

# Trends in Kidney Donation among Kidney Stone Formers: A Survey of US Transplant Centers

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## Key Words

Complex living donors · Nephrolithiasis · Kidney transplantation

## Abstract

**Background:** Living kidney donation is on the rise and acceptance criteria for potential donors are evolving to include more 'complex' patients such as kidney stone formers. Transplant centers are faced with sparse data on patient outcomes when evaluating potential donors who are stone formers; thus, attitudes and practice can differ greatly between centers. **Methods:** We conducted a survey of United States kidney transplant programs to assess current trends in the approach to dealing with stone formers who are evaluated for kidney donation. **Results:** Based on the survey results, there appears to be a tendency toward increased acceptance of donors with a history of kidney stones. 77% of responding centers allowed stone formers to donate. Nearly 40% of centers reported that their attitude towards accepting donors with kidney stones has changed over the last 5–10 years. Among these, the overwhelming majority reported that they were more likely to accept these donors. **Conclusions:** Such trends are likely based on organ need, as published patient outcomes and evidence-based guidelines are lacking for this unique group of patients. We propose the need for a study to formally evaluate the outcome of stone formers

who donate a kidney in order to systematically examine whether appropriately selected stone formers can safely donate.

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## Introduction

Kidney transplantation offers longer survival and a better quality of life than dialysis [1–3]. Thus more patients with end-stage renal disease (ESRD) choose to go on the waiting list for a kidney transplant every year, and waiting time continuously increases. The median waiting time for a deceased donor transplant is approximately 3 years and is expected to lengthen [4]. It is unlikely that the number of deceased donor kidneys will ever be sufficient to meet the increasing demand of ESRD patients [5]. While efforts are being made to increase the supply of deceased donor kidneys for transplantation, recipients are encouraged to seek out potential living donors.

Kidney donation is a unique situation in which the individual undergoing the procedure has the potential for harm with no physical benefit [6]. Thus, it poses an ethical dilemma of how much risk is acceptable for a living donor [6]. Nonetheless, because of the organ donor shortage, some transplantation centers have relaxed their acceptance criteria for living kidney donation and are al-

lowing what has been termed 'complex living donors' [7]. Complex living donors are individuals with normal renal function at the time of evaluation who possess potential risk factors for kidney disease in the future. Reese et al. [7] noted the sparse data that the transplant professional must deal with when counseling a potential complex donor about long-term risks. A donor with nephrolithiasis is a complex donor.

There are data to suggest that patients with kidney stones may have worse kidney function when compared with non-stone formers. Worcester et al. [8] reported that renal function as measured by creatinine clearance decreases with age in stone formers at a higher rate than non-stone formers. A study of NHANES III revealed that overweight and obese individuals ( $BMI \geq 27 \text{ kg/m}^2$ ) with a history of nephrolithiasis have reduced kidney function when compared with similar individuals without a history of kidney stones [9]. The loss of kidney function after donation has been evaluated, although not specifically in donors with a history of kidney stones. In the published literature on renal function following donation, one finds that healthy donors are not at any higher risk for ESRD than their age-matched peers [10–13]. However, it is not known whether harvesting a kidney from a stone former would accelerate loss of renal function or increase albuminuria with age more than occurs among stone formers who do not donate.

The risk of stone recurrence after donation in healthy stone formers is also unknown. There are two published case series which address recurrence of stones in patients with non-donor nephrectomies. Lee et al. [14] reported a stone recurrence rate of 30% in the contralateral kidney in a series of 50 patients who underwent nephrectomy a mean of 70.6 (range 60–84) months earlier for complications related to a previous stone. Worcester et al. [8] compared stone recurrence rates in 115 patients who underwent nephrectomy for various reasons with 3,151 patients with 2 kidneys and found a 14% recurrence rate in the nephrectomy group after a mean follow-up of 6–8 years. All patients were given preventive treatment guided by metabolic workup, such as thiazide, citrate, allopurinol, fluids and dietary advice, in order to lower urinary supersaturation. During treatment, recurrent stones formed at the rates of 1.3 and 0.9 stones per decade in male and female patients, respectively, with 2 kidneys, compared to rates of 0.5 and 0.4 stones per decade for male and female patients with a single kidney; the difference was significant ( $p = 0.012$ ). Although these data should be interpreted with caution, they suggest that the single kidney patients did not do worse with regard to stone recurrence

than the 2 kidney patients when given preventive treatment. Rate of loss of kidney function with age was higher among male stone formers with a single kidney versus male stone formers with 2 kidneys, particularly below the age of 45 [8]. While these patient groups that are seen for stone complications likely have a higher risk for stone recurrence than potential stone-forming donors (who presumably do not suffer from stone complications), the lack of data on donors with nephrolithiasis makes it difficult to accurately assess the risks for uncomplicated stone formers who wish to donate a kidney.

