

Kidney Transplant allocation in Portugal

Alocação de rins para transplante em Portugal

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■ ABSTRACT

Factors such as: patient age, place of residence, socioeconomic status, cause of kidney failure, prognosis, duration of dialysis and co-morbidities influence transplantation outcome. Also the quality of available donors must be taken into account when looking for the balance between utility and justice. In the USA, UK and Portugal deceased donor kidney allocation rules are based on systems of points assigned to each possible receptor. However, the key factor in organ allocation is time on dialysis (first come, first served basis). The discussion about access to kidney transplantation with deceased donors never comes to a close and must be done clearly and systematically in order to enable the best decisions at any given moment.

Key-words: Organ allocation system; kidney transplant.

■ RESUMO

Tendo em conta o fato de que o dador cadáver de órgãos é um bem escasso, a sua distribuição deve ser equilibrada, a fim de maximizar a utilidade e justiça. Um sistema de distribuição de rins de dador cadáver deverá ser alicerçado em políticas transparentes. Deve ter em conta a relação entre oferta e procura, buscando um equilíbrio entre o benefício neto mais elevado de sobrevivência que pode ser fornecido por um determinado órgão e o tempo de espera dos candidatos a transplante (assim como a probabilidade de estes serem transplantados). Fatores como: idade do doente, local de residência, nível socioeconómico, causa de insuficiência renal, o prognóstico, o tempo de diálise e co-morbididades influenciam os resultados do transplante. Também a qualidade dos dados disponíveis deve ser considerada quando se olha para o equilíbrio entre a utilidade e justiça na distribuição dos órgãos. Nos EUA, Reino Unido e Portugal as regras de alocação de rins de dadores cadáver são baseados em sistemas de pontos atribuídos a cada possível receptor. No entanto, o fator-chave na alocação de órgãos é o tempo em diálise (numa base: primeiro a chegar, primeiro a ser servido). A discussão sobre o acesso ao transplante renal de dador cadáver é constante e deve ser feita de forma clara e sistemática, de modo a permitir as melhores decisões em todos os momentos.

Palavras-chave: Sistema de alocação de órgãos; Transplante Renal.

■ INTRODUCTION

For patients with end stage renal disease, kidney transplantation provides a lower mortality, reduction of cardiovascular problems and a better quality of life compared with those on dialysis, even for those with advanced age or co-morbidities¹. In light of the fact that deceased donor organs are a scarce resource, their distribution must be balanced in order to maximize utility and justice². Criteria such as: clinical urgency, waiting time, diagnosis, duration of ischaemia, transplant outcomes, number of organs available for paediatric transplants, transplantation in the elderly, time on dialysis, human leukocyte antigen (HLA) compatibility and the presence or absence of HLA antibodies; should and must always be taken into account when discussing access to kidney transplantation³.

An allocation system for deceased donor kidneys should be anchored to transparent policies. It should take into account the relationship between supply and demand, hence seeking a balance between the higher net benefit of survival that can be provided by a particular organ and the transplant candidates' waiting time (as well as the probability of being transplanted)⁴.

■ A NEW KIDNEY ALLOCATION SYSTEM

If one assumes a utilitarian standpoint, the goal is to maximize the overall benefit that can be drawn from an available organ. From the standpoint of access equality, all transplant candidates should have the same opportunities to receive an organ, regardless of the post-transplant outcome⁵, assuming that a particular organ being distributed is equally a good choice and non-damaging to all the candidates (*primum non nocere*).

Factors such as: patient age, place of residence, socioeconomic status, cause of kidney failure, prognosis, duration of dialysis and co-morbidities influence transplantation outcome¹. Also the quality of available donors must be taken into account when looking for that balance between utility and justice.

A numerical indicator of the donor risk applicable to any donor at any time gives clinicians an idea of what they can expect from a particular transplant⁶. This kind of index would also aid in education of

transplant candidates as far as the potential benefit of a transplant from a living donor compared with deceased donor transplantation⁷, making them more aware of the advantages of the first.

A kidney distribution based only on the number of HLA compatibility, although it may be efficient, will result in longer patients' waiting times for transplantation (due to patients with rare HLA typing). This inequality resulting from the strict criteria of HLA compatibility has been recognized in several countries leading to changes in their respective organ allocation systems⁸. Portugal has also followed suit and attempted to correct this issue with Ordinance nº 6537/2007 put into effect April 3rd⁹.

Nowadays, many deceased donor distribution protocols are based on candidates' waiting time (or time on dialysis) not taking into account graft and patient post-transplant survival².

In the USA, UK and Portugal deceased donor kidney allocation rules are based on systems of points assigned to each possible receptor. However, the key factor in organ allocation is time on dialysis (first come, first served basis)^{8,10}. Assigning kidneys to patients who have longer time on dialysis, are sicker or are more sensitized to HLA antibodies, without regard to the compatibility with the donor, has had the negative effect of increasing the graft rejection rate and reducing the number of transplanted patients¹¹⁻¹³.

The presence of donor specific antibodies (DSA) anti-HLA is a recipient's immunologic risk factor¹⁴ and a risk for graft acute rejection¹⁵. Identification of DSA (defined by solid phase techniques) clinically relevant for transplantation is one of the current challenges of histocompatibility^{16,17}. Transplanted patients with DSA are generally subjected to more intense immunosuppression regimens¹⁶. Also in the long run results of transplantation show that they are worse in patients with pre-existing DSA than in those without such antibodies¹⁸.

