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Living-donor kidney transplantation: the experience of a single centre

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ABSTRACT

Introduction: Living-donor kidney transplantation is the best option treatment for end-stage renal disease. It has been associated with better patient and graft survival than cadaveric transplantation. The authors describe the living-donor transplantation experience at the Hospital de Santo António, Oporto.

Patients and Methods: The outcome of the first 100 living-donor kidney transplants was retrospectively analysed and included patient and graft survival, acute rejection rate and graft function.

Results: The recipient's mean age was 34±11 years. Eighteen patients had a retransplant. The donor's mean age was 43±11 years and the majority was genetically related to the recipient (96%). After a follow-up of 46±38 months [6-267], three recipients died (all from infectious complications) and seven grafts were lost. The main causes of graft failure were death of the recipient (n=3) and renal artery stenosis (n=2). One-year rejection rate was 15.3%. The plasmatic creatinine and glomerular filtration rate of the functioning grafts at the last evaluation were 1.42±0.46 mg/dl and 69±24 ml/min/1.73 m^2, respectively. One, three and five-year patient survival were 98%, 95% and 94%, respectively. One, three and five-year graft survival were 95%, 92% and 91%. None of the donors died or suffered any permanent disability.

Conclusions: The outcome of the first 100 living-donor kidney recipients was very satisfactory, meaning kidney transplantation from living donors should be encouraged. Careful selection of donors and recipients is a condition for a successful outcome.

Key-Words:
Kidney transplantation; living-donor; outcome.

INTRODUCTION

One of the major factors restricting wider use of renal transplantation for end-stage renal disease (ESRD) treatment is the limited donor availability. Many strategies have been implemented to increase the donor pool as deceased donors are insufficient to meet the increasing demand. Some of these options include the acceptance of related (RLD) or unrelated living donors (URLD) and expanded criteria donors.

Living-donor transplants are associated with a better short- and long-term patient and graft survival than cadaveric kidneys. Five-year patient and graft survival of 90% and 80%, respectively, have been described[1].

In Portugal at the end of 2009 more than 2000 patients were on the waiting list for a kidney trans-

plant, despite an increase in the donor pool. Only 6% of the kidney transplants were from living donors[2], but the trend is for a progressive increase, as is already happening in other countries worldwide. The recent changes in legislation have allowed unrelated donors to donate to their loved ones or altruistically.

In this review article, we describe the living-donor transplantation experience with the first 100 recipients at the Transplantation Department of the Hospital de Santo António, Oporto.

PATIENTS AND METHODS

Between November 1987 and September 2009, 100 patients were transplanted with kidneys from living donors. All candidates and donors were submitted to routine medical screening, including ABO and HLA typing and cross-matching. The goal of this evaluation is to ensure that the recipients are suitable for surgery, have no important cardiac or systemic problems, no neoplastic or infectious diseases that could be aggravated by immunosuppression and no vascular disease that impedes the implantation and good perfusion of the kidney. The potential donor must be under the care and follow-up of a different transplant expert doctor and undergo a systematic physical and psychosocial evaluation.

Our data was retrospectively collected from hospital records. Patient and graft survival were estimated using the Kaplan-Meier method. The glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease (MDRD) equation[3]. The diagnosis of acute rejection was based on clinical and histological criteria.

RESULTS

Mean patient age at the time of transplantation was 34±11 years [9-62], with a slight predominance (58%) of males. All were Caucasians. Baseline characteristics of the patients are shown in Table I. Five patients had preemptive renal transplant and the remaining were in renal replacement treatment for median 25 months [2 days-283 months]. Eighteen patients had been previously transplanted (one previous kidney transplant in 17 cases and 2 previous transplants in one case).

