KDOQI US Commentary on the 2017 KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors

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Living kidney donation is widely practiced throughout the world. During the past 2 decades, various groups have provided guidance about the evaluation and care of living donors. However, during this time, our knowledge in the field has advanced substantially and many agreed on the need for a comprehensive, unifying document. KDIGO (Kidney Disease: Improving Global Outcomes) addressed this issue at an international level with the publication of its clinical practice guideline on the evaluation and care of living kidney donors. The KDIGO work group extensively reviewed the available literature and wrote a series of guideline recommendations using various degrees of evidence when available. As has become recent practice, NKF-KDOQI (National Kidney Foundation–Kidney Disease Outcomes Quality Initiative) convened a work group to provide a commentary on the KDIGO guideline, with a focus on how these recommendations apply in the context of the United States. In the United States, the United Network for Organ Sharing (UNOS) guides and regulates the practice of living kidney donation. While the KDIGO guideline for the care of living kidney donors and UNOS policy are similar in most aspects of the care of living kidney donors, several important areas are not consistent or do not align with common practice by US transplantation programs in areas in which UNOS has not set specific policy. For the time being, and recognizing the value of the KDIGO guidelines, US transplantation programs should continue to follow UNOS policy.

Complete author and article information provided before references.

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As they are designed to reflect the views and recommendations of the responsible KDOQI Commentary work group and because they are reviewed and approved by KDOQI and NKF leadership, KDOQI Commentaries are not peer reviewed by AJKD. This article was prepared by a KDOQI Commentary work group comprising the authors and co-chaired by Drs Didier Mandlebrot and Emilio E. Poggio. It was reviewed and approved by the NKF Scientific Advisory Board.

Introduction

Living donor kidney transplantation has been a critical component in the treatment of kidney failure for more than 7 decades in the United States, currently representing ~30% of all kidney transplantations performed annually.[1] A comprehensive evaluation of potential living kidney donors is paramount to the success of this practice, in order to properly select donors who are at minimal risk of developing future kidney disease or other medical complications. While for many decades, the long-term medical risks—especially incident kidney failure—of living kidney donors were considered to be negligible, more recent publications have shown that there is an increased risk of kidney failure.[2,3] This increase in knowledge and awareness of potential medical complications following kidney donation has led the transplantation community during the past decade to further research the short- and long-term outcomes of living kidney donation, paying special attention to the evaluation and acceptance criteria of donor candidates.

Living kidney donation is practiced in many countries around the world.[4] Although in the United States, the United Network for Organ Sharing (UNOS) provides specific policies stipulating the minimum required evaluation process and follow-up of living kidney donors and oversees compliance with this policy by transplantation centers, this is not the case in other countries. Furthermore, there is heterogeneity in the evaluation of potential living kidney donors across various professional associations and countries.[5-10] Therefore, comprehensive recommendations addressing the care and follow-up of living kidney donors, such as the KDIGO (Kidney Disease: Improving Global Outcomes) clinical practice guideline on the evaluation and care of living kidney donors, are important to kidney donors and the transplantation community.[11,12]

The KDIGO guideline recommendations on living donation were created by an international group of experts with broad expertise and differing regulations in each of their home countries. The product of this collaborative work is an extremely comprehensive review of the field that addresses very important issues and generated a needed set of general recommendations that will be of use to the transplantation community. Notwithstanding, it is important to note that the difficult task of creating a comprehensive practice guideline in this field is limited by published data that lack strong evidence and therefore the recommendations are mostly based on

sound opinion by the KDIGO work group. Likewise, our review, commentary, and suggestions are subject to the same limitations.

To assist the US practitioner in interpreting and applying the KDIGO guidelines, NKF-KDOQI (National Kidney Foundation–Kidney Disease Outcomes Quality Initiative) convened a work group to write a commentary. In this commentary, we focus on how these guidelines may or may not strictly apply in the US context (Table 1), given the explicit regulatory requirements of UNOS and the Centers for Medicaid & Medicare Services (CMS), as well as the history of living donor practices and conventions in the United States. The structure of this commentary lists each of the guidelines followed by a commentary from an expert group of US transplantation practitioners. Each of the KDIGO guideline recommendations was reviewed and then discussed via teleconference to determine areas of agreement and controversy. Sections were subsequently written by specific group members and the entire document was reviewed by all co-authors.

We thank the KDIGO work group for their thorough review of the issues related to living donor care and evaluation and for an important contribution to patient care globally. All guideline statements are reproduced with permission of KDIGO.

Guideline Statements and Commentary

Goals of Evaluation, Framework for Decision Making, and Roles and Responsibilities

Goals and Principles of Evaluation

1.1 The donor candidate's willingness to donate a kidney voluntarily without undue pressure should be verified.

1.2 The benefits and risks of kidney donation should be assessed for each donor candidate.

1.3 The decision to accept or exclude a donor candidate should follow transplant program policies.

1.4 Donor candidate decision-making should be facilitated through education and counseling on individualized risks and benefits, methods to minimize risks, and the need for postdonation follow-up.

1.5 For an accepted donor candidate, a plan for donation care and follow-up should be formulated to minimize risks of donation.

1.6 For an excluded donor candidate, a plan for any needed care and support should be formulated.

Framework for Decision-Making

1.7 The donor candidate, the intended recipient, and the transplant program must all agree with the decision to proceed with donation in concordance with transplant program policies and informed consent.

1.8 Transplant program policies must be defensible based on current understanding of the risks and benefits of kidney donation, and should apply to all donor candidates evaluated at the center.

1.9 Each transplant program should establish policies describing psychosocial criteria that are acceptable for donation, including any program constraints on acceptable relationships between the donor candidate and the intended recipient.

1.10 All donor candidates should be evaluated using the same criteria, regardless of whether donation is directed towards a designated recipient.

1.11 Each transplant program should establish policies describing medical criteria that are acceptable for donation, addressing when possible, numeric thresholds for short-term and long-term postdonation risks above which the transplant program will not proceed with donation. Risks should be expressed as absolute rather than relative risks.

1.12 When possible, transplant programs should provide each donor candidate with individualized quantitative estimates of short-term and long-term risks from donation, including recognition of associated uncertainty, in a manner that is easily understood by donor candidates.

1.13 Transplant programs should evaluate donor candidate risks in comparison to predetermined thresholds for acceptance. If a donor candidate's postdonation risk is above the transplant program's acceptable risk threshold, the risk is not acceptable for donation. If a donor candidate's postdonation risk is below the transplant program's acceptance threshold, the candidate makes the decision whether or not to proceed with donation.

1.14 If a donor candidate is not acceptable, the transplant program should explain the reason for nonacceptance to the donor candidate.

1.15 Transplant programs should protect donor candidate's privacy regarding the evaluation, including all considerations in the decision to donate or not.

Roles and Responsibilities

1.16 A multidisciplinary transplant program team knowledgeable in kidney donation and transplantation should evaluate, care for, and formulate a plan for donor care including long-term follow-up.

1.17 Transplant programs should minimize conflict of interest by providing at least one key team member not involved in the care or evaluation of the intended recipient who evaluates the donor candidate and participates in the determination of donor acceptance.

1.18 Transplant programs should conduct as efficient a donor evaluation as possible, meeting the needs of donor candidates, intended recipients and transplant programs.

