THE ASSOCIATION BETWEEN RENAL TUBULAR DAMAGE AND MORTALITY IN GENERAL JAPANESE POPULATION: THE TAKAHATA STUDY.

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OBJECTIVES

Renal tubular damage has an influence on renal deterioration, however the effect of renal tubular damage on mortality is unknown. To clarify this, we conducted a longitudinal study in community-based population.

METHODS

Subjects of this study were 3443 Japanese over 40-year-old. Renal tubular damage was assessed using urinary beta 2-microglobulin-creatinine ratio (UBCR) in morning spot urine specimen. We investigated the association between the level of UBCR and mortality during 7-year observational period.

CONFLICT OF INTEREST

All authors declared no conflict of interest.

FIGURES AND TABLES

Table 1. Comparisons of baseline characteristics among subgroups classified by UBCR

	UBCR subgroups				
UBCR (μg/g)	<100	100-199	200-299	300≤	P value
Number	1346	1061	305	374	
Male (%)	47.2	38.1	46.4	49.6	<0.001[a]
Age (yrs)	60.3 ± 10.4	63.5 ± 9.7	65.6 ± 9.8	67.9 ± 9.1	<0.001
Systolic BP (mmHg)	131.8 ± 16.1	134.4 ± 15.1	136.0 ± 15.8	140.7 ± 15.6	<0.001
Diastolic BP (mmHg)	78.5 ± 10.0	78.4 ± 9.6	80.1 ± 10.4	82.3 ± 10.5	<0.001
Body mass index (kg/m²)	23.7 ± 3.2	23.3 ± 3.2	23.3 ± 3.1	23.5 ± 3.6	0.003
Hypertension (%)	48.7	55.0	59.9	73.9	<0.001[a]
Obesity (%)	33.0	27.6	28.1	29.7	0.029[a]
Smoker (%)	35.2	30.3	29.7	28.9	0.017[a]
Drinker (%)	43.5	37.5	40.4	38.4	0.020[a]
Diabetes (%)	8.5	6.3	7.6	8.7	0.190[a]
Hypercholesterolemia (%)	34.8	35.3	28.7	27.6	0.008[a]
Albuminuria (%)	12.0	21.0	32.2	53.5	<0.001[a]
Current medication (%)	41.8	43.6	48.6	56.8	<0.001[a]
Serum creatinine (mg/dl)	0.69 ± 0.15	0.64 ± 0.14	0.66 ± 0.15	0.73 ± 0.48	<0.001
eGFR (ml/min/1.73m²)	79.9 ± 15.3	83.6 ± 16.1	82.7 ± 17.5	78.4 ± 19.0	<0.001
Hemoglobin (g/dl)	13.9 ± 1.5	13.6 ± 1.4	13.6 ± 1.4	13.6 ± 1.4	<0.001
Serum albumin (g/dl)	4.52 ± 0.26	4.49 ± 0.25	4.48 ± 0.24	4.44 ± 0.27	<0.001
Uric acid (mg/dl)	5.30 ± 1.39	4.87 ± 1.28	4.79 ± 1.22	4.95 ± 1.35	<0.001
Fasting blood sugar (mg/dl)	89.3 ± 27.9	86.8 ± 27.3	89.6 ± 28.6	88.7 ± 29.1	0.130
HbA1c (%)	5.24 ± 0.69	5.22 ± 0.56	5.35 ± 0.90	5.28 ± 0.69	0.016
e24hUNa (mEq/day)	193.2 ± 53.7	216.4 ± 54.9	228.1 ± 58.1	246.0 ± 60.7	<0.001
Past history of MI/stroke (%)	1.9	2.3	3.8	4.3	0.017[a]

One-factor ANOVA; [a]Chi-square test. UBCR, urine beta 2-microglobulin-creatinine ratio; BP, blood pressure; eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1c; e24hUNa, estimated 24-h urinary sodium excretion.; MI, myocardial infarction.