Table I

Patients' baseline characteristics

Recipient characteristics	
Mean age (years)	34 ± 11 [9 – 62]
Male gender	58%
Caucasian race	100%
Median time on RRT (months)	25 [2 days – 283 months]
Preemptive (*n*)	5
Previous renal transplant (*n*)	18
one (*n*=17); two (*n*=1)	
Hepatitis C (n)	2
Aetiology of ESRD	***n***
– Chronic glomeulonephritis	49
IgA nephropathy (*n*=18), FSGS (*n*=8), Others (*n*=23)	
– Unknown	21
– Reflux nephropathy	9
– Urologic malformation	7
– Others	14
Median PRA	0% [0% – 96%]
HLA-identities	3 ± 1 [0-6]
Donor characteristics	
Mean age (years)	43 ± 11 [19 – 65]
Female sex	64%
Mean creatinine (mg/dl)	0.78 ± 0.18 [0.40 – 1.20]
Relationship to the recipient	Siblings (53%); parents (42%); spouses (4%); descendents (1%)

The median of peak and last titres of panel reactive antibodies (PRA) were 0% [0%-96%]. Three patients with a history of a previous transplant presented a last PRA >20%. Two patients had hepatitis C virus infection. In 49% of the cases, ESRD was secondary to chronic glomerulonephritis, mainly IgA nephropathy (18%) and focal segmental glomerulosclerosis (8%).

Mean donor age was 43±11 years [19-65]. Most were female (64%) and genetically related to the recipient (siblings in 53% of cases, parents in 42% and descendents in 1%). Their plasmatic creatinine and GFR were 0.78±0.18 mg/dl and 130±46 ml/min/1.73 m^2, respectively. The mean number of HLA identities was 3±1 [0-6] and only three patients were transplanted with a complete mismatch. In 80% of the cases, the recipient had a positive cytomegalovirus (CMV) serology and in only 6% the recipient was negative with a positive donor.

Until 2007, the immunosuppression protocol consisted of ciclosporin, mycophenolate mophetil (MMF) and prednisolone. Induction was performed with an IL-2 receptor antagonist (daclizumab/basiliximab) and this was the scheme received by the majority of the patients (44%). From that date, patients underwent the same protocol, but with tacrolimus instead of ciclosporin (33% of the transplants). Induction with antithymocyte globulin was performed in all cases of higher immunological risk (11%) – Table II. Mean hospital stay was 14±11 days [5-64]. Four patients needed transitory haemodialysis due to delayed graft function (DGF).

Table II

Immunosuppression protocols

Protocol	%
IL2-antagonist, Ciclosporin, MMF, Prednisolone	44%
IL2-antagonist, Tacrolimus, MMF, Prednisolone*	33%
ATG, Tacrolimus, MMF, Prednisolone	11%
Ciclosporin, MMF, Prednisolone	11%
Ciclosporin, Prednisolone	1%

*From 2007

IL2-antagonist: basiliximab/daclizumab; **MMF:** mycophenolate mophetil; **ATG:** antithymocyte globuline

Complications during the hospital stay were registered in 18 recipients. The most frequent was acute rejection (n=10) followed by renal artery stenosis (n=4), significant haematoma of the renal loca (n=2), urinary fistula (n=1) and urinary sepsis (n=1). Two patients with renal artery stenosis underwent renal artery angioplasty and the other two surgical intervention.

After a follow-up of 46±38 months [6-267], three recipients died and seven grafts were lost. The deceased patients suffered bacterial infectious complications at the first (n=2) and 31st month after transplantation (n=1). The causes of graft failure were death of the recipient with a functioning graft (n=3), renal artery stenosis (n=2), acute tubular necrosis in the context of severe sepsis (n=1) and chronic rejection (n=1). The median time after transplantation until graft loss was 10 months [25 days-31 months].

The one-year acute rejection rate was 15.3%. Until the end of follow-up, we registered 13 acute rejections in 13 patients, which occurred a median 7 days after transplantation [2-180]. Five of those rejection episodes were humoral. All patients responded to treatment and no graft was lost due to acute rejection.

The plasmatic creatinine and GFR of the functioning grafts at the last evaluation were 1.42±0.46 mg/dl and 69±24 ml/min/1.73 m^2, respectively. The proteinuria was 0.21 g/day [0-2.2], in median. Only 5.4% of the patients presented proteinuria ≥ 0.5 g/day. The maintenance immunosuppression consisted of a calcineurin inhibitor (tacrolimus in 58 patients; ciclosporin in 35) in association with MMF in 92 cases.

One, three and five-year patient survival were 98%, 95% and 94%, respectively. One, three and five-year graft survival were 95%, 92% and 91%, respectively (Fig. 1). During the process of donation, none of the donors died, had a complication implying intensive care treatment or suffered any permanent disability.

