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Genetic Assessment of Living Kidney Transplant Donors: A Survey of Canadian Practices

Somaya Zahran[1], Ke Fan Bei[2,3], Aisha Adil[3,4,5,*], Princess Okoh[4,6,7,*], Thomas Kitzler[8,9,10], and Ahsan Alam[11]

Abstract

Background: Kidney failure is a prevalent condition with tendency for familial clustering in up to 27% of the affected individuals. Living kidney donor (LKD) transplantation is the optimal treatment option; however, in Canada, more than 45% of LKDs are biologically related to their recipients which subjects recipients to worse graft survival and donors to higher future risk of kidney failure. Although not fully understood, this observation could be partially explained by genetic predisposition to kidney diseases. Genetic testing of potential LKDs may improve risk assessment and inform the safety of donation. The strategies to evaluate these donors are still evolving. In Canada, little is known about the practice of assessing for genetic conditions among LKDs.

Aim: The aim was to examine the Canadian practices regarding LKDs genetic assessment.

Methods: Questionnaires were sent to 23 Canadian adult transplant centers to examine their protocols for LKDs genetic assessment.

Design: The questionnaire comprised of 10 sections and 21 questions including case scenarios of different LKD encounters. Major domains of the survey addressed general demographics, information sharing practices, effect of mode of inheritance on candidacy decision, having a policy for LKD genetic evaluation, and case scenarios covering the following conditions: autosomal dominant polycystic kidney disease (ADPKD), Alport syndrome, Fabry disease, familial focal and segmental glomerulosclerosis (FSGS), atypical hemolytic uremic syndrome (aHUS), autosomal dominant tubulointerstitial kidney disease (ADTKD), sickle cell, and apolipoprotein L1 mutation (APOL1).

Participants: The questionnaire was sent to the living-donor assessment committee representative (nephrologist) in adult and pediatric kidney transplant centers across Canada.

Results: In total, 16 of 23 Canadian centers responded to the survey. Of the 8 surveyed genetic conditions, ADPKD, Alport syndrome, and aHUS were the most frequently encountered. More centers have specific policies for donor evaluation for ADPKD (25%) and aHUS (21.4%) vs none to very few for other genetic conditions. The most cited guidelines are Kidney Disease Improving Global Outcomes (KDIGO), Canadian Society of Nephrology/Canadian Society of Transplantation (CSN/CST), and the Canadian Blood Services' Kidney Paired Donation Protocol.

Conclusions: Canadian transplant centers follow a case-by-case approach rather than a standard protocol for genetic assessment of LKDs given that current guideline recommendations are based on expert opinion due to a lack of a reliable body of evidence. With the expected rise in utilization of the increasingly available genetic testing, early multidisciplinary assessment including medical geneticists has the potential to improve personalized management. Studies examining long-term donor and graft outcomes are needed to construct the basis for evidence-based recommendations and inform the safety of donations.

Abrégé

Contexte: L'insuffisance rénale est une affection prévalente qui, pour jusqu'à 27 % des personnes touchées, comporte une tendance au regroupement familial. La transplantation de reins provenant de donneurs vivants constitue l'option de traitement optimale. Au Canada, plus de 45 % des donneurs de rein vivants (DRV) ont un lien biologique avec leur receveur, ce qui expose ces derniers à une moins bonne survie du greffon et les donneurs à un risque plus élevé de souffrir éventuellement d'insuffisance rénale. Bien qu'elle soit encore mal comprise, cette observation pourrait s'expliquer en partie par une prédisposition génétique aux maladies rénales.Le dépistage génétique des DRV potentiels peut améliorer l'évaluation

