was 385 days (IQR 800). Repeat UNa correlated with first UNa (R=0.56, p<0.001) with a difference between mean first and second UNa of 2.0mmol/24h. Average change in urinary sodium was -2.5%**.** Primary renal disease (PRD) was specified in 199 (47.0%) patients and was renovascular disease (n=68), diabetic nephropathy (n=39), tubulointerstitial disease / polycystic kidney disease (n=51), glomerulonephritis (n=39) and others (n=8). The remainder were recorded as CKD of unknown cause.

Urinary sodium excretion in patients with CKD

Patients with lower eGFR had lower UNa levels, particularly in CKD stage 5 (Figure 1a), although there were significant differences across all CKD groups (one way ANOVA p<0.001). UNa:Cr increased with progressive CKD (Figure 1b). To ascertain factors correlated with urinary sodium excretion, the following factors were entered into a correlation matrix: UNa, UNa:Cr, age, weight, eGFR, blood pressure, and uACR. UNa correlated with higher weight (R=0.37, p<0.001), higher eGFR (0.206, p=0.001), $\log_{10}$uACR (-0.15, p=0.003), mean arterial pressure, (0.10, p=0.041) but not systolic blood

pressure (SBP) or diastolic blood pressure (DBP). UNa was not significantly correlated with age. UNa was higher in men (174 vs. 137mmol/24h, p<0.001). UNa was lower in patients prescribed diuretics (mean 145 vs. 159 mmol/24h, p=0.05) but there were no significant differences in UNa between those receiving and those not receiving ACEi.

UNa:Cr correlated with age (R=0.30, p<0.001), SBP (0.22, p<0.001), MAP (0.12, p=0.02) lower eGFR (-0.23, p<0.001) and higher $\log_{10}$uACR (0.15, p=0.003). There were no significant correlations with DBP or weight. UNa:Cr was higher in women (17.5 vs. 15.3, p<0.001) and in patients prescribed diuretics (p<0.001) but not ACEi.

Urinary sodium and albumin excretion

To assess to interaction between uACR and UNa:Cr, subjects were divided into groups based on 'high' or 'low', uACR and UNa:Cr respectively with subjects allocated to high or low groups based on uACR and/or UNa:Cr being above or below the median value for the cohort. The cut points were 11mg/mmol and 16.0 for uACR and UNa:Cr respectively. The four groups are shown in Table 2 with significant differences in age, renal function and blood pressure demonstrated across the groups.

Urinary sodium and albumin excretion and need for RRT or death

90 patients (21.3%) required renal replacement therapy (RRT) and 102 patients died (24.1%) during follow-up. Cause of death was cardiovascular disease (n=25), infection (n=13), malignancy (n=2), known other (n=19), unknown (n=43). 48 patients died after receiving RRT. 144 (34.0%) patients

either required RRT or died. Censoring for death or RRT, median follow-up for the cohort was 8.5 (IQR 6.7) years. Mean slope decline in eGFR was -2.8 (4.0) ml/min/1.73m^2/yr. Characteristics of patients who died or required RRT during follow up a shown in data supplement Table S1. Kaplan-Meier analysis demonstrated that highest UNa or UNa:Cr groups exhibited reduced patient survival and combined patient and renal survival ($p<0.001$, data supplement Figure S2). Higher UNa:Cr was not associated with significantly reduced time to requirement for RRT ($p=0.087$). Effect of interaction between uACR and UNa:Cr was tested using the groups in Table 2. Patients with higher UNa:Cr were at greater risk of both death and requirement for RRT, irrespective of uACR status (Figure 2b). Increased uACR was an additional risk for reduced patient and renal survival (Figure 2). Effect of the interaction between UNa:Cr and uACR on survival analysis to death, RRT or either death or RRT was also performed with patients stratified by diuretic use (supplementary Figures S3, S4) or by eGFR above or below 45ml/min/1.73m^2 (supplementary Figure S5). To assess the implications of UNa and albuminuria, survival analysis was performed with patients stratified into high and low UNa and albuminuria groups based on median UNa (143mmol/24h) and uACR (11mg/mmol). In these analyses, patients with lower UNa had relatively improved outcome, with patients in higher albuminuria groups having poorer outcome (supplementary Figure S6).

