ONE-YEAR (PATIENT AND RENAL ALLOGRAFT) SURVIVAL FOLLOWING RENAL TRANSPLANTATION

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Abstract

Background: Renal transplantation offers a realistic therapeutic option to patients with end-stage renal disease (ESRD).

Objective: To evaluate one- year (patient and renal allograft) survival and comparing age and HLA-matching results as possible risk factors.

Methods: Fifty (50) patients underwent renal transplantation in the renal transplantation unit of Surgical Specialties Hospital-Baghdad from September 2000 to October 2002. None had diabetes mellitus or clinical evidence of symptomatic cardiac disease. All the transplanted kidneys were from living donors. Direct matching between the serum of recipient and lymphocytes of the donor was negative. HLA class I matching was performed. Recipients were followed for one year following renal transplantation clinically and by regular laboratory tests. Ultrasound and color Doppler examinations were performed when there was evidence of decreased urinary output, allograft dysfunction, or clinical suspicion of rejection. Graft nephrectomy, when needed, was done in the same center.

Results: Thirty-nine patients (78%) continued their lives one year following renal transplantation while eleven patients (22%) died during the first year following renal transplantation, due to cardiovascular complications and sepsis. Death following renal transplantation was compared with age and HLA-matching as possible risk factors. The comparison was not statistically significant. In thirty-eight patients (76%) the transplanted kidney was functioning normally after one year from renal transplantation. Twelve (12) patients (24%) needed graft nephrectomy on the basis of clinical picture of acute rejection aided by conventional sonographic and color Doppler examinations. Acute rejection was not confirmed by histopathological examination prior to graft nephrectomy.

Conclusions: Cardiovascular disease is common in renal transplant recipients and is a major cause of mortality in this population followed by sepsis. Age of recipient and HLA- matching results were not correlated to the one-year recipient mortality.

Key words: Acute rejection, cardiovascular diseases, one-year survival, renal transplantation.

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Introduction

Renal transplantation can restore patients with end-stage renal disease (ESRD) to nearly normal health. Regardless of whether the treatment modality is dialysis or transplantation, the major causes of death are, in order, heart disease, sepsis, and stroke[1].

It has been known for some time that cardiovascular mortality and morbidity are higher in renal transplantation than in the general population[2]. There is an approximate 10-fold higher incidence of cardiovascular mortality in renal transplant recipients than equivalent patients without renal disease. In contrast, when one considers all patients with ESRD, cardiovascular mortality is lower in transplant recipients than patients on maintenance hemodialysis. Kasiske[3] examined a large cohort of renal transplant

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recipients and found that, in a broad sense, traditional factors such as lipids, HgbA1C, and diabetes mellitus were associated with cardiac morbidity and mortality in a similar quantitative manner as in the general population.

An often-overlooked phenomenon in renal transplant recipients is cardiomyopathy, which in this population is thought to be multifactorial. Once again, the incidence of cardiomyopathy is significantly less in renal transplant recipients (10%) compared with patients on maintenance dialysis. Unfortunately, several commonly used immunosuppressive drugs interfere with the cardiovascular system.

One year graft survival rates are reported to be 80% for mismatched cadaveric renal grafts, 90% for non-identical living related grafts and 95% for human lymphocyte antigen-identical grafts[4]. A variety of medical and surgical catastrophes can occur following renal transplantation which compromise graft outcome. Technical failures, infections, and recurrence of the disease for which the transplant was performed are among the problems occasionally encountered in these patients. However, except for transplants performed between identical twins, transplant rejection continues to be the most important contributor to graft loss.

The aim of the study is to evaluate one- year (patient and renal allograft) survival and comparing age and HLA-matching results as possible risk factors and under the difficult circumstances of sanctions.

Patients & Methods

From September 2000 to October 2002, 50 patients underwent renal transplantation in the renal transplant unit of Surgical Specialties Hospital, Baghdad. The recipients and their potential donors were evaluated prior to transplantation. None was shown to have diabetes mellitus or clinical evidence of symptomatic cardiac disease. All transplanted kidneys were from living donors (LDs).

Recipients and their potential donors were ABO compatible. Direct matching was negative. HLA-matching class I only was performed as class II was not available. Panel reactive antibodies (PRA) test was performed. Recipients with less than 30 per cent reaction were chosen.

