

# ETHICAL ISSUES IN INCREASING LIVING KIDNEY DONATIONS BY EXPANDING KIDNEY PAIRED EXCHANGE PROGRAMS

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Overview

## **Abstract Author Information Article Outline**

**Introduction.** In 1997, Ross et al. proposed to increase the supply of living kidney donations by using kidneys from living ABO-incompatible donors through an exchange arrangement between two living kidney donor-recipient pairs. Although many transplant centers are exploring this option, only a small fraction of potential donor-recipient pairs are eligible for an exchange on the basis of ABO incompatibility. In this article, we explore three variations that have potentially great clinical relevance.

**Methods.** The three potential variations discussed are: (1) altruistically unbalanced living donor-recipient exchanges; (2) an indirect exchange (an exchange between a living donor-recipient pair with a cadaveric donor-recipient pair) on the basis of a positive crossmatch; and (3) an indirect exchange on the basis of ABO incompatibility.

**Discussion.**

The goal of kidney paired exchange programs is to increase the supply of kidneys available for transplantation ethically. We acknowledge that all exchanges increase the potential for coercion, and we currently reject the proposal of altruistically unbalanced exchanges because of the potential for coercion. However, we believe that voluntary consent can be achieved for indirect exchanges. The indirect ABO-compatible exchange creates no new ethical concerns to our original living paired exchange program and we support its implementation. The indirect ABO-incompatible exchange does create a new ethical concern because it may increase the vulnerability of O blood group recipients. If mechanisms can be developed to avoid increasing the waiting time for blood group O recipients, we would support the implementation of the indirect ABO-incompatible exchange.

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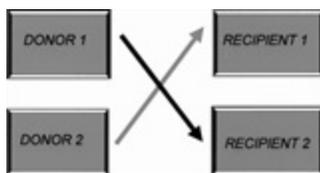
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In 1997, Ross et al. (<sup>1</sup>) proposed to increase the supply of living kidney donations by using kidneys from living ABO-incompatible donors through an exchange arrangement between two living kidney donor-recipient pairs in which donor 1 provides a kidney to (ABO-compatible) recipient 2 and donor 2 provides a kidney to (ABO-compatible) recipient 1 (Fig. 1). Although many transplant centers are exploring this option, only a small fraction of potential donor-recipient pairs are eligible for an exchange on the basis of ABO incompatibility (<sup>2</sup>, <sup>3</sup>). The only potential pairs are blood type A and B mismatches; these mismatches account for just 6% of patients in end-stage renal disease (<sup>2</sup>). The most common blood type (blood type O) recipients are not eligible because all potential O donors may donate directly unless there is a positive crossmatch. Positive crossmatches between potential kidney donors and recipients may provide a more frequent option for kidney paired exchanges because the number of potential donors rejected on the basis of a positive crossmatch approaches 15% for all living donors (<sup>4</sup>) and is even higher between spouses (<sup>4</sup>, <sup>5</sup>).



**Figure 1**

In a second article on kidney paired exchanges, Ross and Woodle (<sup>6</sup>) explored the ethics of several variations on living donor kidney paired exchanges. Further work in this area reveals three possibilities that have potentially great clinical relevance: (1) altruistically unbalanced living donor-recipient exchanges; (2) an indirect exchange (an exchange between a living donor-recipient pair with a cadaveric donor-recipient pair) on the basis of a positive crossmatch; and (3) an indirect exchange on the basis of ABO incompatibility. In this article, we will discuss the ethical issues raised by these three options.

## THE UNBALANCED KIDNEY PAIRED EXCHANGE

We did not discuss the issue of the blood group O recipient who requires a blood group O donor in our initial

proposed kidney paired exchange protocol. Blood group O is the most common blood type in the population and in patients with end-stage renal disease waiting for a cadaveric kidney donor (7). Blood group O recipients require a blood group O donor, but blood group O donors are universal donors and can give to any ABO recipient. Because these donors are universal donors, they will rarely find themselves eligible for a kidney paired exchange. Exceptions will occur if the blood group O donor and his or her potential recipient are otherwise incompatible (e.g., a positive crossmatch).

