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Simultaneous Heart and Kidney Transplantation in Patients with End-stage Heart and Renal Failure

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Combined simultaneous organ transplantation has become more common as selection criteria for transplantation have broadened. Broadening selection criteria is secondary to improved immunosuppression and surgical techniques. The kidney is the most common extrathoracic organ to be simultaneously transplanted with the heart. A series of 13 patients suffering from both end-stage heart and renal failure underwent 14 simultaneous heart and kidney transplantations at Temple University Hospital between 1990 and 1999. This is the largest series reported from a single center. Three patients died during the initial hospitalization for an in-hospital mortality of 21%. Of 10 patients who left the hospital, 1-year survival was 100% and 2-year survival 75%. One patient required retransplant for rejection within the first year. Overall mortality at 1 and 2 years was 25 and 41%, respectively. Four out of nine (44%) patients greater than 5 years post-transplant were alive. Of the 10 patients who left the hospital, 66% were alive at 5 years. One patient succumbed to primary nonfunction of the cardiac allograft, while the four other deaths were secondary to bacterial or fungal sepsis. The patient's racial backgrounds were equally divided between African-American and white. These results are similar to those reported in a United Network of Organ Sharing Database (UNOS) registry analysis of 84 simultaneous heart and kidney transplants that found 1- and 2-year survival to be 76 and 67%, respectively. Simultaneous heart and kidney transplantation continues to be a viable option for patients suffering from failure of these two organ systems, although the results do not match those of heart transplant alone.

Key words: Combined heart kidney transplantation, end-stage renal disease, heart failure, heart transplantation, renal transplantation

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Introduction

Simultaneous transplantation of two organs for combined end-stage organ failure has been a reality since 1967 when Kelly et al. (1) described the first simultaneous pancreas and kidney transplant for diabetic nephropathy. Later, in 1978, Norman et al. (2) described the first combined simultaneous heart and kidney transplant in a patient maintained on an left ventricular assist device (LVAD) for 5 d prior to transplant. Since then two series of six patients have been published on this subject along with a review of the United Network of Organ Sharing Database (UNOS) registry data on 84 simultaneous heart and kidney transplants from the same cadaveric donors (3). The number of simultaneous heart and kidney transplants is increasing every year in the United States and 154 such procedures were performed in the United States over the 10-year period between 1989 and 1998 (4). We present our experience of 14 simultaneous heart and kidney transplants in 13 recipients.

Materials and Methods

Between January 1990 and October 1999, a series of 14 simultaneous heart and kidney transplants in 13 patients were undertaken at our institution (5,6). A retrospective review of medical records was completed on these 13 patients. The charts were reviewed for patient demographics, mortality, immunosuppression, graft function, donor characteristics, preoperative panel of reactive antibodies (PRA), human leukocyte antigen (HLA) typing and etiology of organ failure. A review of the literature on combined heart and kidney transplantation was also conducted. These results were compared with UNOS data for heart and kidney alone, UNOS data on simultaneous heart and kidney transplants and outcomes from heart and kidney alone at our institution.

The patient selection criteria include all patients with New York Heart Association class III and IV congestive heart failure, congestive heart failure with a high risk of sudden cardiac death, ischemic heart disease refractory to medical therapy and not amenable to bypass surgery or angioplasty, and malignant ventricular arrhythmias refractory to other therapies. The patients must have concomitant renal failure with creatinine clearances less than 30 mL/min and/or require hemodialysis. The patients were transplanted based on ABO blood group compatibility and cross-matching. Due to the time constraints, HLA typing was not done preoperatively but is reported. The hearts were procured by the cardiac transplantation service at our institution, and the kidneys by the surgical team designated by the organ procurement organization. The heart transplant was performed, and then the renal allograft was placed immediately following this procedure.

The patients were given perioperative cefazolin or vancomycin and gentamycin in the case of a penicillin allergy.

Postoperative immunosuppression was given according to our standard regimen which includes steroids, azathioprine or mycophenolate mofetil (MMF) and cyclosporine. Anti-lymphocyte induction was used selectively. Any early rejection episodes were treated with anti-T-lymphocyte antibodies, and in a case of humoral rejection, plasmapheresis. Steroids were given as a bolus at the time of transplantation and then tapered to a dose of between 10 and 20 mg/d of prednisone. Azathioprine was dosed at 1–3 mg/kg per day. MMF was given at a dose of 1000 mg twice daily and decreased if gastrointestinal side-effects could not be tolerated. Cyclosporine was started at 4 mg/kg each morning and 3 mg/kg each evening and doses were adjusted to maintain a trough level range of between 250 and 400 ng/mL. Patients who failed cyclosporine-based immunosuppression were placed on FK 506 with trough levels maintained between 10 and 15 ng/mL. Later episodes of rejection of the heart or kidney were treated with a steroid bolus and taper.

