



Canadian Kidney Transplant Recipients', Transplant Candidates', and Caregivers' Perspectives on Precision Medicine and Molecular Matching in Kidney Allocation: A Qualitative Analysis

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Fabian Ballesteros¹, Aliya Affdal², Mohamad Issa³ ,
Marie-Françoise Malo^{2,4}, Savannah-Lou Cochran-Mavrikakis⁵,
Carina Sancho⁴, Stirling Bryan⁶, Paul Keown⁷,
Ruth Sapir-Pichhadze^{8,9} , and Marie-Chantal Fortin^{1,8,10}

Abstract

Background: Antibody-mediated rejection (AMR) is an important cause of kidney transplant loss. A new strategy requiring application of precision medicine tools in transplantation considers molecular compatibility between donors and recipients and holds the promise of improved immunologic risk, preventing rejection and premature graft loss.

Objective: The objective of this study was to gather patients' and caregivers' perspectives on molecular compatibility in kidney transplantation.

Design: Individual semi-structured interviews.

Setting: The Centre hospitalier de l'Université de Montréal (CHUM) and McGill University Health Centre (MUHC) kidney transplant programs.

Participants: Kidney transplant candidates, kidney transplant recipients, and caregivers.

Methods: Twenty-seven participants took part in semi-structured interviews between July 2020 and November 2021. The interviews were digitally recorded, transcribed, and analyzed using the qualitative description approach.

Results: Participants had different levels of knowledge about the kidney allocation process. They expressed trust in the system and healthcare professionals. They indicated that a fair organ allocation system should strive to maximize graft survival as it would decrease the demand for deceased donor kidneys and allow more patients to access transplantation. Molecular matching and precision medicine were seen as important improvements in the kidney transplant allocation process given their potential to improve graft survival and decrease the need for retransplantation. However, participants were concerned about increased waiting times that may negatively impact some patients upon implementation of molecular matching. To address these concerns, participants suggested integrating safeguards in the form of maximum waiting time for molecularly matched kidneys.

Limitations: This study was conducted in the province of Quebec most of the participants were white and highly educated. Consequently, the results could not be generalizable to other populations, including ethnic minorities.

Conclusions: Molecular matching and precision medicine are viewed as promising technologies for decreasing the incidence of AMR and improving graft survival. However, further studies are needed to determine how to ethically integrate this technology into the kidney allocation scheme.

Trial registration: Not registered.

Abrégé

Contexte: Le rejet médié par les anticorps (RMA) est une cause majeure de perte des reins greffés. L'application en transplantation de technologies de la médecine de précision, une nouvelle stratégie tenant compte de la compatibilité moléculaire entre les donneurs et les receveurs, promet de réduire le risque immunologique, et ainsi prévenir le rejet et la perte prématurée du greffon.

Objectif: Recueillir les points de vue des patients et des proches aidants sur l'utilisation de la compatibilité moléculaire en transplantation rénale.



Conception: Entrevues individuelles semi-structurées.

Cadre: Les programmes de transplantation rénale du Centre hospitalier de l'Université de Montréal (CHUM) et du Centre universitaire de santé McGill (CUSM).

Sujets: Candidats à la transplantation rénale, receveurs d'une greffe et proches.

Méthodologie: Vingt-sept personnes ont participé à des entrevues semi-structurées entre juillet 2020 et novembre 2021. Les discussions ont été enregistrées numériquement, transcrites et analysées selon une approche de description qualitative.

Résultats: Le niveau de connaissances du processus d'attribution des reins variait parmi les participants qui, par ailleurs, ont dit faire confiance au système et aux professionnels de la santé. Ils ont en outre indiqué qu'un système équitable d'attribution des organes devrait s'efforcer de maximiser la survie des greffons, car cela réduit la demande pour des reins de donneurs décédés et permet à un plus grand nombre d'individus d'accéder à une greffe. L'appariement moléculaire et la médecine de précision ont été jugés comme des améliorations importantes du processus d'allocation des organes, vu leur potentiel d'accroître la survie des greffons et de diminuer les besoins de retransplantation. Les participants s'inquiétaient toutefois de l'allongement des temps d'attente qui pourrait entraîner des conséquences négatives pour certains patients pendant la mise en œuvre de l'appariement moléculaire. Pour répondre à cette préoccupation, les participants ont suggéré d'intégrer des garanties sous forme d'un temps d'attente maximal pour les reins attribués par appariement moléculaire.

Limites: Cette étude a été réalisée au Québec et la majorité des participants étaient blancs et très instruits. Par conséquent, les résultats pourraient ne pas être généralisables à d'autres populations, notamment aux personnes issues de minorités ethniques.

Conclusion: L'appariement moléculaire et la médecine de précision sont vus comme des technologies prometteuses pour réduire l'incidence du RMA et améliorer la survie des greffons. D'autres études sont nécessaires pour préciser la façon d'intégrer cette technologie de façon éthique dans le schéma d'attribution des reins.

