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Stone Disease in Living-Related Renal Donors: Long-Term Outcomes for Transplant Donors and Recipients

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Abstract

Background and Purpose: Historically, patients wishing to donate their kidney to living related recipients were deemed ineligible if preoperative imaging demonstrated nephrolithiasis. We assess the outcomes of donors with nephrolithiasis and the outcomes of their recipients.

Methods: Donors undergoing nephrectomy between 2001 and 2011 who had nephrolithiasis on preoperative computed tomography (CT) imaging or a history of stone passage were identified. A retrospective chart review documented donor and recipient demographics, donor 24-hour urine collections, stone size and location, stone events after transplant, and graft function. A seven-question telephone survey regarding development and/or presence of symptomatic nephrolithiasis was conducted.

Results: Fifty-four donor-recipient pairs met the inclusion criteria. Twenty-eight (51.9%) patients had valid preoperative 24-hour urine collection, seven (25%) of whom had hypercalciuria. Seven (13%) patients had previous symptomatic nephrolithiasis, but no stones on imaging. Forty-one patients donated a kidney with at least one stone, with a mean stone size of 2.4 mm (range 1–6 mm). Median follow-up for donors and recipients was 22.5 months (interquartile range [IQR] 1–79.3) and 47.4 months (IQR 25.1–76.1), with 50% and 77.7% having a follow-up of more than 2 years, respectively. One donor with nephrolithiasis on preoperative imaging who donated the contralateral kidney passed a stone spontaneously after visiting the emergency department. Otherwise, no other donors or recipients experienced any stone episodes during the follow-up period.

Conclusion: The risk of clinical stone recurrence in donors and recipients is low: As such, presence of small caliceal stones should not constitute an exclusion for living-related kidney donation.

Introduction

Historically, patients wishing to donate their kidney to living related recipients were deemed ineligible if preoperative imaging demonstrated nephrolithiasis. The Ad Hoc Clinical Practice Guidelines Subcommittee of the Patient Care and Education Committee of the American Society of Transplant Physicians developed a guideline[1] stating that "nephrolithiasis is at least a relative contraindication to living donor nephrectomy because of the future risk that recurrent stones, obstructions, and infections will injure the remaining kidney," and that "nephrolithiasis not only places the donor at risk; inadvertent transplantation of a kidney with stone places the recipient at risk." The guideline goes on to recommend that "a history of stone formation need not be an absolute contraindication if the donor has passed only one stone, has stone disease that has been inactive for over 10 years, and if nephrolithiasis is not currently present on radiographic studies." Furthermore, the guideline recommends that patients with metabolic stone-forming abnormalities or patients with stone history, who have abnormal 24-hour urine measurements should be excluded from donation.

Since the publication of this guideline in 1996, attitudes and practices toward donors with a history of nephrolithiasis or with nephrolithiasis on preoperative imaging has shifted in the United States. In 2009, Ennis and associates[2] reported that 77% of responding centers allowed stone formers to donate and that about 40% of centers reported that their attitude toward accepting donors with kidney stones has changed over the last 5 to 10 years. Among these centers, the overwhelming majority (93%) reported that they were more likely to accept these donors.[2] There has been only few recent studies, however, exploring the outcomes of these donors and their recipients.

One such study was conducted by Kim and colleagues,[3] who looked at 16 donors with nephrolithiasis (nonobstructing and small (median 2 mm; range 1–9 mm) on preoperative imaging who proceeded with kidney donation. Eleven recipients received kidneys containing stones. Symptomatic

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nephrolithiasis developed in one recipient after transplantation. The remaining 10 recipients have stable graft function, postoperative ultrasonography negative for nephrolithiasis, and no sequelae fromstones. Symptomatic nephrolithiasis did not develop in any donor donation. The results of the study were limited by the number of patients (16) and by the exclusion of patients with abnormal 24-hour urine collection values.

We assess the long-term outcomes of living-related donors with a history or presence of nephrolithiasis and their respective recipients. In performing this study, we aim to offer a more accurate and practical risk assessment for these donors and their recipients.

Methods

We performed a retrospective chart review of all living-related donors who underwent donor nephrectomy between 2001 and 2011. Donors with a history of symptomatic nephrolithiasis or presence of nephrolithiasis on preoperative computed tomography (CT) imaging and their respective recipients were identified. For those patients, we documented donor and recipient demographics, donor 24-hour urine collections, stone size and location, stone events after transplant, and graft function in an Institutional Review Board approved database.

