Kidney Transplantation in a Veterans Administration Medical Center: 40 Years' Experience

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Objectives: **Advances in immunosuppressive therapy have led to substantial improvements in kidney transplant outcomes in the past 20 years. Kidney transplantation activity started in 1963 at the Veterans Administration Medical Center in Nashville, Tennessee, and continues to grow with increasing numbers of transplants from living-related and unrelated donors. In this study, patient and graft survival rates during 2 different periods were evaluated and compared with non–veterans-administration centers.**

Materials and Methods: **Six hundred fourteen kidney transplants were performed between March 1963 and December 2002. For analytic purposes, the 40-year experience was divided into 2 eras based on the immunosuppressive agents used. Azathioprine and prednisone were the immunosuppressive agents used in era 1. A calcineurin-inhibitor–based triple immunosuppressive regimen initially including azathioprine and prednisone and later, mycophenolate mofetil and prednisone, was the preferred immunosuppressive regimen in era 2.**

Results: **In era 1, 1-year patient and graft survival rates were 72.5% and 50%, and 89% and 75% for deceased-donor and living-donor transplants respectively. In era 2, patient survival rates increased to 95.1% and 87.8% for 1 and 3 years respectively, while graft survival increased to 87.6% and 74.9%. Forty-three percent of deceased-donor and 21% of living-donor kidneys were lost owing to rejection in era 1. In era 2, the incidence of acute rejection was 14.5% overall.**

Conclusions: **Overall, our results are comparable with non–veterans-administration centers and the national average and show that kidney transplantation offers veteran patients with end-stage renal disease a safe and effective treatment with increased quality of life.**

Key words: *Deceased donor, living related, kidney transplantation*

Patient and graft survival rates in renal transplantation have increased substantially since the early days of transplantation. In addition, long-term outcomes and quality-of-life data provide a strong argument for kidney transplantation when compared with chronic dialysis [1,2]. Advances in immunosuppressive therapy in the last 20 years have increased our ability to control and prevent acute rejection and therefore, improve the outcome of patient and graft survival [3].

The first kidney transplant at the Veterans Administration Medical Center in Nashville, Tennessee, was performed in March, 1963, and a summary of the first 20 years' experience was published in 1985 [4]. The present study reviews the Veterans Administration Medical Center, Nashville, Tennessee, experience with renal transplantation in the past 40 years (1963-2003).

Materials and Methods

Between March 20, 1963, and December 27, 2002, 614 renal transplants were performed in our center. After obtaining approval from our center's institutional review board, patient charts were evaluated retrospectively, and clinical and demographic data

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were analyzed. Of these transplants, 119 were from living donors and 495 were from deceased donors.

For analytic purposes, the 40-year experience was divided into 2 eras based on immunosuppression used: era 1 (1963-1983) and era 2 (1984-2002). In era 1, the mean age of recipients was 40.9 years (range, 19-59 years). There were 269 male and 4 female recipients. Seventy-nine percent of the recipients were white and 21% were African-American. Etiology of end-stage renal disease (ESRD) included chronic glomerulonephritis in 157, previous graft failure in 51, nephrosclerosis in 34, membranous nephropathy in 5, trauma in 2, and other/unknown in 75 recipients. Initial immunosuppression in era 1 consisted of azathioprine and prednisone. Cyclophosphamide also was used in selected cases. Treatment of rejection was with bolus methylprednisolone and graft irradiation. Between 1970 and 1981, thoracic duct drainage was employed in 43 patients for immunologic advantage. In 1978, rabbit-antihuman thymocyte serum (ATS) was introduced as an adjunct to azathioprine and prednisone for prophylaxis and treatment of rejection.

Era 2 started in 1984 with the introduction of cyclosporine. The mean age of recipients was 52.7 years (range, 29-72 years). Forty-four percent of the recipients were between the ages of 50-64 years, 41% were between 35-69 years, 10% were between 18-34 years, and 5% were older than 65 years. There were 278 male and 12 female recipients. Sixty-four percent were white, 31% were African-American, 4% were Hispanic, and 1% was Asian. Etiologies of ESRD were hypertension in 23%, diabetes in 16%, polycystic kidney disease and glomerulonephritis in 10% each, focal glomerulosclerosis in 8%, failed previous transplant and membranoproliferative glomerulonephritis in 6% each, immune globulin A nephropathy in 4%, and other in 17% of patients. In era 2, 186 patients were given Nashville-antihuman thymocyte serum (N-ATS), 76 recipients were given basiliximab, 72 patients were given thymoglobulin, 4 patients were given OKT3, and 2 were given daclizumab. Cyclosporine, azathioprine, and prednisone triple immunosuppressive protocol was used between 1984 and 1995. Between 1996 and 2001, cyclosporine, azathioprine, and prednisone, or cyclosporine, mycophenolate mofetil (MMF), and prednisone combinations were used. Starting in 2002, the preferred triple immunosuppressive regimen was tacrolimus, MMF, and prednisone. Rejection episodes were diagnosed by clinical parameters and ultrasound-guided biopsy and scored according to Banff criteria. Acute cellular rejections were treated with bolus steroid doses for 3 days. Steroid-resistant rejections were treated with polyclonal antibodies (thymoglobulin or N-ATS). Monoclonal anti-T-cell antibodies (OKT3) also were administered in patients with steroid-resistant rejections and in patients with vascular rejection. For the patient and graft survival rates in era 1, previously published data were used [4]. The Organ Procurement and Transplantation center specific database was the source for era 2. Patient and graft survival rates were calculated with the Kaplan-Meier method.