Most potential living donors are excluded from participation because of immunological, psychological, or other medical reasons (4). One possible way to increase the number of altruistic living donors who actually donate is to ask a potential living O donor to participate in a kidney exchange even though he or she could donate directly to his or her emotionally related recipient. That is, to ask donor 1 to provide a kidney to recipient 2 and donor 2 to provide a kidney to recipient 1, when donor 1 can provide a kidney to recipient 1 or 2 and when donor 2 cannot provide a kidney to recipient 2 but can provide a kidney to recipient 1 (Fig. 2). We call this an altruistically unbalanced exchange: an exchange in which one donor-recipient pair can participate in a direct donation, but the second donor-recipient pair cannot. The exchange is unbalanced because of differences in the degree of altruism required by the two donor-recipient pairs. Although donor-recipient pair 2 cannot undergo living donor kidney transplantation without an exchange, donor-recipient pair 1 can choose either to donate directly or through an exchange. Historically, donor-recipient pair 2 has been told that live donation is not feasible; the recipient would have the option of dialysis or a cadaveric transplant. Donor-recipient pair 1 undergoes donation and transplantation. Under this proposed exchange program, donor-recipient pair 1 is being offered the new option of helping two potential recipients by participating in an exchange.



Figure 2



Figure 5



Figure 6



Figure 7



Figure 8

A direct donation and an exchange donation offer the same physical risks for the donor. There are rare but significant perioperative risks. Recent surveys find less than 2% major complications (8, 9), including a perioperative mortality of 3 in 10,000 (10, 11). The major concern with altruistically unbalanced exchanges is the possible coercion that donor 1 may experience; there may be psychological pressure on donor 1 to participate in the exchange to maximize the number of organs available. The donor who may have consented to donate solely

to benefit his or her paired recipient may feel coerced to participate even though he or she has no interest in doing so.

There are potential medical and psychological reasons for a donor to prefer to give his or her kidney directly to an emotionally related recipient. If the donor and recipient are siblings, minor haplotype antigen matches may increase the probability of a successful graft<sup>(12)</sup>. To ask an already altruistic donor to be more altruistic and risk a slightly lower graft survival for his or her emotionally related recipient in order that two patients receive transplants rather than one is difficult to justify from an individualistic perspective. Even if the donor was willing to take a more communitarian perspective, a question remains as to whether the emotionally related recipient should have a say in this decision because the small percentage point decrease in graft survival affects the recipient most intimately.

A second reason the potential unbalanced donor-recipient pair may prefer a direct donation is the psychological assurance concerning the “quality” of the donated kidney that the recipient receives. Data regarding direct donations of blood suggest that direct donations are not safer than the general pool<sup>(13, 14)</sup>. Nevertheless, there are specific criteria that do correlate with graft survival. One such criterion is the age of the donor<sup>(12, 15, 16)</sup>, which could create the need to grade organs to ensure equity in the exchange, particularly given the current trend to expand the criteria for eligible donors<sup>(17, 18)</sup>. At a minimum, information about donor health and organ quality must be provided to the unbalanced altruistic donor-recipient pair in such a way that they can make a truly informed decision about whether to participate in an exchange.

There is also a possibility that direct donation offers a greater psychological benefit and that recipient compliance with posttransplantation treatment may be better when recipients face their donors on a daily basis<sup>(19)</sup>.

Most donors agree to donate because a loved one is ill. To ask a donor to participate in an unbalanced exchange requires the donor to modify his or her reason for donating to a more generalized concept of altruism. Under the circumstances, this request may be construed as quite coercive. As such, we currently do not support the implementation of unbalanced kidney paired exchanges. Empirical data of the attitudes of potential and former organ donors and living kidney recipients would be useful to prove or disprove our concerns.

## INDIRECT EXCHANGES: EXCHANGES BETWEEN LIVING AND CADAVERIC DONORS

Another possible type of kidney exchange is to allow a potential donor who is immunologically incompatible with his potential recipient to donate his kidney to the cadaveric waiting list with the agreement that his paired recipient would receive priority for the next ABO-compatible crossmatch-negative cadaveric kidney. We call an exchange between a living donor and a cadaveric donor an indirect exchange. A living donor-cadaveric donor exchange provides an individual on the cadaveric waiting list with a living donor kidney, which has a better chance of graft survival (>80% versus >70% three-year graft survival)<sup>(12)</sup>. However, a living donor-recipient pair may decide to accept this arrangement to minimize waiting time. From their perspective, the decreased waiting time may offset the lower graft survival of a cadaveric kidney. From the perspective of those on the cadaveric waiting list, an indirect exchange seems to be neutral if not slightly positive because it exchanges a cadaveric kidney for a living kidney.

