

Original Article | Laterality of Symptomatic Recurrent Calcium Nephrolithiasis

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ABSTRACT

Objective: Although it is presumed that both kidneys excrete similar urinary constituents, it is a general observation that the majority of patients present with unilateral stone disease. The aim of this work was to study the laterality of recurrence in calcium stone formers.

Patients and Methods: In a retrospective study of 154 patients treated for recurrent symptomatic nephrolithiasis at our institution between January 1982 and December 2006, the side of stone formation was determined by an analysis of radiographic findings and symptomatic history. Patients with hydronephrosis, major renal anatomic anomalies and non-calcium stones were excluded from the study. The features of unilateral stone forming and bilateral stone forming were compared. Statistical analysis was done using Student's t-test.

Results: Of the 154 patients, 102 were males and 52 females with a male-to-female ratio of 1:2. One hundred and fourteen patients had unilateral stones (Group A), 64 (56%) on the left and 50 (44%) on the right side. In 40 patients they were bilateral (Group B). Comparing Groups A and B, the mean age at the first stone episode was 41.5 versus 38.3 years, the mean interval between the first stone and recurrence was 9.6 versus 9.9 years, and the mean follow-up was 13.3 versus 14.9 years (differences not statistically significant). In Group A, 101 patients (89%) had unilateral stone recurrence episodes with 86 of these 101 patients (85%) developing stones on the same side as the primary stone. Of the 40 patients with bilateral stone formation, 30 patients (75%) had bilateral stone recurrence episodes.

Conclusion: Recurrent stone formers commonly present with calculi on the same side and the etiology of this phenomenon is unclear, but anatomic and external triggers should be considered.

Keywords : Laterality, kidney, renal stones, recurrence, urinary calculi.

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INTRODUCTION

Urolithiasis is a common disorder, affecting 2% to 3% of the population in industrialized countries; its lifetime risk is 20% in white men and 5-10% in women¹. The highest incidence of urinary stone formation is found in the second to fourth decades, with a male/female predominance of 3:1²⁻³. About 80% of all stones contain calcium, mainly in the form of calcium oxalate⁴. It is well known that renal stones have a marked tendency to recur, with reported rates as high as 50% within 10 years of the first stone episode⁵⁻⁶.

Nephrolithiasis is a heterogeneous disorder. The etiology of stone formation has been evaluated extensively in the literature, with regard to the impact of epidemiologic intrinsic (genetics, age and sex) and extrinsic factors (geography, climatic and seasonal factors, water intake, occupation, diet and stress), the physical chemistry of urine and of inhibitors playing a role in crystal formation, growth and aggregation. However, the exact mechanism of stone formation remains unclear¹. Although it is presumed that both

kidneys excrete similar urinary constituents, it is a general observation that the majority of patients present with unilateral stone disease⁷. Little statistical evidence is available with regard to the laterality of stone disease. Many urologic surgeons believe that patients with recurrent stone formation may develop only unilateral calculi, but few data are available to prove this hypothesis⁸.

This study was carried out in order to examine the laterality of recurrence in calcium stone formers.

PATIENTS AND METHODS

The clinical records of patients presenting consecutively with recurrent urinary stones between January 1982 and December 2006 were reviewed retrospectively. All patients suffered from symptomatic renal or ureteric stone disease. Patients with residual stones after the initial intervention were excluded from the study, as were those with residual fragments 3 months after endoscopic or extracorporeal lithotripsy and after open surgery. After further exclusion of patients with hydronephrosis, major renal anatomic anomalies (horseshoe, pelvic and malrotated kidney, bifid pelvis, bifid ureters, ectopic pelvic fusion anomaly) and non-calcium stones, 154 patients were enrolled into the study. The side of stone formation was determined by an analysis of radiographic findings and symptomatic history. The subsequent history of urolithiasis was evaluated at follow-up every 12 months. Pyelography and full metabolic investigation were performed in all the patients during the first as well as during the recurrent stone episodes. The features of unilateral and bilateral stone formation were compared. The statistical significance for each medical variant was calculated with Student's t-test.

RESULTS

Of the 154 patients, 102 were males and 52 females with a male-to-female ratio of 1:2. One hundred and fourteen patients had

unilateral stones (Group A), 64 (56%) on the left and 50 (44%) on the right side. In 40 patients they were bilateral (Group B). The mean age at the first stone episode was 41.5 (range 17 – 65) years for the patients of Group A, and 38.3 (range 13 – 57) years for the patients of Group B. The mean follow-up from initial stone presentation to the last follow-up visit was 13.3 years for patients in Group A compared to 14.9 years in Group B. Recurrences developed within 10 years after the initial episode in both groups. The demographic patient data are summarized in Table 1. In Group A, 101/114 patients (89%) had unilateral stone recurrence episodes with 86 of the 101 patients (85%) developing stones on the same side as the primary stone. There were 15 of the 114 patients (15%) who had more than one recurrence on the same side. Of the 40 patients with bilateral stone formation, 30 patients (75%) had bilateral stone recurrence episodes.

