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RENAL TRANSPLANTATION IN PATIENTS 65 YEARS OLD OR OLDER

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ABSTRACT

Between January 1982 and August 1989, cadaveric renal transplantation was performed in 22 patients 65 years old or older. Mean recipient age was 68 years (range 65 to 73 years). There were 17 men and 5 women. Additional risk factors included retransplantation (3 patients), high (greater than 30%) panel reactive antibody (4) and diabetes (1). All patients received cyclosporine as part of the immunosuppressive regimen. The 3-year actuarial patient and allograft survival rates were 89% and 71%, respectively. There were 6 graft losses due to chronic rejection (2 patients), renal vein thrombosis (1), myocardial infarction (1), withdrawal of immunosuppression because of sepsis (1) and primary nonfunction (1). Of the 16 patients with a functioning graft 12 currently have a serum creatinine of less than 2.0 mg./dl. These results suggest that cadaveric renal transplantation is an acceptable form of treatment for patients older than 65 years with end stage renal disease.

KEY WORDS: kidney transplantation, geriatrics

Of 28,944 new Medicare patients with end stage renal disease accepted for dialysis in 1985, 10,285 (35.5%) were 65 years old or older.[1] However, in the same year only 57 (0.8%) of the 6,910 transplants performed were in recipients in this age group.[1] The reluctance to perform transplantation in these patients is due partly to the belief that the risks of transplantation outweigh the advantages. This assumption is based to a large extent on studies that were performed in the 1970s, before the advent of cyclosporine.[2, 3] However, since the introduction of cyclosporine and the subsequent decrease in steroid requirements, there has been improved graft and patient survival in this recipient age group (table 1). We evaluate the role of renal transplantation in the management of end stage renal failure in patients older than 65 years.

MATERIAL AND METHODS

Between January 1982 and August 1989, cadaveric renal transplantation was performed in 22 patients 65 years old or older (mean age 68 years). The causes of renal failure were hypertension in 5 patients, glomerulonephritis in 5, pyelonephritis in 2, Wegener's granulomatosis in 1, intravenous contrast-induced nephropathy in 1, polycystic kidney disease in 1, gouty nephropathy in 1, interstitial nephritis in 1, insulin-dependent diabetes in 1 and unknown in 3. There were 17 men and 5 women. Three patients were undergoing retransplantation. Panel reactive antibody was greater than 30% in 4 patients.

All men underwent a voiding cystometrogram performed as part of the pretransplant evaluation. Ultrasound of the gallbladder has become a routine part of this evaluation since 1988, and elective pretransplant cholecystectomy is performed if calculi are present. Cardiac evaluation consisted of a stress thallium and/or MUGA scan and cardiac catheterization was performed when these were abnormal. In 7 patients a stress thallium test was performed and 6 of these underwent a cardiac catheterization before transplantation. One of these patients underwent coronary angioplasty before transplantation. No coronary artery bypass procedures were done. Additional risk factors for transplantation are outlined in table 2.

The minimal transplant requirements were ABO compatibility and a negative lymphocytotoxic crossmatch on current sera. No attempt was made to match for HLA-A, B or DR antigens and there was no formal transfusion policy during this period. A total of 16 patients received cyclosporine plus prednisone and 6 received triple therapy (cyclosporine, azathioprine and prednisone). Rejection was treated with high dose steroids. One patient received OKT3 for steroid resistant rejection. Actuarial patient and allograft survival, and statistical analysis were calculated using BMDP software.

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RESULTS

Patient survival. The 1 and 3-year actuarial patient survival rates were identical at 89% (see figure). Followup ranged from 5 months to 7 years (median 27 months). There were 2 deaths. One patient died of a myocardial infarction after sepsis from a perforated sigmoid diverticulum. A 73-year-old man had a history of myocardial infarction, an ejection fraction of 28% and significant coronary artery disease that was not surgically correctable. The allograft never functioned and he died of a myocardial infarction 2 months after transplantation.

