



POINT OF VIEW

Kidney transplantation and patients who decline SARS-CoV-2 vaccination: an ethical framework

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SUMMARY

As SARS-CoV-2 vaccines have started to be rolled out, a key question facing transplant units has been whether listing for transplantation should be contingent on recipients having received a vaccine. We aimed to provide an ethical framework when considering potential transplant candidates who decline vaccination. We convened a working group comprising transplant professionals, lay members and patients and undertook a literature review and consensus process. This group's work was also informed by discussions in two hospital clinical ethics committees. We have reviewed arguments for and against mandating vaccination prior to listing for kidney transplantation and considered some practical difficulties which may be associated with a policy of mandated vaccination. Rather than requiring that all patients must receive the SARS-CoV-2 vaccine prior to transplant listing, we recommend considering vaccination status as one of a number of SARS-CoV-2-related risk factors in relation to transplant listing. Transplant units should engage in individualised risk–benefit discussions with patients, avoid the language of mandated treatments and strongly encourage uptake of the vaccine in all patient groups, using tailor-made educational initiatives.

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Introduction

The COVID-19 pandemic has had a major impact on kidney transplantation and on patients with end-stage kidney disease. Transplantation activity has been substantially reduced, and kidney transplant recipients have suffered increased mortality. The introduction of vaccines against SARS-CoV-2 has offered considerable hope that it may be possible to protect patients from the risks associated with SARS-CoV-2 infection and that more

patients may once again have access to kidney transplantation. However, as the SARS-CoV-2 vaccines have started to be rolled out, it has become clear that a significant proportion of the population has been hesitant about being vaccinated, and uptake of the vaccines in potential kidney transplant recipients has not been universal. Although data from the UK Household Longitudinal study showed overall high levels of willingness (82%) to take up the SARS-CoV-2 vaccine, high levels of vaccine hesitancy were noted in certain groups [1].

Similar variations in intention to be vaccinated have been shown in the USA [2], Italy [3] and other national surveys [4]. Unpublished data from one centre in London show that between 3.5% and 18.6% of patients undergoing satellite haemodialysis have declined vaccination to date.

In this context, one of the key questions facing transplant units has been whether listing for transplantation should be contingent on potential transplant recipients having received the vaccine. This paper aims to review the ethical arguments for and against mandating vaccination as a prerequisite for transplant listing and to support transplant units in their approach to potential transplant candidates who are hesitant towards or decline vaccination in countries where patients have access to vaccination.

Process

In the UK, joint guidance on SARS-CoV-2 vaccination in adult solid organ and islet transplant waitlisted patients and adult living donor transplant recipients was published by NHS Blood & Transplant and the British Transplantation Society on 22 January 2021 [5]. This document includes the following guidance concerning patients who decline vaccination:

Patients who are deemed clinically suitable for solid organ or islet transplantation but decline the offer of SARS-CoV-2 vaccination (full course or second dose) or have contraindications to vaccination should still be considered for transplantation. Clinical multidisciplinary teams must have detailed discussion of risks versus benefits with the patient, document the discussions and the patient decision before activation or remaining active on the waiting list or proceeding to living donor transplantation.

In order to provide more detailed practical guidance for transplant units for this group of patients, the Pan London Transplant Collaborative (PLTC) convened a Collaborative Ethics Group comprising lay members, patients and transplant professionals, many of whom had a special interest in medical ethics. Group membership was selected to reflect the diversity of the local population, and patient representatives included both kidney transplant recipients and patients on the kidney transplant waiting list.

The group's cochairs undertook a literature review, which was followed by a moderated group discussion focusing on describing and evaluating ethical arguments for and against mandating vaccination. The cochairs

also took the issue to the clinical ethics committees at Guy's and St Thomas' NHS Foundation Trust and Imperial College Healthcare NHS Trust, each with similarly broad membership comprising professionals and lay members, but with expertise outside the field of transplantation. The perspectives of the clinical ethics committees were fed back to the PLTC Collaborative Ethics Group; a summary guidance document was prepared by the cochairs and presented to the group for consensus. A summary of this guidance has been provided to UK transplant centres [6]; this review aims to broaden the scope of this guidance for transplant units internationally.

Arguments for mandating vaccination in kidney patients prior to activation or reactivation on the deceased donor transplant waiting list

Duty to protect patients: first do no harm

1.1.1. There is concern that the risks associated with kidney transplantation without prior vaccination against COVID-19 may be excessive. Data from our own cohorts in London have shown that although COVID-19 infections were more common in waitlisted patients, COVID-19-associated mortality is higher in transplant recipients (hazard ratio 3.36) [7]; this has also been demonstrated in a national UK registry-based cohort analysis [8]. A similar increase in the risk of more severe disease in kidney transplant recipients as compared with haemodialysis patients has been reported in both retrospective and prospective analyses of European registry data [9,10]. There is further concern that SARS-CoV-2 infection in the immediate post-transplant period is likely to bring significant additional risk of mortality [10]. This risk can be compounded by other COVID-associated risk factors, including age, diabetes and obesity [11–13].

