Selection of Donor-Recipient Pairs in Renal Transplantation: Comparative Simulation Results

Seleção do Par Dador-Recetor em Transplante Renal: Resultados Comparativos de uma Simulação

Bruno Alves LIMA✉[1], Helena ALVES[2]
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ABSTRACT

Introduction: Implemented in 2007 by Ordinance No. 6357, allocation rules of cadaveric donor kidneys seek to distribute equitably a scarce community resource to patients who can improve their survival and quality of life. As stated in the aforementioned ordinance these rules must be updated whenever the state of the art recommends it. The objective of this work is to evaluate and compare three cadaveric donor allocation models: scoring criteria of ordinance nº 6537/2007 (model 1); similar to the previous model but with a lower score for the dialysis time (model 2); and a model adapted from the previously proposed color allocation system (model 3).

Material and Methods: For the purpose of this analysis we generated data about 70 cadaveric donors taking into account information published regarding blood group distribution and human leucocyte antigens allelic and haplotype frequencies of Portuguese voluntary donors. We generated also data for a simulated waiting list of 500 first-time kidney transplant candidates.

Results: We observed fewer candidates selected by model 3 with more than 3 human leucocyte antigens mismatches (39.3%) when compared to those selected by model 1 with more than 3 human leucocyte antigens mismatches (57.1%, $p < 0.01$).

Discussion: In our analysis, model 3 selects transplant candidates with a lower number of human leucocyte antigens mismatches when compared to the adapted rules for kidney allocation of Ordinance No. 6537/2007 (model 1) without penalizing candidates with a longer time on dialysis.

Conclusion: The analysis and discussion of the best rules for allocation of such a scarce resource as organs from deceased donors should be a continuous and adaptive process inherent to transplant candidate's waiting list evolution and mutation.

Keywords: Donor Selection; Histocompatibility Testing; HLA Antigens; Kidney Transplantation; Portugal; Tissue and Organ Procurement

RESUMO

Introdução: Implementadas em 2007 pelo Despacho nº 6357, as regras de alocação de rins de dador cadáver procuram distribuir de forma equitativa um bem escasso da comunidade destinado a doentes que com ele possam ver melhorada a sua sobrevivência e qualidade de vida. Tal como exposto no referido despacho estas regras devem ser atualizadas sempre que o estado da arte o recomendar. O objetivo deste trabalho é o de avaliar e comparar três modelos de alocação de rins de dador cadáver: critérios de pontuação das regras do despacho nº 6537/2007 (modelo 1); modelo semelhante ao anterior mas com menor pontuação para o tempo de diálise (modelo 2); e um modelo adaptado do sistema de alocação por cores previamente proposto (modelo 3).

Material e Métodos: Para efeitos desta análise foram gerados dados para 70 dadores tendo em conta a informação publicada relativa à distribuição de grupo sanguíneo e de frequências alélicas e haplotípicas do sistema de antigénios leucocitários humanos de dadores voluntários portugueses. Foram também gerados dados para uma lista de espera simulada de 500 candidatos a primeiro transplante renal.

Resultados: Para a frequência do número de incompatibilidades de antigénios leucocitários humanos dos candidatos selecionados por cada modelo verifica-se que há menos candidatos no modelo 3 com mais de 3 incompatibilidades de antigénios leucocitários humanos (39,3%) do que no modelo 1 (57,1%, $p < 0,01$).

Discussão: Em comparação com as regras adaptadas do despacho nº 6537/2007 (modelo 1) para alocação de rins, o modelo 3 seleciona candidatos com menor número de incompatibilidades de antigénios leucocitários humanos sem penalizar os candidatos com um maior tempo de diálise.

Conclusão: A análise e discussão das melhores regras a utilizar na alocação de um bem tão escasso como os órgãos de dador cadáver deve ser um processo contínuo e adaptável à evolução e mutação inerentes à lista de espera de candidatos a transplante.

