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Association of kidney stones with atherosclerotic cardiovascular disease among adults in the United States: Considerations by race-ethnicity

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HIGHLIGHTS

- Research demonstrates that kidney stone history increases the risk of future CVD.
- Little research has examined whether race-ethnicity moderates this relationship.
- We observed that non-Hispanic blacks with kidney stones had an increased risk of CVD.

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ABSTRACT

Background: There is a paucity of research examining the relationship between kidney stones and risk of cardiovascular disease while considering individuals of different race-ethnicities.
Purpose: The purpose of this study was to examine the association between history of kidney stones and increased odds of atherosclerotic cardiovascular disease (via the Pooled Cohort Equations) across race-ethnicity groups.
Methods: 5571 participants aged 40–79 from the 2007–2012 cycles of the NHANES were used for this study. A history of kidney stones was collected from survey data. Predicted odds of having a 10-year atherosclerotic cardiovascular disease (ASCVD) event was assessed from the Pooled Cohort Equations.
Results: After adjustments, having kidney stones was not associated with an increase odds of having an ASCVD event within the next 10-years (OR 1.03; 95% CI: 0.58–1.82, $P = 0.91$). However, among non-Hispanic blacks, those with kidney stones had a 2.24 increased odds (OR 2.24; 95% CI: 1.08–4.66; $P = 0.03$) of having an ASCVD event within the next 10-years when compared to non-Hispanic blacks with no history of a kidney stone.
Conclusion: Kidney stones were associated with 10-year risk of a future ASCVD event among non-Hispanic blacks.

1. Introduction

Nephrolithiasis, or kidney stone events, affect approximately 10% of the U.S. population [24]. Risk factors for kidney stones, cardiovascular disease and stroke overlap and are interrelated. High kidney stone events are more prevalent among people with hypercholestermia, hypertension, obesity, and diabetes [7, 11, 19, 21, 23]. Non-Hispanic white men have been identified as having the highest risk for development of kidney stones and associated medical conditions, such as gout, diabetes, and gallstone disease [7]. Although these findings are well established, little research has been conducted to describe the relationship between kidney stones and risk of cardiovascular disease and stroke across race-ethnicities, even though minority populations have significant health disparities in relation to hypertension, obesity, type-2 diabetes, high cholesterol, cardiovascular disease, and stroke [5]. For example, a recent meta-analysis that examined the relationship between kidney stones and cardiovascular disease only identified 6 studies (addressed in the Discussion section), and differences across race-ethnicities were not investigated.

The purpose of this study was to examine the association between kidney stones and increased odds of a first atherosclerotic cardiovascular disease (ASCVD) event within the next 10 years, and to also see if race-ethnicity moderates this potential relationship. ASCVD was evaluated using the recently developed Pooled Cohort Equations. To

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maximize generalizability, data from the population-based National Health and Nutrition Examination Survey (NHANES) were used.

2. Methods

2.1. Study design

The *continuous* NHANES represents the total civilian, non-institutionalized population in the United States after 1999. The data collected in this survey includes questionnaires administered at home and from physical examinations in mobile examination centers (MECs). A complex, multistage, clustered probability sampling design was used to select a representative sample of the U.S. civilian population. For this study's purposes, we evaluated cycles 2007–2012 as these are the only cycles with kidney stone data.

2.2. Measurement of kidney stones

Trained interviewers inquired about participants' history of kidney stones at the participants' home using a Computer-Assisted Personal Interviewing (CAPI) system. The CAPI system is programmed with built-in consistency checks to reduce data entry errors. CAPI also uses online help screens to assist interviewers in defining key terms used in the questionnaire. The interviewer asked the respondent, "*Have you ever had a kidney stone*?" If the participant replied "Yes," the participant was considered to have a history of kidney stones.

2.3. Measurement of future cardiovascular risk

Predicted 10-year risk for a first ASCVD event for adults 40–79 years (age range equations derived) was calculated using the Pooled Cohort Equations, developed by the American College of Cardiology/American Heart Association (ACC/AHA) Task Force on Practice Guidelines (see Table A in the ACC/AHA reference for the Pooled Cohort Equations) [9]. These equations have demonstrated evidence of validity [13, 17].

Pregnant women or participants on cholesterol medication or who had been told by a doctor or other health professional that they had congestive heart failure, coronary heart disease, angina, heart attack, or stroke were excluded from these ASCVD analyses, which resulted in a sample of 5571 adults 40–79 years of age. Separate equations were developed for black and white/other men and women, which included the following variables in the equations: age (years), concentration of total cholesterol (mg/dL) and HDL-cholesterol (mg/dL), treated or untreated systolic blood pressure (mm Hg), diabetes status (defined as physician diagnosis or A1C ≥ 6.5%), and self-reported smoking status (yes/no). Participants with an ASCVD score of ≥20% were considered to be at high risk for future ASCVD events [9].