1.1.2. The desire to protect patients against excessive risks has underpinned the decision to defer reactivation on the deceased donor transplant waiting list for many patients during the pandemic in risk-stratified groups and therefore represents a consistency of approach. However, to date there are no published empirical data allowing assessment of this cautious approach.

Potential harm to others

1.2.1. It may be argued that admitting unvaccinated patients onto transplant wards may put other patients

and staff at risk, and potentially affect the hospital as a whole. While clinicians will need to act in the best interests of individual patients, they will also need to ensure the safety of others.

1.2.2. The idea that certain freedoms may be accessible only to those who have been vaccinated has already become more familiar, as travel and other aspects of easing lockdown restrictions may become contingent on individuals having received vaccinations.

Inappropriate use of a scarce resource

1.3.1. The increased mortality risk of COVID-19 for transplant patients associated with not being vaccinated may lead us to consider unvaccinated patients not to be suitable recipients for the scarce resource of deceased donor kidneys. One of the central principles of transplantation ethics is to maximize the benefit derived from the scarce resource of donated organs; there is legitimate concern that kidneys may be expected to have better outcomes when transplanted into vaccinated recipients as compared with recipients who have declined vaccination.

1.3.2. In addition, a greater risk of graft loss may be expected if recipients are not able to receive optimal treatment for acute rejection as a consequence of having acquired SARS-CoV-2 infection.

1.3.3. Transplant recipients and other patient representatives are particularly keen to emphasize the personal responsibility that many recipients feel to ensure the best possible outcomes from organ donation. Some patients feel strongly that entry to the transplant waiting list should be contingent on an acceptance of this responsibility.

1.3.4. Transplant programmes also need to be mindful of the damage which might be done to public perceptions of organ donation and the enterprise of transplantation as a whole due to allocation of organs to patients in whom less than optimal outcomes may be expected.

Possible precedents

1.4.1. It is possible to argue that SARS-CoV-2 vaccination is an inseparable component of transplantation care. Just as patients who declare that they would decline immunosuppression after transplantation would not normally be considered suitable for transplantation, those who decline to protect themselves against SARS-CoV-2 in the context of the current pandemic may be considered as not consenting to standard transplantation care.

1.4.2. There are also precedents for predicating transplantation listing on aspects of patient choice or

behaviour, such as mandating abstinence from alcohol for liver transplant listing. In this setting, the main argument relates to inferior transplant outcomes in recipients who continue to consume alcohol, which may have parallels with patients who decline vaccination. Once again, this relates to inappropriate use of the scarce resource of donated organs. As noted above in section 1.3.4, this may cause potential reputational harm to organ donation and transplantation.

Arguments against mandating vaccination

Autonomy and human rights

2.1.1. Mandating a particular treatment overrides the fundamental principle of autonomy. Healthcare professionals are well-accustomed to respecting patient decisions which may be associated with increased risk, and with which they themselves might disagree.

2.1.2. Public Health England and the UK Government have not issued specific guidance on consent to SARS-CoV-2 vaccination, and whether there may be any basis for mandated vaccination. By comparison, The Council of Europe has urged EU member states to ensure that citizens are informed that vaccination is not mandatory and that no one is discriminated against for not having been vaccinated [14].

2.1.3. There are ways in which a decision not to have the SARS-CoV-2 vaccine may not be analogous to not consenting to post-transplantation immunosuppression or other essential parts of the transplant pathway. Most importantly, the risk of graft loss associated with not being vaccinated is not as high as would be expected if individuals decline immunosuppression.

2.1.4. Similarly, while 'vaccination passports' may be contemplated as a means to reopen the tourism industry, many would see a clear difference between restricting access to overseas travel with restricting access to transplantation.

Equity of access

2.2.1. It has become clear that vaccine hesitancy is common in particular patient groups [1,15]. This includes but is not restricted to minority ethnic populations, who already have reduced access to transplantation and have been particularly impacted by the COVID-19 pandemic, especially in London. In this context, there is significant concern that mandating vaccination prior to transplant listing would cause more damage to trust in the medical profession and further exacerbate health

inequalities [16]. Irrespective of any theoretical reasons for considering vaccination to be a valid prerequisite for transplant listing, this potentially harmful practical impact on equity of access and trust within disadvantaged communities has emerged as a key objection to any such approach.

Practical uncertainties

There may be number of potential uncertainties associated with a policy of mandating vaccination, some of which might render such an approach unworkable. These include the following:

2.3.1. To what extent can we protect each and every patient with the vaccine? The efficacy of SARS-CoV-2 vaccines in generating antibody responses has been shown to be diminished as compared with the general population [17–21]. If the goal is to ensure immunity prior to transplantation listing, should listing be limited to those with proven antibody responses?