Keywords

molecular matching, kidney allocation, precision medicine, qualitative study, kidney transplantation

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Introduction

Kidney transplantation is the best medical treatment for patients with end-stage kidney failure.¹ Kidney transplantation significantly improves patients' quality of life and health status.²⁻⁴ Unfortunately, transplants do not last for the entire patients' lifetime and result in eventual graft loss. For instance, in Canada, the 10-year graft survival rate is 58% for deceased donor kidney transplantation and 77% for living donor kidney transplantation.⁵ One major cause of graft loss is antibody-mediated rejection (AMR) for which there are no well-proven effective therapies. Antibody-mediated rejection could occur early or late during the transplantation

course.⁶⁻⁹ Antibody-mediated rejection is associated with the development and/or the presence of donor-specific antibodies (DSA) which occur when there is an immune recognition by the transplant recipient of non-self epitopes on human leukocyte antigens (HLA).¹⁰

Worldwide, deceased donor kidney allocation algorithms strive to balance equity and medical utility.¹¹ In Canada, kidneys are allocated on a provincial basis. The allocation scheme differs from one province to another, but time spent on dialysis, pediatric priority, HLA compatibility and medical urgency are criteria considered by the different organ donation organizations.¹²⁻¹⁶ In addition, deceased donor kidneys are shared between provinces for highly sensitized

¹Centre hospitalier de l'Université de Montréal, QC, Canada

²Bioethics Program, École de santé publique de l'Université de Montréal, QC, Canada

³Faculté de médecine et des sciences de la santé, Université de Sherbrooke, QC, Canada

⁴Centre de recherche du Centre hospitalier de l'Université de Montréal, QC, Canada

⁵Department of Philosophy, Université de Montréal, QC, Canada

⁶School of Population and Public Health, University of British Columbia, Vancouver, BC, Canada

⁷Faculty of Medicine, University of British Columbia, Vancouver, BC, Canada

⁸Canadian Donation and Transplantation Research Program, Edmonton, AB, Canada

⁹Faculty of Medicine, McGill University, Montréal, QC, Canada

¹⁰Faculty of Medicine, Université de Montréal, QC, Canada

Corresponding Author:

Marie-Chantal Fortin, Full Clinical Professor, Researcher, Centre de recherche du Centre hospitalier de l'Université de Montréal (CRCHUM), Université de Montréal, 900 Saint-Denis Street, Room R12-418, Montréal, QC H2X 0A9, Canada.

Email: Marie-chantal.fortin.med@ssss.gouv.qc.ca

patients (calculated Panel Reactive Antibody (cPRA) > 95%) through a national registry managed by Canadian Blood Services.¹⁷

In recent years, molecular-based matching was proposed for kidney allocation.^{18,19} This is a more precise method of HLA compatibility assessment, which consists of breaking down each HLA at the molecular level and considering the combination of amino acid polymorphisms informing antibody development.²⁰ Molecular compatibility could decrease the development of DSA by the recipient and, therefore, the incidence of AMR.²¹ The Genome Canada Transplant Consortium set an objective for itself to develop a national molecular-compatibility-based kidney allocation program to decrease the incidence of acute rejection.¹⁹ While molecular compatibility may improve long-term outcomes for kidney transplant recipients (KTRs), it could also result in decreased access to transplantation in patients who have a distinct molecular profile in comparison with the donor pool, raising concerns around fairness.¹¹

Patients and caregivers share important perspectives on the issue of how one should distribute a scarce resource such as a deceased donor kidney fairly. First, any new policies affecting organ allocation may affect their chances of being transplanted. Also, patients' preferences on organ allocation are shaped by their medical concerns and their experiential knowledge when awaiting an organ and/or living with the consequences of AMR. Different studies have shown that patient preferences in terms of organ allocation, such as deservingness, are not necessarily aligned with existing allocation criteria.^{22,23}

This study is part of a larger research project, CanPREVENT AMR, the objective of which is to use genetic technologies to improve donor-recipient compatibility and reduce the risks of AMR.¹⁹ The CanPREVENT AMR project also aims to document various stakeholders' perspectives on the ethical issues related to molecular matching in deceased kidney allocation. We have previously reported the Canadian transplant professionals' perspectives on precision medicine and molecular matching.²⁴ The objective of this study was to gather Canadian KTRs', kidney transplant candidates' (KTCs'), and caregivers' perspectives on precision medicine and molecular matching in kidney transplantation, with the vision of informing future allocation rules when incorporating molecular compatibility into deceased donor kidney transplantation in Canada.

Methods

This study was exploratory in nature. We used the consolidated criteria for reporting qualitative research checklist.²⁵ We conducted individual semi-structured interviews to gather KTRs', KTCs', and caregivers' perspectives on precision medicine and molecular compatibility in kidney

transplantation. The Centre hospitalier de l'Université de Montréal (CHUM) and the McGill University Health Centre (MUHC) research ethics boards approved the study and all participants provided their informed consent (CHUM CE20.054, MP-02-2021-9021; MUHC MEO-02-20221-6938).