The hot ischemia time was ranging between 4-14 minutes. The cold ischemia time was ranging between 60-180 minutes. In (45) patients (90%) arterial anastomosis was to the external iliac artery (according to the surgeon's preference), while in (5) patients (10%) the anastomosis was to the internal iliac artery. The renal vein was anastomosed to the external iliac vein. The arterial anastomosis was done in an interrupted fashion, while the venous one was continuous. Extravesical technique for ureteroneocystostomy was used. Triple immunosuppressive therapy that consisted of cyclosporine, corticosteroids and azathioprine was used. Newer agents were not available.

Data collection

The recipients were followed for one year clinically and biochemically. Renal allograft dysfunction was defined as a persistent/or progressive elevation of serum creatinine. Conventional sonographic and color Doppler examinations were performed when there was clinical evidence of decreased urinary output, and/or laboratory findings of graft dysfunction.

Statistical analysis

Data were tabulated in a mean (±SD), number and percentage. Association between different variables was measured by using Fisher's exact test. P value < 0.05 was considered as statistically significant.

Results

Fifty patients aged (15-62) years; with a mean age (34.46 ± 12.4) years underwent renal transplantation. They were (35) males

(70%) and (15) females (30%). Thirty-nine patients (78%) continued their lives one year following renal transplantation while eleven patients (22%) died during the first year following renal transplantation, due to cardiovascular complications and sepsis. Cardiothoracic complications were responsible for death of (7) patients (63.63%).

Two of them died (they were 46 years and 25years) due to cardiac arrest in the immediate 24-hour period. No autopsy could be performed so the real cause of death could not be verified. Two patients developed acute rejection and after failure of anti-rejection medical therapy, graft nephrectomy was done and they were returned to hemodialysis but later died due to acute pulmonary edema. The remaining three patients died due to respiratory failure secondary to chest infection. Sepsis was responsible for death in (4) patients (36.36% of cases). One developed disseminated pulmonary tuberculosis. The other three had septic shock leading to death.

Table (1) shows the causes of death among recipients of transplanted kidney. Death following renal transplantation was compared with recipients' age and HLA matching as possible risk factors. The comparison was not statistically significant. Table (2) and table (3) show the correlation between death and both HLA matching and recipients' age respectively.

Table 1: Causes of death among recipients of transplanted kidney

Cause of death	**(n=11)**
Cardiopulmonary complication (s)	7 (63.63%)
Sepsis	4 (36.36%)

Table 2: Donor- recipient HLA class I – matching and recipients' death

One-year recipients' fate *	**Less than one haplotype (n=20)**	**One haplotype (n=30)**	**Total (n=50)**
Death	4	7	11 (22%)
Survival	16	23	39 (78%)

*** P value not significant**

Table 3: Age and recipients' death *

Age (years)	Dead (n=11)	Survived (n=39)	Total (n=50)
10-19	1	4	5 (10%)
20-29	2	13	15 (30%)
30-39	0	12	12 (24%)
40-49	6	5	11 (22%)
50-59	1	5	6 (12%)
60-69	1	0	1 (2%)

Thirty-three patients (68.75%) developed renal allograft dysfunction, which ranged from mild reversible dysfunction to severe deterioration that necessitated graft nephrectomy. After one year from renal transplantation the transplanted kidney was functioning normally in thirty-eight patients (76%) while twelve (12) patients (24%) needed graft nephrectomy on the basis of clinical picture of acute rejection aided by laboratory, conventional sonographic and color Doppler examinations. The diagnosis of acute rejection was confirmed by biopsy in two patients. Figure (1) illustrates the monthly percentage of deaths and renal allograft nephrectomy during the first year following renal transplantation.

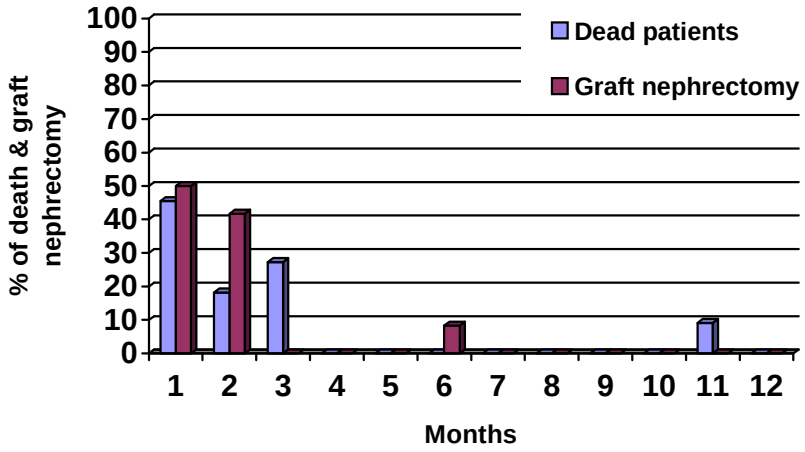

Figure 1: Monthly percentage of recipients' death and renal allograft nephrectomy

