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Racial and Ethnic Differences in the Association of Body Mass Index and Survival in Maintenance Hemodialysis Patients

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Abstract

Background—In maintenance hemodialysis (HD) patients, overweight and obesity are associated with survival advantages. Given greater survival of minority maintenance HD patients, we hypothesized that elevated body mass index (BMI) is more strongly associated with lower mortality among Blacks and Hispanics relative to non-Hispanic whites.

Study design—Retrospective, cohort study.

Setting and participants—We examined a 6 year (2001–2007) cohort of 109,605 maintenance HD patients including 39,090 Blacks, 17,417 Hispanics and 53,098 non-Hispanic white maintenance HD outpatients from DaVita dialysis clinics. Cox proportional hazards models examined the association between BMI and survival.

Predictor—Race and BMI.

Outcomes—All cause mortality.

Results—Patients were (mean±SD) 62±15 years old and included 45% women and 45% diabetics. Across 10 a priori selected BMI categories (<18 to ≥40 kg/m²) higher BMI was associated with greater survival in all 3 racial/ethnic groups. Hispanic and Black patients,

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however, experienced consistently higher survival gains compared to non-Hispanic Whites across almost all BMI categories. Hispanics in the ≥ 40 kg/m² category had the lowest death hazard ratio (HR, 0.57; 95% confidence interval [CI], 0.49–0.68) compared to non-Hispanic Whites in the 21.5–<23 kg/m² group (reference category). While the inverse association was observed for all subgroups, Black maintenance HD patients exhibited the largest decline in death HR with increasing BMI.

Limitations—Race and ethnicity categories were based on self-identified data.

Conclusions—Whereas survival advantage of high BMI is consistent across all racial/ethnic groups, Black maintenance HD patients had the strongest association of high BMI with improved survival.

Index Words

obesity; survival; hemodialysis; race; non-Hispanic white; Black; Hispanic

Approximately 23 million people in the U.S. have chronic kidney disease (CKD) with over 400,000 having CKD stage 5 and requiring maintenance dialysis treatment to survive.(1) According to the United States Renal Data System (USRDS), dialysis patients have an average life expectancy of 5 years, although this varies by race.(2) For example, Black and Hispanic maintenance dialysis patients have a lower mortality rate than their non-Hispanic white counterparts.(3–6) This survival advantage persists even after adjusting for such important factors as co-morbid diseases and laboratory abnormalities.(4, 7) Furthermore, race may confound the association between dialysis adequacy and survival.(8) In patients with non-dialysis-dependent chronic kidney disease (CKD) racial differences are also observed. Among non-dialysis-dependent CKD patients, Blacks have a lower observed mortality when compared to non-Hispanic Whites.(9) However, higher mortality of Blacks in early stages of CKD may result in the selection of a subgroup with fewer co-morbid diseases and better survival in later stages of CKD.(9) Among dialysis patients, Blacks and Hispanic have greater survival,(6, 10, 11) which may be related to their better nutritional status.(12)

Along with co-morbid diseases and certain laboratory abnormalities, overweight and obesity, defined as a body mass index (BMI) of 25–29.9 kg/m² and ≥ 30 kg/m² respectively, correlate with greater survival in maintenance hemodialysis (HD) patients(13–16) despite their associations with increased morbidity and mortality in the general population without CKD.(17) Notwithstanding the occasional observation that abdominal (visceral) obesity is associated with a high risk of all-cause and cardiovascular mortality, even in maintenance HD patients,(18) in virtually all observational studies a higher BMI is associated with greater survival in this population.(13–16)

In the general population, the prevalence of obesity varies substantially by race and ethnicity along with gender.(19) Black women, for instance, have higher rates of obesity than non-Hispanic White women of all ages; by contrast, the inverse association is found in men, in that non-Hispanic White men have higher rates of obesity than their Black counterparts.(19) Additionally, the prevalence of obesity in Hispanic men and women is higher than in the non-Hispanic White population.(19) Maintenance HD patients also display similar patterns of racial differences in obesity. Glanton et al. reported a 22% higher adjusted prevalence of obesity in Blacks than in non-Hispanic Whites in ~150,000 End Stage Renal Disease (ESRD) patients in the USRDS database.(20) The same study also reported slightly higher hazard ratios for mortality in non-Caucasian than in Caucasian ESRD patients with BMI<22 kg/m².(20) To our knowledge this is the only study that reports racial differences in the

association of BMI with mortality but with known USRDS database limitations such as lack of laboratory measures or dialysis treatment data.

