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Original Research Article

Outcomes of Spousal Versus Related Donor Kidney Transplants: A Single Center Experience

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Abstract

Background: Kidney transplantation is the preferred modality of treatment, and it provides the better quality of life than dialysis in patients with end stage renal disease. Living donation constitutes the vast majority of cases in India. The demand and availability of organ gap is fulfilled by spousal donation.

Objective: To assess the graft and patient outcomes of spousal transplant compare with those of related transplant.

Methods and Materials: This retrospective observational study was conducted among the transplant patients during the period of 2012 and 2022. The spousal donors as well as related donors with their demographic details, pre- and post-transplant evaluation, immunosuppressive therapy and followed up with post-transplant complications, were obtained and recorded.

Result: A total number of transplants were179. After exclusion of unrelated and cadaveric transplants, 135 cases were taken in the study. They were analysed,45 cases were spousal, and 90 cases were related. Mean age of recipient was 42.8+/-7.5 in the spousal and 30.3+/-7.7 in related transplants. Delayed Graft Function (DGF) was 8.8% in spousal and 10% in related transplants. Rejection episodes were13% in spousal and 20% in related donors. Serum creatinine at one year was 1.39+/-0.7 and 1.26+/-0.37 in spousal and related donors respectively. Patientr survival was 93% and 97% in spousal and related donors respectively. One year graft survival was 91% in both. Rejection episodes were also comparable.3-year survival was 90.2%in spousal donor group and 89.0% in related donor group.

Conclusion: Spousal donation particularly wife is the major source of donor in our country and the post-transplant complication and survival is compared to related transplant groups.

Keywords: Spousal Donor, DGF, Related.

Introduction

Kidney transplantation provides the best hope for rehabilitation to normal life in end stage renal diseases. Living donor transplants constitutes the vast majority of

all kidney transplants in India. With the use of effective immunosuppressants like CNIs, HLA matching has become less important in renal transplantation. Keeping this in view spousal donors can fulfil the huge gap between the demand and availability of the organ. A large number of studies have been conducted to compare results of related and spousal kidney donation and have shown similar outcomes[1-9]. Few studies in India have looked into this aspect[10-12]. In most of them cyclosporine and azathioprine have been used as maintenance immunosuppression and induction done selectively. Therefore, this study was designed to assess the graft and patient outcomes of SD transplants and to compare them with those of RD transplants in the setting of use of highly effective immunosuppressants like MPAA, tacrolimus and uniformly used induction agent.

Patients and Methods

Adults aged 18 years or above who underwent renal transplantation at Renal Transplant Unit of SCB Medical College Hospital, Odisha, from a SD or RD between March 2012 and October 2020 were included in the study. Our centre is a tertiary care centre in eastern India where renal transplantation is a Govt supported programme. Patients undergoing deceased or living unrelated donor (other than SD) transplantation were excluded from the study. Data on outcomes at one year and 3 years post-transplant was collected retrospectively (2012-2020).

Pre-Transplant Evaluation and Post-Transplant Management Protocol

Pre-transplant crossmatch was done using complement dependent cytotoxicity (CDC) technique only. Induction therapy with basiliximab/antithymocyte globulin (ATG) was administered to all patients. Basiliximab was given at 20 mg intravenous (i.v.) 2 h before transplantation and 20 mg i.v. at day 4 post-transplant. ATG was given at 1 mg/kg i.v. on day 0, 1 and 2 post-transplants. Maintenance immunosuppression was a combination of calcineurin inhibitor (tacrolimus was used in >90% of patients), mycophenolate mofetil (MMF) and steroid. All patients received 500 mg of hydrocortisone at the time of clamp release intra-operatively and 20 mg of prednisolone orally from post-operative day 2. Prednisolone was tapered to 5 mg once daily over the next 2 months. Tacrolimus trough levels were targeted at 8-11 ng/ml over 3 months post-transplant,5-8 ng/ml till 1year,3-5ng/ml thereafter. All patients received MMF 1 g twice a day. The calcineurin inhibitor and MMF were started 24 h before transplant.

