



Communicating About Precision Transplantation Tools

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Abstract

Purpose of review: Precision tools that ensure molecular compatibility can help prevent rejection and improve kidney transplantation outcomes. However, these tools will generate controversy because they are perceived to and can in fact impact equity in the ethics of allocation. They may also affect the extent to which physicians can advocate for their patient fiduciaries, as generally required by Canadian professional ethics and law.

Sources of information: Electronic databases such as Google Scholar and PubMed were searched for peer-reviewed literature, and Google search engine was used to identify the news articles, jurisprudence, legal information, and other relevant websites cited.

Methods: We discuss controversies precision transplantation tools will likely generate, consider what challenges will arise from their implementation, and provide recommendations of avenues and content for communication to address these issues.

Key findings: Communication about the translation of new precision tools will be challenging as media portrayals of transplantation often focus on individual narratives about access to transplantation and fail to center the issues of utility, allocation, and rejection. Incomplete portrayals of this nature will need to be countered with explanations of how new precision tools can be of net benefit when implemented equitably, as maintaining trust in the donation and transplantation system is key.

Limitations: Our manuscript focuses on precision medicine applications pertaining to the implementation of molecular compatibility in transplantation. Distinct communication content and avenues may need to be considered in other contexts.

Implications: Clear, accurate, and strategic communication is key to managing translation of precision medicine tools. For this purpose, we provide detailed recommendations for stakeholder engagement, content, and avenues for communicating about precision transplantation tools.

Abrégé

Motif de la revue: Les outils de précision assurant la compatibilité moléculaire peuvent aider à prévenir le rejet et à améliorer les résultats de la transplantation rénale. Or, ces outils susciteront une controverse parce qu'ils sont perçus comme ayant une incidence sur l'équité dans l'éthique de l'allocation, et qu'ils peuvent effectivement en avoir une. Ces outils sont également susceptibles d'influer sur les limites au sein desquelles les médecins peuvent défendre les intérêts de leurs patients fiduciaires, comme l'exigent l'éthique professionnelle et le droit canadien.

Sources: Des bases de données électroniques telles que Google Scholar et PubMed ont été consultées à la recherche de la documentation évaluée par des pairs. Le moteur de recherche Google a servi à répertorier les articles de presse, la jurisprudence, les informations juridiques et les autres sites Web pertinents cités.

Méthodologie: Nous discutons des controverses qui seront vraisemblablement générées par les nouveaux outils de précision liés à la transplantation. Nous examinons également les défis qui découleront de leur mise en œuvre et nous formulons des recommandations sur les stratégies et le contenu à adopter dans les communications qui aborderont ces questions.

Principales observations: La communication entourant l'application des nouveaux outils de précision posera un défi, car les représentations médiatiques de la transplantation se concentrent le plus souvent sur des récits individuels liés à l'accès à la transplantation, et ne mettent pas en lumière les problèmes liés à l'utilité, l'attribution et le rejet. Ces représentations incomplètes devront être contrebalancées par des explications sur la façon dont les nouveaux outils de précision pourront être bénéfiques s'ils sont mis en œuvre équitablement; car il est essentiel de maintenir la confiance dans le système de don et de transplantation.



Limites: Notre article porte sur les applications de la médecine de précision en lien avec la mise en œuvre d'outils mesurant la compatibilité moléculaire en transplantation. Il faudra possiblement envisager des stratégies et un contenu de communication distincts dans d'autres contextes.

Conclusion: Une stratégie de communication claire et précise est essentielle pour gérer l'application des outils de la médecine de précision. À cette fin, nous fournissons des recommandations détaillées sur l'engagement des intervenants, ainsi qu'en matière de contenu et de stratégies pour les communications liées aux nouveaux outils de précision en transplantation.

Keywords

bioethics, biomarker, kidney transplantation

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Introduction

Precision medicine tools can help prevent antibody mediated rejection by ensuring molecular compatibility at the time of kidney allocation. Precision medicine has been described as an approach to diagnosis, treatment, and prevention that “takes into account precise delineation of genetic, molecular, environmental, behavioral, and other factors that contribute to health and disease.”^{1,2} Examples of precision tools for donation and transplantation include next generation sequencing and long-read nanopore sequencing.³

Precision tools can potentially allow transplant teams to be more exact in allocation of kidneys to more compatible patients, thus improving utility by increasing average longevity.⁴ Moreover, greater compatibility between kidneys and recipients may help personalize immunosuppression. This can be achieved in patients allocated highly molecularly compatible donors by minimizing the need for immunosuppression, and thus its associated toxicity. In addition, for those recipients with less compatible kidneys, it can ensure sufficient immunosuppression to prevent rejection. Reduced immunosuppression needs from well-matched organs may also improve utility by decreasing rates of other adverse events such as infection and cancer.