des risques et informer la sécurité du don. Les stratégies d'évaluation de ces donneurs continuent d'évoluer. Au Canada, les pratiques qui ont cours pour évaluer les conditions génétiques des DRV sont mal connues.
Objectif: Examiner les pratiques ayant cours au Canada pour l'évaluation génétique des DRV.
Méthodologie: Un questionnaire a été envoyé à 23 centres canadiens de transplantation pour adultes afin d'examiner leurs protocoles d'évaluation génétique des DRV.
Conception: Le questionnaire en 10 sections et 21 questions explorait notamment différents scénarios de rencontres avec les DRV. Les principaux domaines de l'enquête portaient sur la démographie, les pratiques de partage de l'information, l'effet de l'hérédité sur la décision de candidature, la présence de politiques d'évaluation génétique des DRV et des scénarios de cas couvrant les affections suivantes: la polykystose rénale autosomique dominante (ADPKD), le syndrome d'Alport, la maladie de Fabry, la glomérulosclérose segmentaire et focale (FSGS) d'origine familiale, le syndrome hémolytique et urémique atypique (SHUa), la néphropathie tubulo-interstitielle autosomique dominante (ADTKD), la drépanocytose et la mutation de l'apolipoprotéine L1 (APOL1).
Participants: Le questionnaire a été envoyé aux personnes (néphrologues) représentant le comité d'évaluation des DRV dans des centres de transplantation rénale pour adultes et enfants partout au Canada.
Résultats: Le questionnaire a été rempli par 16 des 23 centres. Des huit maladies génétiques étudiées, les plus fréquemment rencontrées étaient l'ADPKD, le syndrome d'Alport et le SHUa. Une plus grande proportion de centres disposait de politiques spécifiques pour l'évaluation de l'ADPKD (25 %) et du SHUa (21,4 %) chez les donneurs; aucun ou très peu de centres en avaient pour d'autres conditions génétiques. Les lignes directrices les plus souvent citées étaient celles de KDIGO, de la CSN/CST et du Protocole de don croisé de rein de la Société canadienne du sang.
Conclusion: Pour l'évaluation génétique des DRV, les centres de transplantation canadiens suivent plutôt une approche au cas par cas qu'un protocole standard, car, en absence d'un ensemble fiable de preuves, les recommandations actuelles des lignes directrices reposent sur l'opinion d'experts. Les tests génétiques sont de plus en plus disponibles; l'augmentation attendue de leur utilisation pour une évaluation multidisciplinaire précoce, incluant les généticiens médicaux, des donneurs pourrait améliorer la personnalisation de la prise en charge. Des études examinant les résultats à long terme des greffons et des donneurs sont nécessaires pour élaborer des recommandations fondées sur des données probantes et informer la sécurité des dons.

Keywords
kidney transplantation, living kidney donor, genetic testing, donor evaluation, Canadian transplant centers

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Introduction

Kidney transplantation offers the best treatment option for patients with kidney failure. Living kidney donor transplantation (LKDT) accounts for up to one third of all kidney transplantations in Canada.[1] The LKDT is a superior treatment option for kidney failure than deceased donation as it offers better patient and graft survival[2,3] with similar or less health care costs.[4] However, in Canada, more than 45% of all living kidney donors (LKDs) are biologically related to their recipients.[5] There is evidence showing higher risk for developing chronic kidney disease (CKD) if there is a positive family history of renal disease,[6-8] with particularly the highest risk in first-degree relatives. Although likely multifactorial, this tendency for familial clustering could be related to underlying genetic predisposition or monogenic kidney disease. Moreover, approximately 10% of CKD in adults and up to 20% of nephropathy of unknown etiology is caused by a genetic cause.[9,10] It is reported that living kidney donation to a recipient who is biologically related is associated with worse graft survival,[11] and donors are subject to higher risk of future kidney failure[12-14] and shorter life expectancy.[15] This is presumed to be due to the higher risk of genetic

[1]Division of Nephrology, Department of Medicine, McGill University Health Center, Montreal, QC, Canada
[2]Department of Immunology, Temerty Faculty of Medicine, University of Toronto, ON, Canada
[3]Latner Thoracic Surgery Research Laboratories, Toronto General Hospital, The University Health Network, ON, Canada
[4]Institute of Medical Science, Temerty Faculty of Medicine, University of Toronto, ON, Canada
[5]Canadian Donation and Transplantation Research Program, Edmonton, AB, Canada
[6]Kidney Health Education and Research Group, Toronto, ON, Canada
[7]Ajmera Transplant Center, Toronto General Hospital, The University Health Network, ON, Canada
[8]Department of Human Genetics, McGill University, Montreal, QC, Canada
[9]Division of Medical Genetics, Department of Specialized Medicine, McGill University Health Centre, Montreal, QC, Canada
[10]Child Health and Human Development Program, Research Institute of MUHC, McGill University Health Centre, Montreal, QC, Canada
[11]Multiorgan Transplant Program, Division of Nephrology, Department of Medicine, McGill University Health Centre, Montreal, QC, Canada

*Equal authorship.