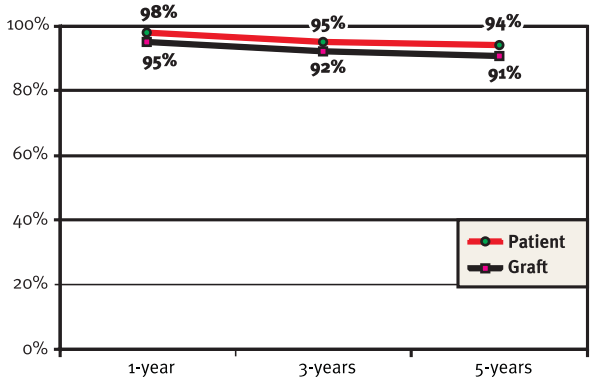

Figure 1

Patient and graft survival at one, three and five years.

DISCUSSION

The outcome of renal transplantation has improved over the years. The main reasons for that were the improvement of the immunosuppressive protocols, the development of infection surveillance measures together with more effective treatments, and the higher quality of dialysis care, allowing a better state-of-health of transplant candidates at the time of transplantation[4].

The 22 years of our living-donor transplantation programme have seen many improvements in surgical technique, immunosuppression and recipient preparation. In the first years of the programme, we performed only a few of these transplants, with marked growth occurring in recent years, explaining why patients have been offered different immunosuppressive regimens over time. Our patient and graft survival were excellent in comparison to published series[1]. Our good results could be explained by such factors as the recipients' young age, high HLA-match, small number of high-immunological risk patients and the immunosuppression protocols.

The majority of our recipients had a sibling or a parent as a compatible donor and this may explain their young age at transplantation. Although a younger age may be regarded as a risk factor for acute rejection because of the stronger immunological environment[5], our rejection rate was lower than in other reviews with a similar follow-up[6]. Our one-year acute rejection rate was 15.3%. This rate has varied widely in recent series because of discrepancies in diagnostic criteria and immunosuppression protocols, ranging from 18.5% and 52.2% in RLD and 30% and 54.2% in URLD[4,7,8]. The main factor to explain our low rejection rate is the immunosuppressive induction with monoclonal or polyclonal antibodies in the majority of the patients (88%). The 2009 Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines on the monitoring, management and treatment of kidney transplant recipients recommend that an IL2-receptor antagonist should be the first-line induction therapy and that a lymphocyte-depleting agent should be used in high immunologic risk patients[9]. IL2-receptor antagonists have already been shown in a large review to reduce the risk of acute rejection and graft loss without affecting all-cause mortality, malignancy or CMV infection[10].

Some studies have demonstrated a higher incidence of acute tubular necrosis and acute rejections in recipients of kidneys from unrelated donors[11], and that could be another explanation for our low rate of acute rejection, since the majority of our donors were RLD. The rate of DGF (4%) was similar to other series[12].

The small number of URLD in this study did not allow for a comparison of graft survival with RLD, but other series have reported no differences[13,14]. Gjertson *et al.*[15] concluded that unrelated living donors remain an underutilised resource despite their high graft survival rates, similar to genetically related donors and significantly better than cadaveric donors. Nowadays, ethical issues and possible commercialisation are the main obstacles for the expansion of genetically unrelated donor transplantation[16].

The predictability of HLA compatibility on graft survival is different depending on the type of organ transplanted. In renal transplantation this is a subject of debate. Although studies from 100 transplantation centres in the US recommend six-antigen match and other studies report better graft function and survival rate with HLA-matching[11], its significance in the era of more potent immunosuppressive therapy has diminished[17] and good survival has been reported with lesser matched patients as well[18,19]. In our review, only three patients were transplanted with a complete mismatch.

Living-donor renal transplantation is becoming increasingly popular because of better quality organs and outcomes. Although the risks of donation are recognised, mainly related to perioperative morbidity, it appears that there is no impact on short- and long-term survival compared to the general population[20], probably because living donors are a selected population and also have regular medical supervision after donation. The potential donor may choose or not to accept the risks. In our review none of the donors died, had a complication implying intensive care admission or suffered from any permanent disability after the donation process.

Conflict of interest statement. None declared.

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