Comparison of Survival of Patients with Heart and Lung Transplants on Peritoneal Dialysis and Hemodialysis

Organ transplantation is the most successful treatment available for patients with failure of the kidney, heart, and lungs. With the advent of improved surgical techniques and the availability of potent immunosuppressant drugs like calcineurin inhibitors in the last 3 decades, patients with heart and lung transplants are living longer with a functioning graft. However, one of the most severe side effects of the use of calcineurin inhibitor therapy is the development of chronic kidney disease (CKD) leading to end-stage renal disease (ESRD) (1,2). In the seminal paper by Ojo *et al.* in 2003, the incidences of advanced CKD (defined as estimated glomerular filtration rate < 30 mL/min/1.73m² body surface area) at 5 years after transplant of heart, lung, and combined heart and lung were 10.9, 15.8, and 6.9%, respectively (1). Twenty-nine percent of those who develop CKD after transplantation progressed to ESRD. The reported incidence of ESRD in the literature varies from 3.1 – 6.7% among patients with heart or lung transplant (1,3–7). These patients constitute 3 to 5% of the prevalent chronic hemodialysis (HD) patients in the USA (1). Both CKD and ESRD have a significant negative impact on survival as well as lifestyle and socioeconomic status (1,6,8).

The treatment options for organ transplant recipients who develop ESRD include home dialysis, in-center HD, or a kidney transplant, with the best results from renal transplantation, similar to other patients with ESRD. Most patients with heart and lung transplants are managed by HD as shown in the Canadian study in which 83.8% were on HD (6). Peritoneal dialysis (PD) is less frequently used (6,8). There is no consensus statement or randomized control trial to guide decisions for dialysis modality for ESRD patients with heart, lung, or both transplants (9). The perceived risk of peritonitis and poor technique survival are 2 possible reasons for the underutilization of PD in these immune-compromised patients (8,10,11). However, recent reports support the use of PD in non-renal

solid organ transplant patients (7,11). The benefits of PD in patients with heart and lung transplant include slower loss of residual renal function, better hemodynamic stability, and decreased risk of viral transmission and catheter-related bacteremia (9). The literature on patient outcomes comparing HD and PD is sparse. The current study evaluates mortality, dialysis-related infections, and hospitalizations in patients with heart, lung, or both heart and lung transplants on PD or HD at a single center over a span of 13 years.

METHODS

This is a single-center, retrospective analysis of data collected prospectively from Institutional Review Board (IRB)-approved registries of PD and HD at an outpatient dialysis unit affiliated with a large transplant program. All included patients signed informed consents at the initiation of dialysis at the outpatient center from January 1, 1999, to December 31, 2012. Heart, lung, or both heart and lung transplant patients were included in the analysis. Time on dialysis in the hospital prior to outpatient dialysis was not included. Patients with kidney and abdominal organ transplant and also 2 patients with heart and lung transplant who had switched between the 2 modalities of PD and HD before enrolling in the registries were excluded from the analysis. The registry data were collected from the time the patient began PD or HD in the outpatient center until the end points of transfer to another center or to death. The registry contains demographic information at the start of dialysis, the initial serum albumin, co-morbidity conditions allowing calculation of a co-morbidity index (Charlson Comorbidity Index), all hospitalizations, and

all infectious complications leading to hospitalization or related to dialysis.

STATISTICAL ANALYSIS

Demographic characteristic differences between PD and HD patients were examined using Student's t-test, chi-squared test, and Kruskal-Wallis test as appropriate. Cox regression examined association of survival with Charlson Comorbidity Index (CCI), diabetes, initial serum albumin, demographic characteristics, age, and dialysis modality. Kaplan-Meier analysis was performed to detect survival differences by dialysis modality.

RESULTS

The cohort of patients with heart, lung, or both transplants on dialysis at one outpatient dialysis center between 1999 and 2012 consisted of 26 patients: 10 on PD and 16 on HD. Patients were provided information on modalities and allowed to choose. The demographics, clinical characteristics of the patients, and outcomes are shown in Table 1. The rate of hospitalizations was significantly higher in the HD group. The most common cause of hospitalization was related to pulmonary diseases (22.4%), followed by vascular access-related hospitalization (19%). Pulmonary causes accounted for 8/40 (20%) of the admissions in the lung transplant patients (only 1 of whom was a patient on PD) and 5/19 (26%) in the heart transplant patients (all on HD) ($p = 0.58$). Ten percent of the hospitalizations were due to cardiac issues like arrhythmia and heart failure. The rates of dialysis-related infections were not significantly different in the PD compared to the HD group (0.36 vs 0.08 per dialysis year

