

Altruistic Donor Triggered Domino-Paired Kidney Donation for Unsuccessful Couples from the Kidney-Exchange Program

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Between January 2000 and July 2009, 132 individuals inquired about altruistic kidney donation to strangers. These donors were willing to donate to genetically and emotionally unrelated patients. Some altruistic donors wished to donate to a specific person, but most wished to donate anonymously. In domino-paired donation, the altruistic donor donates to the recipient of an incompatible couple; the donor of that couple (domino-donor) donates to another couple or to the waiting list. In contrast to kidney-exchange donation where bilateral matching of couples is required, recipient and donor matching are unlinked in domino-paired donation. This facilitates matching for unsuccessful couples from the kidney-exchange program where blood type O prevails in recipients and is under-represented in donors. Fifty-one altruistic donors (39%) donated their kidney and 35 domino-donors were involved. There were 29 domino procedures, 24 with 1 altruistic donor and 1 domino-donor, 5 with more domino-donors. Eighty-six transplantations were performed. Donor and recipient blood type distribution in the couples limited allocation to blood type non-O waiting list patients. The success rate of domino-paired donation is dependent on the composition of the pool of incompatible pairs, but it offers opportunities for difficult to match pairs that were unsuccessful in the kidney-exchange program.

Key words: Altruistic donor chains, anonymous kidney donation, directed stranger donation, Domino-paired donation, Good Samaritan donor, nondirected donation

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Introduction

Living donor renal transplantation is the most promising solution for closing the gap between organ supply and demand. However, in our center 17.3% of couples with willing donors are either ABO incompatible (52%) or have a positive cross match (48%) (1,2). The introduction of the living kidney-exchange program led to an increase in the success rate of living donor renal transplantation. However, even in the successful Dutch National kidney-exchange program, 42% of couples cannot be matched (2). This unsuccessful pool is dominated by ABO incompatible pairs (71%), and further matching is hampered because blood type O recipients are over-represented, whereas O donors are under-represented (2–4).

Altruistic, anonymous or Good Samaritan donor transplantation is increasingly accepted to deal with organ shortage (5). A significant number of individuals are sincerely motivated to donate a kidney when they are informed about the organ shortage and the suffering of dialysis patients (6,7). In our experience, increasing the awareness of living anonymous donation among the general public (e.g. through attention in the media) has a direct effect on the enrolment of potential donors. Ethical and psychological aspects regarding anonymity, voluntariness and justice of this form of donation have been the subject of research and discussion worldwide (8–14). Actually, there is no unambiguous term to describe the phenomenon of altruistic, directed or nondirected kidney donation to an unknown person. All living donors are altruistic, whether they donate to a loved one or to a stranger. In some situations the kidney donation is not anonymous as the donor and recipient are acquainted, but not familiar with each other. The term Good Samaritan is appropriate, but incomprehensible for people without a Christian background. Eventually, the term altruistic donation to a stranger appears to be best applicable.

As the population of altruistic donors that wishes to donate to strangers is a representation of the general population a large number of O donors can be expected. In our center, the domino-paired program was initiated in an attempt to match the unsuccessful couples from the Dutch kidney-exchange program (15). The availability of an altruistic donor unlinks the matching of donor and recipient of

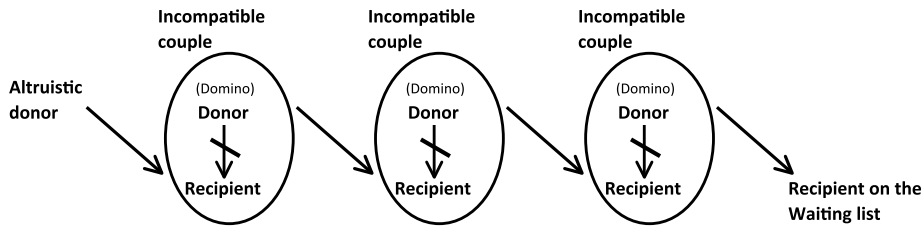


Figure 1: Example of a domino procedure with one altruistic donor, three incompatible couples and one recipient on the waiting list (chain-length 4).

an unsuccessful couple, thus enlarging their chances of a successful match (16). The altruistic donor donates to the recipient of an incompatible couple from the kidney-exchange program provided that the donor of that couple (domino-donor) donates to a patient on the waiting list. A much larger number of transplantations are made possible when the domino-donor donates to the recipient of another incompatible couple (Figure 1). Chains with one or more incompatible couples are possible (17). In this article we describe how altruistic donation to strangers triggered our domino-paired donation program.

