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Osteoporosis, Fractures, and Bone Mineral Density Screening in Veterans With Kidney Stone Disease

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ABSTRACT

Whether a link exists between kidney stone disease and osteoporosis or fractures remains an open question. In this retrospective cohort study, we sought to determine the prevalence of osteoporosis and fractures and rate of bone mineral density screening by dual-energy X-ray absorptiometry (DXA) in patients with kidney stone disease. We examined nationwide data from the Veterans Health Administration and identified 531,431 patients with kidney stone disease between 2007 and 2015. Nearly 1 in 4 patients (23.6%, 95% confidence interval [CI] 23.5–23.7) with kidney stone disease had a prevalent diagnosis of osteoporosis or fracture. In patients with no prior history of osteoporosis or bone mineral density assessment before a kidney stone diagnosis, 9.1% were screened with DXA after their kidney stone diagnosis, of whom 20% were subsequently diagnosed with osteoporosis. Our findings provide support for wider use of bone mineral density screening in patients with kidney stone disease, including middle-aged and older men, a group less well recognized as at risk for osteoporosis or fractures. © 2021 American Society for Bone and Mineral Research (ASBMR).

KEY WORDS: OSTEOPOROSIS; SCREENING; DXA; FRACTURE RISK ASSESSMENT; GENERAL POPULATION STUDIES

Introduction

Kidney stones affect approximately 1 in 11 persons in the United States.[1] The majority of kidney stones are composed of calcium,[2] and the most common metabolic abnormality underlying stone risk is high urine calcium excretion or hypercalciuria.[3] In a subset of patients with kidney stones, dysregulated calcium homeostasis may be present in which calcium is resorbed from bone and excreted into the urine, which can lead to osteoporosis and the formation of calcium stones.[4,5] However, the magnitude and significance of bone loss in patients with kidney stone disease is currently underappreciated in the clinical setting; for example, guidelines still do not exist for evaluation or management of osteoporosis in patients with kidney stone disease.

The prevalence of fractures in patients with kidney stone disease has been reported to range from 19% to 24%, but the prevalence of osteoporosis in this group of patients remains unclear.[6,7] Clinicians may miss the opportunity to screen patients with kidney stone disease for osteoporosis because of financial barriers to reimbursement, and so the prevalence of osteoporosis in patients with kidney stone disease may be underestimated. The Veterans Health Administration (VHA) is the largest national integrated health care system in the US and offers distinct advantages for studying the link between kidney stone disease and osteoporosis or fractures, including the presence of a large cohort with long times for longitudinal follow-up and the absence of financial barriers for osteoporosis screening in patients with kidney stone disease. Moreover, the VHA is enriched for male patients with kidney stone disease;[8,9] although the risk of osteoporosis and fractures in women has been well appreciated, this risk is less well studied or recognized in men.[10,11]

In this cohort study, we used national VHA data to estimate the prevalence of osteoporosis and fractures in patients with kidney stone disease and determine clinical factors associated with a diagnosis of osteoporosis or fractures. In addition, we sought to determine the contemporary use of bone mineral density screening with dual-energy X-ray absorptiometry (DXA) in patients with kidney stone disease.

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Materials and Methods

Data and study population

The Stanford University School of Medicine Institutional Review Board and the Veterans Affairs Research and Development Committee approved this study and waived the requirements for patient informed consent because the data were de-identified and presented in aggregate. We identified patients with kidney stone disease who received care from January 1, 2007, to December 1, 2015, using VHA national data stored in the Corporate Data Warehouse and hosted by the Veterans Affairs Informatics and Computing Infrastructure (VINCI).[12] We defined persons with kidney stone disease as those with one or more inpatient encounters that included International Classification of Diseases, Ninth Revision and Tenth Revision (ICD-9 and ICD-10) codes for kidney or ureteral stones, two or more outpatient encounters for kidney or ureteral stones, or one or more kidney or ureteral stone procedures within 1 year using Current Procedural Terminology (CPT) codes (Supplemental Table S1). Each person was counted once, at the time of his or her first qualification for kidney stone disease during the observation period.