Corresponding Author:
Ahsan Alam, Multiorgan Transplant Program, Division of Nephrology, Department of Medicine, McGill University Health Centre, 1001 Decarie Boulevard, D05.7176, Montreal, QC H4A 3J1, Canada.
Email: ahsan.alam@mcgill.ca

kidney disease in donors who have positive family history of CKD.

Genetic testing of LKD candidates has the potential to improve risk assessment and inform the safety of donation.[16,17] Previously, it has been reported that biologically related donors may be at risk for the same kidney disease as their intended recipient's primary renal disease[18] as new familial kidney disease diagnoses were made after donation.[19] With the rapidly decreasing cost of genetic testing technologies, it is important to consider their impact on living donation and carefully weigh the risks and benefits associated with their administration as part of donor assessment. Although the strategy to evaluate LKDs for underlying genetic kidney diseases is still evolving, there are few recommendations in the currently available clinical practice guidelines. Aside from autosomal dominant polycystic kidney disease (ADPKD)[20] where expert opinions are available, there exists a lack of a reliable body of evidence to support strong recommendations for genetic testing in LKDs and non-standardized implementation of testing modalities.

Here, we survey all Canadian transplant centers regarding their policies for genetic evaluation of LKD and report the donation assessment methodologies of genetic kidney diseases across Canadian LKDs programs.

Methods

Questionnaires

A questionnaire was developed by the authors, and the final version of the questions was agreed upon after multiple rounds of revisions over virtual meetings before it was sent to all transplant centers (see full survey in the Supplementary Material). The questionnaire does not follow a standard structure; rather, it comprised of 10 sections and 21 questions which were structured as follows[1]: current approaches taken for donor evaluation: which genetic diseases are tested for and what policies are in place for evaluation.

Subsequent sections included questions pertaining to the specific kidney disease conditions and current practices in place for[2] ADPKD,[3] X-Linked Alport syndrome (this case scenario focused on X-linked as it is the most prevalent form[21] and its association with kidney failure risk is more established and less ambiguous[22] than for the autosomal dominant form),[4] Fabry disease,[5] familial focal and segmental glomerulosclerosis (FSGS),[6] atypical hemolytic uremic syndrome (aHUS),[7] autosomal dominant tubulointerstitial disease (ADTKD),[8] sickle cell disease (SCD)[9], and apoliprotein L1 (*APOL1*) risk alleles. These 8 case scenarios were selected based on relative commonality in our institutions. Thus, in addition to being clinically relevant, these case scenarios also highlight a decision-making dilemma given the lack of evidence to guide their management. The survey also briefly alluded to CKD of unknown etiology (CKDu) (survey question 2—Supplementary Material), as it is a relatively new concept which we did not expect LKD assessment centers to have standard operating procedures (SOPs) for. For each of the case scenarios, transplant centers are asked to pick one or multiple courses of action. Options included declining donation, allowing donation, discussing with candidates, deciding on a case-by-case basis, or performing genetic testing.