2.4. Covariates

The following covariates were included in the analytic models: poverty-to-income ratio (continuous), age (years; continuous), gender, self-reported engagement in moderate-to-vigorous physical activity in the past 30 days (yes/no), education (9th grade; 9th–11th grades; high school; some college; college or more), self-reported smoking status (current smoker, former smoker, never smoker), total dietary energy intake (kcals), dietary protein intake (g), dietary calcium intake (g), dietary sodium intake (g) and alcohol consumption (non-drinker, light-to-moderate drinker [1 or less drinks/day for women and 1–2 for men], and heavy drinker [2 + for women, 3 + for men]). The dietary-related covariates were assessed in the MEC using the "multi-pass" 24-hour dietary interview format.

2.5. Analysis

All statistical analyses were computed in Stata Version 13 (StataCorp, College Station, TX) and accounted for the complex survey design employed in NHANES. Multivariable logistic regression was used to examine the association between having been diagnosed with a kidney stone and having an increased 10-year risk for a first ASCVD event. Statistical significance was set at $P < 0.05$.

3. Results

Among the 5571 participants, the weighted mean (SE) age was 53.5 years (0.1); 52.7% (0.6) were female; 60.4% (1.4) had some college or more; 19.9% (0.9) smoked; 26.6% (1.0) were non-drinkers; and 72.5% engaged in moderate-to-vigorous physical activity in the past 30 days. With regard to dietary behavior, weighted mean (SE) kcals was 2168.4 (19.9); dietary protein was 82.8 g (0.7); dietary calcium was 978.1 mg (13.0) and dietary sodium was 3524.9 mg (35.4).

The weighted mean (SE) ASCVD score was 7.1 (0.2), with a range of 0.09–87.8. The weighted proportion of participants with an elevated ASCVD (≥20%) was 7.7% (N = 703). The weighted ASCVD score across race-ethnicity groups for the entire sample was as follows: Mexican American, 5.98% (95% CI: 5.21–6.75); other-Hispanic, 6.27 (5.63–6.92); non-Hispanic white, 7.10 (6.68–7.52); non-Hispanic black, 8.56 (7.93–9.18); and other race, 6.45 (5.46–7.43). The weighted ASCVD score across race-ethnicity groups for those with kidney stones (N = 522) were as follows: Mexican American, 6.86 (4.78–8.49); other-Hispanic, 8.16 (5.88–10.43); non-Hispanic white, 8.40 (7.21–9.60); non-Hispanic black, 13.86 (10.77–16.96); and other race, 9.55 (5.89–13.20).

After adjustments, and for the entire sample, having kidney stones was not associated with an increase odds of having an ASCVD event within the next 10-years (OR 1.03; 95% CI: 0.58–1.82, $P = 0.91$). When stratified by race-ethnicity, results were also non-significant for Mexican Americans (OR = 1.35; 95% CI: 0.42–4.29; $P = 0.59$; N = 901), other Hispanic (OR 1.02; 95% CI: 0.21–4.85; $P = 0.97$; N = 640), and non-Hispanic whites (OR 0.81, 95% CI: 0.40–1.61; $P = 0.54$; N = 2512). However, among non-Hispanic blacks (N = 1162), those with kidney stones had a 2.24 increased odds (OR 2.24; 95% CI: 1.08–4.66; $P = 0.03$) of having an ASCVD event within the next 10-years when compared to non-Hispanic blacks with no history of a kidney stone. When adding thiazide prescription use as a covariate, the results were unchanged (OR 2.23; 95% CI: 1.07–4.67; $P = 0.03$). Although the previous analyses controlled for gender, further sensitivity analyses were computed to see if, in addition to an interaction relationship between race-ethnicity and kidney stones on ASCVD, whether an interaction relationship between gender and kidney stones on ASCVD was observable. This is important to consider as previous research has demonstrated a stronger relationship between kidney stones and CVD for women, compared to men [8]. Notably, in a multivariable logistic regression, there was no gender interaction effect regarding the relationship between kidney stones and ASCVD (cross-product multiplicative interaction term for gender and kidney stones on ASCVD: OR, 1.90; 95% CI: 0.47–7.71; $P = 0.35$).

4. Discussion

The purpose of this study is to investigate whether there was an association between kidney stone formers and increased odds of ASCVD across race-ethnicity groups. Analyses via Pooled Cohort Equations revealed that non-Hispanic blacks, and no other ethnicity groups, had an increased risk of a first ASCVD event. Specifically, non-Hispanic black kidney stone formers had a 2.24 increased odds of having an ASCVD event within the next 10-years when compared to non-Hispanic blacks with no history of a kidney stone.