Urolithiasis (2019) 47:115–123
https://doi.org/10.1007/s00240-018-1092-4

INVITED REVIEW

Living kidney donation from people at risk of nephrolithiasis, with a focus on the genetic forms

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Received: 17 September 2018 / Accepted: 8 November 2018 / Published online: 23 November 2018

Abstract

Deciding whether to accept a donor with nephrolithiasis is a multifaceted task because of the challenge of finding enough suitable donors while at the same time ensuring the safety of both donors and recipients. Until not long ago, donors with a history of renal stones or with stones emerging during screening on imaging were not considered ideal, but recent guidelines have adopted less stringent criteria for potential donors at risk of stones. This review goes through the problems that need to be approached to arrive at a wise clinical decision, balancing the safety of donors and recipients with the need to expand the organ pool. The risk of declining renal function and worsening stone formation is examined. Documents (consensus statements, guidelines, etc.) on this issue released by the most important medical societies and organizations are discussed and compared. Specific problems of living kidney donation associated with certain systemic (chronic hypercalcemia due to CYP24A1 gene mutations, primary hyperoxaluria, APRT deficiency) and renal (medullary sponge kidney, cystinuria, distal renal tubular acidosis, Dent's disease, Bartter syndrome, familial hypomagnesemia with hypercalciuria and nephrocalcinosis) Mendelian disorders that cause nephrolithiasis are also addressed.

Keywords Guidelines · Kidney transplantation · Living donation · Mendelian disease · Renal stone

Introduction

The prevalence of nephrolithiasis is high. In Italy, a survey found that 7.5% of a sample of the general population had a history of renal stones [1]. Its prevalence could be even higher, however, with more in-depth imaging. In fact, CT scans show that up to 11% of potential living kidney donors have asymptomatic stones [2]. The problem of deciding whether to accept donors with renal stones is consequently very common. The majority of such potential donors has small stones, less than 4 mm in diameter [2, 3]. In the past, donors with a history of renal stones, or with stones emerging during screening on imaging (and therefore asymptomatic) were not considered ideal for donation purposes due to concerns about: (1) the transmission to the recipient of potentially harmful donor-gifted stones, or a predisposition to stones formation; and (2) the complications of recurrent stones in a person with only one kidney (having donated the other).

Given the shortage of organs, many transplant centers are now accepting some of these less than ideal donors, however, and adopting an "extended criterion" regarding nephrolithiasis. In fact, recent guidelines (GLs) have proposed less stringent criteria for potential donors at risk of stones.

Deciding whether to accept a donor with nephrolithiasis is a multifaceted task because of the challenge of finding suitable donors while at the same time ensuring the safety of both donors and recipients. This review covers the problems that have to be approached to make the right clinical decision, balancing the safety of donors and recipients with the need to expand the organ pool. We examine the risk of a declining renal function and a worsening stone activity. We discuss and compare the documents (consensus statements, GLs, etc.) on this issue published by the most important medical societies and organizations (Table 1). Finally, we

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Table 1 Consensus statements, documents and guidelines considered in this review

American Society of Transplant Physicians Guidelines (1996)
Amsterdam Forum on the Care of the Live Kidney Donor (2005)
European Renal Best Practice Transplantation Guideline (2013)
KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors (2017)
ERA-EDTA DESCARTES Working Group. Long-term risks of kidney living donation: review and position paper (2017)
US Organ Procurement and Transplantation Network (2018)
British Transplantation Society Guidelines for Living Donor Kidney Transplantation (2018)

address the specific problems of living kidney donation associated with some Mendelian disorders responsible for nephrolithiasis.

