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IMPROVING LIVING DONOR TRANSPLANTATION IN CHILE**

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Number of figures and tables: 1 Table 3 figures

Abstract

Chile has a very low cadaveric organ donation rate; at the same time, living donor transplantation activity is low. The purpose of this paper is to analyze the impact on the number and quality of transplants of the potential application of different mechanisms for kidney exchange from living donors to patients on Chile's waiting list.

Methods

A computerized model was developed, to simulate five different options for living kidney donation: i) direct donation, ii) direct donation plus pair wise and three-way exchange iii) pair wise exchange, iv) three-way exchange, and v) allocation of donors based on the Top Trading Cycles (TTC) mechanism. The projected number of transplants, adjusting for the risk of a positive crossmatch, was calculated as well as the average quality in terms of HLA match.

Results

If all patients in the waiting list have a direct donor willing to donate, 47,7% of patients will get a transplant. Allowing incompatible pairs and those with a positive cross match to exchange kidneys can increase the number of transplants to 51,8%. This figure rises to 60 and 61% for pair wise or three way exchanges respectively. Although TTC assures that 55% of the patients could be transplanted the quality is better with an average HLA match of 3,5 vs 1,25 for the others.

Conclusions

These results show that kidney exchange mechanisms can increase the number of living donor transplants between 4 and 13%.

Introduction

Chile has a very low cadaveric donation rate. Indeed, in 2010 the donation rate was only 5,4 donors per million people (pmp), with a significant decrease in the last 4 years (1).

One possible alternative to relieve the difficult situation of the transplantation system in Chile is to promote living donation. However, the level of development of this activity is very low compared to other countries. In fact, in the last years, only 10% of all kidney transplants come from a living donor compared to around 50% for USA. (2). In order to increase the probability of finding a compatible living donor several mechanisms apart from direct donation have been proposed (3,4,5). In countries like the U.S., Germany, Romania, England and the Netherlands these complex exchanges have been explored and developed (6,7, 8, 9, 10).

The purpose of this paper is to explore the impact on the number and quality of transplants of the implementation of different algorithms of living kidney donation in Chile. We examine not only the possibility of direct living donation where a patient on the waiting list is associated with a donor (typically a family member or direct relative), but also, if they are not compatible, the option to resort to more complex exchange mechanisms that will enable to find compatible pairs among different directly incompatible donor-recipient pairs. (3,4,5).

Methods

We developed a computerized model in order to evaluate a direct donation mechanism and four different exchange mechanisms. The number (percentage) of expected transplant was calculated assuming different proportions of all the patients of the actual Chilean waiting list having a living donor. On the other hand we calculated the average HLA match for each of these mechanisms as a measure of the quality of these mechanisms. Finally a sensitivity analysis was performed, estimating the impact of different criteria of donor-recipient compatibility on the number and quality of transplants of each mechanism. Thus, a donor-recipient pair was considered compatible if: i) it has ABO blood compatibility (criterion 1), ii) it has ABO blood compatibility and at least one HLA compatibility (criterion 2), iii) there is ABO blood compatibility and at least one common HLA-DR (criterion 3).

Mechanisms: i) Direct donation is the baseline situation. It consists in allowing kidney transplant only between a directly (genetically or emotionally related) compatible donor-recipient pair. ii) The “Multi Stage” kidney exchange mechanism (MSKEM), in addition to allowing direct donation, it incorporates, in a second stage, the possibility of cross-exchange between incompatible donor-recipient pairs. Subsequently, it allows cross-exchange between 3 pairs and so on until all possibilities for exchange are exhausted. iii) Pairwise (PW) and three way (3W) kidney exchange only. All donor recipient pairs are included and cross-exchange between two (PW) or three (3W) donor-recipient pairs, respectively are performed. iv) Top Trading Cycles Mechanism (TTC). Again all donor recipient pairs are included, a recipient is randomly selected and chooses the best donor among the whole pool, based on ABO blood-type compatibility and HLA mismatch. Next, that donor’s recipient chooses his preferred organ from those remaining in the pool, and so on, creating a chain of donor and recipients, until all possibilities are exhausted. This chain is eliminated from the pool and for all those remaining without a transplant, the procedure is repeated as many times as necessary. (5,11,12).

