

# Higher Serum Phosphorus Levels at The Initial Visit Predict More Rapid Decline in Kidney Function in Pre-dialysis CKD Patients in Japan

Tomoki Kawasaki 1), Ryoichi Ando 2), Yoshitaka Maeda 1), Yohei Arai 3), Hidehiko Sato 4), Soichiro Iimori 5), Eisei Sohara 5), Tomokazu Okado 5), Tatemitsu Rai 5), Shinichi Uchida 5), and Sei Sasaki 5)

1) Department of Nephrology, JA Toride Medical Center, 2) Department of Nephrology, Musashino Red Cross Hospital, 3) Department of Nephrology, Tokyo Kyosai Hospital, 4) Department of Nephrology, Tokyo Metropolitan Otsuka Hospital, 5) Department of Nephrology, Tokyo Medical and Dental University

## 1. INTRODUCTION

Higher serum phosphorus is associated with increased mortality in patients with end stage kidney disease (ESKD).

Several studies also reported serum levels of phosphorus was a risk factor for decline in kidney function in pre-dialysis CKD patients.

## 2. PURPOSE

We evaluated the association of **serum phosphorus levels at the initial visit** to nephrology centers **with CKD progression**.

## 4. RESULTS

**4-1.** Patients in **Group 4** more frequently had **diabetes, hypertension, and lower eGFR and higher proteinuria**, and were more likely to be treated with **calcium-containing phosphate binders**.

**Table 1.** Baseline characteristics of individuals stratified by quartiles of serum phosphorus level

	All (n=990)	Group 1 (n=229)	Group 2 (n=231)	Group 3 (n=265)	Group 4 (n=265)	P value
Age (Yr)	66.9 ± 13.7	65.9 ± 12.5	68.8 ± 13.7	66.8 ± 14.4	66.4 ± 13.8	n.s
Man (n,%)	688 (69.5)	201 (87.8)	171 (74.0)	172 (64.9)	144 (54.3)	<0.0001
Diabetes (n,%)	367 (37.1)	71 (31.0)	79 (34.2)	94 (35.5)	123 (46.4)	0.002
Hypertension (n,%)	898 (90.7)	200 (87.3)	211 (91.3)	235 (88.7)	252 (95.1)	0.01
Prevalence of CVD (n,%)	264 (26.7)	66 (28.9)	56 (24.2)	74 (27.9)	68 (25.7)	n.s
Use of ACEI/ARB (n,%)	634 (64.0)	132 (57.6)	150 (64.9)	169 (63.8)	183 (69.1)	n.s
Use of calcium (n,%)	13 (1.3)	0 (0.0)	2 (0.9)	1 (0.4)	10 (3.8)	0.0006
Use of VitD (n,%)	45 (4.5)	9 (3.9)	9 (3.9)	10 (3.8)	17 (6.4)	n.s
eGFR (ml/min/1.73 m <sup>2</sup> )	33.0 ± 18.7	39.9 ± 17.0	37.0 ± 17.3	35.0 ± 18.1	21.6 ± 16.8	<0.0001
CKD stage						
G2 (n)	83	25	24	23	11	
G3a (n)	173	63	44	51	15	
G3b (n)	243	60	72	72	39	
G4 (n)	310	70	73	88	79	
G5 (n)	181	11	18	31	121	
Corrected Ca (mg/dl)	9.39 ± 0.56	9.40 ± 0.48	9.44 ± 0.52	9.39 ± 0.44	9.34 ± 0.75	n.s
Urinary Protein (g/gCr)	2.15 ± 3.25	1.12 ± 2.27	1.53 ± 2.38	1.98 ± 2.91	3.76 ± 4.23	<0.0001

Data are mean ± SD, n(% of total). Comparisons were made by ANOVA,  $\chi^2$  test

## 5. SUMMARY

We showed that **higher serum phosphorus at the initial visit** to nephrology centers was a **predictable factor for decline in kidney function** in the following year.

## 6. LIMITATIONS

- The present study was **observational study**.
- We tried to correct for the effect of **confounding factors** with stratification by CKD stages. But sample size in each group might be insufficient for full evaluation.
- We did **not measure the amount of protein intake** which is associated with CKD progression, and with serum phosphorus levels.
- Patients were **followed only for one year**. It might be not long enough for evaluation of the outcome adequately especially in earlier stages CKD.