Stone recurrences, renal function decline and risk of severe renal damage in stone patients, and particularly in those with a single kidney

Though a large meta-analysis of seven cohorts did not disclose any association between a history of renal stones and end-stage renal disease (ESRD) [4], a huge registry-based study on over three million subjects revealed that the risk of ESRD is twice as high in stone formers as in people not prone to stones [5]. Results from the Mayo Clinic fit with such an estimate, but show that only one in three of those cases of ESRD were actually due to stone-related complications [6]. Unlike the renal stone disease common in the general population, nephrolithiasis due to urinary malformations and diversions, malabsorptive bowel syndromes or Mendelian disorders carry a high risk of chronic kidney disease (CKD) and ESRD [7]. Complications of kidney stones and urological treatments may require nephrectomy, though this applied to only 3.5% of a large general case population of over three thousand stone patients [8]; and the prevalence was even lower, < 1%, among 3170 US children hospitalized for renal stones [9]. The risk is certainly much higher for struvite and calcium phosphate stones [7], and in cases of cystinuria [10], however.

The absolute excess risk of ESRD due to the common form of kidney stone disease observed in the general population is therefore quite modest, with an estimated population attributable risk of around 5% [5].

Whether stone activity increases and renal function deteriorates after nephrectomy is an issue that was investigated in two studies. Lee et al. [11] followed up 50 stone patients after nephrectomy for 6 years, finding stone recurrences in 30% of cases, with no deterioration in glomerular filtration rate (GFR). Worcester et al. [8] saw much the same picture in 115 patients with a post-nephrectomy follow-up of 6–8 years. In both studies, none of the patients lost their remaining kidney, and the stone recurrence rate was much lower than the one reported in stone patients with two kidneys in a recent meta-analysis [12]. The reason for this latter finding could lie in the fact that measures are generally taken to prevent stones in nephrectomized subjects.

Four other studies specifically investigated stone activity and GFR after nephrectomy in kidney donors with a nephrolithiasis risk. Kim et al. [13] found no stone recurrences and a stable renal function at a 1-year follow-up of 16 donors. There were also no stone recurrences 12–49 months after donation in the 8 subjects described by Olsburgh et al. [3]. The same was true of the 26 donors with a median follow-up of 22.5 months in the study by Rizkala et al. [14], and of the 18 kidney donors seen 5–8 years after nephrectomy by Serur et al. [15]. In all the above studies, moreover, the recipients fared quite well.

Apart from the possible associated risk of stone recurrences in donors, a Norwegian study on the general population [16] showed that subjects with a blood relative with ESRD caused by non-hereditary diseases (diabetes, hypertension, glomerulonephritis, pyelonephritis) have a fourfold higher long-term risk of ESRD than individuals with no family history of nephropathy. The recent position paper by the ERA-EDTA DESCARTES Working Group on the long-term risks of kidney living donation [17] does not advice against kidney donation, however; it only recommends that donors who have a first-degree relative with non-hereditary renal disease be informed that they carry a higher risk of developing ESRD than the general population. It is worth noting that this risk appears to be higher than the risk of stone formers developing ESRD.

In short, for donors who are or have been stone formers, losing a kidney does not seem to affect their prognosis regarding renal function and stone recurrence rates. Thus, kidney donation from common stone formers would presumably be safe, and generally have no major adverse outcomes.

What do the guidelines and consensus statements recommend?

The publication issued in 2005 by the Amsterdam Forum on the Care of the Live Kidney Donor [18] is the most comprehensive and precise document on the specific topic of the

requirements for donations from renal stone patients. These GLs conclude that stone formers can only donate a kidney if they have a history of only one stone, or if they have a stone less than 15 mm in diameter, or one that is potentially removable during the transplantation procedure, and no previous history of stones. In both the cases, any hypercalciuria, hyperuricemia, or metabolic acidosis contraindicate donation. The Forum also categorically rules out donations from subjects with nephrocalcinosis, ongoing bilateral stone disease, types of stones with a high recurrence rate and/or hard to prevent (struvite and cystine stones), stones secondary to monogenic or systemic disorders (primary and intestinal hyperoxalurias, renal tubular acidosis, sarcoidosis), and stone recurrences despite appropriate treatments. The older American Society of Transplant Physicians GLs were along the same lines [19]. The GLs from the European Renal Best Practice (ERBP) group [20] does not address nephrolithiasis, and endorse the KDIGO GLs [21] on matters it does not cover to avoid duplications. Significant differences between the above-mentioned GLs are discussed point by point below.