Data

Recipients’ characteristics were obtained from the waiting list as of August 2009. At that moment 1412 patients were waiting for a kidney transplant: mean age 43 ± 9 years, 52% male, 70 % blood type O, 22% type A 6% type B and 2% type AB. Sixty nine percent had a Panel Reactive Antibody (PRA) under 10%, 23 % between 10 and 80% and only 8% above 80%. The actual HLA A, B and DR of each recipient were used in all simulations. To simulate the characteristics of potential donors, we used the blood type and HLA frequencies of the cadaveric donor population from January 2000 to August 2009. To establish the probability of transplantation success, we assumed the relationship between PRA and positive Crossmatch in the literature (13). With this, we obtain a weight that is used to calculate the number of expected transplants.

Results

The results of the simulations, using as matching criterion the ABO blood-type compatibility only, show that all of the mechanisms are superior to direct donation which in the best case scenario (all those in the waiting list have a living donor) could yield a total of 47% of transplants while the other

mechanisms yield between 4 and 14% more transplants (Fig N 1). The highest number of transplants is obtained when pairwise or 3-way exchanges are performed. However if we analyze the quality of the HLA match the TTC mechanism outperforms all others with a mean match of 3 vs, 1,5 for all others moreover the number of matches increases as the percent of patients having a donor increases (Table. N 1).

As expected, for all the mechanisms the expected number of transplants increases as the number of patients on the waiting list who have a direct donor grow. Also, the number of expected transplants increases as more complex kidney exchange mechanisms are considered. The PW and 3W mechanisms show similar results and the highest number of expected transplants of near 61% of the population in the waiting list. Direct Donation results in the lowest number of expected transplants (47%). The Multi-Stage mechanism adds a few more transplants and TTC is in between direct donation and PW and 3W (55%). Irrespective of the matching criteria used Direct Donation always yields the least number of transplants followed closely by Multi-Stage. TTC, comes in between and , PW and 3W exchanges are the best (Fig 2).

For the TTC mechanism there is a consistent result in terms of the number of transplant obtainable and the quality in terms of HLA match that is not modified when more stringent matching criteria are simulated (ie at least 1 HLA DR match for all transplants) and as already shown the number of HLA matches consistently increases with the number of patients having a donor (Fig 3 Table1).

Discussion:

In this paper we simulated a mechanism for direct living donation and four different exchange mechanisms using data from Chile's waiting list as of August 2009. Our results could be interpreted as the probability of having a compatible (and cross-match negative) emotionally related living donor. Significant improvements can be achieved in quantity and quality of transplants, when different exchange mechanisms are developed. In fact the chance of having a compatible donor is around 47% Our findings add evidence in favor of exploring different living donation mechanisms to alleviate the situation of the waiting list for a kidney transplant. Although the more complex mechanisms for kidney exchange can increase the number of expected transplants significantly, all of them but the TTC

present, at best, an equal average quality than Direct Donation. Interestingly, however, the differences in quantity between Direct Donation and the other mechanisms are reduced if only the ABO blood-type compatibility matching criterion is used. Indeed, in this case, all the mechanisms yield a number of expected transplants between 50% y 60% of patients who are on the waiting list (for 100% of live-donor recipients). A possible interpretation of this result is that expanding the compatibility criteria is something to consider when evaluating the implementation of policies aimed at encouraging living donation. The natural trade-off is that the donation quality is significantly reduced with this expansion. Estimating these alternatives' monetary cost and quantifying their effect on the quality of life should be the subject of other studies (14). Most probably, a significant economic benefit and quality of life gain could be expected, taking into account the clear superiority of living donation over cadaveric donation (15).

There are other even more complex mechanisms, such as the Top Trading Cycles and Chains mechanism TTCC (3,4) which were not addressed in this study since their implementation is still very unrealistic (6).

