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Canadian Society of Transplantation and Canadian Society of Nephrology Commentary on the 2017 KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors

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Abstract

Purpose of review: To review an international guideline on the evaluation and care of living kidney donors and provide a commentary on the applicability of the recommendations to the Canadian donor population.

Sources of information: We reviewed the 2017 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors and compared this guideline to the Canadian 2014 Kidney Paired Donation (KPD) Protocol for Participating Donors.

Methods: A working group was formed consisting of members from the Canadian Society of Transplantation and the Canadian Society of Nephrology. Members were selected to have representation from across Canada and in various subspecialties related to living kidney donation, including nephrology, surgery, transplantation, pediatrics, and ethics.

Key findings: Many of the KDIGO Guideline recommendations align with the KPD Protocol recommendations. Canadian researchers have contributed to much of the evidence on donor evaluation and outcomes used to support the KDIGO Guideline recommendations.

Limitations: Certain outcomes and risk assessment tools have yet to be validated in the Canadian donor population.

Implications: Living kidney donors should be counseled on the risks of postdonation outcomes given recent evidence, understanding the limitations of the literature with respect to its generalizability to the Canadian donor population.

Abrégé

Justification: Examiner une directive internationale sur l'évaluation et la prise en charge des donneurs vivants d'un rein et formuler un commentaire sur l'applicabilité de ces recommandations à la population des donneurs canadiens.

Sources: Nous avons révisé le guide des pratiques cliniques relatives à l'évaluation et à la prise en charge des donneurs vivants d'un rein (*Clinical Practice Guideline for Evaluation and Care of Living Kidney Donors*) de 2017 du KDIGO (*Kidney Disease: Improving Global Outcomes*) et nous l'avons comparé aux recommandations canadiennes de 2014 du Protocole de don croisé d'un rein par donneurs participants (*Kidney Paired Donation Protocol for Participating Donors*).

Méthodologie: Un groupe de travail réunissant des membres de la Société canadienne de transplantation et de la Société canadienne de néphrologie a été formé. Les membres ont été sélectionnés pour représenter tout le Canada et plusieurs sous-spécialisations relatives au don vivant d'un rein, notamment la néphrologie, la chirurgie, la transplantation, la pédiatrie et l'éthique.

Principales constatations: Plusieurs des recommandations du KDIGO s'harmonisent aux recommandations du protocole de don croisé d'un rein. Les chercheurs canadiens ont contribué en grande partie aux données sur l'évaluation des donneurs et des résultats utilisées pour appuyer les recommandations formulées dans les lignes directrices du KDIGO.

Limites: Certains résultats et outils d'évaluation des risques doivent encore être validés dans la population des donneurs canadiens.

Conclusion: Compte tenu des plus récentes données, les donneurs vivants d'un rein devraient être mis en garde concernant les risques sur leur santé post-don, tout en comprenant les limites de la littérature en ce qui concerne leur généralisabilité à la population de donneurs canadiens.

Keywords
assessment, Canada, evaluation, follow-up care, kidney transplantation, living kidney donor

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What was known before

The Canadian 2014 Kidney Paired Donation Protocol for Participating Donors was developed to harmonize assessment and acceptance criteria between the various transplant programs across Canada involved in the Kidney Paired Donation program. Despite this, there is still variability between transplant centers across the country with respect to donor acceptance criteria.

What this adds

The international 2017 Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors provided recommendations based on systematic reviews of relevant studies, including those published after 2014. Many of the recommendations are ungraded and based on expert opinion. This review highlights the recommendations from the guideline and interprets them within the Canadian context.

Introduction

In 2006, the Canadian Council for Donation and Transplantation (CCDT) held its sixth forum with the goal to enhance living donation in Canada.[1] Recognizing the variability across transplant programs in the nation, the 2014 Kidney Paired Donation (KPD) Protocol harmonized assessment and acceptance criteria for participating donors.[2] In 2017, the Kidney Disease: Improving Global Outcomes (KDIGO) published the Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors.[3] This international collaboration included Canadian experts on the guideline committee and the recommendations were based on critically appraised studies evaluated by the Evidence Review Team (ERT).[3] Where applicable, recommendations were graded based on the quality of the evidence (Table 1). For topics where there was no or insufficient evidence in the literature, the KDIGO working group relied on expert opinion and the recommendations were not graded.

This Canadian commentary represents another national collaboration around living kidney donation, in conjunction with the Canadian Society of Transplantation (CST) and the Canadian Society of Nephrology (CSN). The goal of this working group was to review the 2017 KDIGO Living Kidney Donor Guideline, evaluate its relevance and applicability to Canadian donors, compare the recommendations to the 2014 KPD Protocol, and highlight the impactful research led by Canadian investigators within this area. We considered many Canadian aspects, including our ethnic diversity, universal healthcare system, and our vast and variable geography and landscape. This review is intended to be used with the comprehensive KDIGO Living Kidney Donor Guideline to support shared decision-making in the evaluation of living kidney donor candidates and the care of past and future living kidney donors in Canada.

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Table 1. KDIGO Nomenclature and Description for Grading Recommendations and Final Grade for Overall Quality of Evidence.

	Implications		
Grade[a]	Patients	Clinicians	Policy
Level 1 'We recommend'	Most people in your situation would want the recommended course of action and only a small proportion would not	Most patients should receive the recommended course of action	The recommendation can be evaluated as a candidate for developing a policy or a performance measure
Level 2 'We suggest'	The majority of people in your situation would want the recommended course of action, but many would not	Different choices will be appropriate for different patients. Each patient needs help to arrive at a management decision consistent with her or his values and preferences	The recommendation is likely to require substantial debate and involvement of stakeholders before policy can be determined

Grade	Quality of evidence	Meaning
A	High	We are confident that the true effect lies close to that of the estimate of the effect
B	Moderate	The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
C	Low	The true effect may be substantially different from the estimate of the effect
D	Very low	The estimate of effect is very uncertain, and often will be far from the truth

Note. Reproduced from Lentine et al[3] KDIGO Clinical Practice Guideline on the Evaluation and Care of Living Kidney Donors. KDIGO = Kidney Disease: Improving Global Outcomes.

[a]The additional category 'Not Graded' is used, typically, to provide guidance based on common sense or where the topic does not allow adequate application of evidence. The most common examples include recommendations regarding the monitoring intervals, counseling, and referral to other clinical specialists. Ungraded recommendations are generally written as simple declarative statements, but are not meant to be interpreted as being stronger recommendations than Level 1 or 2 recommendations.

Review Process

A working group was formed consisting of members from the CST and/or CSN. Members were selected to have representation from across Canada and in various subspecialties related to living kidney donation, including nephrology, surgery, transplantation, pediatrics, and ethics. Two co-chairs were selected to oversee the Canadian commentary on the 2017 KDIGO Living Kidney Donor Guideline. Each section was designated to one or more members of the working group based on their clinical expertise and interest in that area. Overall consensus was reached among all members. The commentary was reviewed by the CST and CSN executive, prior to peer review and final approval.

Commentary on Chapter 1: 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.

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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.

The recommendations in Chapter 1 are based on expert opinion and are "Not Graded." In general, they align with the KPD Protocol's ethical principles. Both the 2017 KDIGO Guideline and 2014 KPD Protocol emphasize the importance of respecting donor autonomy, the duty to protect the living donor candidate from anticipated harm from donation, and to proceed with nephrectomy only after informed and freely given consent.[2,3] The Chapter 1 recommendations are clear, reasonable, ethically based, and noncontentious. The KPD Protocol does not detail donor follow-up and the KDIGO recommendation to formulate a donor follow-up plan is an important addition (see Chapter 19). Currently, there is no national standard for living kidney donor follow-up, in part, due to the lack of existing evidence.

