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Impact of abdominal aortic calcification on long-term cardiovascular outcomes in patients with chronic kidney disease

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ABSTRACT

Background: The presence of abdominal aortic calcification (AAC) can predict cardiovascular (CV) outcomes in hemodialysis patients. However, little is known about the predictive value of AAC for CV outcomes in chronic kidney disease (CKD) patients without hemodialysis. The aim of this study was to investigate the prevalence and the predictive value of AAC in asymptomatic CKD patients.
Methods: We prospectively evaluated 347 asymptomatic CKD patients without hemodialysis [median estimated glomerular filtration rate (eGFR): 43.2 mL/min/1.73 m^2]. A non-contrast computed tomography scan was used to determine the abdominal aortic calcification index (ACI) as a semi-quantitative measure of AAC. The patients were divided into three groups according to the tertiles of ACI.
Results: Among the subjects, AAC was found (ACI > 0) in 296 patients (86.3%), and the median ACI was 11.4%. During the median follow-up of 41.5 months, a total of 33 CV events were observed. Patients with the highest tertile of ACI had the highest risk of CV outcomes compared with the other two groups (96.5%, 93.0%, and 74.3%, respectively; $p < 0.001$). The Cox proportional hazard models showed that ACI was an independent predictor of CV outcomes (hazard ratio 1.36, 95% confidence interval 1.17–1.60, $p < 0.001$). The C-index was also significantly increased by adding eGFR and ACI values to the model along with the other conventional risk factors (0.79 versus 0.66, $p = 0.043$).
Conclusion: Evaluation of the AAC provides useful information for predicting adverse clinical outcomes among asymptomatic CKD patients without hemodialysis.

1. Introduction

Chronic kidney disease (CKD) is closely related to increased morbidity and mortality of cardiovascular (CV) disease [1–4]. Moreover, patients with CKD frequently experience CV events associated with accelerated atherosclerosis and vascular calcification before the initiation of hemodialysis [5–7]. Thus, risk stratification for clinical events is clinically important in such populations. One of the main factors for the heightened CV risk in this population is the presence of mineral bone disorders (MBD), which is indicated by an imbalance of serum calcium, phosphorus, and parathyroid hormone (PTH) [8–11].

On the other hand, abdominal aortic calcification (AAC) detected by lumbar radiographs is also associated with increased risk of CV events [12,13]. Semi-quantitative methods, such as noncontrast computed tomography (CT) scans, for the assessment of AAC are highly sensitive for the earlier and precise detection of aortic calcification than previous qualitative methods, such as plain X-ray films. In the present study, we hypothesized that the AAC as detected by CT scans would be a useful indicator of future CV events, and could be used to identify high-risk patients with adverse CV outcomes in patients with CKD. Therefore, the aim of

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this study was to evaluate the predictive ability of the abdominal aortic calcification index (ACI) for future CV events in asymptomatic CKD patients without hemodialysis.

