

The first 100 kidney transplants from living related donors at Groote Schuur Hospital

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Abstract Improved results with cadaver kidney transplantation and the increase in the number of cadaver organs have caused the continued use of donor kidneys from living relatives to be questioned. In this analysis of our first 100 renal transplants involving a living related donor, the 5-year graft survival rate was 70%. The 5-year graft survival rate for recipients of grafts from HLA-identical donors was 81%, as opposed to the 64% survival rate for grafts from one-haplotype donors. Recipients of grafts from one-haplotype-matched donors who received donor-specific blood transfusions demonstrated better graft survival than those who were not transfused. This analysis demonstrates that the results of living related kidney transplantation are good, and suggests that donor-specific blood transfusions may be beneficial.

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The shortage of cadaver donor kidneys and the superior patient and graft survival rates in cases where the donor was a living relative were in the past the major reasons for using organs from living related donors for kidney transplantation in patients with end-stage renal failure.¹⁻³ Since the introduction of the immunosuppressive agent cyclosporin, the results of kidney transplantation with grafts from cadaver donors have improved significantly and the difference in graft survival rate compared with transplants from living related donors is not as great.^{4,5} Furthermore, with the increased acceptance of the concept of clinical brain death and the increased public awareness of organ donation, the shortage of cadaver organs is not as critical as it was before. Added to these considerations is the risk, although minor, to the well-being of a perfectly healthy donor.^{6,9} In the light of the above, the continued use of organs from living related donors for transplantation has been questioned. In this study we reviewed the results of kidney transplantation from living related donors at our institution.

Methods

Recipient selection criteria

Standard criteria were used for the selection of patients with end-stage renal failure for dialysis and transplantation; these took into account the aetiology of the renal disease, the results of an extensive clinical evaluation to

determine the general health of the patient and the presence of any complications of renal failure. A detailed social history was included in the patient evaluation to assess the feasibility of a transplant from a living related donor.

Selection of the donor

All potential living related donors were first screened in respect of ABO compatibility, a leucocyte crossmatch, and emotional stability and motivation. Potential donors remaining after the initial screening process were investigated to confirm excellent general health and bilateral renal function. Tests were directed towards detection of unsuspected extrarenal pathology. The quality of renal function and the possibility of any anatomical abnormalities in the kidneys were also investigated. The final selection of the donor, if several medically suitable relatives were available, was made on the basis of histocompatibility testing; an HLA-identical sibling was the ideal choice. Angiographic evaluation of the selected donor was undertaken to determine the exact status of the renal arteries and to rule out the possibility of any unsuspected intrarenal lesions. When either kidney was demonstrated satisfactory for use, the left was usually chosen since the longer renal vein contributed to the technical ease of the nephrectomy and the subsequent transplant.

Surgical techniques

Donor nephrectomy

Conventional surgical techniques were used for the donor nephrectomy and subsequent transplant.^{10,11} The donor received 1 litre of normal saline overnight to ensure adequate hydration and 200 ml of 20% mannitol at the time of induction of general anaesthesia to maintain a diuresis. Under general anaesthesia and with the patient in the full kidney position, a loin incision either between the 11th and 12th ribs or over the 12th rib was made. The kidney was mobilised by means of an extra-peritoneal approach. When the left kidney was selected, the adrenal and gonadal veins were ligated and divided, and adequate lengths of the renal artery and vein and the ureter mobilised. The ureter was clamped and divided as distally as possible, the renal artery clamped and divided flush with the aorta and the renal vein clamped and divided proximal to the adrenal vein. When the right kidney was used the renal vein was divided with a patch of vena cava and the renal artery clamped and divided as proximally as possible. The kidneys were immediately flushed with and preserved with Euro-Collins solution. Haemostasis was secured, the wound closed in layers and a corrugated drain left *in situ*.

Recipient operation

The transplant procedure was performed through an incision in the right or left iliac fossa and an extra-peritoneal approach used to mobilise the iliac vessels. The donor renal vein was anastomosed end-to-side to the recipient external iliac vein and the donor renal artery anastomosed end-to-end to the recipient internal iliac artery. Finally the ureter was anastomosed to the bladder.