Using a large and contemporary cohort of maintenance HD patients from a single dialysis provider, we examined the hypothesis that, while higher BMI is associated with greater survival, the association differs by race and ethnicity and that these differences in BMI-survival associations may have a bearing on survival advantages of minority maintenance HD patients.

Methods

Patients

We obtained, refined, and analyzed data from all individuals with chronic kidney disease (CKD) stage 5 who underwent maintenance HD treatment from July 2001 through June 2007 in one of 580 outpatient Davita Inc (prior to its acquisition of former Gambro dialysis facilities) dialysis facilities. The study was approved by all relevant Institutional Review Committees. Due to the large sample size, the anonymity of the patients studied, and the non-intrusive nature of the research, the study is exempt from the requirement of written consent.

The original 6-year (7/2001-6/2007) national database of all DaVita maintenance HD patients included 109,605 subjects (Figure S1; available as online supplementary material). The first (baseline) studied quarter for each patient was the calendar quarter in which the patient's hemodialysis vintage was >90 days. Patients who received hemodialysis treatment in the baseline quarter and who had a BMI between 12 – 60 kg/m² and age between 16–99 years in the baseline quarter were included in the present study.

Clinical and Demographic Measures

The creation of the cohort has been described previously.(12, 21–25) To minimize measurement variability, all repeated measures for each patient during any given calendar quarter, i.e., over a 13-week interval, were averaged and the summary estimates were used in all models. Average values were obtained from up to 20 calendar quarters (from July 1, 2001 through June 30, 2006) for each laboratory and clinical measure for each patient over the 6-year cohort period, and quarter was included as a time-dependent variable in the analyses. Patients' outcomes were followed for 4 more quarters, i.e. up to June 30, 2007. Dialysis vintage was defined as the duration of time between the first day of dialysis treatment and the first day that the patient entered our cohort.

Thirteen-week averaged post-dialysis weight and baseline height were used to calculate the body mass index (BMI=weight[kg]/height squared[m²]).(26) We divided BMI into ten *a priori* selected categories and defined the following ranges: moderately to severely underweight (<18 kg/m²), mildly underweight (18–19.99 kg/m²), borderline low normal (20–21.49 kg/m²), low to moderate normal (21.5–22.99 kg/m²), high normal (23–24.99 kg/m²), mildly overweight (25–27.49 kg/m²), moderately overweight (27.5–29.99 kg/m²), mild obese (30–34.99 kg/m²), moderately obese (35–39.99 kg/m²) and severely obese (>=40 kg/m²). Outliers in BMI were defined as subjects with a BMI<12 or >60 kg/m², and together they comprised <1% of the total population and were removed.

The presence or absence of diabetes at baseline and race/ethnicity were obtained directly from the DaVita database. Histories of tobacco smoking and preexisting co-morbid conditions were obtained by linking the DaVita database to the Medical Evidence Form 2728 of the United States Renal Data System (USRDS).(27) There were 10 co-morbid conditions: ischemic heart disease, congestive heart failure, status post cardiac arrest, status

post myocardial infarction, pericarditis, cardiac dysrhythmia, cerebrovascular events, peripheral vascular disease, chronic obstructive pulmonary disease and cancer.

Race and Ethnicity

The DaVita national database, similar to the USRDS database, includes race and ethnicity for over 98% of all patients as “self-identified” data. Race and ethnicity determinations were based on “self-identification” data, in that dialysis patients chose the race or races and/or ethnicity with which they most closely identified according to the definitions set forth by the United States Census Bureau and the Federal Office of Management and Budget.(28, 29) In this study, three mutually exclusive racial/ethnic categories (Blacks, Hispanics, and non-Hispanic Whites) were created. Other racial/ethnic groups such as Asians or American Indians were not included in these analyses due to small sample size, especially for patients with a BMI greater than 30 kg/m².

Laboratory Measures

Blood samples were drawn using uniform techniques in all dialysis clinics and were transported to the DaVita Laboratory in Deland, Florida within 24 hours. All laboratory values were measured by automated and standardized methods. Most laboratory values were measured monthly. Hemoglobin was measured at least monthly in all patients and weekly to bi-weekly in most patients. HbA1c was usually measured semi-annually or quarterly. Normalized protein equivalent of total nitrogen appearance (nPNA), also known as normalized protein catabolic rate (nPCR), was measured monthly as a measure of daily protein intake. Most blood samples were collected pre-dialysis with the exception of the post-dialysis serum urea nitrogen to calculate urea kinetics.

