Impact of Obesity on Modality Longevity, Residual Kidney Function, Peritonitis, and Survival Among Incident Peritoneal Dialysis Patients

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Background: The prevalence of severe obesity, often considered a contraindication to peritoneal dialysis (PD), has increased over time. However, mortality has decreased more rapidly in the PD population than the hemodialysis (HD) population in the United States. The association between obesity and clinical outcomes among patients with end-stage kidney disease remains unclear in the current era.

Study Design: Historical cohort study.

Setting & Participants: 15,573 incident PD patients from a large US dialysis organization (2007-2011).

Predictor: Body mass index (BMI).

Outcomes: Modality longevity, residual renal creatinine clearance, peritonitis, and survival.

Results: Higher BMI was significantly associated with shorter time to transfer to HD therapy (*P* for trend < 0.001), longer time to kidney transplantation (*P* for trend < 0.001), and, with borderline significance, more frequent peritonitis-related hospitalization (*P* for trend = 0.05). Compared with lean patients, obese patients had faster declines in residual kidney function (*P* for trend < 0.001) and consistently achieved lower total Kt/V over time (*P* for trend < 0.001) despite greater increases in dialysis Kt/V (*P* for trend < 0.001). There was a U-shaped association between BMI and mortality, with the greatest survival associated with the BMI range of 30 to < 35 kg/m^2 in the case-mix adjusted model. Compared with matched HD patients, PD patients had lower mortality in the BMI categories of < 25 and 25 to < 35 kg/m^2 and had equivalent survival in the BMI category ≥ 35 kg/m^2 (*P* for interaction = 0.001 [vs < 25 kg/m^2]). This attenuation in survival difference among patients with severe obesity was observed only in patients with diabetes, but not those without diabetes.

Limitations: Inability to evaluate causal associations. Potential indication bias.

Conclusions: Whereas obese PD patients had higher risk for complications than nonobese PD patients, their survival was no worse than matched HD patients.

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The prevalence and severity of obesity among patients with end-stage renal disease (ESRD) has increased over time since the mid-1980s in developed countries.[1] This epidemic has occurred in parallel with trends in the general population, but has been more dramatic among patients with ESRD in the United States.[2-4] This difference in the observed secular trends of obesity can be explained by the heightened risk for chronic kidney disease among obese patients and those with diabetes[5,6] and also by the "obesity paradox" of patients with ESRD, for whom obesity is unexpectedly associated with greater survival.[7-10]

Interestingly, whereas the obesity paradox has consistently been observed among patients with ESRD receiving hemodialysis (HD), there are inconsistent data among those receiving peritoneal dialysis (PD).[11-17] It is generally thought that dialysis clearance may be less adequate in obese PD versus HD patients due to less efficient solute and fluid removal, although a small observational study has shown the feasibility of achieving adequate solute clearance in obese PD patients.[18] Other studies have shown that obesity is associated with higher risk for peritonitis and more rapid decline in residual kidney function,[19,20] both important risk factors for death and transfer to HD therapy.[21-23] A previous study of US Renal Data System (USRDS) data demonstrated that PD patients with obesity, defined as those with body mass index (BMI) ≥ 30 kg/m^2, showed faster transfer to HD therapy yet similar survival compared with PD patients without obesity.[14] Furthermore, among patients with ESRD who are obese, receipt of PD has been associated with equivalent or higher mortality as compared to receipt of HD.[24,25] These data have discouraged nephrologists from recommending PD as a treatment option for obese patients with ESRD,[26,27] and some facilities have listed severe obesity as a contraindication to PD therapy.[28-32]

However, most of these data were derived from noncontemporary cohorts that may not be generalizable to present-day dialysis populations. Mortality has decreased more rapidly in the PD versus HD population in the United States,[4,33] likely due to advances in PD delivery, efficacy, and safety during the past 2 decades. There is a progressive attenuation in mortality risk associated with PD in more recent cohorts.[34] Nevertheless, it remains unclear whether these advances have influenced the association between obesity and clinical outcomes in the current era. Thus, we hypothesized that the severity of obesity, expressed as BMI, is incrementally associated with adverse clinical outcomes and that the survival advantage of PD is attenuated among obese patients with ESRD.