Cox regression analyses

Cox regression analysis was performed to identify independent predictors of death, RRT or RRT or death (Table 3 and supplementary Tables S2, S3).

Albuminuria, eGFR, and age were independent predictors of death, whilst UNa:Cr was not a independent predictor of death (p=0.085). Albuminuria and eGFR were predictors of need for RRT whilst eGFR whilst diuretic use appeared protective. Albuminuria and age were predictors of the combined outcome of death or RRT. Additional analyses were performed separately for subjects receiving or not receiving diuretic therapy with consistent results irrespective of diuretic status (Supplementary Tables S4-9). Figure 3 demonstrates hazard plots for risk of death or RRT stratified by combined UNa:Cr group and albuminuria after adjusting for age, gender, eGFR, MAP, diuretic and ACEi usage. This demonstrates association between cumulative uACR and UNa:Cr grouping and significantly increased risk of death or RRT.

Discussion

In this study we demonstrate an association between urinary sodium excretion, a marker of dietary sodium intake, and mortality in patients with CKD. However, this relationship did not persist after adjusting for age, renal function, blood pressure and albuminuria. Urinary sodium was associated with risk of requiring RRT, but not independent of albuminuria or baseline eGFR, findings similar to *post hoc* analyses of the REIN studies[15].

The mean sodium excretion in our cohort was equivalent to a dietary salt intake of 9.1g per day, lower than the United Kingdom average, reflecting combined effects of dietary advice and malnutrition in CKD[21]. We adjusted urinary sodium for urinary creatinine excretion, which corrects for muscle mass, but may also take into account reduced GFR, or reduced tubular secretion of creatinine in CKD. Use of 24-hour urinary sodium:creatinine ratio rather than 24-hour urinary sodium may reduce bias associated with incomplete urine collections, similar to using the urinary albumin:creatinine ratio to estimate albumin excretion. As urinary albumin:creatinine also depends on urinary creatinine, its prognostic role is also determined by low urinary creatinine which reflects frailty and low muscle mass. Low urinary creatinine may also partly explain the prognostic value of the UNa:Cr ratio in our study. 24-hour urine collection remains the best method for assessing sodium excretion and our sodium:creatinine ratio was derived from a 24-hour collection. Spot samples are less representative due to circadian variation in sodium excretion.

We observed lower urinary sodium excretion in patients with lower eGFR perhaps due to reduced dietary intake related to poor appetite. Alternatively,

despite increasing fractional sodium excretion, the failing kidneys may be unable to excrete sodium fully. However, even if sodium is stored in non-osmotically active form, as recently proposed[22], accumulation of vast amounts of sodium over a prolonged period would overwhelm storage sites. Thus even in advanced CKD, patients are in sodium balance and UNa reflects dietary intake.

There are multiple mechanisms for sodium-mediated damage. Haemodynamic effects mediated via volume retention include increased shear stress, endothelial dysfunction, elevated cardiac preload, vascular stiffness and elevated afterload and LVH. Non-haemodynamic factors such as oxidative stress via superoxide production[23] and inflammation have also been demonstrated[24, 25].

Damaging effects of dietary sodium intake on end-organs have been shown in various populations. A study of normotensive and never treated hypertensives showed high dietary sodium intake was associated with LVH and albuminuria[6]. The Framingham Offspring Study demonstrated increasing urinary sodium to be associated with increasing uACR[7, 8], using spot urinary sodium samples normalized to creatinine. Using spot samples could introduce variability as urinary sodium excretion may vary throughout the day. The large Scottish Heart Health Study, drawn from a similar population to ours, showed that urinary sodium predicted coronary heart disease in women[26].