Epidemiologic and Statistical Methods

Survival analyses, including Kaplan-Meier, log-rank tests and Cox proportional hazard regressions with baseline measures, were examined to determine whether the 6-year survival rates were associated with BMI. Patients are followed up until death or kidney transplant or otherwise assumed to have survived at least until June 30, 2007. Models were analyzed within 3 mutually exclusive race-ethnicity groups: Black, non-Hispanic White, and Hispanic. For each analysis, three models were examined based on the level of multivariate adjustment:

- I. Unadjusted model that included BMI categories and entry calendar quarter (q1 through q20);
- II. Case-mix adjusted model that included all of the above plus age, gender, and 10 pre-existing co-morbid states, categories of dialysis vintage (<6 months, 6 months to 2 years, 2–5 years and ≥5 years), primary insurance (Medicare, Medicaid, private and others), marital status (married, single, divorced, widowed and other or unknown), and residual urinary urea clearance during the entry quarter;
- III. Case-mix plus malnutrition inflammation complex syndrome (MICS)-adjusted model which included all of the covariates in the case-mix model as well as 12 surrogates of nutritional status and inflammation. Eleven laboratory surrogates of MICS have known associations with clinical outcomes in maintenance HD patients (30) including nPNA, serum levels of albumin, total iron-binding capacity, ferritin, creatinine, phosphorus, calcium, bicarbonate, blood white blood cell count, lymphocyte percentage and hemoglobin.
- IV. All descriptive and multivariate analyses were carried out with the SAS version 9.1, SAS Institute, Inc., Cary, North Carolina.

Results

The original 6-year (7/2001-6/2007) national database of all DaVita patients included 164,789 adult subjects (Figure S1). After excluding those without quarter base data ($n=13,312$), those having an outlier BMI (due to incorrect height or weight values, $n=17,277$), those receiving peritoneal dialysis treatment ($n=10,528$), and those without recorded age or with an outlier age at baseline ($n=803$), there were 122,869 maintenance HD patients who met all inclusion and exclusion criteria. Patients with outlier BMI values had similar demographic and laboratory variables compared to those included in the study as shown in Table S1. In the present study we exclusively examined Blacks, Hispanics and non-Hispanic Whites; therefore, we excluded the 13,264 patients with other or unknown race or ethnicity, and the final study population consisted of 109,605 patients.

These patients were followed until death, kidney transplant, or survival until June 30th 2007. Among the 109,605 observed maintenance HD patients with a median time in the study of 733 days, there were 58,294 deaths (53%). The mean age was 62 ± 15 years, 45% were women, and 45% had diabetes mellitus (Table 1). Baseline demographic and laboratory data are presented in Table 1; 48% of patients were non-Hispanic Whites; 36% were Blacks, and 16% were Hispanics. Table S2 compares the demographic, clinical and laboratory characteristics of the 109,605 maintenance HD patients in the 6-year DaVita cohort across BMI categories. Higher BMI was associated with younger age, higher prevalence of diabetes, and higher proportion of Black patients. As shown in Figure 1, the crude mortality was lowest in the highest BMI category ($>40 \text{ kg/m}^2$) in each race. Table S3 shows the distribution of BMI across the different races in the entire cohort.

The association of BMI categories with the risk of death is shown in Figure S2–S4. As shown in Figure S2, compared to BMI of 23 to $<25 \text{ kg/m}^2$ (reference), the case-mix- and MICS-adjusted death risk in Black maintenance HD patients with a BMI of 25 to 30 kg/m^2 , BMI of 35 to 40 kg/m^2 and BMI of more than 40 kg/m^2 was 22%, 25% and 30% lower ($p<0.001$), respectively. A similar linear trend between BMI categories and mortality was detected in non-Hispanic White patients (Figure S3). A BMI $>40 \text{ kg/m}^2$ was associated with a 16% lower death risk after adjusting for both case-mix and MICS variables ($p<0.001$) in non-Hispanic white patients (Figure S3). In Hispanic patients only a very low BMI was associated with higher mortality (Figure S4). In Hispanic patients, compared to patients with BMI of 23– $<25 \text{ kg/m}^2$ (reference), the groups with BMI of 18– 20 kg/m^2 and $<18 \text{ kg/m}^2$ had 23% and 51% higher fully adjusted death risk (Figure S4).