Commentary

In recommendations 1.1 to 1.10 and 1.14 to 1.18, the KDIGO guideline comprehensively summarizes principles of living kidney donor evaluations. These recommendations are sound and generally uncontroversial. We note that recommendation 1.3, focusing on transplantation program policies, is directly applicable to the US context in that CMS and UNOS program audits usually focus less on whether a specific donor candidate should have been accepted or not and more on whether a specific program followed its own protocols consistently. However, we also note that there are currently specific UNOS policies regarding exclusion criteria, such as diabetes mellitus. US

Table 1. Key Differences Between UNOS Regulations and the KDIGO Guideline

	UNOS Policy 14[a]	KDIGO Guideline[11]
Overall framework		
Approach to decision making	Nonquantitative: provides explicit exclusion criteria, eg, HTN with evidence of end-organ damage or diabetes	Quantitative: recommends quantification of risk and establishing numeric thresholds for long-term postdonation risks above which the transplantation program will not proceed with donation
Medical evaluation of living kidney donor candidates		
Predonation kidney function assessment	Requires 1) mGFR using exogenous filtration markers, or 2) CL_{cr} using 24-h urine Use of eGFR alone is not an option	Recommends eGFR assessment followed by confirmation using 1 of the following methods: 1) mGFR using exogenous filtration markers, 2) CL_{cr} using 24-h urine, 3) eGFR from combination of creatinine and cystatin C, or 4) repeat eGFR using creatinine
Selection based on kidney function	Provides no specific exclusion criteria based on kidney function	Recommends - acceptance if GFR ≥ 90 mL/min/1.73 m^2 - exclusion if GFR < 60 mL/min/1.73 m^2 - assessment of overall kidney failure risk compared to the program's pre-established risk threshold if GFR in 60-90 mL/min/1.73 m^2 range
Predonation proteinuria assessment	Requires measurement of both protein and albumin excretion in urine	Recommends measurement of urinary albumin excretion, and *not* total protein excretion
Predonation BP assessment	- No specific BP cutoffs or medication requirement criteria provided - Mandates exclusion if uncontrollable HTN or HTN with evidence of end-organ damage	- Candidates with HTN controlled to SBP < 140 mm Hg and DBP < 90 mm Hg using 1 or 2 antihypertensive agents, who do not have evidence of end-organ damage, may be acceptable for donation - Recommends exclusion based on overall kidney failure risk compared with programs' predetermined threshold
Predonation diabetes	Mandates exclusion of all with T1DM or T2DM	- Recommends exclusion of all with T1DM - Suggests considering older candidates with T2DM with well-controlled glycemia, not requiring insulin and without end-organ damage
Psychosocial evaluation		
Substance abuse disorder	Requires review of donor candidate's alcohol and drug use, past or present	Recommends that donor candidates with a past or present history of substance use disorder should be excluded or not evaluated until resolution

Abbreviations: BP, blood pressure; CL_{cr}, creatinine clearance; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GFR, glomerular filtration rate; HTN, hypertension; KDIGO, Kidney Disease: Improving Global Outcomes; mGFR, measured glomerular filtration rate; SBP, systolic blood pressure; T1(2)DM, type 1 (2) diabetes mellitus; UNOS, United Network for Organ Sharing.
[a]Dated August 15, 2019.

programs clearly need to also consider these national guidelines in assessing donor candidates. Additionally, in reference to recommendation 1.5, we note that in the US context, there are currently specific requirements for donor follow-up, including in postoperative months 6, 12, and 24.

We also suggest that the stipulation in recommendations 1.8 and 1.10 that transplantation program policies should apply to all donor candidates evaluated at the center may be overly prescriptive in the US context. Some donors might be willing to take a higher or lower medical risk for their own psychosocial benefit. Although there are risk factors that would preclude donation in all donor candidates, many programs would reasonably conclude that borderline risk estimates may be tolerable to certain donor candidates and ultimately the decision to donate is the candidate's, as long as he or she is appropriately counseled. For example, many programs would not support using the exact same thresholds for a nondirected donor and a directed donation within a close relationship, such as donation to a spouse or child.

The guideline introduces a novel concept for the decision-making process, a paradigm outlined in recommendations 1.11, 1.12, and 1.13. The KDIGO work group recommends "when possible" that transplantation programs *quantify* risk and provide numeric thresholds for short- and long-term donation risks. This goal is laudable, but we question whether the transplantation community currently has the requisite tools to accomplish this objective with the precision that is needed to set clear parameters for decision making. While a tool to estimate predonation risk of kidney failure in the general population resembling prospective living kidney donors is now available,[13] a complementary tool to estimate with precision the donation-attributable risk of kidney failure over the predonation risk does not exist. Also, the predonation risk predictor tool does not include factors that are likely to affect certain aspects of kidney failure risk, such as

genetics, key health behaviors, and environment. For example, the tool does not include family history of kidney disease or donation to an immediate relative with kidney failure, which have repeatedly been shown to be significant risk factors for donor kidney failure.[2,3,14] The tool does not include other important clinical variables frequently encountered during donor evaluation, such as prediabetes, number of antihypertensive medications a donor candidate requires, nonsteroidal anti-inflammatory drug use, history of recurrent urinary tract infections, and frequency or size of kidney stones. Thus, for donor candidates with these risk factors, the tool may underestimate risk. Furthermore, the risk tool was constructed using a life-table approach, with relative risks estimated from cohorts with short follow-up time. The follow-up time of these cohorts ranged from only 4 to 16 years, whereas the relevant time horizon of risk assessment for most living donors is multiple decades. The lifetime estimates generated are therefore inherently imprecise approximations.[14] The website that enables the risk calculator's convenient use by practitioners (http://www.transplantmodels.com/esrdrisk) does not readily acknowledge most of these limitations. Finally, although the risk tool was compared with actual living donor outcomes, the latter were available only to 15 years postdonation. The diverse and concerning limitations of this calculator have been described more fully elsewhere.[15-18]

Although transplantation centers may reasonably elect to use this tool, we do not believe that the KDIGO work group should imply that the use of this calculator is best practice or the default approach to donor risk assessment. The KDIGO recommendations themselves note that this tool was intended to be a "proof-of-concept" exercise. Given the lack of evidence relevant to the guideline and the limitations listed above, as is acknowledged by the KDIGO work group, the guideline statements were "not graded" by them for the strength of recommendations. However, incorporation of the tool into the KDIGO work group's overarching paradigm for donor selection may appear to overrate the strength of evidence on which this tool was developed. The tool should be used only with a clear understanding that it may well generate incorrect information about long-term outcomes. It should be considered as a possibly valuable step in a multistep scientific quest to determine long-term donor risk.

We note that an additional predictive tool by Massie et al[19] bases risk of kidney failure on former living kidney donors, but was published after this KDIGO guideline. This postdonation risk predictor tool has the advantage of including family history but does not include many other variables, including smoking history, albuminuria, and blood pressure. Both the pre- and postdonation tools require additional validation and study before being considered standard of care.

Therefore, the goal of quantifying postdonation risk is laudable, but the lack of tools to estimate future risk with precision makes the goal unreachable at this time. In addition, transplantation programs currently lack both the data and the experience to be able to follow the KDIGO recommendation to set their own acceptable absolute thresholds for long-term risks of kidney failure. The implementation of this framework for decision making also directly relates to the informed consent process as well.

We also question the prescription in recommendation 1.11 to express risks "as absolute rather than relative risks." We agree that the absolute risk is critical to convey because the donation-attributable increase in absolute risk of future kidney failure will usually be relatively low. However, we believe that full informed consent would reasonably include the disclosure of the best-available estimates of relative risk of kidney failure due to kidney donation.

We also note that in the US context, recommendation 1.17 about providing "at least one key team member not involved in the care or evaluation of the intended recipient" is a UNOS requirement to provide what is termed the "Independent Living Donor Advocate."

Informed Consent

Process of Informed Consent

2.1 Informed consent for donation should be obtained from the donor candidate in the absence of the intended recipient, family members and other persons who could influence the donation decision.

Capacity for Decision Making

2.2 The donor candidate's capacity to provide informed consent (ie, ability to understand the risks, benefits and consequences of donation) should be confirmed before proceeding with evaluation and donation.

2.3 Substitute decision makers should not be used on behalf of a donor candidate who lacks the capacity to provide informed consent (eg, children or those who are mentally challenged), except under extraordinary circumstances and only after ethical and legal review.

Content of Disclosure

2.4 Protocols should be followed to provide each donor candidate with information on:

- The processes of evaluation, donor acceptance, and follow-up
- The types of information that may be discovered during the evaluation, and what the transplant program will do with such information
- Individualized risks, benefits and expected outcomes of the donor evaluation, donation, and postdonation health, including a discussion of the uncertainty in some outcomes
- Treatment alternatives available to transplant candidates, and average expected outcomes
- How personal health information will be handled
- Availability of transplant program personnel for support

Comprehension of Disclosed Information

2.5 The donor candidate's understanding of the relevant information on the risks and benefits of donation should be confirmed before proceeding with donation.

Voluntarism

2.6 Donor candidates should have adequate time to consider information relevant to deciding whether they wish to donate or not.

2.7 A donor candidate's decision to withdraw at any stage of the evaluation process should be respected and supported in a manner that protects confidentiality.

2.8 A donor candidate who decides not to donate and has difficulty communicating that decision to the intended recipient should be assisted with this communication by the transplant program.