The recruitment and interviews were carried out between July 2020 and November 2021. Convenience and purposive sampling²⁶ were used to recruit KTRs, KTCs, and caregivers. Participants were recruited among the KTCs and KTRs followed at the CHUM and at the MUHC, 2 transplant programs located in the Canadian province of Quebec. Figure 1 summarizes the recruitment process. To be included in the study, participants had to be adults and speak English or French. Invitation letters were sent to KTRs and KTCs. Flyers about the study were also distributed at the CHUM and the MUHC transplant clinic, and a research coordinator approached patients during the transplant clinic. Caregivers were invited to participate through KTRs and KTCs. Moreover, we used social media to recruit patients through the Facebook pages of the Canadian Donation and Transplantation Research Program, the Kidney Foundation of Canada and the CHUM.

Forty KTRs, 9 KTCs, and 3 caregivers were interested in having more information about the study and were contacted by the research team. Of these 52 individuals, 8 KTRs declined to participate due to time constraints and personal reasons; 5 KTRs could not be reached; and 9 KTRs, 2 KTCs, and 1 caregiver did not send back a signed informed consent form. Two KTRs and 1 KTC requested to participate with their caregiver (spouse). Of the 30 participants who consented to participate, 2 KTRs and 1 KTC could not be reached to schedule an interview, meaning 27 patients and caregivers participated in this study: 16 KTRs, 6 KTCs, and 5 caregivers (Figure 1).

Twenty-one participants took part in an individual interview: 14 KTRs, 5 KTCs, and 2 caregivers. Two KTRs and 1 KTC took part in an interview with their respective caregivers. Six interviews were conducted by phone and 18 by videoconference, 17 in French and 7 in English, by a male member of the research team (F.B.) who had no clinical relationship with the participants. French interview excerpts were translated by a professional agency. The interviews lasted around 38 (28-61) minutes and were digitally recorded and transcribed. Each participant received CAN\$30 as a financial compensation for their time. The interview transcripts were sent to all participants for review and approval.

Interviews began with a brief PowerPoint presentation about molecular matching and the objectives of the study (see Supplementary Material). The objective of the PowerPoint presentation was to provide background information on molecular matching and to facilitate participation in discussion. Participants had the opportunity to ask questions about the study before the interviews started. The issues

