Asymptomatic Nephrolithiasis Detected by Ultrasound

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Background and objectives: Data from several countries suggest a recent world-wide increase in the prevalence of stone disease. However, these studies have not analyzed the effect that increases in utilization of imaging modalities have had on detection of asymptomatic stones.

Design, setting, participants, & measurements: A retrospective chart review of all patients who had an abdominal or retroperitoneal ultrasound in 2005 at a Department of Veterans' Affairs Medical Center was conducted. The charts of patients who had ultrasounds demonstrating kidney stones were further reviewed. Patients were classified into symptomatic and asymptomatic groups on the basis of their clinical history. Age and sex for all patients were recorded. For those patients with stones, additional data were recorded. Of all patients in the study, the percentage of those with asymptomatic stones was calculated. Taking into account uncertainty about symptomaticity in some patients, a sensitivity analysis for the presence or absence of gross and microhematuria was performed to determine a range for the percent of asymptomatic stones. Appropriate statistical tests were used to determine significance.

Results: The prevalence of all kidney stones in the study group was 8.6 %. Using the sensitivity analysis, 29.8 to 45.7% of all stones were asymptomatic. Of stones found on abdominal ultrasounds, 71.4% were asymptomatic, whereas 36.8% of stones found on retroperitoneal ultrasound were asymptomatic.

Conclusions: Asymptomatic stones have a relatively high prevalence on ultrasound. Epidemiologic estimates of prevalence of nephrolithiasis need to account for increases in utilization of imaging modalities and the resulting detection bias.

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Recent data from several countries suggest a world-wide increase in the prevalence of stone disease in the last 3 to 4 decades (1–5). These studies have relied on patient questionnaires, hospital admission records, and large national health databases (1) to determine the prevalence and incidence of nephrolithiasis. A variety of reasons for increased stone prevalence have been postulated, with the common assumption that environmental factors, rather than genetic ones, are responsible, because of the relatively short time course over which these epidemiologic trends have been observed. However, it is also possible that the increased utilization of imaging studies in recent years has led to greater detection of nephrolithiasis, overestimating the true increased prevalence of stones (1,6–8).

Therefore, although factors such as changing diet and increasing prevalence of diabetes and obesity likely contribute to the observed epidemiologic trends, their relative effect on stone disease can only be assessed after accounting for increases in utilization of imaging modalities. The purpose of this study was to estimate the prevalence of asymptomatic stones and consider how this figure could affect prevalence data for nephrolithiasis that do not discriminate between symptomatic and asymptomatic stones. The data presented are based on a 1-yr retrospective analysis of all retroperitoneal and abdominal ultrasounds conducted at our institution.

Materials and Methods

Data Acquisition

After approval from the local institutional review board, a complete list of all retroperitoneal and abdominal ultrasounds performed at the New York Harbor Veterans' Affairs Medical Center in 2005 was obtained from the radiology service. Using the electronic medical record (EMR) system, we retrospectively reviewed all provided studies (n = 1353). Studies in which the kidneys were not examined, were not mentioned in the radiologist's report, or were difficult to visualize were excluded from the data (n = 24). To prevent inclusion of multiple studies of the same patient, only the first study was included and subsequent repeat studies were excluded (n = 106). The charts of three patients could not be reviewed because of privacy issues. Thus, out of the original 1353 studies, 1220 were included in the data. Therefore the data that were subject to analysis consisted only of ultrasounds in which the kidneys were adequately examined, limited to one study per patient.

Data Review

The goal of this study was to determine the prevalence of stones in patients who did not have symptoms of stones at the time of the study, and who had never had a symptomatic stone. These patients would represent a population who could report a history of asymptomatic stones detected solely by ultrasound. Without this reviewed imaging study, these patients would not have been included in estimates of

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stone prevalence. The sex, race, and age of each patient were recorded. We checked for the presence of stones in each ultrasound by reviewing the radiologist's report. Studies without stones were recorded as negative. If a stone was present, it was considered "definite" if an echogenic density was seen with posterior shadowing and "possible" if the report suggested or could not exclude nephrolithiasis.

