

*Original Article*

## Outcome in emotionally related living kidney donor transplantation

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### Abstract

**Background.** The growing shortage of cadaver kidneys, the limited possibilities to expand the living related donor pool and the good results obtained in our centre with poorly matched cadaver kidneys, led us in 1991 to begin accepting highly motivated, unrelated, living kidney donors who had a strong emotional bond with the recipients.

**Methods.** Between 1 January 1991 and 1 January 1996, 46 potential living kidney donors and their emotionally related recipients were evaluated. Twenty-three cases were accepted for renal transplantation after thorough somatic and psychological evaluation. The mean post-transplant follow-up until 1 April 1996 was of  $28 \pm 3$  months. Compatible blood groups and a negative cross-match were mandatory, but no minimal HLA matching was required.

**Results.** There was a 50% drop-out rate following the initial screening. The main reasons for not performing transplantation were immunological contraindications in 39% of the cases, somatic in 30.5%, psychological in 26% and socioeconomic in 4.5%. In the accepted group of recipients, 48% (11/23) received transplants without chronic dialysis. Donor survival was 91%; two deaths unrelated to nephrectomy occurred 1 year after donation. The 2-year actuarial recipient and graft survivals were 100% and 91% respectively, compared to 99% (recipients) and 93% (grafts) in the non-HLA-identical living related kidney transplant group, and to 93% (recipients) and 83% (grafts) in the cadaver kidney transplant group. Recipient rehabilitation was completed after  $4 \pm 1$  months. Emotionally related donors returned to work  $5 \pm 2$  weeks after nephrectomy, and no donor regretted his decision, even in the case of failure.

**Conclusions.** Kidney transplantation from emotionally related living donors represents a valuable option, allowing more patients with end-stage renal disease to avoid chronic dialysis. Recipient and graft outcomes were superior to cadaver kidney transplantation. Motivated and emotionally related donors should be

allowed to donate one of their kidneys provided that they are carefully selected and thoroughly informed.

**Key words:** kidney transplantation; unrelated living donor; emotionally related donor

### Introduction

Ten years ago, Evans *et al.* [1] stated that kidney transplantation is the renal replacement therapy affording the highest quality of life. Organ shortage and steadily growing waiting time for a cadaver kidney transplant have forced the medical community to look for alternatives, such as living kidney donation. For genetically related donors this is considered ethically and medically acceptable in many transplantation centres [2–4]. However, many patients with end-stage renal disease (ESRD) do not have a willing or suitable genetically related donor. Instead, some of them have the opportunity to receive a kidney from an unrelated donor who has clear emotional bonds with the patient and a strong motivation. Should the transplantation team consider and accept such a donation, potentially placing a healthy individual at risk for the benefit of another individual, or should such donations be disregarded? Most centres deny this option due to ethical and psychological reasons. In 1991 the question arose in our centre. A 44-years-old healthy wife asked what were the reasons forbidding her to donate a kidney to her husband in ESRD, whom she loved, wanted to help and had shared her daily life with for 20 years. This led us to reconsider the question of genetically unrelated living kidney donation. After thorough immunological, somatic, and psychological assessments, our transplantation team considered this donation as a real option, and the first emotionally related living donor kidney transplantation in Switzerland was thus performed on May 16th 1991.

World-wide, kidney transplantation from unrelated living donors is not new [5–7]. Before dialysis became currently available, kidney transplantation involved only living donors, genetically related or not [8]. Later on, ethical considerations [9,10] and the era of HLA-matching favoured the use of well-matched cadaver

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kidney transplantation. In our centre the recipient of a cadaver kidney transplant is chosen on a 'first come, first served' basis within the same blood group as the donor, regardless of HLA histocompatibility, but providing the cross-match is negative. Traditionally in our centre, HLA matching is not a limiting criteria for recipients with a normal immunological risk (i.e. less than 50% anti-HLA antibodies and not known as rejecters of previous grafts). Thus the introduction of a genetically unrelated living donor programme using kidneys from poorly matched or fully mismatched donors did not differ from our HLA allocation criteria for cadaver kidneys. Therefore, our team felt that there was no medical justification against genetically unrelated transplantation.

Since the first case in 1991, the number of potential emotionally related kidney donors has been growing steadily. Forty-six such donor-recipient pairs have been considered, of which 23 transplantations were performed. In this report we present the results of the transplantation screening procedures and follow-up for both groups, those for which transplantation was performed and those for which it was not. Based on our data, we try to ascertain under which circumstances kidney transplantation from an emotionally related living donor is justified or not.