Commentary

The KDIGO work group does excellent work summarizing the approach to evaluating and counseling living kidney donors. They summarize existing data and identify important areas in which additional research to effectively counsel living donors is needed. Guideline chapters 1 and 18 present a conventional framework for living donor ethics and chapter 2 operationalizes this understanding into informed consent recommendations.

We identify some important limitations to the section on approach to informed consent.

First, as outlined in the section above, the KDIGO work group argues for a quantitative and transparent approach to calculating long-term health risk for potential living kidney donors. They argue that centers ought to identify a maximum acceptable risk of outcomes such as kidney failure. They then advocate the use of the predonation risk predictor tool to estimate long-term risk of kidney failure for individual donors. However, as discussed above, there are limitations in the accuracy of this approach.

As mentioned previously, we suggest that the framework for informed consent could reasonably include an accommodation for the strength of the donor's determination or the perceived "benefit" that the donor may derive when considering the decision to donate. While we understand the difficulty that transplantation professionals may have in measuring determination and perceived benefit, we contend that transplantation professionals take these issues into account regularly and that the concept of donor nonmedical benefit has been recognized in multiple research studies and clinical practice guidelines.[20,21]

An additional issue involves the general approach to informed consent. The guideline does not sufficiently address the problem that a large volume of information, enforced in the United States by UNOS, may actually reduce the quality of the informed consent process.[22] Clinicians should attempt to separate out the high-priority items from the lower priority items related to risk.

Last, in the US context, we recommend that the counseling of donors about the small increased risk of kidney failure after donation should also include information about former donors receiving very high priority in the deceased donor list in the unlikely event that they develop kidney failure.[23,24]

Compatibility Testing, Incompatible Transplantation, and Paired Donation

Evaluation

3.1 Donor ABO blood typing should be performed twice before donation to reduce the risk of unintended blood type incompatible transplantation.

3.2 Donor blood group A subtype testing should be performed when donation is planned to recipients with anti-A antibodies.

3.3 Human leukocyte antigen (HLA) typing for major histocompatibility complex (MHC) Class I (A, B, C) and Class II (DP, DQ, DR) should be performed in donor candidates and their intended recipients, and donor-specific anti-HLA antibodies should be assessed in intended recipients.

Counseling

3.4 Donor candidates who are ABO blood group or HLA incompatible with their intended recipient should be informed of availability, risks, and benefits of treatment options, including kidney paired donation and incompatibility management strategies.

3.5 If a donor candidate and intended recipient are blood type or crossmatch incompatible, transplantation should be performed only with an effective incompatibility management strategy.

3.6 Nondirected donor candidates should be informed of availability, risks and benefits of participating in kidney paired donation.

Commentary

The recommendations for the measurement of donor antigens (ABO and HLA) and donor counseling about incompatible transplantation are appropriate and consistent with US regulations and practices. We acknowledge the importance of informing the potential donor about the recipient outcomes following incompatible transplantation and the value of kidney paired donation in certain circumstances. However, we recognize the complexity of this issue. First, incompatible transplantation and/or kidney paired donation are options at most, but not all, US transplantation centers and outcomes of incompatible transplants can vary based on center expertise. When it is available, the outcomes of incompatible transplantation must be weighed against alternative risks including dialysis or waiting for a deceased donor.[25] These issues should be explained to the donor if applicable.

Preoperative Evaluation and Management

4.1 Donor candidates should receive guideline-based evaluation and management used for other noncardiac surgeries to minimize risks of perioperative complications, including a detailed history and examination to assess risks for cardiac, pulmonary, bleeding, anesthesia-related and other perioperative complications.

4.2 Donor candidates who smoke should be advised to quit at least 4 weeks prior to donation to reduce their risk of perioperative complications, and commit to lifelong abstinence to prevent long-term complications.

Commentary

Because donor safety is paramount, a thorough preoperative workup of all donors is imperative to stratify a donor's risk of perioperative complications and long-term kidney function and donor survival. Most centers use a similar set of evaluation laboratory and radiologic tests, which in the US context should include the UNOS list of compulsory studies for all donors.

While we agree with the recommendations set out by the KDIGO work group, we emphasize that the workup and any testing obtained needs to be viewed in the context of being a living donor. While certain findings and results may be acceptable in risk stratification for a needed surgery, all results must be viewed in the context of an optional surgery that the individual does not otherwise require. For example, while a cardiologist may "clear" a donor with mild cardiac disease for surgery, the donor team needs to determine that this is an acceptable risk for an optional procedure. In addition, if certain diagnostic tests carry a higher than reasonable risk (such as a cardiac catheterization), the team may decide that even doing the test is not acceptable.

Definitive studies on smoking risk among living kidney donors do not exist at this point. Extrapolating conclusions from other patient populations clearly indicate a higher risk of kidney failure for smokers, and it is reasonable to discourage smoking to reduce perioperative complications and improve long-term donor health. Some centers do not accept donors who smoke.[26] However, smokers are not a homogeneous group. If a donor candidate is a heavy smoker and already has some health issues attributable to smoking, they are unlikely to be an acceptable donor. However, for more moderate or light smokers, strong counseling and smoking cessation before donation seems reasonable.

Predonation Kidney Function

Evaluation

5.1 Donor kidney function should be expressed as glomerular filtration rate (GFR) and not as serum creatinine concentration.

5.2 Donor GFR should be expressed in mL/min per 1.73 m^2 rather than mL/min.

5.3 Donor glomerular filtration rate (GFR) should be estimated from serum creatinine ($eGFR_{cr}$) for initial assessment, following recommendations from the KDIGO 2012 CKD guideline.

5.4 Donor GFR should be confirmed using one or more of the following measurements, depending on availability:
- Measured GFR (mGFR) using an exogenous filtration marker, preferably urinary or plasma clearance of inulin, urinary or plasma clearance of iothalamate, urinary or plasma clearance of ^{51}Cr-EDTA, urinary or plasma clearance of iohexol, or urinary clearance of ^{99m}Tc-DTPA
- Measured creatinine clearance (mCrCl)
- Estimated GFR from the combination of serum creatinine and cystatin C ($eGFR_{cr\text{-}cys}$) following recommendations from the KDIGO 2012 CKD guideline
- Repeat estimated GFR from serum creatinine ($eGFR_{cr}$)

5.5 If there are parenchymal, vascular or urological abnormalities or asymmetry of kidney size on renal imaging, single kidney GFR should be assessed using radionuclides or contrast agents that are excreted by glomerular filtration (eg, ^{99m}Tc-DTPA).

Selection

5.6 GFR of 90 mL/min per 1.73 m^2 or greater should be considered an acceptable level of kidney function for donation.

5.7 The decision to approve donor candidates with GFR 60 to 89 mL/min per 1.73 m^2 should be individualized based on demographic and health profile in relation to the transplant program's acceptable risk threshold.

5.8 Donor candidates with GFR less than 60 mL/min per 1.73 m^2 should not donate.

5.9 When asymmetry in GFR, parenchymal abnormalities, vascular abnormalities, or urological abnormalities are present but do not preclude donation, the more severely affected kidney should be used for donation.

Counseling

5.10 We suggest that donor candidates be informed that the future risk of developing kidney failure necessitating treatment with dialysis or transplantation is slightly higher because of donation; however, average absolute risk in the 15 years following donation remains low. (*2C*)

Commentary

Recommendations 5.1 to 5.5 on kidney function evaluation of potential kidney donors are comprehensive and discuss the preferred methodology. Recommendations 5.6 to 5.9 discuss the degree of kidney function that would be acceptable for kidney donation. In alignment with the 2012 KDIGO chronic kidney disease (CKD) guideline, the KDIGO work group recommends reporting donor kidney function as glomerular filtration rate (GFR) expressed as mL/min/1.73 m^2.

The guideline recommends that the initial screening be performed by estimated GFR (eGFR) based on serum creatinine (Scr) level, followed by confirmation using either measured GFR (mGFR), creatinine clearance (CL_{cr}) or eGFR. mGFR and CL_{cr} are commonly used in the United States and are the ones recommended by current UNOS policy.[27] What would be new to the current practice in the United States (and not contemplated in the UNOS policy) is confirmation of GFR by a second eGFR as an acceptable option. The second eGFR could either be derived from Scr and cystatin C levels or simply be a repeat assessment of eGFR using Scr level alone.[26-29] This recommendation is a substantial departure from current practice in the United States[27] and would not be compliant with current UNOS policy. For transplantation programs to use this approach yet be compliant with UNOS policy, that policy would first need to be revised.

