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## Living kidney transplantation between spouses: Results in 100 cases

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**Abstract** The use of unrelated living donors in kidney transplantation is still controversial but many transplant centres have accepted this procedure. The main argument against this approach is usually an ethical one. Because of this, at our institution we accept biologically unrelated donors only if they have an emotional closeness to the recipient. From January 1983 to October 1993, out of 654 kidney transplantations we performed at our institution, 364 kidney allografts were from living donors. Of these living donors, 245 were first-degree relatives of the recipient (LRD) while 119 were unrelated (LURD); 100 cases were spouses – wife to husband in 76 cases and husband to wife in 24 cases. Statistical analysis of the results (chi-

square) revealed actuarial patient and graft survival rates of 89.8% and 86.8% at 1 year, 82.9% and 72.3% at 5 years and 72.3% and 60.3% at 9 years, respectively. In our series, the result of living donor kidney transplantation in this group were similar to those obtained in the LRD group, while they were significantly better than those from cadaver donors ( $P = 0.003$ ). In conclusion, cadaver organs given the shortage of kidney transplantation between spouses may be a good alternative and can be performed successfully, providing a "gift of life" for both the patient and the family.

**Key words** Kidney transplantation  
Living unrelated kidney donors  
Spouses

### Introduction

The use of living unrelated donors (LURD) in kidney transplantation is much debated, and different opinions are expressed. However, kidney transplantation from living donors (LD) is a reality for most occidental countries and is widely employed in developing countries where, in some, commercialisation of organs, a practice unacceptable and forbidden in most countries, is allowed and practised.

The validity of kidney transplant from LD is based upon many ethical and clinical considerations including

the free willingness of the donor, limited risk for the donor's health and results that in most reports are better than with cadaver donor (CD) kidney transplantation [1]. Recent studies have focused on results of kidney transplantation from LURD, showing its validity compared to kidney transplantation from living-related donor (LRD). However, this practice yields further ethical problems, particularly in the definition of motivation of the donor. Among the unrelated donors, those emotionally related are preferred [2], the majority being spouses. A small number of donors can be recruited among acquired relatives such as in-laws or friends.

The purpose of this work was to define the ethical issues in LD kidney transplantation, focusing on LURD, and to report the experience of 100 kidney transplants from spouses performed at the University of Rome "La Sapienza".

### Materials and methods

From January 1983 to October 1993, out of 654 kidney transplantations performed at our institution 364 kidney allografts were from living donors. Of these living donors, 245 were first-degree relatives of the recipient (LRD), while 119 were unrelated (LURD), among whom 100 cases were spouses – wife to husband in 76 cases and husband to wife in 24 cases. In all cases, motivation was altruism and no financial incentives were used in our donor-recipient pairs.

The potential donors were initially identified on the basis of ABO compatibility and negative cross-matching, not taking into account HLA A–B and DR donor-recipient matching and no donor-specific transfusion was requested. Regarding the spouses group (100 cases), in 92 pairs 0–1 HLA A–B match was found and 83 cases showed no HLA DR match. Ninety-six patients were undergoing dialysis before transplantation (Table 1).

The preliminary medical evaluation of potential donors included a careful clinical history, physical examination and routine laboratory tests (Table 2). When indicated, psychological or psychiatric consultation was obtained. Many previous contraindications to kidney donation, such as the presence of bilateral multiple renal arteries, have been progressively overcome by improvements in surgical technique.

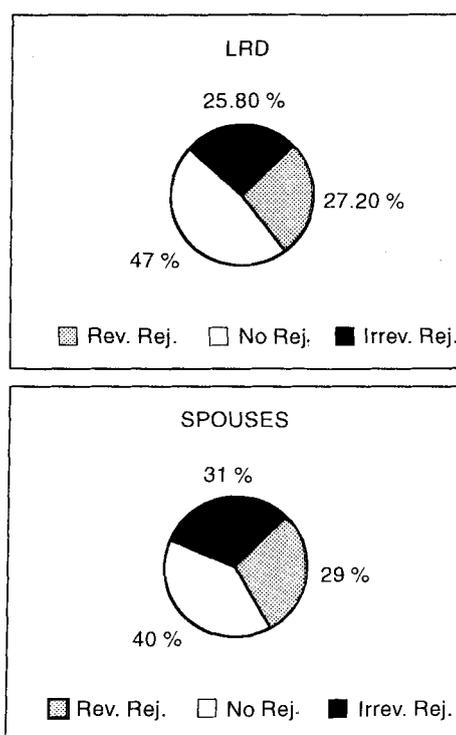
Immunosuppression consisted of a triple-drug regimen with azathioprine, prednisone and cyclosporin A. Acute rejection episodes were treated with a 3-day course of 1 g prednisolone i.v., and steroid-resistant rejection, with a 7-day course of OKT3 or a 14-day course of anti-lymphocyte globulin (ALG) therapy. Statistical analysis of the results was performed using the chi-square test.