## Subjects and methods

Potential donors and recipients referred to our transplantation centre between 1 January 1991 and 1 January 1996 for an emotionally related living donor kidney transplantation were analysed. We defined an emotionally related donor as a donor without genetic relationship (or very distant) but with a long-standing loving relationship and/or a strong emotional bond with the recipient. As for any related living donor, the unrelated donor had to be free of coercion or pressure from the recipient or the family, and the kidney donation had to be without financial counterpart.

The same somatic and psychological criteria for related living donors were applied to unrelated donors. The recipients were also evaluated according to the same criteria as recipients of a living related donor kidney and as recipients on the waiting list for a cadaver kidney.

The records of the cohort of donor-recipient pairs not accepted for transplantation were retrospectively examined for the causes of exclusion and the outcome of the recipient. The characteristics of the transplantation group and the graft outcome until 1 April 1996 (mean follow-up  $28 \pm 3$  months, range 4 to 59 months) were analysed. The outcome was compared with non-hyperimmunized first-graft recipients from non-HLA-identical related living donors ( $n=68$ ) and from recipients of a cadaver kidney ( $n=170$ ) also transplanted between 1 January 1991 and 1 January 1996 with an identical immunosuppression protocol. Recipients of related living donor kidneys and cadaver kidneys were followed over the same period as recipients of unrelated living donor kidney transplants (until 1 April 1996). Hyperimmunization was defined as more than 80% anti-HLA antibodies in the last serum before transplantation.

Quadruple immunosuppressive therapy was employed (cyclosporin A (CsA), steroids, azathioprine (Aza), ATG-F<sup>®</sup> or ATGAM<sup>®</sup>). Maintenance therapy consisted of CsA

alone whenever possible. If required, first azathioprine and then prednisone were added. In case of resistant or relapsing severe rejection, CsA was switched to FK 506 (tacrolimus).

From June 1994 on, three donor-specific transfusions (DST) were administered prior to transplantation in cases of husband-to-wife kidney donation, when the wife had been previously pregnant and the donating husband was the children's father. The same procedure was used in cases of dubious B-cell and negative T-cell cross-matches. The protocol was adapted from the transfusion protocol used by Salvatierra *et al.* [11] and consisted of transfusion of 200 ml fresh blood with a cross-match control 14 days later. Three transfusions were given if the crossmatch reaction remained negative. Azathioprine was administered (2 mg/kg/day, maximal dose 150 mg/day, adapted to the leukocyte count) throughout the whole procedure and until transplantation.

All donor and recipient pairs were first evaluated by their referring nephrologist, then interviewed by a nephrologist in our centre and separately by a psychologist. Immediately before donation, 1 week after nephrectomy and again 1 year later, donors underwent a standardized renal haemodynamic evaluation with inulin and para-aminohippurate (PAH) clearances.

In February 1995 an anonymous questionnaire was sent to 15 of the donors after nephrectomy; 11 were returned and analysed (2 were lost, 2 were not returned). The questions investigated the motives leading to donation, the changes donation had brought in daily life and recovery after the nephrectomy. Additional psychosocial information was collected in a non-standardized way, from written data in the files and from interviews with the donors at various times before and after donation.

## Statistics

Results are expressed as mean values  $\pm$  standard error of the mean. The Student *t* test was used to compare donor and recipient characteristics before and after transplantation, and log-rank-test to compare graft and recipient survivals in the three groups (living unrelated donor kidney, living related donor kidney, and cadaver kidney). The value of  $P < 0.05$  was considered significant.

## Results

### *Characteristics of the group not accepted for transplantation*

Tables 1 and 2 summarize the characteristics and the causes of exclusion of donors and recipients considered not suitable for donation and/or transplantation. When

**Table 1.** Characteristics of donors and recipients in the group not accepted for transplantation

Pairs not accepted for transplantation	Donors ( $n=23$ )	Recipients ( $n=23$ )
Age (years)	$53 \pm 2$	$56 \pm 2$
Female: male	16:7	6:17
Relationship	21 spouses 1 heterosexual partner 1 friend	

