


Revision of the Portuguese Rules for the Selection of the Donor-Recipient Pair in Kidney Transplantation

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Abstract

The process of reviewing and updating the rules for the selection of donor-recipient pairs in transplantation is underway, 16 years after the implementation of the current rules. Shortly after the implementation of the 2007 rules, some voices questioned the effectiveness of their results. Therefore, in addition to technical and scientific advances, the errors identified in the past should also serve as lessons learned for this new process underway.

We hope that the current review will lead to simpler, more transparent and fairer allocation rules for such a precious commodity as deceased donor kidneys for transplantation.

Keywords: Donor Selection; Kidney Transplantation; Portugal; Resource Allocation; Tissue and Organ Procurement

INTRODUCTION

The current rules for selecting the donor-recipient pair in transplantation with kidneys from deceased donors were approved by Order No. 6537/2007.¹ These rules repealed those implemented in 2000,² maintaining the text: “Organs for transplantation are a community asset, destined for patients who, with this gesture, will be able to improve their survival and quality of life. For this reason, the choice of donor-recipient pair should always follow the criteria that can best fulfill these objectives, being updated whenever the state of the art recommends it, thus respecting the principles of equity and medical ethics.”

While the current rules were updated seven years after the implementation of the 2000 rules, we had to wait more than 16 years for the Portuguese Ministry of Health, through Order no. 5908/2023 of 25 May,³ to create a working group with the power to analyze and review the rules for selecting the donor-recipient pair in transplantation with deceased donor. This Order from May now states, in relation to Order no. 6537/2007, that “the experience acquired in the meantime with its application and technical scientific progresses demonstrate the need to revise it, in order to updating the clinical and laboratory criteria and the donor eligibility criteria”. But in fact, shortly after they came into force, several voices questioned the results of implementing the 2007 standards.⁴ Furthermore, to date

there is no published evidence to justify the implementation of the 2007 rules from a technical-scientific point of view.

Now that a new process is underway to update the rules for selecting the donor-recipient pair in kidney transplantation, we can only hope that the mistakes of the past are not repeated and that the criteria used to define the new standards are in fact transparent, respecting the principles of fairness and medical ethics.

ASSESSMENT OF PATIENTS AND DONORS

The assessment of the rules for allocating deceased donor kidneys for transplantation must be based on a continuous process adaptable to the evolution of both the patients on the transplant waiting list and the organ donors themselves.⁵ This assessment should be as objective as possible, based on the most up-to-date data and systematic information that can describe both the evolution of the waiting list and the kidney transplants carried out over the last few decades.⁶

Data on end stage renal disease patients who have been or are still on the waiting list for transplantation can come from various sources, such as histocompatibility laboratories, nephrology consultants, hemodialysis centres or transplant units. The definition of objective and systematic

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metrics that can be obtained from this data would allow for better decision-making, also in the evaluation of health policies applicable to the distribution of deceased donor kidneys for transplantation.⁷

In Portugal, there are many entities involved in transplantation activities, namely: the Instituto Português do Sangue e da Transplantação (IPST) with its three *Centros de Sangue e Transplantação*; the five *Gabinetes Coordenadores de Colheita e da Transplantação*, whose focal point is the Hospital Donation Coordinator; and the seven Transplant Centres spread across the country. Each patient on the waiting list can also be registered at two transplant centres, so the process of assessing the candidate for a kidney transplant (and generating all the data that needs to be analyzed) is not simple for either the patients or the medical teams dedicated to this activity.⁸

Currently, the data available on kidney transplantation in Portugal is clearly insufficient. In particular, and because transplantation activities are sponsored by the National Health System, it would be expected that the IPST, as the entity responsible for managing the transplant waiting list, would be able to make data and public information available that would benefit individual patients and could promote research in this area.⁹ Making this type of data available would also be a way of increasing health literacy and community involvement in defining new health policies.¹⁰ It is not intended that individual data be made available, but with the correct characterization of both patients and donors it would be possible to generate more accurate synthetic data and apply data science technologies with which we could obtain new answers to old questions.¹¹ Nevertheless, there are also great examples of efficient data collection and management for kidney transplant recipients and donors. For instance, the CRISTAL application, initiated in 1996 and overseen by the Agence de la Biomédecine, is a nationwide database that systematically gathers information on organ transplants in France. Similarly, the Scientific Registry of Transplant Recipients in the United States is a noteworthy model that Portugal might contemplate adopting.

EQUITABLE DISTRIBUTION

A system for allocating deceased donor kidneys for transplantation must take into account not only the relationship between supply and demand, but also a balance between the net survival benefit that can be attributed to an organ and the waiting time for candidates, along with their likelihood of having access to a transplant.⁶ In other words, any kidney allocation system in transplantation has to take into account the scarcity of available organs, in the search for a fair distribution that can maximize efficiency and allow equitable access, while respecting *Leges Artis*. Unfortunately, the rules of Order No. 6537/2007, which are still in force, have long failed to fulfill this conjecture.¹²

From a utilitarian point of view, the aim of a kidney allocation system is to maximize the total benefit that can be obtained from an organ, while from an egalitarian point of view, all transplant candidates should have the same probability of being transplanted.⁶ According to the ethical principle of justice, equals should be treated equally so that all patients have a similar chance of access to transplantation. On the other hand, considering utilitarian values, some inequalities can be allowed if this gives society - as a group - the greatest benefit by maximizing the utility of resources. Thus, deceased donor kidneys can be directed to patients who can put them to better use and who are less likely to return to the waiting list due to graft rejection.¹³