To determine the prevalence of osteoporosis and fracture, we identified patients with kidney stone disease who had a diagnosis of osteoporosis or fracture in the 5 years before or 5 years after their index stone diagnosis. To assess the rates of bone mineral density evaluation in patients who present with kidney stone disease, we determined the number of patients who underwent DXA up to 5 years after their index stone diagnosis. In the subset of patients who had a 24-hour urine calcium or citrate measurement, we examined the prevalence of osteoporosis and fractures according to the level of 24-hour urine calcium and citrate excretion.

Statistical analysis

We expressed continuous variables as mean ± SD or median with 25th, 75th percentile range and used Student's *t* test or the Wilcoxon rank sum test to compare groups. We expressed categorical variables as proportions and used the chi-square test to compare groups. We performed multivariable logistic regression to identify factors independently associated with a diagnosis of osteoporosis or fracture after the index kidney stone diagnosis in patients with no prior history of osteoporosis and fracture. We also performed multivariable logistic regression to identify factors independently associated with receipt of DXA after an index kidney stone diagnosis in patients with no prior history of osteoporosis or fracture. We considered two-tailed $p < .05$ as statistically significant. We conducted all statistical analyses with SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Prevalence of osteoporosis and fracture in patients with kidney stone disease

Of the 531,431 unique patients with kidney stone disease from January 1, 2007, to December 31, 2015, 125,247 (23.6%, 95% confidence interval [CI] 23.5–23.7) had a diagnosis of either osteoporosis or fracture around the time of their kidney stone diagnosis. The most common diagnosis was a non-hip fracture in 101,047 (19.0%) of patients, followed by osteoporosis in 32,613 (6.1%) and hip fracture in 11,284 (2.1%). Patients with kidney stone disease and osteoporosis or fracture had a mean (SD) age of 64.2 (14.1) years, included 114,184 (91.2%) men and 11,063 (8.8%) women, and more than three-quarters were white (Table 1).

Table 1. Baseline Characteristics of Patients With Kidney Stone Disease and Osteoporosis or Fracture

Characteristics	With osteoporosis or fracture (n = 125,247)	Without osteoporosis or fracture (n = 406,184)
Osteoporosis	32,613 (26.0)	—
Non-hip fracture	101,047 (80.7)	—
Hip fracture	11,284 (9.0)	—
Age (years), mean (SD)	64.2 (14.1)	62.6 (13.5)
Sex (n, %)		
Male	114,184 (91.2)	384,863 (94.8)
Female	11,063 (8.8)	21,321 (5.2)
Race (n, %)		
White	95,975 (76.6)	300,758 (74.0)
Black	17,350 (13.9)	64,016 (15.8)
Other or unknown	11,922 (9.5)	41,410 (10.2)
Body mass index, mean (SD)	28.6 (6.2)	29.6 (6.2)
Stone diagnosis (n, %)		
Inpatient	3027 (2.4)	10,399 (2.6)
Outpatient	32,789 (26.2)	142,306 (35.0)
Procedure	89,431 (71.4)	253,479 (62.4)
Stone procedure (median, IQR)	1.0 (1.0, 3.0)	1.0 (1.0, 2.0)
Comorbid conditions		
Type 2 diabetes mellitus	40,073 (32.0)	124,781 (30.7)
Enteric disease	1314 (1.0)	3035 (0.7)
Metastatic cancer	3420 (2.7)	10,686 (2.6)
Prostate cancer	1840 (1.5)	6514 (1.6)
Breast cancer	644 (0.5)	790 (0.2)
Paralysis	6097 (4.9)	9246 (2.3)
Primary hyperparathyroidism	1535 (1.2)	2089 (0.5)
Hypogonadism	3531 (2.8)	8328 (2.1)
Charlson comorbidity index, mean (SD)	2.7 (2.5)	2.2 (2.3)
Stone specialty care		
Nephrology		
Before stone dx	1157 (0.9)	2340 (0.6)
After stone dx	3159 (2.5)	7953 (2.0)
Urology		
Before stone dx	8709 (7.0)	22,858 (5.6)
After stone dx	19,539 (15.6)	64,087 (15.8)
Endocrinology care		
Before stone dx	1922 (1.5)	3569 (0.9)
After stone dx	4045 (3.2)	7988 (2.0)
Region		
Midwest	30,118 (24.0)	101,824 (25.1)
Northeast	19,722 (15.7)	60,432 (14.9)
West	41,257 (32.9)	140,094 (34.5)
Southeast	34,150 (27.3)	103,834 (25.6)

SD = standard deviation; IQR = interquartile range; dx = diagnosis.