Participants and Methods

All individuals who made inquiries about altruistic kidney donation to strangers in the Erasmus Medical Center, Rotterdam in the period between January 1, 2000, and July 1, 2009, were included in this analysis. In the first contact information is given about preparatory medical and psychological examinations and the long and short-term implications of donation for donor health. It is stressed that for nondirected donation, anonymity will be maintained and that profit seeking is an absolute contra-indication for donation. Thereafter, an information package is sent. It is left to the potential donor to take the initiative to make an appointment to see a nephrologist. Health professionals from the transplant unit do not actively recruit altruistic donors.

The donor screening follows a four-step plan. This plan is executed by dedicated live-donor coordinators. The same nephrologist sees the donor at each consultation. This procedure has been described thoroughly (1). During the donor work-up, it is emphasized that donor consent can be withdrawn at any moment. All potential altruistic donors that wish to donate to strangers are referred to the psychologist to assess motives and psychological flexibility. The reasons and motivations of the donor are examined, based on the 'Symptom Checklist' (SCL-90) and an in-depth interview (18). If medical contra-indications are found the potential donor is referred to a specialist in that field. All potential donors that eventually undergo nephrectomy (actual donors) are followed up annually for the rest of their lives.

Our program for altruistic donors who wish to donate to strangers includes three possibilities for donor-recipient couple selection: (1) Nondirected donation: The altruistic donor donates to a recipient on the waiting list. The recipient is selected according to the allocation criteria that are used by the Dutch Transplant Foundation for deceased donor organ assignment. The donor is not allowed to specify characteristics of the potential recipient. (2) Directed donation: In less than 10% of cases the potential altruistic donor became aware of a specific person with end stage renal disease (ESRD). Although there is no emotional or genetic relationship, the volunteer wishes to donate to this person. Donor and recipient know each other but are not actively involved in each other's lives (19). (3) domino-paired donation: The altruistic donor donates to the recipient of a couple that is unsuccessful in our National Kidney-Exchange Program and the donor of that couple (domino-donor) donates to the waiting list or to the recipient of another unsuccessful couple, provided that the potential donor of that couple also donates a kidney. As domino-paired donation increases transplantation possibilities beyond the single altruistic donation to a stranger, this procedure is encouraged in our center.

The couple with the longest waiting time in the donor-exchange program is selected for the domino procedure, provided there is ABO compatibility and absence of recipient HLA antibodies against the potential donor. We aim for a fair HLA match for couples selected in our altruistic donation program. When it turns out to be impossible to find a match between an altruistic donor and an incompatible couple within 6 months the altruistic donor is asked to donate to the pool. There is a 6-month period for reconsideration between admission and actual donation and it is stressed that withdrawal is always possible. For most domino-procedures, transplantations were performed on the same day. In a few cases transplantations were performed on two consecutive days. For logistical reasons, in one chain-length 3 and in one chain-length 4 procedure, altruistic donors donated the day after all domino-donations took place. This means that the incompatible or domino donors donated before their recipient was transplanted. This is justified by the fact that, in our experience, the altruistic donors are so motivated that they never withdraw at the last moment. The last domino-donor of the chain donates to a recipient on the waiting list.