Precision medicine innovations are bound to generate controversy within the scientific and bioethics communities, as well as in broader discourse. These advancements will impact how people perceive and experience decisions around the allocation of kidneys. Health and science communications are known to be affected by multiple forces that can impact how accurately and completely they are received, including but not limited to hyping, message creep, narrativizing, and disinformation campaigning.⁵⁻⁸ Here, we discuss controversies precision transplantation tools related to molecular compatibility of human leukocyte antigens will likely generate, consider what challenges will arise from its implementation, and provide suggestions of avenues and content for communication to address these issues.

Precision Transplantation Controversies

As noted, precision transplantation tools will generate controversies. Some will be bioethical, involving the balance of

equity and utility. There is an ongoing tension between those 2 principles, where measures that can improve utility can sometimes be understood to diminish equity. New interventions that increase utility through precision allocation may exacerbate existing systemic inequities in a way that is unjust. For example, we know that ethnic minority transplant candidates are disproportionately excluded from access to organs when human leukocyte antigen B (HLA-B) is given weight in kidney matching.⁹ It is possible for this type of inequity to be exacerbated if we do not carefully pre-empt and audit the impacts and consequences of new precision transplantation tools. Indeed, systemic inequities that impact organ availability, donor pool, and recipient waitlists can cause improvements in utility to generate outcomes that many would consider morally problematic—outcomes in which individuals with greater privilege are granted priority access to transplantation and also experience better post-transplant outcomes than those who are systemically disadvantaged due to socioeconomic or other factors.

Precision transplantation tools will also generate controversy because of the pressure on physicians to protect and treat as paramount the best interests of identifiable patients. This is both an ethical pressure codified in professional ethical standards and a legal pressure codified in common law and elsewhere.^{10,11} Physicians' legal duties in Canada, for example, have been to prioritize the interests of identifiable patients to which they are fiduciaries over and above system-level interests, such as cost containment or resource allocation considerations, other than when official triage protocols are implemented during public health emergencies.¹²⁻¹⁴ The legal and ethical pressures physicians experience has at times led to problematic conduct such as “gaming” the transplant wait list to attempt to prioritize patients whose care doctors

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are personally managing.¹⁵ It is important to recognize that these behaviors are not merely idiosyncratic but are at least in part a by-product of dominant ethical principles and law, both of which are consistently reinforced in the profession. Physicians' sense of agency may be diminished in the presence of greater reliance upon precision interventions in allocation decision-making. This will generate controversy.

Survey data support the idea that precision interventions will be controversial among health care professionals. One qualitative study found that while the benefits of precision tools were acknowledged, physicians believed that a "place must be retained for clinical judgment that allows a physician to make decisions based on medical data, professional expertise and knowledge of the patient."¹⁶ Moreover, a survey of nephrologists found they disapproved of precision medicine tools if those tools raised equity concerns relating to access by disadvantaging certain groups.¹⁷ Clearly, precision tools in transplantation create concern among physicians about reductions in equity and the erosion of their ability to advocate for patients.

The Challenge of Communicating About Precision Tools

Communicating discoveries and implementations of precision tools in donation and transplantation will be challenging. Despite the fact that allocation in North America is very systematic and accounts for many factors relating to equity and utility,¹⁸ media portrayals of transplant do not always reflect this reality. Research has found that portrayals of transplantation in the popular press focus disproportionately on individual patients, using a narrative approach with an emotional, inequity-driven, and patient-centered framing.⁴ They often focus on individuals and their struggle for access to an organ.^{8,19} There is little representation of system-level utility or allocation challenges in the popular press. In addition, transplantation can sometimes be wrongly represented as the final goal of patients when it is not, and wait time can be portrayed as the ultimate burden with little attention given to the risks of rejection and graft failure.

