

Nephrolithiasis and Risk of Incident Bone Fracture

Eric N. Taylor,* Diane Feskanich, Julie M. Paik and Gary C. Curhan

From the Channing Division of Network Medicine (ENT, DF, JMP, GCC) and Renal Division (JMP, GCC), Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts, and Department of Epidemiology, Harvard T.H. Chan School of Public Health (JMP, GCC) and Division of Nephrology and Transplantation, Maine Medical Center (ENT), Portland, Maine

Abbreviations and Acronyms

BMI = body mass index

FFQ = Food Frequency Questionnaire

HPFS = Health Professionals Follow-up Study

NHS = Nurses' Health Study

THIN = The Health Improvement Network

WHI = Women's Health Initiative

Accepted for publication December 9, 2015.

No direct or indirect commercial incentive associated with publishing this article.

The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.

Supported by National Institutes of Health Research Grants DK94910, DK100447, CA186107 and CA167552.

* Correspondence: Division of Nephrology and Transplantation, Maine Medical Center, 22 Bramhall St., Portland, Maine 04102 (e-mail: entaylor@partners.org).

Purpose: Higher urine calcium is a common feature of calcium nephrolithiasis and may be associated with lower bone mineral density in individuals with kidney stones. However previous population based studies of kidney stones and the risk of bone fracture demonstrate conflicting results. We examined independent associations between a history of kidney stones and incident fracture.

Materials and Methods: We performed prospective studies using data from the Nurses' Health Study of 107,001 women with 32 years of followup and the Health Professionals Follow-up Study of 50,982 men with 26 years of followup. We excluded premenopausal women, men younger than 45 years and individuals who reported osteoporosis at baseline. Study outcomes were incident wrist (distal radius) or incident hip (proximal femur) fracture due to low or moderate trauma. Cox proportional hazards regression was used to adjust for multiple factors, including age, race, body mass index, thiazide use, supplemental calcium and dietary intakes.

Results: There were 4,940 wrist and 2,391 hip fractures in women, and 862 wrist and 747 hip fractures in men. All fractures were incident. The multivariable adjusted relative risk of incident wrist fracture in participants with a history of kidney stones compared to participants without kidney stones was 1.18 (95% CI 1.04–1.34) in women and 1.21 (95% CI 1.00–1.47) in men. The pooled multivariable adjusted relative risk of wrist fracture was 1.20 (95% CI 1.08–1.33). The multivariable adjusted relative risk of incident hip fracture in participants with kidney stones was 0.96 (95% CI 0.80–1.14) in women and 0.92 (95% CI 0.74–1.14) in men. The pooled multivariable adjusted relative risk of hip fracture was 0.94 (95% CI 0.82–1.08).

Conclusions: Nephrolithiasis is associated with a significantly higher risk of incident wrist but not hip fracture in women and men.

Key Words: kidney calculi; osteoporosis; fractures, bone; wrist; hip

KIDNEY stones are a major cause of morbidity and they are common. The prevalence of nephrolithiasis in the United States increases with age but in the overall population it is about 11% in men and 7% in women.¹ Calcium nephrolithiasis accounts for more than 80% of kidney stones.²

Some previous studies reported lower bone mineral density in individuals with a history of nephrolithiasis compared to those without nephrolithiasis^{3–6} and bone demineralization in calcium stone formers may be related to higher urine calcium.^{7,8} Previous reports also suggest

that individuals with nephrolithiasis may be at higher risk for bone fracture.^{9–11} A recent study using data from THIN in the United Kingdom compared more than 50,000 individuals with diagnostic codes for urolithiasis to more than 500,000 participants without such codes. The risk of incident bone fracture in individuals with a history of kidney stones was 10% higher in men and it varied by age in women with the highest relative risk of 1.52 in women 30 to 39 years old.⁹

However, the association between nephrolithiasis and bone fracture remains unclear for several reasons. 1) The THIN study was not able to adjust for race or diet.⁹ Because black individuals are less likely to form kidney stones than white individuals¹ and also less likely to experience bone fracture,¹² it is possible that THIN results reflect a higher proportion of black individuals in the referent group. It is also possible that associations in THIN were due to differences in diet. For example lower intakes of fruits and vegetables and higher intakes of red and processed meats, and sugar sweetened beverages are associated with a higher risk of nephrolithiasis and fracture.^{13–17} 2) Not all longitudinal studies have identified kidney stones as a risk factor for bone fracture. A recent series using WHI data including almost 10,000 women with a self-reported history of kidney stones who were followed more than 8 years showed no independent association between nephrolithiasis and incident fracture.¹⁸ 3) No population based study to date has excluded fracture due to major trauma. Bone fracture in the setting of high trauma likely occurs regardless of kidney stone status.