Controversy exists regarding the influence of very low sodium intake on cardiovascular events in the general population. A large pan-European study in patients without cardiovascular disease found low urinary sodium excretion to be associated with increased cardiovascular risk[27]. *Post hoc* analyses of

the ONTARGET and TRANSCEND trials in patients at high cardiovascular risk demonstrated J-shaped relationships between urinary sodium and outcome[28], whilst data from ONTARGET suggest that sodium intake does not *per se* increase risk of CKD in diabetics[29]. Therefore in non-CKD populations, whilst reduction in dietary sodium intake may be beneficial, there may be a lower threshold of optimum sodium intake.

In patients with CKD, proteinuria (or albuminuria) is major predictor of both CKD progression[30] and predicts cardiovascular disease in both CKD and the general population[31, 32]. In univariate analyses, we have demonstrated increased urinary sodium excretion has cumulative effects with albuminuria on both renal and patient survival, in patients with low and high urinary albumin excretion. Lowering dietary sodium intake has been shown to reduce proteinuria, independent of blood pressure[12]. The anti-proteinuric response to renin-angiotensin system inhibitors is augmented by a low sodium diet[33]. A recent crossover study has shown salt restriction to have dramatic effects on blood pressure, vascular function and proteinuria in CKD patients[34]. These results provide powerful arguments for salt restriction in CKD. Although observational, our study adds weight to the notion that sodium restriction is beneficial. A prospective randomized controlled trial in optimally treated CKD patients is required, addressing effects of reduced sodium intake on mortality, cardiovascular events and commencement of renal replacement therapy.

Our study has several limitations. This was a retrospective cohort study using prospectively collected data. Patients were prescribed a number of different medications. Variations in diet during follow-up are not accounted for, but in a subset of patients with two collections, urinary sodium was relatively constant

over time. An assessment of nutritional status would be useful. We do not have causes of death for all patients. Despite attempting to ensure complete urinary collections, some may be incomplete. As an observational study we report associations and cannot prove causality. There may be co-linearity between some of the variables in the multivariate model. We have not assessed the impact of sodium intake on non-fatal cardiovascular events. As low urinary creatinine is a major component of poor outcome and it is difficult to dissociate any relationship between UNa:Cr, urinary ACR and outcome and that driven solely by urinary creatinine[18]. A larger study would be required to prove this. Nonetheless, UNa:Cr represents a useful marker for monitoring sodium intake and may be a target for interventional studies examining long-term effect of sodium reduction in CKD.

Perspectives

A high 24-hour urinary sodium to creatinine ratio, reflective of proportionally high dietary sodium intake in CKD, is associated with significantly increased risk of death but not independent of eGFR, age and albuminuria. There is a cumulative relationship between urinary sodium:creatinine ratio and albuminuria on adverse outcomes. These are novel findings and the first to observe a relationship between sodium intake and mortality in CKD. Further long-term studies to determine optimal sodium intake in CKD are required.

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Novelty and Significance

What Is New?

- Urinary sodium to creatinine ratio is higher with increasing severity of chronic kidney disease

- High urinary sodium intake reflected by a high urinary sodium or high urinary sodium to creatinine ratio is associated with reduced survival in chronic kidney disease patients irrespective of albuminuria status

- Association between high urinary sodium or high urinary sodium to creatinine ratio and increased need for renal replacement therapy is not independent of baseline renal function or albuminuria

What Is Relevant?

- These data support the notion of reducing dietary sodium intake in patients with chronic kidney disease

- The major benefit of sodium reduction is likely to be on patient survival and not on progression of renal disease

- Further study is required to inform target levels of sodium intake in patients with chronic kidney disease

Summary

We have demonstrated an association between urinary sodium excretion and mortality in chronic kidney disease and a cumulative relationship between sodium excretion, albuminuria and reduced survival.

Table and figure legends

Figure 1 (a) Bar chart of mean urinary sodium excretion (mmol/24h) and 1SD by CKD stage, p<0.001 by one-way ANOVA **(b)** Bar chart of mean UNa:Cr and 1SD by CKD stage, p<0.001 by one-way ANOVA.