In addition, we have concerns with this recommendation because there is limited evidence that evaluation of kidney function by only using eGFR is safe for a nephrectomy, considering the limitations of estimating

equations in the setting of normal-range GFR. We also believe that the confirmatory test to evaluate the GFR should not be the same as the screening test. Rather, the confirmatory test could be either an mGFR using exogenous filtration markers or measured CL_{cr}, especially considering the practical consideration that a 24-hour urine collection to measure albumin excretion rate (AER) is already recommended in statement 6.3. All laboratories in the United States will also be able to measure Scr in the same sample that would permit the measurement of CL_{cr}. While CL_{cr} has well-known limitations, it is readily available and is current practice in most transplantation programs in the United States.[27]

In regard to levels of GFR acceptable for donation, KDIGO recommends a GFR ≥ 90 mL/min/1.73 m^2, which is higher than that previously recommended by some guidelines (GFR ≥ 80 mL/min/1.73 m^2). This cutoff is also in accordance with the levels of GFR used to define stages of kidney disease, including the normal range of GFR in the general population. We agree with the newer threshold. For donor candidates with GFR below this threshold, the KDIGO work group recommends the holistic evaluation of donors based on their demographic and clinical profile based on the predicted lifetime incidence of kidney failure (using the predonation risk predictor tool) as determined by the transplantation center's acceptance risk threshold. This approach represents a paradigm shift in the medical evaluation of live donors. As described previously, we believe that relying solely on the risk tool is premature.

We agree that candidates with a GFR < 60 mL/min/1.73 m^2 should be excluded from donation. However, we have concerns about the recommendation that candidates with GFRs of 60 to 89 mL/min/1.73 m^2 can be approved based on demographic and clinical profiles derived from the estimated risk of kidney failure. It is important to note that these recommendations do not differentiate thresholds based on the methodology of GFR assessment. CL_{cr} usually overestimates GFR, while eGFR usually underestimates GFR in the normal range. We have already described the limitations of the risk tool; even if the tool provides an overall estimate of future kidney failure risk in an acceptable range, we find it unlikely that candidates with GFRs (especially as assessed by CL_{cr}) in the lowest part of this range, for example, between 60 and 70 mL/min/1.73 m^2, would be acceptable candidates. We also have concerns with the GFR cutoffs to determine eligibility being independent of age. For example, a GFR of 85 mL/min/1.73 m^2 would be considered excellent kidney function for a 65-year-old donor, but would be unusually low for a 25-year-old and may justify exclusion of the younger candidate. We appreciate that the risk tool already incorporates age and agree that a wide range of GFRs may be acceptable depending on other clinical variables. However, given the importance of GFR in predicting future CKD and kidney failure, we do not think that the risk tool is reliable enough to provide the sole guidance regarding acceptable predonation GFR. The limitations of using estimation equations and of ignoring age in the assessment of donor kidney function are highlighted in a recent study by Gaillard et al.[30]

Predonation Albuminuria

Evaluation

6.1 Donor proteinuria should be measured as albuminuria, not total urine protein.

6.2 Initial evaluation of donor albuminuria (screening) should be performed using urine albumin-to-creatinine ratio (ACR) in a random (untimed) urine specimen.

6.3 Donor albuminuria should be confirmed using:
- Albumin excretion rate (AER, mg/day [mg/d]) in a timed urine specimen
- Repeat ACR if AER cannot be obtained

Selection

6.4 Urine AER less than 30 mg/d should be considered an acceptable level for donation.

6.5 The decision to approve donor candidates with AER 30 to 100 mg/d should be individualized based on demographic and health profile in relation to the transplant program's acceptable risk threshold.

6.6 Donor candidates with urine AER greater than 100 mg/d should not donate.

Commentary

The recommendations for predonation albuminuria screening are based on the 2012 KDIGO CKD guideline because studies have not been performed to directly examine the impact of predonation albuminuria on living donor kidney function or kidney allograft function. We agree with this approach because the correlation between albuminuria, CKD, and other comorbid conditions is well documented in the general population. The initial kidney donor evaluation of albuminuria should be performed using a random urinary albumin-creatinine ratio (UACR) and if abnormal, confirmed with a timed urine specimen. If a timed urine specimen is not possible, a repeat UACR is recommended.

Our main concern with the recommendations on albuminuria is the explicit statement that albuminuria and not total proteinuria be used for living kidney donor evaluation. This recommendation is not consistent with UNOS policy, which requires the measurement of both urine protein and urine albumin. Additionally, while we appreciate the difficulties standardizing the measurement of proteinuria, in some circumstances, donor candidates may have clear proteinuria identified that is not albuminuria. This proteinuria may be indicative of an underlying tubular defect, tubular interstitial disease, or abnormal paraprotein associated with eventual CKD. While we agree that these disorders are rare and are likely to be suggested by other abnormal findings during the evaluation, a urinary protein-creatinine ratio is an inexpensive screening test that can be easily added to a urine sample. We do not recommend changing UNOS policy regarding measurement of proteinuria and albuminuria.

Though this section of the guideline is entitled "Predonation Albuminuria," a substantial portion of the text is dedicated to postdonation proteinuria. While of uncertain long-term significance, the incidence of proteinuria is higher in kidney donors (~12%) than in non–kidney donors. Clinicians should be discouraged from dismissing proteinuria found after donation to the kidney donation itself. We recommend a complete workup for postdonation proteinuria, as would be done in the general population. These are additional reasons why having a baseline proteinuria measurement may be useful, as a comparison for future findings.

Predonation Hematuria

Evaluation

7.1 Donor candidates should be assessed for microscopic hematuria.

7.2 Donor candidates with persistent microscopic hematuria should undergo testing to identify possible causes, which may include:

- Urinalysis and urine culture to assess for infection
- Cystoscopy and imaging to assess for urinary tract malignancy
- 24-hour urine stone panel to assess for nephrolithiasis and/or microlithiasis
- Kidney biopsy to assess for glomerular disease (eg, thin basement membrane nephropathy, IgA nephropathy, Alport syndrome)

Selection

7.3 Donor candidates with hematuria from a reversible cause that resolves (eg, a treated infection) may be acceptable for donation.

7.4 Donor candidates with IgA nephropathy should not donate.

Commentary

We agree with the assertion that microscopic hematuria should be based on microscopic evaluation of the urine and not dipstick alone. Causes for false-positive or true-positive dipstick testing for hematuria in the absence of red blood cells on microscopic examination are discussed.

An algorithm is put forth for sequential evaluation of donor candidates with microscopic hematuria that does not resolve, up to and including kidney biopsy if necessary. There is appropriate discussion of recommendations from other societies about potential donors with hematuria and thin basement membrane disease or Alport syndrome seen on biopsy.

Kidney Stones

Evaluation

8.1 Donor candidates should be asked about prior kidney stones, and related medical records should be reviewed if available.

8.2 The imaging performed to assess anatomy before donor nephrectomy (eg, computed tomography angiogram) should be reviewed for the presence of kidney stones.

8.3 Donor candidates with prior or current kidney stones should be assessed for an underlying cause.

Selection

8.4 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.

Counseling

8.5 Donor candidates and donors with current or prior kidney stones should follow general population, evidence-based guidelines for the prevention of recurrent stones.

Commentary

Although living donor candidates are among the healthiest individuals in the general population, the guideline points out that routine use of computed tomography (CT) for evaluation of these candidates reveals a 5% to 10% incidence of asymptomatic calcific densities in the kidneys consistent with kidney stones. In the general population with stone disease, there is a significant risk of stone growth or new stone formation and patients with kidney stones may have an increased risk of CKD and kidney failure. Following living donation, stone disease in the remaining kidney could have serious consequences, including acute kidney injury from obstructive nephropathy and severe pyelonephritis. Thus, it is appropriate to be concerned about stone disease, both symptomatic and asymptomatic, in living donor candidates. As described in the guideline, the reported incidence of recurrent stone events in donors with stone disease appears to be extremely low, although there are an insufficient number of studies that have examined the outcome of living donors with kidney stones.

The recommendations on evaluating donor candidates for stone disease are reasonable and follow available guidelines for the general population. However, the guideline does not detail the conditions that should be considered as exclusion criteria, such as multiple or recurrent kidney stones, large stones, or the presence of nephrocalcinosis.