Trimethoprim-sulfamethoxazole prophylaxis was given to all patients for 6 months after transplant. Testing for cytomegalovirus (CMV)/BK virus was done using nucleic acid testing/allograft biopsy when clinically indicated. Prophylactic or pre-emptive therapy for CMV was given to all patients in form of oral valganciclovir 450mg once a day. Testing for CMV serostatus prior to transplant was done routinely. Delayed graft function was defined as the requirement of dialysis in the 1st week after transplant. Evaluation for an acute rise in serum creatinine level included ultrasonography, calcineurin inhibitor C_0 level and urine microscopy and culture. If no obvious cause of renal dysfunction was identified, a renal biopsy was performed. Rejection was classified as per Banff classification. Acute cellular rejection (ACR) was treated with 3 pulses of methyl prednisolone (500 mg each). In case of steroid resistance, ATG was administered (1 mg/kg/d for 5-7 pulses). Antibody mediated rejection (AMR) was treated with plasmapheresis (PP) (40-60 ml/kg/session; replacement with fresh frozen plasma/albumin) and IvIg (100 mg/kg after each PP session). Combined ACR and AMR were treated with an initial steroid pulse followed by ATG (if steroid

resistant). PP/IvIg therapy was also used in some cases depending on the treating physician's discretion. Response to therapy was classified as a complete response (CR) if serum creatinine decreased to ≤1.5 mg/dl or baseline after therapy, partial response if serum creatinine decreased by 50% of maximum but was still >1.5 mg/dl or baseline and no response if there was a less than 50% decrease in serum creatinine and serum creatinine >1.5 mg/dl on follow-up.

Results

A total of 179 transplants were done during the period of 2012 and 2022 out of which 135 patients were included in the study. After excluding deceased and unrelated donor(other than spouse) transplants,149 patients were analyzed. Among them the patients who have not completed 6 months after transplant, those with prolonged cold ischemia time (>2hours), those non-compliant with medicines and those who were lost to follow up were excluded. Data on outcomes at 1 year post transplant was collected retrospectively. Three year patient survival and graft survival was studied.

Out of 135 cases included in the study in 45 cases spouse was the donor and in 90 cases parents and siblings (related donor). Mean age of recipient was 30.3±7.7 and 42.8±7.5 in case of related donor and donor respectively. The difference was not statistically significant. Mean age of donors in related and spouse donor group were 49.9±7.6 and 38.9 ± 7.7 respectively. Like recipient age group donor age group was not statistically significant.

Male female ratio was significantly different in both groups. Females contributed to 80.0% and 95.5% donors in related donor and spouse donor group respectively (p value=0.016).

Table 1: Baseline Characteristics

Donor and recipient characteristics	Related donor	Spouse donor	Significance
Recipient age	30.3±7.7	42.8±7.5	0.652
Donor age	49.89±7.6	38.96±7.7	0.755
Donor sex (M: F)	1.8:1	9:1	0.016
Induction agent: ATG Basiliximab	 40(44%) 50(55%)	 18(40%) 26(45%)	0.127
Maintenance immunosuppression: Pred+tacrolimus+MMF Pred+cyclosporine+MMF Pred+tacrolimus+azathioprine Pred+everolimus+MMF	 83(92.2) % 5 1 1	 42(93.3%) 2 1 0	 0.816

Induction agents were used in all patients as per our institutional protocol. Basiliximab was used in 50 (55%) and 26 (45%) cases of RD and SD respectively whereas ATG was used in 40 (44%) and 18 (40%) cases of RD and SD respectively. In 83 (92.2%) patients of RD group and 42 (93.3%) cases prednisolone, tacrolimus and mycophenolate mofetil was used for maintenance immunosuppression. The difference in use of induction agent and maintenance immunosuppressants were not significant.

Table 2: Outcomes

Outcomes	Related donor	Spouse donor	significance
DGF	9(10%)	4(8.8%)	0.837
Rejection episodes	18(20.0%)	6(13.3%)	0.732
1 year survival	97%	93%	0.111
Cr at 1yr	1.26±0.37	1.39±0.71	0.167
Graft survival at 1 year	91%	91%	0.837
3year survival	89.0%	90.2%	0.48
Graft survival at 3 years	81.9%	78.2%	0.56

Delayed graft function occurred in 9 (10%) cases in RD and 4 (8.8%) cases in SD group. The difference was not statistically significant (p value=0.873). A total of 24 rejection episodes (17%) were recorded out of which 18 (20.0%) occurred in related donor group and 6 (13.3%) in spouse donor group. Rejection episodes were similar in both groups (p value=0.732). Mean serum creatinine at 1year was 1.26±0.37 and 1.39±0.71 respectively (p value=0.167). 1 year survival was 97% in related donor group and 93% in spouse donor group. (p value=0.111). Three-year survival was 89% in related donor group and 90.2% in spouse donor group (p value=0.48). Graft survival was 81.9% and 78.2% in RD and SD respectively.