Among the 462,681 patients with kidney stone disease and no prior history of either osteoporosis or fracture, 56,497 (12.2%) had administrative claims for osteoporosis or fracture in the 5 years after a diagnosis of kidney stone disease. The most

Table 2. Multivariable-Adjusted Odds Ratios for Patients Who Have a Diagnosis of Osteoporosis or Fracture After a Kidney Stone Diagnosis

Variable	OR (95% CI)	*p* Value
Age (per 10 years)	1.03 (1.02–1.03)	<.0001
Male	0.61 (0.59–0.63)	<.0001
Race		
White	Ref.	<.0001
Black	0.80 (0.77–0.82)	
Other	0.88 (0.85–0.91)	
Body mass index		
<19	Ref.	<.0001
19–25	0.83 (0.78–0.87)	
26–30	0.67 (0.63–0.71)	
>30	0.60 (0.57–0.64)	
Index stone diagnosis (surgery versus inpatient or outpatient)	1.37 (1.34–1.40)	<.0001
Metastatic cancer	1.15 (1.11–1.20)	<.0001
Primary hyperparathyroidism	1.59 (1.43–1.76)	<.0001
Type 2 diabetes mellitus	1.07 (1.05–1.09)	<.0001
Enteric disease	1.19 (1.08–1.31)	<.0001
Hypogonadism	1.22 (1.14–1.29)	<.0001
Stone specialty care (5 years before stone)		
Neither	Ref.	<.0001
Nephrology or urology	1.14 (1.10–1.18)	
Both	1.50 (1.11–2.01)	
Endocrine care (5 years before stone)		<.0001
None	Ref.	
Endocrinology	1.28 (1.18–1.40)	
Region		
Northeast	Ref.	<.0001
Midwest	0.93 (0.90–0.96)	
Southeast	0.92 (0.89–0.94)	
West	1.02 (0.99–1.05)	

OR = odds ratio; CI = confidence interval.

Table 3. Multivariable-Adjusted Odds Ratios for Receipt of DXA in Patients With No Prior History of Osteoporosis or Fracture or Bone Mineral Density Testing Before a Kidney Stone Diagnosis

Variable	OR (95% CI)	*p* Value
Age (per 10 years)	1.19 (1.18–1.20)	<.0001
Male	0.17 (0.16–0.17)	<.0001
Race		
White	Ref.	<.0001
Black	1.00 (0.97–1.03)	
Other	0.92 (0.89–0.96)	
Body mass index		
<19	Ref.	<.0001
19–25	1.01 (0.94–1.09)	
26–30	0.94 (0.87–1.01)	
>30	0.88 (0.81–0.94)	
Index stone diagnosis (surgery versus inpatient or outpatient)	1.22 (1.20–1.25)	<.0001
Metastatic cancer	0.93 (0.88–0.98)	.0037
Primary hyperparathyroidism	4.99 (4.57–5.44)	<.0001
Type 2 diabetes mellitus	1.01 (0.98–1.03)	.063
Hypogonadism	2.07 (1.95–2.20)	<.0001
Stone specialty care (5 years before stone)		
Neither	Ref.	<.0001
Nephrology or urology	1.42 (1.36–1.47)	
Both	2.95 (2.24–3.88)	
Endocrine care (5 years before stone)		<.0001
None	Ref.	
Endocrinology	1.57 (1.44–1.72)	
Region		
Northeast	Ref.	<.0001
Midwest	0.90 (0.87–0.93)	
Southeast	0.80 (0.77–0.82)	
West	1.02 (0.99–1.05)	

DXA = dual-energy X-ray absorptiometry; OR = odds ratio; CI = confidence interval.