A central component of the KDIGO Chapter 1 recommendations is establishing postdonation risk for each donor.[3] Providing living kidney donor candidates with a numeric assessment of their individual long-term risk is ideal but in practice is limited by the lack of validated risk assessment tools. To assist with this, the KDIGO working group developed a tool to estimate the 15-year and lifetime incidence of end-stage renal disease (ESRD) in the absence of donation based on various demographic and health characteristics (http://www.transplantmodels.com/esrdrisk/).[4] There are limitations and considerations with this risk assessment tool. First, the tool was developed using population-level incidence rates of ESRD and mortality from the United States and has not been adapted to the Canadian population. The tool is also limited in its ability to confidently predict long-term risk (ie, beyond 15 years postdonation) for younger donors and ethnically diverse donors, including Indigenous populations. Lastly, the model does not take into account the donor candidate's genetic relationship with the recipient, which is a key factor for long-term risk.[5]

The KDIGO Chapter 1 recommendations also include having each transplant center set a quantitative threshold of "acceptable risk."[3] In practice, this also poses difficulty when the absolute individual risk assessment has wide confidence intervals (CI). Instead of relative risk, absolute contraindications modified by age and donor-recipient genetic relationship may be preferable. In addition to this, if transplant centers establish a uniform acceptance threshold for all donor candidates, they lose the flexibility to account for potential psychosocial benefits and harms that could occur to some candidates if they are beyond the threshold. For example, a nondirected donor would be considered equally as a directed donor to their spouse or child. There are reasonable ethical arguments on each side of this principle. Nonetheless, we agree that each center should have a transparent threshold for donor risk estimated using the best tools available beyond which they would not accept donation.

Commentary on Chapter 2: 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.

The recommendations in Chapter 2 are based on expert opinion and are "Not Graded." The recommendations pertaining to informed consent are clear and reasonable. They are in alignment with the KPD Protocol's ethical principles of proceeding with a living donor nephrectomy with the living donor candidate's informed and freely given consent, to respect the autonomy of the living donor candidate, and to be transparent with respect to the knowledge of health risks associated with living donation.[2] The KDIGO Guideline places more emphasis than the KPD Protocol on obtaining informed consent for the evaluation process, not just the donor nephrectomy. The evaluation process includes risks of discovery such as health conditions or misattributed biological relationships. For example, misattributed paternity is estimated to occur in up to 0.5% of Canadian living kidney donor evaluations and transplant centers should have established protocols on how this information is handled (Table 2).[8] As well, while both the KDIGO Guideline and KPD Protocol discuss having separate evaluation teams for the living donor candidate and the intended recipient, the KPD Protocol does not explicitly discuss that informed consent should be obtained in the absence of individuals who could influence the decision, such as the intended recipient. Lastly, the KPD Protocol does not address substitute decision makers, whereas the KDIGO Guideline recommends against their use except under extraordinary circumstances.[3] We recommend that the KPD Protocol consider these issues in their recommendations.

Commentary on Chapter 3: 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.

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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 their 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.

The recommendations in Chapter 3 are based on expert opinion and are "Not Graded." The recommendations for evaluation and counseling on issues relating to compatibility and options for incompatible pairs are clear and consistent with program norms in Canada, although the specifics of this have not been addressed by the Canadian KPD Protocol.

Since Canada has a national KPD program, counseling should highlight the benefits of enrolment in the national KPD program versus provincial or local exchanges, yet also highlight the increased requirement for travel for donors across Canada in the national program. In addition, donor candidates should be counseled on the anticipated expenses associated with KPD and the availability of provincial programs that offer partial re-imbursement for travel expenses incurred by the donor and a travel companion. Future considerations for enrolment of compatible pairs in KPD algorithms should also be considered and may also be offered to selected donors, particularly if there is an anticipated advantage to the recipient.

Commentary on Chapter 4: 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 before donation to reduce their risk of perioperative complications, and commit to lifelong abstinence to prevent long-term complications.

The recommendations in Chapter 4 are based on expert opinion and are "Not Graded." The first recommendation addressing preoperative risk assessment uses sound clinical practice, including a history and physical examination, and applies general population guidelines for preoperative evaluation to minimize surgical risks to the donor.[3] We agree with this recommendation and it aligns with the KPD Protocol, despite variable practices in Canada in preoperative donor evaluations.[2] Given the altruistic nature of the surgery, some programs advocate additional testing (eg, nuclear stress testing) that would usually not be considered for a similar patient undergoing another operation. Given the lack of direct evidence in the donor population, there will always be some degree of practice variation in preoperative assessment but adhering to appropriate guidelines (eg, American Heart Association, Canadian Heart and Stroke Foundation) seems appropriate.[51]

The second recommendation suggests that donor candidates should quit smoking at least 4 weeks before donation and continue smoking abstinence lifelong.[3] We agree with this recommendation, and it is consistent with the KPD Protocol.[2] While the KDIGO recommendation provides a timeline, the KPD Protocol advises donors to stop smoking before the donation surgery, without a specified timeline. The optimal time predonation to quit smoking is not known, but it seems reasonable to quit as early as possible before surgery to maximize the perioperative benefits.

Commentary on Chapter 5: 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 GFR should be estimated from serum creatinine ($eGFR_{cr}$) for initial assessment, following recommendations from the KDIGO 2012 Chronic Kidney Disease (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 chromium-51-ethylnediamine tetraceteic acid (^{51}Cr-EDTA), urinary or plasma clearance of iohexol, or urinary clearance of technetium-99m-diethylene-triamine-pentaacetate (^{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 ($eGFR_{cr}$)

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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)

Most of the recommendations in Chapter 5 are based on expert opinion and are "Not Graded," except for recommendation 5.10 which is graded as 2C. Having sufficient kidney function is the *sine qua non* for being a living kidney donor. Unfortunately, estimates of glomerular filtration rate (eGFR) are numerous and imperfect. Even with standardized laboratory methods, measurements of serum creatinine are subject to variation (analytical and intra-patient day-to-day) and so a single measurement is insufficient. Multiple measurements for the initial screen should be considered prior to further full evaluation.[52] The KDIGO Guideline recommends eGFR assessment using the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation to screen for kidney function adequacy.[3,53] The KPD Protocol recommends 2 eGFR measurements using either the CKD-EPI or Cockcroft-Gault.[2] For most Canadians, including those of diverse ethnic backgrounds, eGFR by the CKD-EPI equation is practical and accurate.