We compared the unadjusted, case-mix, and case-mix and MICS-adjusted mortality risk in different BMI categories across different races (Figure 2A–C and Figure S5–S7). Non-Hispanic white patients had the lowest overall survival in our cohort. Among patients with BMI $<30 \text{ kg/m}^2$, Black patients had a lower survival than Hispanic patients (Figure S6). Non-Hispanic white patients had a higher mortality risk in almost all BMI categories than Hispanic patients (Figure S7).

Using continuous BMI in Cox models, we compared the coefficient estimates and standard errors in all races to examine the impact of race on the association between BMI and mortality in the entire cohort (Figure 3). A 1 kg/m^2 -higher BMI was associated with a 2.0% lower mortality rate in non-Hispanic White patients, 2.5% lower mortality rate in Blacks and 1.0% lower mortality rate in Hispanics. We also examined whether Black, White or Hispanic race/ethnicity had any effect modification on the association between BMI and mortality. Black race exhibited a more pronounced effect modification (interaction term $p\text{-value}<0.01$) compared to White or Hispanic groups (interaction term p values of 0.2 and 0.1, respectively).

Discussion

We found that lower BMI was associated with higher mortality in a cohort of 109,605 maintenance HD patients. Obesity ($>30 \text{ kg/m}^2$) and that even morbid obesity ($>40 \text{ kg/m}^2$) was associated with greater survival compared to normal or low BMI ranges. The inverse association of higher BMI with survival was strongest in Blacks and weakest in Hispanic maintenance HD patients. Whereas survival was higher in most BMI categories for Hispanic patients compared to other racial/ethnic categories, the benefit associated with each 1-kg/m^2 higher BMI appeared to be stronger in Blacks and also to some extent in non-Hispanic white patients. In accordance with previous findings, Black and Hispanic dialysis patients had lower mortality rates compared to non-Hispanic Whites in our cohort. These findings present an important picture of the survival paradox observed in maintenance HD and how this pattern differs across racial/ethnic groups.

Even though obesity is associated with deleterious outcomes in the general population, in maintenance HD patients the association between BMI and mortality is reversed, a phenomenon known as the “obesity paradox” or “reverse epidemiology”.(13–16) The concept of the “altered risk factor pattern” may seem counterintuitive, especially since obesity is an established risk factor for poor health outcomes in the general population.(31, 32) Even so, given the consistency of the observations, there may be aspects of these and other chronic disease populations that make them more resistant to poor outcomes at greater BMI levels. Suggested reasons for this effect have been published(33, 34), including a hemodynamic status that is more stable in obese individuals,(35) a higher concentration of tumor necrosis factor alpha receptors in obesity,(36) neurohormonal alterations of obesity,(37) endotoxin-lipoprotein interaction,(38) differences in bone and mineral and vitamin D,(24, 39) reverse causation,(40) survival bias,(41) time discrepancies among competitive risk factors (over- vs. under-nutrition),(41) and the overwhelming effect of malnutrition inflammation complex on traditional cardiovascular risks.(42, 43) Since the majority of maintenance HD patients in the US die within 5 years of beginning dialysis treatment,(44) the long-term effects of conventional risk factors on future mortality may be irrelevant in the face of their potential short-term benefits or by other risk factors intrinsic to dialysis populations, such as under-nutrition and inflammation. On this note, perhaps dialysis patients do not survive long enough to die of the consequences of over-nutrition, since they face more pressing mortality risks from other health conditions such as protein-energy wasting.(45–48) Hence, obesity, by providing more nutritional reserve, may protect them against early death.(15)

The incidence and prevalence of CKD and ESRD have been rising in the United States and in most other countries.(49) Differences in incidence and prevalence of CKD by racial/ethnic lines have been present for at least the past 20 years.(50–52) The annual ESRD incidence for Blacks and Hispanics in 2006 reached 1,010 and 520 per million population, respectively, which is 3.6 and 1.5 times greater than the incidence in non-Hispanic Whites.(49) The prevalence of ESRD continues to be highest for Blacks and Hispanics, at 5,004 and 2,326 per million population, respectively, as compared to 1,194 per million among non-Hispanic Whites.(49) Compared with non-dialyzed Medicare patients of the same age group, mortality of dialysis patients is 10–100 times greater, irrespective of race or ethnicity.(49, 53, 54) Almost half of the deaths in maintenance HD patients are attributed to cardiovascular disease.(52, 55, 56) Black and Hispanic dialysis patients have higher survival than their non-Hispanic White counterparts while in the general population without CKD the opposite is observed; and this so-called “CKD racial survival paradox” has existed over the past two decades.(51, 54) The higher dialysis survival of the minorities is rather consistent and independent of demographic or residency status or the modality of dialysis treatment