TABLE 1
Demographics, Clinical Characteristics at the Start of Dialysis, and Outcomes of Heart and Lung Transplant Recipients on Chronic Outpatient Dialysis

	Peritoneal dialysis	Hemodialysis	<i>p</i> value
Total patients	10	16	
Women, <i>n</i> (%)	2 (20%)	3 (19%)	NS
African American, <i>n</i> (%)	0	5 (31%)	0.05
Age in years, mean (SD)*	55.9 (12.7)	54.9 (13)	NS
Diabetes mellitus, <i>n</i> (%)	3 (30)	8 (50)	NS
Charlson Comorbidity Index, median (range)*	5 (3–10)	5 (2–10)	NS
Median serum albumin, g/dL (range)*	3.8 (2.6–4.1)	3.1 (2.5–4.2)	0.03
Type of transplant:			NS
Lung transplant, <i>n</i> (%)	2 (20)	6 (37.5)	
Heart transplant, <i>n</i> (%)	8 (80)	9 (56)	
Combined heart-lung, <i>n</i> (%)	0	1 (6)	
Deaths per 1,000 patient years	273	308	0.89
Hospitalizations per 100 patient years	72.7	231.4	0.001
Dialysis-related infection per patient year	0.36 (peritonitis)	0.08 (bacteremia)	0.08
Exit-site infection per patient year	0.28	0.08	0.10
Total dialysis time, years	10.62	25.54	
Mean dialysis time per patient, months	12.74	19.15	0.34

SD = standard deviation.

* At the start of outpatient dialysis.

at risk, respectively, $p = 0.08$). However, the type of dialysis-related infection was quite different as the PD patients had peritonitis and the HD patients had bacteremia (2 episodes, both of which were in patients using a central venous catheter). The peritonitis rate of 0.36 episodes per year compares favorably to that of the entire cohort on PD at this single center during this time period of 0.25 episodes per year ($p = 0.23$).

There were 3 deaths on PD (30%) and 8 deaths on HD (50%). One of the patients on PD died from a complication of a pulmonary infection and the other 2 after withdrawal from dialysis. While the causes of death for 5 of the HD patients are unknown, 3 died from complication of sepsis, pneumonia, and stroke respectively. Survival was 90% and 88 % at 6 months ($p = 0.08$); and 80 % and 81% at 1 year ($p = 0.27$) for PD and HD patients respectively. Cox regression analysis controlling for initial serum albumin showed no difference in survival by modalities (hazard ratio [HR] 1.37, $p = 0.7$).

DISCUSSION

The development of moderate to advanced chronic kidney disease is frequent in heart and lung transplant patients. According to one report, 60% of patients with a heart transplant and ESRD had renal biopsy evidence of calcineurin inhibitor toxicity-related changes (2). Diabetes, hypertension, increasing age, smoking, and cardiac dysfunction also contribute to the risk for chronic kidney disease and subsequent ESRD in some of these patients (12). Development of ESRD increases mortality in these patients, most of whom are placed on in-center HD. We found that the survival on PD and in-center HD was similar in patients with heart or lung transplants while hospitalizations were less frequent on PD, suggesting that PD is a modality that should be considered more often. Ours is one of the largest and longest follow-up studies reported so far. The number of heart transplant patients in the present study is 17, which is lower than Goldstein but higher than Jayasena and the prior study from our center (5,8,13). The studies done prior to the 21st century favor HD as the preferred mode of dialysis (5,8,13). In the first description of the role of dialysis in heart transplant patients, Goldstein *et al.* followed 19 heart transplant patients on HD for 3 years and found that survival was 75% and 44% in the first year and second year, respectively (5). In an earlier study from our center, in the 12 patients (4 HD and 8 PD) with heart transplants followed for 2 years, there were 6 deaths (2 HD and 4 PD), and overall survival of the group was 81% and 44% in the first and second year, respectively (13). The mortality was higher in the PD than in the HD group (451 vs 273 deaths/1000 patient years, $p = 0.0001$).

In contrast to this earlier study from our program, with the more recent results we did not find any survival difference between HD and PD. While the previous paper pointed out that failed heart transplants with worsening cardiac function contributed to increased mortality in PD patients, in the more recent period we did not find any death related to failed allograft, suggesting improved management of immunosuppression. In addition the care of PD patients with respect to prevention of exit-site infection and peritonitis during more

recent times might have contributed to better survival. This is substantiated by the rate of peritonitis (0.36 per patient year) in the PD group that is almost the same as other PD patients without non-renal solid organ transplant in the registry.

