Correlation between Carotid Intima–Media Thickness and Early-Stage Chronic Kidney Disease: Results from Asymptomatic Polyvascular Abnormalities in Community Study

Yu Wu, PhD,*,[1] JinHong Hou, MD,†,[1] JunJuan Li, MD,† Yang Luo, MD, PhD,‡ and ShouLing Wu, MD§

Objective: Chronic kidney disease (CKD) might be a potential independent risk factor for increased carotid intima–media thickness (IMT). Our aim is to determine whether mild to moderate kidney dysfunction is associated with increased carotid IMT. *Methods:* We employed 3629 subjects free from clinical cardiovascular diseases at the baseline visit of the Asymptomatic Polyvascular Abnormalities in Community Study. Kidney function was evaluated in terms of estimated glomerular filtration rate (eGFR) calculated by the Chronic Kidney Disease Epidemiology Collaboration China equation. The mean of the maximal internal and common carotid IMT was measured by means of high-resolution B-mode ultrasound. Univariable linear regressions and multivariate logistic regressions were used to evaluate the independent association between kidney function and carotid IMT. *Results:* In the unadjusted linear analysis, carotid IMT showed a significant negative correlation with eGFR in both male ($r = -.346$, $P < .001$) and female ($r = -.253$, $P < .001$) subjects. After adjustment for age, traditional vascular risk factors (smoking, diabetes, systolic blood pressure, diastolic blood pressure, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total cholesterol, and antihypertensive drug use), and nontraditional risk factors (C-reactive protein and homocysteine), the association remained significant. The odds ratio for increased IMT was 1.299 (95% confidence interval [CI], 1.062-1.588) in the group with an eGFR of 60-89 mL/minute/1.73 m^2 and 1.789 (95% CI, 1.203-2.660) in the group with an eGFR of 30-59 mL/minute/1.73 m^2. *Conclusions:* Increased IMT is associated with early-stage CKD. This association is independent of traditional and nontraditional cardiovascular risk factors. Early detection of kidney dysfunction

From the *Department of Nephrology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China; †Department of Nephrology, Kailuan Hospital, Hebei United University, Tangshan, China; ‡Department of Nephrology, Beijing Shijitan Hospital, Capital Medical University, Beijing, China; and §Department of Cardiology, Kailuan Hospital, Hebei United University, Tangshan, China.

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Address correspondence to Yang Luo, Department of Nephrology, Beijing Shijitan Hospital, Capital Medical University, Beijing 100038, China. E-mail: luoyang96@163.com.; Address correspondence to ShouLing Wu, Department of Cardiology, Kailuan Hospital, Hebei United University, Tangshan 06300, China. E-mail: drwusl@163.com.

[1] Y.W. and J.H. contributed equally to this work.

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is important to improve risk stratification of atherosclerotic disease. **Key Words:** Carotid intima–media thickness (IMT)—chronic kidney disease (CKD)—estimated glomerular filtration rate (eGFR)—atherosclerotic disease.

Introduction

As a noninvasive marker of arterial wall hypertrophy, increased intima–media thickness (IMT) has been used as an indicator of generalized atherosclerosis.[1,2] Previous studies have shown that risk factors of increased carotid IMT include hypertension, diabetes mellitus, dyslipidemia, smoking, and so on.[3] Recently, it has been recognized that chronic kidney disease (CKD) is not only a strong predictor for cardiovascular disease but also a potential risk factor for increased carotid IMT.[4-6] However, the role of kidney dysfunction as an independent risk factor for increased carotid IMT remains controversial, especially in the low-risk general population.[7-9]

We hypothesized that subjects with kidney dysfunction would have a greater quantity of increased IMT compared with individuals with normal kidney function. We therefore tested this relationship between kidney function and carotid IMT in a group of general Chinese individuals from the Asymptomatic Polyvascular Abnormalities in Community (APAC) Study.

Materials and Methods

Study Population

This is a cross-sectional population-based study. The subjects are participants of the APAC Study, which is a community-based, prospective, long-term follow-up observational study designed to investigate the epidemiology of asymptomatic polyvascular abnormalities. From June 2010 to June 2011, participants older than 40 years with no history of stroke, transient ischemic attack, and coronary disease at baseline were included in the APAC study. Study design and sampling have been described previously.[10,11] In the present study, we used the cohort consisting of 3629 subjects of whom the estimated glomerular filtration rate (eGFR) was higher than 30 mL/minute/1.73 m^2, carotid IMT measurements were available, and lipid-lowering drugs were not used. Informed consent was obtained from all participants.

Assessment of Carotid IMT

The carotid artery was scanned by trained and certified sonographers blinded to clinical information. The near and the far wall of the bilateral internal and the common carotid arteries and the carotid bifurcations were measured off-line using a duplex ultrasound system with a 5~12 MHz scanning frequency in the B-mode, pulsed Doppler mode, and color mode (Philips HD-15; Philips Corp., Amsterdam, The Netherlands). Carotid IMT was defined as the mean of the maximal IMT of the near and far walls on both the left and right sides. In the present study, higher carotid IMT was defined as measures above the 75th percentile of the sample distribution (.9 mm).

Calculation of GFR

Serum creatinine was measured on an autoanalyzer (Hitachi 747; Hitachi, Tokyo, Japan). Kidney function was evaluated in terms of eGFR calculated according to the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) China equation with adjusted coefficient of 1.1 for the Chinese population[12]: $eGFR_{CKD\text{-}EPI(CN)} = 1413 \min(SCr/k, 1)^{\alpha} \times \max(SCr/k, 1)^{-1.209} \times .993^{Age} \times 1.018$ (if female) $\times 1.1$, where SCr is serum creatinine, k is .7 for females and .9 for males, α is 20.329 for females and 20.411 for males, min is the minimum of SCr/k or 1, and max indicates the maximum of SCr/k or 1. Kidney function was classified into stage 1: eGFR 90 or higher, stage 2: 60-89 mL/minute/1.73 m^2, or stage 3: less than 60 mL/minute/1.73 m^2, based on the modified Kidney Disease Outcomes Quality Initiative clinical practice guidelines on CKD.[13]

Other Variables

Information on demographic variables (e.g., age, gender, and previous history of diseases) and smoking was collected through questionnaires. The smoking status was classified as "never," "former," or "current" according to self-reported information. The body mass index (BMI) was calculated as body weight (kg) divided by the square of height (m^2). Arterial hypertension was defined based on the following information alone or in combination: (1) presence of a history of arterial hypertension; (2) using antihypertensive medication; or (3) a systolic blood pressure (SBP) of 140 mmHg or higher, or a diastolic blood pressure (DBP) of 90 mmHg or higher. Diabetes mellitus was defined as a self-reported history, current treatment with insulin or oral hypoglycemic agents, or fasting blood glucose level of 6.1 mmol/L or higher.

At each examination, blood samples were collected from the antecubital vein in the morning under fasting conditions. They were stored in vacuum tubes containing ethylenediaminetetraacetic acid for storage. Cholesterol and triglyceride concentrations were measured enzymatically (interassay coefficient of variation: <10%; Mind Bioengineering Co. Ltd, Shanghai, China). Serum creatinine, urea nitrogen, glucose, high-density lipoprotein