A seven-question telephone survey (Appendices 1 and 2) regarding development and/or presence of symptomatic nephrolithiasis was conducted on both donors and recipients. Two weeks before the telephone calls, a letter was mailed to the donors and eligible recipients introducing the telephone survey, describing the reason that the patient was chosen for the telephone survey, and that partaking in the survey was completely voluntary. When conducting the telephone calls, a voicemail message was left for those patients who had a valid telephone number and did not respond. Three more attempts were made at contacting those patients.

The follow-up period was measured from the time of surgery to: (1) The time of most recent follow-up (either our telephone survey or chart, if the patient was not available for the survey), (2) time to death, or (3) time to allograft nephrectomy. Donor preoperative estimated glomerular filteration was calculated by the Modification of Diet in Renal Disease equation. Twenty-four-hour urine samples were considered valid if the creatinine measurement was 1 g or greater. Descriptive continuous variables were summarized using means, medians, and ranges. Descriptive categoric variables were summarized using frequencies and percentages. All statistical calculations were performed using JMP® Pro 9.0.0.

Results

Between 2001 and 2011, 732 living-related donor nephrectomies were performed. Of these, 54 donor-recipient pairs met the inclusion criteria. Donor and recipient mean ages were 44 and 45.6 years, and males constituted 44.4% (n = 24) and 68.5% ($n = 37$), respectively (Tables 1 and 2). Twenty-eight (51.9%) patients had valid preoperative 24-hour urine collection, seven (25%) of whom had hypercalciuria, and 10 (35.7%) had two or more risk factors for nephrolithiasis (Table 1). Seven (13%) patients had previous symptomatic nephrolithiasis, but no stones on imaging. Only four (7.5%) recipients had symptomatic stone history.

A total of 41 patients donated a kidney with at least one stone, with a mean stone size of 2.4 mm (range 1–6 mm) and a median of one stone per kidney (IQR 1–1), and 76.3% if stones were located in the midpolar area or lower pole of donated kidneys. Nineteen (35.2%) donors underwent right-sided nephrectomies. Six patients had right nephrolithiasis, but underwent left donor nephrectomies, four of whom had complex right renal vasculature (two patients had two renal arteries, one patient had three renal arteries, and one patient had three right renal veins join a common trunk approximately 9 mm before entering the inferior vena cava). The other two patients had left nephrectomies (performed in July 2009 and July 2010) because of surgeon preference.

The donor telephone survey response rate was 48.1% (26 patients). Two donors refused, 13 patients had disconnected telephone numbers, and 13 patients did not respond or call back after multiple attempts at reaching them. The recipient telephone survey response rate was 79.5% (31 of 39 survey eligible patients; nine deceased patients and six patients who had an allograft nephrectomy were excluded from the survey). One patient refused, four patients had disconnected telephone numbers, and three patients did not respond or call back after multiple attempts at reaching them.

Median follow-up for donors and recipients was 22.5 months (IQR 1–79.3) and 47.4 months (IQR 25.1–76.1), with 50% and 77.7% having a follow-up of more than 2 years, respectively. One donor had a bench nephrolithotomy, for which a preoperative CT scan illustrated a total of 12 stones, but bench nephrolithotomy only identified and removed one stone fragment measuring 2 mm. One donor with nephrolithiasis on pre operative imaging (single, 2-mm, midpolar stone) who donated the contralateral kidney passed a stone spontaneously after visiting the emergency department. Otherwise, no other donors or recipients experienced any stone episodes during the follow-up period.

Discussion

There may sometimes be a conflict for the surgeon to want to provide a living-related renal allograft to the recipients so that they are no longer dialysis dependent, while, by the same token, to "first do no harm" to the donor as well as the recipient. The topic of transplanting a kidney from a donor with a history of nephrolithiasis or with nephrolithiasis on preoperative imaging has historically, and until recently, brought about this conflict. As stated earlier, there has been a shift in opinion regarding the safety to the donors and recipients in using these kidneys. It may be that more of these donors are being identified who would otherwise not be identified with the use of sonography or intravenous urography with the advent of more sensitive CT imaging in recent years. Furthermore, the development of multiple minimally invasive strategies for treating patients with transplant nephrolithiasis have prompted many transplant programs to no longer consider renal calculi an absolute contraindication to donation.[4]

In our study, we performed a bench *ex vivo* ureteroscopy and stone basket extraction on one allograft that had a preoperative CT scan that illustrated 12 renal stones. On ureteroscopy, however, only one 2-mm stone fragment was identified and extracted. Therefore, some of these stones that are detected on CT scan may in reality be papillary or intraparenchymal calcifications.

