AJKD

Original Investigation

Impact of the Triglycerides to High-Density Lipoprotein Cholesterol Ratio on the Incidence and Progression of CKD: A Longitudinal Study in a Large Japanese Population

Kazuhiko Tsuruya, MD, PhD,[1,2,3] Hisako Yoshida, PhD,[1] Masaharu Nagata, MD, PhD,[2]
Takanari Kitazono, MD, PhD,[2] Kunitoshi Iseki, MD, PhD,[3] Chiho Iseki, PhD,[4]
Shouichi Fujimoto, MD, PhD,[3] Tsuneo Konta, MD, PhD,[3] Toshiki Moriyama, MD, PhD,[3]
Kunihiro Yamagata, MD, PhD,[3] Ichiei Narita, MD, PhD,[3] Kenjiro Kimura, MD, PhD,[3]
Masahide Kondo, MD, MSc, PhD,[3] Koichi Asahi, MD, PhD,[3] Issei Kurahashi, PhD,[5]
Yasuo Ohashi, PhD,[6] and Tsuyoshi Watanabe, MD, PhD[3]

Background: The impact of the triglycerides to high-density lipoprotein cholesterol (TG:HDL-C) ratio on chronic kidney disease (CKD) is unclear.

Study Design: Longitudinal cohort study.

Setting & Participants: 124,700 participants aged 39 to 74 years in the Japanese Specific Health Check and Guidance System, including 50,392 men, 74,308 women, 102,900 without CKD, and 21,800 with CKD.

Predictor: Quartiles of TG:HDL-C ratio.

Outcomes & Measurements: Changes in estimated glomerular filtration rate (eGFR) and urinary protein excretion during the 2-year study period. Incident CKD in participants without CKD, and progression of CKD in participants with CKD.

Results: In the entire study population, higher quartile of TG:HDL-C ratio at baseline was significantly associated with greater decline in eGFR and increase in urinary protein excretion during the 2-year study period, even after adjustment for confounding factors. A higher ratio was associated with higher risk of incident CKD in participants without CKD and higher risk of rapid decline in eGFR and increase in urinary protein excretion in participants with CKD. Higher TG:HDL-C ratio was more strongly associated with decline in eGFR (P for interaction = 0.002) and with incident CKD (P for interaction = 0.05) in participants with diabetes than without diabetes.

Limitations: Short observation period and single measurement of all variables.

Conclusions: A higher TG:HDL-C ratio affects the decline in eGFR and incidence and progression of CKD in the Japanese population.

Am J Kidney Dis. ■(■):■-■. © 2015 by the National Kidney Foundation, Inc.

INDEX WORDS: Chronic kidney disease (CKD); estimated glomerular filtration rate (eGFR); urinary protein excretion; proteinuria; kidney disease progression; dyslipidemia; triglycerides to high-density lipoprotein cholesterol ratio; lipid nephrotoxicity; diabetes; Japanese population.

Abnormalities of lipid metabolism have been identified as a possible cause of progression of chronic kidney disease (CKD). However, the precise mechanism of the effect of such abnormalities remains unknown.[1,2] In the current era, aggressive reduction of low-density lipoprotein cholesterol (LDL-C) levels is recommended and can be achieved in most patients with dyslipidemia by treatment with 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors, also known as statins. High serum triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) levels have come to be recognized as residual cardiovascular (CV) risk factors. Thus, in various disorders of lipid metabolism, high TG and low HDL-C levels (the dominant type of dyslipidemia in patients with CKD) have recently attracted attention and have been shown to predict the occurrence of ischemic heart disease, myocardial infarction, and CV mortality.[3,4]

TG:HDL-C ratio, which has been considered to be a useful marker of insulin resistance,[5-8] reportedly

correlates with small dense LDL-C level and LDL particle size.[9-11] Recent studies have shown that TG:HDL-C ratio may be a better predictor of CV events[3,8,12] and CV mortality[13,14] than other lipid parameters, including TG level, LDL-C level, and total cholesterol to HDL-C ratio.

We recently reported the association between TG:HDL-C ratio and the prevalence of CKD in a large Japanese population.[15] However, the cross-sectional study design limited the interpretation of causality between TG:HDL-C ratio and prevalence of CKD. In the present study, we hypothesized that an elevated TG:HDL-C ratio is involved in the decline in estimated glomerular filtration rate (eGFR) and the incidence and progression of CKD. We thus examined associations between TG:HDL-C ratio at baseline and changes in eGFR and the incidence and progression of CKD during a 2-year prospective longitudinal study.