**Table 1** Kidney transplantation between spouses; characteristics of recipients

|                            |                 |
|----------------------------|-----------------|
| Cases (n)                  | 100             |
| Age (mean)                 | 44.9 ± 10 years |
| Sex (male/female)          | 76/24           |
| HLA A-B 0–1 match          | 92              |
| HLA DR 0 match             | 83              |
| Dialysis before transplant | 96              |

**Table 2** Kidney transplantation from living donor; characteristics of donors

|                               | Related      | Unrelated    |
|-------------------------------|--------------|--------------|
| Cases (n)                     | 245          | 119          |
| Age (mean)                    | 39 ± 9 years | 46 ± 9 years |
| Sex (male/female)             | 85/160       | 35/84        |
| Mean creatinine value (mg/dl) | 0.8 ± 0.3    | 1 ± 0.3      |
| Blood pressure (mmHg)         |              |              |
| Systolic                      | 125 ± 10     | 130 ± 10     |
| Diastolic                     | 80 ± 9       | 85 ± 8       |
| Creatinine clearance (ml/min) | 104 ± 12.6   | 98 ± 11.3    |



**Fig. 1** Kidney transplant programme: incidence of rejection (*Rev* reversible, *rej* rejection, *irrev* irreversible, *LRD* living-related donors)

### Results

With the exception of the last three cases, all the transplants between spouses were followed up for at least 6 months after surgery. In all patients, it was their first graft and the graft started functioning during surgery without any need for postsurgery dialysis.

Acute rejection and nephrotoxicity were diagnosed by standard clinical criteria and confirmed by fine-needle aspiration biopsy and/or histology. We did not observe any increase in the number of acute rejection episodes compared to the LRD group (Fig. 1). Most rejection episodes developed during the early postoperative period and were usually reversed with corticosteroids alone. Steroid-resistant rejection was found in 15 cases, and 11 patients lost their kidneys due to chronic rejection.

Thirteen patients died 2 days–69 months posttransplantation (four due to myocardial infarction, six due to sepsis, one due to a spinocellular carcinoma and one due to an ictus cerebri). Three patients developed cancers 3–53 months after transplantation (two Kaposi's sarcoma at 3 and 12 months and one spinocellular carcinoma at 52 months). The incidence of viral infection was 9% (6 CMV, 3 HSV) and bacterial infections developed in 26

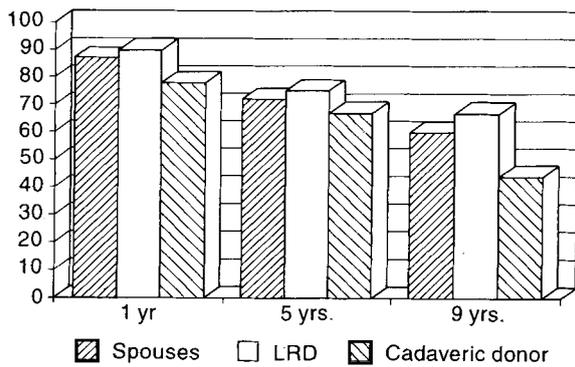


Fig. 2 Kidney transplantation in the cyclosporin era: actuarial organ survival

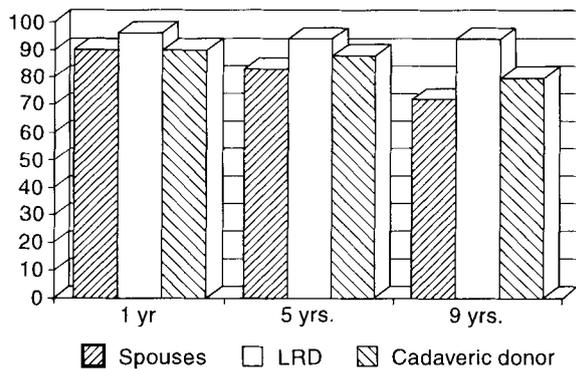


Fig. 3 Kidney transplantation in the cyclosporin era: actuarial patient survival

cases. Out of the 100 patients who underwent successful transplantation between spouses, 66 had well-functioning grafts and were followed-up for a maximum of 10 years.

The mean serum creatinine value was  $2.3 \pm 8$  mg/dl after a mean follow-up of 38 months (range 1–120 months). Actuarial patient and graft survival rates were 89.9% and 86.8% at 1 year, 82.9% and 72.3% at 5 years and 72.3% and 60.3% at 9 years, respectively (Figs. 2 and 3).

In our series, the results of LURD kidney transplantation between spouses were similar to those obtained in the LRD group, while they were significantly better than those from CD ( $P = 0.003$ ).

## Discussion

Our results reconfirmed most recent reports showing that LURD kidney transplantation in the cyclosporin era gives better results than CD transplantation, and similar

results to haploidentical LRD transplantation, whether donor-specific transfusions are used or not. Ethical and moral acceptability of this kind of renal transplantation is based on a number of considerations that are widely debated.