Last, for donors with an existing solitary kidney stone who are accepted for donation, preference should be given to donation of the kidney with the stone, to minimize risk of acute kidney injury due to stone disease in the remaining kidney.

Hyperuricemia, Gout, and Mineral and Bone Disease

Evaluation

9.1 Donor candidates should be asked about prior episodes of gout.

Counseling

9.2 Donor candidates may be informed that donation is associated with an increase in serum uric acid concentration, which may increase the risk for gout.

9.3 Donor candidates and donors with prior episodes of gout should be informed of recommended methods to reduce their risk of future episodes of gout.

Commentary

The recommendations in this section are reasonable, but we acknowledge that few studies have been done in this area. Given the modest increase in serum uric acid levels after donation, donors should be informed of their risk for gout. The lack of studies and/or evidence regarding metabolic bone disease in donors led the authors to not make any recommendations in this area outside of what is suggested for the general population.

Predonation Blood Pressure

Evaluation

10.1 Blood pressure should be measured before donation on at least 2 occasions by clinical staff trained in accurate measurement technique, using equipment calibrated for accuracy.

10.2 When the presence or absence of hypertension in a donor candidate is indeterminate based on history and clinic measurements (eg, blood pressure is high normal or variable), blood pressure should be further evaluated using ambulatory blood pressure monitoring (ABPM) or repeated using standardized blood pressure measurements.

Selection

10.3 Normal blood pressure, as defined by guidelines for the general population in the country or region where donation is planned, is acceptable for donation.

10.4 Donor candidates with hypertension that can be controlled to systolic blood pressure less than 140 mm Hg and diastolic blood pressure less than 90 mm Hg using 1 or 2 antihypertensive agents, who do not have evidence of target organ damage, may be acceptable for donation. The decision to approve donor candidates with hypertension should be individualized based on demographic and health profile in relation to the transplant program's acceptable risk threshold.

Counseling

10.5 Donor candidates should be counseled on lifestyle interventions to address modifiable risk factors for hypertension and cardiovascular disease, including healthy diet, smoking abstinence, achievement of healthy body weight, and regular exercise according to guidelines for the general population. These measures should be initiated before donation and maintained lifelong.

10.6 We suggest that donor candidates should be informed that blood pressure may rise with aging, and that donation may accelerate a rise in blood pressure and need for antihypertensive treatment over expectations with normal aging. (*2D*)

Commentary

The recommendations on the evaluation of blood pressure in a potential living kidney donor are that the acceptance or refusal of the donor candidate should not be based only on actual blood pressure readings alone, but in the context of demographics, clinical characteristics, and risks attributable to donation. Available evidence suggests that well-controlled hypertension is still a risk factor for future kidney failure, but a weaker predictor than many other factors such as African ancestry, albuminuria, and smoking. The KDIGO work group suggests considering candidates with systolic blood pressure < 140 and diastolic blood pressure < 90 mm Hg, based on guidelines such as the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) 8.[31] More recent guidelines, such as the American College of Cardiology/American Heart Association guidelines that came out after the KDIGO guideline, suggest a lower blood pressure target of 130/80 mm Hg.[32,33] No consensus exists to support using a specific blood pressure as an exclusion criterion, but the KDIGO work group provides reasonable minimal criteria in an evolving field. UNOS regulations do not define specific cutoffs for hypertension.

There is likely an increased risk of hypertension associated with living kidney donation, especially in African Americans.[34] While not particularly emphasized in the guidelines, there are no data on the safety of live kidney donation among nonwhite donors (Hispanic and African American) with predonation hypertension controlled with medications, regardless of the rest of the clinical profile at time of donation.

Predonation Metabolic and Lifestyle Risk Factors

Identification of Metabolic and Lifestyle Risk Factors

11.1 Risk factors for kidney and cardiovascular disease should be identified before donation and addressed by counseling to promote long-term health.

Obesity

11.2 Body mass index (BMI) should be computed based on weight and height measured before donation, and classified based on World Health Organization (WHO) criteria for the general population or race-specific categories.

11.3 The decision to approve donor candidates with obesity and BMI >30 kg/m^2 should be individualized based on demographic and health profile in relation to the transplant program's acceptable risk threshold.

11.4 Donor candidates who have had bariatric surgery should be assessed for risk of nephrolithiasis.

Glucose Intolerance

11.5 Donor candidates should be asked about prior diagnosis of diabetes mellitus, gestational diabetes, and family history of diabetes.

11.6 Glycemia should be assessed by fasting blood glucose and/or glycated hemoglobin (HbA_{1c}) before donation.

11.7 2-hour glucose tolerance or HbA_{1c} testing should be performed in donor candidates with elevated fasting blood glucose, history of gestational diabetes, or family history of diabetes in a first-degree relative, and results

should be used to classify diabetes or prediabetes status using established criteria for the general population.

11.8 Donor candidates with type 1 diabetes mellitus should not donate.

11.9 The decision to approve donor candidates with prediabetes or type 2 diabetes should be individualized based on demographic and health profile in relation to the transplant program's acceptable risk threshold.

11.10 Donor candidates with prediabetes or type 2 diabetes should be counseled that their condition may progress over time and may lead to end-organ complications.

Dyslipidemias

11.11 Fasting lipid profile (including total cholesterol, LDL-C, HDL-C and triglycerides) should be measured as part of an overall cardiovascular risk assessment before donation.

11.12 The decision to approve donor candidates with dyslipidemia should be individualized based on demographic and health profile in relation to the transplant program's acceptable risk threshold.

Tobacco Use

11.13 The use of tobacco products should be assessed before donation.

11.14 Donor candidates who use tobacco products should be counseled on the risks of perioperative complications, cancer, cardio-pulmonary disease and kidney failure, should be advised to abstain from use of tobacco products, and should be referred to a tobacco cessation support program if possible.

11.15 The decision to approve donor candidates who are active tobacco users should be individualized based on demographic and health profile in relation to the transplant program's acceptable risk threshold.

Commentary

Cardiovascular disease is the leading cause of death in the general population and hence attention to identifiable and preventable risk factors is important, as suggested by the guideline.

The recommendations regarding obesity are generally reasonable and mention both the quite low kidney failure hazard ratio (HR) from obesity found in the predonation risk prediction tool as well as the much higher risk of kidney failure found in former US live kidney donors who were obese.[35] However, the lower values are given much more specificity and prominence; the HR from the predonation risk tool is listed explicitly (1.16), and there are 2 figures encompassing 8 graphs showing a minimal impact of obesity. The HR for kidney failure found in former US live donors—1.86—is not mentioned. This highlights the potential limitations of the risk tool because the relative risk of kidney failure from obesity may be greater in actual donors than potential donors.

The guideline mentions the need for assessing kidney stone risk after bariatric surgery, a population that may require special attention and is not rare in the United States. In donor candidates who have undergone bariatric surgery, we agree that a stone metabolic evaluation may be advisable even in the absence of incidental nephrolithiasis found during the evaluation because stone formation may take several years. Modification of any abnormalities may prevent future nephrolithiasis.

The discussion of diabetes and prediabetes in donor candidates is also generally reasonable. It mentions other guidelines that either recommend exclusion or possible consideration of candidates with diabetes and takes the position that type 1 diabetes is an absolute exclusion criterion, but that candidates with type 2 diabetes may be considered as donors. Specifically, the KDIGO work group noted that older candidates with type 2 diabetes with well-controlled glycemia, not requiring insulin, and without end-organ damage, may be considered for donation. However, it is not made explicit that in the US context, both type 1 and type 2 diabetic patients are excluded from donation by UNOS regulations.

We agree with the work group's point that candidates with prediabetes may progress to diabetes at a lifetime rate of 5% to 10%, and that the risk of progression is reduced by lifestyle changes and weight loss. However, the guideline does not mention the important point that the World Health Organization (WHO) defines prediabetes as fasting blood glucose level of 110 to 126 mg/dL, while the American Diabetes Association defines prediabetes as a fasting blood glucose level of 100 to 126 mg/dL. It also does not mention that the risk of progressing to diabetes depends on the actual level of hyperglycemia; for example, a candidate with fasting blood glucose level of 112 mg/dL has a substantially higher risk of progression than one with a fasting blood glucose level of 102 mg/dL. Further, the guideline suggests individualizing acceptance decisions for those with prediabetes "based on their predicted long-term risk in relation to the transplant program's acceptable risk threshold."[11(pS61)] We think this is a reasonable statement, but note that the predonation kidney failure risk tool does not include prediabetes as a predictor, pointing out another limitation of relying on that tool.