Surveillance for cardiac allograft rejection was accomplished by routine protocol endomyocardial biopsy weekly for 6 weeks, then every other week for 6 weeks, then every month for 3 months and then every other month for 6 months. The kidney allograft was followed with serial blood urea nitrogen and creatinine determinations. Core needle biopsy of the renal allograft was undertaken if there was an elevation in creatinine over baseline that did not respond to treatment of possible dehydration with intravenous fluid administration and when endomyocardial biopsy was negative for rejection.

Infection prophylaxis included miconazole lozenges four times daily, a single strength bactrim tablet once daily and acyclovir 200 mg three times daily. Patients were given H_2 blockers for prophylaxis against the development of peptic ulcer disease.

Results

The average age of the donors was 26 years (range 4–46). The donors were 71% Caucasian and 14% African-American, and the remaining two donors were Hispanic and Asian. Eight of the donors were male and six were female. The HLA mismatch between the donors and recipients was, on average, four antigens.

The average age the recipients in this study was 44 years (range 20–60). The ethnicity was equally divided between Caucasian and African-American. Sex of the recipients was equally divided. Fifty per cent of the patients had zero PRA prior to transplant and 50% had a measurable PRA ranging from 3 to 35. Two patients had LVADs placed as a bridge to transplantation. One of the LVADs was electric and the other was pneumatic. Preoperative ejection fraction was, on average, 18% (range 5–25). The major etiologies of heart failure were ischemic (43%), hypertensive dilated (22%) and idiopathic (14%). The main causes of renal failure were hypertensive (29%), and diabetic (21%) nephropathies. All patients were on hemodialysis.

In-hospital mortality was 21%. The mortalities at 1 and 2 years were 25 and 41%, respectively. The mortality rates led to an overall survival of 75% at 1 year and 59% at 2 years. Of the patients who survived the hospitalization for transplantation, the 1-, 2- and 5-year survival rates were 100, 75 and 66%, respectively. Kaplan–Meier survival rates for heart kidney transplant recipients in this series were 92 ± 7% at 30 d, 77 ± 12% at 1 year and 60 ± 14% at 2 and 5 years (see Figure 1) Sixty per cent of the deaths were among the African-American patients within the cohort. The causes of death were primarily from infectious complications (see Table 1) Three patients succumbed to overwhelming fungal infections from *Aspergillus* and *Candida* and one to bacterial sepsis due to methicillin-resistant *Staphylococcus aureus*. The remaining death was due to primary nonfunction. Seventy-five per cent of the infectious deaths were in African-American patients.

One patient had acute humoral rejection which was treated with OKT3, steroids, plasmapheresis and cytoxan. The patient underwent 8 months of plasmapheresis starting with three treatments per week and tapering to one treatment per month and is currently off pheresis on a regimen of cyclosporine, MMF and steroids. The patient's most recent BUN and Cr levels were 59 and 1.7, respectively. The patient's most recent heart biopsy showed no evidence of rejection. Another patient was treated for acute cellular rejection with steroids on two occasions.

The two patients who had LVADs placed as a bridge to transplantation both succumbed to fungal sepsis at 13 months following transplantation. During that period, one of the patients required retransplant for rejection of the first heart allograft.

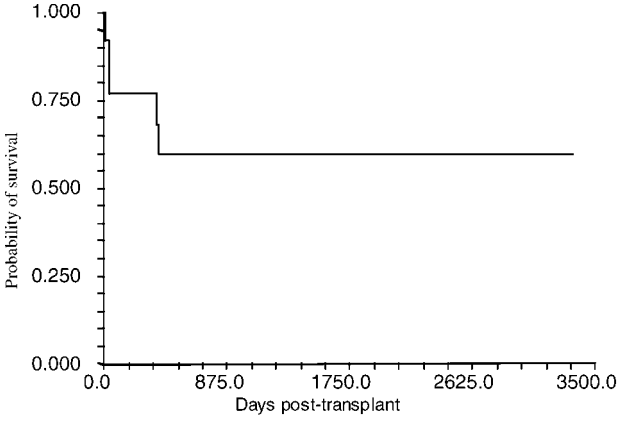


Figure 1: Kaplan–Meier survival curve for heart–kidney transplant recipients.

Table 1: Cause of death

Cause	n
Fungal sepsis (*Aspergillus*, *Candida*)	3
Bacterial sepsis (methicillin-resistant *Staphylococcus aureus*)	1
Primary non-function	1

A Kaplan–Meier analysis of over 600 heart-alone transplants performed at our institution between 1990 and 1999 was performed and yielded survival rates of 91 ± 1% at 30 d, 80 ± 1.5% at 1 year, 75 ± 1.7% at 2 years, 72 ± 1.7% at 3 years and 67 ± 1.9% at 5 years. Actual survival rates for kidney-alone transplants at our institution were 100% at 30 d, 100% at 1 year and 87% at 3 years. Thirty-four per cent of the patients in the heart-alone group had one or more episodes of 3A rejection or greater, while only 15% of the heart kidney recipients had this finding.