In practice, successful transplantation, prevention of rejection, and greatly improved quality and length of life are all goals. For many, transplantation itself is not the "finish line," and many adverse outcomes including death or retransplantation occur frequently post-transplant, often due to rejection. Taking into consideration the retrospective perspectives of patients with failed kidney transplants, underlying patient desire might often be to find a well-matched organ rather than decreasing time to the next organ offer. This illuminates an important challenge in communicating precision medicine advances in transplantation: countering the incomplete portrayals focused on access to transplantation to properly explain how new technologies can be of net benefit when implemented equitably.

The reality that media portrayals of transplant often focus only on part of the larger picture is important, because these portrayals can impact donation and transplantation systems. Because of these portrayals, transplant and health system officials will have to carefully consider the best way to communicate the ethics and background justification for any decision that alters allocation in a manner perceived to impact equity. Indeed, inherent to many representations of donation and transplantation is a key false dichotomy, which is the idea that utility and equity are always mutually exclusive. In some ways, there are hard limits to the ways in which utility and equity can be increased at the same time, and communicating this is important. However, with certain advances, including some of those being studied in precision transplant medicine, both utility and equity can benefit. For example, precision tools that could prevent immune sensitization for members of a disadvantaged group, a cause of failed first transplant, would diminish the added competition and demand for organs for that population in addition to those who are waitlisted for the first time. Careful communication of these possibilities is important to translation of new tools. In addition, some advances that increase the potential pool of donor organs, either through increasing the number of medically viable organs or increasing the number of individuals willing to donate, could increase access across all equity-seeking groups. Indeed, the need to maintain and build trust in the donation and transplantation system is an important factor to consider in communication, as it affects the availability of organs.

As noted, some physicians may have concerns about potential diminishment of their ability to advocate for identifiable patients. Communicating and collaborating with these professionals on precision tools and their implementation are thus another challenge. Importantly, these tools are not intended to replace physicians' role in transplant, nor to supersede their legal duties to patients, but rather to enhance the decision-making process. The use of molecular compatibility testing, for example, can serve as a tool, providing valuable insights and supporting clinical judgment. Physicians will continue to play a pivotal role in patient care, balancing all the medical, emotional, and ethical factors involved. Well-implemented precision tools will complement their expertise and strengthen the overall transplantation process by providing valuable additional resources. Nonetheless, there remains a possibility that precision tools that improve utility and/or equity could over time reduce the ability of physicians to advocate for patients, and this is a topic that will require continual review as new systems are implemented.

Communicating Effectively

Precision tools can improve equity and utility by making systems more efficient and maximizing the effectiveness of organs. There is value to minimizing the risks of rejection and the need for immunosuppression. Boxes 1 and 2 outline

Box 1. Recommendations for Communicating Precision Medicine Discoveries and Implementations in Donation and Transplantation.

1. Engage with the media: Actively engage with journalists and media outlets to provide accurate information on precision medicine advances and correct misconceptions. Offer expert interviews and press releases to help generate media portrayals that are balanced and note both proof of incorporating equity considerations and explanations of the importance of preventing graft rejection. Avoid excessive focus on identifiable patients and their access to transplant.
2. Inform and engage health care professionals: Conduct targeted educational programs for health care providers to enhance their understanding of precision medicine in organ transplantation. This will enable them to communicate accurate and up-to-date information to patients, addressing misconceptions and emphasizing both equity measures and the importance of long-term health outcomes. Engage with physicians and other health care providers about their concerns with precision medicine in transplantation, and their views on its impacts on the physician-patient relationship.
3. Develop patient-oriented materials: Create easily accessible and comprehensive materials that explain current research into, and when applicable, translation of, precision medicine tools. Include conservative appraisals of the potential benefits and limitations. Use clear language and visuals to convey the importance of avoiding rejection and improving long-term health as primary goals.
4. Collaborate with patient advocacy groups: Partner with organizations representing transplant recipients, donor families, and patients on waiting lists to develop clear and accurate messaging. Involve them in communication campaigns to ensure diverse perspectives are considered.
5. Use social media and online platforms: Utilize social media platforms and online forums to share accurate information and engage with the public. Create content that explains the science behind precision medicine and addresses equity concerns. This can also help to “prebunk” misinformation that can spread virally online.
6. Engage with patient ambassadors: Identify and engage with transplant recipients, living donors, and donor families as ambassadors who are willing to share their personal perspectives on precision medicine and the importance of improving long-term health outcomes for recipients. Their stories can humanize the communication efforts and provide a more accurate representation of patients’ experience of the transplantation process.
7. Collaborate with ethicists and policy experts: Work with experts in ethics and policy to create public communications regarding equity and fair access in the context of precision transplantation. Ensure these communications reflect current organ allocation guidelines and address issues of transparency, fairness, and equitable distribution.
8. Monitor and respond to misinformation: Keep track of online conversations and social media platforms to identify misinformation or misconceptions about precision medicine and transplantation, especially relating to inequity. Respond promptly with factual information and credible sources to counteract false narratives and promote accurate understanding.

