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Practice Patterns in Evaluation of Living Kidney Donors in United Network for Organ Sharing-Approved Kidney Transplant Centers

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Key Words
Living donation · Kidney transplant · Evaluation · Practice patterns

Abstract
Introduction: The current pattern of evaluation for living kidney donors was investigated. ***Methods:*** We designed a 37-question electronic survey to collect information about living kidney donor evaluation. Of the 181 United Network for Organ Sharing (UNOS)-approved centers, 72 responded. Survey responses were coded and downloaded into SPSS. Data was expressed as means and standard deviations or the percentage of centers with specific responses. ***Results:*** 66% of the centers used a cut-off of <80 ml/min for exclusion of living kidney donors. 24-hour urine measuring creatinine clearance (CrCl) was the most common screening method for glomerular filtration rate (GFR) assessment in potential living donors. 56% of the centers excluded donors with blood pressure (BP) >140/90, whereas 22.7 and 7.1% excluded patients with pre-hypertension with a cut-off BP of 130/85 and 120/80, respectively. 66% of the centers used 24-hour urine creatinine to assess for proteinuria. 20% of the centers accepted living kidney donors with microalbuminuria and 84% accepted patients with a history of nephrolithiasis. 24% of the centers reported use of formal cognitive testing of potential living donors. ***Discussion:*** There were significant variations in exclusion criteria based on GFR, history of kidney stones, body mass index, BP and donors with urinary abnormalities. The definitions for hematuria and proteinuria were variable. There is a need for uniformity in selection and for a living donor registry. We also recommend raising the cut-off for estimated GFR to 90 ml/min to account for 10–15% overestimation when CrCl is used.

Introduction

In patients with end-stage renal disease (ESRD), kidney transplantation improves the quality of life and increases survival as compared to long-term dialysis [1–3]. Living donation provides a better patient and allograft survival when compared with deceased donor transplantation, especially when the living donor transplant is performed preemptively [4, 5]. Najarian et al. [6] reported no evidence of progressive renal deterioration in living kidney donors when compared to their paired siblings. Other studies have shown minimal long-term risk in healthy kidney donors as compared to the general population [7,

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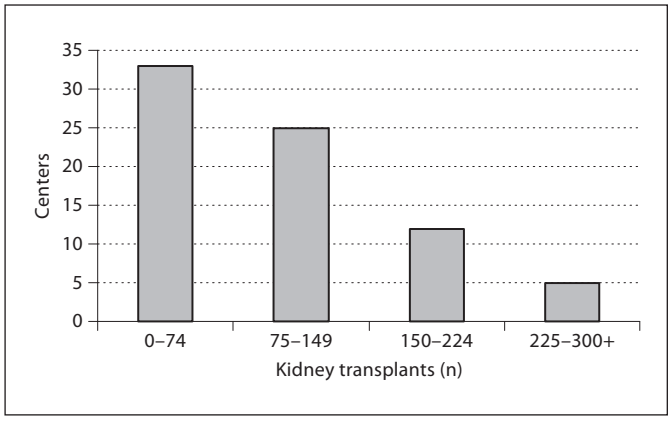

Fig. 1. Number of kidney transplants in the program.

8]. A number of surveys have been carried out in the USA and European countries to determine the criteria for selection of living kidney donors [9–12], however these have become outdated because with ever-increasing waiting times, more centers are considering donors with medical conditions, which were historically considered contraindications to living kidney donation. Our survey was also an attempt to see whether results of the previous surveys and guidelines have led to uniformity in living donor evaluation. The aim of this study was to obtain the latest information about how transplant centers evaluate living kidney donors in the USA.

Methods

We designed a 37-question electronic survey to gather information about living kidney donor evaluation and selection processes. A questionnaire was designed to establish factors related to donor assessment, exclusion criteria and follow-up. Questions were related to how centers evaluated glomerular filtration rate (GFR), urinary abnormalities in living donors and exclusion criteria for obesity, hypertension and nephrolithiasis. A list of all United Network for Organ Sharing (UNOS)-approved transplant programs was obtained from the UNOS website. Transplant nephrologists and surgeons were further identified through transplant program websites or a phone call to the programs.

