

## Survival Experience of Peritoneal Dialysis Patients with Human Immunodeficiency Virus: A 17-Year Retrospective Study

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*Human immunodeficiency virus (HIV)-related renal disease is the third-leading cause of end-stage renal disease (ESRD) among African Americans aged 20 – 64 years. The number of HIV-infected (HIV+) patients reaching ESRD will increase exponentially over the next decade. Because of significant improvements in therapy and management during the last ten years, survival of HIV+ patients has improved. The survival experience of very long-term HIV+ peritoneal dialysis (PD) patients remains to be investigated.*

*The objective of the present study was to examine the important differences in clinical and laboratory parameters between HIV+ and HIV-negative (HIV-) PD patients. To assess the factors associated with better survival in HIV+ PD patients, we retrospectively reviewed the charts of 488 PD patients, including 53 HIV+ patients, for the period 1987 to September 2004. We collected demographic, clinical, and laboratory data, including CD4 cell counts and history of hospitalizations and peritonitis.*

*Maximum survival of HIV+ PD patients was 12.5 years as compared with 15.87 years in HIV- patients. Not surprisingly, HIV was a strong independent predictor of mortality in PD patients [relative risk (RR) = 3.09,  $p < 0.0001$ ]. In HIV+ patients, higher CD4 counts at the initiation of dialysis were strongly associated with better survival (RR = 0.10 and  $p < 0.0001$ ,  $\geq 200$  cells/mm<sup>3</sup> vs.  $\leq 50$  cells/mm<sup>3</sup>). In univariate analysis, use of highly active antiretroviral therapy (HAART) was associated with significantly improved survival in HIV+ PD patients. Patients treated with 1 or*

*2 drugs had a 4.3-times higher mortality risk than those who received HAART therapy ( $p = 0.012$ ). Independent associations were seen between HIV and younger age, African American race, male sex, and lower serum albumin. The rates of hospitalization ( $p < 0.0001$ ) and peritonitis ( $p < 0.01$ ) were significantly higher in HIV+ patients than in HIV- patients. Very long-term survival of HIV+ patients with chronic renal failure is possible on PD therapy. Morbidity and mortality of these patients may be improved with HAART therapy, better nutrition, and treatment of peritonitis.*

### Key words

Human immunodeficiency virus, HIV, survival, CD4 count, highly active antiretroviral therapy, HAART

### Introduction

According to data from the Joint United Nations Programme on HIV/AIDS at December 2004, approximately 39.4 million people (35.9 – 44.3 million) are infected with the human immunodeficiency virus (HIV) worldwide. Infection with HIV is a common cause of nephropathy leading to end-stage renal disease (ESRD), particularly among African Americans (1,2). Although focal segmental glomerulosclerosis with collapsing features is the most common histologic lesion in these patients, other lesion types may also occur (1,3).

Because of improvements in medical therapy, the incidence and mortality of AIDS-defining diseases have both been decreasing in countries where highly active retroviral therapy (HAART) is available (4,5). Because more patients are living with HIV infection, the number of HIV-infected (HIV+) patients reaching ESRD is increasing. The incidence and prevalence of HIV+ ESRD patients are increasing in the U.S.

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ESRD population (5). Despite the encouraging reports regarding improved survival of HIV+ dialysis patients, morbidity and mortality among these patients remain higher than in other ESRD patients (6).

Information on the effectiveness of antiretroviral medication in reducing the mortality of HIV+ peritoneal dialysis (PD) patients is limited. A better understanding of the factors associated with poor outcomes in HIV+ dialysis patients may help to improve outcomes in those patients. More detailed information about the demographic, clinical, and metabolic characteristics of that population, and the benefits of their use of antiretroviral medication, may improve treatment.

The objective of the present study was to examine the differences in various demographic, clinical, and laboratory parameters between HIV+ and other PD patients and to assess the factors associated with survival in the HIV+ patients.