1. The risk for the donor has to be low, with a high expected benefit for the recipient [3]. Also if a restrictive interpretation of the Hippocratic oath should prohibit any intervention that has no therapeutic benefit for the individual patient, kidney donation is considered an exception to that principle based on the small risk for the donor. Five cases of donor death have been reported in more than 8000 kidney transplants from LD [4]; however, most of the large series have reported no deaths and a very low incidence of postoperative complications. As for long-term consequences, some studies have focused on the incidence of hypertension and kidney function impairment. A recent review [4] has reported the incidence of hypertension and kidney disease to be the same as in the general population. An analysis performed on 212 kidney donors followed up for more than 10 years [5] shows a mild, non-progressive increase in proteinuria that remains lower than 200 mg/day, a non-significant increase in blood pressure and an increase in creatinine of 10% preoperative values. Pregnancy did not impair kidney function and the five cases of renal disease reported were not correlated to the nephrectomy and were due to diseases not present at the time of nephrectomy (diabetes, morbid obesity).

Our experience was in agreement with these reports and allowed us to consider the risk for the donor fully balanced with the benefit for the recipient, and consequently acceptable.

The benefit for the recipient is expected to be higher when LRD and LURD are used, compared with CD kidney transplantation. This may be attributed to perfect functioning of donor kidneys, short preservation time and the possibility of starting immunosuppression before transplantation. In contrast, the results of commercialised kidney transplantations are very discouraging, providing a further argument against transplants from paid donors [6].

2. The donor must be extensively informed on the donation procedure, its risks, the benefits and the limits of transplantation. The capacity to express a legally valid consent is necessary, and, therefore, all of our donors are over 18 years of age. Furthermore, it is necessary that the transplant surgeon is satisfied that the donor fully understands all the medical information.

3. Consent has to be free and without any form of coercion. This is the most difficult aspect to be evaluated because some kinds of psychological conditioning can be difficult to recognise in a family setting, while some kinds of economic conditioning can be willingly concealed even by the donor.
4. The analysis of motivation is a further cause of concern and is still controversial. The concept of a gift can be the only motivation for donation, which means that the objective is to provide a benefit to the health of the recipient, not expecting any material reward. This may happen between genetically related persons, between emotionally related persons (spouses, acquired relatives) or in favour of somebody not known and when there is no relationship between donor and recipient. Pure altruism can be easily recognised only in this last, rare situation, while subtle kinds of coercion can exist when a genetic or emotional relationship is present. However, when free willingness can be detected in the donor evaluation, altruistic donation is widely considered acceptable in the genetic or emotional relationship. The concept of "rewarded gifting" has been proposed [7] to reimburse to the donor for the inconvenience and loss of income related to the donation, categorically excluding any role for middlemen. The evaluation of whether this kind of donation can be acceptable is difficult, and questions arise, such as how inconvenience can be quantified and what is the line dividing this kind of rewarding to commerce. The commercialisation of kidneys, where

the paramount consideration is not the health of the donor and recipient but money, payment is not only to the donor, who may receive only a little of what a desperate recipient is willing to pay, but to middlemen and brokers, who may be part of the medical team. The World Health Organization and guidelines from the Transplantation Society categorically exclude this kind of donation as totally unethical, but it is accepted and widely practised in some countries where CD transplantation is rare or not performed, and paying recipients come mainly from rich countries.

According to these considerations, kidney transplantation from living-related donors is ethically acceptable as is kidney transplantation from living unrelated "emotionally related" donor.

In conclusion, we showed that results of kidney transplantation from spouses were similar to those from living-related donors, with no significant increase in rejection or incidence of infectious complications, and significantly better than those from cadaver donors. No ethical issue can be advocated to exclude the use of such genetically non-related, emotionally related donors, and an extensive use of this kind of donor may provide a significant benefit for the recipients and, resulting in a decrease in organ demand, for all those who need kidney transplantation.

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## References

1. Berloco P, Pretagostini R, Poli L, Rossi M, Caricato M, Alfani D, Cortesini R (1993) Living unrelated kidney transplantation: a real source in the cyclosporin era. *Transplant Proc* 25: 3085-3086
2. Velideoglu E, Bilgin N, Haberal M (1993) Is it worth it to use kidneys between spouses? *Transplant Proc* 25:2185-2186
3. Schreiber HL (1991) Legal implications of the principle *primum nihil nocere* as it applies to live donors. In: Land W, Dossetor JB (eds.) *Organ replacement therapy: ethics, justice and commerce*. Springer, Berlin Heidelberg New York, pp 13-17
4. Bonomini V (1991) Medical risk and benefit in renal donors; the use of living donors is justified. In: Land W, Dossetor JB (eds) *Organ replacement therapy: ethics, justice and commerce*. Springer, Berlin Heidelberg New York, pp 25-31
5. Bay WH, Lee AH (1987) The living donor in kidney transplantation. *Ann Intern Med* 106:719-727
6. Sells RA (1991) Voluntarism in consent in both related and unrelated living organ donors. In: Land W, Dossetor JB (eds.) *Organ replacement therapy: ethics, justice and commerce*. Springer, Berlin Heidelberg New York, pp 18-24
7. Daar AS, Salahudeen AK, Pingle A (1990) Ethics and commerce in live donor transplantation: classification of issues. *Transplant Proc* 22:922-924