Discussion

Transplantation has revolutionized treatment of end- stage renal disease (ESRD) by proving more cost effective than hemodialysis, with a lower morbidity and improved quality of life. Both patient mortality and graft loss were excessive prior to 1970, reflecting the limitations of immunosuppressive therapy available at the time. As immunosuppressive therapy was

refined, patient survival improved. This was due to a decrease in the frequency of life-threatening infections. Currently, a 6-month patient survival of 95% is achievable at most centers, despite the fact that criteria for recipient selection have been liberalized to include older individuals and patients with systemic illnesses such as diabetes mellitus[5]. Other Registries now report 2-year patient survival exceeding 90% for HLA identical matches, and 85-90% for cadaveric and living-related non-HLA identical transplants[6-8].

Since cardiovascular disease (CVD) is the main cause of death in renal transplant recipients, optimal control of cardiovascular risk factors is essential in the long-term management of these patients[9]. Evidence is very suggestive that pre-transplant screening for CVD, treatment of hypertension, the use of low-dose aspirin, and smoking cessation will also help to reduce the incidence of post-transplant CVD. Less compelling are data suggesting that intensive glucose control in diabetics will safely decrease the incidence of CVD. Although there is little evidence that treatment of erythrocytosis will reduce CVD, hematocrits above 55% to 60% should probably be treated to prevent venous thrombosis. Vitamins for reducing homocysteine, antioxidant vitamins, and prophylaxis for potentially atherogenic infections are therapies that warrant additional study[3].

An attempt was made to evaluate the effectiveness of the clinical history and current screening techniques available in predicting post-transplant coronary artery disease and also to assess the role of coronary angiography as a pre-transplant screening technique. The conclusion was that clinical history and electrocardiogram (ECG) results are good, practical and low-cost screening methods, and that exercise stress testing and echocardiography were found to be of limited value. Coronary angiography is appropriate in certain high-risk groups but not necessary as part of screening in all potential renal transplant recipients[10].

The first renal transplantation in Iraq was performed in 1973. Renal transplantation surgery started in the Medical City in 1985. Several social and ethical issues of such surgical procedure were encountered.

In this study thirty-nine patients (78%) continued their lives one year following renal transplantation while eleven patients (22%) died during the first year following renal transplantation, due to cardiovascular complications and sepsis. Although recipients did not have symptoms or otherwise clear clinical evidence of diabetes mellitus or active cardiac disease, two of them died due to cardiac arrest in the immediate 24-hour period raising a question of anesthetic protocol during surgery or whether any further preoperative work up was needed. In our study Age of recipient and HLA-matching results were not proved to be correlated to the one-year recipient mortality.

Cardiovascular disease is common among renal transplant recipients and is a major cause of mortality in this population. Calcineurin inhibitors such as cyclosporin, although minimizing early acute rejection, are responsible for considerable nephrotoxicity, leading to progressive renal dysfunction and graft loss. The recent introduction of non-nephrotoxic immunosuppressants offers the possibility of improved renal function post-transplantation.

After one year from renal transplantation the transplanted kidney was functioning normally in thirty-eight patients (76%) while twelve (12) patients (24%) needed graft nephrectomy on the basis of clinical picture of acute rejection aided by laboratory, conventional sonographic and color Doppler examinations. The diagnosis of acute rejection was confirmed by biopsy in two patients.

The indications for allograft nephrectomy are to remove a symptomatic irreversibly rejected kidney and, in the case of a chronically rejected asymptomatic graft, to withdraw immunosuppression and to prevent the development of anti-HLA antibodies that could delay or prevent a subsequent transplantation[1].

In a previous study (42%) of non-functioning renal transplants required removal at some time. Graft failure due to acute or early acute rejection invariably necessitated removal. The recommendation was that transplant nephrectomy is reserved for the symptomatic cases[11].

Our figures of one-year patient and graft survival are less than the standard international figures. This study was undertaken while the country was under sanctions[12, 13]. We were short of many appliances, anesthetic drugs, antibiotics, anti sera, immunosuppressive drugs and kidney perfusion solutions. HLA class II was and still is not available. It was a hard decision to continue working with limited success or to give up. We hope that with a better supply of required drugs and equipment the results will pick up.

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