Subsequent sections questioned whether LKD assessment programs allowed donors with a family history of the aforementioned kidney diseases to participate in kidney donation, providing yes/no/maybe or specific options (relevant to the kidney disease) and an open-ended section was provided with free text comment boxes. Case scenarios were provided to gauge LKD programs' protocol for donor acceptance, and responses were gathered by the following options: allowed, declined, offered case-by-case, if further (clinical and/or genetic) tests were conducted, or other approaches for each genetic condition listed (given as open-ended section). Section 10 questioned which, if any, international guidelines were being used for consultation and guidance at respective donor programs including: Kidney Disease Improving Global Outcomes (KDIGO),[23] Canadian Society of Nephrology/Canadian Society of Transplantation (CSN/CST),[24] Kidney Paired Donation (KPD) Protocol for Participating Donors 2014,[25] European Renal Association/European Dialysis and Transplant Association (ERA-EDTA) 2015,[26] British Transplantation Society (BTS) 2018,[27] or other. An optional open-ended section with free-text comment boxes was provided for additional comments, questions, and concerns regarding the survey and aspects that may have not been addressed regarding genetic testing of LKDs.

Review of Guidelines

The following international guidelines were reviewed to examine their recommendations (if any) for genetic assessment of LKDs for underlying CKD-predisposing genotype; KDIGO,[23] CSN/CST,[24] Canadian Blood Services KPD Protocol for Participating Donors 2014,[25] ERA-EDTA,[26] BTS,[27] The Transplantation Society (TTS), American Society of Transplantation (AST), Francophone Society of Nephrology, Dialysis and Transplantation (SFNDT), Australian/New Zealand Paired Exchange Program Protocol 3 for Living Donor Evaluation Guidelines,[28] Guideline for the Evaluation of Kidney Donors in New Zealand,[29] and the Sociedad Española de Nefrología (SEN) (Spanish Society of Nephrology), the Sociedad Española de Trasplante (SET) (Spanish Transplant Society), and the Organización Nacional de Trasplantes (ONT) (Spanish National Transplant Organisation) SEN-SET-ONT recommendations for living-donor kidney transplantation (Supplementary Tables 1 to 3).[30,31]

We summarized the available relevant guideline-derived recommendations and examined their applicability to practice as informed by different providers in Canada.

Survey Distribution

All contacts received emails from the research group describing the study and inviting them to participate in a questionnaire in November 2022. An optional one-on-one virtual interview was also offered as an alternative to the survey. The questionnaire was translated into French with the help of the Canadian Donation and Transplantation Research Program (CDTRP).

The survey population included 25 kidney LKD assessment programs spanning all 10 Canadian provinces. The questionnaire was administered via email to the respective contacts. If no response had been provided, a reminder email was sent on a weekly basis up until the questionnaire deadline (November 28, 2022). All of the survey questions were answered to completion by all responders, except for optional comment questions.

Ethical Considerations

As per the Centre for Applied Ethics Quality, Evaluation, Performance and Ethics affiliated with the McGill University Health Centre, this study was exempted from research ethics board (REB) approval. As per the Tri-Council Policy Statement (TCPS, 2018), the information we collected would be available as part of the LKD assessment programs' SOPs or usual clinical practice; thus, no REB approval was required at our institution.

Data Analysis

This is a descriptive study of practice patterns of Canadian transplant centers regarding genetic assessment of LKDs. Initial data analysis included calculating percentages of most commonly encountered genetic conditions at transplant centers, any (if) respective donor evaluation protocols in practice, and whether donation was allowed, declined, offered case-by-case, if further (clinical and/or genetic) tests were conducted, or other approaches for the diagnosis or risk assessment of each genetic condition.

Results

Survey Responses

Our survey was sent to 25 Canadian transplant centers. All adult and pediatric kidney transplant centers across Canada were identified. We obtained the contact list of the Canadian Blood Services' Living Donor Assessment Committee (LDAC) representative (nephrologist) for each center and contacted them. Inclusion criteria included the LKD assessment programs that were Health Canada accredited to ensure the responses reflected the current practices and protocols in place in Canada.

As 3 of the centers were managed by the same LDAC representative who informed us that all answers will be identical for all the 3 centers, we opted to merge the 3 centers into 1 response, so the total number is 23 centers. A total of 16 centers responded in total (69.6%); 13 centers (81.3%) of the responders represented English-speaking provinces and 3 (18.7%) represented French-speaking provinces. All Canadian regions were represented in the survey (Figure 1 map), and all responders represented adult centers that are affiliated with academic institutions.