Palavras-chave: Antígenos HLA; Obtenção de Tecidos e Órgãos; Portugal; Seleção do Doador; Teste de Histocompatibilidade; Transplantação Renal

INTRODUCTION

Chronic kidney disease is increasingly frequent worldwide related to an increasing incidence of diabetes and high blood pressure and ageing population.[1] Due to the asymptomatic nature of the disease, patients frequently present with end-stage renal disease and the need for renal replacement therapies such as dialysis and transplantation.[2]

When compared to dialysis, kidney transplantation is associated with a decreased mortality as well as a reduction in cardiovascular events and is the best option for renal replacement therapy, whenever available.[3] Deceased-donor kidneys for transplant are a scarce resource and the most accurate and transparent allocation policy should be followed.[4] Equity in organ allocation is based on a well-balanced relationship between a fair allocation, i.e. giving

1. Oficina de Bioestatística. Ermesinde. Portugal.
2. Instituto Nacional de Saúde Dr. Ricardo Jorge. Porto. Portugal.
✉ Autor correspondente: Bruno Alves Lima. balima78@gmail.com
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priority to patients waiting longer for an organ and a useful or efficient allocation in which it is insured that the patients receiving an organ are those with the best conditions for transplantation [for instance, showing higher grade of human leukocyte antigen (HLA) compatibility].[5,6]

In Portugal, deceased-donor kidney allocation was regulated from 2007 onwards by the ordinance no. 6357 regarding waiting-listed transplant candidates. These are periodically examined in order to be assigned with an immunological profile, which is based on HLA typing and a periodic anti-HLA antibody detection. These unacceptable anti-HLA antibodies are found through single antigen bead (SAB) assays with mean fluorescence intensity (MFI) levels ≥ 1,000.[7,8] In the presence of the immunological profile, a virtual crossmatch can be obtained for each patient whenever a donor is available. Therefore, kidney allocation is established by excluding those candidates with donor-specific antibodies (DSA) (positive virtual crossmatch) and selecting those with ABO-identical blood group as the donor (iso-group distribution). A score is subsequently assigned to patients, based on HLA mismatches, dialysis time, age and the level of panel-reactive antibodies (PRA) by complement-dependent cytotoxicity (CDC).[7] The calculated PRA (cPRA) is not considered by this kidney allocation system. This is an estimation of the likelihood of a positive virtual crossmatch for each candidate taking into account the HLA typing of a certain group of possible donors.[9] In the current organ allocation system, apart from lacking transparency –the relative position in the waiting list is not available to patients – higher priority is given to dialysis time instead of donor-recipient HLA mismatches.[11] The regulations within the ordinance no. 6537/2007 were also associated with higher number of rejection episodes,[12] even though, to our best knowledge, these results were never replicated in subsequent publications.

A colour-based system classification, instead of the current deceased-donor kidney allocation system, has been presented in 2013 by the authors of this study.[10] According with this system, waiting-listed candidates are prioritized according with dialysis time and anti-HLA sensitisation.

This study aimed at the assessment and comparison between three deceased-donor kidney allocation system models, in which the first model is directly adapted from the scoring criteria defined by the ordinance no. 6537/2007, a slight difference regarding scoring assigned to patient's dialysis time is involved in the second model and the third is updated from the abovementioned colour-based system classification.[10]

MATERIAL AND METHODS

Data regarding 70 donors with age randomly selected from a normal distribution with a mean age of 55 and standard deviation of 15, within an 18-75 truncated age range, were generated for the study. The parameters of this normal distribution were arbitrarily selected and reflected the authors' experience. The frequencies of the groups were randomly assigned to each donor considering the frequencies that were previously described for blood donors in Portugal.[13] Therefore, a total of 32 group A, 6 group B, 3 AB and 29 group O donors were selected. Data regarding HLA typing were generated for each patient based on the allele and haplotype frequencies in volunteer bone marrow donors from the Northern region of Portugal.[14]

Data were also generated for a simulated waiting list of 500 candidates for primary kidney transplant. These patients' ages were randomly generated from a normal distribution with a mean of 45 and standard deviation of 15, within an 18-75 truncated age range. Blood ABO group frequencies were defined so that group O candidate group was the most frequent with 46% (230); group A with 43% (215), group B with 8% (40) and group AB with 3% (15) of the patients. Data regarding HLA typing for each patient were generated taking into account the allele and haplotype frequencies in volunteer bone marrow donors from the Northern region of Portugal.[14]

A cPRA group was randomly assigned to each candidate, according with the following frequencies: 80% of the patients with 0% level of cPRA; 5% within the 10-40% range; 5% within the 40-80% and 10% with levels ≥ 80%. Anti-HLA antibodies were assigned to patients in groups with cPRA levels > 0% (necessarily different from corresponding HLA antigens) in order to obtain the percentage of the 70 simulated donors with HLA matched antigens to those antibodies. The cPRA level for each candidate is therefore similar to the percentage of donors with whom a positive virtual crossmatch would be found.