An electronic anonymous survey via a secured hyperlink (www.surveymonkey.com) was sent to transplant nephrologists of 181 UNOS-approved renal transplant centers in May 2011. If the transplant nephrologist did not respond, a request for survey completion was sent to the surgeon. A subsequent request for completion of the survey was re-sent to the non-responders in October and November 2011 via a secured hyperlink. Survey responses were coded and downloaded into Statistical Package for the Social Sciences (SPSS Inc., Chicago, Ill., USA) for analysis. Duplicate responses from the same program were excluded. Data was expressed as means and standard deviations (SDs), or the percentage of centers with specific responses. Survey responses were summarized using descriptive statistics. Institutional review board approval was obtained from SUNY Downstate and WRNNMC.

Results

Respondents from 72 centers completed the questionnaire. Of these, 33 centers performed more than 75 kidney transplants in a year, 25 centers reported 75–149 kidney transplants, while 12 larger centers reported 150–224 kidney transplants and 5 centers performed 225–300 kidney transplants per year (fig. 1). Forty-five percent of the centers reported less than 24 living kidney donor transplants at their center in each year, while 30% of the centers carried out 25–49 living kidney transplants each. Among kidney programs with reported annual transplants between 50–74 and 75–100, the response rate was 19.2 and 5.5% respectively. Of these, 55.4% were university based, 23% were university affiliated and 18.9% were private transplant centers.

Assessment of Glomerular Filtration Rate

An overwhelming majority of centers have a standard operating procedure for measurement of GFR in a potential living donor. Sixty-six percent of the centers used a cut-off of <80 ml/min for exclusion of living kidney donors with some centers using higher GFR cut-off values of <90 ml/min (13.5%) and <100 ml/min (7%). Some centers accepted living donors with a much lower GFR with cut-off values of <70 ml/min (1.4%) and <60 ml/min (4%). Only 4% of the centers used 2 SDs below the expected GFR for age. 24-Hour urine measured creatinine clearance (CrCl) was the most common screening method for GFR assessment in potential living donors (71% of the centers); 23% of the centers used estimated GFR based on the MDRD equation while 9.5% used the CKD EPI equation and 5.4% of the centers used Cockroft-Gault CrCl. A smaller number (15%) used radionucleotide GFR (fig. 2).

Sixty-two percent of the centers required two GFR measurements for the final decision to proceed with the surgery. If initial assessment of GFR was indeterminate, most centers (84%) used a confirmatory method (radionucleotide GFR by 47%, 24-hour CrCl by 42% of the centers with the remaining using timed urine cimetidine GFR). Only 11.7% of the centers adjusted a correction factor (i.e. 10–15%) to account for tubular secretion of cre-

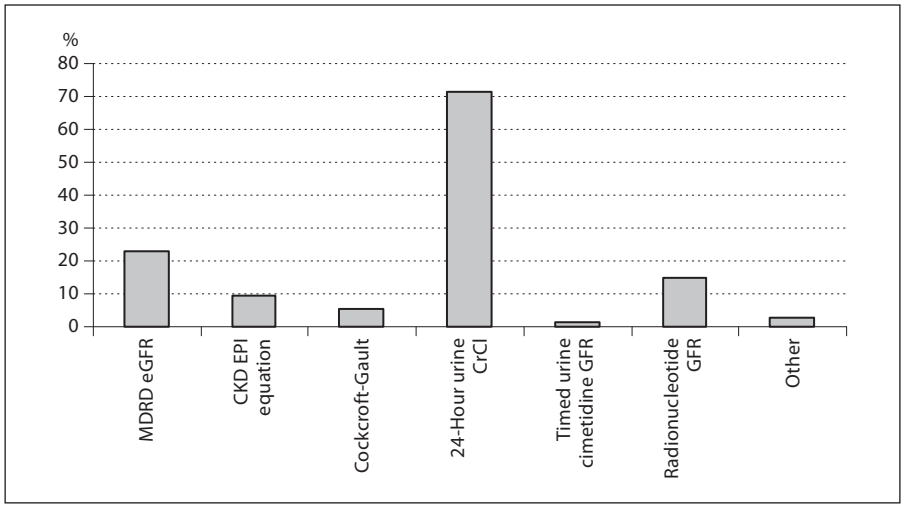

Fig. 2. Screening method for GFR assessment in potential living donors.