Given the need for highly accurate GFR assessment for donor candidate evaluation, confirmatory testing is necessary.[54] The confirmatory measure is also controversial as not all measurements in recommendation 5.4 are considered equivalent. If being conservative (avoiding overestimation), then creatinine clearances, plasma clearances of exogenous markers, and radioactive tracer scintillation counting by nuclear medicine techniques may not be the best confirmatory tests.[55] Few centers use the gold standard of urinary clearance of exogenous markers due to its limitations, including time, expense, and day-to-day variation. Moreover, there is no evidence that using exogenous urinary clearance methods improves decision-making. The KPD Protocol requires two 24-hour urine studies measure creatinine clearance and/or 1 measured GFR to confirm adequate function.[2]

The KDIGO Guideline recommends an eligibility criterion of a GFR $\geq$90 mL/min/1.73 m^2, which is conservative given that the CKD-EPI equation underestimates kidney function. Likewise, a GFR $<$60 mL/min/1.73 m^2 is a reasonable cut point to deny donation, although historically some centers have done so inadvertently.[56] As shown by the KDIGO ESRD risk assessment tool, younger individuals have a higher lifetime cumulative risk of ESRD compared to older individuals.[4] For example, a 20-year-old individual with an eGFR of 90 mL/min/1.73 m^2 has a higher lifetime risk of ESRD, in the absence of donation, than a 60-year-old individual with an eGFR of 60 mL/min/1.73 m^2. Personalized estimates of postdonation ESRD risk have been developed for the U.S. population (http://www.transplantmodels.com/donesrd/), but have not been studied and validated in the Canadian donor population.[57] In contrast, the KPD Protocol recommends age-dependent eGFR cut-offs for donor acceptability, but the KDIGO Guideline did not endorse this either because there is a lack of evidence or need to do so with their ESRD risk assessment tool.[2-4]

In focus groups involving 56 living kidney donors from a single center in British Columbia, donors identified their own postdonation kidney function and kidney failure among their top 5 most important outcomes (Table 2).[50] With respect to counseling, living kidney donor candidates should be informed of their risk of ESRD, in the absence and presence of donation. While this risk may be comparatively higher following donation, the absolute risk for most donors is small ($<$0.5% over 15 years).[58] Nonetheless, the lifetime risk of ESRD may be elevated, particularly for younger donors, justifying the need for increased surveillance postdonation (see Chapter 19).

Table 2. Summary of Studies Involving Canadian Living Kidney Donors.

Study	Design/setting	LKD (n)	Control group (n)	Follow-up	Key findings
Evaluation					
Zimmerman et al[6]	Retrospective/survey Ontario (1 center) 1991-1996	144	N/A	N/A	• Female vs. male donors: o Overall: 28.3% vs. 20.3% (OR 1.54; $P = .027$) o First-degree relatives: 26.9% vs. 22.2% (OR 1.29; $P = .229$) o Spouses: 36.0% vs. 6.5% (OR 8.16; $P = .003$)
Karpinski et al[7]	Cross-sectional study Canada (4 centers) N/A	180	N/A	N/A	• Reason for exclusion: o Positive cross-match: 33% (59/180) o Blood group incompatibility: 22% (40/180) o Hypertension: 10% (18/180) o Proteinuria: 7% (13/180)
Young et al[8]	Retrospective/survey Canada (CORR) 1992-2006	701	N/A	N/A	• 5.7% (40/701) of misattributed paternity involving fathers and children • True prevalence of misattributed paternity may be ~2.5% or 0.25-0.50% of all living kidney donations • Transplant centers varied in their policies/practices about disclosure of this information
Hizo-Abes et al[9]	Cross-sectional survey Ontario (1 center) 2008	43	73 recipients	N/A	• Agree that recipient's information should be shared with the donor: 86% vs. 80% • Agree that donor's information should be shared with the recipient: 97% vs. 89%
Dunsmore et al[10]	Retrospective Manitoba (1 center) 2008	372	N/A	N/A	• Reason for exclusion in donors for Aboriginal vs. Caucasian recipient candidates: o Medical: 23% vs. 21% (P = not significant) o Immunologic: 21% vs. 38% o Nonmedical: 50% vs. 30% ($P < .0001$) o Another donor: 5% vs. 11%
Perlis et al[11]	Retrospective Ontario (1 center) 2002-2008	467	N/A	N/A	• Reason for exclusion: o Initial health screen: 50.2% (121/241) o Multidisciplinary rounds: 10.3% (48/467) o Urologic: 75.0% (36/48) o Medical: 18.7% (9/48) o Malignancy: 4.2% (2/48) o Social: 2.1% (1/48)

(continued)

Table 2. (continued)

Study	Design/setting	LKD (n)	Control group (n)	Follow-up	Key findings
Habbous et al[12]	Prospective Canada/Australia (16 centers) 2009-2015	849	N/A	2.3 weeks [1.3-7.5]	• Total duration of LKD evaluation (months): ○ Start to donation: 10.3 [6.5-16.7] ○ Start to approval: 7.9 [4.6-14.1] ○ Approval to donation: 0.7 [0.3-2.4] ○ First to last consultation: 3.0 [1.0-6.3]
Hanson et al[13]	Focus groups British Columbia/Australia (3 centers) 2015-2016	123	N/A	3.6 years (3.1)	• Themes reflecting donors' experiences of evaluation: ○ Perseverance (eg, emotional investment) ○ Undeterred by low risks (eg, inherent invincibility) ○ Mental preparation (eg avoiding regret) ○ Underlying fears for health (eg, unsettling uncertainty) ○ System shortfalls (eg, questioning risk information) ○ Lifestyle interference (eg, living in limbo)
Financial considerations					
Yang et al[14]	Undercover Canada 2007-2008	N/A	N/A	N/A	• LKD vs. nondonor control profiles: ○ Annual premium quote for life insurance: $191 [145-962] vs. $209 [151-984] ($P = .89$) ○ Time spent on the phone with agent: 7.0 min [5.0-9.8] vs. 9.5 min [7.0-11.0] ($P = .046$)
Klarenbach et al[15]	Prospective Canada (7 centers) 2004-2008	100	N/A	1 year	• Cost, lost pay: $2144 (4167) • Cost, other expenses: $1780 (2504) • Cost, overall: $3268 (4704), 1/3 >$3000, 15% >$8000
Habbous et al[16]	Retrospective Ontario (5 centers) 2004-2014	1099	4396 healthy nondonors	1 year	• Mean incremental healthcare costs: ○ Cost, evaluation period: $3596 (95% CI = 3350-3842; $P < .0001$) ○ Cost, perioperative period (donation-30 days): $11,694 (95% CI = 11,415-11,973; $P < .0001$) ○ Cost, postdonation follow-up period (30 days-1 year): $1011 (95% CI = 793-1230; $P < .0001$) ○ Cost, overall: $16,290 (95% CI = 15,814-16,767; $P < .0001$)
Przech et al[17]	Prospective Canada (12 centers) 2009-2014	821	N/A	3 months	• Cost, out-of-pocket: $1254 [75th percentile: 2589] • Cost, low productivity: $0 [1908] • Cost, total: 25% >$5500
Barnieh et al[18]	Case study Ontario 2009-2014	159	N/A	N/A	• Cost incurred—Cost reimbursed: $3115 • Out-of-pocket: $1313 • Lost income: $1802

(continued)

Table 2. (continued)

Study	Design/setting	LKD (n)	Control group (n)	Follow-up	Key findings
Kidney Paired Donation Program					
Cardinal et al[19]	Retrospective Quebec (1 center) 2005-2012	N/A	N/A	N/A	• A living organ donation team and participating in KPD: ○ Living donor kidney transplants: □ 50 to 73 (IRD 0.029, 95% CI = 0.003-0.056) ○ Donor candidates contacting the program: □ 191 to 304 (IRD 0.143, 95% CI = 0.091-0.196)
Hendren et al[20]	Survey British Columbia (1 center) 2001-2009	86	N/A	N/A	• 93% (78/86) of donors indicated a willingness to participate in KPD program • Increase willingness: ○ Reimbursement for expenses ○ Advantage to the recipient ○ Improved efficiency of KPD
Preoperative imaging					
Feifer et al[21]	N/A Quebec (1 center) N/A	48	N/A	N/A	• 48% (23/48) of donors had aberrant vasculature at laparoscopy • Accurate (n = 14) vs. inaccurate (n = 9) preoperative CT angiography: ○ Accuracy: 85% ○ Arterial imaging: Sensitivity 65%, specificity 100% ○ Venous imaging: Sensitivity 50%, specificity 100%
Neville et al[22]	Prospective Ontario (1 center) 2000-2002	27	N/A	N/A	• Selective renal angiography vs. donor nephrectomy: ○ Sensitivity 86%, specificity 95% ○ Positive predictive value 75%, negative predictive value 97% • MRA vs. donor nephrectomy: ○ Sensitivity 64%, specificity 88% ○ Positive predictive value 58%, negative predictive value 90%
Monroy-Cuadros et al[23]	Retrospective Alberta (1 center) 2002-2006	66	N/A	N/A	• 12% (8/66) of donors had an accessory renal artery at laparoscopy • Accurate (n = 6) vs. inaccurate (n = 2) preoperative MRA: ○ Negative predictive value: 97% ○ False-negative rate: 25% ○ Sensitivity: 75%, specificity: 100%