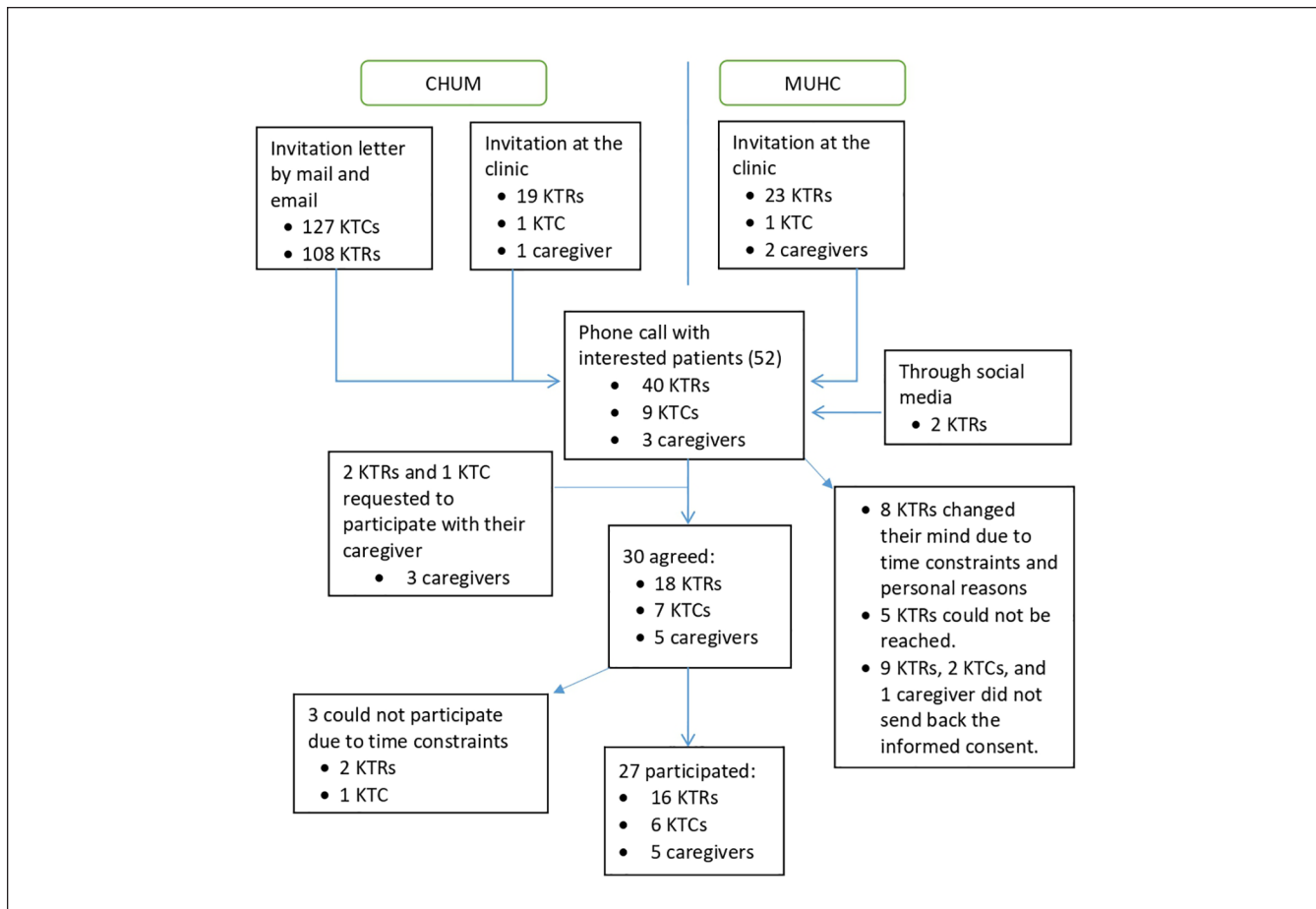


Figure 1. Recruiting flow chart.

covered during the interviews were outlined in an interview guide with open-ended questions that was developed by the research team and pre-tested by 2 patients for question length and clarity, in both English and French. The questions addressed the following themes: (1) knowledge and perspectives on the current organ allocation system, (2) the role of molecular matching in deceased organ and living kidney donation, (3) informed consent and molecular compatibility, and (4) sociodemographic data (see Supplementary Material). Consistent with qualitative methodology, the interview guide was modified during the study as new topics emerged from the interviews.²⁶

We used a qualitative description approach to describe the perspectives of patients and caregivers on molecular matching in kidney transplantation.^{27,28} The goal of this pragmatic approach was to stay close to the data and provide a comprehensive summary of the topic studied,²⁸ using thematic analysis.^{26,29} The latest version of NVivo (Lumivero) software was used to facilitate the analysis. Prior to coding the verbatim, the research team created the initial coding frame based on the interview guide and a review of the literature. New codes were added to the

coding frame based on the interview content. The research team met frequently to discuss the coding frame and data analysis. F.B., a male researcher with more than 10 years of experience conducting qualitative research in the field of organ transplantation ethics, coded the interviews and no new codes were created after the 20th interview. The number of participants allowed for data saturation.^{30,31} A female independent researcher (A.A.) who is completing her PhD in bioethics and has worked in our research team in ethics and organ transplantation for more than 5 years and has experience in qualitative methods coded 37% of the raw data with the rate of coding agreement assessed at 96% and disagreements were discussed. Coded quotes were then organized by themes and subthemes.

Results

Participants' Characteristics

Sixteen KTRs, 6 KTCs and 5 caregivers participated in the study. Fifteen participants were women and most of them were white (89%). Participants were in their fifties and half

of them had a university degree. Notably, more than half of the participants (52%) were currently employed and 56% had an annual family income of more than \$50,000. Table 1 summarizes participants' characteristics.

Perspectives and Knowledge of the Current Allocation System (Table 2)

Participants had some limited knowledge about the current organ allocation system. They were aware of some criteria about the current organ allocation system, such as the HLA and blood group compatibility. Some of them mentioned needing more information and transparency. One caregiver mentioned the need to know the patient's queue place and average waiting time.

Participants trusted health professionals and organ donation organizations in their ability to develop a fair allocation system for deceased kidney donor. When questioned specifically on kidney allocation criteria, most participants viewed compatibility between the donor and the recipient as the most important criterion. For KTCs, time spent on dialysis as well as any factors that could affect graft survival, such as non-adherence, were viewed as important criteria. For KTRs and caregivers, transplant recipients' lifestyle habits were also viewed as a factor to take into account when allocating deceased donor kidney. Participants also believed that a fair allocation system should strive to maximize graft survival as it would decrease the demand for deceased donor kidney and would allow more patients to have access to transplantation.

Perspectives on Precision Medicine and Molecular Matching in Kidney Transplantation (Table 3)

Many participants viewed precision medicine and molecular matching as an interesting avenue to explore as it could improve graft survival, prevent graft rejection, and make the healthcare system more cost-effective. That being said, they also expressed concerns regarding this new technology. Indeed, some participants questioned whether molecular matching could prevent some patients from having access to kidney transplantation or increase waiting time for other patients. They feared that precision medicine could discriminate and disadvantage some patients.