common diagnosis was a non-hip fracture in 47,580 (10.3%), followed by osteoporosis in 14,498 (3.1%) and hip fracture in 7359 (1.6%) (Supplemental Table S2). In multivariable models, the presence of type 2 diabetes (odds ratio [OR] = 1.07; 95% CI 1.05–1.09), metastatic cancer (OR = 1.15; 95% CI 1.11–1.20), enteric disease (defined as ulcerative colitis, Crohn's disease, or Celiac's disease; OR = 1.19; 95% CI 1.08–1.31), hypogonadism (OR = 1.22; 95% CI 1.14–1.29), and primary hyperparathyroidism (OR = 1.59; 95% CI 1.43–1.76) were associated with higher odds of receiving a diagnosis of osteoporosis or fracture after a kidney stone disease diagnosis (Table 2). Patients were also more likely to have a diagnosis of osteoporosis or fracture if they had visited either a urologist or nephrologist (OR = 1.14; 95% CI 1.10–1.18) or endocrinologist (OR = 1.28; 95% CI 1.18–1.40) before their stone diagnosis. Because primary hyperparathyroidism can be associated with both kidney stone disease as well as osteoporosis, we performed companion analyses excluding patients with a diagnosis of primary hyperparathyroidism; results were not materially different (Supplemental Table S3). We also examined the odds of receiving a diagnosis of osteopenia, osteoporosis, or fracture; results were similar to those obtained when examining osteoporosis or fracture. However, we found an unusually low proportion of patients with osteopenia, raising the possibility of under-coding (Supplemental Table S4).

Bone mineral density screening with DXA in patients after a kidney stone diagnosis

Of the 462,681 patients without a prior history of osteoporosis or fracture or DXA assessment before a kidney stone diagnosis, 42,329 (9.1%) were screened with DXA in the 5 years after their stone diagnosis (Supplemental Table S5). Patients who completed DXA had a mean age (SD) of 64.2 (12.1) years, and 35,170 (83%) were men. Of those who completed DXA, 8348 (20%) were subsequently diagnosed with osteoporosis, 8055 (19%) with non-hip fracture, and 1008 (2.4%) with hip fracture. Eight-five percent (7115/8348) of patients with kidney stone disease who were screened with DXA and later diagnosed with osteoporosis were men (Supplemental Table S5).

The odds of being screened with DXA were higher among patients with a prior diagnosis of hypogonadism (OR = 2.07; 95% CI 1.95–2.20) or primary hyperparathyroidism (OR = 4.99; 95% CI 4.57–5.44); the odds of being screened with DXA were lower with a prior diagnosis of metastatic cancer (OR = 0.93;

Table 4. Twenty-Four-Hour Urine Calcium Excretion and Osteoporosis or Fracture in Patients With Kidney Stone Disease

Characteristics	Total patients with 24-hour urine calcium (N = 26,667)			p Value
	<200 mg/d (n = 13,730)	200–400 mg/d (n = 12,844)	>400 mg/d (n = 93)	
24-hour urine calcium, mean (SD)	169.0 (25.9)	234.0 (31.3)	462.5 (55.4)	<.0001
Age (years), mean (SD)	60.1 (13.4)	59.0 (13.5)	59.0 (12.8)	.12
Sex (n, %)				<.0001
Male	12,529 (91.3)	11,784 (91.7)	89 (95.7)	
Female	1201 (8.7)	1060 (8.3)	4 (4.3)	
Body mass index, mean (SD)	30.2 (6.3)	30.6 (6.3)	32.4 (6.8)	<.0001
Osteoporosis (n, %)	813 (5.9)	727 (5.7)	9 (9.7)	.18
Hip fracture (n, %)	135 (1.0)	108 (0.8)	1 (1.1)	.47
Non-hip fracture (n, %)	1286 (9.4)	1181 (9.2)	3 (3.2)	.12

SD = standard deviation.