(continued)

Table 2. (continued)

Study	Design/setting	LKD (n)	Control group (n)	Follow-up	Key findings
Surgical outcomes					
Pace et al[24]	Cost-utility analysis Ontario (1 center) 2000	21	N/A	N/A	• Open (n = 10) vs. laparoscopic (n = 11) donor nephrectomy: o Cost: $9853.70 vs. $10,317.40 o QALY: 0.7062 vs. 0.7683 o Societal ICER: $7471.11/QALY
Pace et al[25]	Cost-utility analysis Ontario (1 center) 2000-2001	61	N/A	N/A	• Open (n = 27) vs. laparoscopic (n = 34) donor nephrectomy: o Cost: $12,631.91 vs. $11,170.71 o QALY: 0.6585 vs. 0.7247 o Societal ICER: $2231.61/QALY
Bettschart et al[26]	Prospective/retrospective Quebec (1 center) 1993-2001	34	N/A	Open: 55.7 months [N/A] (max 102 months)	• Open (n = 17) vs. laparoscopic (n = 17) donor nephrectomy: o Right nephrectomy: 14 vs. 13 o Operative time: 167 vs. 198 min ($P \leq .01$) o Length of stay: 8.2 vs. 4.6 days ($P \leq .01$) • Left (n = 4) vs. right (n = 13) laparoscopic donor nephrectomy: o Operative time: 207 vs. 182 min
Bergman et al[27]	Retrospective Quebec (1 center) 2000-2004	52	N/A	N/A	• Fluid-load (>10 mL/kg/h; n = 24) vs. fluid-restriction (<10 mL/kg/h; n = 28) laparoscopic donor nephrectomy: o Postoperative creatinine: 117.5 vs. 121.5 μmol/L ($P = 0.8$) o Complications: 4.2% vs. 7.1% ($P = .9$)
Salazar et al[28]	Retrospective Alberta (1 center) 2001-2004	50	N/A	20 months (9) (max 32 months)	• Open (n = 15) vs. laparoscopic (n = 11) vs. hand-assisted (n = 24) donor nephrectomy: o Surgical time: 188 vs. 213 vs. 235 min ($P < .001$) o Hospital stay: 5 vs. 3 vs. 4 days ($P < .001$)
Bergman et al[29]	Prospective/retrospective Quebec (1 center) 1998-2004	92	N/A	N/A	• Open (n = 33) vs. laparoscopic (n = 59) donor nephrectomy: o Complications: 21% vs. 10% ($P = .2$) o Length of stay: 5 vs. 3 days ($P < .001$)
Rampersad et al[30]	Retrospective Manitoba (1 center) 2007-2014	183	N/A	N/A	• Mini-open (n = 89) vs. laparoscopic (n = 94) donor nephrectomy: o Estimated blood loss: 347.8 vs. 90.3 cc ($P < .0001$) o Intraoperative complication rate: 11 vs. 4 ($P = .0253$) o Operative time: 108.4 vs. 165.9 min ($P < .0001$) o Length of hospital stay: 3.3 vs. 2.4 days ($P < .0001$) o Discharge creatinine: 110.3 vs. 97.7 μmol/L ($P < .0001$)

(continued)

Table 2. (continued)

Study	Design/setting	LKD (n)	Control group (n)	Follow-up	Key findings
Follow-up care					
Manera et al[31]	Focus groups British Columbia (1 center) Australia (2 centers) 2015-2016	123	N/A	(max 16 years)	• Experiences and expectations of LKD regarding follow-up and self-care after donation: o Lacking identification as a patient (eg, invincibility and confidence in health) o Empowerment for health (eg, self-advocacy) o Safety net and reassurance (eg, continuity/rapport) o Neglect and inattention (eg, hospital abandonment)
Lam et al[32]	Retrospective Alberta (2 centers) 2002-2014	534	N/A	7 years [3-10] (max 13 years)	• 25% of LKD had all 3 markers of care (physician visit, serum creatinine, albuminuria measurement) in each year of follow-up • Adherence to physician visits was higher than serum creatinine or albuminuria measurements (67% vs. 31% vs. 28%)
Medical outcomes (donors vs. nondonors)					
Stothers et al[33]	Survey British Columbia (1 center) 1997-2001	98	243 Friends/family of waitlist candidates	N/A	• Living donor kidney transplants (donors vs. controls): o Knowledge test results: 4.7 vs 2.7 ($P = .000$) o Belief test results: 43.1 vs. 38.5 ($P = .000$)
Gourishankar et al[34]	Prospective Alberta (1 center) 2002-2004	51	N/A	1 year	• Loss of kidney function by day 2 postnephrectomy: ~33-43 mL/min (~30%-35%) • Cystatin C was the only marker to detect changes in kidney function between day 2 and month 1 and day 2 and year 1 (compared to serum creatinine, 24-hour creatinine clearance, Cockcroft-Gault, and MDRD) but there was no advantage to preoperative assessment of kidney function or long-term monitoring
Young et al[35]	Cross-sectional survey Canada (2 centers) 2006	112	111 recipients 51 transplant professionals	N/A	• Willing to accept greater than actual risk for healthy nondonors (potential donors vs. potential recipients vs. transplant professionals): o Hypertension: 78% vs. 34% vs. 68% ($P < .0001$) o Cardiovascular disease: 71% vs. 27% vs. 51% ($P < .0001$) o Kidney failure: 77% vs. 38% vs. 50%
Garg et al[36]	Retrospective Ontario 1993-2005	1278	6359 healthy nondonors	6.2 years (3.2) (max 13 years)	• Death or major cardiovascular event: 1.3% vs. 1.7% (2.0 vs. 2.7 events/1000 person-years; HR 0.7, 95% CI = 0.4-1.2; $P = .225$) • Hypertension: 16.3% vs. 11.9% (29.1 vs. 20.6 events/1000 person-years; HR 1.4, 95% CI = 1.2-1.7; $P < .001$)

(continued)

Table 2. (continued)