Use of Precision Medicine and Molecular Matching in Living Kidney Donation (Table 4)

Precision medicine and molecular matching could also be used in living kidney donation to choose the better-matched living donor or to invite compatible pairs to enter into kidney paired donation to have a molecular-matched kidney. Most participants were open-minded about including molecular matching in living kidney donation and inviting compatible pairs in kidney paired donation. However, they believed that

Table 1. Participants' Characteristics.

Characteristics	N = 27
Category	
Kidney transplant recipients (KTRs)	16
Kidney transplant candidates (KTCs)	6
Caregivers	5
Province of origin	
Quebec	25
Ontario	1
Alberta	1
Sex	
Female/Male	15/12
Age (years \pm SD) (range = 37-70)	56.0 \pm 11.9
Ethnic group	
White	24
Other	3
Employment status	
Employed/self-employed	14
Retired	10
Other	3
Level of education	
University	13
High school and college	12
Elementary	2
Annual family income	
More than \$100K	9
\$50K-\$100K	6
Less than \$50K	11
Prefer not to answer	1
Time since transplant for KTRs (years \pm SD) (range = 1.8-32.1)	8.4 \pm 9.9
Type of renal replacement therapy for KTCs	
Hemodialysis	4
Peritoneal dialysis	2

participation of compatible pairs in kidney paired donation should be voluntary and not mandatory. That being said, some of them believed that certain participants would be reluctant to participate in kidney paired donation to have a better-matched kidney, preferring to donate or receive a kidney from their loved ones. They also questioned whether molecular matching in kidney paired donation could increase the waiting time for a kidney transplant.

Mitigation Strategies and Recommendations for Implementing Precision Medicine and Molecular Matching in Kidney Transplantation (Table 5)

As mentioned above, the possibility that molecular matching and precision medicine could increase waiting time for a kidney transplantation for some patients was a major concern. To mitigate the increased waiting time for a molecular-matched deceased donor kidney, some participants

Table 2. Perspectives and Knowledge of the Current Allocation System.

Themes and Interview Excerpts	N = 27
Limited knowledge and the need for more information <i>I know there's the blood group, that's one of the things I'm aware of, so a certain compatibility. As for the rest, I never really went into detail about it. I was told I was O positive, but they didn't tell me about the average waiting time. We talked about having a certain amount of time, but that it shouldn't take too long either. (KTC2, male)</i> <i>I understand that there is a point system out there. No one will give you a straight answer on how the point system works. . . . [N]o one will sit down and actually say this is how the point system works. It's like a big secret in the world of transplant. . . . So, if we educate people more in regard to what the process is and what they look at and how they can be, like how we can help with the process, that's why I think it's so important to do these things. (KTR2, female)</i> <i>I wanted a bit more visibility on the, how high or low we are in the queue. . . . I mean what really helps the patient is, and that helped us a lot, like when we're on a list and then or we didn't have a . . . prepping for the list, we . . . the average waiting time . . . that helped us prepare, . . . , this lifestyle of dialysis, and then that gave us, you know, it gave us a window at least. (Caregiver2, male)</i>	14
Trust in the system <i>[I] always felt I trusted the caregivers and the way organs are allocated for now, I think it makes a lot of sense, and no, I was very confident. (KTC1, male)</i> <i>So, like time on dialysis for instance, like blood-type matching, cross-type matching, stuff like that, I think it's fair. . . . I think the system right now is fair in a sense that like what we said, we trust that. (KTR5, female/Caregiver2, male)</i>	10
Immunological compatibility and graft survival are the most important criteria to consider when allocating an organ <i>If you're matching from a deceased donor, then you want to make the best match that you're going to make, so it will last the longest. (KTR7, female)</i> <i>Well the compatibility criteria, for sure should be there. I think the most important ones are the blood group and then the anti-HLA. (KTC4, female)</i> <i>Yes, well I mean the waiting time and then the time on dialysis, and then the chances of graft survival. I think these are things that are, that are important. (KTR14, female)</i>	12
Adherence, time spent on dialysis and lifestyle habits need to be considered <i>I would say that time spent on dialysis, I think, is something that is important. (KTC1, male)</i> <i>But the third criterion would be more important, and adherence too. Of course, if you smoke, drink alcohol. . . in any case, if there were too many complications associated with things like that, I'd be less willing to give you a kidney than to someone who's like a normal person, who doesn't have too many comorbidities, as we say. (KTR1, male)</i> <i>We've seen, we've seen dialysis patients come in and they were pretty wrecked, either they drank in between sessions, or, and when we saw that, I'm like ok, well does this person? You know, you ask yourself the question, does this person deserve a transplant because they are abusing their body and that. (Caregiver2, male)</i> <i>I'd say lifestyle habits too might be a factor to consider. People who are going to make good use of it and then all that after a transplant. I know it's part of the interview process when we meet and all that. There are a number of questions, and they really want to see how we're going to act with this, with the question of transplantation and whether we're going to make good use of it. (KTC2, male)</i> <i>[W]e would take points off someone who doesn't take their medication, it's not complicated, if they don't take their medication, they're going to lose their graft. . . . loss of points for taking alcohol, smoking, I don't know what else. (KTC1, female)</i>	8