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Immunosuppression protocol

In the early part of the study patients were treated with azathioprine and steroids. Cyclosporin was introduced at our institution in 1983 and the immunosuppression regimen consisted of cyclosporin and steroids. A 'triple therapy' immunosuppression protocol consisting of steroids, cyclosporin and azathioprine has been used in our unit since 1987. Intravenous cyclosporin 2 mg/kg was given intra-operatively. The oral cyclosporin was commenced the following day at a dose of 10 mg/kg/day in two divided doses. Whole-blood cyclosporin trough levels were maintained at about 500 ng/ml. Azathioprine 1 - 2 mg/kg was given intra-operatively and 2 - 3 mg/kg daily postoperatively. Solu-Medrol 500 mg was given intra-operatively and oral methylprednisolone (Medrol; Upjohn) was given at a dose of 24 mg per day. Cyclosporin was stopped at either 3 or 6 months and the patients maintained on methylprednisolone and azathioprine.

Rejection episodes were initially treated with bolus intravenous doses of steroids. Rejection episodes resistant to steroid therapy were treated in the early part of the study with anti-lymphocyte globulin (ALG). Since 1987 steroid-resistant rejection episodes have been treated with the mouse monoclonal antibody, OKT3.

Donor-specific blood transfusions

Between May 1982 and August 1987 patients who were one-haplotype-matched with the donor were treated with donor-specific blood transfusions. The patients were transfused on three occasions with 200 ml blood from the donor at 2-weekly intervals and were given azathioprine at the time of the transfusion. The transplant procedure was scheduled for a convenient time at least 2 weeks after the last transfusion. A leucocyte crossmatch was performed before each transfusion and before the transplant procedure.

Results

Seven hundred and sixty-six kidney transplants were performed at Groote Schuur Hospital between December 1970 and August 1988. One hundred of the 766 transplants involved living related donors; the incidence of living related transplants at our institution was 13%. Of the 100 patients who received an allograft from a living related donor, 64 were male and 36 female, and the mean age was 29.96 years (range 9 - 52 years).

The total annual number of kidney transplants performed in our unit has increased over the years (Fig. 1) and the proportion of transplants involving living related donors has ranged between 10% and 20%. The number of living related transplants has increased in recent years; two-thirds were performed within the last 6 years.

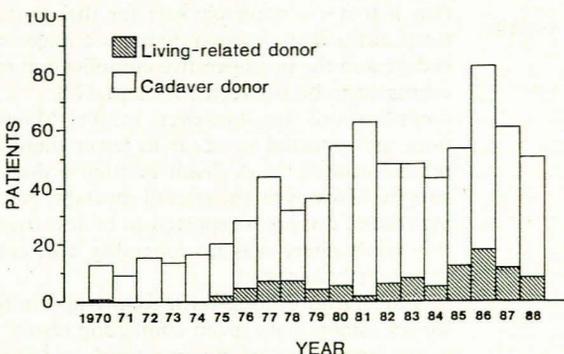


FIG. 1. Total number of kidney transplants and the number of kidney transplants from living relatives each year.

Of the 100 living related transplants, 48 transplants involved grafts from HLA-identical siblings. The remaining 52 transplants were grafts from one-haplotype-matched, related donors. On 82 occasions the transplant involved a sibling and the remaining 18 grafts were from a parent to a child.

Donor-specific blood transfusions were introduced in our unit in May 1982 and were used until August 1987. Thirty-three patients who had a one-haplotype match with the donor received donor-specific transfusions.

The cumulative patient and graft survival of the first 100 transplants involving a living related donor are shown in Fig. 2. The cumulative patient survival rates at 1 and 5 years were 90% and 74% respectively. The cumulative probabilities of the graft surviving 1 and 5 years were 86% and 70% respectively.

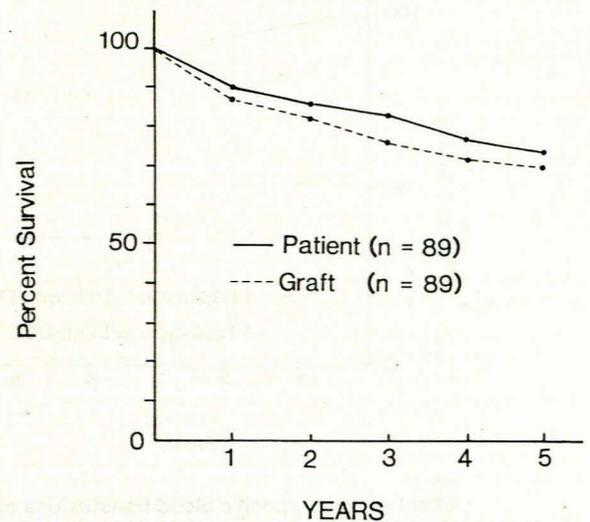


FIG. 2. Overall cumulative patient and graft survival rates in recipients of transplants from living relatives.