Graft survival. The 2-year actuarial allograft survival was 73% (see figure). Six grafts were lost due to rejection in 3, renal vein thrombosis in 1, death from myocardial infarction in 1 and primary nonfunction in 1.

Surgical complications. Surgical complications occurred in 10 patients and resulted in 1 death and 2 allograft losses (table 3).

Rejection. Acute rejection episodes occurred in 9 patients (40%), 8 of whom (89%) responded to either steroids or OKT3. Immunosuppression was discontinued in the remaining patient because of sepsis, which occurred after attempted ureteral repair (an injury that was sustained during lymphocele drainage). Two patients lost the allografts to chronic rejection.

Medical complications. Medical complications are shown in table 4. Two patients had fatal myocardial infarctions 40 and 60 days after transplantation, respectively. These 2 patients previously demonstrated significant coronary disease on cardiac catheterization that was considered unsuitable for surgical correction. One patient who had cytomegalovirus pneumonia suffered a steroid resistant rejection episode that responded to OKT3. He subsequently lost the graft to chronic rejection.

DISCUSSION

The introduction of cyclosporine and the subsequent use of lower doses of steroids have resulted in improved patient and

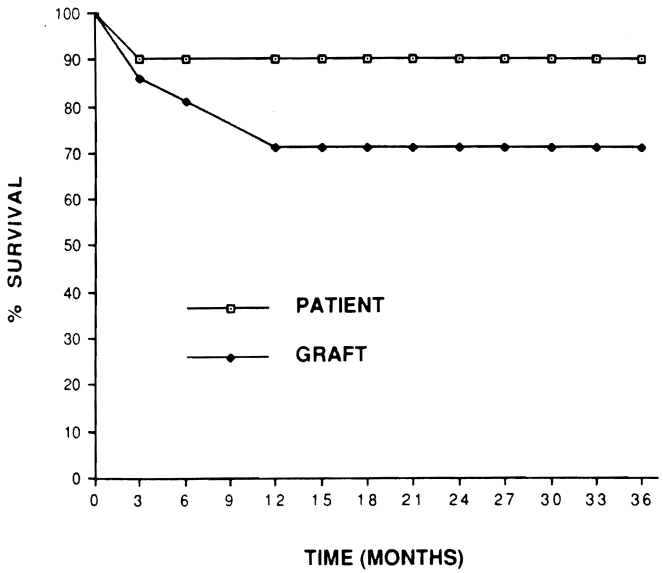
TABLE 1. *Results of renal transplantation in older patients*

Reference	Recipient Age (yrs.)	No. Pts.	1-Yr. Pt. Survival (%)	1-Yr. Graft Survival (%)
Fauchald et al[7]	Older than 60	122	67	87
Fehrman et al[4]	Older than 65	55	71	63
Tapson et al[6]	Older than 60	13	74*	61
Roza et al[8]	Older than 65	17	91	81
Murie et al[5]	Older than 55	56	87	73
Jordan et al[9]	Older than 55	67	88	70
Korb et al[10]	Older than 55	24	82	70
Present series	Older than 65	22	89	71

* 2-year survival.

TABLE 2. *Additional risk factors in renal transplant recipients older than 65 years*

Disease	No. Pts.
Cardiovascular hypertension:	
Hypertension	13
Lt. ventricular hypertrophy	2
Prior myocardial infarction	3
Respiratory:	
Chronic obstructive lung disease	4
Gastrointestinal:	
Peptic ulcer disease	3
Colon Ca	1



Actuarial patient and graft survival rates for renal transplant recipients older than 65 years. Numbers of patients followed at 1, 2 and 3 years are 13, 10 and 7, respectively.