Table 5. Twenty-Four-Hour Urine Citrate Excretion and Osteoporosis or Fracture in Patients With Kidney Stone Disease

Characteristics	Total patients with 24-hour urine citrate (N = 23,855)			p Value
	<200 mg/d (n = 4415)	200–400 mg/d (n = 5773)	>400 mg/d (n = 13,667)	
24-hour urine citrate, mean (SD)	107.3 (55.9)	303.6 (57.7)	779.6 (52.5)	<.0001
Age (years), mean (SD)	61.1 (13.3)	58.3 (14.3)	58.2 (12.7)	<.0001
Sex (n, %)				.44
Male	4094 (92.7)	5390 (93.4)	12,735 (93.2)	
Female	321 (7.3)	383 (6.6)	932 (6.8)	
Body mass index, mean (SD)	30.0 (6.6)	30.4 (6.2)	31.2 (6.0)	<.0001
Osteoporosis (n, %)	197 (4.5)	198 (3.4)	355 (2.5)	<.0001
Hip fracture (n, %)	62 (1.4)	44 (0.8)	54 (0.4)	<.0001
Non-hip fracture (n, %)	400 (9.1)	474 (8.2)	1023 (7.5)	.003

SD = standard deviation.

95% CI 0.88–0.98). Patients were also more likely to be screened with DXA if they visited either a urologist or nephrologist (OR = 1.42; 95% CI 1.36–1.47) or endocrinologist (OR = 1.57; 95% CI (1.44–1.72) (Table 3).

Association between osteoporosis and level of 24-hour urine calcium or citrate measurement

In our cohort of patients with kidney stone disease, 26,667 (5.0%) completed a timed (24-hour) determination of urine calcium excretion. Just over half of patients (13,370/26,667) had a 24-hour urine calcium <200 mg/d, 48.2% (12,844/26,667) had a 24-hour urine calcium between 200 and 400 mg/d, and fewer than 1% (93/26,667) had a 24-hour urine calcium >400 mg/d (Table 4). In patients with a 24-hour urine calcium measurement <200 mg/d, the proportion with a diagnosis of osteoporosis was 5.9% (813/13,370) compared with 5.7% (727/12,844) in those with a 24-hour urine calcium measurement between 200 and 400 mg/d, and 9.7% (9/93) in those with a 24-hour urine calcium measurement >400 mg/d. Differences in the proportion of patients with a diagnosis of osteoporosis by level of 24-hour urine calcium excretion were not significant (p = .18) whether by 24-hour urine calcium excretion in categories outlined above or as a continuous variable (OR = 1.00 per 10 mg/d increase; 95% CI 1.00–1.01). When we excluded patients who were prescribed medications that decrease urine calcium excretion (thiazide and thiazide-type agents: hydrochlorothiazide, chlorthalidone, or indapamide) or increase urine calcium excretion (loop diuretic agents: furosemide, bumetanide, torsemide, or ethacrynic acid), results were not materially different (Supplemental Table S6).

In our cohort, 23,855 (4.5%) completed a 24-hour urine citrate measurement. Almost 60% of patients (13,667/23,855) had a 24-hour urine citrate >400 mg/d, 24.2% (5773/23,855) had a 24-hour urine citrate between 200 and 400 mg/d, and 18.5% (4415/23,855) had a 24-hour urine citrate <200 mg/d (Table 5). In patients with a 24-hour urine citrate <200 mg/d, the proportion with a diagnosis of osteoporosis was 4.5% (197/4415) compared with 3.4% (198/5773) in those with a 24-hour urine citrate between 200 and 400 mg/d, and 2.5% (335/13,667) in those with a 24-hour urine citrate >400 mg/d. The proportion of patients with hip fracture by 24-hour urine citrate was the following: 1.4% (62/4415) in patients with urine citrate <200 mg/d, 0.8% (44/5773) in those with urine citrate between 200 and 400 mg/d, and 0.4% (54/13,667) in those with a 24-hour urine citrate >400 mg/d. The proportion of patients with non-hip fracture by 24-hour urine citrate was the following: 9.1% (400/4415) in patients with urine citrate <200 mg/d, 8.2% (474/5773) in those with urine citrate between 200 and 400 mg/d, and 7.5% (1023/13,667) in those with a 24-hour urine citrate >400 mg/d. Differences in the proportion of patients with a diagnosis of osteoporosis or fracture by level of 24-hour urine citrate excretion were significant (p < .01). Compared with patients with a 24-hour urine citrate excretion >400 mg/d, patients with a 24-hour urine citrate excretion between 200 and 400 mg/d were more likely to have a diagnosis of osteoporosis or fracture after adjustment for age, sex, and body mass index (OR = 1.12; 95% CI 1.04–1.22). Patients with more severe hypocitraturia (24-hour