METHODS

Study Population

This longitudinal cohort study was conducted as part of a prospective ongoing project titled "Study on the design of the comprehensive health care system for CKD based on the individual risk assessment by Specific Health Checkups" and was based on data obtained from the Japanese Specific Health Check and Guidance System. This annual health check program was initiated in 2008 by the Japanese government, and it promotes early diagnosis and intervention strategies for the prevention of metabolic syndrome. Data were collected from 1,120,101 individuals who participated in the health checkups in 2008 to 2011. Inclusion and exclusion criteria for participants are shown in the flow chart in Fig 1.

Of 1,120,101 participants, we selected 261,958 with data for eGFR and urinary protein level from 2 time points at a 2-year interval. We then excluded 136,676 participants without essential data including age; sex; systolic blood pressure; diastolic blood pressure; body mass index (BMI); waist circumference; levels of hemoglobin A_{1c} (HbA$_{1c}$), LDL-C, HDL-C, and TG; information on smoking, alcohol consumption, and exercise habits; histories of stroke and heart disease; and medications for hypertension, diabetes mellitus, and dyslipidemia. We also excluded participants with a history of kidney disease and those with eGFR < 15 mL/min/1.73 m^2. Finally, data from 124,700 participants (50,392 men and 74,308 women) aged 39 to 74 years were analyzed in the present study. This study was conducted in accordance with the Private Information Protection Law and ethics guidelines for epidemiology research published by the Ministry of Health, Labour and Welfare in 2008.

Clinical Evaluation and Laboratory Measurements

All participants completed a self-administered questionnaire that documented medical history, current medications, smoking habit (current smoker or not), alcohol consumption (daily drinker or not), and regular exercise habit. Participants' height and weight were measured, and BMI was calculated (kg/m^2). For these measurements, participants wore light clothing without shoes. Blood pressure measurement and blood and urine sampling were performed at each participant's local medical institute, as stipulated by the health check program.
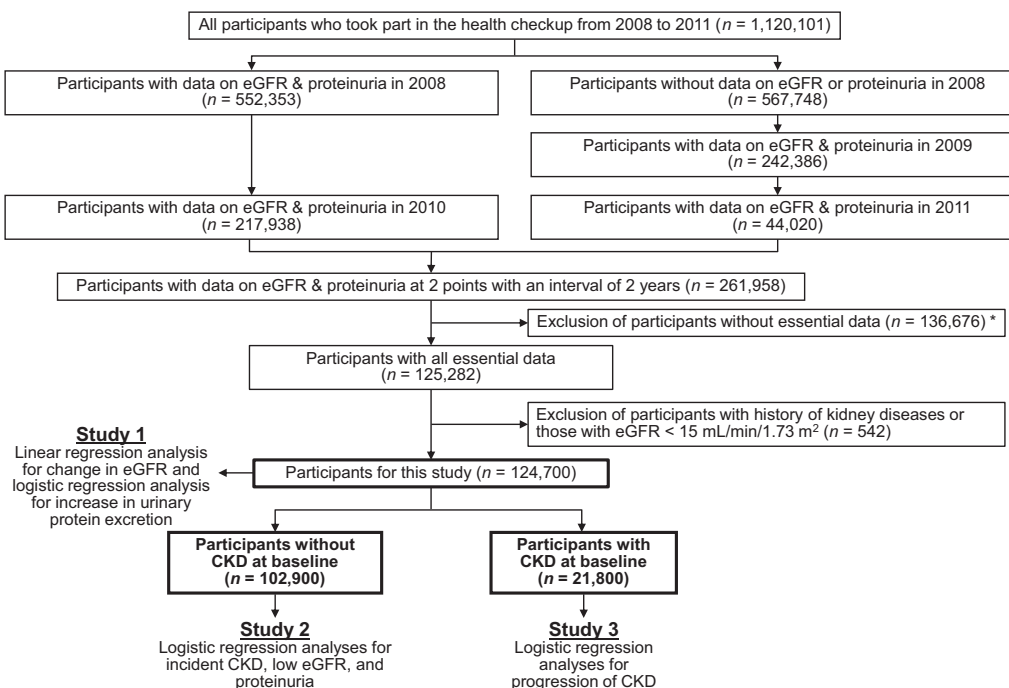
Figure 1. Flow chart of study participants. *Essential data: age; sex; systolic blood pressure; diastolic blood pressure; levels of hemoglobin A_{1c}, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides; waist circumference; information on smoking, alcohol consumption, and exercise habits; histories of stroke and heart disease; and medication for hypertension, diabetes mellitus, and dyslipidemia. Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.