The guideline points out that dyslipidemia is a component of metabolic syndrome and a risk factor for cardiovascular disease, but has not been shown to be directly associated with future risk of kidney failure. While the recommendation is to individualize "the decision to approve donation in persons with dyslipidemia based on their predicted long-term risk,"[11(pS61)] there remains little guidance as to exactly how to factor dyslipidemia in the context of prediabetes and other components of metabolic syndrome.

The discussion on smoking points out that smoking substantially increases mortality and directly increases future risk of kidney failure. Various international guidelines as well as the KDIGO guideline all support efforts toward smoking cessation, but vary as to how strictly to enforce those efforts. The KDIGO work group again recommends individualizing decisions regarding candidates who are active smokers based on their predicted long-term risk.

Preventing Infection Transmission

Evaluation

12.1 Risk for human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) infections should be assessed before donation.

12.2 Donor candidates should be assessed for factors associated with an increased likelihood of endemic or unexpected infections, including geographic, seasonal, occupational, animal and environmental exposures.

12.3 Donor candidates should complete a urinalysis and testing for HIV, HBV, HCV, cytomegalovirus (CMV), Epstein-Barr virus (EBV), and *Treponema pallidum* (syphilis).

12.4 If indicated by regional epidemiology or individual history, donor candidates should complete testing for *Mycobacterium tuberculosis*, *Strongyloides*, *Trypanosoma cruzi*, West Nile virus, Histoplasmosis, and/or Coccidiomycosis.

12.5 Transplant programs should develop protocols to screen donor candidates for emerging infections in consultation with local public health specialists.

12.6 In general, donor infection risk factor and microbiological assessments should be performed or updated as close in time to donation as possible. For HIV, HBV and HCV, screening should be current within 28 days of donation.

Selection

12.7 If a donor candidate is found to have a potentially transmissible infection, then the donor candidate, intended recipient and transplant program team should weigh the risks and benefits of proceeding with donation.

Commentary

For the most part, evaluation of potential living donors is governed by national policy, and these polices (often appropriately) differ from one region to another. Overall, the recommendations reasonably follow a mix of different regional practices. The guideline has an excellent discussion of Chagas disease and discusses posttransplantation monitoring of recipients of seropositive donors. It is worth noting that polymerase chain reaction–based testing, which is the most sensitive of available assays, is not commercially available in the United States but can be performed at the Centers for Disease Control and Prevention. Also, although a section heading refers to "Increased Risk Donors," the text that follows uses the term "high risk donor." The latter term should be avoided because it not only contributes to global confusion about the risk, but is not consistent with US consensus definitions, which specifically recommend the term "increased risk donor."

Cancer Screening

Evaluation

13.1 Donor candidates should undergo cancer screening consistent with clinical practice guidelines for the country or region where the donor candidate resides. Transplant programs should ensure that screening is current according to guideline criteria at the time of donation.

Selection

13.2 In general, donor candidates with active malignancy should be excluded from donation. In some cases of active malignancy with low transmission risk, a clear management plan and minimal risk to the donor, donation may be considered.

13.3 A kidney with a small simple (Bosniak I) cyst can be left in the donor, particularly if there are compelling reasons for donating the contralateral kidney.

13.4 Donation of kidneys with a Bosniak II renal cyst should proceed only after assessment for the presence of solid components, septations, and calcifications on the preoperative computed tomography scan (or magnetic resonance imaging) to avoid accidental transplantation of a kidney with cystic renal cell carcinoma.

13.5 Donor candidates with high-grade Bosniak renal cysts (III or higher) or small (T1a) renal cell carcinoma curable by nephrectomy may be acceptable for donation on a case-by-case basis.

13.6 Donor candidates with a history of treated cancer that has a low risk of transmission or recurrence may be acceptable for donation on a case-by-case basis.

Commentary

The recommendations regarding cancer screening are well written, although based on nongraded evidence. We agree that donors should undergo cancer screening consistent with clinical practice guidelines for the country or region where they reside. In the United States, these would usually be the United States Preventive Task Force or the American Cancer Society guidelines. We agree that the overall goal of cancer screening is to reduce the risk of donor-derived malignancy for the recipient, as well as assess for the presence of current or future risk of cancer development in the donor (both recurrent and de novo). This cancer screening helps reduce the risk of injury to the remaining kidney from drug toxicity or other treatments. The recommendations discuss transmission of a malignancy from the donor to the recipient based on risk classification into 6 categories from no significant risk to high risk, including an unknown risk category.

The recommendations do not specifically address the issue of how to deal with donors who have a high lifetime risk of developing certain cancers, especially those with high risk of developing renal cell cancer such as Von Hippel Lindau, hereditary leiomyomatosis, and Britt-Hogg-Dube syndromes. There may also be concerns about those with other familial cancer syndromes, such as hereditary breast and ovarian cancer from BRCA 1 or 2 variants or hereditary colorectal cancers.

Evaluation of Genetic Kidney Disease

Evaluation

14.1 Donor candidates should be asked about their family history of kidney disease, and when present, the type of disease, time of onset, and extra-renal manifestations associated with the disease.

14.2 When the intended recipient is genetically related to the donor candidate, the cause of the intended recipient's kidney failure should be determined whenever possible. The intended recipient should consent to share this medical information with the donor evaluation team, and with the donor candidate if it could affect the decision to donate.

Selection

14.3 Donor candidates found to have a genetic kidney disease that can cause kidney failure should not donate.

Counseling

14.4 Donor candidates must provide informed consent for genetic testing if indicated as part of their evaluation. Donor candidates should be informed of the possible effects of receiving a diagnosis of a genetic kidney disease, such as any impact on their ability to obtain health or life insurance.

14.5 In cases where it remains uncertain whether the donor candidate has a genetic kidney disease and whether the disease can cause kidney failure, donation should proceed only after informing the donor candidate of the risks of donation if the disease manifests later in life.

Autosomal Dominant Polycystic Kidney Disease (ADPKD)

14.6 Donor candidates with ADPKD should not donate.

14.7 Donor candidates with a family history of ADPKD in a first-degree relative may be acceptable for donation if they meet age-specific imaging or genetic testing criteria that reliably exclude ADPKD.

Apolipoprotein L1 (*APOL1*) Risk Alleles

14.8 Apolipoprotein L1 (*APOL1*) genotyping may be offered to donor candidates with sub-Saharan African ancestors. Donor candidates should be informed that having 2 *APOL1* risk alleles increases the lifetime risk of kidney failure but that the precise kidney failure risk for an affected individual after donation cannot currently be quantified.

Commentary

With growing awareness of an increasing number of monogenic kidney diseases that present later in life, genetic testing may become an increasingly common part of the routine donor evaluation. At the current time, imaging criteria can reliably exclude autosomal dominant polycystic kidney disease (ADPKD) in older donors and genetic testing should be offered to younger donors at risk with equivocal imaging findings. For many other genetic diseases, focused testing or more comprehensive testing panels are available. The guideline recommends offering genetic testing to donors with a family history of heritable kidney disease. These recommendations also emphasize the need to counsel donors on the implications of the results of such testing on their future health and medical insurability. For example, it is unclear whether heterozygous carriers of X-linked diseases such as Fabry or Alport can safely donate.

The presence of certain genetic variants such as *APOL1* renal risk alleles (2 copies) and sickle cell trait (1 copy) have been associated with increased risk of CKD in the general population. There are no studies to date demonstrating increased risk of kidney disease in living kidney donors with sickle cell trait, but it might be reasonable to assume that such a risk would also be present in donors. Whether donation increases the risk of kidney disease in this population is unknown. However, Doshi et al[36] recently reported on the renal risks associated with 2 copies of *APOL1* genetic variants in a single-center study in which black donors with 2 copies had a lower predonation GFR, and importantly a higher postdonation risk for CKD and kidney failure. Other studies reported increased risk of CKD in young males with 2 *APOL1* renal risk alleles with good health at baseline (similar to donors but did not donate).[37] Although it is unknown whether living kidney donation further amplifies this risk, it seems reasonable to consider *APOL1* genetic testing in high-risk donor candidates, with pre- and posttest counseling. We did not reach consensus among our commentary work group regarding whether testing for *APOL1* genetic variants must be part of every donor evaluation of candidates with African ancestry. Each transplantation center should individualize their protocol for *APOL1* genetic testing and their response to positive test results based on their risk tolerance and informed consent discussion with the candidate. While offering such testing, one should be cognizant of the responsibility for counseling and of the donor's right to autonomy.