### Patients and methods

We retrospectively reviewed the medical records of 488 PD patients, including 53 HIV+ patients who attended Long Island College Hospital from 1987 to September 2004. We collected demographic information (age, race, sex), clinical data (diabetes, hypertension, HIV seropositivity), laboratory data (CD4 cell count, albumin, cholesterol, creatinine, and parathyroid hormone levels). We also recorded the history of HIV medication for every HIV+ patient. History of hospitalization and peritonitis were collected up to 1999.

### Statistical analysis

Continuous variables are reported as mean  $\pm$  standard deviation. For selected comparisons between group means, either parametric (*t*-test) or nonparametric (Mann–Whitney test) methods were used, as applicable. Comparisons of proportions and categorical variables used the chi-square test. Observed survival of patients was computed by the Kaplan–Meier method (7). The log-rank test was used to compare survival curves. We performed univariate Cox regression survival analyses to measure the association of various factors with outcomes. Multivariate Cox regression analysis was used to determine independent predictors of survival. All analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, U.S.A.).

## Results

### Demographics and patient characteristics

The HIV+ PD patients were younger than the HIV-negative (HIV–) patients (41 years vs. 56 years,  $p < 0.0001$ ). Among HIV+ patients, the percentages of African Americans (83% vs. 57%,  $p < 0.001$ ) and men (85% vs. 43%,  $p < 0.0001$ ) were significantly higher than among the HIV– patients. The percentage of patients with diabetes was lower among the HIV+ patients (9% vs. 47%,  $p < 0.0001$ ). Among the HIV+ patients, causes of ESRD were diabetes (6%), hypertension (19%), glomerulonephritis (2%), HIV (64%), and other or unknown causes (9%). In HIV– patients, the causes of ESRD were diabetes (39%), hypertension (33%), glomerulonephritis (8%), polycystic kidney disease (4%), obstruction (2%), and other or unknown causes (14%).

### Laboratory data

Baseline levels of serum albumin (2.63 g/dL vs. 3.56 g/dL,  $p < 0.0001$ ), total cholesterol (185 mg/dL vs. 204 mg/dL,  $p = 0.03$ ), and parathyroid hormone (249 pg/mL vs. 384 pg/mL,  $p = 0.021$ ) were significantly lower in HIV+ patients than in HIV– patients. But levels of serum creatinine were significantly higher in HIV+ patients (12.3 mg/dL vs. 10.6 mg/dL,  $p = 0.028$ ). Mean values of all variables measured over the study period showed similar results. In HIV+ patients, baseline levels of mean and median CD4 count were  $187 \pm 217$  cells/mm<sup>3</sup> and 116 cells/mm<sup>3</sup> respectively. Minimum and maximum CD4 counts were 3 cells/mm<sup>3</sup> and 845 cells/mm<sup>3</sup> respectively.

### Outcome and survival

For HIV+ patients, the mean, maximum, and median survivals were  $2.40 \pm 2.87$  years, 12.53 years, and 1.23 years respectively. For HIV– patients, the mean, maximum, and median survivals were  $2.48 \pm 2.49$  years, 15.87 years, and 1.714 years respectively. During the study period, 258 HIV– patients (59%) and 39 HIV+ patients (74%) died ( $p = 0.06$ ). Expectedly, following 17 years of observation, the cumulative observed survival of HIV+ patients was significantly lower ( $p = 0.014$ ) than that of HIV– patients [Figure 1(A)]. Survival adjusted for age, race, sex, and diabetes status yielded results that were more significant [ $p < 0.0001$ , Figure 1(B)]. Using the Cox multivariate regression analysis, age [relative risk