Donors With Family History of Chronic Kidney Disease

When presented with a scenario where a donor and a recipient are biologically related, after obtaining their consent, 62.5% (10/16) of Canadian transplant centers routinely discuss the recipient's etiology of CKD, whereas 31.3% (5/16) might consider this discussion based on the nature of the disease, age of the donor, certainty of diagnosis, and whether genetic testing is available. About 43.8% (7 of 16) reported sharing information regarding the underlying disease with the donor. The decision regarding donor eligibility is affected by the mode of inheritance, according to 62.5% (10/16) of the respondents, whereas 31.3% (5/16) said the eligibility decision varies based on availability and certainty of genetic testing, nature of the disease, and donor age.

When a donor reports family history of CKDu, 68.8% (11 of 16) of Canadian centers would proceed with donation, usually after discussing risks/benefits and performing more investigations. This approach varies based on Family history, donor age, clinical picture, and initial test results.

Conditions Encountered by Canadian Transplant Centers

Almost 100% Canadian centers reported encountering donors with family history of ADPKD (16 of 16) and aHUS (15 of 16). About 81.3% (13/16) of the centers reported encountering donors with a family history of Alport syndrome, whereas FSGS (6/16) and *APOL1* (5/16) follow with a frequency close to 35%. Finally, the least reported conditions are SCD (3/16) and ADTKD (2/16) with a frequency of about 15%. Despite frequently encountering ADPKD, aHUS, FSGS, and *APOL1*, only 43.8% (7/16), 31.3% (5/16), 12.5% (2/16), and 6.3% (1/16) of the Canadian transplant centers have policies for evaluating donors with these respective conditions (Figure 2).

