# RISK FACTORS RELATED TO THE DEVELOPMENT OF CHRONIC KIDNEY DISEASE (CKD) IN MIDDLE-AGED WORKERS

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# Background

- Chronic kidney disease (CKD) is defined by signs of kidney damage such as proteinuria and/or reduced glomerular filtration rate (GFR).
- The significance of CKD has been recognized not only with its progression to renal failure but also to the high occurrence of cardiovascular disease (CVD).
- Especially, proteinuria or albuminuria has been shown to relate strongly to the development of CVD.

- New criteria of CKD severity attaching greater importance to the presence of proteinuria or albuminuria was proposed.

## Objectives

- Against this background, the impact of CKD on the health of working populations in Japan has not yet been throughly evaluated.
- In the present study, we aimed to clarify the distribution of CKD with possible contributing factors to its development and progression.

# Subjects and methods

- 3,964 males and 2,698 females who were aged 35~64 years in 2009 and had serum creatinine (Cr) measured in the health check-ups in both 2003 and 2009.
- Factors contributing to the occurrence of CKD during the 6-year period were analyzed by retrospective longitudinal observation.
- Proteinuria was detected by a dipstick method and glomerular filtration rate (eGFR) was estimated by the equation of the Japanese Society of Nephrology (JSN).

# CKD severity proposed by JSN (2012)

| GFR (mL/min/1.73m$^2$) | Normal urinary protein (<0.15 g/d) | Mild proteinuria (0.15-0.49g/d) | Marked Proteinuria (≧0.50 g/d) |
|---|---|---|---|
| G1: ≧90 | Free of CKD | Mild CKD | Moderate CKD |
| G2: 60－89 | | | |
| G3a: 45－59 | | | |
| G3b: 30－44 | | Severe CKD | |
| G4: 15－29 | | | |
| G5: ＜15 | | | |

CVD Risk RR: 1.5~2.2 RR:2.3~3.9 RR≧4.0

# Distribution of CKD

| | 35~44 y.o. | | 45~54 y.o. | | 55~64 y.o. | |
|---|---|---|---|---|---|---|
| | M | F | M | F | M | F |
| CKD signs / Number | 1,204 | 630 | 1,559 | 1,232 | 1,201 | 836 |
| Proteinuria (Dipstick) | | | | | | |
| 1+ | 1.7 | 0.8 | 1.6 | 1.2 | 2.3 | 0.7 |
| 2+~ | 0.6 | 0.0 | 0.9 | 0.2 | 1.5 | 0.1 |
| eGFR (mL/min/1.73m$^2$) | | | | | | |
| G1 (90~) | 8.2 | 13.8 | 3.4 | 5.5 | 3.6 | 2.4 |
| G2 (60~89) | 85.7 | 80.2 | 82.3 | 79.0 | 74.2 | 75.0 |
| G3a (45~59) | 5.7 | 6.0 | 13.8 | 15.5 | 21.0 | 22.0 |
| G3b (30~44) | 0.1 | 0.0 | 0.4 | 0.0 | 1.0 | 0.5 |
| G4 (15~29) | 0.0 | 0.0 | 0.1 | 0.0 | 0.1 | 0.1 |
| G5 (~14) | 0.2 | 0.0 | 0.1 | 0.0 | 0.2 | 0.0 |
| CKD severity | | | | | | |
| Mild | 7.0 | 6.5 | 14.0 | 15.5 | 21.0 | 22.2 |
| Moderate | 0.6 | 0.2 | 1.3 | 0.6 | 2.3 | 0.6 |
| Severe | 0.3 | 0.0 | 0.5 | 0.1 | 1.0 | 0.2 |