Table 1. Donor Demographics and Stone Characteristics

Variables	*Values*
N	54
Age (years)	44.0 [21–62]
Sex (male)	24 (44.4)
BMI (kg/m^2)	26.1 [16.8–36.6]
American Society of Anesthesiologists score	1.33 [1–2]
Charlson Comorbidity Index	0.02 [0–1]
Previous abdominal surgery	20 (38.5)
Previous symptomatic stone history	7 (13.0)
Median time since stone history (years)	10 [2–22]
[a]Valid 24-hour urine obtained preoperatively	28 (51.9)
[a]Specific 24-hour urine results	
pH > 6.5	8 (28.6)
pH < 5.5	3 (10.7)
Calcium > 250 mg	7 (25.0)
Oxalate > 45 mg	6 (21.4)
Sodium > 200 mmol	5 (17.9)
Uric Acid > 700 mg	4 (14.3)
Citrate < 320 mg	3 (10.7)
Two or more of the above	10 (35.7)
[b]Preoperative eGFR	96.0 [63.4–138.0]
Stone laterality	
Right	25 (46.3)
Left	20 (37.0)
Bilateral	2 (3.7)
No stone	7 (13.0)
[c]Median number of stones per kidney	1 [IQR 1–1]
[c]Stone size (mm)	2.4 [1–6]
[d]Stone location	
Upper pole	9 (23.7)
Midpolar	13 (34.2)
Mid-lower pole	5 (13.2)
Lower pole	11 (28.9)
Nephrectomy laterality – right	19 (35.2)

Percentages represented in parentheses and ranges represented in brackets.

[a]Samples with at least a 24-hour creatinine measurement of 1 g.

[b]Estimated glomerular filtration rate (mL/min/1.73 m^2) using the Modified Diet of Renal Disease (MDRD) equation.

[c]Total of 41 patients who donated a kidney with at least one stone.

[d]38 patients who donated kidneys with ipsilateral stones that had stone location data.

BMI = body mass index; eGFR = estimated glomerular filtration rate; IQR = interquartile range.

Table 2. Recipient Demographics

Variables	*Values*
N	54
Age (years)	45.6 [9–71]
Sex (male)	37 (68.5)
BMI (kg/m^2)	27.3 [10.5–37.4]
American Society of Anesthesiologists score	2.9 [1–4]
Charlson Comorbidity Index	2.9 [2–8]
Previous abdominal surgery	27 (50)
ESRD etiology	
Glomerulonephritis	13 (24.1)
Polycystic kidney disease	11 (20.4)
Diabetes mellitus	7 (13.0)
Hypertension	4 (7.5)
Diabetes mellitus and hypertension	3 (5.5)
Surgical removal due to malignancy	3 (5.5)
Drug-induced	3 (5.5)
[a]Other	7 (13.0)
Unknown	3 (5.5)
Dialysis	
Hemodialysis	27 (50.0)
Peritoneal dialysis	6 (11.1)
Hemodialysis and peritoneal dialysis	1 (1.9)
[b]None (preemptive)	20 (37.0)
Previous symptomatic stone history (%)	4 (7.5)

Percentages represented in parentheses and ranges represented in brackets.

[a]Calcium oxalosis, congenital renal dysplasia, hemolytic-uremic syndrome, medullary cystic disease, multiorgan system failure, neurogenic bladder, reflux nephropathy.

[b]19 patients with chronic kidney disease (CKD) stage 5 and one patient with CKD stage 4.

ESRD = end-stage renal disease.

To further assess the safety of using these historically viewed "risky kidneys," we must understand the natural history and risk of recurrence for patients with a history of symptomatic stone passage, as well as those patients who have asymptomatic renal calculi on CT scan. Trinchieri and colleagues[5] prospectively evaluated the recurrence rate and risk factors for recurrence in 195 patients after a first renal stone. At a mean follow-up of 7.5 years, 27% of patients experienced symptomatic recurrence. Of interest, a cohort of 36 symptom-free patients without a history of recurrence during follow-up included 5 with asymptomatic renal calculi greater than 3 mm. This group found no difference in patients with and without recurrence with regard to the male-to-female ratio, family history of stones, age at onset, or the incidence of various metabolic disorders. Age at disease onset, however, was lower in patients who had two or more stones during follow-up than in those who had only one stone or no recurrence.