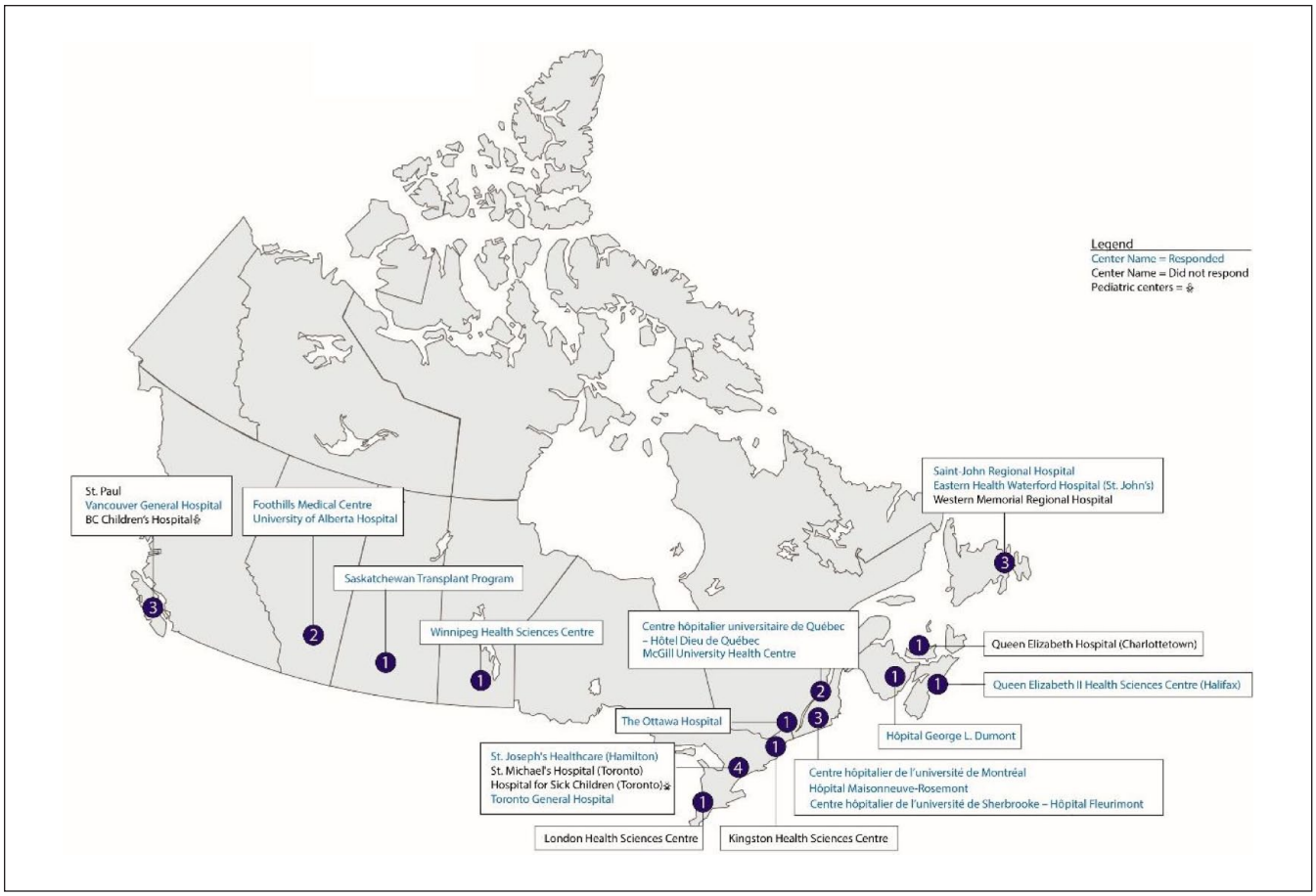

Figure 1. Map of Canadian transplant centers to which the survey was sent. Centers that did not respond are indicated in blue. Centers who responded are indicated in black. The child sign indicates a pediatric center.

Case Scenarios

Responses are summarized in Table 1.

For a 25-year-old donor with a first-degree family history of ADPKD, 75% of Canadian centers reported genetically testing the intended recipient with kidney failure, then performing targeted genetic testing of the donor, and only 50% reported performing high-resolution imaging. Only 2 centers reported having relevant SOPs or protocols, one of which cited the CST assessment of living donation,[24] and the other reported referral to medical genetics based on age and risk factors. For assessment of mothers as donors for their Alport syndrome-affected sons, female donors with Fabry disease, heterozygous carriers of FSGS, and donors with family history of ADTKD, majority (72%, 87.5%, 93.8%, and 75%, respectively) of transplant centers reported proceeding with donation on a case-by-case basis. Although more than half of centers reported either genetically testing the potential donors with a first-degree family history of aHUS or deciding based on a case-by-case assessment, all or majority (75%) of centers would individualize donation decision for

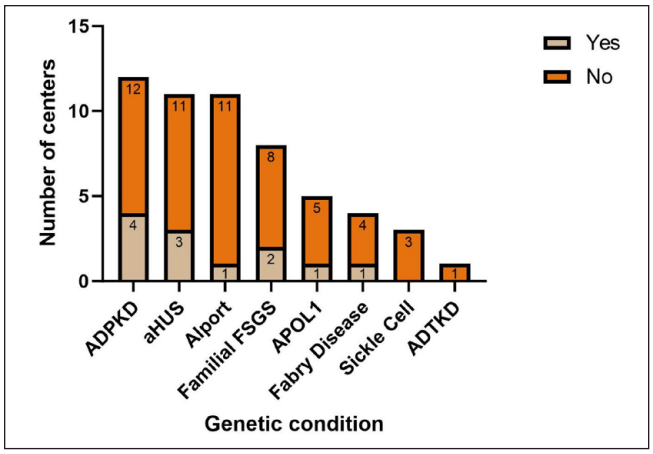

Figure 2. Encountered genetic conditions in the Canadian LKD programs are represented on the x-axis. Bars represent the number of centers that have encountered the genetic condition. Bar colors represent the responses regarding LKD evaluation protocol status (orange: response as no protocol—beige: response as having a protocol).

Table 1. Survey Response to Some of the Living Kidney Transplant Donor Case Scenario Questions—Responders Were Allowed to Pick More Than 1 Answer.