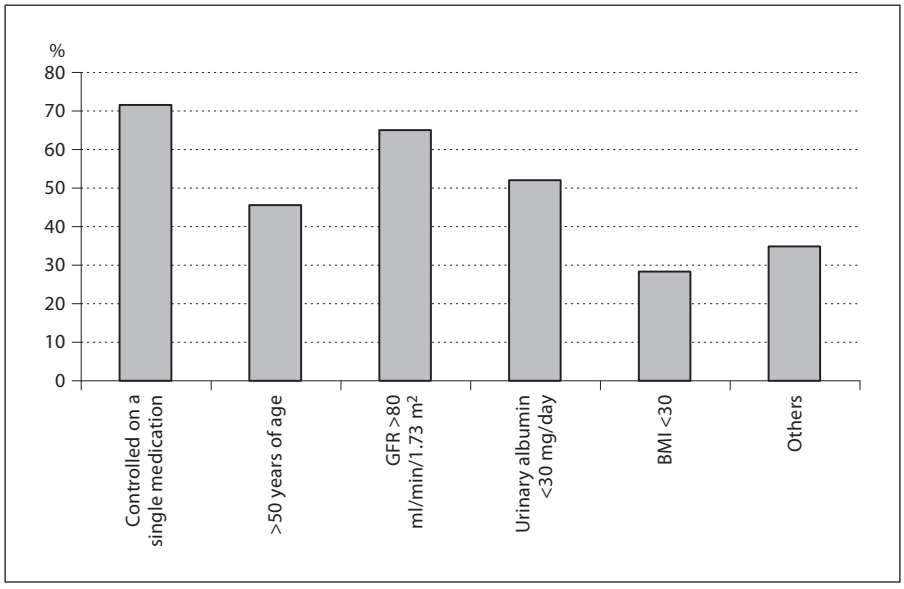

Fig. 3. Criteria for inclusion of kidney donors with a history of hypertension.

atinine while 62% of the centers reported adjusting GFR for body surface area (1.73 m^2). To assess adequacy of collection, 73% reported using creatinine index.

Hypertension

Half of the centers did not exclude potential living donors with hypertension, however cut-off for blood pressure (BP) at which patients were excluded from donation was widely variable. Fifty-six percent excluded donors with BP >140/90, whereas 22.7 and 7.1% excluded patients with pre-hypertension with a cut-off BP of >130/85 and >120/80, respectively. A variety of methods were used to assess hypertension: 24-hour ambulatory BP monitoring alone (31.9%), multiple BPs (31.9%), 15.2% used both of these modalities and 6.9% used a single BP reading. Of those who accepted patients with hypertension, criteria for proceeding with living kidney donation included patients on single antihypertensive medication (73.3%), age >50 years (44.4%) and body mass index (BMI) <30 (28.9%), as shown in figure 3. More frequent follow-up for donors who were hypertensive was recommended by 37.1% of the centers.

Proteinuria

Sixty-six percent of the centers used 24-hour urine collection to assess for proteinuria, whereas 25% used a random protein:creatinine ratio or random albumin:creatinine ratio with the rest using urine dipstick and 24-

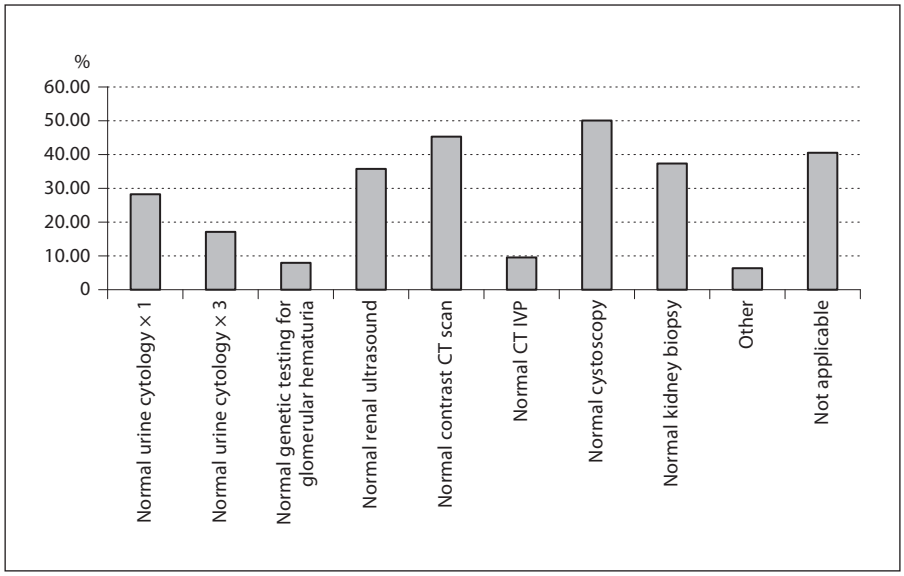

Fig. 4. Criteria for inclusion of potential living donors with hematuria.

hour urine albumin. The cut-off level for proteinuria for exclusion from donation was >150 mg (47.1%), 200 mg (26.5%) and 300 mg (13.2%), respectively. Twenty percent of the responding centers accepted living kidney donors with microalbuminuria.