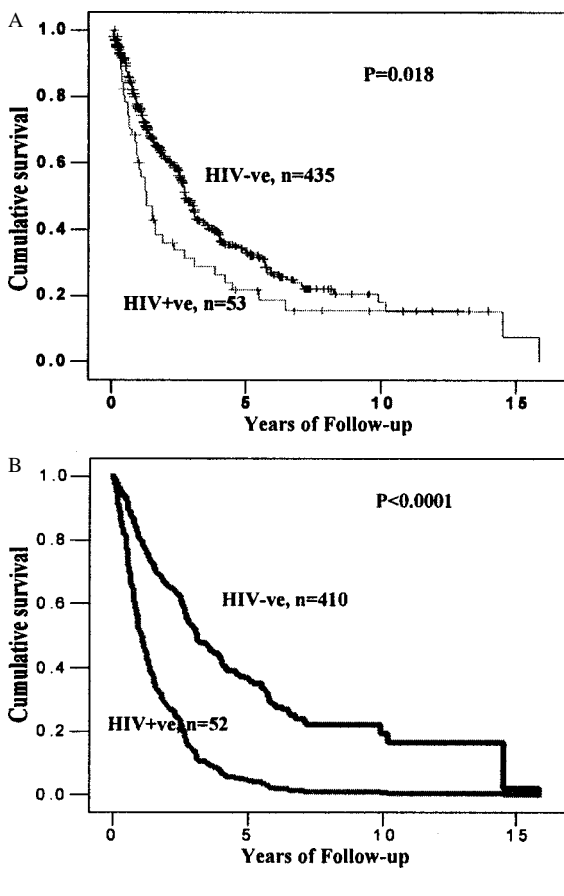


FIGURE 1 (A) Observed survival in peritoneal dialysis (PD) patients by human immunodeficiency virus (HIV) status. (B) Survival of PD patients by HIV status, adjusting for age, race, and diabetes status.

(RR = 1.036,  $p < 0.0001$ ], race (African American vs. other race: RR = 0.75,  $p = 0.025$ ), diabetes (RR = 1.51,  $p = 0.002$ ), and HIV status (RR = 3.09,  $p < 0.0001$ ) were independent predictors of mortality in PD patients. The HIV+ patients had a relative risk of mortality 3 times that of the HIV- patients.

We stratified the HIV+ patients into three groups by baseline CD4 count. Survival of HIV+ patients with a baseline CD4 count of 200 cells/mm<sup>3</sup> or more and 50 – 199 cells/mm<sup>3</sup> was significantly better than the survival of patients with a CD4 count of 50 cells/mm<sup>3</sup> or fewer ( $p < 0.0001$ , Figure 2). By univariate Cox regression analysis, higher levels of serum albumin, higher CD4 count, and HIV therapy with HAART were associated with a reduced risk of mortality in

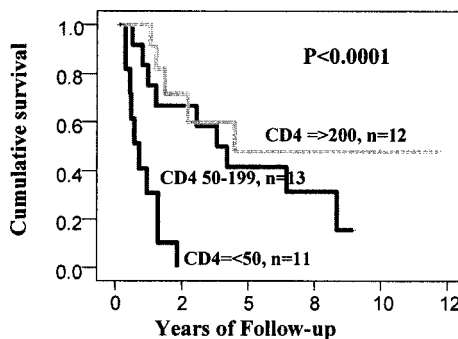


FIGURE 2 Observed survival in peritoneal dialysis patients positive for the human immunodeficiency virus, by enrollment CD4 count.

HIV+ patients. Each 1 g/dL increase in baseline serum albumin level was associated with a 43% reduction in relative risk of death. Patients with a CD4 count of 200 cells/mm<sup>3</sup> or more had a 90% reduction in relative risk of death as compared with patients whose CD4 counts were 50 cells/mm<sup>3</sup> or fewer. Patients who received single or double antiretroviral therapy had a 4.3-times greater risk of death than did those who received HAART therapy ( $p = 0.012$ ). No significant difference in the relative risk of death was seen between patients taking single or double therapy and those receiving no drug therapy at all ( $p = 0.20$ , Table I). In the multivariate Cox regression analysis, after adjustment for confounding variables that influenced survival in the univariate model, only CD4 count was an independent predictor of mortality risk in HIV+ PD patients.