Donor age The Amsterdam Forum [18] and the KDIGO GLs [21] emphasize donor age among the criteria to consider. They argue that younger donors would be exposed to a risk of stone recurrence for longer. Other documents do not stress this point, but we think it is important.

Stone burden This depends on the dimension and number of the stones. The Amsterdam Forum [18] recommends excluding donations from subjects with a stone larger than 15 mm in diameter. This is disputable, in our opinion. We would argue that it is prompted by two considerations: first, the size of a stone is a proxy for its composition: larger stones are likely to be composed of struvite or cystine (i.e., stone types that advise against donation); second, larger stones are more likely to have damaged the kidney (by causing an obstruction). These assumptions cannot be taken for granted, however, and a careful assessment is required. For instance, Olsburgh et al. [3] routinely perform a DMSA scan to exclude renal scars and assess split renal function in potential donors found to have asymptomatic stones. We also suggest that large stones be removed and analyzed ahead of donation, as such large stones are relatively infrequent nowadays, and might well be composed of struvite or cystine, for which a specific contraindication to donation exists.

That said, for the most common, much smaller stones, we agree with the general recommendation that stones be removed before kidney implantation.

Finding bilateral and multiple stones do suggest a significant metabolic activity, i.e., a propensity to form stones, but that does not necessarily mean that this activity is still ongoing. Potential donors may have had a period of strong metabolic activity many years earlier, before reaching a current quiet metabolic situation.

Stone activity The Amsterdam Forum [18], and the very recent British GLs [22] do not recommend any stone-free period before kidney donation, whereas the older American Society of Transplant Physicians GLs [19] suggested a prior 10-year latency. Of course, this was a way to enable donations only from donors with a very modest stone activity, or none at all. Such subjects make up the majority of cases, as truly recurrent stone formers are relatively infrequent [23]. The British GLs consider subjects with a history of moderate nephrolithiasis and with minor urine metabolic abnormalities eligible for donation [23]. The KDIGO GLs are even more flexible: "The acceptance of a donor candidate with prior or current kidney stones should be based on an assessment of stone recurrence risk and knowledge of the possible consequences of kidney stones after donation." [21]. The stone recurrence risk is difficult to estimate, however. At stone clinics, this is generally based on a post-hoc definition after some years of follow-up [24]. Regrettably, no biomarkers of such a risk are available, and single and recurrent stone formers have very similar metabolic profiles. The recent ROKS nomogram for predicting a second symptomatic stone is based largely on clinical variables and identifies only 56% of cases in subgroups of patients at highest risk [25]. It is also only applicable to symptomatic stones, while those most frequently encountered during screening for living kidney donation are incidental findings.

We thus come to the conclusion that there is no good way to distinguish between recurrent and non-recurrent stone formers, or between metabolically active and metabolically inactive stone patients. We personally assume that truly recurrent stone formers are individuals who have passed at least 3 stones in 5 years [24], but we admit that this approach is based more on experience than on clear evidence. In our opinion, these are the subjects who should not donate.

Metabolic evaluation This assessment complements and corroborates findings concerning stone activity. All the GLs recommend looking for metabolic stone risk factors in 24-h urine collections. This is also a requirement of the US Organ Procurement and Transplantation Network (OPTN) Policies for potential donors with a history of nephrolithiasis or actual stones > 3 mm [26].

The KDIGO GL suggests performing the full evaluation of nephrolithiasis recommended by the urological societies (AUA, EAU) in candidates with past or present renal stones. This involves one or two 24-h urine collections for total volume, pH, calcium, oxalate, uric acid, citrate, sodium, potassium and creatinine.