**Table 2.** Main reason leading to non-acceptance of an unrelated living kidney donor transplantation

Immunological reason	Somatic reason	Viral problem	Motivation problem	Insurance problem
9/23 (39.1%) Blood group incompatibility ( <i>n</i> =2) Positive cross-match ( <i>n</i> =6*) Repeated HLA-Ag mismatch with previous graft ( <i>n</i> =1)	7/23 (30.4%) Donor with medical contraindication ( <i>n</i> =5) Recipient with medical contraindication ( <i>n</i> =2)	0	6/23 (26.1%) Ambivalence of the donor ( <i>n</i> =3) Refusal of the recipient ( <i>n</i> =2) Donor's motivation not convincing for the medical team ( <i>n</i> =1)	1/23 (4.4%) Recipient's insurance not valid in Switzerland ( <i>n</i> =1)

\*2/6 also showed a repeated mismatch with a previous graft.

only considering the main reason for exclusion of these 23 pairs, immunological criteria were the most frequent cause (39.1%), followed by somatic contraindications of the donor to nephrectomy (hypertension, diabetes, obesity, lymphoma) or of the recipient to transplantation (high cardiovascular or pulmonary operative risk) (30.4%). In 20% (4/20) of the rejected spouses, the cross-match was positive in the absence of previous transplantation, the distribution between husband recipients and wife recipients was equal. Motivation was a problem in 26.1% of the cases, and in 4.4%, transplantation could not be performed because the costs in Switzerland were not covered by the patient's insurance. Virology profiles were not a contraindication for anyone in this group (see Table 3 for the viral exclusion criteria). In 39% of the cases (9/23), additional reasons beside the main cause of exclusion were involved in the final decision. The particularly low incidence of blood group incompatibility does reflect a major selection bias, as the incompatible pairs were in most cases primarily excluded by the referring nephrologist.

#### Outcome of the group not accepted for transplantation

At the end of the follow-up period the outcome of 20/23 potential recipients was available. The three recipients whose somatic condition excluded an emotionally related donor kidney transplantation were consequently also excluded from the waiting list for a cadaver kidney and are currently still on dialysis. Thus 17 recipients remained potential candidates for transplantation; for 88% (15/17) of these, there was no alternative living donor, and they were placed on the waiting list for a cadaver kidney. Three of them received transplants and one died on dialysis before surgery was possible. In 12% (2/17) of the cases,

transplantation with a kidney from another potential living donor (one related, one unrelated) could be performed.

#### Characteristics of the group accepted for transplantation

The characteristics of donors and recipients who underwent transplant surgery are listed in Table 4. The mean age of the recipients was  $50 \pm 2.5$  years at the time of transplantation, which is significantly younger than the non-transplanted group ( $56 \pm 2$  years). In 65% of the cases, the wife or partner donated to her husband, while in only 26% the husband donated to his wife. On average, donor and recipient knew each other or lived together for 20 years (10–40 years). Love was by far the prevalent motive for donation (82%), often combined with partnership (68%). In 55% of the cases the referring nephrologist had first raised the possibility of living donation, 30% of the donors came spontaneously to this idea, 15% knew about the possibility of living donation through the media, and no donor was primarily asked by the potential recipient.

Thirty percent (7/23) of the recipients received a transplant as primary replacement therapy for ESRD; their mean serum creatinine on the day before transplantation was  $725 \pm 45$   $\mu\text{mol/l}$ . Four additional patients required dialysis through a central venous catheter during 1 month, before transplantation could take place. Thus, through transplantation, 48% of the recipients avoided chronic dialysis including avoidance of an arteriovenous shunt or a peritoneal dialysis catheter. Overall, the mean interval between starting dialysis and transplantation was  $7 \pm 2$  months for

**Table 3.** Viral profiles excluding transplantation

Donor		Recipient
HBs-Ag positive	And	HBs-Ab negative
HCV-Ab positive	And	HCV-Ab negative
EBV-Ab positive	And	EBV-Ab negative
HIV-Ab positive	Or	HIV-Ab positive

**Table 4.** Characteristics of donors and recipients in the group accepted for transplantation

Pairs accepted for transplantation	Donors ( <i>n</i> =23)	Recipients ( <i>n</i> =23)
Age (years)	$50 \pm 2$	$50 \pm 2.5$
Female: male	16:7	7:16
Relationship	19 spouses 2 heterosexual partners 1 father-in-law 1 distant cousin	

**Table 5.** Characteristics of the recipients of living unrelated donor kidney (LURD), of living related donor kidney (LRD), and of cadaver kidney (CAD)

	LURD (n=23)	LRD (n=68)	CAD (n=170)
Age at transplantation (years)	50±2.5	35.5±2	51±1
Pre-emptive transplantation	48%* (11/23)	26% (18/68)	6% (10/170)
Mean time between dialysis and transplantation (months)	7±2*	12±2	21±1

\* $P < 0.001$  with LRD and CAD.

recipients of an unrelated living donor kidney, significantly shorter than for the groups receiving related living donor kidneys ( $12 \pm 2$  months) and cadaver kidneys ( $21 \pm 1$  months) ( $P < 0.001$ ) (see Table 5). All recipients had less than 50% anti-HLA antibodies in their last serum before transplantation. On average,  $4.3 \pm 1$  HLA-A, -B and -DR mismatches were present, ranging from 3 to 6. This was comparable with the mean HLA-mismatches for cadaver kidney recipients in our centre ( $4.3 \pm 1.1$ ).