The survival of grafts in patients who were HLA-identical and those who had a one-haplotype match with the donor are shown in Fig. 3. The patients who were HLA-identical with the donor had a significantly better

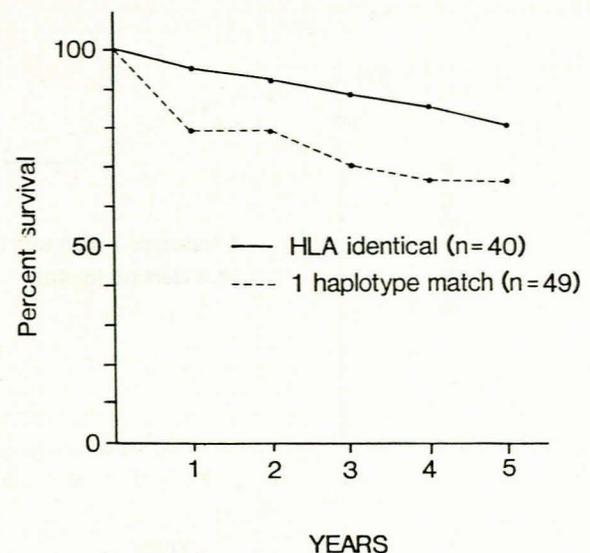


FIG. 3. Cumulative graft survival in recipients of HLA-identical and one-haplotype-matched kidney grafts from living related donors.

graft survival than the patients who only had a one-haplotype match with the donor ($P < 0,05$). The cumulative graft survival rates at 1 and 5 years in the patients who were HLA-identical with the donor were 95% and 81% respectively. In patients who had a one-haplotype match with the donor, the 1- and 5-year graft survival rates were 79% and 64% respectively.

The effect of donor-specific blood transfusions on graft survival in patients who were matched for only one haplotype with the donor is shown in Fig. 4. The cumulative graft survival rates at 1 year and 5 years were 97% and 81% respectively in patients who received donor-specific transfusions, and 51% and 36% respectively in the patients who did not ($P < 0,05$).

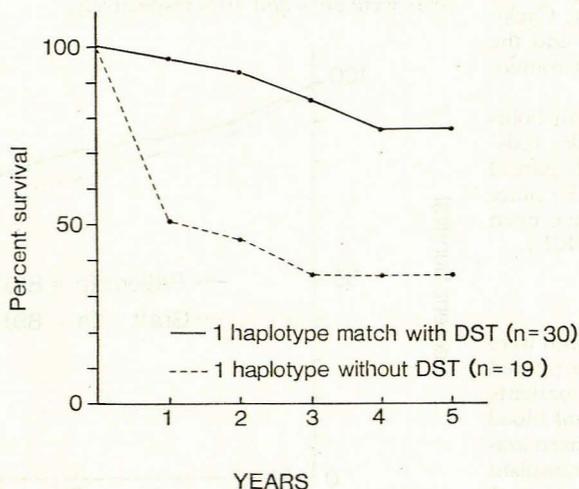


FIG. 4. Effect of donor-specific blood transfusions on the survival of one-haplotype-matched kidney grafts from living related donors.

As can be seen from Fig. 5, there was no difference in the graft survival rates of the patients who were HLA-identical with the donor and the patients who were one-haplotype-matched with the donor and who received donor-specific blood transfusions.

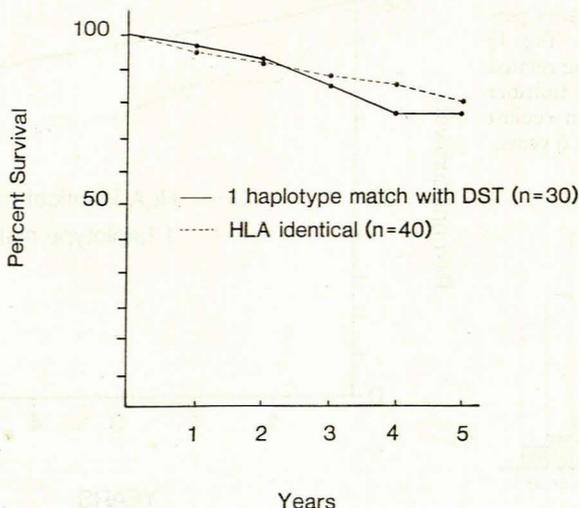


FIG. 5. Cumulative graft survival rates in recipients of HLA-identical grafts and recipients of one-haplotype-matched grafts who received donor-specific blood transfusions.