Study	Design/setting	LKD (n)	Control group (n)	Follow-up	Key findings
Prasad et al[37]	Prospective Ontario (1 center) 2004-2007	58	N/A	6 months	• Pre- vs. postdonation: ○ 24-hour systolic blood pressure: 118.9 vs. 118.1 mmHg ($P = .77$) ○ eGFR: 91.9 vs. 61.6 mL/min/1.73 m^2 ($P < .0001$)
Prasad et al[38]	Prospective Ontario (1 center) 2004-2007	51	N/A	12 months	• Dippers (n = 25) vs. nondippers (n = 16) at 12 months postdonation: ○ 24-hour systolic blood pressure: 111.4 vs. 114.3 mmHg ($P = .384$) ○ Serum creatinine: 97.9 vs. 97.7 μmol/L ($P = .810$) ○ 24-hour urine protein: 0.139 vs. 0.111 g/day ($P = .360$)
Storsley et al[39]	Retrospective Manitoba (1 center) 1971-2007	38 Aboriginal donors	76 Caucasian donors	14 years (N/A)	• Hypertension: 42% vs. 19% (OR 6.3, 95% CI 1.8-22.1; $P = .004$) • Diabetes: 19% vs. 2% ($P = .005$) • eGFR: 77±17 vs. 67±13 mL/min/1.73 m^2 (Mean difference 5.9, 95% CI = -0.6 to 12.5; $P = .07$)
Clemens et al[40]	Retrospective Canada (7 centers) Scotland (1 center) Australia (1 center) 2004-2008	203	104 healthy nondonors	5.5 years [3.8-8.4]	• Quality of life (15D): 0.93 (0.09) vs. 0.94 (0.06) ($P = .55$)
Lam et al[41]	Retrospective Ontario (5 centers) 1992-2009	2027	20,270 healthy nondonors	6.9 years [N/A] (max 17.7 years)	• Acute dialysis: 0.05% vs. 0.07% (6.5 vs. 9.4 events/100,000 person-years; HR 0.58, 95% CI = 0.08-4.47; $P = .61$)
Garg et al[42]	Retrospective Ontario (5 centers) 1992-2009	2028	20,280 healthy nondonors	6.8 years [3.7-10.9] (max 17.7 years)	• Death or major cardiovascular event: 2.1% vs. 3.0% (2.8 vs. 4.1 events/1000 person-years; HR 0.66, 95% CI = 0.48-0.90; $P = .008$) • Death-censored major cardiovascular event: 1.3% vs. 1.4% (1.7 vs. 2.0 events/1000 person-years; HR 0.85, 95% CI = 0.57-1.27; $P = .43$)
Young et al[43]	Cross-sectional Canada (7 centers) Scotland (1 center) Australia (1 center) 2004-2008	198	98	5.3 years [3.3-8.4]	• Serum fibroblast growth factor 23: 38.1 vs. 29.7 pg/mL ($P < .001$) • Renal fractional excretion of inorganic phosphate: 17.8% vs. 12.3% ($P < .001$) • Serum phosphate: 0.97 vs. 1.02 mmol/L ($P = .03$) • Plasma intact parathyroid hormone: 5.7 vs. 5.0 pmol/L ($P = .03$)

(continued)

Table 2. (continued)

Study	Design/setting	LKD (n)	Control group (n)	Follow-up	Key findings
Garg et al[44]	Retrospective Ontario (5 centers) 1992-2009	2015	20,150 healthy nondonors	6.9 years [3.8-11.0] (max 17.7 years)	• Fragility fracture: 16.4 vs. 18.7 events/10,000 person-years (RR 0.88, 95% CI = 0.58-1.32; *P* = .5) • Prescription for bisphosphonate: 17.1% vs. 15.2% (*P* = .4)
Thomas et al[45]	Retrospective Ontario (5 centers) 1992-2009	2019	20,190 healthy nondonors	8.8 years [5.6-12.9] (max 19.7 years)	• Kidney stones with surgical intervention: 8.3 vs. 9.7 events/10,000 person-years (RR 0.85, 95% CI = 0.47-1.53; *P* = .58) • Hospitalization with kidney stones: 12.1 vs. 16.1 events/10,000 person-years (RR 0.75, 95% CI = 0.45-1.24; *P* = .27)
Thomas et al[46]	Retrospective Ontario (5 centers) 1992-2009	2009	20,090 healthy nondonors	8.8 years [5.6-12.9] (max 19.7 years)	• Gastrointestinal bleeding: 18.5 vs. 14.9 events/10,000 person-years (Rate of hospitalization: RR 1.24, 95% CI = 0.85-1.81; *P* = .26; Time to first hospitalization: HR 1.25, 95% CI = 0.87-1.79; *P* = .236)
Garg et al[47]	Retrospective Ontario (5 centers) 1992-2009	85	510 healthy nondonors	11.0 years [N/A] (max 20.0 years)	• Gestational hypertension or preeclampsia: 11% vs. 5% (OR 2.4, 95% CI = 1.2-5.0; *P* = .01) • Gestational hypertension: 5% vs. 2% (OR 2.5, 95% CI = 0.9-6.5; *P* = .06) • Preeclampsia: 6% vs. 3% (OR 2.4, 95% CI 1.0-5.6; P = 0.05)
Lam et al[48]	Retrospective Ontario (5 centers) 1992-2010	1988	19,880 healthy nondonors	8.8 years [N/A] (max 20.8 years)	• Gout diagnosis: 3.4% vs. 2.0% (3.5 vs. 2.1 events/1000 person-years; HR 1.6, 95% CI = 1.2-2.1; *P* < .001) • Prescription for allopurinol/colchicine: 3.8% vs. 1.3% (OR 3.2, 95% CI = 1.5-6.7; *P* = .002)
Ordon et al[49]	Retrospective Ontario (5 centers) 1992-2010	2119	21,190	9.9 years [6.6-14.3] (max 21.7 years)	• Nephrectomy: 0% vs. 0.18% (0 vs. 1.78 events/10,000 person-years; *P* = .037)
Hanson et al[50]	Focus groups British Columbia (1 center) 2015-2016	56	N/A	3.6 years (3.1) (max 16 years)	• Most important outcomes to donors (0-1, 1=most): • Kidney function (0.57), Surgical complications (0.29), Kidney failure (0.26), Life satisfaction (0.20), Time to recovery (0.19)

Note. Data are presented as mean (*SD*) or median [IQR]. LKD = living kidney donors; IQR = interquartile range; OR = odds ratio; CORR = Canadian Organ Replacement Registry; CI = confidence interval; IRD = incidence rate difference; KPD = Kidney Paired Donation; CT = computed tomography; MRA = magnetic resonance angiography; QALY = quality-adjusted life year; ICER = incremental cost-effectiveness ratio; eGFR = estimated glomerular filtration rate; MDRD = Modifications of Diet in Renal Disease; N/A = not applicable/available; RR = rate ratio; SD = standard deviation; HR = hazard ratio.

Commentary on Chapter 6: 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.

The recommendations in Chapter 6 are based on expert opinion and are "Not Graded." The KDIGO Guideline recommends that predonation albuminuria should be evaluated using a 2-stage testing approach, with urine albumin-to-creatinine ratio (ACR) as the initial test and albumin excretion rate (AER) or repeat ACR as the confirmatory test.[3] These recommendations are reflective of a strong body of evidence from general population studies demonstrating an association between albuminuria and an increased risk of ESRD, cardiovascular disease, and death.[4,59,60] The KPD Protocol recommends that predonation proteinuria be evaluated using a 24-hour urine collection for total protein and ACR.[2] We agree with the KDIGO recommendations that the assessment of albuminuria, rather than proteinuria, is the preferred approach in living kidney donors. Albuminuria is a more sensitive marker of kidney damage than proteinuria and is one of the earliest markers of glomerular disease, often occurring prior to the decline in kidney function. As such, the KPD Protocol has been revised to recommend a two-stage testing approach for albuminuria in living kidney donors similar to the KDIGO Guideline.

The KDIGO Guideline acceptance criteria for albuminuria in living kidney donors align with the KDIGO Chronic Kidney Disease (CKD) Guideline definition and classification.[3,61] Donors with an AER of <30 mg/day, which is considered normal or mildly increased, are acceptable for donation. The risk to living kidney donors with predonation albuminuria of >30 mg/day is unclear. Therefore, the KDIGO Guideline recommends that living kidney donors with albuminuria of 30 to 100 mg/day be accepted on a case-by-case basis, based on the individual risk profile of the donor candidate. The KDIGO Guideline recommends that individuals with >100 mg/day of albuminuria should not donate. Accounting for the different methods for assessment of albuminuria and proteinuria, the albuminuria thresholds for donor acceptance in the KDIGO Guideline are similar to the proteinuria thresholds in the KPD Protocol. However, the KPD Protocol has also been modified to align with the albuminuria acceptance thresholds in the KDIGO Guideline. In light of donor safety, we agree with the KDIGO Guideline predonation albuminuria recommendations for donor selection. It is important to note that the recommendations are largely based on data from general population studies. The association between predonation albuminuria and postdonation outcomes needs further study to better define acceptance thresholds for living kidney donors.