2.3.2. To what extent will vaccination limit infectivity and transmission of the virus? This is particularly unclear for new virus variants. It is likely to remain of the utmost importance to maintain measures to prevent infection, such as physical distancing and use of appropriate PPE.

2.3.3. If existing SARS-CoV-2 vaccines are found to have limited efficacy against new virus variants, would there still be any argument for vaccination to be mandated?

2.3.4. Should those with evidence of natural immunity be exempted from being vaccinated?

2.3.5. When community prevalence falls, would there be a point when vaccination will no longer be mandated?

2.3.6. Can those unable to receive the vaccine for medical reasons maintain access to transplantation?

2.3.7. If it has been determined that it may be in the best interests of a patient that lacks capacity to be listed for deceased or living donor transplantation, would that imply that vaccination should also be undertaken, in the potential recipient's best interests?

Living donor recipients

Many of the same arguments as stated above for deceased donor kidney transplantation would also apply to directed living donor transplantation, with the key exception of any consideration given to optimal utilization of a scarce public resource. If a recipient declines the opportunity to be vaccinated prior to receiving a

living donor kidney transplant, both recipient and donor will need to consider the increased risks to recipient and graft survival associated with this. The transplant team may feel that the transplant may proceed if donor and recipient have both given informed consent taking into account these additional risks: this may be analogous to situations where recipients have a high risk of graft loss due to recurrent primary disease but donors nevertheless consent to donation.

Suggested approach

4.1. As set out above, cogent arguments can be made both for and against mandating vaccination prior to listing for deceased or living donor kidney transplantation. However, fundamental concerns regarding equity of access, public trust and practical uncertainties have led many in the transplant community to conclude that a blanket policy of mandating vaccination prior to listing for deceased or living donor kidney transplantation would not be ethically desirable, would be unworkable and may do more harm than good. It would go against the principle of autonomy and patient choice and may deprive potential recipients of the benefits of transplantation.

4.2. Nevertheless, these concerns must be reconciled with our duty to protect patients from harm and to act as responsible stewards of the scarce resource of donor organs.

4.3. We suggest the following approach to vaccine hesitancy among potential kidney transplant recipients:

4.3.1. Explore and understand the reasons behind any individual's vaccine hesitancy and address their concerns. The emphasis should be on encouragement rather than enforcement.

4.3.2. Use peer educators or champions as advocates for the vaccine. Valuable resources for encouraging uptake of vaccination are already available; in the UK, many of these are signposted on the Kidney Care UK website [22]. Specific resources for black and minority ethnic (BAME) patients include the Kidney Care UK webinar on vaccination in BAME communities, broadcast on 9 February 2021 [23].

4.3.3. Assess risks and benefits on an individual basis, moving away from the language of mandated treatments.

4.3.4. Discussions with patients who are hesitant about the vaccine should include consideration not only of the risks of not being vaccinated for themselves, but also of the potential impact on others (other patients, hospital staff) and the greater good.

4.3.5. Given the importance of patient risk factors in determining individuals' SARS-CoV-2-associated risk, it is unlikely that it will be possible to predetermine thresholds of community prevalence or reproduction rate which might prompt changes in vaccination policy applicable to all patients.

4.3.6. When making these risk assessments, it is unlikely that unvaccinated patients will be included in the first phase of cautious reopening of transplant programmes, when it will be important to ensure that risk is minimized as far as possible. However, conversations with patients should centre on an overall assessment of risk and strong encouragement to take up opportunities for vaccination.

4.3.7. Patients should continue to be encouraged to practice means of protecting themselves against SARS-CoV-2 infection, including social distancing and, where possible, avoiding crowded indoor spaces.

Summary recommendations

5.1. We suggest the following approach with individual transplant candidates who are hesitant about SARS-CoV-2 vaccination:

5.1.1. Consider vaccination status as one component of clinical risk in transplant waitlisting, along with other

evidence-based clinical risk factors for poor outcomes in SARS-CoV-2 infected transplant patients including age, diabetes, obesity and surgical and anaesthetic complexity. This will mean that there will be high-risk patients where it is deemed that listing would not be appropriate in the absence of vaccination, until community prevalence and transmission rates fall significantly. It is the duty of individual transplant units to review vaccination status and other clinical risk factors in all patients being considered for kidney transplantation.

5.1.2. Given the rapidly evolving knowledge base regarding SARS-CoV-2 and vaccination efficacy in kidney and transplant patients, we suggest reviewing this guidance frequently and updating recommendations as needed.

5.1.3. It will remain important to emphasize the importance of continuing with protective measures including social distancing and rigorous infection control in dialysis facilities and other hospital environments, public transportation and other public areas.

5.1.4. Transplant units should collect data on vaccination uptake, transplantation listing and outcomes for all patients who are listed, those that undergo transplantation and those that remain off the transplant waiting list.

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