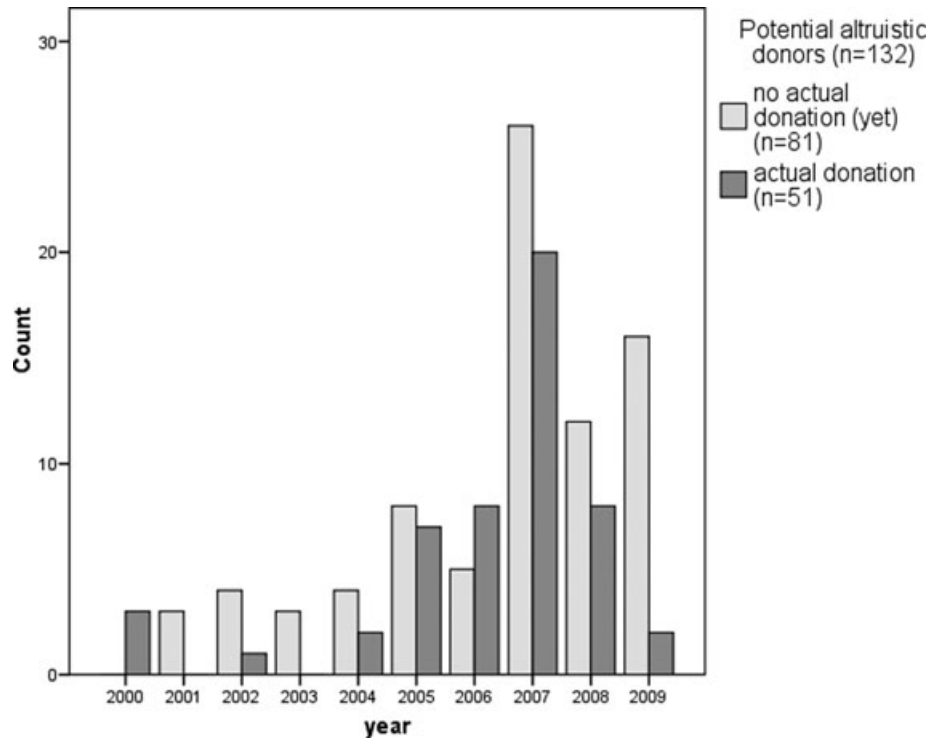


Figure 2: Number of altruistic potential donors per year. As the observation stopped in July 2009, a lot of potential donors still await either donation or the decision.

Results

In the study period 132 potential altruistic donors inquired about living kidney donation (Figure 2). The number of persons that inquired about donation and eventually donated a kidney steeply increased in 2007. There were 12 donors who aimed at directed donation (Figure 3): One of them started as a potential nondirected donor, but he met a potential recipient during donor work-up. The rest started the donor work-up as a directed donor with a predetermined recipient. One of the potential donors was an ex-colleague of the recipient, three donors lived in the same street as the recipient, six met in societies, clubs or public places, one partner of a deceased hemodialysis patient decided

to donate to another dialysis patient at the dialysis center. Of 12 potential donors, 9 eventually donated, 1 of them via domino-paired donation because of incompatibility with the first-choice recipient. One couple is on the waiting list for donation. One potential directed donor withdrew because the recipient died. For one couple decision is pending (Figure 3).

There were 120 donors who opted for nondirected donation; 14 donated to the waiting list and 28 donated via the domino-paired program (Figure 3). Two potential donors await donation. Sixty-six potential donors withdrew (n = 41), were declined (n = 15), or were referred to another transplantation center in the Netherlands (n = 10).

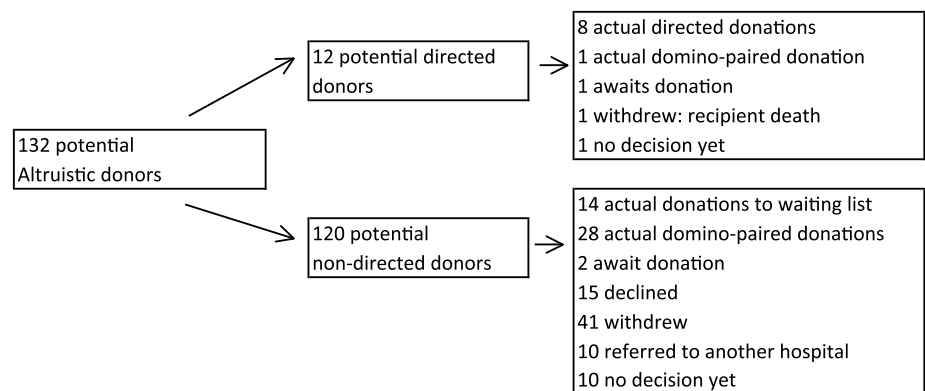


Figure 3: Diagram showing the results of the Good Samaritan/Domino-Paired Donation Program.

