Kidney International, Vol. 66 (2004), pp. 2017–2021

Kidney function is inversely associated with coronary artery calcification in men and women free of cardiovascular disease: The Framingham Heart Study

CAROLINE S. FOX, MARTIN G. LARSON, MICHELLE J. KEYES, DANIEL LEVY, MELVIN E. CLOUSE, BRUCE CULLETON, and CHRISTOPHER J. O'DONNELL

NHLBI's Framingham Heart Study, Framingham, Massachusetts; Department of Endocrinology, Diabetes, and Hypertension, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts; Departments of Neurology, and Preventive Medicine and Epidemiology, Boston University School of Medicine, Boston, Massachusetts; Department of Mathematics, Boston University, Boston, Massachusetts; Department of Radiology, Beth Israel-Deaconess Hospital, Boston, Massachusetts; University of Calgary Foothills Hospital, Calgary, Alberta; Division of Cardiology, Department of Medicine, Massachussetts General Hospital, Boston, Massachusetts; and National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Maryland

Kidney function is inversely associated with coronary artery calcification in men and women free of cardiovascular disease: The Framingham Heart Study.

Background. Among patients with end-stage renal disease (ESRD), the risk of cardiovascular disease is 10 to 20 times higher than the general population. Adults with ESRD have increased coronary-artery calcification (CAC) detected by electron-beam computed tomography (EBCT). Because the risk of coronary heart disease is increased even at moderate declines in kidney function, we sought to test whether high CAC scores are seen among those with mild reductions in kidney function.

Methods. Men and women free of symptomatic cardiovascular disease underwent EBCT. Coronary calcium was quantified using the method described by Agatston. Renal function was estimated by glomerular filtration rate (GFR). Spearman correlation coefficients were used to test the association between GFR and CAC.

Results. Three hundred nineteen subjects (162 men/157 women), mean age 60, were included. Mean GFR was 86 ± 23 mL/min/1.73 m^2 (range 31–169; 10% with GFR <60 mL/min/1.73m^2). The median CAC scores by quartile of GFR were 85.9, 48.1, 7.9, and 2.7. Overall, the unadjusted correlation of GFR and CAC was -0.28 ($P < 0.0001$). This remained significant after adjustment for age and sex (-0.11, $P < 0.05$), and additionally after adjustment for body mass index (-0.11, $P < 0.05$), hypertension (-0.11, $P < 0.05$), or total cholesterol (-0.12, $P = 0.04$). A similar correlation was noted after multivariable adjustment (-0.10, $P < 0.08$).

Conclusion. Mild declines in kidney function are associated with subclinical coronary artery calcification in a sample of subjects free of clinically apparent cardiovascular disease. This might help explain the increased risk of cardiovascular disease among individuals with renal dysfunction. Larger ongoing studies are needed to better quantify this finding.

This work was supported by the National Heart, Lung and Blood Institute's Framingham Heart Study (N01-HC-25195).

Key words: coronary calcification, kidney disease, risk factor.

Received for publication March 31, 2004
and in revised form May 21, 2004
Accepted for publication June 2, 2004

© 2004 by the International Society of Nephrology

Kidney disease increases the risk of coronary mortality [1] and all-cause mortality [2]. Among patients with end-stage renal disease (ESRD), the risk of cardiovascular disease is 10 to 20 times higher than in the general population [3], and cardiovascular disease accounts for 50% of all deaths in this population [4]. However, this increased risk occurs even at moderate reductions in kidney function, independently of cardiovascular risk factors [5, 6].

The mechanism of this increased risk of cardiovascular disease in individuals with kidney disease is not known. Coronary artery calcification (CAC), detected by electron-beam computed tomography (EBCT), is a sensitive marker for coronary artery disease [7]. There are significantly increased quantities of CAC in young adults with ESRD compared with healthy age-matched control patients [8–10].

Given the association between accelerated CAC in ESRD patients, one can hypothesize that an increased risk for CAC might be seen in subjects with mild to moderate kidney dysfunction. The documentation of increased CAC among individuals with moderate kidney disease might partially explain the elevated risk of coronary heart disease in those with kidney disease. Thus, we hypothesized that declining glomerular filtration rate (GFR), a measure of kidney function, is inversely associated with CAC as measured by EBCT in the Framingham Heart Study.