Pregnancy

Evaluation

15.1 Female donor candidates should be asked about future childbearing plans.

15.2 Female donor candidates should be asked about prior hypertensive disorders of pregnancy (eg, gestational hypertension, preeclampsia, or eclampsia).

15.3 Local guidelines should be followed to confirm the absence of pregnancy before performing radiologic tests, including abdominal computed tomography (with iodinated contrast) or nuclear medicine GFR testing.

Selection

15.4 Women should not donate while pregnant.

15.5 Women should not be excluded from donation solely because they desire to conceive children after donation.

15.6 Women with a prior hypertensive disorder of pregnancy may be acceptable for donation if their long-term postdonation risks are acceptable.

15.7 A decision to proceed with donation in the year after childbirth should consider the psychological needs of mother and child, and should include anesthesia and analgesia planning for nursing mothers.

Counseling

15.8 Women with childbearing potential should be informed of the need to avoid becoming pregnant from the time of approval for donation to the time of recovery after nephrectomy; a quantitative human chorionic

gonadotropin (β-hCG) pregnancy test should be performed and confirmed as negative immediately before donation.

15.9 We suggest that women with childbearing potential be counseled about the effects donation may have on future pregnancies, including the possibility of a greater likelihood of being diagnosed with gestational hypertension or preeclampsia. (*2C*)

15.10 Women with a prior hypertensive disorder of pregnancy should be informed about their long-term risks.

15.11 Women with childbearing potential who proceed with donation should be counseled on how to reduce the risk of complications in future pregnancies.

Commentary

The guideline provides an excellent overview of potential issues associated with pregnancy in young female donors. They cover 3 general areas: the need to ensure that a woman is not pregnant during the workup or peridonation period, the potential risk from past pregnancy complications on future kidney function, and the risk that donation might bring to future pregnancies.

The guideline highlights the need to make sure women are not pregnant or planning to become pregnant during the workup because there are a number of investigations that could expose a fetus to ionizing radiation. In addition, any new mother planning to donate should be made aware of the typical recovery period postdonation and potential complications that could affect her ability to care for her offspring, allowing her to make support arrangements.

Pregnancy complications and kidney disease are closely associated. Both gestational hypertension and preeclampsia, especially severe and early-onset disease, increase the risk for future hypertension, CKD, and kidney failure.[38-40] A careful pregnancy history that includes the presence, severity, and onset of preeclampsia is therefore necessary in the evaluation of all female donors.

The guideline notes the increased risk of pregnancy complications postdonation and suggests making women aware of these risks, as well as preventive strategies. In the rationale, the guideline reviews 3 recent retrospective studies and incorporates a very helpful summary table.[41-43] These data are actually relatively encouraging. Although increased gestational hypertension and preeclampsia are more common in women after donation than prior and more common than among the general population, overall event rates are low. UNOS requirements for informed consent for live donation require providing information to women of childbearing age about the risks of gestational hypertension and preeclampsia after donation. In this respect, clinicians counseling these women can state that overall the rates of either gestational hypertension or preeclampsia increase from ~5% to 11%.

We suggest that decreased renal mass from donation is an additive risk factor for adverse pregnancy outcomes, which may be of greater concern in populations already at increased risk for preeclampsia, including certain ethnic groups (eg, African American and Hispanic), those with higher body mass indexes, and more advanced maternal age. As such, individualized risk stratification is required and will influence appropriate pregnancy surveillance and preventative strategies. The need to share this portion of medical history with other members of the donor's health care team, especially obstetricians, is an important message that should be delivered to all potential young female donors.

Psychosocial Evaluation

Evaluation

16.1 Donor candidates should receive in-person psychosocial evaluation, education and planning from health professionals experienced in the psychosocial concerns of donor candidates and donors.

16.2 To ensure voluntariness, at least a portion of the psychosocial evaluation of the donor candidate should be performed in the absence of the intended recipient, family members and other persons who could influence the donation decision.

16.3 Whenever possible, the psychosocial evaluation of the donor candidate should be performed by health professionals not involved in the care of the intended recipient.

16.4 Transplant programs should follow protocols for assessing the donor candidate's psychosocial suitability, available support, preparation and concerns for donation.

Selection

16.5 Transplant programs should follow protocols defining psychosocial factors that either exclude donation, or prevent further evaluation until resolution.

Disclosures and Support

16.6 We suggest that donor candidates be informed that donors usually have good quality of life after donation (*2D*).

16.7 Transplant programs should assist donor candidates and donors in receiving psychosocial or psychiatric support as needed.

Commentary

Despite the lack of an evidence base, these evaluation recommendations are consistent with general clinical practice in the United States and mirror other published guidelines. We agree that all potential living donors should undergo psychosocial assessment as part of their candidacy evaluation, that this assessment should be performed face to face, and that it be conducted by a trained mental health clinician with experience in transplantation and living donation. Additionally, we agree with the recommended content of the psychosocial evaluation, as highlighted in Table 23 of the guideline. We note that the KDIGO work group stopped short of recommending that the entire psychosocial assessment be performed independent of

other family members, the recipient, or others who potentially could influence the donor candidate's decision-making process. One rationale provided is that the inclusion of others in at least a portion of the evaluation may lead the donor candidate to be more forthcoming and candid during the evaluation, yet this inclusion—paradoxically—could seem subtly coercive by some donor candidates.

Regarding the selection of donor candidates, we agree that transplantation programs should develop clearly defined criteria that would result in being declined as a potential donor due to psychosocial risk factors. These recommendations were "not graded," and it must be emphasized that such protocols and associated psychosocial exclusion criteria have no empirical basis because there is scant (or no) scientific evidence that the psychosocial contraindications listed in Table 24 of the guideline are predictive of adverse outcomes following donation. Some of the listed contraindications may be considered good clinical practice, but there is considerable programmatic variation on how such criteria should be operationally defined.

However, we caution against the recommendation that donor candidates with a past or present history of substance use disorder should be excluded or not evaluated until resolution. There is no evidence to support this broad recommendation, and the substance type, severity, treatment received, or abstinence period are not described. Quite often, a psychosocial evaluation is warranted to assess whether the level of substance use (eg, alcohol and marijuana) meets criteria for substance use disorder, as defined by the *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition: DSM-5* criteria. Excluding these donor candidates without offering a thorough evaluation would be premature in certain cases. We also note that UNOS policy 14.1 on the psychosocial evaluation of living donors is not so restrictive regarding former substance abuse. Furthermore, an evaluation in some of these candidates may be an opportunity to motivate them and help them access available mental health services. We agree with the recommendation that "A psychosocial profile that predicts a level of postdonation risk that exceeds a transplant program's acceptable risk threshold"[pS82] should be considered a contraindication, which is consistent with the KDIGO work group's position that each program should develop its own criteria regarding psychosocial inclusion/exclusion criteria.

We agree with the recommendation that transplantation programs should do more to help potential and former donors access mental health services, as needed. For potential donors who may be excluded for psychosocial reasons, programs should determine whether these psychological, psychiatric, or behavioral health factors are modifiable and refer the donor candidate for treatment if she or he desires to pursue it. As noted by the KDIGO work group, an emerging area of clinical importance is the psychological consequences associated with being turned down as a donor candidate and the transplantation program's obligation to assist such individuals in finding psychological support.[44] Finally, although only a small proportion of former living donors experience clinically significant adverse psychosocial consequences, we agree that programs should develop a process for psychosocial screening postdonation and either provide or assist donors in finding appropriate psychological or psychiatric services.

Acceptable Surgical Approaches for Donor Nephrectomy

17.1 Renal imaging (eg, computed tomographic angiography) should be performed in all donor candidates to assess renal anatomy before nephrectomy.

17.2 The surgeon should have adequate training and experience for the surgical technique used for donor nephrectomy.

17.3 We suggest that "mini-open" laparoscopy, or hand-assisted laparoscopy by trained surgeons should be offered as optimal approaches to donor nephrectomy. However, in some circumstances, such as for donors with extensive previous surgery and/or adhesions, and at centers where laparoscopy is not routinely performed, open nephrectomy (flank or laparotomy) may be acceptable. (*2D*)

17.4 Robotic, single-port, and natural orifice transluminal nephrectomy should generally not be used for donor nephrectomy.