#### Recipient outcome after transplantation

Overall recipient survival was 100%, compared to 99% for the recipients of a non-HLA-identical living related kidney, and to 93% for recipients of a cadaver kidney over the same follow-up period (Figure 1). None of these differences reached statistical significance.

At the time of transplantation, seven patients worked full-time, two worked at 75%, seven worked at 50%, and two had a working capacity of 0% (since 1 and 3 months respectively), one additional recipient could not find a job. Within on average  $4 \pm 1$  month (range 1–8 months) after transplantation 14 recipients worked full-time and five worked at 50%. The two recipients

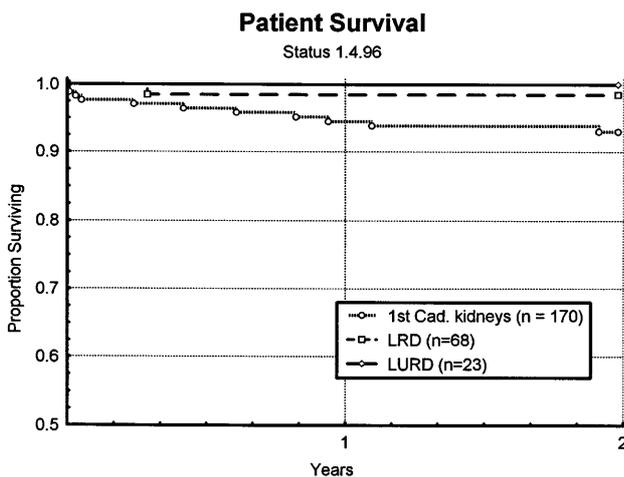
with graft failure did not change their working hours before and after unsuccessful transplantation (both worked half-time). Finally, two recipients were retired and two received a disability pension not directly related to the nephropathy and, therefore, not reversible even with a successful transplantation.

#### Graft outcome

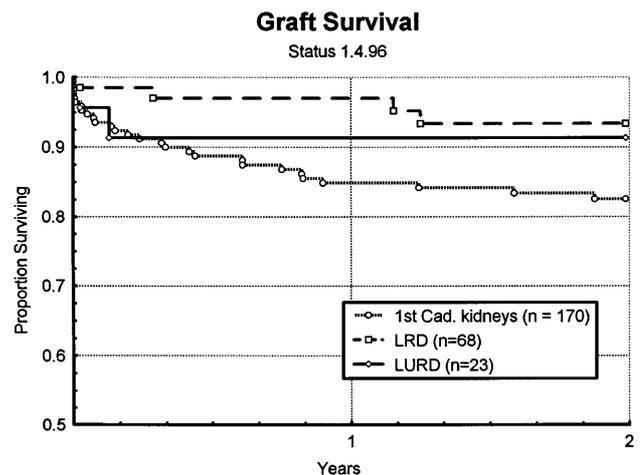
The 2-year actuarial graft survival reaches 91% for kidneys of unrelated living donor. This was statistically comparable to the results obtained with grafts from non-HLA-identical related living donors (93%). Cadaver kidney grafts showed a lower survival of 85% (Figure 2); however, the difference did not reach significance, probably because of the relatively small number of transplantation from unrelated living donors.

Two secondary graft failures occurred during the follow-up period. In one, a severe therapy-resistant accelerated vascular rejection appeared in the first week after a husband-to-wife kidney donation. This led to transplant nephrectomy in the third week after transplantation. Thereafter the recipient developed anti-HLA antibodies against her husband's mismatched antigens. Before transplantation no anti-HLA antibodies were detectable and the cross-match was clearly negative. As she had earlier borne two children by her husband, this accelerated rejection prompted us to introduce routine donor-specific transfusions for similar husband-to-wife transplantations in order to pick up silent immunizations secondary to pregnancies. The second failure occurred after a wife-to-husband kidney donation; the transplant was lost because of severe non-reversible vascular rejection 10 weeks after transplantation.

