LETTER TO THE EDITORS

Kidney paired donation in Brazil – a single center perspective

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Dear Editors,

The number of kidney transplants (KT) performed annually in Brazil is less than half of the estimated necessity, leading to a waitlist containing over 26 thousand patients [1]. A recent Brazilian analysis showed that highly sensitized patients (panel-reactive antibody (PRA) > 80%) make up 7.6% of the waitlist. They have only a 19% chance to receive a transplant after 10 years (vs. 44% chance for patients with PRA 0%) and 20% higher mortality rates [2].

Living donor kidney transplant (LDKT) represents about 20% of the total KT per year in Brazil [1]. Unfortunately, up to 35% of the willing donors will not donate for immunological reasons – ABO incompatibility (ABOi) or positive crossmatch (CDC+) [3]. Desensitization protocols have been developed to overcome incompatibilities, but they are expensive and limited to specialized programs [4]. Besides that, these techniques may be associated with higher patient morbidity and inferior long-term outcomes [4,5].

Kidney paired donation (KPD) represents a strategy for increasing the number of LDKT, offering an incompatible donor/recipient pair, the chance to exchange with another pair in the same situation [4]. In Brazil, KPD is still prohibited by law. We designed a study to show mathematically how KPD could increase LDKT in a single center in Brazil.

All the potential donors evaluated between January 2013 and April 2019 in Santa Casa de Misericórdia de Juiz de Fora were retrospectively analyzed (N = 790). Of those, 622 were contra-indicated, and immunological incompatibility was the leading cause (18%). We selected those immunologically incompatible pairs (100 intended donors involving 89 different recipients) to compose the pool. CDC+ was the reason for contra-indication in 42% of the pairs.

An optimized algorithm was used to estimate the number of matches. As ABOi donors did not have HLA testing performed, it was randomly assigned to them by resampling from the pool of all previous donors (living and deceased) from the center in the period. We considered a scenario with and one without prioritization of highly sensitized recipients. In each scenario, we conducted 10 simulated match runs and determined the average number of transplants. The random factor between the match runs was HLA randomly assigned to the ABOi donors. We also simulated two different programs: One allowing only 2-way exchanges and another also allowing 3-way exchanges.

The cutoff for considering a pair compatible was if they had ≤2 DSAs with MFI sum <3000, determined based on actual center criteria, but it can be changed according to each center preference. The hospital ethical committee approved this study in February 2019 (CAAE: 07000819.0.0000.5139).

The results of the match runs are shown in the Table. In the simulated program allowing only 2-way exchanges, we found 27.8 possible transplants. As the algorithm maximizes the number of transplants, there is no difference in the total transplants, despite prioritization. The number of highly sensitized recipients transplanted increases (from 4.6 to 7.7) and the number of transplants with 2 or fewer mismatches decreases slightly (from 0.9 to 0.6) when highly sensitized candidates are prioritized.s

In the simulated program allowing 2- and 3-way exchanges, the number of transplants increases to 35.3. In the prioritization model, the number of highly sensitized recipients transplanted increases from 9.3 to 11.

There were 506 KT in our center in the referred period, 31% were LDKT and only 14 highly sensitized were transplanted. Considering this simulated KPD program,

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Table 1. KPD match runs results

	Total recipients N = 89 (100%)	No priority to sensitized recipients	Priority to highly sensitized recipients
2-way exchanges			
No of transplants		27.8	27.8
Type O recipient	51 (57.3%)	12.3	12.5
No PRA*	5 (5.6%)	0.9	1.0
PRA 0–20%	42 (47.2%)	6.2	4.4
PRA 21–40%	9 (10.1%)	5.8	5.1
PRA 41–60%	7 (7.9%)	5.8	5.1
PRA 61–80%	9 (10.1%)	4.5	4.5
PRA 81–100%	17 (19.1%)	4.6	7.7
Retransplant	14 (15.7%)	6.9	6.6
No DSA		19.8	20.0
Less than 3 mismatches		0.9	0.6
2- and 3-way exchanges			
No of transplants		35.3	35.3
2-way exchanges		5.6	5.3
3-way exchanges		29.7	30.0
Type O recipient	51 (57.3%)	15.3	15.2
No PRA*	5 (5.6%)	1.6	1.7
PRA 0–20%	42 (47.2%)	7.3	5.8
PRA 21–40%	9 (10.1%)	6.5	6.5
PRA 41–60%	7 (7.9%)	6.1	6.0
PRA 61–80%	9 (10.1%)	5.6	5.4
PRA 81–100%	17 (19.1%)	8.2	9.9
Retransplant	14 (15.7%)	8.9	8.9
No DSA		23.9	24.3
Less than 3 mismatches		0.7	1.0

*Missing data.

the number of LDKT could increase by 23% if kidney exchanges were permitted. The number of sensitized recipients transplanted could increase by 70.7% when using the prioritizing model. This augment in transplantation shows promising hope, especially to highly sensitized patients. Overall, more than a third of our recipients and more than half of our highly sensitized recipients with incompatible donors could be transplanted through KPD.

These results are from a pool of six years of accumulated pairs. The annual number of transplants might decrease once an active program is developed, as the hard-to-match recipients accumulate. On the other hand, the benefits of KPD are not limited to quantity, because KPD could improve transplant outcomes and make KT available to more highly sensitized recipients. Another limitation of this study is that we do not have the real HLA for most donors (N = 58). We randomly assign HLA to donors based on our previous pool of donors. Also, we ran 10 match runs for each scenario, randomizing HLA of these donors to mitigate this limitation.

Around the world, kidney paired donation is no longer just a concept. Local, regional, and national KPD programs with different acceptance rules are being used in many countries to help those patients waiting for transplantation. This model is responsible for 12% of LDKT in the United States [6]. In Europe, KPD already represented 8% of LDKT in 2016 [7].

KPD programs are not restricted to developed countries; India had facilitated more than 200 LDKT through KPD in 2014, showing excellent outcomes compared with other LDKT [8]. During the First Latin American Bioethics and Transplant Forum (2010), the "Document of Aguascalientes" was written, recognizing the legality of KPD [9]. Despite that, KPD has not fully developed in Latin America. The first exchange was performed in Argentina in 2015 [10] and since then, there are only a few case reports.

A KPD program is less expensive than desensitization and results are clinically superior. That aspect becomes even more important in Brazil, where there is no reimbursement for desensitization from the public health system. Therefore, KPD should be the preferred option

to overcome donor/recipient incompatibilities, especially in low-to-middle income countries [3,8]. In conclusion, our results show that allowing KPD programs in Brazil can substantially increase the number of high-quality transplants in our country. These results support the implementation of KPD in South America.

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Conflict of interest

The authors have declared no conflicts of interest.

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