Figure 2 (a) Kaplan-Meier survival plot of time to death by group of UNa:Cr and albuminuria **(b)** Kaplan-Meier survival plot of survival to requirement for RRT by group of UNa:Cr and albuminuria (1 = low UNa:Cr, low uACR, 2 = high UNa:Cr, low uACR, 3 = low UNa:Cr, high uACR, 4 = high UNa:Cr, high uACR). Comparison by log rank test and estimate of significance, for both (a) and (b) p<0.001.

Figure 3 Hazard plot of risk of death or RRT by combined UNa:Cr and albuminuria (1 = low UNa:Cr, low uACR, 2 = high UNa:Cr, low uACR, 3 = low UNa:Cr, high uACR, 4 = high UNa:Cr, high uACR) after adjusting for age, gender, eGFR, proteinuria, MAP and diuretic or ACEi usage. Variables included in the Cox regression model were age, eGFR, gender, mean arterial pressure, $\log_{10}$uACR, UNa:Cr, ACEi use, diuretic use.

Table 1: Baseline demographics of cohort.

Mean ± SD or median (IQR) values are displayed or number and percentage of total cohort. eGFR = estimated glomerular filtration rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; MAP =mean arterial pressure; uACR = urinary albumin to creatinine ratio; UNa = 24h urinary sodium excretion; UNa:Cr = urinary sodium to creatinine ratio; UCr = 24h urinary creatinine excretion; ACEi = angiotensin converting enzyme inhibitor; RRT = renal replacement therapy.

Table 2: Demographics of patients by stratum of combined urinary sodium: creatinine and urinary albumin: creatinine ratio

Subjects were divided into groups based on ‘high’ or ‘low’, urinary albumin excretion and UNa:Cr respectively with subjects allocated to high or low groups based on uACR and/or UNa:Cr being above or below median value for the cohort- 11mg/mmol and 16.0 for ACR and UNa:Cr respectively. Data shown are mean with standard deviation in parentheses for continuous variables and number and percentage of the group for categorical variables. Comparisons are one-way ANOVA for continuous variables and Chi-square for categorical variables. UNa:Cr = urinary sodium to creatinine ratio; uACR = urinary albumin to creatinine ratio; eGFR = estimated glomerular filtration rate; SBP = systolic blood pressure; MAP =mean arterial pressure; $\log_{10}$ACR = log transformed uACR; UNa = 24h urinary sodium excretion; UCr = 24h urinary creatinine excretion; RRT = renal replacement therapy

Table 3: Cox regression survival analyses for end point of death

Data presented as hazard ratio (HR), 95% confidence interval (95% CI) and estimate of significance (p). eGFR = estimated glomerular filtration rate; $\log_{10}$ACR = log transformed urinary albumin:creatinine ratio; age in years; MAP = mean arterial pressure; UNa:Cr = urinary sodium:creatinine ratio; ACEi = angiotensin converting enzyme inhibitor (0=yes). Variables included in the Cox regression model were age,

eGFR, gender, mean arterial pressure, log_{10}uACR, UNa:Cr, ACEi use, diuretic use.