		Allow donation after discussion	Decline donation	Case by case	Genetic tests[a]	Clinical tests[b]	Other
X-linked Alport mother to donate to son		13% (2/16)		75% (12/16)			
Heterozygous female Fabry				88% (14/16)			
Heterozygous carriers of Familial FSGS		6% (1/16)		94% (15/16)			
First degree family history of aHUS		6% (1/16)	6% (1/16)	56% (9/16)	63% (10/16)		
FHx of ADTKD		6% (1/16)		75% (12/16)	19% (3/16)		
FHx of SCD				100% (16/16)	13% (2/16)		
Confirmed sickle cell trait			6% (1/16)	75% (12/16)			13%[c] (2/16)
APOL1	Confirmed 1 risk allele	6% (1/16)		81% (13/16)		6% (1/16)	
	Confirmed 2 risk allele	25% (4/16)		88% (14/16)		13% (2/16)	

[a]Genetic tests were not explicitly specified to allow answers based on what is available in different center for each if the conditions.
[b]Clinical tests are meant to describe any functional testing for phenotype diagnosis (blood tests, imaging, or others).
[c]Decision varies based on age, comorbidities.
%: percentage of responding centers.
(#/16): total number of responding centers of the 16 centers.
FSGS = Focal and segmental glomerulosclerosis; aHUS = atypical hemolytic uremic syndrome; ADTKD = autosomal dominant tubulointerstitial kidney disease; SCD = sickle cell disease; *APOL1* = apolipoprotein 1.

SCD and hemoglobin SS trait candidate donors, respectively, considering age and comorbidities. Minority of centers reported proceeding with genetic testing for SCD (12.5%) and for target populations for *APOL1* (positive family history [18.8%] or African descent [12.5%]). If a candidate carries a confirmed *APOL1* risk allele, 18.3% of centers would manage on a case-by-case basis, comments included whether the allele is G1 or G2. One center did not consider a single risk allele high risk for donation, so no special consideration is required. However, if 2 *APOL1* risk alleles are present (eg, G1/G1, G2/G2, or G1/G2), 87.5% would decide on a case-by-case basis, whereas 25% would discuss with the candidate and 12.5% would perform more tests. Factors taken into consideration include candidate's age and comorbidities.

Guidelines Followed by Canadian Transplant Centers

The KDIGO is the most referenced guideline (100%) followed by CSN/CST and Kidney Paired Donation consensus protocol (87.5% each).

Discussion

Our study was conducted using a survey with numerous case scenario questions (Supplementary Material) to examine Canadian practices regarding LKD genetic assessment. Our results show that Canadian transplant centers use diverse strategies which are mostly based on a case-by-case basis. There is no consistent practice that unifies LKD assessment programs, and most of the programs do not have protocols or SOPs for LKD genetic assessment. This reflects the lack of evidence to guide decision-making regarding LKD genetic evaluation, as shown in our review of the available guidelines. For example, in a relatively common encounter like family history of ADPKD in a young donor candidate as presented in our case scenario, there was significant variability in the assessment of LKD, from referral of the candidate, family member, or both to genetic testing, performing high-resolution imaging, or a mix of both. Although this reflects the relevant KDIGO recommendation statement,[23] it highlights the lack of standardization for the assessment of such a relatively common genetic renal condition.

Our survey results emphasize the need for higher-quality evidence to support stronger recommendations for the utility of the increasingly available genetic tests. As case reports of related kidney donors revealed primary recipient's disease emergence (as in FSGS and aHUS[32-34]) or de novo diagnosis of a genetic disease affecting the kidney (like Fabry disease[35]), there is a growing need for more research in this field. A recent set of recommendations published by the Living Donor Community of Practice Genetics Workgroup proposed an algorithm to serve this purpose,[36] focusing mainly on monogenic kidney diseases. The group recommends limiting genetic testing for living donors with

a first-degree family history of confirmed or suspected genetic kidney disease or CKDu; this approach should be considered mainly for autosomal dominant conditions and in a cascade manner, ie, testing the affected family member first if can be identified, then performing targeted genetic testing of the candidate. Other recommendations include testing individuals with a second-degree family history of genetic diseases (like Fabry disease) and not testing those with a family history of non-genetic etiology of kidney failure. It is notable, though, that accurate risk assessment of the related LKD can be accomplished by establishing whether there is a known genetic cause in the family member with kidney failure. The genetic ascertainment should ideally begin with the related kidney transplant recipient before they reach kidney failure.[37]