recommended setting a maximal waiting time. The maximum acceptable additional waiting time for a molecular-matched kidney would be 4 years or 1 or 2 years over the average waiting time. After this delay, if the KTC did not receive a molecular-matched deceased donor kidney, they would be prioritized to receive a deceased donor kidney based on the former allocation criteria. Other participants would, however, prefer to receive a non-molecularly matched kidney to be transplanted more rapidly and stop dialysis.

Some participants addressed the difficult situation of highly sensitized patients who are hard to match in the current allocation system. These patients suffer from high anxiety waiting for the perfect match, worrying they will never be able to get a transplant. Some participants suggested that

highly sensitized patients should not be considered for precision medicine, as it might further complicate finding suitable matches. Other participants suggested that these hard-to-match patients should still have access to current programs, such as national sharing of kidneys, while being considered for molecular-matched deceased donor kidneys simultaneously.

One important recommendation was about informed consent and education about precision medicine and molecular matching in kidney transplantation. Patients wanted to be informed on how molecular matching will increase their graft survival and decrease the risk of rejection. Patients also want to be informed about the chances of finding a molecular-matched kidney in an acceptable timeframe. Percentages were described as a good way to communicate

Table 3. Perspectives on Precision Medicine and Molecular Matching in Kidney Transplantation.

Themes and interview excerpts	N = 27
<p>Precision medicine and molecular matching is an innovative way to allocate organs</p> <p><i>I think that if we can improve, I, for one, don't have any objections to that. What's more, this program can just make things better. To avoid rejection, I think, I think it's a win-win. (KTC5, male)</i></p> <p><i>[W]ith better organ allocation, well after that you avoid your potential hospitalizations, you avoid potential problems, you obviously possibly avoid rejection, we agree there, so you avoid major pressure on the healthcare system, and on the person living it, and on all their entourage as well. I think this is a good thing. (KTR9, male)</i></p> <p><i>It's a very positive, that's a very positive possibility I find. It's a real advancement. I'm impressed. (KTR10, female)</i></p> <p><i>I think that's wonderful, I mean if they can match you better and it lasts longer, I think that's the goal, right? We want to do it and make it last as long as it possibly can and let the person have the healthiest life for the longest amount of time without having to go through another surgery and another waiting list and another. Yes, I think that's, if we could do that, it would be amazing. (KTR11, female)</i></p>	19
<p>Concerns</p> <p><i>I have mixed feelings. Yes, we want the graft's survival rate to be the best possible, but we also want to look at we don't want to leave people out from not taking the route of transplant. . . . I don't want the best match to having to turn somebody down for a transplant. (KTR2, female)</i></p> <p><i>My reaction right away was this, whenever you target it as precisely as possible, you have a better chance of success, there's no question, however if that takes more time and if that restrains a person from getting it when they really need it, then that's my concern. . . . I think ethically you can't just rely on that, it's that just even a bigger level of discrimination too. (Caregiver3, female)</i></p> <p><i>Well for those, for those who are waiting, I think it's not super good news. In fact, if there are risks, are there more risks of not being transplanted or? If that's what it is, I don't quite agree with it. (KTR15, female)</i></p>	12

Table 4. Use of Molecular Matching in Living Kidney Donation.

Interview excerpts	N = 27
<p>Precision medicine is an avenue to explore in kidney paired donation</p> <p><i>Well, I tend to trust the medical specialists at the research centre. If they tell me I'm not in danger of complications and to delay, I'd be willing to delay for a period of time, but if no match can be found within a reasonable time, well I'd revert to my donor who's here next to me, the member of my entourage, to receive the transplant. (KTR14, male)</i></p>	24
<p>Preferences to donate or receive from their loved ones</p> <p>Section 1.01 <i>That may not be an option, just for my experience I'll say, to put into a paired exchange, and the reason I say that is, there are people out there who only want to give to their loved ones. So, once they hear paired exchange, they are like no, I'm not donating. . . . And so, if you tell them they are a match and then you want them to go into a chain to get a better one, you might have some problems. (KTR2, female)</i></p>	8
<p>Participation in kidney paired donation should be voluntary</p> <p><i>Yes, well listen, I think it's fine to offer it, it's not, as long as it's not compulsory, because there are many things that come into play. . . (KTR4, female)</i></p>	15

risk. Participants also believed that the information provided should be adapted to every patient's situation and preferences.

Lastly, although participants found that molecular matching and precision medicine are interesting avenues, they also stressed the need to pursue research to develop renal replacement therapy that would improve patients' health and quality of life. Even if molecular matching and precision medicine could improve graft survival, participants also highlighted the need to support patients and caregivers throughout their transplant journey.