Table 1: Donor characteristics

| | Altruistic donors | Domino-donors | p-Value |
|--------------------|-------------------|---------------|------------------------|
| Number | 51 | 35 | |
| Males (%) | 57 | 51 | ns ¹ |
| White (%) | 98 | 86 | ns ¹ |
| Age (years) | 57 ± 10 | 55 ± 11 | ns ² |
| ABO blood type (%) | O | 61 | p = 0.003 ¹ |
| | A | 29 | |
| | B | 6 | |
| | AB | 4 | |

¹Chi-square.

²ANOVA.

For 10 potential donors no decision has been made yet. Eventually 51 of 132 altruistic donors actually donated a kidney (39%).

Twenty-nine of the actual altruistic donors were married or lived with a partner. The other 22 donors lived alone: 7 were divorced, 5 were widowers, 10 were single. Twenty-eight donors stated that they were Christians; the other 23 donors stated that they were not religious. Ten donors had vocational, secondary education, 15 had academic, secondary education and twenty-six donors were highly educated (College or University). There was 1 Asian donor; the other 50 donors were White (Table 1).

Twenty-two altruistic donors donated to the waiting list: 8 directed and 14 nondirected (Figure 3). Of the 14 nondirected donations to the waiting list, 4 were performed before the domino-paired program had started. Three of these 14 donors had a medical reason for nephrectomy and decided to donate this kidney: 2 donors had irreversible ureteral lesions after abdominal surgery; 1 had persisting pain after a urological operation because of kidney stones. They were not included in the domino procedure for logistical reasons. For the remaining seven donors it was not possible to find a match with an incompatible couple within a period of six months. Having ABO blood type A (n = 5) or AB (n = 2) was the main reason. There were 29 altruistic donors who donated to an incompatible pair: 1 of them with a directed donor, 28 with nondirected donors (Figure 3).

Thirty-five incompatible couples were involved in domino-paired donation procedures. ABO blood type incompatibility (69%) and positive crossmatch (31%) were the reasons for incompatibility. Efforts to match the couples in the kidney-exchange program had been unsuccessful. Domino-donors are the potential donors from the incompatible couple for whom donation and transplantation became possible via the domino-paired procedure. Twenty-four domino procedures included one altruistic donor and one domino-donor (chain-length 2, Figure 4). Four domino-procedures included one altruistic donor and two domino-donors (chain-length 3) and one procedure included one al-

| | Altruistic donors (N) | Domino-donors (N) |
|--------------------------|-----------------------|-------------------|
| directly to pool | 22 | 0 |
| 24 Domino chain-length 2 | 24 | 24 |
| 4 Domino chain-length 3 | 4 | 8 |
| 1 Domino chain-length 4 | 1 | 3 |
| Total | 51 | 35 |

Figure 4: Scheme showing how Altruistic donors and domino-donors participated in the Good Samaritan/Domino-Paired Donation Program.

truistic donor and three domino-donors (chain-length 4). In total: twenty-nine domino-donors donated to the waiting list, six donated to the recipient of another incompatible couple. Thanks to the domino-paired procedure 35 extra transplantations were made possible. This means that 51 altruistic donors enabled 86 transplantations.

Only 15 altruistic donors were declined because of medical (n = 7) or psychological (n = 8) reasons (Figure 3). From the 41 potential donors that withdrew there were 33 who never made an appointment to see the nephrologist, 6 withdrew during the donor screening procedure and 2 potential altruistic donors withdrew after medical and psychological approval and shortly before donation (Figure 3).

Table 1 shows characteristics of the actual donors. There are no significant differences between altruistic donors and domino-donors concerning gender, age and ethnicity. As expected, the percentage of blood-type O donors is low in the domino-donor population, while this percentage is normal to high in the altruistic donor population. Table 2 shows the recipient population divided into recipients from the waiting list and recipients from an incompatible couple. There are slightly more males in the population of recipients from an incompatible couple (ns). The percentage of Whites is high in both populations, but in the population of recipients from the waiting list the proportion comes close to that in the general population. Most blood type O donors donate to blood type O recipients from an incompatible couple. As a result, an extraordinarily high number of recipients from the waiting list had blood type A (Table 2). The patients from the waiting list had significantly longer waiting times compared to recipients from an incompatible couple but historic PRA was higher in the population of recipients from an incompatible couple. Current PRA was not significantly different. The number of HLA mismatches and HLA-DR mismatches was not significantly different between patients from the waiting list and recipients from an incompatible couple.