An increased use of genetic testing in LKD assessment may have multiple implications. In addition to improved prognostication and personalized decisions,[37] the overall safety of donation will likely increase as, currently, some genetically susceptible LKDs who are accepted without genetic testing may carry increased long-term risks compared to the general population.[38] However, this might be at the expense of increased cost and time for LKD evaluation and potentially declining LKD rates as the identification of abnormal genetic variants in some candidates might exclude them from donation. In addition, given the current uncertainty regarding the relevance of positive genetic tests in asymptomatic individuals[36] and the numerous factors affecting their interpretation (eg, patient, family, phenotype, variant, etc),[38] it would be difficult to inform donor candidates about any future risks of kidney disease, resulting in anxiety.

The LKD assessment programs may benefit from a multidisciplinary approach bringing together clinical and molecular geneticists, genetic counselors, and nephrologists. An efficient and streamlined approach would be important to minimize workup times for the donors. Nephrologists may select from pre-established genetic testing panels appropriate for the condition in question and provide pre-analytical counseling, whereas geneticists assist with interpretation and post-testing counseling, with ongoing psychological support to LKD candidates throughout the process to minimize anxiety. To help overcome the discomfort displayed by some nephrologists in adopting genetic testing,[39] educational platforms with periodic review of the fast-evolving literature[40] should be arranged. On a broader level, sharing and harmonizing protocols for genetic testing across LKD assessment programs in Canada would enhance equity and safety of LKD.

To our knowledge, this survey is the first to provide insights into real-world practices regarding genetic assessment of LKDs by transplant centers in Canada. The response rate to our survey was high, representing all regions across Canada, and included programs in both English and French-speaking provinces.

One limitation of our study is that the survey was sent to the medical director of LKD programs, whose response might not reflect the practice of each donor nephrologist within their respective programs, as one might expect some degree of practice variability between clinicians within the same center. Second, our survey was not anonymous as we requested identification of the respective transplant center, which might introduce social desirability bias. Third, as this was not the scope of our protocol, the survey did not seek to identify the perceived barriers or suggestions on how to improve such genetic evaluations. Fourth, our survey case scenarios included only 8 encounters that were most prevalent in our practices. Although deemed clinically relevant, responses cannot be extrapolated to all other genetic conditions.

Future research can be directed to explore several key areas. First, to develop standardized educational platforms for nephrologists regarding utilization and interpretation of genetic testing and examine the impact on referral rates. Second, long-term outcomes studies are needed to delve into post-donation health for donors with underlying genetic variants or family history of genetic kidney diseases and potentially identify risk factors for unfavorable outcomes (ie, development of CKD, hypertension, etc) to improve safety of donation. This focus could lead to building personalized risk assessment models using donors' genetic profiles, along with clinical and demographic data to tailor the assessment and counseling for each donor candidate. An example is the ongoing APOLLO trial, which prospectively examines the effect of *APOL1* gene on graft survival and proteinuria in living donors.[41] Larger-scale collaboration between international societies to facilitate the development of standardized genetic assessment, interpretation, and implementation protocols could improve safety and equity of living kidney donation.

Conclusions

Canadian transplant centers follow a case-by-case approach rather than a standard protocol for genetic assessment of LKDs. Current international recommendations are largely based on expert opinion due to lack of a reliable body of evidence and inefficiency of the current testing modalities. Early involvement of medical genetics offers the opportunity for personalized management. More studies are needed to examine long-term outcomes and construct the basis for evidence-based recommendations to inform safety of donations.

Ethics Approval

After discussion with our research ethics board, formal approval was not required as per the Tri-Council Policy Statement (TCPS 2, 2018) and its official interpretation that information that staff normally provide as part of their work duties does not require REB review.

Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Materials

All data are available for sharing by the corresponding author upon request.

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ORCID iD

Somaya Zahran https://orcid.org/0000-0002-0112-0894

Supplemental Material

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