Burger and coworkers[6] performed a retrospective review 300 male patients with asymptomatic renal stones and evaluated the risk of progression (defined as pain experienced during follow-up, net cumulative stone growth, or intervention [shockwave lithotripsy], ureteroscopy, percutaneous nephrolithotomy). At presentation the mean cumulative stone diameter was 10.8 mm. At a mean follow-up of 3.2 years, 77% of patients experienced disease progression with 26% needing surgical intervention. The group found a positive association with stone size and progression. When stratified by stone size, patients with an isolated stone of 4 mm or greater at presentation were 26% more likely to experience failed observation than patients with a smaller solitary calculus. Patients with isolated upper pole calculi measuring less than 4 mm had a lower rate of observation failure. At a follow-up of 3.7 years none of these patients needed intervention. This population of patients is probably most similar to those evaluated during kidney donor evaluation.

There have been multiple studies that explored the safety of renal allografts containing stones and/or are from donors with a stone history.[3,7–10] They have been limited by the number of patients and/or relatively short follow-up, however. To our knowledge, this is the largest study with long-term follow-up assessing the outcomes and risk of donors with history of

nephrolithiasis or with nephrolithiasis on preoperative CT scan and their recipients. In our current study, we have found that no adverse events occurred to the recipients of donors that may be labeled as "high risk." More specifically, 13% of our donors had a history of symptomatic renal stones and about 36% of donors with valid 24-hour urines had at least two risk factors (i.e., hypercalciuria, aciduria, hyperoxaluria, hyperuricosuria, and/or hypocitraturia, etc.) for stone recurrence. Furthermore, most (76.3%) of the allografts containing stones in our study were located outside the upper pole, which, according to Burger and coworkers,[6] would render them at higher risk for progression, when the stones were less than 4 mm (our study's mean stone size was 2.4 mm). As stated earlier, only one donor had a stone adverse event for which the patient had renal colic and was seen in the emergency department. No surgical intervention was required, however, and the stone spontaneously passed with intravenous fluids.

Our study is limited by its retrospective nature and its relatively small sample size. As stated earlier, however, this is the largest study of its nature with the longest follow-up. Also, our transplant center, along with many others around the United States, has relaxed its donor inclusion criteria over the last 10 years and, therefore, there may have been some donors who were eliminated during the earlier period of our study, who may have otherwise been included if they were considered more recently. On the other hand, 43% ($n = 23$) of the donor nephrectomies that were included in the current study were performed between 2001 and 2005, before the publication by Davis and Delmonico,[11] who reviewed the 1996 guidelines[1] and relaxed the restrictions on potential donors and nephrolithiasis.

Conclusion

The risk of clinical stone recurrence in donors and recipients is low. As such, presence of small caliceal stones should not constitute an exclusion for living-related kidney donation. Furthermore, kidneys with more favorable anatomy for transplantation (i.e., left) can be safely transplanted, without regard to stone laterality.

Disclosure Statement

No competing financial interests exist.

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Abbreviations Used
CT = computed tomography
IQR = interquartile range

(*Appendix follows* →)

Appendix 1

Kidney Donor Survey:

Since you donated your kidney:

1. Have you been told that you have any *new* kidney stones?
2. Have you had any flank pain?
3. If you did have flank pain, have you been to the emergency department or your doctor's office and were told that you are passing or have passed a stone?
4. Is the recipient of your kidney now on dialysis?
5. If he or she is not on dialysis, is the recipient of your kidney still using your kidney or has he undergone another kidney transplant?
6. Have you suffered any complications/side effects after you donated your kidney? If so, when?
7. What is your most recent serum creatinine level? What was the date?

Appendix 2

Kidney Transplant Recipient Survey:

1. How many months/years has the kidney that you received been functional and keeping you off dialysis?
2. Have you had any permanent rejections of this kidney?
3. Have you had any kidney stone attacks from this kidney? If so, how were they treated?
4. Did you suffer any complications/side effects after this kidney transplant was performed?
5. If so, what were the complications/side effects? When did this occur? (Please provide month/year)
6. What was done to treat the complication/side effect?
7. What is your most recent serum creatinine level? What was the date?