Discussion

This is the first study to describe KTRs, KTCs', and caregivers' perspectives on the integration of molecular matching

and precision medicine in deceased donor kidney allocation and in living kidney donation. Most participants had a positive view on the integration of molecular compatibility into organ allocation schemes as it has the potential to improve graft survival, prevent retransplantation, and, therefore, decrease the shortage of organs available for transplantation. They were, however, concerned by the possibility of decreasing access to transplantation for certain groups of patients and increasing waiting time when seeking molecularly compatible kidneys.

The balance between medical utility and fairness is a cause for ongoing tension in the field of organ allocation. Most allocation systems try to balance both utility and fairness.^{11,32} Our study has shown that participants truly value graft survival. For most participants, a fair deceased kidney allocation system should take into account compatibility

Table 5. Mitigation Strategies and Recommendations for Implementing Precision Medicine and Molecular Matching in Kidney Transplantation.

Themes and interview excerpts	N = 27
Setting a maximal waiting time <i>For myself, I consider that maybe there should be a maximal waiting time for this. (KTR4, female)</i> <i>Well, it's been three and a half years, and I'm already at the end of my rope, so it can't be more than four years. (KTC4, female)</i> <i>If the average is two to three years, I say four years. (KTR16, female)</i> <i>Yes, I do, I do, there's, there's a certain amount of waiting that should be reasonable, and beyond that, it's, yes, it doesn't feel right. (Caregiver3, female)</i>	7
The difficult situation of highly sensitized patients Section 1.02 <i>If you already have a high sensitized population, you already know that they are going to be difficult to match. You already have an expectation that your precision medicine will not work on those patients, so leave them in the pool, leave them in the general pool. You already do it now, you just said. I didn't realize that, so it's one of, you know? Leave them in the pool, they wait long enough. It's not like in terms of burden of sharing the burden of us all, you know, having to wait, to go through dialysis, you know? Keep them out of, keep them out of the precision testing. (KTR8, female)</i> Section 1.03 <i>Maybe there could be exceptions made for people who are extremely hard to match, and they get a kidney anyway that lasts less long. [. . .] I think, I think the system is wonderful to make sure that people are getting a really good match, but we can't just forget about the people for whom it's difficult. So, I think there should be some sort of program that's helping them as well, for sure. (KTR11, female)</i>	5
Informed consent and education about precision medicine <i>It's important to have all the information, the keys and the pros and cons. There were risks, which were very significant; they need to be brought up. There were risks and we knew it. We knew what the risks were, it's important that they be well laid out. (KTR3, female)</i> <i>A percentage would be nice. It's true that it comes with caveats too, of course, we're never sure of the exact percentage. But an idea of the proportion of how many people who have had rejections in these targets, in these antigens, you know. . . Like "for one hundred transplant recipients, there have been three rejections," so, on average. . . there are 97 people out of 100 who tolerate it well. That's more information from past transplants. (KTR1, male)</i>	16
Research to develop renal replacement therapy that will improve patients' quality of life and health status <i>Other participants (KTCs and KTRs) are proposing to develop options that would make dialysis more acceptable and consequently optimize quality of life. For example, develop a form of self-dialysis at home or something autonomous so that the person can at least work remotely or more. . . like having something that doesn't require getting hospital care. (KTR16, female)</i> <i>Yes, just give them, give them their last little bit of life, so they could spend at least some time with their families and, you know? No, I mean, cause from what I've heard, especially close to the end, you know when you've been on dialysis for so long, you don't have quality of life, so maybe just getting away from the dialysis machine for a little bit and get some quality of life would be better than nothing. (KTR7, female)</i>	4

between the donor and the recipient as well as other factors that could affect future graft survival, including lifestyle behaviors. These results are aligned with other studies, which have shown that for patients life gained after transplantation, and rejection prevention, are important determinants in the design of deceased donor allocation schemes.^{22,33,34} For some patients who participated in a qualitative study, medical compatibility between the donor and the recipient was an essential prerequisite.³³ The high value given by patients to medical utility and graft survival differs from the results of our previous study looking at transplant professionals' views on molecular matching, prioritizing fairness over utility in organ allocation.²⁴ A recent worst-off scaling survey conducted with community members in Australia showed that the most valued principle was related to equity and fairness. In this study, participants prioritized deceased kidney transplantation to patients who had waited the longest, were hard to match, and those deemed the sickest.³⁵

Participants in our study were open-minded about including molecular compatibility in kidney paired donation. Wide-scale buy-in prioritizing the enrollment of molecularly compatible pairs into the kidney paired donation program is expected to further decrease immunological risk. Recently, Jackson et al invited the transplant community to revisit the existing paradigm on compatibility in living donation. For these authors, compatibility should be viewed more broadly than ABO/HLA compatibility and include molecular matching.³⁶ However, participants in our study found that participation of compatible pairs in the kidney paired donation program should be considered voluntary rather than mandatory. This is aligned with our previous study, which showed that the prospect of receiving a better kidney was a factor that increased the willingness of compatible pairs to participate in kidney paired donation; however, participants also expressed a strong desire to donate or receive from their intended donor or recipient.³⁷