graft survival in renal transplantation. Fehrman et al reported 1 and 3-year actuarial patient and graft survival rates of 71%, 57%, 63% and 49%, respectively, in 55 recipients older than 65 years.[4] Murie et al reported 1-year patient and allograft survival rates of 87% and 73% in 63 patients older than 55 years.[5] These researchers failed to show any significant difference in allograft survival compared to younger recipients. Tapson et al reported a 74% 2-year patient survival rate and that 8 of 13 allografts (61%) were functioning at a mean of 15 months after transplantation.[6] Others have reported good results in terms of patient and allograft survival (table 1).[7-10] Our results of 89% 1-year actuarial patient and 71% 1-year actuarial allograft survival compare favorably with what has been reported recently. Of the 16 kidneys still functioning 12 have serum creatinine levels of less than 2 mg./dl. The 2 deaths in this group occurred in patients with known but surgically uncorrectable coronary artery disease. Of the 6 grafts that failed 4 were lost within the first 6 months and all had failed by 1 year.

The improvement in patient and allograft survival noted may be attributable partly to the introduction of cyclosporine. In 1971 Simmons et al, using azathioprine and prednisone, reported 1-year patient and allograft survival rates of 40% and 20%, respectively, in patients older than 45 years.[3] In the same era Delmonico et al reported 1-year patient and allograft survival rates of 57% and 50%, respectively, in patients older than 51 years.[2] These lower survival rates reported from the precyclosporine era were attributed largely to the high dose of steroids used. In the series reported by Fehrman et al 17 patients were treated with azathioprine and steroids, and these patients had 1 and 3-year allograft survival rates of 59% and 41% compared to 65% and 54% in 38 cyclosporine treated patients.[4]

Death with a functioning transplant is a major cause of graft failure in elderly patients. The chief causes of death are cardiovascular disease and infection. These are inherent problems in this population of patients. Among 17 patients older than 65 years reported on by Roza et al 10 grafts were functioning at 3 to 28 months.[8] One kidney was lost to chronic rejection and 6 patients died with a functioning graft: 1 of infection and 5 of cardiovascular disease. In the series reported by Tapson et al 10 of 13 patients had a functioning graft 15 months after transplantation, 1 had primary nonfunction and the other 4 died with a functioning graft.[6]

The role of invasive pretransplant cardiac assessment is debatable. Jordan et al performed cardiac catheterization on all patients older than 55 years.[9] However, only 4 of these 67 patients required coronary revascularization before transplantation. Of the 3 coronary deaths 2 occurred in patients with minimal or no coronary artery disease. Howard et al performed stress thallium testing on 16 patients older than 65 years who had no cardiac symptoms before transplantation.[11] Of these patients 8 underwent cardiac catheterization based on these results but none required an operation. One patient with angina had cardiac catheterization and required coronary bypass surgery before transplantation. Four patients died of cardiovascular disease in the current series. Of our 22 patients 7 underwent a stress thallium test because of clinical symptoms and 6 had coronary arteriography. Only 1 patient had angioplasty preoperatively as a result of these studies with a successful outcome.

As reported by others,[12] we found a low incidence (3 allografts, or 13%) of allograft loss secondary to rejection. This low incidence of graft loss secondary to rejection occurred despite

TABLE 3. *Surgical complications, management and outcome*

Complication	No. Pts.	Management (No.)	Outcome
Cholecystitis	3	Cholecystectomy	Excellent
Ogilvie's syndrome	2	Colostomy (1), colonoscopy (1)	Excellent
Retroperitoneal hematoma	2	Observation	Excellent
Lymphocele	1	Ureteral injury, sepsis	Immunosuppression stopped, graft rejected
Renal artery thrombosis	1	Allograft nephrectomy	Pt. died of myocardial infarction at 10 days
Sigmoid colon perforation	1	Colostomy drainage	Sepsis, myocardial infarction, pt. died at 40 days