The British GLs [23] state that 24-h urine excretion of calcium, oxalate, citrate and urate, together with pH assessment in early-morning spot urine, is mandatory for potential donors with a personal or family history of stones, or current stone disease. When no urine metabolic abnormalities

come to light, or if they regress after appropriate treatment, a candidate could be eligible for donation [23].

It is noteworthy that the KDIGO GLs also suggest the full-panel 24-h urine evaluation for potential donors with persistent microhematuria of unknown origin—with the draconian recommendation that subjects with any 24-h urine biochemistry abnormalities be ruled out (Fig. 13, page S48 of the KDIGO) [21]. This is unjustified, in our opinion, and looks like a sort of short-circuit, because the KDIGO experts do not come to such a stringent conclusion a few paragraphs later, when addressing potential donors with previous or current stones. At odds with the American Society of Transplant Physicians GL [19], we strongly agree with the recommendation in the British GLs that potential donors with 24-h urine metabolic abnormalities should not be ruled out automatically [23]. We also find it very reasonable to perform a trial in the potential donor to see if the abnormality can be reversed with appropriate treatment—and most documents wisely recommend that donors with a stone risk be appropriately treated after their donation to prevent lithogenesis.

Stone composition The Amsterdam Consensus and the British GLs exclude donors with a history of cystine or struvite stones [18, 23] (Table 2). The document from the American Society of Transplant Physicians [19] implicitly confirms this stance when it recalls the challenges of treating these types of stone and the frequently severe renal damage they can cause.

It should be noted, however, that the British GLs [23] are somewhat ambiguous when addressing infectious (struvite) stones: at one point they exclude subjects with struvite stones from donation, but elsewhere they contemplate consenting to donations from such subjects if any coexisting anatomical abnormality causing the infectious stone is resolved. Since there is a consensus on the use of the stone-bearing kidney for donation purposes, we agree with the recommendation in most GLs that infectious/struvite stone formers be ruled out (even if the stone is removed) because of the high risk of stone recurrence, infections [27], and worsening renal damage in the (immunosuppressed) patients receiving the transplant.

In candidates for donation with a history of a single stone, the Amsterdam Forum [18] considers ineligible those at high risk of recurrence, or with types of stone that are difficult to prevent, or associated with inherited or systemic disorders [18]. Generally speaking, these conditions tend to coexist: apart from cystine and struvite stones (specifically excluded by several GLs), brushite stones also fall into these categories. Though not mentioned by the GLs, we consider it unsafe to let subjects who have formed brushite stones donate a kidney.

Systemic disorders The British GLs [23] seem to consider the possibility of allowing kidney donations from patients with inflammatory bowel disease (IBD) when they suggest metabolic screening (urine and plasma biochemistry) of potential donors with conditions carrying a significant stone risk (including IBD). This statement clearly refers to the possibility of intestinal hyperoxaluria and resembles the Amsterdam Forum's recommendation [18]. We judge it unwise to allow donations by subjects with IBD with or without any hyperoxaluria: such patients could also experience episodes of low diuresis due to diarrhea exacerbation, which would in any case favor stone formation, nephrocalcinosis, and acute kidney injury (AKI).

Nephrolithiasis may occur in up to 20% of subjects with primary gout, while only a part of hyperuricemic subjects develop gout [28]. Most uric acid stone patients are normouricemic with metabolic disease, and their stones form due to a hyperacidic urine [29]. This disorder is easily preventable, and that is why we question the Amsterdam Forum's inclusion of hyperuricemia among the criteria precluding living donation: while we would exclude potential candidates with a history of gout (not because of any stones, but because of the potential risk of ESRD), we like to consider donors with hyperacidic urine who form uric acid stones, providing prevention measures are in place.