HISTOCOMPATIBILITY

The success of kidney transplantation depends (to a large extent) on the genetic and immunological compatibility between donor and recipient. Human leucocyte antigens (HLA) are highly polymorphic proteins that play a key role in transplantation. An important barrier to transplantation is HLA sensitization of transplant candidates. The most common sensitization events are blood transfusions, pregnancies and organ transplants, the latter having the greatest potential for sensitization.¹⁴ After the loss of an organ, the risk of a patient developing HLA antibodies *de novo* increases exponentially.¹⁵ Donor-specific antibodies (DSAs), both those present at the time of transplantation and those that arise *de novo*, are a risk factor for rejection and potential organ loss.¹⁶

The identification of HLA antibodies and consequently the definition of non-acceptable HLA antigens for transplant candidates have made it possible to develop concepts of calculated panel reactive antibody (cPRA) and virtual crossmatch (vXM). The cPRA value of a given transplant candidate serves as an estimate of the likelihood that the next available transplant donor will be incompatible with that candidate. This value depends not only on the identification of HLA antigens that are not acceptable for the patient, but also on the HLA frequencies of the population to which the organ donors belong.¹⁷ The way in which these non-acceptable antigens are defined can restrict the chances of finding a possible donor for the patient.¹⁴ Therefore, the cPRA value and the vXM result have to be read as two sides of the same coin.¹⁸

The number of patients on the waiting list for re-transplantation has increased progressively in recent years. Re-transplantation also offers these patients a survival benefit when compared to those who remain on dialysis.¹⁴ This group of patients represents the largest portion of all hypersensitized patients on the waiting list. HLA sensitization compromises access to subsequent transplantation¹⁵ and the difficulty of transplanting these patients means that they remain on the waiting list forever.¹⁴

Kidney transplantation requires a careful immunological study of the donor-recipient pair. Although a positive vXM is a contraindication for transplantation, it can be seen only as an increased risk factor, depending on the patient's history and level of sensitization.¹⁶ Stratifying a transplant candidate's risk of DSAs is fundamental for a clinical assessment of the implications they may represent.¹⁶

Hypersensitized patients have a clear disadvantage in access to kidney transplantation¹⁵ and the current allocation system does not compensate for this disadvantage in an efficient way. The characterization of hypersensitized patients using a measure such as the cPRA is essential for clinicians to be able to inform patients about their real chances of being transplanted.¹⁵

One way of preventing sensitization in re-transplant candidates is to improve the HLA match at the first transplant.¹⁴ In addition, allocation programs aimed at hypersensitized candidates have been proposed as a way of mitigating the disadvantage to which they are subjected in terms of access to transplantation.¹⁴

TRANSPARENT RULES

When possible and compared to dialysis treatments, kidney transplantation increases patient survival, increases their quality of life, has a lower long-term cost and has a much lower environmental impact.⁸ However, the current rules for selecting the donor-recipient pair in kidney transplantation, which have been in force since 2007, are unnecessarily complex, non-transparent and inequitable.⁵ More than enough time has passed to justify an evaluation of the results of these rules and the introduction of improvements in the light of new clinical data available.¹⁹ Given the limitations of healthcare resources, decisions on how best to distribute these scarce goods (such as deceased donor kidneys for transplantation) should be based on the conditions: of publicity (decisions to implement new health policies must be publicized), of relevance (the rationale for decisions must be supported by data), of appeal (a mechanism for challenging decisions taken must be guaranteed) and of regulation (the decision-making process must be regulated to ensure that the previous conditions are met).¹³ Only by applying these four conditions can the legitimacy of the process for defining new rules for selecting the donor-recipient pair in kidney transplantation be guaranteed.

A change is needed, but first it is necessary to carry out simulations that allow us to understand the implications they may have on the waiting list and to anticipate other repercussions that may arise.¹² This type of simulation

must be carried out transparently and based on methods that have been previously tested and evaluated.²⁰ While simplicity alone should not dictate the choice of new rules, it is essential to consistently evaluate them against straightforward and comprehensible rules that act as a reference point for transparency.

The definition of new standards can result from the evaluation of existing models, or from a systematic review of the literature, or from an idea based on empirical knowledge, or even from the consensus of a group of experts. In any case, it would always be desirable for these new rules to first be published in a scientific journal before being published in the Portuguese Republic Official Journal (*Diário da República*).²¹

CONCLUSION

Order no. 5908/2023 defines a working group, which lists some names of indisputable professional and technical-scientific competences for the task assigned to them. Even so, it was given to the IPST's *Coordenação Nacional da Transplantação* (CNT) the task of coordinating the work of this group (with a casting vote). Unfortunately, we do not know of any published scientific work on access to transplantation from CNT, so our expectations can not be very high.

The politician who signed Order 5908/2023 did not have the foresight to give this working group the task of monitoring the implementation of the solutions it was asked to find. The definition of rules for the selection of the donor-recipient pair in deceased donor kidney transplantation cannot be seen as a one-off task at a given moment in time. Any type of rules that may emanate from this endeavor, in addition to a systematic evaluation, must be followed up with an analysis of their impact, both on the outcome of new transplants and on the evolution of the waiting list of transplant candidates.

It would be desirable for the working group now formed to have access to indicators and systematic information every six months, based on reliable (and preferably public) data, which would allow it to draw conclusions about the evolution of kidney transplantation in Portugal. Moreover, considering that it has been over 15 years since the reassessment of rules that have been questioned almost since their introduction, legislators should now seize the opportunity to prescribe a specific timeframe for their revision. Whatever new rules are implemented, we can only hope that they will be the result of a transparent, verifiable and auditable process, unlike the one that took place in 2007.

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BAL: Writing the original draft, Study conception. Read and approved the final manuscript

HA: Conceptualization and supervision. Read and approved the final manuscript

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