The clinical history of each patient was also abstracted from the EMR using the indication given for the ultrasound study, and, if unclear, using preceding clinical notes. From the history, the patients were categorized into symptomatic and asymptomatic groups on the basis of the presence or absence of typical clinical symptoms for nephrolithiasis (*i.e.*, flank pain, hematuria). In cases where the patient was already known to have a symptomatic stone, or if the patient had a procedure (*e.g.*, lithotripsy, stenting), the patient was categorized as symptomatic. No time constraints were placed on prior symptomaticity. Therefore, a documented incident of flank pain or hematuria attributable to nephrolithiasis in the distant past precluded the classification of a patient into the asymptomatic category, even if the 2005 study in question seemed to suggest an asymptomatic stone.

If the monitoring of known kidney stones was given as the indication for the ultrasound, stones that were previously detected incidentally and had remained asymptomatic up to the time of the imaging were considered asymptomatic. Cases that were difficult to interpret ($n = 6$) were adjudicated by all of the authors and a consensus was reached.

Data Analyses

All of the above data were entered in a secure, de-identified database to preserve patient privacy. Analyses were performed to determine the percentage of kidney stones detected via ultrasound that were asymptomatic. Descriptive analyses of the type of ultrasound (abdominal *versus* renal) in these asymptomatic patients were calculated. Other demographic data regarding those found to have symptomatic and asymptomatic stones were compared. Statistical significance was calculated using Fisher's exact test with two-tailed P values. When appropriate, 95% binomial proportion confidence intervals were reported.

Sensitivity Analyses

The use of subjective judgment in some patients to classify stones on the basis of symptomaticity precluded reporting the final percentage of asymptomatic stones as a single value. The presence of varying degrees of hematuria (from microhematuria to gross hematuria) introduced a variable that could not be neatly classified as categorical. In our initial analysis, stones were classified as asymptomatic provided that no gross hematuria was present. Thus, patients who had microhematuria could still technically have asymptomatic kidney stones if it could be attributed to causes unrelated to stones. These causes included recent or current bladder catheterization, recent prostatic resection, hemorrhagic cystitis, urinary tract infection, or intrinsic renal disease. Allowing microhematuria to be present among cases of asymptomatic stones may cause the percentage of such cases to be falsely elevated. Therefore, the data were reanalyzed to only allow those patients with no degree of microhematuria to be classified as asymptomatic. Using these more stringent criteria enabled us to generate a minimum value for the percentage of asymptomatic stones. We then report the percentage of asymptomatic stones as a range instead of a single value.

Results

A review of all abdominal and retroperitoneal ultrasounds revealed 105 records that were positive for kidney stones. After exclusion of duplicate and incomplete ultrasound studies, this represents 8.61% of all ($n = 1220$) reviewed ultrasounds. Table 1, a and b, show the general demographic characteristics of those patients who were found to have kidney stones.

Table 1a. Details of records reviewed

Total number of ultrasounds reviewed	1353
Number of ultrasounds excluded	133
Number of ultrasounds included in study	1220
Total number of patients with stones	105
Mean age of all patients in study (SD)[a]	65.5 (13.4)
Mean age of patients without stones	65.4 (13.5)
Mean age of patients with stones	66.0 (12.0)
Mean age of patients with asymptomatic stones	67.8 (11.1)
Mean age of patients with symptomatic stones	64.5 (12.6)

[a]All means are listed in years as mean (SD).

Table 1b. General demographic characteristics and patient history information from records with stones

Characteristic	Number of Patients	Percent
Gender		
male	104	99.0
female	1	1.0
Race		
white	58	55.2
black	21	20.0
Hispanic	17	16.2
other	2	1.9
unknown	7	6.7
Prior history of stones	61	58.1
No prior history of stones	43	41.0
Undocumented history of prior stones	1	1.0
Number of inpatients at time of ultrasound	13	12.4
Number of patients with unknown inpatient or outpatient status	15	14.3