Our results differ from a study of patients with heart and lung transplants on PD with a median follow-up of 10 months who had a high rate of peritonitis (0.8 episodes per year at risk) compared to the other patients (0.4 episodes per year at risk) (8). Two-year survival was also worse in the heart and lung transplants compared to the other patients on PD (25.2% vs 79%). However, the authors concluded that PD is a good choice in patients with poor cardiac function. Our survival was much better than reported in this study, and our peritonitis rates much lower.

The more recent literature is consistent with the present report showing favorable outcomes for patients with heart and lung transplants on PD. In comparison with patients on HD, patients on PD had fewer episodes of congestive heart failure and hospitalizations in the study by Ahmad *et al.* (7). The Canadian registry study highlighted the benefits of home-based therapy (PD and home HD) in patients with non-renal solid organ transplants (11). During the 24 months of follow-up of 25 patients (including 11 patients with liver transplant), these researchers found that the peritonitis rate was 0.41/year, similar to ours at 0.36/year. This study differs from our study in that we followed the patients for longer periods, there were no liver transplant patients included in our series, and none of our patients were on home HD.

To summarize, we found a higher hospitalization rate in heart and lung transplant patients on HD compared to PD, a non-significant higher but acceptable rate of infection (peritonitis) on PD, and similar survival with the 2 modalities. These results suggest that patients should be fully informed of the modality options so they can make an informed choice for the type of dialysis which fits their lifestyle best.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

Pramod Guru
Rachita Prakash
Heena Sheth
Filitsa Bender
Renee Burr
Beth Piraino*

University of Pittsburgh School of Medicine
518 Scaife Hall, Pittsburgh, PA

*email: piraino@pitt.edu

REFERENCES

1. Ojo AO, Held PJ, Port FK, Wolfe RA, Leichtman AB, Young EW, *et al.* Chronic renal failure after transplantation of a nonrenal organ. *N Engl J Med* 2003; 349(10):931–40.

2. Greenberg A, Egel JW, Thompson ME, Hardesty RL, Griffith BP, Bahnson HT, *et al.* Early and late forms of cyclosporine nephrotoxicity: studies in cardiac transplant recipients. *Am J Kidney Dis* 1987; 9(1):12–22.
3. Greenberg A, Thompson ME, Griffith BJ, Hardesty RL, Kormos RL, el-Shahawy MA, *et al.* Cyclosporine nephrotoxicity in cardiac allograft patients—a seven-year follow-up. *Transplantation* 1990; 50(4):589–93.
4. Pattison JM, Petersen J, Kuo P, Valentine V, Robbins RC, Theodore J. The incidence of renal failure in one hundred consecutive heart-lung transplant recipients. *Am J Kidney Dis* 1995; 26(4):643–8.
5. Goldstein DJ, Zuech N, Sehgal V, Weinberg AD, Drusin R, Cohen D. Cyclosporine-associated end-stage nephropathy after cardiac transplantation: incidence and progression. *Transplantation* 1997; 63(5):664–8.
6. Alam A, Badovinac K, Ivis F, Trpeski L, Cantarovich M. The outcome of heart transplant recipients following the development of end-stage renal disease: analysis of the Canadian Organ Replacement Register (CORR). *Am J Transplant* 2007; 7(2):461–5.
7. Ahmad M, Robert R, Bargman JM, Oreopoulos D. Advantages of peritoneal dialysis in comparison to hemodialysis, in cardiac allograft recipients with end stage renal disease. *Int Uro Nephrol* 2008; 40(4):1083–7.
8. Jayasena SD, Riaz A, Lewis CM, Neild GH, Thompson FD, Woolfson RG. Outcome in patients with end-stage renal disease following heart or heart-lung transplantation receiving peritoneal dialysis. *Nephrol Dial Transplant* 2001; 16(8):1681–5.
9. Perl J, Bargman JM, Jassal SV. Peritoneal dialysis after nonrenal solid organ transplantation: clinical outcomes and practical considerations. *Perit Dial Int* 2010; 30(1):7–12.
10. Andrews PA, Warr KJ, Hicks JA, Cameron JS. Impaired outcome of continuous ambulatory peritoneal dialysis in immunosuppressed patients. *Nephrol Dial Transplant* 1996; 11(6):1104–8.
11. Cornelis T, Rioux JP, Bargman JM, Chan CT. Home dialysis is a successful strategy in nonrenal solid organ transplant recipients with end-stage renal disease. *Nephrol Dial Transplant* 2010; 25(10):3425–9.
12. Bloom RD, Reese PP. Chronic kidney disease after nonrenal solid-organ transplantation. *J Am Soc Nephrol* 2007; 18(12):3031–41.
13. Bernardini J, Piraino B, Kormos RL. Patient survival with renal replacement therapy in heart transplantation patients. *ASAIO* 1998; 44(5):M546–8.
doi: 10.3747/pdi.2013.00299