Results

Three hundred twenty-four (296 deceased-donor, 28 living-donor) kidney transplants were performed between 1963-1983. Overall 1-year patient and graft survival rates were 72.5% and 50% respectively for deceased-donor kidney transplants. One-year patient and graft survival rates for living-donor transplants were 89% and 75% respectively. Patient survival, which was 45% at the beginning of the first era (1963-1969), improved to 84% toward the end of the era (1981-1983). One-year graft survival also improved from 45% to 70% in the same period. One hundred eighteen (43%) deceased-donor and 5 (21%) living-donor kidneys were lost to rejection. Technical failure caused 3 graft losses in the deceased-donor group. Sixty-one patients (22%) in the deceased-donor and 3 (12.5%) patients in the living-donor group died with a functioning graft. Causes of death in era 1 were sepsis (31%), cardiovascular (20%), gastrointestinal (6%), and neoplasm (2%). Sixty-two patients (23%) in the cadaveric group had functioning grafts between 1 and 17 years after transplant, while 14 patients (58%) in the living-donor group had functioning grafts between 16 months and 11 years after transplant. Two hundred ninety (199 cadaveric, 91 living-donor) transplants were performed in era 2 (1984-2002). Delayed graft function was seen in 45 recipients (15.5%). There were 42 (14.5%) acute rejection episodes; 31 (74%) were seen within the first 3 months after transplant. Late rejection (after 3 months) was seen in 11 (26%) patients. Acute rejection episodes were treated with bolus steroids (42), OKT3 (8), thymoglobulin (18) and N-ATS (7). In 5 patients, the grafts were lost to acute rejection and

had to be removed. Twenty-seven (9.3%) patients experienced chronic allograft nephropathy (CAN) between 2 and 7 years after transplant.

Twenty-one patients (56%) died with a functioning graft. Causes of death were cardiovascular (5), sepsis (3), liver failure (3), posttransplant lymphoproliferative disorder (2), anesthesia complication during spinal surgery (1), and unknown (7). Posttransplant complications were seen in 25 patients and included myocardial infarction (7), liver failure (4), development of polyoma virus infection (4), recurrence of focal segmental glomerulosclerosis (3), recurrence of proliferative glomerulonephritis (1), posttransplant malignancy (4), cytomegalovirus infection (3), urinary tract infection (8), calcineurin inhibitor toxicity (1), cerebrovascular accident (1), pancreatitis (1), pulmonary edema (1), herpes simplex virus retinopathy (1), renal cell carcinoma in the transplanted kidney (1), and noncompliance (1). There were 7 surgical complications seen: lymphocele (3), hematoma (2), and incisional hernia (2).

One- and 3-year patient survival rates in era 2 were 93.7% and 86.2% for deceased-donor kidney transplants and 92.6% and 93.2% for living-donor transplants. The overall patient survival rate was 95.1% and 87.8% for 1 and 3 years respectively. One- and 3-year graft survival rates were as follows: 83.1% and 67.2% for cadaveric, 95% and 88.3% for living donor, and 82.6% and 76.9% overall.

Discussion

Kidney transplants have become the preferred treatment for most patients with ESRD. In the last 2 decades, improvements in immunopharmacology, basic sciences, and clinical transplantation have resulted in substantial improvements, not only in short-term outcomes, but also in long-term outcomes. Kidney transplantation offers the greatest potential for return-to-normal renal function, increased longevity, improved quality of life, and lower healthcare costs [5]. Currently, more than 400,000 Americans receive treatment for ESRD [6], and the number of patients with ESRD awaiting kidney transplantation is more than 60,000—more than 3 times the number who actually receive kidney transplants [7]. Only 14% of Americans with ESRD receive new grafts. Furthermore, there is a widespread geographic variation in organ donor rates. Organ donation among minorities, especially in African-Americans, is also low [8]. Despite the advances that have been made in immunopharmacology, histocompatibility testing, and modulation of the immune system, acute rejection and CAN continue to play a significant role in short- and long-term graft loss respectively. The two major factors associated with long-term graft loss are death with a functioning graft and CAN, with CAN being the most prevalent cause of late kidney graft loss [9]. Our results are in agreement with these findings. In era 1, 43% of the grafts in deceased-donor and 21% in living-donor groups were lost to rejection, while death with a functioning graft was 22% in deceased-donor and 12.5% in the living-donor groups.

The introduction of cyclosporine in 1983 marked the beginning of era 2 in our program and resulted in the decrease of acute rejection rates to 14.5%. The introduction of mycophenolate mofetil and tacrolimus resulted in a further decrease in acute rejection rates to less than 10%. This finding is also in agreement with other authors' results [10,11]. In era 2, 9.3% of the grafts were lost to CAN and 58% of the recipients died with functioning grafts.

One-year patient and graft survival rates increased from 45% and 45% in the beginning of era 1 to 86% and 70% in the early 1980s. In era 2, these rates improved to 95% and 88% respectively. Currently, 3-year survival rates in our program are: patient survival (84.7%) and graft survival (67.2%) in deceased-donor transplants and patient survival (93.2%) and graft survival (88.3%) in living-donor transplants, with overall patient and graft survival rates of 87.8% and 74.9%. These results are comparable to non–veterans-administration results and the national average [12].

Although veteran kidney transplant recipients differ from the other transplant recipient populations in that they are older, 95% male, and have an increased number of multiple medical problems, these recipients still can expect good results in terms of patient and graft survival. This shows that renal transplantation offers the veteran patient with ESRD a safe and effective alternative treatment to dialysis with increased quality of life.

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