urine citrate <200 mg/d) were even more likely to have a diagnosis of osteoporosis or fracture (OR = 1.36; 95% CI 1.25–1.48) (Supplemental Table S7).

Discussion

In this cohort study, we found that approximately 1 in 4 patients with kidney stone disease have a history of osteoporosis or fracture at the time of kidney stone diagnosis. Even though bone and kidney stone disorders commonly occur together, fewer than 1 in 10 patients with kidney stone disease complete DXA screening after a kidney stone diagnosis. Since our cohort of US Veterans was enriched with male patients, these findings suggest that the risk of osteoporosis or fractures in patients with kidney stone disease is not restricted to postmenopausal women but is also observed in men, a group that is less well recognized to be at risk. Our findings provide support for wider use of bone mineral density screening in patients with kidney stone disease, including men, so that osteoporosis can be diagnosed and treated earlier to prevent fractures.

Among patients with kidney stone disease and a mean age of 64 years, 6.1% carried a previous diagnosis of osteoporosis, a proportion similar to the reported age-adjusted prevalence of osteoporosis in men over the age of 65 years (5.6%) but much lower than the age-adjusted prevalence among women over the age of 65 years (24.8%).[13] However, among patients who were subsequently screened, 20% were diagnosed with osteoporosis, which approximates the age-adjusted prevalence of osteoporosis in women over the age of 65 years for whom bone mineral density screening is recommended.[14] Given that almost 20% of patients in our cohort had a non-hip fracture, we contend that osteoporosis is underdiagnosed and undertreated in older men with kidney stone disease.

Prior studies assessing fracture risk in patients with kidney stone disease have yielded conflicting results.[6,15–17] One reason for discrepant findings in these studies is the presence of sex-specific differences in fracture risk. Data from the Osteoporotic Fractures in Men (MrOS) study revealed lower bone mineral density in men with kidney stone disease;[18] moreover, cross-sectional data from the Third National Health and Nutrition Examination Survey (NHANES III) found that men with kidney stones, but not women, were more likely to report a history of spine and wrist fractures.[16] In contrast, the Women's Health Initiative found no increase in fracture risk among women with kidney stone disease.[11]

We showed a low rate of bone mineral density screening with DXA after a stone episode and a relatively high prevalence of osteoporosis. Prior studies have noted a higher incidence of fractures in patients with kidney stone disease, but few studies have assessed the rate of bone mineral density screening for osteoporosis, osteopenia, or other forms of bone disease in this population.[6,7,15] The US Preventive Task Force recommends bone mineral density screening for women older than 65 years with DXA because of their high rates of osteoporosis. DXA screening is also recommended for women younger than 60 years with specific risk factors for osteoporosis, but clinical practice guidelines do not address bone mineral density screening for men, whether or not they have kidney stone disease.[14] A missed opportunity to diagnose osteoporosis in men is problematic; if they go on to develop a fracture, the consequences can be severe. It has been estimated that a 60-year-old man has a 25% lifetime risk for sustaining an osteoporotic fracture, and rates of osteoporosis in men are expected to increase by nearly 50% in the next 15 years.[19,20] The 1-year mortality rate in men after hip fracture is twice that of women.[21] In our study, patients with kidney stone disease, the majority of whom are men, appear to be at unusually high risk of osteoporosis and fractures, yet they remain largely unscreened for osteoporosis and could benefit from more timely diagnosis and possible treatment.