Although the living donation activity yet to be developed in Chile, it is important to stress the potential benefits it could bring to the population that remains on the waiting list. It is clear that letting all the donors (even if the recipient is compatible) incorporate into to a large pool and then to assign it to the most suitable recipient (given that that donor's original recipient is transplanted with an equal or better donor) using one of the above exchange mechanisms, would be of great benefit to the whole community of patients on the waiting list. However we as doctors are not generally prone to these exchanges, even though studies that have evaluated the willingness to participate in kidney exchange programs, have found that direct donors are generally willing to participate in these programs involving two pairs, compared to other policies such as donation in exchange for better ranking on the waiting list, because they see the benefit of their patients directly (16).

These results are broadly consistent with the findings in the related the literature (3,4,5). Roth, using data from the USA waiting list showed that under direct donation near 54% of the patients on the waiting list could get a living unrelated transplant with a mean HLA match of 1,2 and that more

complex exchange mechanisms could reach up to 92 % of transplant with a mean HLA match of 3,4. These significant differences with the current paper are probably related to the size and heterogeneity of the study populations.

Choosing which mechanism is more suitable depends on many factors, however given that PW and 3W exchanges consistently yield the most transplants and that the logistics of scheduling 2 or 3 parallel transplantations is easier than implementing a transplant chain, they seem the better way to go.

Implementing a kidney exchange mechanism however is no easy task; most importantly the system has to be transparent, with universal access and following rules that are a consensus involving all the actors in the Transplant field i.e. Healthcare authorities, transplant physicians, patients, etc.. Most probably creating a government sponsored agency in which all of these actors have a saying could be a good solution.

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Figure 1 Number of expected transplants using different exchange mechanisms.