TABLE 4. *Medical complications and outcome management*

Complication	No. Pts.	Management	Outcome
Infection:			
Urinary tract infection	6	Antibiotics	Resolved without sequelae
Bacterial pneumonia	3	Antibiotics	Resolved without sequelae
Pneumocystis pneumonia	2	Trimethoprim-sulfamethoxazole	Resolved without sequelae
Cytomegalovirus pneumonia	1	Ganciclovir	Lost graft to chronic rejection
Herpes:			
Zoster	1	Acyclovir	Resolved without sequelae
Laryngitis	1	Acyclovir	Resolved without sequelae
Cardiovascular:			
Myocardial infarction	2		Died
Miscellaneous:			
Nephrotic syndrome	1		Stable
Steroid-induced diabetes mellitus	2	Steroids decreased	Resolved without sequelae
Gastritis	1	Antacids	Resolved without sequelae

the fact that HLA matching was not an important selection criterion in this series. With the use of cyclosporine many single center studies, including our own, currently report no effect of HLA matching or mismatching on renal transplant outcome.[13–15] Other reports of multicenter studies indicate a beneficial effect of matching.[16] However, this may partly reflect results from the pre-cyclosporine era. More recent data would suggest that matching is of benefit primarily for 6-antigen matched kidneys.[17] Regardless of matching, older patients may be less immunocompetent and, therefore, less likely to reject the grafts.

Historical comparison of survival statistics in end stage renal disease treatment programs is confounded by several issues. The results of transplantation in general have improved during the last decade due to increased sophistication of patient care, and the use of safer and more effective immunosuppression. Also, it is difficult to identify the selection bias inherent in most programs. Our patient and graft survival rates are comparable with those reported in other series (table 1). An alternative to renal transplantation is hemodialysis. Patient survival on dialysis is equivalent to that with transplantation. The European Dialysis and Transplant Association report of 1984 showed a 2-year actuarial survival of 71% for 60 to 69-year-old and 60% for 70 to 79-year-old patients on hemodialysis.[18] These results are comparable to the rates in the aforementioned transplant series (table 1).[4–10] Given that survival percentage is satisfactory with either form of therapy, quality of life may be more important in choosing treatment modality. Westlie et al reported a detailed retrospective analysis of mortality, morbidity and life satisfaction in 157 patients 70 years old or older who had started hemodialysis up to April 1983.[19] For patients who started dialysis after 1976 the 3-year survival rate was 50%. Quality of life was considered to be high. From the same institution, Husebye et al reported a prospective followup study in 1987 on 79 patients who had been interviewed in 1983.[20] At that time (1987) 54% of the 79 patients had died. Despite the optimism of the earlier 1983 report, 43% of the deaths followed voluntary withdrawal from dialysis, perhaps a reflection of the quality of life on dialysis. Analysis showed that psychosocial and not physical factors were prognostically important. The patients in this later series were apparently unselected, with less than 1% of all candidates being considered unfit for dialysis.

No formal assessment of the quality of life has been done in our study. However, no patient has chosen to discontinue therapy after transplantation. Compliance with medications is good and our impression is that patients are generally satisfied. Patients are considered for transplantation at the University of Pittsburgh once they are referred by their attending nephrologist. Patients are rarely rejected because they are considered medically unfit for transplantation. As would be expected, this group of patients has a high incidence of significant risk factors. However, a striking difference between this population and younger transplant recipients is the incidence of insulin-dependent diabetes mellitus. Approximately 30% of all transplant recipients at our center are diabetics. Nevertheless, only 1 of 22 patients older than 65 years had insulin-dependent diabetes mellitus as a cause of the renal failure in this series. Presumably, most diabetics have end stage renal disease at a younger age and, therefore, they undergo transplantation earlier.

In conclusion, these data support an integrated approach to the management of renal failure in elderly patients, that is either continuous ambulatory peritoneal dialysis, hemodialysis or transplantation may be appropriate for the individual patient at a particular time. Certainly, renal transplantation should not be denied on the basis of patient age alone. In fact, it may well be the treatment of choice for older patients in terms of survival and quality of life.

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