# Factors possibly contributing to the development of CKD

- Sex
- Age (2009)
  - 35~44 y.o.
  - 45~54 y.o.
  - 55~64 y.o.
- BMI
  - ~18.4
  - 18.5~24.9
  - 25.0~29.9 mild obesity
  - 30.0~ marked obesity
- Health conditions
  - Hypertension BP≧140/90 mmHg
  - DM FPG≧126 mg/dL, HbA1c≧6.5%
  - high-Chol LDLc≧140 mg/dL
  - high-TG TG≧150 mg/dL
  - low-HDLc HDLc＜40 mg/dL
- Cigarette smoking
  - Nonsmoker
  - Ex-smoker
  - Smoke up to 1 pack/d
  - Smoke more
- Alcohol consumption
  - Nondrinker
  - Drink up to 29 mL/d
  - 30~59 mL/d
  - 60 mL/d or more
- Occupation
  - Clerk
  - Manager/Professional
  - Sales/Service
  - Operator/Driver
  - Miscellaneous

# Results of MLR analysis on factors contributing to the development of proteinuria

| Factors: Reference category | OR | (95% C.I.) | *p* |
|---|---|---|---|
| BMI: 18.5~24.9 | | | |
| 25.0~29.9 | 1.51 | (0.92—2.47) | 0.103 |
| 30.0~ | 4.52 | (2.31—8.84) | < 0.001 |
| Hypertension (+) | 2.49 | (1.59 – 3.91) | < 0.001 |
| DM (+) | 3.51 | (2.02 – 6.08) | < 0.001 |
| Smoking: Non-smoker | | | |
| Smoke up to 1 pk/d | 2.61 | (1.36 – 5.02) | 0.004 |
| Smoke more | 4.51 | (2.27 – 9.41) | < 0.001 |
| Alcohol: Non-drinkers | | | |
| Drink up to 29 mL/d | 0.59 | (0.34 – 0.99) | 0.048 |
| Occupation: Clerk | | | |
| Miscellaneous | 3.40 | (1.11—10.4) | 0.032 |

# Results of MLR analysis on factors contributing to the development of moderate or severe CKD

| Factors: Reference category | OR | (95% C.I.) | *p* |
|---|---|---|---|
| Age: 35~44 years | | | |
| 45~54 | 1.97 | (0.88—4.42) | 0.101 |
| 55~64 | 2.44 | (1.07—5.57) | 0.034 |
| Hypertension (+) | 3.01 | (1.78 – 5.11) | < 0.001 |
| DM (+) | 3.69 | (1.94 – 7.03) | < 0.001 |
| Smoking: Non-smoker | | | |
| Smoke up to 1 pk/d | 2.58 | (1.21 – 5.49) | 0.014 |
| Smoke more | 2.98 | (1.22 – 7.27) | 0.016 |
| Alcohol: Non-drinkers | | | |
| Drink 60 mL/d or more | 0.40 | (0.16 – 0.96) | 0.041 |
| Occupation: Clerk | | | |
| Miscellaneous | 5.89 | (1.84—18.7) | 0.003 |
| Reduced eGFR (+) | 9.39 | (4.80—18.4) | < 0.001 |
| Proteinuria (+) | 38.8 | (18.1—83.2) | < 0.001 |

# Limitations

- Not randomized selection of the subjects.
- Drop-outs of subjects from the study may have caused an underestimation of CKD frequency.
- Some problems exist in the validities of the measurement of proteinuria by a dipstick method and the estimation of GFR from serum Cr.
- Single measurements of CKD signs did not meet the clinical definition of CKD requiring the persistence of the signs for 3 months or longer.
- The effects of renal toxic substances possibly exposed in some occupations have not evaluated in this study.

# Conclusions

- CKD was present in 16% of Japanese workers aged 35~64 years similarly in both sexes.
- Moderate or severe CKD having a high risk of CVD amounted to 3.3% of males aged 55~64 years, which is especially significant since workers of that age group are becoming rapidly more numerous in workplaces in Japan.
- Lifestyle modifications, adequate treatment of hypertension and DM if present are important to prevent the development and progression of CKD and thus CVD in workplaces.
- Some occupations characterized by heavier physical work load or lower socioeconomic status may be related to the higher development of CKD