Commentary on Chapter 7: 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 the following:
- 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.

The recommendations in Chapter 7 are based on expert opinion and are "Not Graded." Overall, the KDIGO Guideline and KPD Protocol are similar in their recommendations on the assessment and selection of donor candidates with predonation microscopic hematuria. The KPD Protocol recommends kidney biopsy following a negative cystoscopy in the assessment of persistent hematuria in donor candidates.[2] For younger donors, cystoscopy is controversial given the low risk of malignancy in this population.[62]

The KDIGO Guideline recommends that donor candidates with hematuria from a reversible cause that resolves (eg, treated infection) may be eligible for donation.[3] The KPD Protocol is more specific in its eligibility criteria, including potential donors with thin basement membrane disease when all other testing is normal and those with hematuria who have no abnormality on imaging, cystoscopy, and kidney biopsy.[2] In addition to IgA nephropathy, the KPD Protocol also recommends exclusion of donor candidates with Alport syndrome.[2,63]

Commentary on Chapter 8: 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.

The recommendations in Chapter 8 are based on expert opinion and are "Not Graded." We concur with these recommendations. The Canadian Urological Association (CUA) guidelines strongly advocate for performing two 24-hour urine collections as part of the metabolic evaluation, noting that a second collection will change management for a significant number of patients.[64,65] In addition to this, the CUA guidelines recommend measuring vitamin D levels in those with elevated parathyroid hormone levels and/or low normal serum calcium.[64]

The KPD Protocol does not specify the number of 24-hour urine collections needed but does recommend that all donor candidates with stones should be assessed by an urologist.[2] In Canada, many centers have kidney transplant surgeons who are also urologists. This may not be necessary for the majority of donor candidates who have asymptomatic, unilateral, small (<15 mm) stones found incidentally on imaging as these patients likely have a low risk of recurrence, particularly if the metabolic workup is negative.[3] Donor candidates with a history of predonation kidney stones should be counseled on modifiable risks, which may affect the candidate's ability to donate. One study from Ontario compared 2019 living kidney donors with 20,190 matched, healthy nondonors without a history of kidney stones (Table 2).[45] Reassuringly, after a follow-up of 8 years, there was no significant difference between the 2 groups with respect to the rate of hospitalizations for kidney stones or the rate of kidney stones treated with surgical intervention.[45]

Commentary on Chapter 9: 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.

The recommendations in Chapter 9 are based on expert opinion and are "Not Graded." The decrement in GFR associated with living donor nephrectomy is associated with a rise in serum uric acid levels,[66,67] which may in turn increase the incidence of gout. Whether this occurs is unclear. In a retrospective study of 1988 living kidney donors and 19,880 matched, healthy nondonors from Ontario, the incidence rate of gout and incidence of

medications used to treat gout were higher in donors than nondonors (Table 2).[48] The KPD Protocol does not make any recommendations regarding the assessment or counseling of hyperuricemia or gout. We recommend that donor candidates be asked about prior episodes of gout. The most compelling reason to do so in donor candidates may be the potential for associated nonsteroidal anti-inflammatory drug (NSAID) use postdonation. Given the uncertainty surrounding the role of donation in future episodes of gout, transplant programs may elect to defer lifestyle and dietary counseling to reduce the risk of hyperuricemia and gout to the primary care physician.

Commentary on Chapter 10: 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)

Most of the recommendations in Chapter 10 are based on expert opinion and are "Not Graded," except for recommendation 10.6 which is graded as 2D. The KDIGO Guideline makes 6 recommendations regarding blood pressure in the living kidney donor candidate. The first 2 recommendations deal with the evaluation and measurement of blood pressure. At the time the KDIGO Guideline was published, the recommendations were very similar to the KPD Protocol. Recently, Hypertension Canada (previously known as Canadian Hypertension Education Program, CHEP) revised its guideline for the evaluation and diagnosis of hypertension.[68] Rather than office readings using auscultation, Hypertension Canada recommends measuring blood pressure using a validated digital oscillometric device (eg, BpTRU, OMRON HEM 907XL, MicroLife WatchBP Office, or PRO BP2400) as the preferred method.[68] These devices take an automated series of measurements while the patient is alone in a quiet room (usually 3-6 measurements spaced 1 minute apart over 4-7 minutes) with averaging of the results. This technique has repeatedly been demonstrated to correlate more closely with daytime ambulatory blood pressure measurement (ABPM) compared to manual office measurements and is already widely used in Canada.[69,70] If blood pressure is normal (systolic blood pressure $<$135 mmHg and diastolic blood pressure $<$85 mmHg) using an office-based automated device, then hypertension can safely be excluded.[68] Values above this will need confirmation using ABPM or a series of home-based readings.[68] We recommend that the new Hypertension Canada guidelines be followed for the evaluation of living donor candidates. This will allow hypertension to be excluded in many patients with just 1 office visit. In addition, it will align with guidelines being used by Canadian primary care practitioners. If donor nephrectomy is delayed, we suggest that the blood pressure be re-checked at annual intervals using an office-based automated device.

The KDIGO Guideline and KPD Protocol differ in the criteria for selection of hypertensive donors. The KDIGO Guideline states that donors with controlled hypertension on 1 or 2 agents may be suitable for donation, regardless of age.[3] The decision to proceed should be based on the donor candidate's predicted lifetime incidence of ESRD in relation to the program's acceptance risk threshold. In contrast, the KPD Protocol requires that hypertensive donors be $\geq$50 years of age and well controlled on just 1 agent.[2] While we understand the need to minimize variability between programs for KPD to function properly, the data supporting the age cutoff are weak. The medical risks postdonation are unlikely to be different for a 48-year-old donor compared to a 51-year-old donor. The assessment of overall risk seems like a more logical approach. To operationalize this in a Canadian context, programs will need to agree on the same methods for determining risk postdonation (eg, use of an ESRD risk assessment tool that is validated in a Canadian population).[4]

In a retrospective cohort study from Ontario matching 1278 living kidney donors to 6359 healthy nondonors, donors were more frequently diagnosed with hypertension than controls after a mean follow-up of 6 years (Table 2).[36] However, the authors concluded that while the observed increase in hypertension diagnoses may have been associated with the nephrectomy, it could also have been noted due to the increased surveillance for hypertension among living donors by their primary care physicians. The KDIGO Guideline has 2 specific recommendations regarding counseling that are not addressed in the KPD Protocol. First, the KDIGO Guideline recommends that hypertensive donors be counseled on lifestyle interventions to reduce their blood pressure and cardiovascular risk (eg, healthy body weight, regular exercise, smoking cessation).[3] Second, they suggest that donor candidates be informed that nephrectomy may accelerate the rise in blood pressure that accompanies aging, necessitating earlier treatment for hypertension than might be expected based on age.[3] We agree with both of these recommendations. Implementation would not be onerous and may already be occurring in many Canadian programs, given the first recommendation applies to all members of the general population, including living kidney donors.

Commentary on Chapter 11: 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 (HbA1c) before donation.
11.7: 2-hour glucose tolerance or HbA1c 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, low-density lipoprotein cholesterol [LDL-C], high-density lipoprotein cholesterol [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.

