Coronary Artery Calcium Score and Association with Recurrent Nephrolithiasis: The Multi-Ethnic Study of Atherosclerosis

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Purpose: Subclinical coronary artery calcification is an established predictor of cardiovascular events. While a history of kidney stones has been linked to subclinical carotid atherosclerosis, to our knowledge no study has examined its relationship with coronary artery calcification. We studied the association between kidney stone history and prevalent coronary artery calcification in MESA (Multi-Ethnic Study of Atherosclerosis).

Materials and Methods: MESA is a multisite cohort study of participants 45 to 84 years old without known cardiovascular disease at baseline from 2000 to 2002. Computerized tomography was done in 3,282 participants at followup in 2010 to 2012 to determine coronary artery calcification and kidney stone history was assessed by self-report. Coronary artery calcification scores were categorized as none—0, mild—1 to 99, moderate—100 to 399 or severe—400 or greater. Cross-sectional analysis was performed adjusting for demographic and dietary factors related to kidney stones.

Results: The prevalence of kidney stone disease history was approximately 9%, mean ± SD participant age was 69.5 ± 9.3 years, 39% of participants were Caucasian, 47% were men and 69% had detectable coronary artery calcification (score greater than 0). No difference in the score was seen between single stone formers and nonstone formers. Recurrent kidney stone formation was associated with moderate or severe calcification on multivariable logistic regression vs none or mild calcification (OR 1.80, 95% CI 1.22–2.67). When coronary artery calcification scores were separated into none, mild, moderate and severe calcification, recurrent stone formation was associated with a higher score category on multivariable ordinal logistic regression (OR 1.44 per category, 95% CI 1.04–2.01).

Conclusions: Recurrent kidney stone formation is associated with subclinical coronary atherosclerosis. This association appeared stronger with coronary artery calcification severity than with coronary artery calcification presence.

Key Words: kidney, urolithiasis, coronary artery disease, arteriosclerosis, recurrence

Abbreviations and Acronyms

CAC = coronary artery calcification

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KIDNEY stone disease is linked to systemic conditions, including chronic kidney disease,[1] hypertension,[2] obesity[3] and diabetes mellitus.[4] Recent longitudinal studies have also shown an association of kidney stone disease with coronary heart disease.[5,6] Therefore, biological pathways that result in CAC may also lead to the development of nephrolithiasis.

CAC, which is present only in atherosclerotic arteries, is a marker of subclinical atherosclerosis.[7] CAC is quantified noninvasively by computerized tomography and the calculated CAC score reflects the presence and extent of atherosclerotic disease. In 2010 ACC (American College of Cardiology) and AHA (American Heart Association) guidelines indicated that measuring CAC for cardiovascular risk assessment in asymptomatic adults may be reasonable in those at intermediate risk, defined as a 10% to 20% 10-year risk of cardiovascular events.[8] Adding CAC to the Framingham Risk Score improves disease prediction and it is considered an independent predictor of cardiovascular events.[7,9,10]

While atherosclerotic disease and nephrolithiasis have shared risk factors, to our knowledge the relationship between CAC and kidney stone disease has not been previously examined. The purpose of this study was to evaluate our hypothesis that participants reporting a history of kidney stones have a greater prevalence and extent of coronary artery calcification.

MATERIALS AND METHODS

Data Source and Study Population

MESA is a cohort study of 6,814 men and women designed to evaluate the prevalence of and risk factors for subclinical cardiovascular disease.[11] Participants who were free of clinical cardiovascular disease at the time of study entry (2000 to 2002) were recruited from 6 communities in the United States, including Baltimore, Maryland; Chicago, Illinois; Forsyth County, North Carolina; Los Angeles County, California; Northern Manhattan, New York; and St. Paul, Minnesota. Specific details about sampling, recruitment and data collection were reported previously.[11] The study included a racial/ethnic distribution of 38% Caucasian, 28% African-American, 22% Hispanic and 12% Chinese-American participants. Of the original participants 4,716 attended Exam 5 in 2010 to 2012, when they were queried about kidney stone history and evaluated for interval development of cardiovascular disease. Institutional review boards at each site approved the study and all participants provided written informed consent.

Assessment

Kidney Stones. Participants were asked whether their doctor or health care provider had ever told them that they had a kidney stone. Participants who answered yes were also asked the number of kidney stones. Participants were categorized into those who had previously had 0, 1, or 2 or more stones and were termed never, single and recurrent, respectively.

Coronary Artery Calcification. Multidetector row computerized tomography using a standardized protocol was performed in 3,305 of the participants followed through Exam 5 to evaluate for CAC.[12] The Agatston scoring method was used to evaluate calcium levels, normalized to a calcium phantom with 4 bars of known calcium density that were scanned along with the participant. The Agatston score is based on the area of calcification and weighted by the highest density of calcification in each plaque.[13] The phantom adjustment method serves to calibrate results across sites and evaluators.

Covariates

Exam 5 covariates included age (continuous), gender, race/ethnicity, diabetes status (normal, impaired fasting glucose, or untreated or treated diabetes) and body mass index (weight in kg/height in m^2, continuous). Dietary variables were treated continuously and derived from a validated food frequency questionnaire administered at Exam 5.[14] Dietary covariates selected as plausibly related to kidney stone formation included energy intake in kcal per day, animal protein consumption level in gm per day, calcium intake level in mg per day and sodium intake level in mg per day.

Statistical Analysis

We included in analysis 3,282 participants who attended Exam 5, responded to the kidney stone questionnaire, underwent computerized tomography and had no missing covariates. Of these participants 69.4% had detectable coronary calcium and 3.3% had previously experienced myocardial infarction or stroke, indicating that the majority had subclinical atherosclerosis. When comparing the baseline characteristics of those with vs without CAC among the original MESA cohort, there were no appreciable differences in the baseline characteristics measured at Exam 5.

To evaluate the relationship of kidney stones to CAC prevalence 4 models were performed, adjusting first for age, gender and race/ethnicity category, and then additionally adjusting for the nutrition and health related variables. Post hoc adjustment was done to account for smoking status, hypertension status, education level and health insurance status.

In the first model logistic regression was performed with the presence of CAC (CAC score greater than 0) as the outcome and with kidney stone history (0, 1, or 2 or greater stones) as the potential predictor of interest. In the second model linear regression was performed with log-transformed CAC score as the outcome and kidney stone history (0, 1, or 2 or greater) as the predictor of interest. Only participants with detectable CAC (greater than 0) were included in this model. Coefficients of interest were exponentiated and, thus, are interpretable as ratios of geometric means between the kidney stone groups. In the third model logistic regression was performed with a CAC score less than 100 vs 100 or greater as the outcome and kidney stone history (0, 1, or 2 or greater) as the predictor of interest. An Agatston score threshold of 100 defines medium to high levels of coronary