There are, however, two different types of indirect exchanges depending on the ABO compatibility of the living donor-recipient pair (Figs. 3 and 4). In the next two sections, we discuss the different ethical issues raised by these two scenarios.



Figure 3



Figure 9



Figure 10



Figure 11



Figure 12

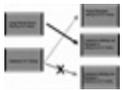


Figure 4



Figure 13



Figure 14



Figure 15

## INDIRECT EXCHANGES BETWEEN ABO-COMPATIBLE LIVING AND CADAVERIC DONORS

One type of living-cadaveric donor exchange involves a living donor and recipient who are ABO compatible but have a positive crossmatch. The person on the waiting list who is offered the living kidney is the person who would otherwise receive the cadaveric kidney (Fig. 3). For this person, the choice is between a cadaveric kidney or a living kidney. The decision of the potential recipient on the waiting list who is offered the choice between a

cadaveric or a living kidney is relatively simple: given the greater likelihood of graft survival, it is rational and reasonable that the individual will accept the exchange.

The biggest concern in the scenario of an ABO-compatible indirect exchange is logistical: are the transplantations to be done simultaneously or does the living donor give a kidney preemptively and his or her emotional loved one then moves up to the highest position on the waiting list and get the next available ABO-compatible, crossmatch negative kidney? Donating electively avoids the need for the potential altruistic donor to be “on-call.” Being “on-call” may result in the need to harvest the organ at non-optimal times or under non-ideal circumstances either medically (e.g., the patient would not be fasting) or personally (e.g., the individual needs to be available on pager). Because a donor must be able to renege at any time, delaying the harvest until an urgent moment may increase the likelihood of renegeing and thus of disappointing two potential recipients. We believe that the donor should donate electively with the promise that his or her potential recipient be given highest priority on the United Network of Organ Sharing (UNOS) waiting list.

Indirect exchanges involving ABO-compatible crossmatch-positive donor-recipient pairs is an obvious extension to our original kidney paired exchange proposal. The only twist is in the timing of the donations because cadaveric kidneys do not become available electively. To ensure the elective nature of the living kidney donation, the living donation should be done before and not simultaneous to the cadaveric donation. Performed in this manner, these exchanges offer no new ethical challenges. They raise concerns about whether the donors are acting voluntarily and altruistically, but these are the same ethical challenges raised by all potential exchanges and were addressed in our original article (<sup>1</sup>). They also raise the same legal challenges raised in our original article about whether exchanges are within the scope of altruistic donations permitted by U.S. federal law (<sup>20</sup>, <sup>21</sup>), the United Nations declaration (<sup>22</sup>), and the laws and regulations of transplant authorities (<sup>23</sup>).

## INDIRECT ABO-INCOMPATIBLE EXCHANGES AND THEIR IMPACT ON POTENTIAL O RECIPIENTS

The more likely indirect exchange, however, involves an ABO-incompatible donor-recipient pair such that the person who would receive the living donor’s kidney is not the individual who would get the cadaveric kidney now to be transplanted into the paired recipient (Fig. 4). This is because the most likely living donor who cannot donate directly will be an A, B, or AB donor who cannot donate to the potential O recipient. As such, the individual on the waiting list who benefits from the exchange will have the same blood type as the living donor, and individuals on the waiting list with the same blood type as the paired recipient may have longer waiting times because the paired recipient gets priority for the next cadaveric kidney of that blood type. The problem is that although the number of kidneys available for individuals on the cadaveric waiting list could be numerically increased by ABO-incompatible indirect exchanges, and the quality of kidneys for cadaveric waiting list recipients improved, changes in beneficiaries will occur.

Because there are two possible beneficiaries from the cadaveric waiting list when the cadaveric kidney becomes available, depending on whether or not a living donor-cadaveric donor exchange takes place, indirect exchanges between ABO-incompatible cadaveric and living donors logistically require that the harvest of the living donor be done electively, before the cadaveric kidney is even identified. If the exchange were to take place simultaneously and the living donor reneged (as he or she must be able to do until the moment of surgery), the recipient from the cadaveric list would change. The results are disappointed individuals and the greater storage

time of the cadaveric kidney, which is inversely related to graft function and survival. Everyone is worse off than if the actual recipient were known beforehand.