17.5 Nontransfixing clips, (eg, Weck Hem-O-lok) should not be used to ligate the renal artery in donor nephrectomy; instead, renal artery transfixation by suture ligature or anchor staple within the vessel wall should be used.

17.6 In the absence of reasons to procure the right kidney (vascular, urological or other abnormalities), the left kidney should be procured in laparoscopic donor nephrectomy because of the relative technical ease associated with a longer venous pedicle.

17.7 We suggest laparoscopic procurement of the right rather than the left living donor kidney may be performed if the surgeon has adequate training and experience. (*2D*)

17.8 Procurement of a living donor kidney with 3 or more arteries should only be undertaken by surgeons with adequate experience.

17.9 A donor candidate with atherosclerotic renal artery disease or fibromuscular dysplasia involving the orifices of both renal arteries should not donate.

Commentary

We agree with the excellent summary of surgical approaches for donor nephrectomy in the guideline. Regarding preoperative imaging, centers in the United States usually prefer CT over magnetic resonance imaging because of ease of interpretation by surgeons and completeness of information. It is critical that the radiologist understand the laparoscopic nephrectomy procedure and therefore what important information needs to be conveyed to the surgeon.

In recent years, there have been several reports of single-port transumbilical and robotic donor nephrectomy being adopted by a few centers. Small-volume studies have shown promising results.[45-47] However, most donor surgeons are not trained in single-port or robotic techniques nor has conclusive evidence been reported that these techniques are superior to the current standard of care. Keeping in mind the most important tenet of donor safety, the commentary work group cannot recommend that these techniques be widely used at this time. Surgical research protocols in select institutions with experienced surgeons should result in the necessary objective data to evaluate the need for broader use of these techniques.

Early studies showed an increased rate of venous thrombosis with the use of right kidneys associated with very short right renal vein length. In addition, the anatomic location of the right kidney increases the potential risk of vascular injury to the inferior vena cava and small venous branches originating from the cava. There is a slightly higher reported rate of conversion to open procedure when operating on the right kidney. However, comfort in right nephrectomy has grown over time, and many centers do not shy away from this approach if there are the proper indications. One single-center study concluded that reluctance toward right donor nephrectomy is not justified.[48] There are certainly cases in which a right nephrectomy is the necessary choice given the premise that the "better" kidney remains with the donor, including those for whom the right kidney is clearly smaller than the left, has lower function than the left kidney based on split kidney function, an abnormality such as a large cyst, or there is a significantly more complicated vascular anatomy on the left side. Although the vast majority of nephrectomies are left sided, the decision to as to whether to perform a right-sided nephrectomy should focus on the needs of the donor and expertise of the surgical team.

Ethical, Legal, and Policy Considerations

Ethical and Legal Framework

18.1 Local laws and regulations on living donation should be followed and explained as needed to donor candidates.

18.2 Where local laws or policies impede the ethical practice of living donation, avenues to advocate for change should be explored.

18.3 Autonomy (self-determination) in the willingness or not to be considered as a living donor should be respected during all phases of the evaluation and donation processes. Transplant programs should support autonomy through a fully informed consent process.

Policies for Donor Candidate Identification

18.4 Public awareness of opportunities for living donation should be increased through education, donor advocacy, evaluation efficiencies, and removal of disincentives.

18.5 Transplant candidates should be assisted in identifying living donor candidates, as long as these efforts respect donor autonomy and do not exert undue pressure to donate.

18.6 Donor candidates should be informed of the dangers of transplant tourism.

18.7 Transplant programs should define and disclose their policies for the acceptance of donor candidates identified through public solicitation.

Financial Support

18.8 Donor candidates should be informed of the availability of legitimate financial assistance for expenses from evaluation and donation.

Communication of Policies

18.9 Nondirected donors and donors participating in paired donation should be informed of the transplant program's policy on contact with the recipient and other paired donation participants at all stages in the donation process.

18.10 Transplant programs should disclose the extent of the expected postdonation program-patient relationship before donation, including whether the donor can seek medical care at the transplant center after donation.

18.11 Regional policies should ensure access to kidney replacement therapy (dialysis and/or transplantation) for donors who develop kidney failure.

Commentary

The guideline emphasizes the important ethical principle of respecting the autonomy of donors and potential kidney donors, which is chiefly operationalized through the informed consent process. We agree with the affirmations that the informed consent process should extend, when relevant, to: (1) the potential risk of transplant tourism; (2) center policies about paired exchange, including contact between donors and recipients; and (3) resources for financial assistance related to the financial burdens of kidney donation.

We also support the general concept that transplantation centers ought to make reasonable efforts to facilitate the process through which transplantation candidates identify living donors. These efforts by the transplantation center should include educating transplantation candidates and their families about outcomes for living donors and living donor transplant recipients, as well as the process for donor evaluation. We endorse the idea that donors should be educated about the center's approach to donor follow-up and how the center would handle the workup and treatment for complications plausibly related to kidney donation. We note that UNOS Policy 14.3 includes a list of more than 50 specific requirements for informed consent for donor candidates. While all requirements are to be addressed, given the lengthy and complex elements of informed consent for

kidney donors, we suggest that centers exercise some judgment as to the approach to donor informed consent, to prioritize the most relevant and important elements of the decision-making process.

Postdonation Follow-up Care

19.1 A personalized postdonation care plan should be provided before donation to clearly describe follow-up care recommendations, who will provide the care, and how often.

19.2 The following should be performed at least annually postdonation:
- Blood pressure measurement
- BMI measurement
- Serum creatinine measurement with GFR estimation
- Albuminuria measurement
- Review and promotion of a healthy lifestyle including regular exercise, healthy diet and abstinence from tobacco
- Review and support of psychosocial health well-being

19.3 Donors should be monitored for CKD, and those meeting criteria for CKD should be managed according to the 2012 KDIGO CKD Guideline.

19.4 Donors should receive age-appropriate healthcare maintenance, and management of clinical conditions and health risk factors according to clinical practice guidelines for the regional population.

Commentary

We agree with the recommendations for personalized postdonation care. In the United States, some follow-up information must be reported by the transplantation center to UNOS for 2 years postdonation.

The 2012 KDIGO CKD guideline defined CKD as "abnormalities of kidney structure or function, present for > 3 months, *with implications for health* [emphasis added]." Although studies show an increased relative risk of kidney failure among donors, it is still an uncommon occurrence. Currently, there is no evidence to support the premise that living donors with eGFR < 60 mL/min/1.73 m^2 for more than 3 months face an accelerated rate of progression to kidney failure, as long as the eGFR is stable or increasing, and there are no structural abnormalities or proteinuria/albuminuria. As such, we question whether such individuals should be treated according to the CKD guideline. In the US context, such labeling of former donors as having CKD GFR category 3 (G3) may have negative consequences on their ability to obtain health and life insurance and on their perception of well-being.

We agree that donors with eGFRs < 60 mL/min/1.73 m^2 with structural changes to the remnant kidney, histologic abnormalities, presence of albuminuria/proteinuria, abnormal urinary sediment, or electrolyte abnormalities due to tubular disorders should be treated as having CKD according to the KDIGO CKD guideline and managed accordingly.

We also agree that donors should receive age-appropriate care to maintain health and manage clinical conditions and risk factors according to clinical practice guidelines. While all donors are encouraged to adopt healthy lifestyles and follow up regularly with their primary care physician, the commentary group suggests particularly careful follow-up of medically complex donors such as those with hypertension.

Conclusions

The evaluation, selection, counseling, and care of living kidney donor candidates is a common practice in the field of transplantation in the United States. With a growing number of former living kidney donors (~5,000 to 6,000 new donors per year as of 2018), not only transplant providers but importantly, primary care practitioners will be caring for donors throughout their lives. The medical and psychosocial complexity of this population has increased over past decades; therefore, as with other clinical practice guidelines, the KDIGO clinical practice guideline on the evaluation and care of living kidney donors serves as a valuable tool that will facilitate clinical decision making with the ultimate goal of continuously advancing the field of living kidney donation. While most of the KDIGO recommendations, as well as this group's suggestions, are based on limited evidence, opinion in conjunction with sound judgment are their basis. However, the limited evidence also underscores the need for further research in the field. Regardless, the efforts put into developing these guideline recommendations are welcomed by the transplantation community.

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