Three recipients were enrolled in the donor-specific-transfusions (DST) protocol before transplantation. In two cases involving a husband-to-wife kidney donation, the transfusions did not elicit detectable anti-



**Fig. 1.** Two-year actuarial recipient survival after living unrelated donor (LURD) kidney transplantation, after living related donor (LRD) kidney transplantation, and after first cadaver kidney (CAD) transplantation.



**Fig. 2.** Two-year actuarial graft survival for living unrelated donor (LURD) kidney grafts, for living related donor (LRD) kidney grafts, and for first cadaver kidney (CAD) grafts.

HLA antibodies and the post-transplantation follow-up was totally free of rejection. One case involved a slightly positive B-cell cross-match, while the T-cell cross-match was negative. After three DSTs there was no increase in positivity of the B-cell cross-match and the T-cell cross-match remained absolutely negative. Three weeks after transplantation interstitial and vascular rejection were diagnosed, but could be successfully treated with ATG<sup>®</sup>. Under a combination of tacrolimus + Aza + prednisone, the serum creatinine remains stable around 150  $\mu\text{mol/l}$ .

The rejection episodes for the 14 functioning grafts transplanted for at least 1 year were analysed. Clinical rejections as defined by Bock *et al.* [12] occurred in 7/14 patients (50%) and biopsy-proven rejection in 3/14 patients (21%) (one interstitial, one combined interstitial and vascular, one vascular). These results are comparable to our overall graft outcome as previously published [12] of 58% clinical rejections and 36% biopsy-proven rejections. Hummel and Thiel [13] looked at the number of methylprednisolone-pulses given during the first year after transplantation in all transplant recipients in our centre. Recipients of kidneys with 6 HLA mismatches received on average  $7.7 \pm 5.6$  pulses (mean  $\pm$  SD) which was not different from the recipients of kidneys with  $>3$  HLA-matches:  $7.2 \pm 7.4$ . For the recipients of unrelated living donor kidneys studied here,  $3.5 \pm 0.95$  (mean  $\pm$  SEM) pulses were administered per patient during the first year after transplantation. Proteinuria can be used as a marker for chronic rejection. In recipients of fully mismatched kidneys [13] proteinuria reached  $0.35 \pm 0.37$  g/day 1 year after transplantation. Surprisingly, proteinuria was higher in recipients of kidneys with  $>3$  matches:  $0.79 \pm 2.1$  g/day. For the recipients of unrelated living kidney donors proteinuria was on average  $0.29 \pm 0.09$  g/day.

For the 21 functioning kidneys, 38% (8/21) of the recipients reached the aim of CsA monotherapy at the end of the follow-up period (on average  $28 \pm 3$  months after transplantation). Twenty-four per cent (5/21) could be maintained on a two-drug regimen (CsA + Aza or Aza + prednisone). Because of vascular or recurrent interstitial rejection, 38% (8/21) required further triple combination with either CsA + Aza + prednisone or tacrolimus + Aza + prednisone. The mean serum creatinine at the end of the follow-up period was  $131 \pm 8$   $\mu\text{mol/l}$  (range 61–230  $\mu\text{mol/l}$ ).

#### *Donor outcome after kidney donation*

Hospitalization for nephrectomy lasted on average  $13 \pm 2$  days (range: 9–17 days). No donor required a regular intake of painkillers at the time of discharge.

Immediate donor survival was 100%, but dropped to 91% at 1 year due to two deaths. The first death occurred 1 year after donation in the context of a primary malignant cerebral tumour. The second death occurred by suicide 2 years after donation. A documented bipolar depression had been treated for many years. At the time of donation, however, the donor

was stable, neither manic nor depressive. Six months before committing suicide he stated that the kidney donation was the most valuable deed in his life.

At the end of the follow-up period, 15/23 donors were more than 1 year post-surgery and could have their kidney function evaluated. Donor parameters before nephrectomy (Nx), 1 week after and 1 year after nephrectomy are detailed in Table 6. There is no evidence of progressive deterioration of the kidney function over the 12 months following the post-Nx clearance evaluation. None of the differences between the 1 week post-Nx and 1 year post-Nx values were statistically significant. Blood pressure and microalbuminuria remained unchanged after 1 year. Serum creatinine increased by 40% and inulin clearance decreased by 28%. Surprisingly, a mean increase in body weight of 6 kg was observed during the first year after nephrectomy.