Table 2 Stone composition and kidney donation according to several GLs

Stone composition	ASTP GL	Amsterdam[a]	KDIGO	ERBP	British GL
Cystine	Reject	Reject	NS	NS	Reject
CaOx	NS	Accept	NS	NS	NS
Ca-P[b]	NS	Accept	NS	NS	NS
Struvite	Reject	Reject	NS	NS	Acceptable[c]
Uric acid	Reject[d]	Accept	NS	NS	NS

NS not specified, *ASTP* American Society of Transplant Physicians, *ERBP* European Renal Best Practice

[a]If not rejected for genetic and certain secondary forms

[b]This class should be better specified. For instance, brushite stones have a very different natural history from apatite stones

[c]Providing the anatomical defect (pathogenic cofactor) is corrected

[d]If mixed with calcium oxalate

Stone-promoting inherited systemic disorders and living kidney donation

As these disorders are systemic in the donor, recipients are not at risk of stone recurrence.

Chronic hypercalcemia from vitamin D 24-hydroxylase gene (CYP24A1) mutations This autosomal recessive disorder characterized by hypercalcemia, hypercalciuria, nephrocalcinosis and nephrolithiasis is due to mutations causing loss of function of the 1,25(OH)2D24-hydroxylase gene (CYP24A1). It may lead to CKD and ESRD. Heterozygous carriers could manifest a mild clinical and biochemical phenotype [renal stones, mild PTH-independent hypercalcemia and high plasma levels of 1,25(OH)2D] [30, 31]. Since this condition may be difficult to treat, we recommend caution in considering living kidney donations from heterozygous relatives.

Primary hyperoxaluria The very rare genetic forms of oxaluria usually cause ESRD due to nephrocalcinosis and stone-related complications [32]. They are all inherited as a recessive trait. Heterozygous relatives (parents and 50% of siblings) or siblings not carrying the mutated allele (25%) have normal oxaluria, and can therefore all be candidates for organ donation. Not all apparently healthy siblings are heterozygous or not carrying the mutated allele, however. In fact, the disease has a variable expression, with some homozygous individuals manifesting it only in adult age, with a single stone and a normal kidney function [33], or developing ESRD in their sixth decade of life [34]. If nephrectomized (for donation purposes), the remaining kidney would be exposed to twice the burden of oxalate and—in an already hyperoxaluric subject—this would mean a huge quantity, which would considerably accelerate the disease in the donor. Of course, such subjects must be identified (with 24-h urine oxalate evaluation and genetic analysis) and not allowed to donate.

2,8-dihydroxyadeninuria (APRT deficiency) The disease is autosomal recessive and heterozygous subjects are asymptomatic. A case has been reported of kidney donation from the mother [35]. Although the report does not provide details on the donor follow-up, living donations from healthy carriers seem to be safe. The disease is amenable to treatment with high doses of allopurinol or febuxostat [36].

Stone-promoting inherited kidney diseases and living kidney donation

Nephrolithiasis due to inherited renal tubular disorders [37] is a concern for both donors and recipients. The risk of stone recurrence and ESRD is significant and needs to be carefully evaluated.

Medullary sponge kidney (MSK) MSK can be a cause of very recurrent stones [38, 39]. The pathogenesis of nephrolithiasis is a combination of metabolic urine abnormalities (defective distal acidification, hypoacidic urine, hypocitraturia, hypercalciuria) and urine stasis (because the renal papillary ducts are dilated, forming pseudocysts) [40]. Familial clustering of MSK has been observed in 50% of patients with this condition, with an apparently autosomal dominant inheritance [41]. It could be associated with renal and non-renal malformations [42]. There is a limited risk of renal failure and ESRD due to renal infections and/or obstructive episodes [43]. The favorable experience of living kidney donations from 26 MSK subjects is reassuring [44]. Nevertheless, because MSK patients risk renal failure, and the onset of severe loin pain [39], and because it is sometimes difficult to prevent stone recurrences, we recommend caution in using kidneys from living donors with MSK. In fact, the above-mentioned study on living donations from MSK subjects [43] was retrospective, and a selection bias in considering for donation only MSK patients with a low stone-forming metabolic activity cannot be ruled out. In fact, their urine stone risk must have been quite low, since none had hypercalciuria or hypocitraturia. This population has all the features of that subgroup of MSK patients who experience few or no stone episodes [38, 45].