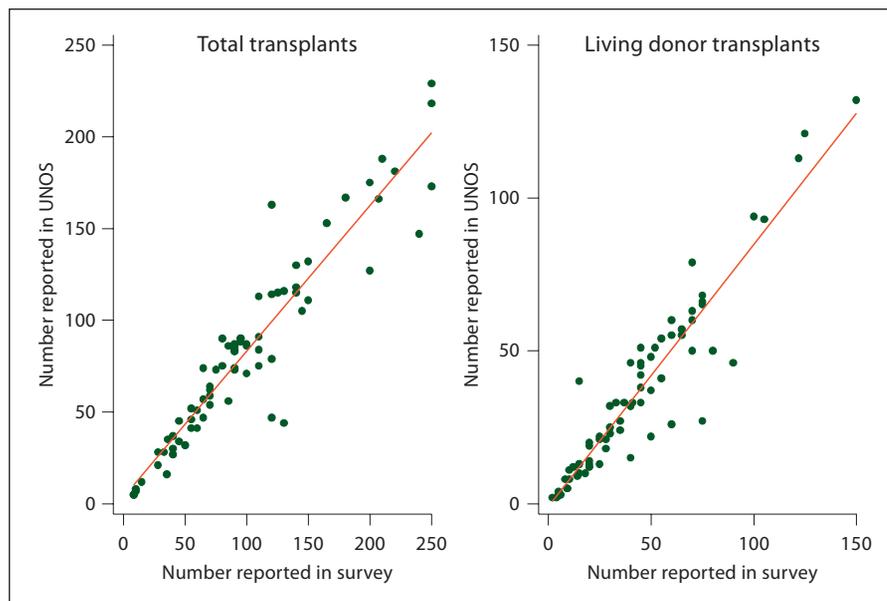
Stone recurrence in a single kidney poses a special risk to kidney function because obstruction by stone passage could result in acute renal failure in that situation. Modern urologic techniques for stone removal, such as extracorporeal shock-wave lithotripsy or percutaneous nephrolithotomy, although generally safe, have some potential risk for renal damage [15]. Whether that risk is increased in patients with a single kidney is still unsettled [16–20].

The American Society of Transplantation position paper [21] proposes guidelines that a kidney stone former may donate a kidney if: (a) only one stone has ever formed; (b) stones have been multiple, but none have formed for >10 years and none are seen on radiograph; (c) the donor is screened for metabolic abnormalities, and is offered life long follow-up that includes periodic risk reassessment, medical treatment, and hydration. It is unclear whether these guidelines represent actual practice, as stone formers can donate in some programs but not others. This variation reflects a general uncertainty regarding the safety of kidney donation for stone formers. Such uncertainty stems from a lack of data to assess outcomes of stone formers who donate a kidney.

With this in mind and in order to better characterize the current variation in practice, we contacted United States kidney transplant programs to assess the current climate in the approach to dealing with stone formers who are evaluated for kidney donation. We also asked whether attitudes toward kidney donation in stone formers are changing.

## Materials and Methods

A survey to capture data about current practices regarding kidney donation in stone formers was designed by one of the authors (M.A.J.) of this paper and sent out in 2 waves (in 2001–2002, appendix 1, and 2007–2008, appendix 2) to surgical and medical directors of all 236 pediatric and adult United States kidney transplant centers. Contact information for each center was obtained from the United Network of Organ Sharing (UNOS). Each re-



**Fig. 1.** High correlation was observed between the self-reported and UNOS-based number of transplants and live donor transplants per year ( $\rho = 0.94$  for each measure).

spondent identified him or herself as a nephrologist, surgeon, other transplant physician, or nurse. The number of total and living donor kidney transplants performed yearly was reported by each respondent, as well as independently obtained from UNOS. Several survey questions sought to address the center's approach to asymptomatic individuals with a history of one or more stones or radiographic evidence of stone formation. If a center had previously allowed a stone former to donate, the respondent was asked questions about follow-up of these donors (if known or available). Finally, respondents were asked to comment on any changes in attitude over the preceding 5–10 years about accepting donors with history of or with current stones in the second wave.