We also showed that the odds of DXA screening and a diagnosis of osteoporosis were higher when patients see an endocrinologist, nephrologist, or urologist. Perhaps these specialists are more likely to recognize the possibility of osteoporosis in these patients, or perhaps primary care physicians, who recognize the possibility of osteoporosis, are more inclined to refer to specialists. Nonetheless, raising awareness of osteoporosis in patients with kidney stone disease among primary care providers could increase DXA screening and potentially mitigate fracture risk; even a single DXA test appears to be sufficient in discriminating fracture risk.[22]

To determine which patients with kidney stone disease are more likely to carry a diagnosis of osteoporosis (and benefit most from DXA screening), we assessed shared risk factors for osteoporosis and kidney stone disease, including levels of urine calcium and citrate excretion. We found no correlation between osteoporosis and the level of 24-hour urine calcium excretion, consistent with findings from smaller studies.[5,23] We identified no correlation between osteoporosis and level of 24-hour urine calcium excretion even when we excluded patients who were treated with thiazide diuretics, a class of medications that decrease urine calcium excretion. It is possible that the cause of hypercalciuria in the majority of patients with kidney stones relates more closely to overabsorption of calcium from the gut ("absorptive hypercalciuria") rather than overresorption of calcium from the bone ("resorptive hypercalciuria"). Nonetheless, our findings indicate that patients with kidney stone disease could benefit from DXA screening even in the absence of hypercalciuria.

By contrast, the level of 24-hour urine citrate excretion was associated with osteoporosis and fractures in our cohort. This association persisted after accounting for differences in age and body mass index, key confounders of bone mineral density. These findings support previous studies showing that alkali therapy for patients with osteoporosis improves markers of bone turnover or lowers fracture risk.[23–26] Because urine citrate excretion increases in response to alkali therapy, the presence of low urine citrate excretion may identify which patients should be screened for osteoporosis or which patients may benefit from alkali therapy for the prevention or treatment of osteoporosis. There may be additional 24-hour urine indices associated with osteoporosis, such as 24-hour urine sodium, potassium, magnesium, or phosphate, but we were unable to examine these indices because of the low number of patients who completed these measurements in our cohort.

This study has several strengths. First, we identified a sizeable cohort of patients with kidney stone disease from the largest integrated national health care system in the US, and we had access to both inpatient and outpatient diagnostic claims that interfaced with laboratory results. This cohort was diverse in age, race/ethnicity, geographic location, and presence of comorbid conditions. Earlier studies assessing bone mineral density measurements in patients with kidney stone disease were limited by smaller sample size and a more regional sample population.[27–30] Second, patients who receive care in VHA facilities face fewer financial restrictions in completing diagnostic

procedures, such as DXA, which enables them to have similar access to disease screening and medical care across the country.

The study has several limitations. First, the Veterans study population comprised mostly male patients, which may limit generalizability of these results to women. Postmenopausal women are known to be at higher risk for osteoporosis. By sex-stratified analysis, we found that 34% of women with kidney stone disease had a diagnosis of osteoporosis or fracture around the time of kidney stone diagnosis, suggesting that women with kidney stone disease may be particularly vulnerable (Supplemental Table S8). Second, we only used diagnosis codes, and not information from radiologic imaging, to determine the presence of fractures. Therefore, fractures that may be clinically silent or nearly so, for example vertebral compression fractures, may have been missed or unrecognized. Third, although our findings suggest that wider use of DXA screening in patients with kidney stone disease may identify more patients with osteoporosis at heightened risk for fracture, future studies should examine the comparative safety and effectiveness of antiresorptive and other agents aimed at enhancing bone mineral density in patients with kidney stone disease.

In conclusion, roughly 1 in 4 patients with kidney stone disease carry a diagnosis of osteoporosis or fracture around the time of a kidney stone diagnosis. Fewer than 1 in 10 patients with kidney stone disease complete DXA screening after a kidney stone diagnosis, while approximately 1 in 8 patients are newly diagnosed with osteoporosis or fracture within 5 years of a kidney stone diagnosis. Our findings provide support for wider use of bone mineral density screening in patients with kidney stone disease, including middle-aged and older men, for whom efforts to mitigate risks of osteoporosis and fractures are not commonly emphasized.

Disclosures

All authors report no conflicts of interest with this work.

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PEER REVIEW

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