Cystinuria Some of the documents considered here do not recommend testing for cystinuria in candidates for living kidney donation at risk of nephrolithiasis. This is the case of the GLs issued by the KDIGO [21], and the American Society of Transplant Physicians [19], and of the OPTN Policies [27]. We believe that testing for cystinuria should be mandatory in all potential donors at risk of nephrolithiasis because:

1. those whose first stone episode occurs in adulthood could take many years to diagnose correctly, and it is not unusual for them to receive just a nonspecific diagnosis of renal stone disease [46];
2. these patients may also pass non-cystine stones [47], and could consequently be misdiagnosed as idiopathic calcium stone formers.

In addition, relatives of cystinuric patients with ESRD should be screened for cystinuria before allowing them to

donate [48]. In fact, both heterozygous type A and type B cystinuric subjects may have abnormally high 24-h cysteine excretion levels (though not as high as homozygous patients), sufficing to prompt stone formation [49]. This challenges the common notion that subjects with single heterozygous mutations in the dibasic amino acid exchanger genes are healthy carriers.

Distal renal tubular acidosis Genetic forms of distal renal tubular acidosis (dRTA) are typically characterized by nephrocalcinosis, nephrolithiasis, mineral bone disease, and growth retardation [50, 51].

The distinctive biochemical profile of this condition includes metabolic acidosis, hypokalemia, hyperchloremia, hypercalciuria, hypocitraturia, and inappropriately high urinary pH. The condition is genetically heterogeneous in terms of inheritance mode and molecular defect. Either recessive or autosomal inheritance is possible.

Some heterozygous subjects with recessive mutations or polymorphisms of the ATP6V1B1 gene have incomplete dRTA, i.e., a urinary acidification defect without any systemic acidosis; they have hypocitraturia and a greater prevalence of calcium phosphate nephrolithiasis [52, 53]. In a cohort of stone formers, the prevalence of said polymorphism was 5.8% [52]. On the other hand, the prevalence of incomplete dRTA in stone formers with osteoporosis/osteopenia (a frequent finding in calcium stone formers) was 23% in a cohort of 183 patients [54]. The diagnosis of incomplete dRTA is frequently overlooked in calcium stone formers, who are consequently misdiagnosed as idiopathic cases [25]. These subjects can therefore be considered safe as kidney donors. We think that they can indeed donate, providing they undergo metabolic assessment (calciuria, citraturia, and arterial pH and bicarbonate) soon afterwards. The risk is that, with the halving of their already defective capacity to handle acids after nephrectomy, some of these subjects' incomplete form of the condition will turn into overt dRTA if they continue on their usual diet. If this happens, potassium citrate can easily cure the condition, however [25, 55].

Dent's disease This rare, X-linked recessive disease [38] is usually seen in males. Mutations have been found in either the CLCN5 gene (Type 1 Dent's disease) or the OCRL1 gene (Type 2). Dent's disease becomes manifest with nephrocalcinosis, hypercalciuria, renal stones, tubular proteinuria, other tubular dysfunctions, and ESRD. A milder phenotype may be found in female carriers; there is only one report of a female carrier developing ESRD [56]. The variable phenotype in female carriers is probably attributable to the phenomenon of lyonization. Fathers and 50% of male siblings are healthy and could donate. Mothers and 50% of sisters are obligate carriers. To the best of our knowledge, we were the first to successfully perform a kidney transplant in an ESRD Type 1 Dent's patient with a kidney donated by his mother, who exhibited none of the typical signs of the disease [57].