After transplantation, the global quality of the relationship between donor and recipient remained unchanged or improved and it did not worsen even in the cases of graft loss. In cases of a functioning graft and mostly in spousal donation, donors profited from greater availability and a better overall shape of the recipient. Donors returned to work after  $5 \pm 2$  weeks; however, their full ability to cope with all aspects of daily life only returned after  $9 \pm 2$  weeks. Even though some donors still felt easily tired up to 1 year after nephrectomy, they admitted they would donate again. This information was collected from the questionnaires and obtained through informal talks when the donor accompanied the recipient in the ambulatory controls and could be seen on his/her own. In particular, the two donors whose kidneys were rejected were interviewed in the absence of the recipients.

## **Discussion**

The results of our 5 years experience with kidney transplantation from living unrelated donors (LURD) illustrates the advantages and the limitations of this programme. A high motivation of the donors was required and commercialism, as well as coercion, were definitely excluded. The deliberate restriction to emotionally related donors and the role of the psychologist as independent donor advocate were in accordance with the guidelines of the Council of the Transplantation Society [14] and represent in our view the essential ethical basis for unrelated living kidney donation. The following discussion thus applies only to the issue of emotionally related donor and recipient, and the term LURD refers exclusively to emotionally related donors.

If transplantation is the therapeutic goal for ESRD, then the first advantage of emotionally related donation is to expand the pool of potential donors. This means a better chance for pre-emptive transplantation, or a shorter delay between starting dialysis and transplantation than for those without a living donor. Pre-emptive transplantation avoids the necessity to create

**Table 6.** Donors characteristics before nephrectomy (pre-Nx), 2 weeks after nephrectomy (2 weeks post-Nx) and 1 year after nephrectomy (1 year post-Nx)

	Body-weight (kg)	Systolic/diastolic BP (mmHg)	Serum-creatinine ( $\mu\text{mol/l}$ )	Inulin clearance (ml/min/1.73 m <sup>2</sup> )	PAH clearance (ml/min/1.73 m <sup>2</sup> )	Urine albumin (mg/day)
Pre-Nx	72 $\pm$ 3	119 $\pm$ 4/ 76 $\pm$ 2	68 $\pm$ 4	93 $\pm$ 5	506 $\pm$ 36	9 $\pm$ 1
1 week post-Nx		126 $\pm$ 2/ 79 $\pm$ 2	102 $\pm$ 5	63 $\pm$ 3	356 $\pm$ 19	
1 year post-Nx	78 $\pm$ 4	121 $\pm$ 4/ 75 $\pm$ 3	98 $\pm$ 5	64 $\pm$ 3	316 $\pm$ 26	7 $\pm$ 1

No statistical significance for all values between 1 week post-Nx and 1 year post-Nx.

an access for dialysis. More importantly, it also avoids the psychological and socioeconomical consequences of chronic dialysis, namely reduced professional capacity, limited active life, and eventually disability. Nearly half of our recipients transplanted with a kidney from an emotionally related donor avoided chronic dialysis. This was in significant contrast with the marginal number of pre-emptive transplantation in recipients of cadaver kidneys (6%) ( $P < 0.001$ ) because of the difficulty of finding a suitable organ when dialysis is required. Surprisingly, we also found a significant difference with kidney recipients from related living donors (LRD) where only 26% ( $P < 0.001$ ) could directly have transplant surgery. Explanation for this phenomenon is probably multifactorial: selection bias in recruitment or referral, higher motivation and quicker decision of spouses, more accurate evaluation and anticipation of the practical issues implied by ESRD from the life-partner, easier co-ordination in spousal kidney donation because only one couple is involved, while in case of LRD, donors and recipients do not live together and have their own life-partners who may not always fully sympathize with donation.

The interval between starting chronic dialysis and transplantation was significantly shorter for recipients of LURD and represented one-third of the waiting time for a cadaver kidney (CAD) in our centre ( $P < 0.01$ ), which certainly contributed to the high success in rehabilitation. Thus the opportunity to receive a transplant early or without dialysis was higher when a motivated unrelated living donor was present. The analysis of the recipient outcome in the group not accepted for transplantation, further shows the contribution of this expanded donor group. Namely, for 75% of these recipients, the emotionally related donor represented the only possible living donor with no other alternative than to wait for a cadaver kidney. In the meantime most (75%) are still waiting, and one patient has died.