Discussion

In India where deceased donor transplantation is still in infancy, live donors remain the major source for allograft and constitutes 90% of allografts. Near relatives made the major donor pool until a near relative status was conferred to spouse donor by THOA,1994 amendments. Over last 10 years a striking change in the spectrum of living renal donors has been seen in India[13]. At PGI Chandigarh, where spouses constituted just 17.2% of all donors between 2002 and 2006, the percentage has already doubled to 34%.the percentage of related donors (parents, siblings and offsprings decreased from 73.6 in 2002-06 to 48.4% in 2012-13 mainly due to a decrease in sibling donors[13]. In our study spouse donor constituted 33.3% cases and related donor, 66.6% cases.

In the present study, the mean age of donors was higher than that of spouse donor, but the difference was not statistically significant.

Female donors contributed to 80% in RD group and 95.5% in SD group. Zimmerman et al[14], showed that females constituted 90% of spousal donors and 58.1% of 1st degree relative donors. Similar trend is seen in various Indian studies[11,12]. Higher incidence of kidney diseases in men, fearing of losing earning member, and perception of renal donation as an extension of responsibility towards family in females have been suggested as reasons for female preponderance among living donors[15].

Unlike most of the previous studies all the recipients of our study received induction therapy in form of Inj basiliximab and Inj ATG which were equally distributed among the recipients. Present evidence in literature strongly supports the use of induction therapy as a part of initial immunosuppressive therapy in kidney transplant recipients[16-18]. In a Cochrane review of 30 RCTs on the efficacy and safety of of IL-2 receptor anagonists[17] it was shown that these agents decrease the rate of acute rejection and graft loss ,without significantly affecting all-cause mortality, malignancy or infection rates. A meta-analysis of RCTs comparing lymphocyte depleting agents with placebo or no treatment showed a reduction in graft failure particularly in high immunological risk[16].

In our study, recipients from RD group were found to have more DGF episodes

than SD group, but the difference was not statistically significant (10% vs 8.8%, p value=0.837).

A total of 20 episodes of rejections were recorded during the study period. Out of which 18 (20.0%) occurred in RD group and 6(13.3%) in SD group. The difference was statistically non-significant (p value=0.082). Out of all rejection episodes 3 episodes occurred after 1yr of transplantation. ABMR was seen in 50% of cases and TCMR and mixed ABMR and TCMR constituted 25% each.

Despite of use of induction agents uniformly in both groups and favorable HLA mismatch in RD group more number of rejection episodes were observed in RD group though the difference was statistically not significant. This could be explained by higher median age in RD group and is supported by significantly higher no of DGF in RD group.

Currently pretransplant crossmatch is performed by CDC technique at our center in majority of patients and flow cytometry/Luminex in selected cases. As CDC cross match is a less sensitive technique in determining preformed antibodies, this can be a reason for more episodes of rejection, particularly more number of ABMR.

Patient survival at 1 year was similar in both groups (p value=0.111). The results of the present study are similar to the previous studies where patient survival has been found to be statistically similar in the spousal and related transplant recipient groups[3,6,9,19].

3-year survival was 89.0% in RD group and 90.2% in SD group. Graft loss was defined as the patient became dialysis dependent or underwent second renal transplantation. Graft outcome at 3 years was 81.9% in RD group and 78.2% in SD group. Abraham et al surveyed evolution of renal transplantation in last four decades and found that in Govt run free of cost hospitals 92% graft survival at 1 year,82% at 3 years and 75% at 5 years which is comparable to our results.[20] The results were comparable with Terrasaki et al ,Shah et al and Kute et al who did not find statistical difference in long term survival of related donor and spouse donor renal grafts[21-23].

Conclusion

With increasing age of marriage and decreasing age of onset of diabetes and hypertension getting healthy parents as kidney donors will be more difficult with time. Getting willing siblings for donation will also be difficult as one and two child norm and nuclear families are becoming popular. In that case the spouse can serve as an important source of donor kidney. The majority of spousal donors would recommend other spouses to donate and the gift of life also results in better family and sexual relations and improved relations with children as concluded by similar studies to ours. However, one needs to be very careful to ensure that our enthusiasm on this issue does not result in coercion of spousal donation in the presence of other compatible donors. As seen in our study as well as other Indian studies wife is the major source of spousal donor.in a country like India where wife is the one who has the most to lose from the death of the prospective recipient, such a thing is a very real possibility. Transplant units need to have very clear guidelines in keeping with the socio-economic conditions in their regions, which will ensure that the donor is capable of making independent decision and is free from coercion.

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