Effect of Medical Management on Recurrent Stone Formation Following Percutaneous Nephrolithotomy

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Purpose: Percutaneous nephrolithotomy is a commonly used procedure for treatment of large or complex renal calculi. In some instances postoperative residual stone fragments are an unavoidable result. Yet to our knowledge no study has examined the impact of medical management on stone formation in patients with or without residual fragments following percutaneous nephrolithotomy. Thus, we have conducted the first investigation of aggressive medical management following percutaneous nephrolithotomy and its impact on stone formation rates in patients with and without residual fragments.

Materials and Methods: A total of 70 patients who underwent percutaneous nephrolithotomy and received counseling regarding selective medical management following a comprehensive metabolic evaluation, were identified. Patients were placed into 4 groups following percutaneous nephrolithotomy, that is stone-free or residual fragments, who underwent or did not undergo medical therapy. New stone formation was assessed by spontaneous stone passage in the absence of residual stone fragments, stone passage without change in the number of residual fragments, surgical removal of newly formed stones, or appearance of new stones or increase in size of stone or fragments on abdominal radiographs. Stone remission rates were also calculated.

Results: Selective medical therapy significantly decreased stone formation rates in the stone-free (0.67 stones per patient per year vs 0.02) and residual fragment groups (0.67 stones per patient per year vs 0.02) as determined by the Wilcoxon signed rank test ($p < 0.0001$). Moreover, remission was observed in a higher proportion of patients in the medically treated stone-free and residual fragment groups (87% and 77%) when compared to the same groups without medical therapy (29% and 21%, chi-square test $p < 0.0001$).

Conclusions: Our findings suggest that comprehensive metabolic evaluation and aggressive medical management can control active stone formation and growth in patients with or without residual stone fragments after percutaneous nephrolithotomy. Given the inherent morbidity and increased costs attendant with repeat procedures, medical management should be instituted in patients following percutaneous nephrolithotomy without regard to stone-free status.

Key Words: nephrostomy, percutaneous; calculi, nephrolithiasis

Percutaneous nephrolithotomy is an established procedure for the surgical treatment of complex or large renal calculi. However, even when a stone-free state is achieved, the patient's underlying metabolic abnormalities remain. There are no studies which have evaluated the impact of medical management on recurrent stone formation in patients with or without residual fragments after PNL. Findings from such an investigation could validate the role of medical management in decreasing the recurrence rate in patients after PNL, thereby decreasing the need for additional invasive procedures following initial PNL.

Herein we evaluate whether appropriate medical treatment after PNL can control active stone disease in patients with or without residual calculi. We hypothesize that patients on medical therapy will exhibit an increased remission rate and decreased stone formation rate regardless of their stone-free status.

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PATIENTS AND METHODS

Patients

Following Institutional Review Board approval the records of patients seen at the Duke University Medical Center Comprehensive Kidney Stone Center between 1994 and 2002 were reviewed. Patients who underwent percutaneous stone removal during this time period were identified. Inclusion criteria were recurrent nephrolithiasis, completion of a 24-hour comprehensive urinary metabolic evaluation and counseling to begin medical management following PNL. Subjects were required to have a minimum of 1 year of followup, to have data available regarding stone formation or growth after PNL, and to have preoperative and postoperative abdominal radiographs or noncontrasted spiral computerized tomography for inclusion in the review. Length of followup was defined as the time between the first visit or intervention and last clinic consultation at the Comprehensive Stone Center.

All patients underwent a comprehensive evaluation of their history of stone disease at the initial consultation. After surgical intervention each patient was followed according to a standard protocol, which included 2, 24-hour

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comprehensive urine collections and followup imaging at 3 months postoperatively. Patients completing metabolic evaluation were offered selective medical therapy following PNL. Medical therapy included potassium citrate for hypocitraturia, renal tubular acidosis, chronic diarrheal syndromes and gouty diathesis; thiazide diuretics for hypercalciuria; and allopurinol for hyperuricosuria. Some patients were prescribed more than 1 medication. Conversely, some patients chose not to undergo selective medical therapy and opted for conservative measures alone. All patients were placed on a high fluid intake to achieve a minimum urine output of more than 2 L per day and dietary modification to avoid excessive intake of salty foods and red meat protein. Patients were evaluated every 6 months thereafter with repeat 24-hour urine collections and radiographic evaluation every 18 to 24 months. Patients were also asked about the incidence of stone events, including colic, hematuria, spontaneous stone passage or the actual need for stone removal.