As shown in Table 1, the mean age of all patients who underwent abdominal or retroperitoneal ultrasonography at New York Harbor Veterans' Affairs Medical Center in 2005 was 65.5 yr. The mean age of the patients who had ultrasounds that showed no stones was 65.4 yr. The mean age of the patients who had ultrasounds showing nephrolithiasis was 66.0 yr. Of these patients, those who had asymptomatic stones had a mean age of 67.8 yr and those with symptomatic stones had a mean age of 64.5 yr. A two-tailed t test assuming unequal variance showed no statistically significant difference ($P = 0.1$) between patients with asymptomatic stones and those with no stones. There was also no significant difference in mean age between

Table 2a. Indications for asymptomatic group ($n = 48$) in descending order of frequency[a]

Indication	Number of Patients
Microhematuria	11
Prior stone[b]	9
Hepatitis B or C	8
BPH	7
Chronic renal insufficiency	6
Elevated LFTs	4
Diabetes	4
Prostate cancer	4
Hypertension workup	4
Flank pain[c]	2
Acute renal failure	2
Increased creatinine	2
Ascites evaluation	2
AAA	2
Right upper quadrant pain	2
Pyuria	1
Chronic renal disease	1
Left lower quadrant pain[d]	1
Neurogenic bladder	1
Recurrent UTI	1
Cholecystitis	1
Urinary incontinence	1
Renal artery stenosis	1
Malignant hypertension	1
ESRD	1
Hepatomegaly	1
Rule out nephrolithiasis	1
N/V/D	1
FUO	1
Rule out pancreatitis	1
H/O hydroureteronephrosis	1
Hemorrhagic cystitis	1
Nocturia	1
Follow-up pyelonephritis	1
Hypertensive nephropathy	1
Chronic back pain	1
Ruptured ovarian cyst	1
Prostatitis	1
Hypercalcemia	1
Hyperparathyroidism	1
H/O stents	1
Groin pain	1
Renal mass	1
Gout	1
Abdominal pain	1
GERD	1
Elevated PSA	1

[a]AAA, abdominal aortic aneurysm; BPH, benign prostatic hypertrophy; FUO, fever of unknown origin; GERD, gastroesophageal reflux disease; H/O, history of; LFT, liver function test; N/V/D, nausea, vomiting, diarrhea; UTI, urinary tract infection.

[b]Regardless of stone type (includes calcium oxalate, uric acid, and staghorn calculi). For this group, the indication "prior stone" refers to monitoring of a previously asymptomatic stone.

[c]Refers to both acute and chronic flank pain.

[d]This patient was recently diagnosed with diverticulitis.

patients with symptomatic stones and asymptomatic stones ($P = 0.1$). Lastly, there was no significant age difference between patients who had stones (regardless of symptomaticity) and those who did not ($P = 0.6$).

Of the 105 ultrasound studies that were positive for stones, 48 [45.7%; 95% confidence interval (CI), 35.5 to 54.5%] fit criteria for being asymptomatic whereas 57 (54.3%; 95% CI, 44.5 to 63.5%) were considered symptomatic. The asymptomatic group includes patients who had microhematuria on urinalysis. If the presence of microhematuria was considered to be an exclusion criterion for classifying stones as asymptomatic, then the number of asymptomatic stones fell to 31 (29.8%; 95% CI, 20.3 to 37.9%). Therefore, among all ultrasounds that show nephrolithiasis, the prevalence of asymptomatic kidney stones can be reported as a range of 29.8 to 45.7%.

Patients with asymptomatic stones had 48 unique indications for undergoing ultrasonography. Those in the symptomatic category had 32 unique indications. Table 2 summarizes all of the indications for both groups in descending order of frequency. The indications listed in Table 2 were abstracted from the EMR of every patient who had an ultrasound showing a stone(s). Some patients had multiple conditions/diagnoses listed as indications for the ultrasound, and in these patients all of these indications were included in Table 2. Therefore, each patient was allowed to have more than one indication associated with the ultrasound study in question. As a result, the sum of the columns labeled "number of patients" exceeds how many patients there were in each group. Furthermore, Table 2 includes indications for both abdominal and retroperitoneal ultrasounds. It is important to emphasize that the entries in Table 2 represent indications for the ultrasounds, not diagnoses associated with them. Therefore, although some conditions listed may seem to preclude classification of a patient as asymptomatic, these indications may be associated with other etiologies unrelated to nephrolithiasis.