METHODS

Study sample

The Framingham Heart Study began in 1948 with the enrollment of 5209 men and women, 28 to 62 years of age, with subjects undergoing examinations every 2 years [11, 12]. In 1971, 5124 men and women were enrolled into the Framingham Offspring Study, which included the children or spouses of the children of the original cohort. Offspring subjects underwent examinations approximately every 4 years; the design and methodology have been previously described [13, 14]. The current investigation is composed of 327 subjects from the Framingham Offspring Study who attended the sixth examination cycle and participated in a pilot study of EBCT imaging.

Subjects were selected as previously described [15]. Of the first 3219 subjects attending the sixth examination cycle (1995 to 1998), 349 subjects with clinical cardiovascular disease, 357 who did not reside in New England, and 7 who were not between 35 and 84 years of age, were excluded from sampling. The remaining 2506 subjects were stratified by sex, age quartile, and Framingham coronary heart disease (CHD) risk score quintile. Subjects were randomly sampled from each stratum, and invited to undergo EBCT. Thirteen percent declined participation; refusals were handled by randomly selecting another person from that stratum. A total of 327 subjects underwent EBCT, 319 of which had serum creatinine assessment.

Covariate data were obtained during the seventh cycle of the Framingham Heart Study (1998–2001). Details regarding the methods of risk factor measurement and laboratory analysis have been described [16]. Each examination included a cardiovascular disease assessment and blood testing. Subjects with fasting glucose level ≥126 mg/dL (7.00 mmol/L), and/or receiving oral hypoglycemic or insulin treatment for diabetes were defined as diabetic. Subjects with a systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg (average of 2 readings taken by the examining physician), or receiving medication for treatment of hypertension were defined as hypertensive. Fasting lipid measures included total and high-density lipoprotein (HDL) cholesterol. Smoking status was defined as smoking 1 or more cigarettes/day in the year preceding the examination. Body mass index was defined as weight (kg) divided by the square of height (m).

GFR and EBCT determination

GFR was estimated using the simplified Modification of Diet in Renal Disease (MDRD) Study equation [17, 18], defined as GFR $= 186.3 \times (\text{serum creatinine})^{-1.154} \times \text{age}^{-0.203} \times (0.742$ for women). Serum creatinine was measured using the modified Jaffe method. Because the measure of creatinine can vary across different laboratories, creatinine was calibrated using a 2-step process. First, NHANES III creatinine values were calibrated to the Cleveland Clinic Laboratory, requiring a correction factor of 0.23 mg/dL [19]. Then, mean creatinine values from Framingham, by sex-specific age groups (20–39, 40–59, 60–69, 70+), were aligned with the corresponding corrected NHANES III age-and sex-specific means.

EBCT scans were conducted between 1998 and 1999 (Imatron C-150 XP scanner, GE Medical Systems, Waukesha, WI, USA) following previously published protocols [20, 21]. Scans were read preliminarily by a technologist and over-read by a radiologist (M.E.C.), blinded to clinical data. CAC scores were calculated using the method described by Agatston [20]. Reproducibility was assessed by rereading 20 scans ($r = 0.97$ for replicate readings), and image noise was determined by the SD of pixel numbers in a region of interest within the aorta.

Table 1. Baseline characteristics

	Study sample ($N = 319$)
Age *years*	60 ± 9
% Male	51
Body mass index kg/m^2	28.5 ± 5.4
Total cholesterol *mg/dL*	202 ± 37
HDL cholesterol *mg/dL*	51 ± 17
Glomerular filtration rate $mL/min/1.73m^2$	86 ± 23
Current smoking %	11
Hypertension %	45
Diabetes %	17

Values are expressed as mean ± SD unless otherwise indicated.

Statistical methods

We calculated Spearman correlations for GFR and CAC, including unadjusted correlations, adjusted for age and sex, and adjusted for age, sex, plus 1 additional risk factor. Finally, we adjusted for age, sex, BMI, current tobacco use, diabetes, hypertension, total cholesterol, and HDL cholesterol. Covariate data were obtained from the seventh examination cycle. The SAS CORR procedure was used to perform correlation analyses [22]. A two-sided P value of < 0.05 was considered statistically significant. For descriptive purposes, we graphed median and interquartile range of CAC by quartile of GFR.

RESULTS

EBCT imaging was performed on 327 participants, 319 of whom had creatinine measured. Baseline characteristics are shown in Table 1. GFR ranged from 31 to

Download English Version:

https://daneshyari.com/en/article/3888585

Download Persian Version:

https://daneshyari.com/article/3888585

Daneshyari.com