Dialysis time of each patient has been randomly generated considering the ABO blood group and cPRA level assigned to each one. Therefore, values with a normal distribution and a 70-month mean time and standard deviation of 20 were generated for group O patients with cPRA levels ≥ 80%, values with a normal distribution and a 55-month mean time and standard deviation of 20 for patients with at least one of these characteristics (group O or cPRA ≥ 80%) and random values with a normal distribution and 40-month mean time and standard deviation of 20 for the remaining patients.

Table 1 - Colour-based allocation system (model 3)

	Donor ≤ 65 anos		Donor > 65 anos	
Candidates ≤ 65	Medical urgency	Red	Medical urgency	Candidates > 65
	cPRA ≥ 85% or DT ≥ 3th Quartile	Orange	cPRA ≥ 85% or DT ≥ 3th Quartile	
	cPRA ≥ 50% or DT ≥ Median	Yellow	cPRA ≥ 50% or DT ≥ Median	
	cPRA < 50% and DT < Median	Green	cPRA < 50% and DT < Median	

cPRA: calculated panel-reactive antibody level; DT: dialysis time

A colour has been assigned to each patient according with the colour-based system classification for deceased-donor kidney allocation, as shown in Table 1.

The frequencies and distributions of the values that were generated for the 500 simulated candidates were arbitrarily defined and reflected the authors' experience, taking into account the available information regarding the waiting-listed Portuguese candidates for kidney transplant.[15]

Donors (one by one) were allocated to the two best possible recipients according with each different model (according with the rules of each model), in order to obtain groups up to 140 recipients per model and simulation. Therefore, those with the same blood group as the first donor and presenting with a negative virtual crossmatch were selected from the 500 candidates according with model 1 and a score was calculated for each candidate (according with what is shown in Table 2) and the first donor was allocated to the two patients with the highest score; the same procedure has been followed for the available 498 candidates and so forth until all the 70 donors were allocated up to a maximum number of 140 recipients. A similar procedure has been followed for model 2 with only 0.05 points assigned per each dialysis month, instead of 0.1 points assigned with the model 1.

The colour-based system classification that was previously presented aimed at a fair and efficient allocation of scarce resources such as deceased-donor kidneys.[10] A fair kidney allocation system would be based mainly on dialysis time, while an efficient allocation would favour the number of donor-recipient HLA mismatches. According with model 3, which is analysed in this study, waiting-listed candidates are classified based on medical urgency (those assigned with red) or on dialysis time and cPRA level (remaining colours of the system - orange, yellow and green) (Table 1). Waiting-listed candidates with cPRA levels ≥ 85% or with a dialysis time over the third quartile of dialysis time to transplant (i.e. dialysis time until 75% of the candidates undergo a transplant) were ranked as orange. Candidates with cPRA levels ≥ 50% or with a dialysis time over the median dialysis time to transplant (i.e. dialysis time until 50% of the waiting-listed patients undergo a transplant), were ranked as yellow. The remaining candidates were ranked as green. According with this colour-based model, ABO-identical group candidates with negative virtual crossmatch and within the same age group were initially selected for each available donor for transplant, i.e. only candidates aged 65 and older were selected for donors ages 65 and older, while those under the age of 65 were selected for donors under that age. HLA mismatches (HLAmm) were subsequently calculated and patients were ranked by colour priority and then on a scale of an increasing number of mismatches. In the event of a tie, candidates with longer dialysis time were selected. A corresponding donor was allocated to the two candidates with the lowest number of mismatches within the colour group with the highest priority.

Kruskall-Wallis test has been used for the comparison between median dialysis time and the age of those recipients who were selected with each model. Chi-square test (or Fisher's exact test, whenever appropriate) was used for the comparison between the recipient frequencies per group of cPRA levels and HLA mismatch obtained with each model and *p*-values < 0.05 were considered as statistically significant.

The RStudio software for R language and programming environment was used for all the statistical analyses and graphic representations.