Methods

Patients

We retrospectively extracted, refined, and examined data from all incident patients with ESRD who were 18 years or older in facilities operated by a large dialysis organization in the United States from January 1, 2007, through December 31, 2011.[35] Data used for analyses were deidentified. We selected patients who underwent PD more than 1 day during the follow-up period. We then excluded patients without data for BMI or residual renal clearances of urea and creatinine during the first 91 days of PD therapy (Fig 1). We further excluded patients with weekly renal creatinine clearance (CL_{cr}) > 300 L/1.73 m^2. Differences in characteristics at PD therapy initiation between included versus excluded patients were compared by standardized differences due to the relatively large sample size of this study (Table S1).[36,37]

This study was approved by the institutional review committees of the Los Angeles Biomedical Research Institute at Harbor-UCLA, University of California Irvine Medical Center, and the University of Washington, with the exemption of obtaining written consent given the large sample size, anonymity of the patients studied, and nonintrusive nature of the research.

Demographic, Clinical, and Laboratory Measures

All information was obtained from the electronic database of the dialysis provider. Blood samples were drawn using uniform techniques in all dialysis clinics and were transported to a central laboratory in Deland, FL, typically within 24 hours. To minimize measurement variability, all repeated measures for each patient during the first quarter (or 91 days) of PD therapy were averaged and then used as baseline data in all analyses. We calculated residual renal CL_{cr} as the average of renal urea and creatinine clearances, indexing to body surface area.[38] Actual body weight, not ideal body weight, was used to calculate Kt/V.

BMI was categorized in 6 groups (<20, 20-<25, 25-<30, 30-<35, 35-<40, and ≥40 kg/m^2). Given the established cardiovascular risk profiles among HD patients, severe obesity was defined as BMI ≥ 35 kg/m^2.[39]

Statistics for Clinical Outcomes Among Patients Receiving PD

Patients were followed up from their first day of PD therapy until their death or 60 days after transfer to HD therapy or kidney transplantation. Outcomes of interest were all-cause death, transfer to HD therapy, kidney transplantation, peritonitis-related and non–peritonitis-related hospitalization, and trajectories of solute clearance indexes (ie, renal CL_{cr} and renal, peritoneal, and total weekly Kt/V). Transfer to HD therapy was defined as not undergoing PD for 60 or more days.

Associations of the BMI categories with the competing outcomes of death, transfer to HD therapy, and kidney transplantation were examined in the entire PD cohort using cause-specific hazards models by treating competing events as censoring. Proportional hazards assumptions were tested using log-log plots and Schoenfeld residuals. Associations with peritonitis-related and non–peritonitis-related hospitalizations were also examined by the negative binominal regression model.

Models were examined with 3-level sequential adjustments as follows: (1) unadjusted model that included BMI categories only; (2) case-mix adjusted model that included age, sex, race/ethnicity, cause of ESRD, the 6 comorbid conditions in Table 1, log-transformed dialysis vintage, and log-transformed 5-year cumulative number of incident PD patients treated per facility (as a proxy for PD facility experience); and (3) fully adjusted model that included all covariates in the case-mix model plus log-transformed weekly renal CL_{cr}, weekly peritoneal Kt/V, normalized protein nitrogen appearance, and the 6 laboratory variables in Table 1. The case-mix–adjusted model was a priori defined as the primary model given the potential over-adjustment in the fully adjusted model.

To examine the association of BMI with change in solute clearance indexes over time, patient follow-up time was divided into quarters (or 91-day periods) from the date of PD therapy initiation up to 2 years, and we used the

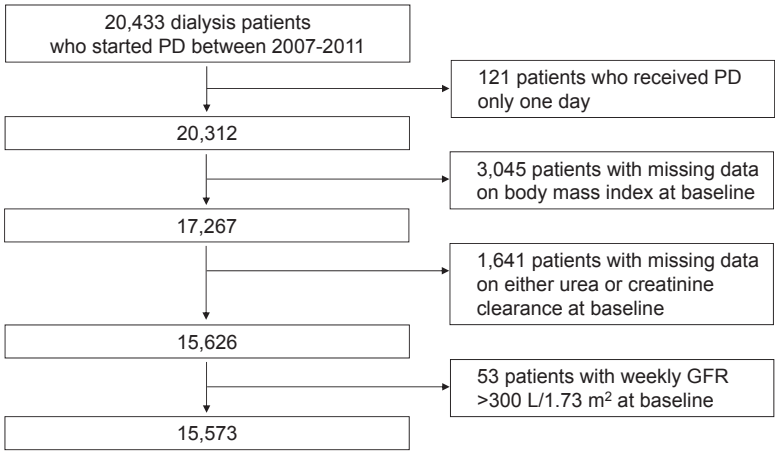

Figure 1. Flow diagram summarizes the criteria used to constitute the analytic cohort. Abbreviations: GFR, glomerular filtration rate; PD, peritoneal dialysis.