Data Analysis

Extensive clinical data including age, sex, race, stone composition and metabolic abnormalities were extracted from each patient chart. Preoperative stone formation rates in number of stones formed per patient per year were determined based on clinical history. Abdominal x-rays (including tomograms) or noncontrasted renal computerized tomography conducted within 1 month before surgery were reviewed. Stone burden preceding PNL was calculated by determining the aggregate surface area of the stones visualized on radiographs. The surface area (mm^2) of each stone fragment was determined by multiplying the maximum length and width of each fragment. The initial postoperative radiographs obtained 3 months after PNL were then reviewed, and patients were divided into 2 cohorts, those with no evidence of residual stones and those with residual fragments following PNL. For the purpose of defining the stone-free cohort, only the kidney or kidneys treated by PNL were considered (patients with stones or fragments in the contralateral untreated kidney could still be designated stone-free as a result of their treatment). These 2 groups were further divided into subgroups of patients based on review of each patient's clinical history: those who underwent or did not undergo postoperative medical therapy. Thus, a total of 4 cohorts were formed.

Serial followup radiographic examinations for all cohorts were reviewed. The SFR following percutaneous stone removal was calculated for each patient. New stone formation was assessed by spontaneous stone passage in the absence of residual stone fragments, stone passage without change in the number of residual fragments, surgical removal of newly formed stones, the appearance of new stones, or an increase in size of stones or stone fragments on abdominal radiographs. Remission rates were assessed following initiation of medical therapy and were calculated as the percentage of patients with no further evidence of active stone disease throughout the length of their followup.

Statistical Analysis

Cohort demographic characteristics were compared using the Kruskal-Wallis test for continuous variables and chi-square test for categorical variables. The Kruskal-Wallis test was used to compare postoperative SFR between cohorts, and the Wilcoxon signed rank test was used to compare preoperative and postoperative SFR for each cohort. Comparisons of remission rates between medicated and nonmedicated groups during the period after PNL were conducted using the Wilcoxon rank sum test.

RESULTS

Patient Population

A total of 226 patients undergoing 247 PNL procedures performed between 1994 and 2002 were identified. Of these subjects, comprehensive metabolic evaluations were recorded in 106 patients. Of these patients 36 were excluded due to conservative management (4), cystinuria (10), neurogenic bladder dysfunction (6), incomplete followup (5), anatomical abnormalities (8) or other comorbidities (3). Thus, a total of 70 patients were included in the study. Of these patients 49 (70%) continued on selective medical therapy whereas 21 (30%) did not undergo medical therapy.

Review of cohort demographics revealed that 81% were white, 13% black, 3% Hispanic and 3% Asian. Half of all patients were male, and mean followup of all subjects was 33.5 months. Patients were initially divided into 2 groups based on their initial postoperative abdominal radiographs: those rendered stone-free (30) and those with residual fragments (40). These 2 groups were further divided into subgroups of patients: those who underwent medical therapy and those who did not undergo therapy. Thus, 4 cohorts were formed, that is stone-free on medical therapy (23), stone-free and not on medical therapy (7), residual fragments on medical therapy (26) and residual fragments not on medical therapy (14). Significant differences in median age and length of followup were observed among cohorts. However, there was no significant difference in preoperative rate of stone formation among groups. Patient demographics divided by cohort are reviewed in table 1. There was no statistically significant difference in type of metabolic abnormality (table 2) or stone composition (table 3) among all groups with 2 notable exceptions: the percentage of patients in each group with struvite or uric acid stones. Stone burdens were similar for patients receiving medical therapy vs those declining medical therapy (40.0 mm vs 43.0 mm, respectively, Wilcoxon 2-sample test $p = 0.73$).

TABLE 1. *Patient demographics by group*

	Age	No. Male	Mos Followup	Preop SFR
All	52	35	31.4	0.67
Stone-free:				
Medical treatment	56	11	24.2	0.67
No medical treatment	38	5	37.8	0.67
Residual fragments:				
Medical treatment	53	10	30.9	0.67
No medical treatment	51	9	40.2	1.00
p Value*	0.02	0.28	0.05	0.39

* Kruskal-Wallis test for continuous variables, chi-square test for categorical variables.

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