Table 2 - Scoring table according with the ordinance no. 6357/2007, modified for the analysis (model 1)

Criterion	Score
HLA mismatch*	
a) No A, B and DR mismatch	12
b) No B and DR mismatch	8
c) One B or DR mismatch	4
d) One B and one DR mismatch	2
e) Remaining possibilities	1
cPRA ≥ 85%	8
cPRA ≥ 50%	4
Dialysis time (per month)	0.1
Age difference between donor and recipient	
Donor > 60 and recipient < 55	0
Donor < 40 and recipient > 55	0
Remaining possibilities	4

* HLA-A mismatches were considered in case of a tie; HLA: human leucocyte antigen system; cPRA: calculated panel reactive antibody level

Table 3 - Demographic and immunological data of the 500 waiting-listed candidates

	n (%)	Median (Q1 - Q3)
ABO blood group		
A	215 (43)	
AB	15 (3)	
B	40 (8)	
O	230 (46)	
Age (years)		46 (36 - 55)
Dialysis time (months)		48 (31 - 62)
cPRA		
0%	400 (80)	
(0%; 50%)	34 (6.8)	
(50; 85%)	43 (8.6)	
≥ 85%	23 (4.6)	
Colour *		
Orange	143 (28.6)	
Yellow	134 (26.8)	
Green	223 (44.6)	

Q: quartile; cPRA: calculated panel reactive antibody level
* colour-based classification system

RESULTS

The demographic and clinical characteristics of the simulated 500 candidates within a wait-list are shown in Table 3. Almost half of the wait-list candidates (44.6%) were ranked as green, while 28.6% as orange.

Similar patient ages have been found among the models, showing a median age of 46 in model 1 and 47 in both remaining models (Table 4).

When median dialysis times of the recipients selected through each model were compared, no statistically significant differences were found between model 2 (median of 62.5 months) and model 1 (median of 67 months) nor between model 3 (median of 67 months) and model 1, even though recipients selected by model 2 were those with the lowest and widest-ranging dialysis times. Less recipients with different HLA mismatches were selected by model 3 and less recipients with at least 3 HLAmm (39.3%) were selected by using the model 3 than with model 1 (57.1%) and showing a statistically significant difference ($p < 0.01$). Less recipients with at least 3 HLAmm (46.4%) were selected with the model 2 than with the model 1, even though with a statistically non-significant difference. When only mismatches at B* and DRB1* loci were considered, more recipients with more than 2 mismatches at B and DRB1 (45.7%) loci were found among those selected with model 1 *vs.* those selected by model 2 and 3 (37.1 and 34.4%, respectively), although these differences were not statistically significant. As regards the distribution of recipients that were selected in each model by groups of cPRA levels, less patients with cPRA level ≥ 85% (9.4%) were selected with model 3 when compared to the two remaining models (15%) and the comparison with model 1 showed a statistically significant difference ($p < 0.01$).

DISCUSSION

More clear priorities are shown by waiting listed candidates selected through the colour-based system classification model (model 3), according with each candidate's waiting time as well as the likelihood of not being selected for a future donor (through cPRA levels).

Candidates with less HLA mismatches are selected by the model 3, leaving the candidates with a longer dialysis

Table 4 - Comparison of the characteristics of the candidates selected by each model

	Model 1		Model 2			Model 3		
	n (%)	Median (Q1 - Q3)	n (%)	Median (Q1 - Q3)	*p* *	n (%)	Median (Q1 - Q3)	*p* †
Age (years)		46.0 (36.8 - 55.0)		47.0 (37.0 - 55.0)	0.857		47.0 (37.0 - 56.5)	0.529
DT (months)		67.0 (51.5 - 81.0)		62.5 (46.8 - 79.0)	0.103		67.0 (58.0 - 80.5)	0.43
HLAmm					0.525			0.009
1	8 (5.7)		10 (7.1)			4 (2.9)		
2	21 (15.0)		24 (17.1)			22 (15.8)		
3	31 (22.1)		41 (29.3)			58 (41.7)		
4	42 (30.0)		30 (21.4)			32 (23.0)		
5	24 (17.1)		24 (17.1)			17 (12.2)		
6	14 (10.0)		11 (7.9)			6 (4.3)		
Up to 3 HLAmm	60 (42.9)		75 (53.6)		0.073	84 (60.4)		0.003
Mais de 3 mmHLA	80 (57.1)		65 (46.4)			55 (39.6)		
mmBDR					0.573			< 0.01
0	7 (5.0)		9 (6.4)			0 (0)		
1	34 (24.3)		41 (29.3)			20 (14.4)		
2	35 (25.0)		38 (27.1)			68 (48.9)		
3	38 (27.1)		27 (19.3)			36 (25.9)		
4	26 (18.6)		25 (17.9)			15 (10.8)		
Até 2 mmBDR	76 (54.3)		88 (62.9)		0.145	88 (63.3)		0.126
More than 3 HLAmm	64 (45.7)		52 (37.1)			51 (36.7)		
BDR					0.685			0.001
(0; 50)	82 (58.6)		77 (55.0)			112 (80.6)		
(50; 85)	37 (26.4)		42 (30.0)			14 (10.1)		
≥ 85	21 (15.0)		21 (15.0)			13 (9.4)		