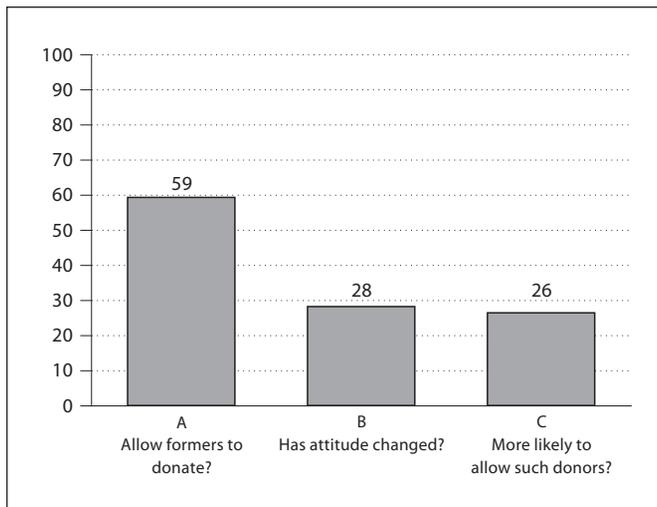
Survey responses were summarized using descriptive statistics. Responses from those centers that had ever allowed stone formers to donate a kidney were compared with responses from centers that had never allowed stone formers to donate. Proportions of positive responses were compared between the two groups using Fisher's exact test. Differences in continuous variables (e.g. total number of transplants) were compared between groups using the Wilcoxon rank sum test. Changes in responses to Yes/No questions that were present both in wave 1 and wave 2 surveys were analyzed using the McNemar test, which tests whether the 'Yes' to 'No' changes are as likely to occur as the 'No' to 'Yes' changes, and only centers responding to both waves were included in this analysis. Overall changes in response to the same Yes/No question between the waves were also evaluated using Generalized Estimating Equations (GEE) models [22] which include all responses. Data regarding the actual number of transplants performed yearly at each center was obtained from the UNOS website. The number of total and living donor transplants was averaged over the preceding 5 years (or less, if <5 years of data were available, which was the case for 8 centers of which none responded to wave 2 of the survey). The actual numbers of transplants performed were compared to the numbers cited by the respondents.

## Results

Surveys were sent to 236 transplant centers. Among these centers, the average number of kidney transplants performed yearly was  $68.8 \pm 60.4$ , ranging from 0 to 315 transplants per year. The average number of living donor transplants performed yearly was  $27.6 \pm 30.1$ , ranging from 0 to 179. On average, the proportion of living donor transplants was 39%, but ranged from 4–100%. The self-reported number of transplants was highly correlated with the published number ( $\rho = 0.94$ ) for both total and living donor transplants (fig. 1).

Of the 236 centers, 92 (39%) responded to wave 1 of the survey and 76 (32%) responded to wave 2. 38 (16%) centers responded to both surveys. The centers that responded to wave 2 survey tended to perform more total transplants than those that did not respond ( $84.2 \pm 51.7$  vs.  $62.1 \pm 62.8$ ,  $p < 0.001$ , Wilcoxon rank sum test), and more live donor transplants ( $36.0 \pm 28.3$  vs.  $23.9 \pm 30.1$ ,  $p < 0.001$ , Wilcoxon rank sum test) on a yearly basis. The trend was similar among wave 1 responding centers.

We have focused our analyses on the second wave of the survey as it reflects more recent practice and attitudes toward stone formers and kidney donation. Of the 76 transplant centers that responded, 59 (77%) responded that their center allows stone formers to donate (fig. 2). 28 of the 76 (36.8%) centers reported that their attitude towards accepting donors with a history of or with current kidney stones has changed over the last 5–10 years.



**Fig. 2.** Number of centers responding ‘yes’ to wave 2 questions: (A) Do you allow any stone former to donate (no matter what the circumstances)? (B) Have you changed your attitude about accepting donors with a history of or with current kidney stones over the last 5–10 years? (C) If your attitude has changed, are you more likely to accept these donors?

Among these, the overwhelming majority (93%) were more likely to accept these donors.

Overall, the proportion of centers that allow stone formers to donate increased from 74.7 to 80.8% between the two surveys, although this increase was not statistically significant ( $p = 0.165$ , GEE model). Of the 36 centers that responded to this question on both waves of the survey, more centers ( $n = 6$ ) began allowing stone formers to donate, whereas only one center switched from allowing to disallowing stone formers to donate ( $p = 0.06$ , McNemar test).