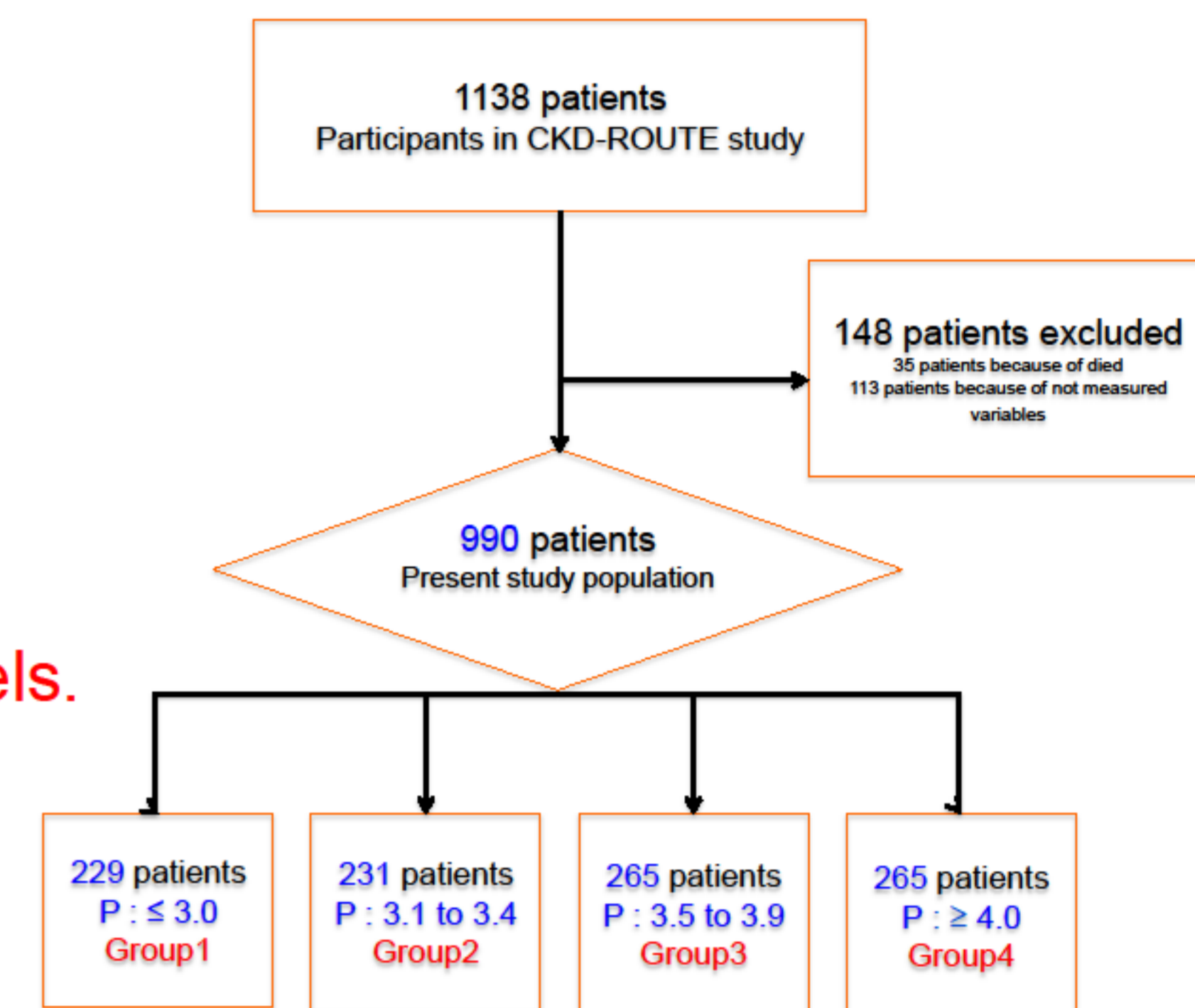
**Conclusion Higher serum phosphorus at the initial visit predicted more rapid progression of CKD**

## 3. METHODS

- This study was done as part of CKD-ROUTE. CKD-ROUTE was **prospective observational cohort study in Japan**.
- Pre-dialysis patients** with age above 20 **at the initial visit** to 16 nephrology centers were **recruited** in CKD-ROUTE study.
- In present study, patients were **stratified by quartiles of serum phosphorus levels**.
- The study **endpoint** was **composite of reached ESKD and 50% reduction of eGFR during one year**.