The recommendations in Chapter 11 are based on expert opinion and are "Not Graded." Overall, we agree with the recommendations in this chapter and they align with the recommendations in the KPD Protocol, with a few exceptions. First, in the KPD Protocol, donor candidates with type 2 diabetes mellitus and those with a body mass index (BMI) >35 kg/m^2 would be excluded from donation.[2] One retrospective study from Japan followed 225 living kidney donors, 14 had predonation diabetes mellitus, and 211 did not, over a median follow-up of 4.3 and 4.6 years, respectively.[71] At the end of follow-up, the eGFR was not significantly different between the 2 groups (51.7 vs. 52.1 mL/min/1.73 m^2; $P = .9$). Similar results were found in a larger cohort of living kidney donors from the United States who developed postdonation diabetes

mellitus.[72] In this study, donors who developed diabetes had a significantly higher risk of hypertension and proteinuria compared to donors who did not develop diabetes mellitus.

Given that many of the studies guiding these recommendations are based on Caucasian donors, Canadian transplant programs should be cautious in generalizing these results given the ethnic diversity of our population. Although the prevalence of living kidney donation and transplantation in the Canadian Indigenous population is low,[10] medical clearance must consider the unique pathophysiology in this group. Diabetes mellitus has a more aggressive course in Indigenous peoples and the incidence of associated ESRD and death is higher compared to non-Indigenous Canadians.[73,74] Since the ESRD risk assessment tool for living kidney donor candidates does not take into account family history or race (beyond Caucasian or African-American),[4] it is limited in predicting ESRD risk in young Indigenous donor candidates with a family history of diabetes. Similar limitations exist for other high-risk ethnic minority populations, such as South Asian Canadians. These unique differences in Canadian living donor candidates support a more conservative approach in medical acceptance until more robust Canadian data on living donor outcomes in these populations are available.

Large cohort studies document an increased risk of postdonation ESRD with increasing BMI >30 kg/m^2.[4,57,75] As the prevalence of obesity in the Canadian population increases, it is likely that individuals with elevated BMI will proceed to kidney donation. Canadian transplant programs must be aware of these risks and ensure donor safety is not compromised. Further research is required to understand the impact of BMI on the development of ESRD following donation including the accuracy of BMI vs. waist-to-hip ratio and the effect of predonation weight loss or postdonation weight gain.

Commentary on Chapter 12: 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.

The recommendations in Chapter 12 are based on expert opinion and are "Not Graded." Every Canadian transplant program is closely monitored to ensure the prevention of infectious transmission in the process of cell, tissue, and organ donation. All programs must comply with Health Canada's regulations pertaining to the safety of human cells, tissues, and organs for the purpose of transplantation.[76] Within these regulations, Health Canada outlines which infectious diseases need to be monitored and the timing and method of testing. These align with the KDIGO Guideline; however, do not include the seasonal and geographic endemic infections.[3] Although these infections are rare in Canada, the ease of global travel and the increasing approval of out-of-country donors make testing for these pathogens prudent.

Currently, there are no reports of kidney transplants from living donors who are hepatitis C virus (HCV) or human immunodeficiency virus (HIV) infected, only deceased donor cases.[77,78] Individuals infected with HCV have a high chance of cure following therapy with newer direct-acting antiviral therapy.[79,80] Certain Canadian transplant centers with access to these newer therapies are already accepting kidneys from deceased donors who are HCV positive to be transplanted into recipients who are HCV negative. It is conceivable that living donor candidates with HCV may proceed to donation and research protocols will need to be developed to ensure the long-term safety of both the donor and recipient. With respect to HIV, 1 study from the United States reported that the 9-year cumulative incidence of ESRD in individuals with HIV is higher than in individuals without HIV, yet the absolute risk was low and varied by age, sex, and race.[81] Thus, we would advocate that the risks and benefits of living donation be thoroughly discussed with HIV-positive individuals who are motivated to donate.

Commentary on Chapter 13: 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 a kidney 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.

The recommendations in Chapter 13 are based on expert opinion and are "Not Graded." The KDIGO Guideline and the KPD Protocol both recommend cancer screening based on recommendations from local/national agencies, but the KPD Protocol specifically provides screening instructions for breast, cervical, prostate, and colon cancer.[2,3]

The KDIGO Guideline and the KPD Protocol have similar selection and exclusion criteria for kidney donation related to cancer. Both documents suggest excluding donors with active cancer. However, in the KDIGO Guideline, this position is nuanced by mentioning that donors with active cancer, but low risk of transmission to the recipient (for instance, cancers with low risk of progression in the donor), may be considered.

In both documents, a living kidney donor with a history of cancer associated with a low risk of recurrence or low risk of transmission is acceptable on a case-by-case basis. Patients with a history of melanoma are formally excluded from donation. In the KDIGO Guideline, this recommendation is not found in the summary, but rather in the rationale section. Lastly, the KDIGO Guideline formulates specific recommendations for the donor with renal cysts.

Commentary on Chapter 14: 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.

The recommendations in Chapter 14 are based on expert opinion and are "Not Graded." We agree with the KDIGO Guideline recommendations regarding the evaluation, selection, and counseling of donor candidates with potential genetic kidney diseases.[3] The KDIGO Guideline recommendations align with the KPD Protocol, particularly in the diagnostic testing of donor candidates with a family history of autosomal dominant polycystic kidney disease (ADPKD).[2,3]

There are some notable considerations and exceptions. First, the KPD Protocol does not address the impact on obtaining health or life insurance in the event of a diagnosed genetic kidney disease. Second, the KDIGO Guideline and KPD Protocol disagree in their recommendations regarding cases where there is uncertainty whether the donor candidate has a genetic kidney disease that can cause kidney failure. The KPD Protocol recommends that in these cases, donor candidates should not proceed with donation in the interest of their own safety.[2] In contrast, we agree with the KDIGO Guideline that, in this situation, donation should only proceed after informing the donor candidate of the risks of donation, if the disease occurs later in life.[3] The donor candidate should also be informed of any potential impact of the genetic disease on survival and function of the graft. Lastly, the KPD Protocol does not make any comments on the utility of apolipoprotein L1 (APOL1) genotyping in donor candidates of sub-Saharan African ancestry. We agree with the KDIGO Guideline recommendations that these donor candidates be offered APOL1 genotyping and informed of the increased risk of kidney failure associated with having 2 APOL1 risk alleles; however, the precise kidney failure risk for an affected individual after donation is unknown.

Commentary on Chapter 15: 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.

Most of the recommendations in Chapter 15 are based on expert opinion and are "Not Graded," except for recommendation 15.9 which is graded as 2C. We agree with the KDIGO Guideline recommendations surrounding pregnancy considerations. For female donor candidates with a history of a hypertensive disorder of pregnancy, a detailed description should be obtained and documented. This includes the number of pregnancies, episodes of hypertensive or other disorders of pregnancy, and any clinical sequelae. The evidence suggests that a prior history of hypertensive disorder during pregnancy (particularly preeclampsia/eclampsia) is associated with a higher risk of ESRD.[82-84] Donor candidates with a mild hypertensive disorder during pregnancy, or a single event that occurred more than 10 years ago who have normal eGFR, normal blood pressure, and no microalbuminuria and who have completed their families are likely at lower risk of postdonation ESRD and can be considered for living kidney donation. Female donor candidates with recurrent episodes of preeclampsia/eclampsia during subsequent pregnancies have a higher risk of ESRD and should be excluded from donation.[83]

Three retrospective cohort studies (from Norway,[85] United States,[86] and Canada)[47] suggest a greater likelihood of being diagnosed with gestational hypertension or preeclampsia after kidney donation although the overall risk remains low. In the Canadian study, the risk of gestational hypertension or

preeclampsia was twofold higher in living kidney donors compared to matched female nondonors over a median follow-up 11 years (Table 2; 11% vs. 5%; odds ratio 2.4, 95% CI = 1.2.-5.0; $P = .01$).[47] To reduce the risk of complications in postdonation pregnancies, female donors should be counseled to maintain general good health, ensure adequate follow-up, and receive proper prepregnancy counseling and prenatal care.