The second advantage and a strong medical justification for transplantation from LURD, are the graft and recipient outcomes. The 2-year actuarial graft and recipient survivals in our centre was higher with LURD kidneys than after CAD transplantation (91% versus 83%) and was close to the results obtained with LRD grafts (93%). The difference in the number of CAD

graft recipients ( $n = 170$ ) and of LURD grafts recipients ( $n = 23$ ) most probably accounts for the lack of statistical significance for this parameter between the two groups. No immunological bias could explain the outcome as the same immunosuppressive protocol and immunological guidelines were applied, i.e. blood group compatibility, negative cross-match, and no HLA compatibility mandatory. The recipients of LURD had a number of HLA mismatches comparable to the recipients from CAD in our centre. Explanations must be related to the circumstances of retrieval: healthy donor, planned operation for donor and recipient, optimal kidney perfusion until nephrectomy, short cold-ischaemia time and therefore minimal reperfusion damage, and no delayed graft function. Furthermore, in our centre, nephrectomy and implantation in living donor kidney transplantation are always performed by the same two surgeons.

The same pattern of higher survival with LURD than after CAD kidney transplantation is consistently found in the literature [15–17]. Long-term graft survival of our LURD group cannot be evaluated so far. However, Pretagostini *et al.* [18] report a 5-year graft survival of 72.3% with LURD compared to 66.8% with CAD. In Sollinger's group [19], the 4-year graft survival was 85% with LURD and 76% with CAD. Data from the United Network for Organ Sharing Renal Transplant Registry (UNOS) show a 3-year graft survival of 85% for kidneys from spouses, (81% for kidneys from non-married unrelated donors) comparable to a graft from a parental donor (82%) against 70% for cadaver kidneys [20].

Recipient survival of LURD grafts did not differ from survival with LRD in our centre (100 versus 99%) but was higher than after CAD kidney transplantation (93%). Again, the small number of LURD transplantations in our series accounts for the lack of statistical significance. The reasons for better recipient survival are certainly multifactorial: shorter duration of ESRD, shorter delay between screening and operation, thus diminishing the risk of unrecognized comorbidities at the time of transplantation. A selection bias of the potential recipients cannot be incriminated, as those rejected for somatic reasons were also excluded from the waiting list for cadaver kidneys, and the mean age of CAD and LURD kidney recipients was comparable.

Spouses represent 90% of the emotionally related donors in our centre and in addition to graft survival, quality of life and functional improvement represent major end-points for the couple. Therefore, it seems particularly important that the preoperative screening ensures a low mortality risk, obviously for the donor but also for the recipient.

A special issue in kidney transplantation from husband to wife is the potential deleterious role of previous pregnancies on graft outcome. There is evidence that maternal alloimmunization against the paternal HLA antigens occurs during pregnancy [21,22]. The UNOS data [20] demonstrated a difference in graft outcome at 3 years between wife-to-husband grafts (or grafts from husband to wife without pregnancy) (87%), and grafts from husband to wife with previous pregnancy (76%). In our experience, the graft outcome was not influenced by the direction of the interspousal kidney donation as from the two graft losses, one involved a husband-to-wife kidney in a couple with three children, and the other occurred after a wife-to-husband kidney donation. However, after the first graft loss involving the husband-to-wife donation and due to an early and severe vascular rejection, a humoral rejection process with undetected presensitization before transplantation was strongly suspected. In the spouses who had a cross-match, only 10% were spontaneously positive in the absence of previous transplantation (20% in 20 couples not accepted for transplantation and 0% in 21 couples accepted). Therefore, to unmask preformed anti-HLA sensitization despite the absence of detectable antibodies, DST with blood containing leukocytes were administered in situations of husband-to-wife kidney donation with previous pregnancies or in case of weakly positive B-cell cross-match. To avoid hypersensitization the transfusions were performed with azathioprine [23,24]. Three patients received DST, none developed anti-HLA antibodies, but conclusions from this small number would be premature. For the same reason, it is not possible to evaluate the potential impact of transfusions on graft survival. To improve graft outcome through transfusions was not the aim of our protocol; however, the data published by Terasaki *et al.* [20] showed a significantly higher graft survival in transfused recipients (90% at 3 years *versus* 81% without transfusion). This could be a reason to extend the use of DST to all LURD before transplantation.