**CKD-ROUTE study**  
CKD Research of Outcomes in Treatment and Epidemiology

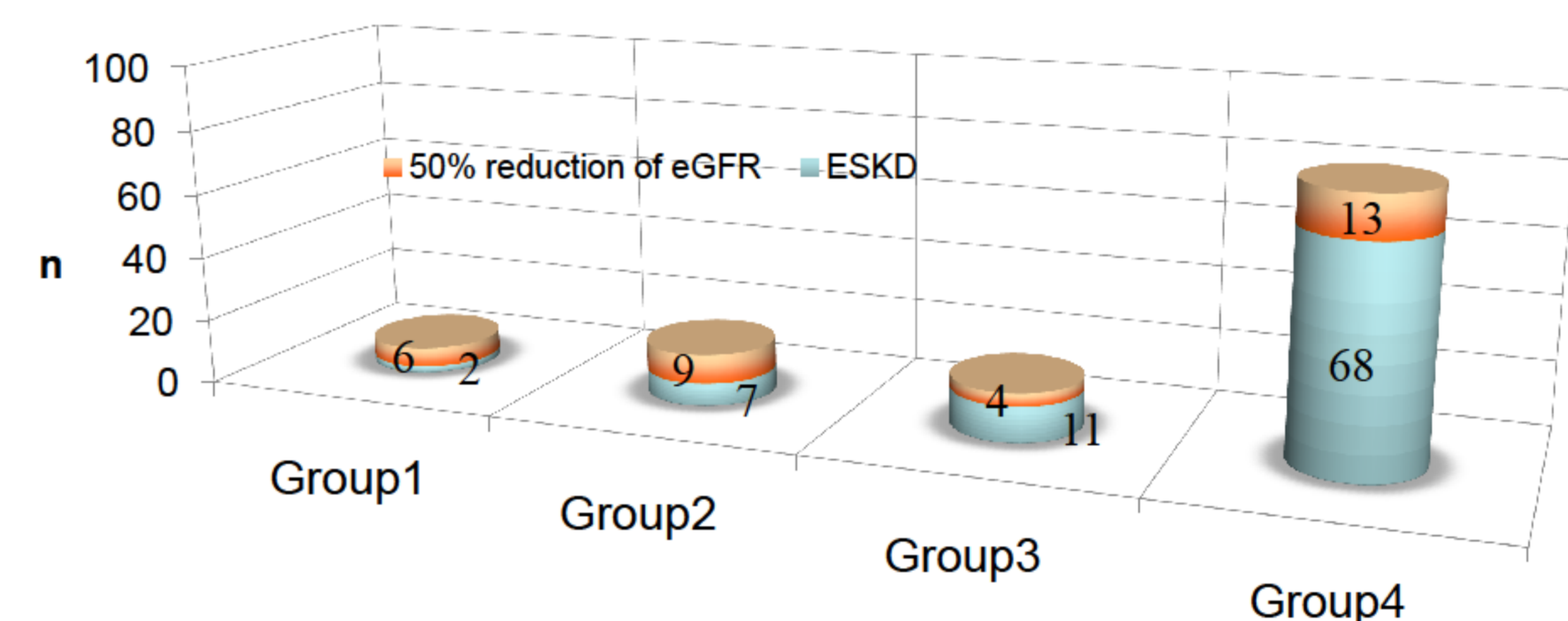
**Figure 1.** Study flowchart



**4-2.** A total of **120 patients** reached the **composite endpoint** of reached ESKD and 50% reduction of eGFR **during one year** (88 patients reached ESKD, and 32 patients had greater than 50% reduction of eGFR).

**Overall incident rate was 136.8/1000 patient-year.**

**Figure 2.** Distribution of events, by quartiles of serum phosphorus



**4-3.** Higher serum phosphorus was associated with a higher risk for the composite endpoint for phosphorus levels **Group 4 versus Group 1; adjusted hazard ratio 1.84 [1.27 to 2.84]**

**Figure 3.** Hazard ratio(HR) with 95%confidence interval (CI) of the composite endpoint of ESKD and 50% reduction of eGFR associated with quartiles of serum phosphorus level **Group 2, Group 3, and Group 4 versus Group 1**

	Unadjusted HR [95%CI]	Adjusted HR [95%CI]
Group 1	1.00	1.00
Group 2	1.41 [0.93 – 2.21]	1.32 [0.86 – 2.09]
Group 3	1.26 [0.83 – 1.99]	1.14 [0.74 – 1.82]
Group 4	3.20 [2.30 – 4.79]	1.84 [1.27 – 2.84]

Adjusted :after adjustment for age, sex, diabetes, hypertension, history of cardiovascular disease (CVD), use of angiotensin-converting enzyme inhibitors(ACEI)/ angiotensin II receptor blockers(ARB),use of calcium containing phosphate binders, estimated GFR(eGFR), corrected calcium and urinary protein.