Of all of the asymptomatic stones, 71.4% were found on total abdominal ultrasound, whereas 36.8% ($P < 0.003$) were found on retroperitoneal ultrasound. Furthermore, 89.5% of symptomatic stones were read as definite and 85.4% ($P = 0.5$) of asymptomatic stones were read as definite. Of all symptomatic stones, 14.0% were newly identified, whereas 75.0% ($P < 0.001$) of asymptomatic stones were newly identified. Stones that were not newly identified could have been detected through previous imaging studies not necessarily limited to ultrasonography [*i.e.*, computed tomography (CT) and intravenous pyelography were both methods that identified previous stones in patients].

Discussion

Evidence from multiple countries reporting a recent increase in the prevalence of kidney stones (1,2,9) may not account for the detection bias introduced by the large number of patients undergoing CT and ultrasound imaging. Conceivably, these studies find asymptomatic stones that are reported to patients who then can answer affirmatively to questions about stone prevalence when surveyed.

Recent epidemiologic data (1) suggest that overall stone prevalence has increased by 62.5% between 1976 to 1980 and 1988 to 1994 in adults between the ages of 20 and 74, but these

Table 2b. Indications for symptomatic group ($n = 57$) in descending order of frequency[b]

Indication	Number of Patients
Prior stone[c]	42
Gross hematuria	8
Microhematuria	6
Flank pain	6
HTN	5
Hepatitis B or C	4
Diabetes	4
UTI	4
F/U lithotripsy	4
Increased creatinine	3
Prostate cancer	3
Dysuria	3
Weak urinary stream	3
Chronic back pain	2
F/U renal cyst	2
CRI	1
Elevated LFTs	1
Right or left lower quadrant pain	1
Urinary incontinence	1
ARF	1
Pyelonephritis	1
Hyperparathyroidism	1
Gout	1
Medullary sponge kidney	1
Hepatic encephalopathy	1
Elevated PSA	1
Bladder stone	1
Medullary calcinosis	1
Ureteral kink	1
CVA tenderness	1
Urosepsis	1
BPH	1

[b]ARC, acute renal failure; CRI, chronic renal insufficiency; CVA, costovertebral angle; F/U, follow-up; HTN, hypertension.
[c]Regardless of stone type (includes calcium oxalate, uric acid, and staghorn calculi).

data do not account for the more frequent application of imaging studies in the latter periods. When men were divided by age into three groups (20 to 39, 40 to 59, and 60 to 74) all experienced increases in stone prevalence, but the last group was the only one in which the increase between the two time periods was statistically significant. Dividing men by decades, only those ages 70 to 74 had a statistically significant increase in stone prevalence between the two study periods (6.7 *versus* 13.3%, $P < 0.001$); among women, both those 70 to 74 yr of age (3.7 *versus* 6.9%, $P = 0.024$), and those 40 to 49 yr of age (2.2 *versus* 4.2%, $P = 0.03$) had statistically significant increases. With the important exception of 40- to 49-yr-old women, one could reasonably speculate that these older groups were more often studied by CT and ultrasonography.

As Table 1 shows, the mean age of our overwhelmingly male population (65.5) is similar to the older men (60 to 74 yr) in the later time period (1988 to 1994) of the National Health and Nutrition Examination Survey (NHANES) study of stone prevalence. Given that our range for the percentage of asymptomatic stones (29.8 to 45.7%) approximates the reported percentage increase in stone prevalence (45 to 48%), it is clear that increased utilization of ultrasonography could contribute significantly to the reported increase in the prevalence of nephrolithiasis. Further quantification of the effect that increased utilization has on prevalence data is only possible if the rate at which asymptomatic stones convert to symptomatic stones is known. Asymptomatic stones that eventually become symptomatic during a given time period would not lead to an increase in estimated stone prevalence attributed to detection bias. Only small data sets regarding this question are available. Inci *et al.* (10) prospectively followed asymptomatic stone carriers and found that 7 of 24 (29.2%) patients had progression of their nephrolithiasis over a mean period of 52.3 mo because of onset of pain (with or without the passage of the stone) or need for urologic intervention. Burgher *et al.* (11) showed that up to 77% of patients with nephrolithiasis had "progression" of their disease, defined as an increase in stone size, onset of pain, or need for urologic intervention over 3.26 yr. If we use our minimum value of 29.8% for the prevalence of asymptomatic stones, and the rates of conversion to symptomatic stones reported by Inci *et al.* and Burgher *et al.*, we estimate that at least 15 to 45% of the reported rise in stone prevalence could be attributable to the increased utilization of imaging studies.