2. Materials and methods

2.1. Subjects

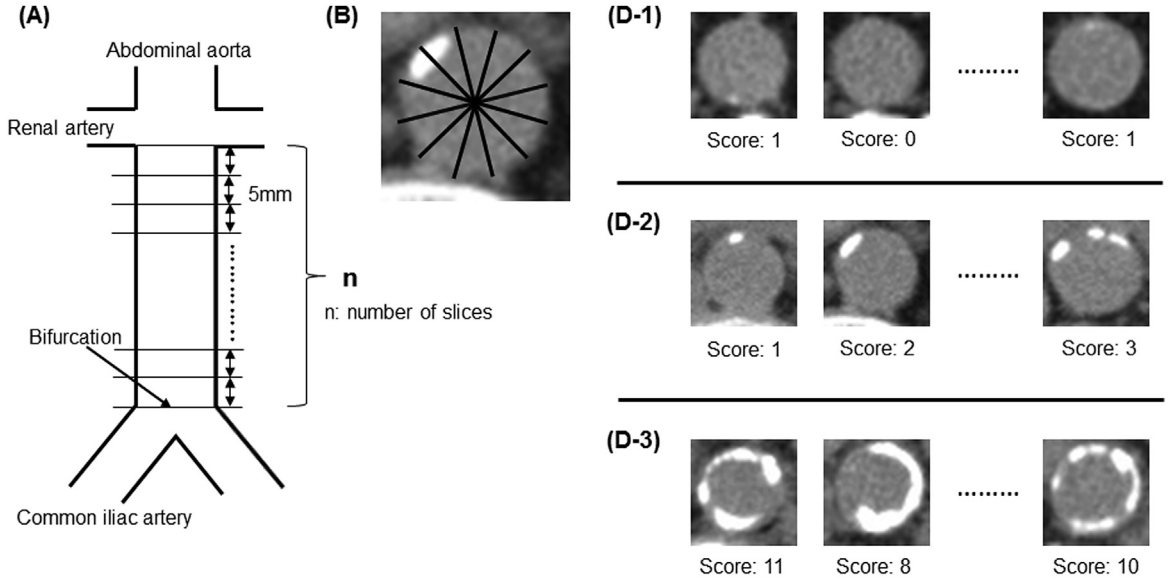
We prospectively evaluated 347 asymptomatic CKD patients without hemodialysis in the outpatient clinic at the Department of Nephrology in Nagoya University Hospital from November 2008 to October 2012. Patients with an estimated glomerular filtration rate (eGFR) < 60 mL/min/1.73 m^2 or the presence of proteinuria and renal disease as a complication at study entry, or both, were defined as having CKD [14]. To investigate the renal morphology and degree of subclinical atherosclerosis in individuals, AAC were quantified by noncontrast CT scan, and the relationships between AAC and the clinical outcomes were analyzed. Clinical outcomes were defined as CV death, nonfatal stroke, nonfatal myocardial infarction, angina pectoris requiring revascularization, and heart failure requiring admission. Patient exclusion criteria were hemodialysis, active malignancy, and had undergone previous abdominal aortic artery repair or stenting. This study was approved by the local ethics committee, and was conducted in accordance with the ethical principles stated by the Declaration of Helsinki. Written informed consent was obtained from all patients. Body mass index (BMI) was calculated as body weight divided by height squared (kg/m^2). Hypertension was defined as systolic blood pressure (SBP) of ≥140 mmHg, diastolic blood pressure of ≥90 mmHg, and/or receiving hypertensive treatments. Diabetes mellitus (DM) was defined as the use of any anti-hyperglycemic medication, a current diagnosis of diabetes and/or having a fasting plasma glucose concentration of >126 mg/dL and/or a glycosylated hemoglobin concentration of ≥6.5% (National Glycohemoglobin Standardization Program). Dyslipidemia was defined as low-density lipoprotein cholesterol ≥140 mg/dL, high-density lipoprotein cholesterol ≤40 mg/dL, triglycerides ≥150 mg/dL, and/or receiving hyperlipidemia treatments. Current smokers were defined as those who declared active smoking at all available examinations.

2.2. Data collection

After an overnight fast of 12 h, blood samples were obtained from all patients. Serum creatinine was measured using the isotope-dilution mass spectrometry traceable enzymatic method, and the eGFR was calculated using the equation for Japanese subjects recommended by the Japanese Society of Nephrology: e-GFR (mL/min/1.73 m^2) = $194 \times SCr^{-1.094} \times age^{-0.287} \times 0.739$ (if female) [15]. The eGFR levels were classified according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative guidelines (eGFR ≥ 90, 60–89, 45–59, 30–44, 15–29, and <15 mL/min/1.73 m^2 for G1, G2, G3a, G3b, G4, and G5, respectively) [14]. Serum calcium levels were corrected for albumin using the following formula: corrected calcium = total calcium + (4.0 − albumin) × 0.8, if albumin was <4.0 g/dL. Intact PTH was measured by electrochemiluminescence immunoassay (Roche Diagnostics, Tokyo, Japan).

2.3. Measurement of the abdominal aortic calcification index

All patients were scanned in the supine position in the craniocaudal direction using a 64-slice non-contrast CT scan (Siemens Medical Solutions, Forchheim, Germany), from which images were obtained with a 5-mm slice thickness. Calcification was considered



(C)

$$ACI\ (\%) = \frac{(\text{total score for calcification in all slices})}{12 \times n} \times 100$$

Fig. 1. The method of calculating aortic calcification index (ACI). (A) The images were obtained from the takeoff of the renal artery to the bifurcation of the aorta into the common iliac arteries at 5-mm intervals. (B) The cross-section of the abdominal aorta on each slice was divided into 12 radial segments. The number of calcified segments was counted on each slice. (C) This formula was used to calculate the ACI. (D) Representative cross-sectional images of the abdominal aorta in patients with 2.9% (D-1), 15.7% (D-2), and 50.8% ACI (D-3).