* p-value for the comparison of model 1 vs. model 2; † *p*-value for the comparison of model 1 *vs.* model 3; Q: Quartile; DT: Dialysis time; HLA: Human leucocyte antigen system; HLAmm: number of HLA-A mismatches*. -B* and -DRB1*; BDRmm: number of HLA-B* and -DRB1 mismatches*; cPRA: calculated panel reactive antibody level

time unaffected, when compared with the regulation adapted from the ordinance no. 6537/2007 (model 1) for kidney allocation. Dialysis time has been less weighted by model 2 (0.05 points per month) when compared to model 1 (0.1 points per month) and, as a direct consequence, candidates with shorter dialysis time were selected, even though there is no statistically significant gain in terms of reduction in the number of HLA donor/recipient mismatches.

The rules for deceased-donor kidney allocation should allow for a well-balanced selection of candidates for transplant between the waiting time (and/or dialysis time) and a successful outcome of the transplant (which may be supported as far as possible by minimising the number of transplants in candidates with a large number of HLA mismatches). With the reduction of the number of transplants carried out in Portugal from 2012 onwards[16] the definition of rules allowing for the most successful transplants becomes even more crucial. According with our study, this desirable trade-off was better reflected by deceased-donor kidney allocation model 3.

Model 3 allows for an easier and more comprehensible use (even for patients) due to the fact that colours are used to mainly rank waiting-listed candidates for transplant rather than a point-based model (faced as an intricate 'black box'). When a colour showing a certain level of priority is assigned to each waiting-listed candidate, it does not mean that orange-ranked patient A will be transplanted earlier than green-ranked patient B; nevertheless, it means that orange-ranked patients will on average be transplanted earlier than green-ranked patients. In the present simulation, 69.8% of the patients selected by model 3 were orange-ranked, while only 1.4% were green-ranked. We may therefore say that model 3 is more transparent than the currently used model.

An ABO blood group match and the absence of donor-specific anti-HLA antibodies (virtual crossmatch) were given the priority in the selection of candidates for a possible donor (in line with the regulations within the ordinance no. 6537/2007), in order to minimize known risks for organ rejection. The definition of the immunological profile of each waiting-listed candidate for transplant is crucial for the definition of the results of the virtual crossmatch with the possible donors. The value of 1,000 MFI (mean fluorescence intensity) has been considered as a high-sensitive threshold for the identification of these antibodies, allowing for the identification of anti-HLA antibodies with a low clinical risk of graft rejection. Even though a higher MFI cut-off has been suggested for the identification of risk antibodies, cumulative MFI values should be considered (and not only the values for each antibody) in order to reach any conclusions on a positive virtual crossmatch,[17,18] i.e. apart from considering a positive virtual crossmatch whenever a candidate presents with a donor-specific anti-HLA >3,000 MFI, this should also include a situation in which the candidate only presents with 3 donor-specific anti-HLA antibodies with 1,000 MFI value each. This same principle should be applicable to cPRA level, i.e. cumulative values of donor-specific anti-HLA antibodies >3.000 MFI should also be considered into this calculation. Virtual crossmatch and cPRA levels should be considered as two sides of the same coin and are crucial for the selection of the best candidates for transplant from a certain donor.[19] Genotype frequencies used for the cPRA level should as much as possible match those of future organ donors and should be known[14] and not belonging to any specifically selected group.

Extra points for PRA levels >50% by CDC are assigned by the ordinance no. 6537/2007, even though these values of PRA by CDC tend to underestimate the number of positive crossmatches with future donors.[19,20] Anti-HLA antibodies have been assigned to candidates in this analysis and cPRA levels were subsequently defined, showing that more candidates with cPRA levels ≥ 85% were selected with model 1, when compared to model 3. Hypersensitised waiting-listed candidates are challenging for any kidney allocation program. These patients tend to wait longer for a compatible organ, therefore increasing their risk of co-morbidity and/or mortality and reducing their likelihood for transplant.[21] More than 25 years have elapsed since the implementation of an acceptable mismatch program by Eurotransplant aimed at increasing the number of transplants of hypersensitised patients.[22] Even though this measure does not respond to all the issues, the possibility of the implementation of such a program should also be discussed in Portugal. According with model 3, candidates with cPRA levels ≥ 85% are orange-ranked in addition to those with the longest dialysis times, even though not hypersensitised. When these candidates are ranked by an ascending number of mismatches with a possible donor, hypersensitised patients (mostly with less common HLA typing as these tend to present with more common HLA antibodies, according with the definition of cPRA) who were not excluded due to a positive crossmatch, tend to be those with the highest number of mismatches and are subsequently rejected for transplant once again. In search for a well-balanced kidney allocation (both fair and useful) in which model 3 is based on, hypersensitised patients are disadvantaged and will eventually tend to accumulate within the waiting list as these are only selected when presenting with a small number of mismatches. Therefore, the possibility of adding a first level of priority in organ allocation for hypersensitised patients (ranked between red and orange) should be considered.