ABO-incompatible indirect exchanges raise the possibility that certain subgroups may be disproportionately harmed. While the specific individual who will benefit and the specific individuals who will be harmed because of an ABO-incompatible indirect exchange is not known beforehand, there is reason to be concerned that some groups of recipients will have increased waiting times. In particular, individuals waiting for blood group O kidneys may experience a lengthened waiting period because over two thirds of ABO-incompatible donor-recipient pairs involve a potential O recipient (<sup>2</sup>). Because these individuals already have the longest waiting time, the exchange may harm this vulnerable population. Even if one were to decrease the waiting list overall by increasing supply, it may be unjust to do so if it entails harming the most vulnerable group (<sup>24</sup>).

A modification in the way that donors are selected could minimize if not entirely eliminate the potential problem that blood group O waiting times will be increased by ABO-incompatible indirect exchanges. In our original article (<sup>1</sup>), we proposed that when all of a recipient's potential living donors are determined to be unsuitable, the potential donor(s) rejected solely on the basis of ABO incompatibility and positive crossmatches would be offered the opportunity to participate in an exchange. We had planned to call all potential donors rejected on the basis of ABO incompatibility and positive crossmatches and have the donors and transplant team make a mutual medical and social decision as to who would be the donor. Given the real concerns of increased waiting time for O recipients, one could argue that the potential O blood group exchange donors should be used preferentially on the basis of utility and justice for those on the waiting list. For example, if a potential O recipient has two willing relatives, one of whom is blood type A (ABO incompatible) and one of whom is blood type O with a positive crossmatch, equitable access would be promoted by preferentially asking the potential O donor to participate. Work in progress includes preliminary calculations that indicate that the preferential selection of O donors will eliminate the negative impact of indirect exchanges on potential O recipients on the cadaveric waiting list.

Coercion is the greatest ethical concern for the use of living donors in general. Concerns about coercion may be exacerbated by indirect exchanges because a reluctant or hesitant donor may no longer be able to invoke ABO incompatibility or a positive crossmatch as a convenient way to withdraw from consideration as a living donor. While we raised this concern with respect to direct paired exchanges, coercion may be of even greater concern in our proposal, which would empower the transplant team to choose the donor on the basis of utility and distributive justice. The traditional way of choosing between potential altruistic donors is to allow individuals who truly want to donate to "step forward." That is, the traditional selection of an individual donor when a potential recipient has more than one willing donor is based on the individual's determination to be a donor by contacting the transplant center, by expressing unwavering interest in donation to the team on any occasion possible, or by emphasizing this desire to the potential recipient who then informs the transplant team of this desire. This allows "willing" but ambivalent donors to be excused without having to admit their ambivalence. In contrast, our approach to minimize the harm to wait-listed blood group O recipients has the transplant team choose between "willing" donors. Although the selected donor will be given many opportunities to renege, his or her selection by the transplant team may be interpreted quite coercively.

Given the serious potential that donors may feel coerced about participating in an exchange, we believe that exchanges should include a series of social work consultations as well as formal psychiatric evaluation to ensure that the "selected" donor is a "willing" donor and that the consent to donate is given voluntarily. While acknowledging the complex dynamics of donation (<sup>25, 26</sup>), we hope that repeated interactions with different members of the transplant team will allow the unwilling "selected" donor the opportunity to renege. We encourage empirical studies to determine how potential donors, previous donors, and wait list candidates react

to indirect exchanges in general as well as their attitudes and beliefs about empowering the transplant team to preferentially select O donors among “willing” living donors.

## CONCLUSION

The goal of kidney paired exchange programs is to increase the supply of kidneys available for transplantation in an ethically sound way. While we acknowledge that all exchanges increase the potential for coercion because they eliminate the easy medical excuses for donors, we believe that voluntary and informed consent can be procured from all parties. We have examined the ethics of altruistically unbalanced kidney exchanges and currently reject their implementation because of their potential for coercion. We also have examined the ethics of indirect exchanges between a living donor to an individual on the cadaveric kidney waiting list with the intention that the living donor’s paired recipient receives highest priority for the next ABO-compatible crossmatch-negative cadaveric kidney. We believe that indirect ABO-compatible exchanges create no new ethical concerns to our original living paired exchange program and support their implementation. Indirect ABO-incompatible exchanges, on the other hand, do create the potential for increasing the vulnerability of O blood group recipients. We have suggested one possibility to minimize this risk by preferentially selecting willing living donors of blood group O. If protocols can be developed that are not coercive but provide a means to avoid increasing the waiting time for blood group O recipients, we would support the implementation of such indirect exchanges.