The biggest controversy and what is often considered as a major limiting issue for organ transplantation from living donors, is indeed that the donor undergoes an intervention which carries a mortality and morbidity risk not balanced by direct benefit for his or her own health. From the literature, the death risk associated with a donor nephrectomy is estimated to be 0.06–0.03% [25,26]. Thorough donor screening and a honest explanation of the donor's risks are the basis for a real informed consent. To achieve the lowest possible mortality and morbidity, an experienced surgical team is required. Also, donor operative procedure should be restricted to nephrectomy without concomitant

elective surgery such as appendectomy, cholecystectomy, fundoplication, etc., as reported in one series [27]. Long-term prognostic data can be assimilated from what is already known from related living donors. A slightly higher prevalence (10%) of hypertension and proteinuria has been described [28,29]; however, when compared to their siblings, the incidence of hypertension in donors was no longer statistically different [26,30] over 10 to more than 20 years follow-up. After donor nephrectomy, pregnancy outcome does not seem to carry an increased risk of complication for mother and child [31]. The survival curve of individuals after unilateral nephrectomy has been found to be similar to the normal population [18], and moreover, the premium of most life insurance policies in the USA do not increase in case of kidney donation [3,32]. These data suggest that unilateral donor nephrectomy in a healthy individual can be regarded as a relatively safe procedure.

The literature emphasizes concerns regarding underlying motives for donation which would be based on psychological disturbances [19,33,34]. An important goal of psychological screening prior to transplantation is to detect such psychopathology although it is seldom the case. In our experience only one case of 46 revealed an unconvincing motivation. As in other centres [15], we found love and partnership to be the main motivations as well as the hope to have two healthy partners in the couple instead of one 'healthy' and one 'sick'. Donors are not unconcerned bystanders when their partner has terminal renal failure and when they share a common daily life. Uraemia, the restraints imposed by diet and dialysis, and the reduced professional possibilities all indirectly influence the well-being of the healthy partner. From this point of view, a successful transplantation can reverse a reduced quality of life for both donor and recipient. The emotionally related donors in our centre have reported an overall improvement in the quality of life for the whole family after successful transplantation. Furthermore, as for LRD, emotionally related donors' self-esteem can be increased as they are the contributors of this improvement [33,35]. In cases of non-functioning grafts, the donors were disappointed but remained confident in themselves and did not regret their decision to donate. As in our experience, positive feelings after donation have also been reported in cases of graft loss [36]. In spite of this, the possibility of failure is an important issue to be discussed with the donor before transplantation. Particularly, the psychologist has to evaluate how the donor and the donor–recipient relationship could be affected by a graft loss.

The psychological and somatic evaluation should be continued after donation. The postoperative pain experienced by donors despite analgesic care, the potential somatic complications after nephrectomy, the rehabilitation of donor and recipient, and the new psychological equilibrium in the couple require a follow-up. The purpose is to validate the ethical basis for kidney transplantation from emotionally related living donors, and to gather objective data for better

information for future donors. To our knowledge, there is currently no data based on prospective studies regarding this issues. Therefore the Swiss Registry for Living Organ Donors was started in our institution in 1993. It provides for a standard medical follow-up over the years after nephrectomy for all living donors in Switzerland. Furthermore, a study supported by the Swiss National Research Foundation investigates the psychological and social outcome of the donor-recipient pairs after living kidney donation in our centre, comparing genetically related to emotionally related kidney donation.

In conclusion, we regard our 5-year experience with transplantation from genetically unrelated, but emotionally related living kidney donors as positive. It has given the chance for prompt transplantation to patients with ESRD who experienced a successful social rehabilitation and a higher graft survival than if they had waited for a cadaver kidney transplant. The donors, mostly spouses, showed high motivation. Their donation was based on love and altruism, but indirectly they themselves gained benefits through the improvement of the recipient's condition. However, for such a programme to remain ethically justified, criteria have to be respected: exclusion of donation with a commercial or coercive background, transplantation in an experienced transplantation centre, careful somatic and psychological screening of donor and recipient before acceptance, intervention of an independent donor advocate, and follow-up of the donors after nephrectomy. When these criteria are fulfilled, patients with ESRD who are candidates for transplantation should certainly not be discouraged from the possibility of kidney transplantation from an emotionally related living donor, but should rather be encouraged. Data from the Swiss Registry of Living Donors and from the psychosocial study undertaken in our centre will hopefully provide prospective information about the long-term status.

### Addendum

At the time of submission of this article, donor-specific transfusions (DST) have been administered prior to transplantation in six additional cases of husband-to-wife kidney donation. The cross-match after each transfusion remained negative in four cases. In two couples, the potential recipient developed a strong positive T- and B-cell cross-match after the first transfusion despite the administration of azathioprine. Transplantation was consequently not performed in this case.

Since the beginning of the protocol a total of eight wives have received DST from their husbands. In two spouses, it triggered a positive cross-match and thus probably unmasked a presensitization which would otherwise have only become manifest after transplantation.

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