Box 2. Recommendations for the Content of Communications Relating to Precision Medicine Tools in Donation and Transplantation.

1. Follow principles of good science communication: Communicate research findings in a carefully measured and contextualized way, avoid jargon, explain limitations, tailor communications toward the communities targeted, ensure messages are brief and shareable, provide visual accompaniment where possible, and focus on the potential impacts and implications.
2. Explain the science behind precision medicine: Provide clear and concise explanations of the scientific principles underlying precision medicine in transplantation. Use simplified terms to help patients and the general public understand concepts such as molecular compatibility, genetic testing, intended and adverse effects of immunosuppression, and personalized treatment plans. Ensure communication is transparent and does not frame the issue in a way that may decrease trust.
3. Highlight ongoing research, advancements and challenges: Explain the ongoing nature of scientific research and advancements in precision medicine for transplantation. Share updates on innovative approaches, emerging therapies, and clinical trials to instill hope and provide a balanced representation of progress being made in the field. Acknowledge challenges and future directions, including potential limitations to the extent to which matches can be optimized.
4. Emphasize long-term health outcomes: Highlight that the primary goal of precision medicine in transplantation is not only to achieve successful transplantation but also to ensure long and healthy lives for recipients. Emphasize the importance of avoiding rejection and managing post-transplant complications in order to improve quality of life.
5. Address equity concerns: Acknowledge the concerns related to equity in access to (molecularly) compatible transplants. Note that there has always been a tension between equity and utility in the context of donation and transplantation, citing examples such as the existence of highly sensitized individuals. Consider explaining where relevant that new tools may differentially impact equity depending on geographic location for donations that lack a national organ sharing system, noting that provinces with smaller donor genetic pools may experience greater equity impacts. Highlight efforts being made to ensure fairness, such as adjustments to allocation systems to protect or improve equity in light of new precision medicine tools. Reinforce the commitment to reducing disparities and improving access for all patients. Explain that better compatibility and overall better outcomes for many patients will be made possible the larger and more diverse the living and deceased donor pool becomes.
6. Avoid hyping: Hype about the power of precision medicine could create a misperception about the potential for the technology to have a greater impact on utility than it may have. In order to avoid exaggeration, clearly convey that donor, recipient, and transplant-related factors, including factors as simple as age and sex of donor and recipient, may continue to more greatly inform outcomes, to avoid distrust related to expectations not being met.
7. Debunk myths and misconceptions: Address common misconceptions about transplantation, such as the portrayal of transplantation as a one-time cure-all solution. Clarify that while transplantation can be life-saving, it requires lifelong management and monitoring to prevent rejection and maintain good health. These facts help explain the importance of precision tools.
8. Provide reliable resources: Direct individuals to trusted sources of information, such as reputable websites, patient education materials, and scientific publications. Ensure that the provided resources are up-to-date, evidence-based, and easily accessible to those seeking more information about precision medicine in transplantation.

recommendations for avenues and content of communications relating to advances in precision medicine for transplantation.

In order to manage the impacts of continual discovery and translation, we must recognize that precision medicine tools may be accompanied by a perception of inequity. We must also recognize that actual inequities could arise from precision tools. These should be pre-emptively mitigated by ensuring decisions remain multifactorial, and we should take into account patients' values and receptiveness to risk when there is low likelihood of a timely match. In addition, we must monitor and measure any equity impacts and develop strategies to mitigate them as they emerge. This will require engaging with patients and stakeholder communities. Clear, accurate, and strategic communication is key to managing translation of these tools. Good communication will ensure accurate understanding of these exciting new developments and the steps being taken to ensure they are equitably implemented.

Ethics Approval and Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

Availability of Data and Materials

Not applicable.

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