DISCUSSION

The pathogenesis of calcium oxalate stones is multifactorial and still not completely understood⁹.

The nucleation theory postulates that urinary stones originate from immersion of crystals or foreign bodies in supersaturated urine¹⁰. However, stones do not form in all patients who are relatively dehydrated or hypersecretors of crystals¹¹. Moreover, 24-hour urinalysis demonstrates a normal concentration of stone forming ions in many stone forming patients¹².

In contrast, the crystal inhibitory theory suggests that absence or a low concentration of natural stone inhibitors favors stone formation; but this is not true for all patients, as some individuals who lack these inhibitors may never form a stone. Conversely, many patients with an abundance of urinary inhibitors may form stones¹³.

If we consider that the risk factors for stone formation are similar for both kidneys, it is very difficult to explain, by metabolic factors

Table 1: Demographics

Patient data	Unilateral stone formers	Bilateral stone formers	P- values
	(Group A)	(Group B)	(B vs. A)
Total number of patients	114	40	---
- Male	75	27	---
- Female	39	13	---
Mean age at first stone episode (years)	41.5 ± 15.7	38.3 ± 16.2	NS
Mean interval between the first stone and recurrence (years)	9.6 ± 4.2	9.9 ± 3.9	NS
Mean follow-up (years)	13.3 ± 5.7	14.9 ± 4.8	NS

NS = no significant difference

alone, why a calculus is primarily formed in one but not in the contralateral kidney. From this point of view, it is logical to consider that different anatomic properties of normal and stone-bearing kidneys are the key factors for the lateralization of the stone and also constitute a risk factor for their etiology.

It is striking that many patients with urolithiasis form stones exclusively on one side, as shown in our study. Although the exact mechanism is not apparent, an attractive hypothesis is that a change in renal blood flow may promote stone formation. Early experimental studies in animal models have demonstrated that acute unilateral renal ischemia enhances nephrolithiasis¹⁴. This observation may explain why the peak incidence of urinary stone disease occurs in the third and fourth decades. Our results confirm this data on the predisposition to form symptomatic calcium oxalate calculi during the third and fourth decades of life.

Shekarriz et al. demonstrated an association between sleep posture and ipsilateral urinary stone disease¹⁵. There may be relative

ischemia of the kidney on one side in the recumbent position, thus resulting in low urine output and supersaturation of crystals leading to stone disease.

A morphologic study of the pelvicalyceal system revealed significant differences in various parameters on the stone side as compared with the normal side: the number of minor and major calices and the number of branches were higher; the lower calyx radius was longer; the total calyx area, the renal pelvic area and the total area were larger^{16,17}. A study of the urodynamic factors revealed that on the stone side the peristaltic frequency in the upper third of the ureter was less, the difference in peristaltic interval was longer and the rhythm of the peristaltic discharge was irregular¹⁷. Therefore, morphological and urodynamic disorders of the upper urinary tract may be considered as factors contributing to stone formation.

In another study, Nabi et al. evaluated 100 consecutive patients with lower calyceal stones, and they found that the lower pole had a more acute pelvicalyceal angle on the

stone-forming side compared to the normal contralateral kidney in 74% of cases¹⁸. They concluded that the infundibuloureteropelvic angle is a significant risk factor, which predisposes to urolithiasis in the inferior calyx. On the other hand, crystals must remain in the pelvicalyceal system for some time to form urinary stones, and Schulz found that patients with urolithiasis were characterized by larger areas of renal pelvis or calyx on urography¹⁹.

It is well known that kidney stones have a marked tendency to recur, with reported rates as high as 50% within 10 years of the first stone episode^{5,6}. On the other hand, Ahlstrand and Tiselius reported that only 26% of their patients had recurrent stones within 10 years after the first stone²⁰. The etiology of this phenomenon is unclear, but suggests important anatomic, intrinsic, and possibly physiologic factors. None of these patients had clear evidence of traditional anatomic risk factors for stone formation, such as ureteropelvic junction obstruction or vesicoureteral reflux. Additionally, stone recurrence was not secondary to residual calculi, because all interventions for residual calculi, for both unilateral and bilateral stones, were evaluated as one treatment unit.

Our findings indicate that stones can recur as long as 10 years after the first episode and recurrent stone formers commonly present with calculi on the same side. Although the mechanism of laterality of recurrent urolithiasis remains to be elucidated, this observation should be considered in the evaluation and prevention of unilateral nephrolithiasis.

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