Commentary Chapter 16: 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.

Most of the recommendations in Chapter 16 are based on expert opinion and are "Not Graded," except for recommendation 16.6 which is graded as 2D. Both the KDIGO Guideline and the KPD Protocol recommend a comprehensive psychosocial evaluation for donor candidates.[2,3] The KPD Protocol further specifies that the psychosocial evaluation should be conducted by a trained health care professional, such as a social worker or psychologist.[2] This role may vary across transplant centers according to resources and expertise. We agree that the psychosocial assessment of the donor candidate should occur in the absence of other people to minimize the risk of potential coercion and be performed by members of the health care team who are not directly involved in the care of the intended recipient.[87] Currently, there is no evidence-based tool or systemic protocol for assessing a donor candidate's psychosocial suitability and further research is needed.[88,89]

The KPD Protocol does not have recommendations regarding postdonation quality of life.[2] One retrospective study involving 7 centers in Canada found that the quality of life scores (using 15D) was high and similar between living kidney donors and healthy nondonors (Table 2).[40] Donor candidates should be informed about the benefits of living kidney donation but also the potential psychological impact after transplantation, particularly if they or their intended recipient suffers complications. Transplant programs have a responsibility to ensure the long-term medical and psychosocial well-being of living kidney donors.

Commentary on Chapter 17: 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 approach used for the 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.

Most of the recommendations in Chapter 17 are based on expert opinion and are "Not Graded," except for recommendations 17.3 and 17.7 which are graded as 2D. Both the KDIGO Guideline and the KPD Protocol appropriately recommend renal imaging for assessment of renal anatomy, which is essential prior to undertaking donor nephrectomy.[2,3] The KDIGO Guideline contains a number of prescriptive statements about the surgical technique to be utilized for donor nephrectomy, while the KPD Protocol does not make any specific recommendations.

We disagree with the surgical recommendations 17.3, 17.4, 17.6, and 17.7. In Canada, there is discrepancy in the number of surgeons and clinical volumes between transplant centers participating in KPD. Due to limitations on the shipping of live donor kidneys in Canada, donors may need to travel to the center of their matched recipient in order to donate, which may incur additional costs and out-of-pocket expenses to the donor. Given that the priority for the surgeons is to achieve the safest possible outcome for the donor, the decisions about surgical technique (open, mini-open, hand-assist laparoscopic, pure laparoscopic, robotic, etc.) and which kidney to remove (right vs. left) should be at the discretion of the surgeon. The surgical experience in Canada suggests that compared to the open technique, laparoscopic donor nephrectomies have longer operative times but are associated with lower blood loss, reduced intraoperative complication rates, and shorter hospital stays.[26,28-30] We also agree with the recommendation 17.5, but would modify this to state that Weck Hem-o-lok clips should not be used as the sole method for control of the main renal artery during donor nephrectomy.

Commentary on Chapter 18: 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.

The recommendations in Chapter 18 are based on expert opinion and are "Not Graded." Many of these recommendations are not considered in the KPD Protocol.[2] In Canada, provincial and federal laws state that organ donation should be gratuitous and organs should not be sold and bought in exchange of valuable consideration.[90] Moreover, living organ donation should be done in compliance with Health Canada standards.[76] Currently, there are no laws or policies that impede the ethical practice of living donation and every effort should be made to remove all disincentives for living kidney donors. Autonomy should always be respected in the process of living organ donation; however, relational autonomy should also be taken into account. Relational autonomy considers the social context, social relationships, and emotions that are embedded in decision making.

In 2017, the CST published a position statement on the issue of public solicitation.[91] It is legally and ethically acceptable for transplant centers to consider potential living organ donor from public solicitation provided that it is made in compliance with the Canadian laws; however, it is not mandatory for transplant programs to assess these donors. Transplant professionals could have conscientious objection towards public solicitation. In such cases, transplant centers should be transparent in disclosing the reasons for declining to evaluate these donors and should refer them to another center for evaluation.

A 2014 prospective study of 7 Canadian transplant centers found that the average overall cost incurred by donor candidates was $3268 with 15% of donors spending >$8000 (Table 2).[15] While there is some credit at the Canadian federal level, reimbursement programs for living kidney donors vary in their policies across the provinces.[92] One study from Ontario's reimbursement program found that the average financial gap between costs incurred and costs reimbursed to donors was $3115 CAD.[18] Transplant centers should continue to advocate for financial neutrality for the donor during the evaluation and donation process.

Canadian Blood Services recommends that anonymity be maintained between nondirected donors and donors participating in paired donation to prevent unwanted requests from the donor or the recipient. In the rare event that a living kidney donor develops ESRD, most programs have allocation policies that allow for certain priority for living donors on the deceased donor kidney transplant waiting list.

Commentary on Chapter 19: 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 and 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.

The recommendations in Chapter 19 are based on expert opinion and are "Not Graded." We agree with the KDIGO Guideline recommendations as an essential component of the donor evaluation process.[3] The KPD Protocol does not address postdonation follow-up care.[2] Since the publication of the KPD Protocol in 2014, there has been increasing literature to further our understanding of long-term postdonation outcomes. Two studies, 1 from Norway and 1 from the United States, have shown that the relative risk of ESRD in living kidney donors is higher than in selected nondonors of similar baseline health; however, the absolute estimates are small (<0.5% over 15 years for most donors).[58,93,94] In addition to this, over a follow-up of ~10 years in Ontario, the risk of gestational hypertension or preeclampsia and gout was higher in donors compared to matched, healthy nondonors,[47,48] whereas the risk of cardiovascular disease, acute dialysis, kidney stones with surgical intervention, gastrointestinal bleeding, and fractures was similar (Table 2).[41,42,44-46,95]

There are many potential benefits of postdonation follow-up care. It allows for prevention, early detection, and management of diseases and is an opportunity to inform and educate prior donors on new research on long-term outcomes.[32] It can also promote the transplant center's collaborative role in the long-term care of donors, rather than leaving them with a sense of abandonment. Although all Canadian center's perform short-term follow-up as part of the surgical postoperative care, there is wide variability in the involvement of centers in the longer-term follow-up. This is mainly due to the role of the primary care physician in follow-up care, donor or professional opinion of well-being, and lack of proven efficacy that close surveillance and monitoring results in improved outcomes.[31] One study from Alberta found that, over a median follow-up of 7 years, only 25% of donors had all 3 markers of care recommended in the KDIGO Guideline (physician visit, serum creatinine, albuminuria measurement) in each year of follow-up (Table 2).[32]

While the United States has mandatory reporting by transplant centers to the national transplant registry, it is limited to 2 years postdonation, and has high rates of missing data and loss-to-follow-up.[96,97] No such policy exists in Canada and while there is enthusiasm for living donor registries in Canada and the United States, there are challenges including limited resources, infrastructure, and funds.[98]

Conclusion

Overall, the recommendations in the 2017 KDIGO Guideline on the Evaluation and Care of Living Kidney Donors aligns with our national 2014 KPD Protocol for Participating Donors. There are some notable differences that we have highlighted in our review, including considerations of our ethnically diverse population, such as the Indigenous population.

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