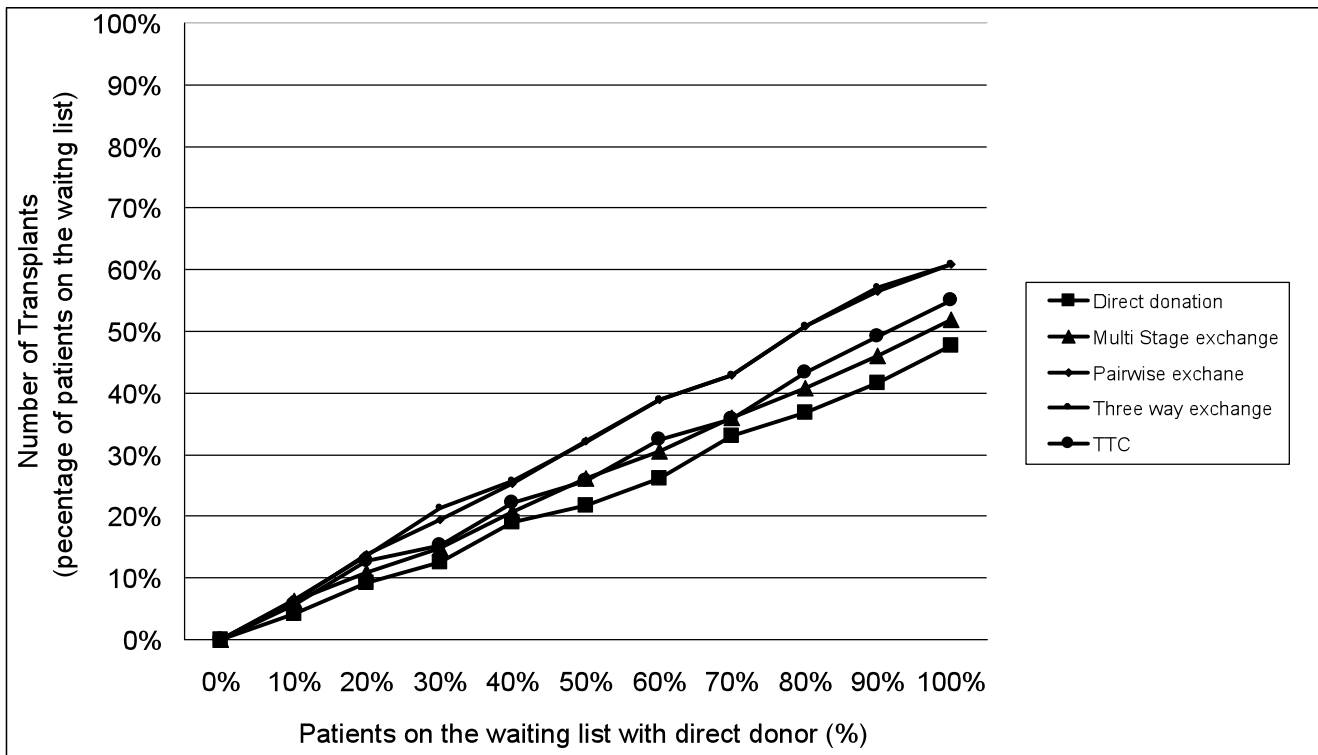


Figure N 2 Effect of different matching criteria on the number of Kidney transplants for the PW and 3W exchange mechanisms.

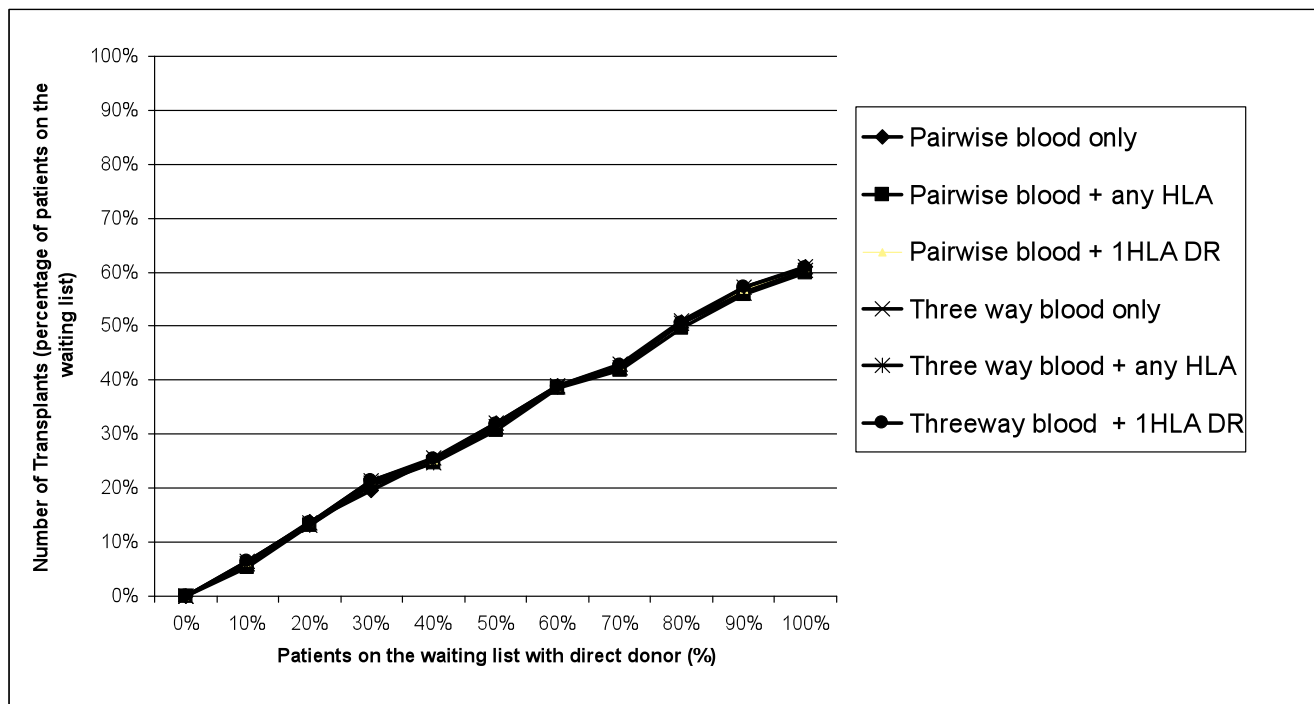


Figure N 3 Effect of different matching criteria on number of transplants for the TTC exchange mechanism