Discussion

The results of our single center series of 13 patients undergoing simultaneous heart and kidney transplantation are encouraging. The mortality at 1 year was 25% which compares favorably with the published 24% mortality of the UNOS series (3) (see Table 2) Kaplan–Meier analysis revealed a 1-year survival of 77% for heart–kidney recipients and 80% for heart alone at our institution. According to our data and the UNOS data, there is a 3–10% increase in mortality at 1 year in the combined transplant patients over heart-alone patients (3). This is most likely secondary to the morbidity of having two failing organs. Results from UNOS data show that African-American heart recipients have a significantly higher mortality at every stage than their white counterparts. Sixty per cent of the deaths in this series were in African-Americans (see Table 3) If the mortality rates of heart alone and kidney alone are combined, the 1-year mortality can be expected to be 20%. This value is close to the measured value of 25% mortality and 23% probability of death in our series and 24% in the UNOS series (3).

There was a significant amount of in-hospital mortality which was primarily from overwhelming sepsis due to bacterial or fungal infection. The patients waiting for heart transplants spend a significant period of time in the hospital, an average of 105 d preoperatively at our institution. The combination of additional morbidity and potential infectious risk related to dialysis access puts these patients at a significant likelihood for colonization and intermittent bacteremia. We question whether more rigorous postoperative or preoperative fungal prophylaxis might decrease the rate of fungal infections in this set of patients, since fungal infection was responsible for three of five deaths. Increased fungal and bacterial prophylaxis in the perioperative period for noncardiac transplants has been evaluated by Edmiston and Johnson (7) and found to improve outcome. Treating these patients with perioperative diflucan or liposomal amphotericin may decrease the incidence of fungal sepsis. Several of the septic deaths were in African-Americans. Increased septic complication in African-Americans has not been reported before; in fact, no effect of race on the incidence of infections after kidney transplantations is documented (8). The African-American patients in our series did indeed have equivalent immunosuppression as their white counterparts.

Table 2: Simultaneous heart–kidney transplant data

	Temple	UNOS registry (3)
Number of patients	13	84
Survival 1 year		
Actual	75%	
Kaplan–Meier probability	77%	76%
Survival 2 years		
Actual	59%	
Kaplan–Meier probability	60%	67%
In-hospital mortality	21%	N/A
Survival in patients surviving initial hospitalization		
1 year	100%	N/A
2 years	75%	N/A
5 years	66%	N/A

Table 3: Mortality of kidney and heart alone from UNOS registry and Temple (4).

	UNOS	Temple
Kidney transplant mortality		
1 year	5.6%	0%
3 years	11.4%	13%
5 years	18.4%	
Heart transplant mortality UNOS		
1 year	14.3%	20%
White	20.9%	
Africa-American	13.2%	
3 years	23.3%	28%
White	22.9%	
A frican-American	31.8%	
5 years	30.5%	33%
White	29.5%	
African-American	41.6%	

The outcome of patients on the waiting list for organ transplant is also informative. UNOS data report mortality of patients on the waiting list for kidney transplants between 4.7 and 5.4% from 1996 to 1998 (4). Over this same period, the mortality on the heart transplant list has been between 19.8 and 33% (4). There is no doubt that the mortality of combined heart and kidney transplantation is worth facing when the percentage of patients who die each year waiting is greater than the 1-year mortality figures. The survival of 77% of heart–kidney patients compared with 80% in heart alone is encouraging.

Analysis of the percentage of patients having rejection revealed a decreased rate in the heart kidney versus heart alone (15 vs. 34%). This may be indicative of the protective phenomenon of receiving two organs simultaneously.

The results of this 13 patient series confirm that treating combined end-stage renal and heart failure with simultaneous heart and kidney transplantations has a reasonable outcome. The mortality associated with the procedure is greater than a heart or kidney alone, but this is probably due to the increased morbidity of having two failing organs. Our mortality

figures are somewhat greater than those reported in the UNOS registry data, but this may be secondary to a higher percentage of African-American recipients in our series and patient population. Our data parallel those of UNOS, which show higher mortality in African-American recipients (4). Comparing survival of kidney alone to heart–kidney might show a large disparity, but the morbidity and mortality of maintaining a heart transplant alone on hemodialysis would most likely be prohibitive. The results do indicate that simultaneous heart and kidney transplantation should be offered to these patients with end-stage heart and renal disease. We feel that offering these patients simultaneous transplants is a reasonable use of the organs that are available to allocation.

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