(thrice-weekly maintenance HD vs. daily peritoneal dialysis), dialysis dose, or other factors related to dialysis treatment or techniques.(49, 53)

There are some potential explanations for the differences in life expectancy seen in different races among maintenance HD patients. In the U.S. general population, disparities in income, education, and health status have been implicated in the increased total mortality and shorter life expectancy of Blacks compared with non-Hispanic Whites.(57–59) However, among dialysis patients Blacks have a substantially lower annual mortality rate (18%) than non-Hispanic Whites (28%).(52) On the other hand, in a 3-year contemporary cohort of 15,859 HD patients, Blacks were the only racial group in whom a high serum LDL cholesterol level (>100 mg/ml) was associated with increased risk of cardiovascular mortality, whereas, paradoxically, LDL-hypercholesterolemia was protective in other races.(30) Additionally, two recent studies by Wolf et al.(60) and Kalantar-Zadeh et al.(24) suggests that therapy with active vitamin D may potentially explain greater survival of Black maintenance HD patients. Additionally, Volkova et al. found racial differences in coronary heart disease and heart failure in incident dialysis patients.(61) Our findings indicate that higher BMI is strongly associated with longer survival. This association may be due to increased food intake having a short-term salutary effect on survival, which may be particularly advantageous in populations with short-term life expectancies. Such an effect could in turn be due to micronutrient intake, attenuation of the malnutrition-inflammation complex syndrome, and/or neurophysiologic modulation of oxidative stress.

Despite the lesser likelihood of Hispanics developing many chronic diseases, they are nearly twice as likely to develop ESRD as non-Hispanic Whites.(62–64) This striking ‘paradox-within-a-paradox’ might relate to the increased incidence and prevalence of diabetes mellitus in this group. Hispanics who are at greatest risk of developing CKD may have a genetic background and ‘thrifty genotype’ in common with Native American Indians, who as a group are also at high risk of developing diabetes mellitus and CKD.(62, 65) Even so, when diabetic Hispanics receive maintenance dialysis, they have a greater likelihood of surviving than non-Hispanic Whites;(66, 67) which is still another example of a paradox-within-a-paradox. In our study, we found that Blacks have a lower mortality than non-Hispanic Whites for higher BMI groups while Hispanics have a consistently lower mortality than Non-Hispanic Whites for almost every BMI groups.

There may be another potential explanation for the stronger survival advantage of higher BMI in Blacks compared to other races. BMI per se may not be an appropriate measure to characterize nutritional status, body composition, obesity or muscle mass in dialysis patients.(18, 23, 42, 68, 69) Blacks at any given BMI may have a greater muscle mass than other races/ethnicities. Indeed density of lean body mass is higher in Blacks than in Whites;(70) and more muscle mass appears to have an association with better survival.(23) Moreover, in Blacks without CKD higher BMI (>25 kg/m²) tends to associate with only slight increase in risks of death.(71) Hence, in Black maintenance HD patients, higher muscles mass could be responsible for the observed association between BMI and survival.

Our study is limited by its observational nature. Like all observational studies, this analysis cannot distinguish direct causation from confounding associations (here, association of BMI with other factors related to survival). It is also important to note the limitation of BMI as a measure of “obesity per se”, and the potential that higher BMI may be a marker of better nutrition/higher muscle mass/edema as well as higher visceral adiposity. Another potential limitation is that we excluded more than 17000 patients with outlier BMI; however, this is unlikely to lead to substantial bias, because excluded patients had similar demographic and laboratory values compared to individuals in the study (see Table S1). Additionally, race and ethnicity categories were based on self-identified data. Our study did not have detailed

serum markers of inflammation, oxidative stress, or oxidized lipids, which could have provided additional evidence to reinforce proposed mechanistic pathways for our findings of powerful associations. A notable strength of our study is its large sample size and the availability of laboratory values, which allowed us to account for important covariates in the multivariate analyses and to examine specific associations, thus providing points of focus in future studies. To the best of our knowledge our study is the first to compare the association between BMI and survival among Blacks, Non-Hispanic Whites and Hispanics in maintenance HD patients.