The survival benefit for patients with a successful kidney transplant is regardless of the age of the deceased donor when compared to those who remain in dialysis.[23] The fact that donor's age is associated with a poorer outcome regarding graft and patient survival is worth mentioning.[24] Ageing-related changes, including decreased glomerular filtration volume or the increased immunogenicity of older organs, may have an impact in outcome.[25]

The use of donors with extended criteria may allow for an increasing number of donors available for transplant and subsequent reduction in waiting time to transplant, even though this should be carefully managed. A kidney transplant of older candidates with older deceased donors is a

good alternative for the former. There is in fact a benefit from this kind of transplant in older patients in terms of survival, when compared to the patients who remain in dialysis.[26,27] Therefore, older donors should be assigned to older candidates, according with the colour-based model that we recommend, even though no statistically significant differences were found between the age of the candidates that were selected by using the model 1 *vs.* those with the model 3.

With an increasing number of candidates for retransplantation upon a first graft rejection,[28] this group of patients should also be taken into consideration by any new rules for organ allocation. The benefit of retransplantarion in low-risk candidates is similar to the benefit of a primary transplant and the waiting time for retransplantation is one of the major risk factors for a non-successful transplant.[29] Only candidates for primary transplant were considered in this study, by convenience of the simulation.

The results were obtained through simulated data for hypothetical waiting-listed transplant candidates and a group of possible deceased donors. Despite some recent initiatives such as for instance the development of the webpage of the Portuguese National Health Service (*Serviço Nacional de Saúde*),[30] open data are still not available[31] regarding the access to a kidney transplant that would allow for a study of the models with real data.

Supported by the reports provided by the *Sociedade Portuguesa de Nefrologia*[32] and the *Sociedade Portuguesa de Transplantação*,[33] it is worth mentioning that this information is not based on any open data that would allow for an analytical and careful assessment. National data on (i) time to transplant, (ii) median waiting time to transplant or (iii) number of donors and transplants per age group or transplantation unit[11,34] are only some examples of indicators that were never published on any scientific review. The possibility of data analysis using inadequate statistical and methodological techniques, or giving a misinterpretation of the results, or selectively reporting results have long been identified,[35] even though these could be minimised with public data disclosure.

The number of waiting-listed deceased-donor transplant candidates corresponds to the inflow (new registrations to the waiting list and re-registrations of patients having suffered from transplant rejection) and the outflow (carried out transplants, removal from the waiting list by medical reasons, patient's own decision or deceased candidates while waiting for transplant). Each candidate's registration is allowed in two transplant units, particularly in Portugal (i.e. inclusion into two waiting lists). More detailed data are unfortunately not available, that would allow for a more detailed analysis of the evolution of the waiting list. Data regarding re-registrations into the waiting list upon a primary transplant or the percentage of patients in need for retransplant and the weight of these patients into the waiting list are also unknown. The best way for the allocation of deceased-donor kidneys will always depend on a correct characterisation of the waiting list for transplant.

CONCLUSION

In conclusion, an organ-allocation model based on levels of priority assigned to transplant candidates and a selection of these based on HLA mismatches will be easier, more clear and fair than the currently used model from 2007 onwards. To the best of our knowledge, this is the first study with an objective assessment of the current rules for the selection of donor-recipient pairs. The analysis and discussion of the best rules for the allocation of such a scarce resource as deceased-donor organs should be an ongoing process adapted to the evolution and changes in waiting-listed transplant candidates.

HUMAN AND ANIMAL PROTECTION

The authors declare that the followed procedures were according to regulations established by the Ethics and Clinical Research Committee of the IPO Porto and according to the Helsinki Declaration of the World Medical Association.

DATA CONFIDENTIALITY

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

CONFLICTS OF INTEREST

The authors declare that there were no conflicts of interest in writing this manuscript.

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