Anti-HLA sensitized candidates are more likely to have a positive crossmatch (usually a contraindication of transplant) with an available donor for transplantation. The definition of a calculated panel-reactive antibody value (cPRA) based on non-acceptable HLA for which the patient is sensitized is an indicator for the probability of transplantation and for the difficulty of patient's access to transplant^{19,20}. The cPRA is a

more accurate and trustworthy measure for wait listed sensitized patients candidates than the one currently in use in Portugal (complement-dependent cytotoxicity PRA)²¹. To avoid transplant difficulties in hypersensitized candidates (PRA > 85%), they used to be prioritized in the distribution of deceased donor kidneys³ or are benefited with extra points²⁰.

The quest for a deceased donor allocation system should be a continuous process, as exemplified by the rules of the European Kidney Allocation System. From the time of its introduction in 1996, it has been continuously redefined in order to: reduce the maximum waiting time for a transplant, balance the exchange of organs between countries that are part of the program, and look for the HLA ensuring the success of transplants²². A transparent kidney allocation system requires stating which patients are likely to be at a disadvantage as far as access to transplantation²³.

The point system from the Portuguese rules for the selection of donor-recipient pair in transplantation with cadaveric donors, implemented in August 2007, is opaque and tends to over select patients with longer time on dialysis⁹. These rules have also been associated with an augmentation in the number of acute rejections¹³.

As an alternative to the existing allocation system, we propose a colour system classification (Table I) that will allow clinicians to know the position of a particular patient in the access to kidney transplantation at all times. Red will be attributed to all clinically urgent candidates, as is already defined by the current rules (“patient with terminal chronic renal failure without possibility of constructing definitive vascular access for whom peritoneal dialysis is not possible”). Orange would be allocated to candidates with values of cPRA > 85% or their time on dialyses being higher than the third quartile of wait listed patients’ time on dialysis to transplantation (i.e., how long it takes for 75% of wait-listed candidates to receive a transplant). Yellow would be given to candidates with cPRA > 50% or time on dialysis being higher than the median of wait listed patients’ time on dialysis to transplantation (i.e., how long it takes for 50% of wait-listed candidates to receive a transplant). Green will be for the remaining candidates. Within each colour group, the candidates order will be determined taking into account the number of HLA compatibilities with the donor and, if a tie still persists, the decision is made by the time on dialysis.

Table I

Kidney allocation colour system

	Not ECD		ECD	
	Clinically Urgent	RED	Clinically Urgent	
Recipients ≤ 65 years old	cPRA ≥ 85% or ToD ≥ 3 rd Quartile ¹	ORANGE	cPRA ≥ 85% or ToD ≥ 3 rd Quartile ¹	Recipients > 65 years old
	cPRA ≥ 50% or ToD ≥ Median ¹	YELLOW	cPRA ≥ 50% or ToD ≥ Median ¹	
	cPRA < 50% and ToD < Median ¹	GREEN	cPRA < 50% and ToD < Median ¹	

ECD – Extended Criteria Donor; cPRA – calculated PRA; ToD – time on dialysis

¹ wait listed patients’ time from first dialysis to transplantation

It tends to be a common practice in many countries to allocate organs of extended criteria donors (ECD) (aged 60 years or over 50, plus two of three conditions: a history of hypertension, serum creatinine levels greater than 1.5 mg/dL, or cerebrovascular cause of death) to older candidates expected to live less time^{24,25}. Organs from older donors may also be particularly suitable for older recipients which have a smaller muscle mass and reduced immunoreactivity enabling the use of less aggressive immunosuppressive regimens²⁶.

This proposed colour system could also be applied in a manner similar to the Eurotransplant “old for old” programme²², i.e., organs from ECD would be allocated to recipients older than 65 years, while organs from the other donors would be allocated to recipients aged 65 or less. The proposed colour system would be applied in both cases for candidate ordering.

High-risk renal transplant candidates have a very poor prognosis while waiting for a transplant, on the other hand, healthier candidates benefit from waiting for a more appropriate donor, even when subjected to a longer time on dialysis²⁷. The possibility of organs with a shorter life expectancy being allocated to candidates with shorter life expectancy has been advocated by many⁸. This would facilitate better organ designation to better candidates thus providing a more efficient organ allocation system, in which organs that are expected to function for many years are assigned to patients with a greater life expectancy¹⁰.

■ CONCLUSION

Although it must be validated with real data, this proposed new allocation system for kidney transplantation has the advantage of being more transparent than the current Portuguese rules; with it clinicians can explain to the patient in a more intuitive manner how far they are from being transplanted. Also, the realization that patients classified as green will likely wait too long for an organ, can easily sway them toward the solution of transplantation with a living donor.

This system of colours also takes into account the criteria of utility and justice for kidney distribution. By setting only 4 colour groups on the basis of justice (time on dialysis and probability of transplantation) and, within each of these groups, candidates are ordered based by efficiency (HLA compatibilities); the proposed criteria meant to be balanced. Whenever the risk of a poor transplant outcome exists and is predictable, this fact must be explained to the patient. That responsibility should be shared using an informed signed consent.

The discussion about access to kidney transplantation with deceased donors never comes to a close and must be done clearly and systematically in order to enable the best decisions at any given moment.

Conflict of interest statement. None declared.

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