Bartter syndrome Living donations have been performed successfully from the parents of ESRD patients with Bartter syndrome [58]. Heterozygous carriers of the mutated genes in this genetically heterogeneous autosomal recessive disorder do not have any of the biochemical manifestations of the disease.

Familial hypomagnesemia with hypercalciuria and nephrocalcinosis This is an autosomal recessive disease involving two genes (claudin 16; claudin 19). Heterozygous relatives may reveal a milder expression of the disease, i.e., isolated hypercalciuria and stones [59, 60].

In a Brazilian family in which two sisters had mutated claudin 19 alleles, one of them successfully received a kidney from her heterozygous father, who showed no signs of the disease either before or during the post-donation follow-up [61].

Conclusions

The policies for accepting a subject at risk of nephrolithiasis as a kidney donor have changed over time, and have varied considerably between different transplant centers. In 2008, already a few years after the Amsterdam Forum [18], a survey of 28 German centers [62] bears witness to such changes and multiple policies. While 36% of the centers followed a strict policy that the discovery of a renal stone was an absolute contraindication to living kidney donation, and one center even ruled out donors with a history of nephrolithiasis, another 50% of the centers adopted much broader criteria, even accepting stone formers with a stone-free period of less than 2 years—instead of the 10 years recommended by the Amsterdam Forum [18]. In addition, 1 and 9 centers, respectively, accepted donors with cystine and struvite stones. While we feel that these latter criteria go too far, and that such individuals should not be considered for donation, we also find some of the criteria recommended by the older GLs excessively stringent.

Attitudes to the enrolment of "marginal" living kidney donors have been captured by the more recent GLs. In fact, the KDIGO and British GLs use very generic terms regarding the eligibility of candidate donors with nephrolithiasis [21, 23]—basically leaving this decision to the discretion of the transplant doctor. Given the complexity of the diagnostic and prognostic aspects of nephrolithiasis, however, such general recommendations should call for an in-depth assessment of stone-forming donors and recipients. It is best to involve a specialist (a nephrologist/internist or urologist) with specific expertise on nephrolithiasis in the decision. That said, our personal convictions are summarized in Table 3. A trial in potential donors to test the feasibility of improving their

Table 3 Characteristics of potential donors that constitute absolute or relative contraindications to living kidney donation

Characteristics that warrant caution:
Risk of intestinal oxalate hyper-absorption
Abnormal cystinuria (without history of stones)
Distal renal tubular acidosis
Nephrocalcinosis
Medullary sponge kidney
Correctable metabolic abnormality in a truly recurrent disease
Characteristics that rule out a donor
Struvite stone
Brushite stone
Cystine stone
Primary and secondary hyperoxaluria
Uncorrectable metabolic abnormality in a truly recurrent disease

urine metabolic profile is always warranted, both in subjects with abnormalities (i.e., hypercalciuria, hypocitraturia, etc.) and in those with no known anomaly, in which case it may be helpful to assess the effect of general measures for kidney stone prevention on urine supersaturation [63].

As suggested by all the GLs, kidney donations from subjects at risk of nephrolithiasis should only take place after thorough counselling of the donor and recipient, who both need to be aware of the limited data available regarding the long-term outcomes in these circumstances.

Donors at risk of stones should be advised about symptoms of renal/ureteric colic and anuria, and be informed about the availability of local urological expertise. Donors should also be advised to maintain a high fluid intake for life (at least 2 liters of fluid a day), and also (where appropriate) to continue any medication prescribed to reduce the risk of future stone formation. Regular follow-up imaging, e.g., annual or biennial renal ultrasound, may be advisable, and regular re-assessment of the metabolic profile should be considered.

Acknowledgements This review was supported by an in-house grant from the Università Cattolica del Sacro Cuore.

Compliance with ethical standards

Conflict of interest Authors have no conflict of interest.

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