Hematuria

Hematuria was defined as >5 cells/HPF (43.3%), >3 cells/HPF (26.9%), >2/HPF (17.9%) and positive dipstick (22.4%). Donors with hematuria were accepted by 38.8% of the centers. Renal biopsy to exclude glomerular cause of hematuria was performed by 58.2%, whereas only 22.7% used the currently available genetic tests. Centers which accepted donors with hematuria required patients to have normal cystoscopy, imaging and kidney biopsy (fig. 4).

Pyuria

Sterile pyuria defined as >3 WBC/HPF with negative urine culture did not exclude donation in 45.8% of the centers.

Nephrolithiasis

The survey results reflected a temporal trend toward increased acceptance of donors with a history of kidney stones. Eighty-four percent of the responding centers accepted patients with a history of nephrolithiasis. Sixty-six percent of the centers accepted donors with a history of single stone, whereas 57% centers accepted donors only if they did not have hypercalciuria, hyperoxaluria, cystinuria, metabolic acidosis and hyperuricemia. Forty-one percent of the centers accepted donors with unilateral stone disease, while 43% required a normal CT-IVP before accepting a donor with a history of nephrolithiasis (fig. 5).

Obesity

The upper limit of BMI that precludes living kidney donation was BMI >30 for 32% of the centers, BMI >35 for 47%, BMI >40 for 9%, while 17% excluded donors based on the presence of other risk factors. Five percent of the centers did not have an official policy for exclusion based on BMI. More frequent follow-up for obese donors was recommended by 30% of the centers.

Psychological Measures

Twenty-four percent of the programs used formal cognitive testing of potential living donors by instruments such as the Minnesota Multiphasic Personality Inventory or any other psychometric tests.

Donor Follow-Up

Duration of follow-up of the donor after kidney donation was variable. Thirty-nine percent of the centers followed up to 1 year, 18% annually up to 3 years, 21% followed annually indefinitely, while 7% of the centers reported no donor follow-up. Investigations for follow-up were serum creatinine evaluated by 88% of the respondents, urinalysis for protein (70%) and single clinic BP reading (67%). Only 7% responding centers performed renal ultrasound and 4.5% used 24-hour urine measured CrCl for follow-up of living kidney donors.

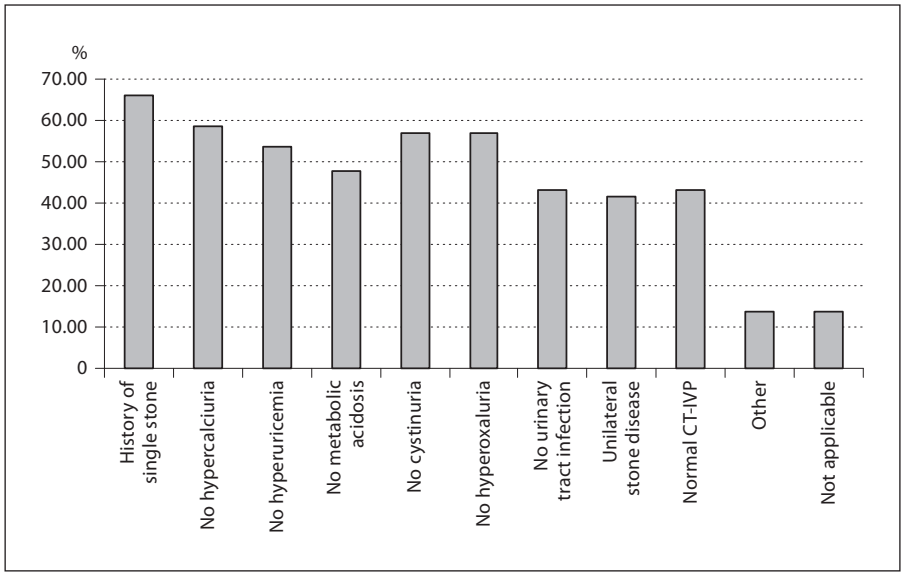

Fig. 5. Criteria for inclusion of potential living donors with a history of nephrolithiasis.