As variations on kidney paired exchange programs continue to evolve, we expect that a number of new clinical and ethical issues will arise. Professional and lay consensus about these issues are essential before such exchanges are introduced into the clinical research setting.

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## REFERENCES

1. Ross LF, Rubin DT, Siegler M, Josephson MA, Thistlethwaite JR Jr, Woodle ES. Ethics of a paired-kidney-exchange program. *N Engl J Med* 1997; 336:1752.
2. Terasaki PI, Gjertson DW, Cecka JM. Paired kidney exchange is not a solution to ABO incompatibility. *Transplantation* 1998; 65:291.
3. Woodle ES, Ross LF. Paired exchanges should be part of the solution to ABO incompatibility in living donor kidney transplantation [Letter; Comment]. *Transplantation* 1998; 66:406.
4. Fehrman-Ekholm I, Gabel H, Magnusson G. Reasons for not accepting living kidney donors. *Transplantation* 1996; 61:1264.
5. Lee P-C, Liang C-C, Lei H-Y, Lee P-H, Lee C-J. Use of living unrelated kidney donors. *Transplantation* 1994; 57: 1134.
6. Ross LF, Woodle ES. Kidney paired exchange programs: an expanded view of the ethical issues. In: Touraine JL, Traeger J, Betuel H, Dubernard JM, Revillard JP, Dupuy C, eds. *Organ allocation: Proceedings of the 30<sup>th</sup> International Conference on Transplantation and Clinical Immunology*. Dordrecht: Kluwer Academic Publishers, 1998
7. Harper AM, Rosendale JD, McBride MA, Cherikh WS, Ellison MD. The UNOS OPTN waiting list and donor registry. *Clin Transpl* 1998: 73.

8. Bia MJ, Ramos EL, Danovitch GM, et al. Evaluation of living renal donors: the current practice of US transplant centers. *Transplantation* 1995; 60:322.
9. Johnson EM, Najarian JS, Matas AJ. Living kidney donation: donor risks and quality of life. *Clin Transpl* 1997: 231.
10. Bay WH, Hebert LA. The living donor in kidney transplantation. *Ann Intern Med* 1987; 106:719.
11. Najarian JS, Chavers BM, McHugh LE, Matas AJ. 20 years or more of follow-up of living kidney donors. *Lancet* 1992; 340:807.
12. Cecka JM. The UNOS Scientific Renal Transplant Registry. *Clinical Transplants* 1998: 1.
13. Kruskall MS, Umlas J. Acquired immunodeficiency syndrome and directed blood donations: a dilemma for American medicine. *Arch Surg* 1988; 123:23.
14. Pink J, Thomson A, Wylie B. Infectious disease markers in autologous and directed donations. *Transfus Med* 1994; 4:135.
15. Lee CM, Scandling JD, Shen GK, Salvatierra O, Dafoe DC, Alfrey EJ. The kidneys that nobody wanted: support for the utilization of expanded criteria donors. *Transplantation* 1996; 62:1832.
16. Ratner LE, Kraus E, Magnuson T, Bender JS. Transplantation of kidneys from expanded criteria donors. *Surgery* 1996; 119:372.
17. Cho YW, Terasaki PI. Impact of new variables reported to the UNOS Registry. *Clin Transpl* 1997: 305.
18. Cho YW. Expanded criteria donors. *Clin Transpl* 1998: 421.
19. Terasaki PI, Cecka JM, Gjertson DW, Cho YW. Spousal and other living renal donor transplants. *Clin Transpl* 1997: 269.
20. National Organ Transplantation Act Public Law Number 98–507, 1984.
21. Uniform Anatomical Gift Act of 1987, §§ 1–17, 1989.
22. World Health Organization: Guiding principles on human organ transplantation. *Lancet* 1991; 337: 1470.
23. Sells RA. Paired-kidney-exchange programs [Letter]. *N Engl J Med* 1997; 337:1392.
24. Rawls J. *A theory of justice*. Cambridge, MA: Belknap Press of Harvard University Press, 1971.
25. Simmons RG, Marine SK, Simmons RL. *Gift of life*. New Brunswick, NJ: Transaction Books, 1987.
26. Siegler M, Lantos JD. Ethical justifications for living liver donation. *Cambridge Quarterly of Health Care* 1992; 1:320.

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