## Discussion

Between 1988 and 2004, kidney donation from live donors increased 267% from 1,812 to 6,647/year [4]. In 2001, the number of transplants performed from live kidney donors surpassed the number of transplants performed from deceased donors [4]. Living donor transplants, particularly preemptive ones, provide better outcomes than deceased donor transplants [23]. Graft survival rates are better when patients have less exposure to dialysis. The main disadvantages of living donor transplantation rest with the donor: the potential perioperative morbidity and mortality of the donor, as well as the potential long-term

adverse effects of living with a solitary kidney. Fortunately, perioperative mortality is low, approximately 0.03% [10, 24, 25], and morbidity is less than 10% [26]. There are few studies on the long-term consequences of living with a solitary kidney. There are no studies that examine the long-term consequences of elective kidney donation in kidney stone formers.

Based on NHANES II and III data, at least 4–6% of adults are kidney stone formers. Kidney stones are more common in men (6.3%) than in women (4.1%) [27]. Improvements in imaging technology have led to the identification of more asymptomatic kidney stone formers than in the past [28]. Prior to donor evaluation, many potential donors are unaware of their stone-forming condition. Whether the seemingly indolent nature of their disease distinguishes them from symptomatic kidney stone formers or whether they are destined to become symptomatic kidney stone formers is unknown. Physicians evaluating these potential donors are uncertain about whether to proceed with the donation.

This uncertainty is reflected in the findings of our survey. Our survey suggests variability in practice with regard to the issue of allowing kidney donation in kidney stone formers. Nevertheless, the majority of centers that responded have previously or do currently allow stone formers to donate a kidney. The centers that responded to the survey tended to perform more living donor transplants than those that did not respond. This helps to enhance the generalizability of these survey results.

The survey results reflect a temporal trend toward increased acceptance of donors with a history of kidney stones, both in attitude and in practice. This trend likely signifies recognition of the need for more living donors rather than prior experience with or knowledge about outcomes of kidney stone-forming donors. In fact, survey respondents had little follow-up information on the stone formers who had donated. There is no formal donor registry in which to follow these patients over time [29]. In the absence of data, physician practices are probably based on trends of need rather than published patient outcomes or evidence-based guidelines.

Given that the need for kidney donors is rapidly reaching crisis proportions, one would desire to use stone formers if that were safe. It is impossible to calculate the precise number of patients awaiting a cadaver organ that could be taken off the wait list if use of donors with kidney stones became standard practice. Karpinski et al. [30] recently explored the impact of using ‘marginal’ living

donors with mild hypertension or proteinuria. They found a potential modest increase of donors of 3%. The authors imply that given the small potential increase, efforts in increasing donation might be better spent elsewhere. However, in the accompanying editorial, Matas [6] points out that every little bit counts. Using the UNOS data of 6,647 living donor transplants performed in 2004 [4], an additional 265 living transplants would be done yearly if we increased the donor pool by 4% and allowed stone formers to donate. This potential increase has benefits for patient outcomes as well as potential cost savings in the care of these patients [31].

We propose the need for a study to prospectively evaluate the outcome of stone formers who donate a kidney in order to systematically examine whether appropriately selected stone formers can safely donate. A critical aspect of such a study is that we identify stone formers in whom donation may contribute to accelerated loss of kidney function or other stone complications and prevent them from donating. While some stone-forming patients are clearly not candidates (i.e. those with enteric or primary hyperoxaluria and cystinuria), the most common type of stone formers, calcium oxalate stone formers who have metabolic abnormalities such as idiopathic hypercalciuria, do not seem obviously unsuitable. If it can be determined that such patients who donate do no worse than calcium oxalate stone formers who do not donate (and their recipients do no worse than waiting for a deceased donor kidney), this may identify a greater pool of donors for potential recipients without other options for living donation. Studies to further evaluate complex living kidney donors such as those with kidney stones are critical for many reasons. Such knowledge allows the potential donor to better make an informed decision regarding donation, and it allows the involved physicians to adhere to the duty of 'doing no harm' to the potential donor [7]. Finally, it serves to identify potential risks in this population that may be prevented or at the very least followed and appropriately treated if necessary. Given the increasing rate of living kidney donation as a partial solution to the ESRD epidemic, we will be faced with the task of risk stratifying these complex donors for years to come. The time has come for a more standardized approach to evaluating stone formers as potential kidney donors. Such an approach should be borne out by dedicated research to evaluate outcomes in this population with unique characteristics and risk factors for donation.