To delineate independent associations between a history of nephrolithiasis and the subsequent risk of incident bone fracture due to low or moderate trauma we performed prospective analyses in the NHS and HPFS cohorts.

MATERIALS AND METHODS

Source Population

A total of 121,700 female registered nurses between 30 and 55 years old enrolled in NHS in 1976 by completing and returning an initial questionnaire providing detailed information on medical history, lifestyle and medications. Like the HPFS cohort, the NHS cohort is followed by biennial mailed questionnaires, which include inquiries about the incidence of newly diagnosed diseases. For this study we started followup in 1980 since before that date we lacked information on diet. A total of 51,529 male dentists, optometrists, osteopaths, pharmacists, podiatrists and veterinarians between ages 40 and 75 years enrolled in HPFS in 1986 by completing and returning an initial questionnaire.

Study Population

The primary analysis included postmenopausal women and to make the 2 cohorts more consistent men 45 years old or older. Women who were premenopausal at baseline entered analysis at the biennial questionnaire when they reached menopause and men younger than 45 years entered when they became 45 years old. Participants with previous wrist, hip or vertebral fracture and those with a history of self-reported osteoporosis were excluded at the start of analysis. A total of 101,319 NHS and 50,893 HPFS participants were included in wrist fracture analysis, and 107,001 NHS and 50,982 HPFS participants were included in hip fracture analysis. Fewer participants contributed to wrist fracture analysis because the assessment of wrist fracture ended before the assessment of hip fracture.

Ascertainment

Kidney Stones. Questions about a history of kidney stones were first asked in 1992 in NHS and in 1986 in HPFS. Thus the current analysis was limited to NHS participants who answered questionnaires in 1992 or later. Subsequent biennial questionnaires asked about a history of kidney stones in the previous 2 years. Participants who reported an incident kidney stone were mailed a supplementary questionnaire asking about the date of occurrence and symptoms. The self-reported diagnosis was confirmed in 97% of participants who completed the supplementary questionnaire in 2 separate validation studies.^{19,20} In a subset of individuals with nephrolithiasis and available kidney stone composition reports 77% of NHS and 86% of HPFS participants had a stone that contained 50% or greater calcium oxalate.¹⁷

Wrist and Hip Fractures. Participants reported wrist and hip fractures on biennial questionnaires, which also assessed information on bone site, date of fracture and circumstances under which the fracture occurred. Wrist fracture assessment ended in 2004 for NHS and in 2008 for HPFS. The primary outcomes of the study were fractures of the distal radius (wrist) or the proximal femur (hip) that occurred in the setting of low or moderate trauma. Fractures due to motor vehicle accident, horseback riding, skiing and other high trauma events were excluded from study because major trauma can cause fracture regardless of bone mineral density. In a validation study in NHS a medical record review confirmed reported fractures in all 30 sampled cases.²¹

Diet. The semiquantitative FFQ, which asks about the average use of more than 130 individual foods and 22 beverages during the previous year, has been mailed to study participants every 4 years. The FFQ also includes an open-ended section. The reproducibility and validity of the FFQ in NHS and HPFS have been documented.^{22,23}

Nutrient intake was calculated from the reported frequency of consumption of each specified unit of food and from USDA (United States Department of Agriculture) data on the content of the relevant nutrient in specified portions. Nutrient values were adjusted for total caloric intake.^{24,25} Intakes of supplemental calcium and vitamin D

Download English Version:

<https://daneshyari.com/en/article/3858978>

Download Persian Version:

<https://daneshyari.com/article/3858978>

[Daneshyari.com](https://daneshyari.com)