Table 2. Multiple logistic regression model to predict high UBCR (≥300 μg/g)

	Odds ratio	(95% CI)	P value
Gender male	1.448	(0.995, 2.108)	0.053
Age (per 10-year increase)	1.508	(1.303, 1.745)	<0.001
Drinking	0.803	(0.584, 1.102)	0.174
Smoking	0.761	(0.554, 1.044)	0.090
Obesity	0.680	(0.519, 0.893)	0.006
Hypertension	1.843	(1.364, 2.490)	<0.001
Hypercholesterolemia	0.803	(0.612, 1.054)	0.113
Diabetes	0.990	(0.567, 1.728)	0.973
Current medication	0.942	(0.706, 1.257)	0.684
Hemoglobin (per 1.0 g/dl increase)	0.984	(0.885, 1.094)	0.766
Serum albumin (per 0.25 g/dl increase)	0.765	(0.680, 0.860)	<0.001
Uric acid (per 1.0 mg/dl increase)	0.856	(0.769, 0.952)	0.004
Hemoglobin A1c (per 1.0% increase)	0.898	(0.709, 1.137)	0.371
Albuminuria	3.288	(2.558, 4.227)	<0.001
eGFR (per 10 ml/min/1.73m² decrease)	1.264	(1.164, 1.372)	<0.001
e24hUNa (per 50 mEq/day increase)	1.932	(1.724, 2.164)	<0.001

CI, confidence interval; eGFR, estimated glomerular filtration; e24hUNa, estimated 24-h urinary sodium excretion.

Table3. Cox proportional analysis for values of UBCR predicting death during follow-up period.*

A) All-cause death.

UBCR(μg/g)	Adjusted HR	95% CI	P value
<100	1.000		
100-199	1.361	(0.852, 2.419)	0.2006
200-299	1.472	(0.809, 2.678)	0.2006
≥300	1.904	(1.103, 3.287)	0.0207

B) Noncardiovascular death.

UBCR(μg/g)	Adjusted HR	95% CI	P value
<100	1.000		
100-199	1.255	(0.724, 2.174)	0.4185
200-299	1.470	(0.723, 2.991)	0.2874
≥300	1.952	(1.021, 3.729)	0.0430

*Cox proportional analysis adjusted for age, gender, eGFR, albuminuria, and other confounding factors.

Fig. 1. The distribution of UBCR.

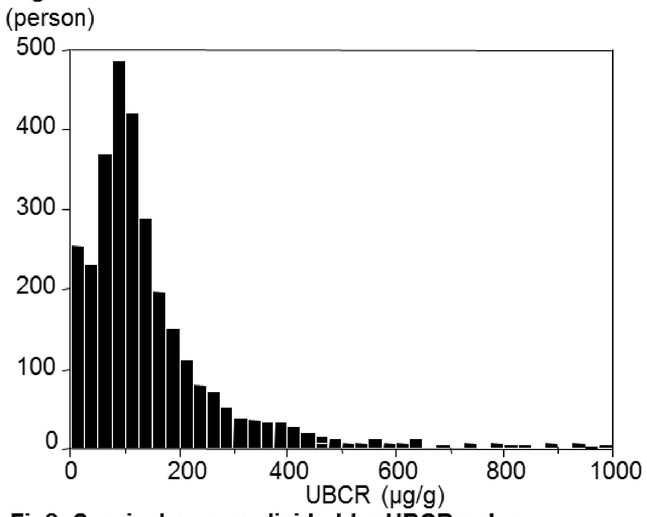


Fig2. Survival curves divided by UBCR value.