Discussion

In the early days of renal transplantation, when chronic haemodialysis was in its infancy and not readily available to all patients, the diagnosis of end-stage renal failure was virtually a death sentence for the majority of patients. A successful renal transplant appeared the only means of saving these patients but unfortunately, not only were cadaver donor organs in short supply, but the results of such transplants were very poor. Transplantation from a living related donor was therefore frequently the only hope for recipient survival.¹²

However, the situation has changed in recent years. With refinements in surgical technique and peri-operative management, the introduction of new immunosuppressive regimens, particularly the use of cyclosporin,^{4,5} and improvements in organ preservation, the results of cadaveric renal transplantation have improved significantly.^{13,14} Furthermore, chronic haemodialysis and peritoneal dialysis have also improved and become more readily available, while the shortage of cadaver donors, although still a problem, is not as critical. The continued use of living related donors for transplantation has therefore been questioned. This report analyses the results of the first 100 kidney transplants from living related donors at Groote Schuur Hospital.

This analysis confirms the good results that can be achieved with kidney transplantation involving living related donors. As expected, the outcome in the patients who were HLA-identical with the donor was better than in the patients who only had a one-haplotype match with the donor. The results after renal transplantation in the one-haplotype-matched patients before the use of donor-specific transfusions were extremely poor. It was because of these initial bad results that we abandoned using one-haplotype-matched living related donors. The reports of the favourable effects of donor-specific transfusions in transplantation led to the re-introduction of one-haplotype-matched transplants from living related donors at our institution.^{15,16} In this study the graft survival rate in the patients who had a one-haplotype match with the donor and who received donor-specific transfusions was better than in the patients who did not receive transfusions and as good as in the patients who were HLA-identical with the donor. Unfortunately the true impact of donor-specific transfusions in the recipients who had a one-haplotype match with the donor cannot be accurately assessed because cyclosporin was introduced at about the same time. This potent immunosuppressive agent may account for the improved results in the one-haplotype-matched patients who received donor-specific transfusions.

The debate about the use of living related donors remains unresolved. One of the most compelling arguments against kidney donation from living relatives is that it is not completely safe for the donor. Nephrectomy in the living related donor is a major surgical procedure and the postoperative complication rate has been estimated to be between 15% and 47%.^{6,17-20} Most of the complications are, however, minor. Major complications are reported to occur in fewer than 3% of living related donors.¹⁷⁻²⁰ A death in such a donor is a catastrophe.⁸ However, the overall mortality rate among living related donors is reported to be less than 0,1%.⁶⁻⁹ In this study there was no mortality and complications were mostly minor.

Furthermore, long-term follow-up studies of living kidney donors have given conflicting results with regard to the prevalence of hypertension²¹ and the amount of urinary protein excretion.²¹⁻²³ However, the renal function does not deteriorate after donation at a rate more rapid than expected for the normal ageing process.²⁴⁻²⁶

The use of living related kidney donors has several advantages over cadaver donors. Most important is the superior graft and patient survival rate following renal transplantation from such donors. The use of cyclosporin has, however, narrowed the gap in the graft survival rate between living related and cadaver renal transplantation. Grafts from living related donors still have a 10 - 15% advantage in survival at 1 year.^{2,3}

The shortage of cadaver donor kidneys is another reason in favour of organs from living related donors. Some patients on dialysis have to wait a long time before a cadaver kidney can be found. During this time they risk needing a blood transfusion and possible sensitisation. The shortage of cadaver donor organs is related in part to a problem of physician awareness — many donor organs are lost because physicians looking after potential donors do not know about organ donation or are reluctant to refer donors to transplant centres.²⁷ At present only a small proportion of potential cadaver donors are referred. An increase in the number of cadaver donor referrals would provide more than enough kidneys for patients on dialysis who could benefit from a transplant. The shortage of organs for transplantation would thus best be resolved by an increase in physician and public awareness about organ donation and transplantation rather than the use of living related donors. In our unit, as a result of several awareness programmes, the number of donor referrals, especially from smaller peripheral hospitals, continues to increase.

In summary, this analysis confirms the good results obtained with transplants from living relatives and suggests that donor-specific blood transfusions in patients with a one-haplotype match with the donor are beneficial. However, the continued use of living related donors could be avoided if there were not a shortage of cadaver kidneys. The shortage of cadaver organs for transplantation can be improved by education of physicians and the public about organ donation. In addition the results of cadaver renal transplantation may improve further with the introduction of new immunosuppressive agents and protocols.

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