Discussion

Worldwide, anonymous kidney donation is slowly gaining acceptance, but the numbers in actual practice are still limited. In most centers with anonymous donation programs, kidneys are allocated to recipients on the waiting

Table 2: Recipient characteristics

| | Waiting list recipients | Incompatible couple recipients | p-Value |
|---------------------|-------------------------|--------------------------------|------------------------|
| Number | 51 | 35 | |
| Males (%) | 51 | 69 | ns ² |
| White (%) | 73 | 86 | ns ² |
| Age (years) | 54 ± 14 | 49 ± 15 | ns ¹ |
| ABO blood type (%) | O | 22 | p < 0.001 ² |
| | A | 61 | |
| | B | 4 | |
| | AB | 14 | |
| PRA current | 5 ± 17 | 7 ± 21 | ns ¹ |
| PRA historic | 10 ± 22 | 22 ± 33 | 0.047 ¹ |
| Waiting time (days) | 936 ± 666 | 492 ± 685 | 0.004 ¹ |
| HLA mismatches | 3.3 ± 1.8 | 3.6 ± 1.5 | ns ¹ |
| DR mismatches | 1.0 ± 0.7 | 1.3 ± 0.8 | ns ¹ |

¹Chi-square.²ANOVA.

list (12,13,20,21). In Europe only a few centers have experience with nondirected living donation (4,22).

Theoretically, application of the so-called domino-paired donation program is preferred because of the potential increase in the number of transplantations (16,23). Recently Gentry et al. described a simulated recipient–donor pair pool in a clinically detailed domino-paired donation model. They expect a considerable increase in the number of transplantations when the domino-paired procedure is consistently applied (24). Real life domino-paired kidney donation has been described in case reports (16,17,25). Rees described in 'A nonsimultaneous, extended altruistic-donor chain' a chain of 10 kidney transplantations initiated by one anonymous donor (17). In this procedure there is no donation to a patient on the waiting list. Recently Lee et al. were the first to describe the evaluation of their multicenter domino-paired kidney donation program (26). They performed 179 renal transplantations with domino-procedures starting with 70 anonymous donors in the Korean population.

In Rotterdam the first anonymous donation to a stranger was conducted in 2000. At the start of this program, these kidneys were allocated to patients on the waiting list. In 2002 one domino procedure was performed because a directed donor was incompatible with his recipient. In 2003 a regional kidney-exchange program was initiated in Rotterdam and in 2004 the National kidney-exchange program was started. It soon became clear that even in the National kidney-exchange program approximately half of the pairs could not be matched with another couple (2–4). This led to the introduction of the Rotterdam domino-paired kidney donation program in 2005. In the Netherlands the media played an important role in the recruitment of living donors during the last years. A famous Dutch television personality suffered from renal failure and received a renal transplant. His kidney failed and he died at the age of 35. In his honor, the 'Big Donor Show' was organized in 2007. In the show

a woman suffering from a brain tumor decided to donate a kidney to one of three patients present. She turned out to be an actress and the whole situation was faked. Long before and after this show there was a storm of discussions on ethical issues, but the number of persons that inquired about donation and eventually donated a kidney steeply increased (Figure 2).

Altruistic donors prefer domino-paired donation because it generates more than one transplantation from their gift. Nowadays, only those nondirected altruistic donors who are unwilling to participate in the domino procedure and those that cannot be matched to an incompatible couple donate to the waiting list.

The motivations of our altruistic donors were not described in this study, but they are a subject of separate study in our center (18,27). Most altruistic donors and slightly fewer domino-donors were White, which is in agreement with other studies (20). However, as about 38% of the patients on the waiting list are non-White, it is clear that both anonymous and domino-donors are not representative samples of the general population. Kidneys donated to recipients on the waiting list are allocated according to the standard criteria of the Dutch Transplant Foundation for deceased donor kidney allocation. This might explain why there is a tendency toward a higher percentage of non-Whites in the population of recipients from the waiting list in comparison to the recipients from an incompatible couple.