Discussion

Estimating GFR in donors is critical in assessment of living donors. Most centers (70.8%) used a 24-hour urine collection to estimate GFR, but 88.3% did not adjust for tubular secretion of creatinine, which can overestimate GFR by 10–15%. With 10–15% overestimation it means that centers targeting CrCl of 80 ml/min are evaluating donors with a true CrCl of 68–72 ml/min, which is potentially problematic and will lead to suboptimal donor selection. In order to target an actual CrCl of 80 ml/min, the cut-off of 24 h CrCl cannot be <88 ml/min otherwise suboptimal selection based on estimated GFR will occur. After kidney donation the median value of the GFR is 65% of its initial value as reported by ter Wee et al. [13], which would have serious implications in a donor with CrCl of 68–72 ml/min pre-donation. Of note, 23.6% used the MDRD equation to estimate GFR in potential donors, despite a lack of validation in persons with normal kidney function. Radionucleotide GFR was frequently used for screening and confirmation, but 64% either did not know which method was used or deferred to the nuclear medicine service. Due to operational variability, non-standardization of technique, increased cost and possible risk of radiation exposure, routine use of iothalamate to assess GFR cannot be advocated [14].

Exclusion criteria for hypertension have become more flexible with more centers accepting patients with hypertension. There is significant variability in the methods for screening for hypertension and different cut-offs were being used to exclude patients with hypertension and prehypertension. More centers were willing to accept patients with urinary abnormalities; 38.8% of the centers accepted donors with hematuria after urological work-up and or renal biopsy and almost half of the centers did not exclude donors with pyuria (defined as >3 WBC/HPF). Cut-off for proteinuria was variable; 20% of the centers accepted patients with microalbuminuria. Attitudes towards accepting donors with a history of kidney stones have changed over the last 10 years with the majority of centers accepting donors with a history of nephrolithiasis.

In 1995, Bia et al. [9] published practice patterns regarding how living donors are evaluated the USA and highlighted the variability of exclusion criteria for living donors with larger centers likely to be less stringent in their exclusion criteria. More recently, Mandelbrot et al. [10] reported increased acceptance of donors with treated hypertension or a history of kidney stones but variability in exclusion criteria was still widely present. However, they did not find an association between a smaller program size and more strict application of exclusion criteria. Reese et al. [15] examined variations in the use of kidney donors among US transplant centers using organ procurement and transplantation network data. Among 9,319 donors, 2,254 (24.2%) were considered medically complex, 1,194 (12.8%) were obese, 956 (10.3%) hypertensive, and 392 (4.2%) had a low GFR.

Bia et al. [9] found that only 16% excluded donors for obesity while Mandelbrot et al. [10] found that only 10%

Table 1. Amsterdam forum guidelines on the care of the live kidney donor: data and medical guidelines [taken from 29]

Hypertension – BP >140/90 by ambulatory BP monitoring are generally not acceptable as donors – BP should preferably be measured by ambulatory BP monitoring, particularly among older donors (>50 years) and/or those with high office BP readings – Some patients with easily controlled hypertension, who meet other defined criteria, e.g. >50 years of age, GFR >80 ml/min, and urinary albumin excretion <30 mg/day may be acceptable as kidney donors – Donors with hypertension should be regularly followed by a physician
Obesity – Patients with a BMI >35 should be discouraged from donating, especially when other comorbid conditions are present – Obese patients should be encouraged to lose weight prior to kidney transplant – Obese patients should be informed of both acute and long-term risks
Acceptable donor renal function – All potential kidney donors should have GFR estimated – Creatinine-based methods may be used to estimate the GFR, however CrCl (as calculated from 24-hour urine collections) may under- or overestimate GFR in patients with normal or near-normal renal function – Calculated GFR values (MDRD and Cockcroft-Gault) are not standardized in this population and may overestimate GFR – A GFR <80 ml/min or 2 SDs below normal (based on age, gender, and BSA corrected to 1.73/m^2) generally precludes donation
Urine analysis for protein – A 24-hour urine protein of >300 mg is a contraindication to donation – Microalbuminuria determination may be a more reliable marker of renal disease, but its value as an international standard of evaluation for kidney donors has not been determined
Urine analysis for blood – Patients with persistent microscopic hematuria should not be considered for kidney donation unless urine cytology and a complete urologic work-up are performed – If urological malignancy and stone disease are excluded, a kidney biopsy may be indicated to rule out glomerular pathology
Stone disease – An asymptomatic potential donor with a history of a single stone may be suitable for kidney donation if: no hypercalciuria, hyperuricemia, or metabolic acidosis; no cystinuria or hyperoxaluria; no urinary tract infection, and if multiple stones or nephrocalcinosis are not evident on CT scan – An asymptomatic potential donor with a current single stone may be suitable if: the donor meets the criteria shown previously for single-stone formers and the current stone is 1.5 cm in size or potentially removable during the transplant – Stone formers who should not donate are those with nephrocalcinosis on X-ray or bilateral stone disease and stone types with high recurrence rates