Our study participants also made interesting recommendations around safeguards when incorporating precision medicine or molecular matching in deceased organ allocation. First, they proposed that a maximal waiting time be set when awaiting a molecularly compatible kidney. Should this maximal waiting time be exceeded, the recipient should be prioritized for transplantation according to allocation rules excluding molecular compatibility. They also recommended the development of educational tools informing candidates on their likelihood of accessing molecularly compatible kidney within a given timeframe. Given the complexity of molecular HLA compatibility, transplant professionals may experience challenges in communicating the opportunities and challenges expected when incorporating them into organ allocation.³² Future studies are needed to explore the most appropriate educational tools on this topic.

A recent Canadian public deliberation process was conducted to define the guiding principles for incorporating molecular compatibility into kidney allocation schemes. Participants in this public deliberation agreed with the inclusion of molecular-based matching into deceased donor kidney allocation. However, they believed that there should also be safeguards and flexibility must be exercised to ensure fairness in organ allocation. They also recommended that patients with declining health have access to a non-molecularly matched kidney for quicker access to kidney transplantation. It is also important to develop a comprehensive educational program and to reassess the outcomes of precision medicine in organ allocation in 5 years.³⁸ These recommendations are aligned with our participants' perspectives.

Limitations of our study include a small sample size, albeit it is important to recall that data saturation was achieved. Also, most study participants were from the province of Quebec, white and highly educated. Moreover, it was often proposed to include precision medicine in kidney transplantation for pediatric patients first to prevent the development of DSA, which would make future kidney transplantation harder to realize for increased immune sensitization.³⁹ Accordingly, another limitation of this study is the lack of parents' perspectives on molecular compatibility implementation for pediatric patients. It is also possible that the PowerPoint presentation used to inform patients about molecular matching could have biased participants' answers. Finally, it is possible that the results of this study are not generalizable (limiting external validity) and not representative to all Canadian KTRs', KTCs', and caregivers' views on molecular matching. Importantly, however, our findings are congruent with perspectives of the Canadian public arising from prior public deliberation efforts.³⁸ Finally, while questions regarding the ethical issues related to molecular matching and kidney allocation are universal, as kidney allocation and clinical practices vary by country, our results may not be applicable to other parts of the world.

Conclusion

This is the first study to report KTRs', KTCs', and caregivers' perspectives on the integration of precision medicine in deceased and living donor kidney transplantation. While participants viewed precision medicine as a promising avenue that could decrease rejection and the need for subsequent retransplantation, they were concerned about the possibility of discriminating against some groups of patients and decreasing access to transplantation for certain patients. To address these concerns, participants suggested the implementation of a maximum waiting time to receive a molecularly compatible kidney and the development of comprehensive educational tools for providing information about this type of allocation as well as the chances of receiving a molecularly compatible kidney within a specified timeframe. Our findings also indicate a need to develop tools for transplant professionals that can enable them to explain the intricacies and nuances of molecular matching to patients. We believe our findings pave the road for future patient-centered integration of molecular compatibility in the Canadian kidney allocation criteria.

List of Abbreviations

AMR, antibody-mediated rejection; cPRA, calculated panel reactive antibody; CHUM, Centre hospitalier de l'Université de Montréal; MUHC, McGill University Health Centre; DSA, donor-specific antibody; HLA, human leukocyte antigen; KTC, kidney transplant candidate; KTR, kidney transplant recipient.

Author Contributions

F.B. participated in the conduct of the research and the data analysis, and in the writing of the manuscript. A.A. participated in the conduct of the research and the data analysis, and in the writing of the manuscript. M.I. participated in the writing of the manuscript. M.-F.M. participated in the conduct of the research and the data analysis, and in the writing of the manuscript. S.-L.C.-M. participated in the data analysis and in the writing of the manuscript. C.S. participated in the data analysis and in the writing of the manuscript. S.B. participated in the research design and in the writing of the manuscript. P.K. obtained the research funding, participated in the research design and in the writing of the manuscript. R.S.-P. obtained research funding, participated in the research design, conduct of research, and in the writing of the manuscript. M.-C.F. participated in the research design, in the conduct of the research and the data analysis, and in the writing of the manuscript.

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ORCID iDs

Mohamad Issa  <https://orcid.org/0009-0001-8187-4521>

Ruth Sapir-Pichhadze  <https://orcid.org/0000-0003-0745-004X>

Marie-Chantal Fortin  <https://orcid.org/0000-0002-8437-0556>

Supplemental Material

Supplemental material for this article is available online.

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