Recipients from the waiting list have lower PRA values but significantly longer waiting times in comparison to recipients from an incompatible couple. HLA matching was comparable in both populations.

Apart from ABO blood type, altruistic donors and domino-donors are not significantly different. Incompatible couples are a selection of donor–recipient combinations that are difficult to match in the National kidney-exchange program

(3). The most prevalent matching problem is a non-O donor combined with O recipient. As could be expected, blood type O is under-represented in the domino-donor population, but well represented amongst altruistic donors (Table 1). This means that, although the altruistic donor often is an O donor, the second or domino-donor very often is a blood type non-O donor, necessitating a non-O recipient. Non-O recipients with an O donor are scarce in the incompatible population as only cross-match positivity can cause this situation. This explains why the subsequent domino-donor and recipient probably are non-O. The same situation is shown by Rees' domino-chain (17). The chain starts with a blood type O donor, but the second domino-donor is a non-O donor and after that all recipients and donors are blood type non-O. As most recipients from blood type incompatible couples are blood type O, long-chains are only useful for a selection of (non-O) couples. In the present report, non-O altruistic donors and domino-donors more often donate to patients on the waiting list and there are significantly more blood type A recipients in the transplanted waiting list population in comparison to the recipients from the incompatible couple population (Tables 1 and 2). The result of our efforts is that, although more waiting list recipients have been transplanted, blood type O is overrepresented in the patients who remain on the waiting list. However, blood type O-patients on the waiting list already have a longer waiting time, a higher risk of removal from the waiting list without transplantation and a worse survival in comparison to blood type non-O patients because organs from deceased O donors are often (12%) allocated to non-O recipients because of HLA-matching (28). A change in policy restricting living and deceased O donor organ allocation to O recipients seems appropriate. This guideline has already been applied in the United Kingdom in order to prevent discrimination of blood type O-patients (4). Voluntary participation of compatible couples with O donor and non-O recipient, in the domino-paired donation program might increase the chances for O recipients from the waiting list. Indirectly, living-donor transplantation of non-O patients from the waiting list increases the chances for transplantation for the O-patients by decreasing the number of patients waiting.

In the Korean population Lee describes, the kidney-exchange program is modest and started only recently, so inclusion in the domino-paired program was not preceded by match runs in the kidney-exchange program (26,29). This resulted in a less unbalanced blood-type distribution in the populations of both recipients and donors from incompatible pairs. Additionally, in our population incompatible couples are ABO incompatible (69%) or have a positive cross-match (31%). In the Korean population 74.3% is ABO incompatible, 6.4% had a positive cross-match and 19.3% is not incompatible but seeks a better HLA-match. The composition of the pool of incompatible couples certainly influences the matching possibilities in the Korean population.

Lee's results and our results are examples of two different policies. In Lee's policy, couples for the domino-paired procedure were recruited from an unselected pool of incompatible couples. This results in a larger increase in transplant numbers per anonymous donor (2.5 times) and longer chains. Logistically longer chains are a disadvantage. Our domino-paired donation program primarily serves unsuccessful (problematic) couples from the kidney-exchange program. Transplant numbers increased only 1.6 times per altruistic donor and chain length is shorter. The challenging question is: Which of these policies will eventually be most effective regarding both easy and difficult to match couples. A third policy is recruitment of couples from one pool of incompatible couples with one computer algorithm serving both the kidney-exchange and the domino-paired program. Short chains, restricting O-donation to O recipients and reservation of altruistic donors for couples who are difficult to match are indispensable rules. This might be an even more interesting option.

In conclusion: In order to carry out a successful domino donation program, a robust infrastructure and a relatively large number of incompatible couples are indispensable. However, the success rate is also dependent on the blood type distribution in the population. Altruistic donor triggered domino-paired kidney donation is a valuable addition to our living donation programs and significantly increases the number of renal transplantations. As kidney-exchange donation and domino-paired donation are complementary and competing programs, the influence of merging these programs on the success rate is a fascinating question for the future.

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