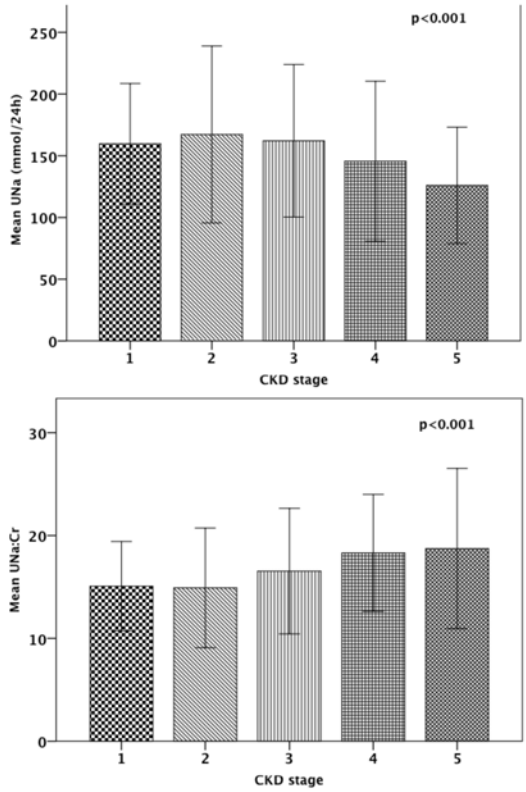

Figure 1

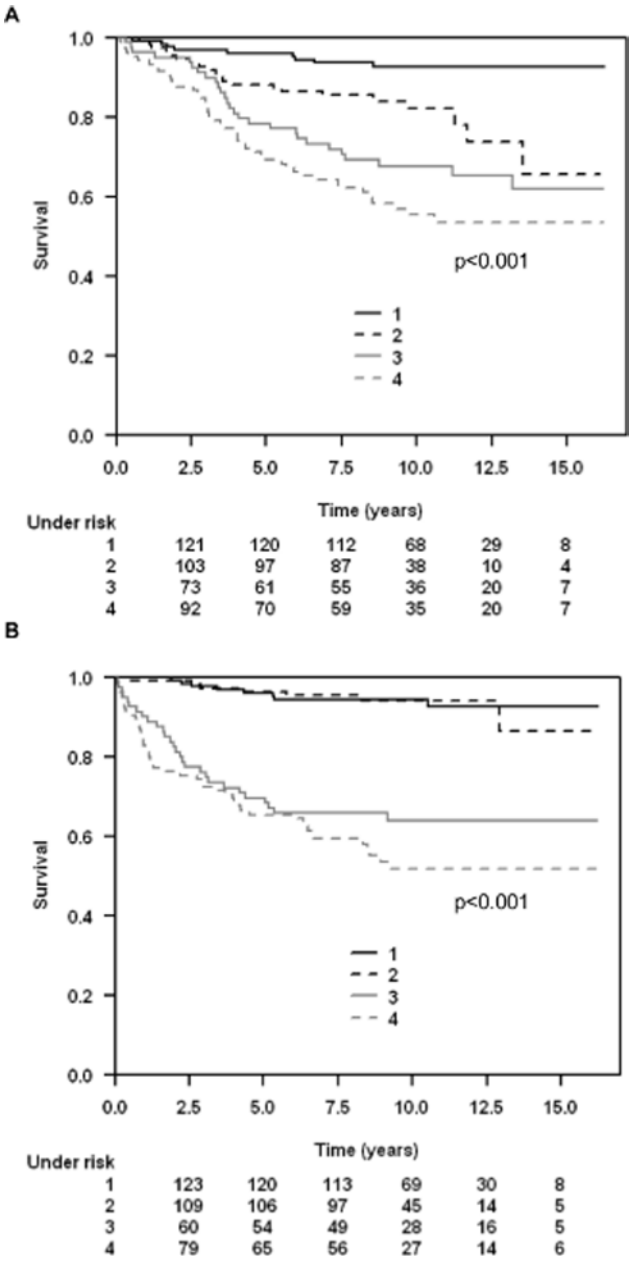
A
1.0
0.8
0.6
0.4
0.2
0.0
Survival
p<0.001
1
2
3
4
0.0
2.5
5.0
7.5
10.0
12.5
15.0
Time (years)
Under risk
1 121 120 112 68 29 8
2 103 97 87 38 10 4
3 73 61 55 36 20 7
4 92 70 59 35 20 7
B
1.0
0.8
0.6
0.4
0.2
0.0
Survival
p<0.001
1
2
3
4
0.0
2.5
5.0
7.5
10.0
12.5
15.0
Time (years)
Under risk
1 123 120 113 69 30 8
2 109 106 97 45 14 5
3 60 54 49 28 16 5
4 79 65 56 27 14 6