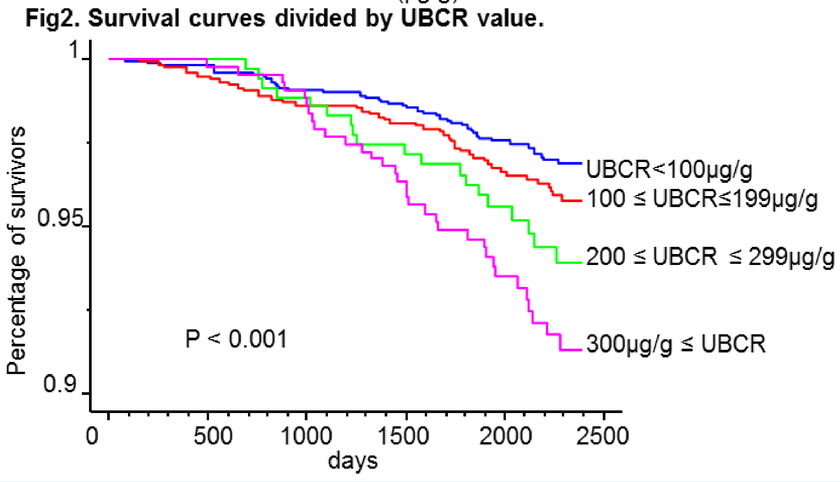
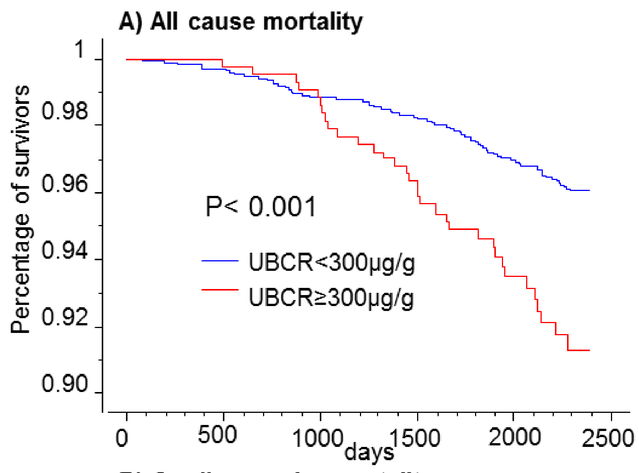
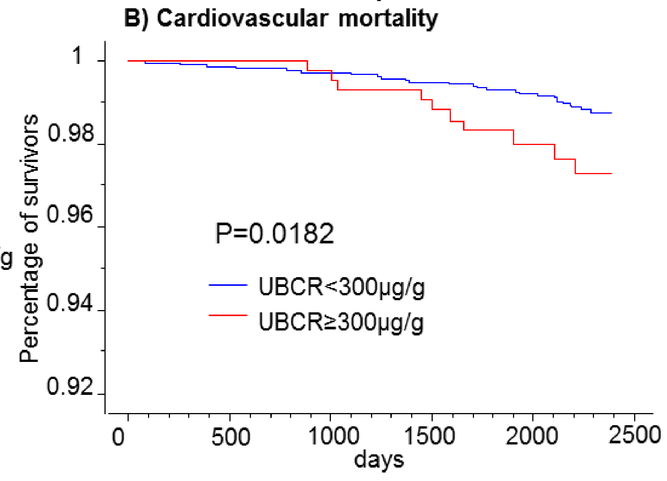


Fig3. Kaplan-Meier curves for seven years mortality with and without high UBCR.

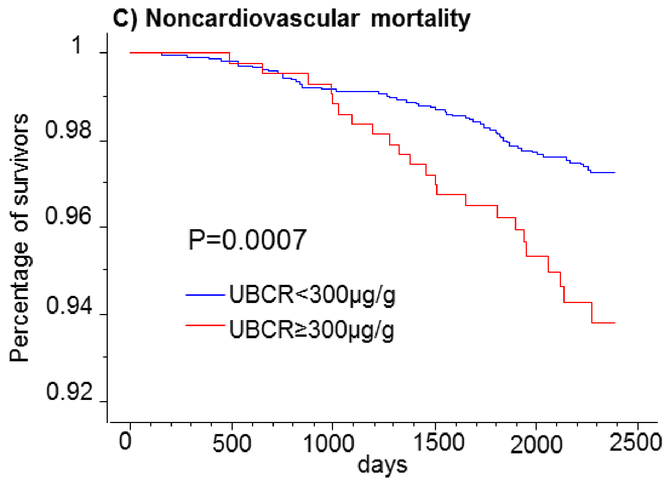
A) All cause mortality



B) Cardiovascular mortality



C) Noncardiovascular mortality



RESULTS

- Median value of UBCR was 112 μg/g, and high UBCR levels (≥300 μg/g) were detected in 394 (12.6%) subjects.
- Kaplan-Meier analysis showed that all-cause, cardiovascular and noncardiovascular mortality was significantly increased along with an increased in UBCR values.
- The subjects with high UBCR showed significantly higher all-cause, cardiovascular and noncardiovascular mortality than those without it (P <0.05).
- Cox proportional analysis adjusted for age, gender, eGFR, albuminuria, and other confounding factors showed that high UBCR was an independent risk for all-cause mortality (hazard ratio 1.90, 95% confidence interval 1.10 to 3.29, P = 0.02).

CONCLUSIONS

This study revealed that renal tubular damage had a significant association with the mortality in general Japanese population.

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