## Appendix 1

Survey wave 1	Yes	No
Kidney donor survey form: _____		
Date: _____		
Program: _____		
Name of individual filling out form: _____		
How many kidney transplants do you perform at your institution yearly? _____		
How many live donor kidney transplants do you perform? _____		
Do you ever allow kidney stone formers to donate kidneys? _____	<input type="checkbox"/>	<input type="checkbox"/>
If yes:		
- Do you include cases where stones are present on radiograph? _____	<input type="checkbox"/>	<input type="checkbox"/>
- Do you limit it to situations where only one stone has formed? _____	<input type="checkbox"/>	<input type="checkbox"/>
- Do you allow formers to donate if stones may have been multiple but none formed for > 10 years and none are seen on radiograph? _____	<input type="checkbox"/>	<input type="checkbox"/>
- Do you limit it only to donors without metabolic abnormalities? _____	<input type="checkbox"/>	<input type="checkbox"/>
Do you allow any stone former to donate or do you have specific criteria? _____	<input type="checkbox"/>	<input type="checkbox"/>
If you have specific criteria, but they were not already mentioned above, what criteria do you use? _____		
If you do allow stone formers to donate, how many have donated kidneys in the last five years? _____		
Do you have follow-up information on these donors? _____	<input type="checkbox"/>	<input type="checkbox"/>
If yes, what is it? _____		
Have they had recurrent stones? _____		
Were they prophylaxed against recurrent stone disease? _____		
Thank you		

## Appendix 2

Survey wave 2	Yes	No
Kidney donor survey form: _____		
Date: _____		
Your name: _____		
Telephone No.: _____		
E-Mail address: _____		
Fax No.: _____		
Program: _____		
Are you a:		
- Nephrologist, surgeon, other transplant physician (not nephrology or surgery), or nurse? _____		
- How many kidney transplants does your institution perform yearly? _____		
- How many live donor kidney transplants does your institution perform yearly? _____		
Do you ever allow kidney stone formers to donate kidneys? _____	<input type="checkbox"/>	<input type="checkbox"/>
Do you allow asymptomatic individuals (people who have not passed a kidney stone) who are unexpectedly found to have <i>one</i> kidney stone on CT to donate? _____	<input type="checkbox"/>	<input type="checkbox"/>
Do you allow asymptomatic individuals (people who have not passed a kidney stone) who are found to have <i>several</i> kidney stones on CT to donate? _____	<input type="checkbox"/>	<input type="checkbox"/>
Do you allow symptomatic individuals who have passed <i>one</i> kidney stone to donate? _____	<input type="checkbox"/>	<input type="checkbox"/>
Do you allow symptomatic individuals who have passed <i>several</i> kidney stones to donate? _____	<input type="checkbox"/>	<input type="checkbox"/>

Survey wave 2	Yes	No	Survey wave 2	Yes	No
Do you allow stone formers to donate if stones may have been multiple but none formed for >10 years and none are seen on radiograph?	<input type="checkbox"/>	<input type="checkbox"/>	Do you instruct <i>all</i> your patients on stones on how to prevent future stones?	<input type="checkbox"/>	<input type="checkbox"/>
Do you allow <i>any</i> kidney stone former to donate (no matter the circumstances: e.g. what type, number, etc.)?	<input type="checkbox"/>	<input type="checkbox"/>	If yes, what do you tell them to do? _____		
Do you <i>never</i> allow a stone former to donate (no matter the circumstances)?	<input type="checkbox"/>	<input type="checkbox"/>	Have you changed your attitude about accepting donors with a history of or with current kidney stones over the last 5–10 years?	<input type="checkbox"/>	<input type="checkbox"/>
Do you <i>only</i> allow a stone former to donate if they meet certain criteria?	<input type="checkbox"/>	<input type="checkbox"/>	If yes, are you:		
If you use specific criteria to decide whether a stone former can or cannot donate, what are the criteria?	<input type="checkbox"/>	<input type="checkbox"/>	– More likely to accept these donors? _____		
Do you do a metabolic evaluation on stone former?	<input type="checkbox"/>	<input type="checkbox"/>	– Less likely to accept these donors? _____		
If you do a metabolic evaluation how does it influence whether or not the individual can donate? _____			– Why have you changed your opinion? _____		
Approximately how many stone formers have donated kidneys in the last 5 years, in your program? _____			Are you interested in participating in this study?	<input type="checkbox"/>	<input type="checkbox"/>
Have any passed stones since donation? _____			If no, is there someone else at your institution that I should contact? _____		
If yes, how many have passed stones after donation? _____			How can I contact that individual? _____		
Have any had acute renal failure from stone formation?	<input type="checkbox"/>	<input type="checkbox"/>	Other individuals who will be involved and their contact information: _____		
			Do you have other comments about this topic?		
			If yes, please feel free to share them: _____		
			What are the specific questions that you feel I should try to answer with this study? _____		
			Thank you		

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