Figure 2

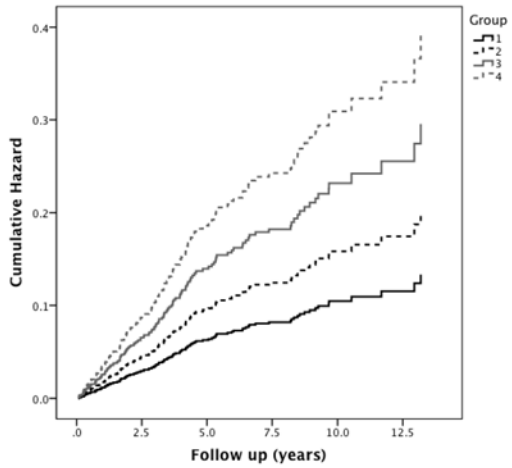
Group
1
2
3
4
Cumulative Hazard
0.4
0.3
0.2
0.1
0.0
.0
2.5
5.0
7.5
10.0
12.5
Follow up (years)

Figure 3

Table 1

Variable	Result
Gender (% male)	212 (50.1)
Age (years)	51.1 ± 16.8
Weight	75.5 ± 18.4
eGFR at baseline (ml/min/1.73m^2)	48 ± 25
SBP (mmHg)	139 ± 25
DBP (mmHg)	79 ± 13
MAP (mmHg)	99 ± 14
uACR (mg/mmol)	11.0 (83)
UNa (mmol/24h)	155.8 ± 66.0
UCr (mmol/24h)	10.1 ± 3.9
UNa:Cr	16.4 ± 5.9
Diuretic therapy (%)	106 (25.1)
ACEi (%)	105 (24.8)
Deaths (n,%)	102 (24.1)
RRT (n,%)	90 (21.3%)
eGFR loss (ml/min/1.73m^2/yr)	-2.8 (4.0)

Table 2

Variable	All patients N=423	Low UNa:Cr Low uACR N=127	High UNa:Cr Low uACR N=111	Low UNa:Cr High uACR N=80	HIgh UNa:Cr High uACR N=105	p
eGFR (ml/min/1.73m^2)	48 (25)	61 (21)	54 (23)	36 (23)	34 (22)	<0.001
Age (y)	52.1 (16.8)	46.9 (16.5)	52.7 (17.8)	51.9 (14.6)	57.9 (15.8)	<0.001
n male (%)	212 (50.1)	73 (57.5)	42 (37.8)	52 (65.0)	45 (42.9)	<0.001
SBP (mmHg)	139 (24)	132 (20)	136 (22)	142 (25)	150 (26)	<0.001
MAP (mmHg)	99 (14)	96 (13)	96 (13)	102 (15)	105 (16)	<0.001
log_{10}uACR	1.14 (0.9)	0.39 (0.40)	0.47 (0.44)	1.99 (0.37)	2.05 (0.43)	<0.001
Weight	75.5 (18.4)	75.3 (17.1)	74.2 (20.0)	79.2 (18.4)	74.3 (17.8)	0.23
UNa (mmol/24h)	156 (66)	140 (46)	192 (82)	127 (46)	160 (64)	<0.001
UCr (mmol/24h)	10.1 (3.9)	12.0 (3.7)	9.4 (3.6)	10.7 (3.8)	7.9 (3.2)	<0.001
Dead (n) (% of group)	102 (24.1)	9 (7.1)	24 (21.6)	27 (33.8)	45 (42.9)	<0.001
RRT (n) (% of group)	90 (21.3)	8 (6.3)	7 (6.3)	28 (35.0)	47 (44.8)	<0.001
RRT or dead (n)(% of group)	144 (34.0)	14 (11.0)	24 (21.6)	40 (50.0)	66 (62.9)	<0.001

Table 3

Death as the dependent variable (n=102)								
Variable	Univariate				Multivariate			
	HR	p-value	95% Confidence interval		HR	p-value	95% Confidence interval	
Age	1.049		1.030	1.069	1.048	<0.001	1.030	1.067
log_{10} uACR	1.767	<0.001	1.303	2.396	1.726	<0.001	1.281	2.325
eGFR	0.976	0.001	0.962	0.989	0.973	<0.001	0.961	0.986
UNa:Cr	1.034	0.057	0.999	1.071	1.030	0.085	0.996	1.064
MAP	0.993	0.32	0.978	1.007				
Diuretic use	1.209	0.42	0.761	1.922				
ACEi use	1.155	0.53	0.738	1.806				
Gender(female)	0.879	0.55	0.578	1.337				