of centers excluded donors with BMI ≥30, whereas in our study 32% of centers excluded living donors with BMI >30. This finding could be explained by the more recent data which shows obesity to be a risk factor for chronic kidney disease [16, 17]. Cuevas-Ramos et al. [18] reported that individuals with metabolic syndrome before nephrectomy showed a GFR <70 ml/min/1.73 m^2 at a significantly shorter follow-up time (5.6 ± 0.8 years) versus persons without metabolic syndrome (12.8 ± 1.0 years; p = 0.001). Another study [19] also reported an increase of 4.6 mm Hg for obese donors and 3 mm Hg for non-obese donors with mean arterial pressure.

Forty-seven percent of the programs excluded donors on any antihypertensive medication [11]. In our study, 50% of the responding programs excluded donors with a history of hypertension. Textor et al. [20] reported that Caucasians with moderate, essential hypertension and normal kidney function had no adverse effects regarding BP, GFR, or urinary protein excretion during the first year after a living kidney donation. On the basis of the limited studies conducted to date, kidney donors may have a 5 mm Hg increase in BP within 5–10 years after donation over that anticipated with normal aging [21]. In a literature review [22], six studies described 125 hypertensive donors with BP cut-off points of 135/85 to 150/90 mm Hg with a follow-up from 10 months to 6.7 years (median 2.6 years). Two studies compared hypertensive donors to normotensive donors on change in inulin or radioisotope GFR with conflicting results. Systolic and diastolic BPs decreased by 5 and 6 mm Hg more, respec-

tively, in hypertensive than normotensive donors with no increase in albumin:creatinine ratio. Ozdemir et al. [23] found that ambulatory BP monitoring was more accurate than in-office BP measurement, but our study showed that ambulatory BP monitoring was limited to a few centers.

The marked donor shortage has seen some transplant centers using donors with isolated hematuria. Kido et al. [24] found that dysmorphic hematuria was significantly associated with progressive kidney disease after donation. Gross et al. [25] found that 3 of 6 donors developed new-onset hypertension and 2 new-onset proteinuria while renal function declined significantly in 4 donors.

Giessing et al. [26] in a survey of surgeons in German centers found that nephrolithiasis at the time of transplant was an exclusion criterion at 36% of the centers; 96% of the centers accepted kidney donors with a history of nephrolithiasis. A US survey [11] found that 77% of responding centers allowed stone formers to donate.

With the advent of imaging, asymptomatic kidney stones are frequently seen. Martin et al. [27] reported five kidneys from living donors were transplanted with asymptomatic renal calculi incidentally detected on CT (8 stones) after excluding metabolic derangements; only 3 of the 8 stones were still in situ at the mean follow-up of 2 years. Worcester et al. [28] compared stone recurrence rates in 115 patients with nephrolithiasis who underwent nephrectomy for various reasons with 3,151 patients with nephrolithiasis and no nephrectomy and found a 14% recurrence rate in the nephrectomy group after a follow-up of 6–8 years.

Our study was a survey based on self-reporting and may not accurately represent actual practice of centers. The possibility of systematic bias cannot be excluded between centers that responded and those that did not. The Amsterdam Forum on the Care of the Live Kidney Donor [29] established guidelines (table 1) but there is still significant variability in exclusion criteria based on GFR, history of kidney stones, BMI, BP and donors with urinary abnormalities. The definitions for hematuria and proteinuria are variable and a variety of screening methods are being used as demonstrated in our study.

We conclude that there is a lack of uniformity and an evidence-based approach to exclude living kidney candidates based on GFR, BMI, BP, use of a psychological instrument and urinary abnormalities. More interesting is that the methodology of estimating GFR, BP and urinalysis was highly variable. We suggest that a living donor registry be established so that data can be collected prospectively, which will allow evaluation of the long-term risk of uninephrectomy and raising the cut-off estimated GFR to 90 ml/min to account for the 10–15% overestimation when CrCl is used.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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