The rate of hospitalization (3.59 admissions vs. 1.64 admissions per patient year,  $p < 0.0001$ ) and the

TABLE I Predictors of mortality in patients positive for the human immunodeficiency virus (HIV)—univariate Cox regression analysis

	Relative risk	p Value
Albumin (g/dL)	0.57	0.03
CD4 count (cells/mm <sup>3</sup> )		
≥200 vs. ≤50	0.10	<0.0001
50–199 vs. ≤50	0.16	0.001
HIV therapy		
Without vs. HAART	2.385	0.067
Single or double vs. HAART	4.3	0.012
Single or double vs. without	1.80	0.20

HAART = highly active antiretroviral therapy.

rate of peritonitis (1.4 episodes vs. 0.84 episodes per patient year,  $p < 0.01$ ) were significantly higher in HIV+ patients than in HIV- patients.

### Discussion

The results of the present study indicate that long-term survival of HIV+ patients—up to a maximum of 12.5 years—is possible on PD therapy. Median survival of our HIV+ patients was 1.23 years. A gradual improvement in the survival of HIV+ ESRD patients has been seen since the mid-1990s (8). Tebben *et al.* (9) reported a median survival of 10 months for HIV+ continuous ambulatory dialysis patients. Kimmel and colleagues (10) reported a median survival of 18.5 months for HIV+ continuous ambulatory peritoneal dialysis patients.

Despite improvement in the survival of HIV+ patients over the years, our study shows that their survival is still extremely low as compared with HIV- PD patients. Interestingly, even though most of our HIV+ patients were African American, younger, and nondiabetic, cumulative observed survival of those patients was significantly lower than the survival of HIV- patients. The survival difference became stronger when adjusted for those confounding variables. The survival of HIV+ dialysis patients has been reported to possibly depend on the clinical and immunologic stage of HIV infection (9,11,12).

The influence of ESRD and PD on the survival of HIV+ patients have not been critically examined. By univariate analysis, we found that higher serum albumin, increased CD4 count, and HAART therapy were associated with better survival in our HIV+ PD patients.

Serum albumin, a marker of nutrition, is a well-established, strong predictor of survival in dialysis patients (13). Levels of serum albumin are lower in PD patients than in HD patients. It may be possible that loss of albumin during PD negatively affected the survival of our HIV+ PD patients. However, some reports have shown no significant difference in survival between HIV+ patients on HD and on PD (10).

In the present study, CD4 count was the best predictor of survival in our HIV+ PD patients. This finding agrees with a previously published report (8). In univariate analysis, HAART therapy was associated with significantly improved survival in our HIV+ PD patients. However, patients not treated with HAART included those from an earlier part of the study (be-

fore 1997) when HAART was not the standard of care and those who were noncompliant. Rodriguez *et al.* (8) could not demonstrate a significant association between HAART use and survival in HIV+ dialysis patients, a result that may have been caused by ineffective prescription of HAART therapy. However, it has been reported that HAART may improve renal outcomes in HIV+ renal disease patients (14).

The observed higher rate of peritonitis in the present study confirms previously published reports by us and by other workers (9,15). In contrast, two other reports could not find a significant difference in the prevalence of peritonitis in HIV+ PD patients (10,16). Our observations regarding the higher rate of hospitalization among HIV+ PD patients as compared with HIV- patients agrees with a report by Tebben and colleagues (9).

The present study has a few limitations. All observational studies, including this one, are subject to potential bias. Also, the clinical and immunologic stages of all HIV+ patients are unknown.

### Conclusions

Very long-term survival (up to a maximum of 12.5 years) in HIV+ chronic renal failure patients is possible on PD therapy. Morbidity and mortality in these patients can be improved with better nutrition, use of HAART therapy, and treatment of peritonitis.

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