Because large health surveys such as NHANES are based mainly on patient questionnaires, their utility for studying epidemiology is greatest when they are accurately validated by medical record review. As the authors of the NHANES stone prevalence study have pointed out, the reliability of this database for nephrolithiasis has not been validated. A patient's positive response to the question, "Have you ever had a kidney stone?" was interpreted as an "episode" of nephrolithiasis (1) even if the stone was discovered because of the results of an imaging study performed for a completely unrelated health issue. The greater percentage of asymptomatic stones found with complete abdominal ultrasound (62.0%) over retroperitoneal ultrasound (37.7%) supports the notion that more stones are being discovered incidentally on imaging studies that were not performed for reasons related to nephrolithiasis or intrinsic renal disease. A consideration for refining stone-related questionnaires in the future may entail asking patients more specific questions related to the symptoms of nephrolithiasis. In this way, some distinction could be possible between patients who have had symptoms *versus* those who are aware of an incidentally discovered stone.

Data for the NHANES III time period (1988 to 1994) show that an annual increase of 7.2% was seen in ultrasound utilization rates in the Medical Expenditure Panel Survey (MEPS) between 1992 and 2001 (6). Therefore, for the years 1992 to 1994, which fall within the NHANES III time period, it can be estimated that there was an approximate 21.6% increase in ultrasound use, a factor that remains unaccounted for in epidemiologic studies of stone prevalence on the basis of information derived from this database.

One limitation of our study is that ultrasonography was used as the imaging modality to assess the number of incidental stones instead of noncontrast CT. The latter is known to be more sensitive (12–16) for detecting nephrolithiasis and has largely replaced ultrasonography for evaluation of patients with symptoms of acute renal colic. One would expect that noncontrast CT would detect even more asymptomatic stones because of its higher sensitivity, yielding more true positives. Because there was no significant difference ($P = 0.5$) in the percentage of definite stones in symptomatic *versus* asymptomatic categories, it can be concluded that false-positive detection of asymptomatic kidney stones by ultrasounds is only minimally affecting our data. Although we cannot be certain if CT would yield higher or lower rates of asymptomatic stones because the point of our study was to assess the effect of asymptomatic stones on patient-reported stone prevalence, the rate we report from ultrasound studies may represent a minimum.

The overwhelming predominance of male patients, which is typical of a Department of Veterans' Affairs Medical Center, prevents our study from being completely applicable to women. However, it is likely that our conclusions can be applied to the female population because the ultrasound utilization trends reported from the MEPS apply to both genders (6).

Furthermore, because the study is retrospective in nature, it is unable to assess definitively if a patient was truly asymptomatic. It is possible that certain patients who we have classified as asymptomatic stone carriers could have had symptoms of renal colic. Although our conservative estimates using the sensitivity analysis prohibit even patients with microhematuria from being classified as asymptomatic, urinalysis studies may not always have been performed concomitant with a patient's symptoms. One way to clarify this uncertainty would be to contact all patients thought to be asymptomatic and inquire about any potential symptoms they may have had. This validation was beyond the scope of this study.

Conclusions

Our results show that asymptomatic stones account for 29.8 to 45.7% of all stones detected with abdominal and retroperitoneal ultrasounds. These stones are found mostly with abdominal ultrasounds for indications unrelated to renal disease, thus pointing toward their incidental discovery. Even when the rate of conversion of asymptomatic stones to symptomatic stones is taken into consideration, our most conservative estimates show that at least 15%, and perhaps as much as 45%, of the reported increase in stone prevalence is due to increased utilization of imaging modalities. Thus, future studies that examine the epidemiology of nephrolithiasis should account for this potential detection bias on the prevalence of nephrolithiasis.

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