In this study we found that obesity, as measured by BMI, was associated with greater survival in maintenance HD patients of all races and ethnicity, but different patterns were observed across the three mutually exclusive racial and ethnic groups. The survival advantage of obesity was most prominent among Blacks. Our analyses suggest a protective but differential role for higher BMI across racial and ethnic groups of maintenance HD patients.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med.* 2009; 150(9):604–612. [PubMed: 19414839]
2. Collins AJ, Foley RN, Herzog C, Chavers B, Gilbertson D, Ishani A, et al. United States Renal Data System 2008 Annual Data Report. *Am J Kidney Dis.* 2009; 53(1 Suppl):S1–374.
3. Collins AJ, Foley RN, Herzog C, Chavers BM, Gilbertson D, Ishani A, et al. Excerpts from the US Renal Data System 2009 Annual Data Report. *Am J Kidney Dis.* 2010; 55(1 Suppl 1):S1–420. A426–427.
4. Wong JS, Port FK, Hulbert-Shearon TE, Carroll CE, Wolfe RA, Agodoa LY, et al. Survival advantage in Asian American end-stage renal disease patients. *Kidney Int.* 1999; 55(6):2515–2523. [PubMed: 10354301]
5. Tanna MM, Vonesh EF, Korbet SM. Patient survival among incident peritoneal dialysis and hemodialysis patients in an urban setting. *Am J Kidney Dis.* 2000; 36(6):1175–1182. [PubMed: 11096042]
6. Eisenstein EL, Sun JL, Anstrom KJ, Stafford JA, Szczech LA, Muhlbaier LH, et al. Do income level and race influence survival in patients receiving hemodialysis? *Am J Med.* 2009; 122(2):170–180. [PubMed: 19185093]
7. Mesler DE, McCarthy EP, Byrne-Logan S, Ash AS, Moskowitz MA. Does the survival advantage of nonwhite dialysis patients persist after case mix adjustment? *Am J Med.* 1999; 106(3):300–306. [PubMed: 10190378]
8. Owen WF Jr, Chertow GM, Lazarus JM, Lowrie EG. Dose of hemodialysis and survival: differences by race and sex. *JAMA.* 1998; 280(20):1764–1768. [PubMed: 9842952]

9. Kovesdy CP, Anderson JE, Derose SF, Kalantar-Zadeh K. Outcomes associated with race in males with nondialysis-dependent chronic kidney disease. *Clin J Am Soc Nephrol*. 2009; 4(5):973–978. [PubMed: 19369403]
10. Bleyer AJ, Tell GS, Evans GW, Ettinger WH Jr, Burkart JM. Survival of patients undergoing renal replacement therapy in one center with special emphasis on racial differences. *Am J Kidney Dis*. 1996; 28(1):72–81. [PubMed: 8712225]
11. Kalantar-Zadeh K, Golan E, Shohat T, Streja E, Norris KC, Kopple JD. Survival disparities within American and Israeli dialysis populations: learning from similarities and distinctions across race and ethnicity. *Seminars in dialysis*. 2010; 23(6):586–594. [PubMed: 21175833]
12. Streja E, Kovesdy CP, Molnar MZ, Norris KC, Greenland S, Nissenson AR, et al. Role of Nutritional Status and Inflammation in Higher Survival of African American and Hispanic Hemodialysis Patients. *Am J Kidney Dis*. 2011
13. Kalantar-Zadeh K, Kopple JD, Kilpatrick RD, McAllister CJ, Shinaberger CS, Gjertson DW, et al. Association of morbid obesity and weight change over time with cardiovascular survival in hemodialysis population. *Am J Kidney Dis*. 2005; 46(3):489–500. [PubMed: 16129211]
14. Kalantar-Zadeh K, Kuwae N, Wu DY, Shantouf RS, Fouque D, Anker SD, et al. Associations of body fat and its changes over time with quality of life and prospective mortality in hemodialysis patients. *Am J Clin Nutr*. 2006; 83(2):202–210. [PubMed: 16469976]
15. Kopple JD, Zhu X, Lew NL, Lowrie EG. Body weight-for-height relationships predict mortality in maintenance hemodialysis patients. *Kidney Int*. 1999; 56(3):1136–1148. [PubMed: 10469384]
16. Kalantar-Zadeh K, Aronoff GR. Hemoglobin variability in anemia of chronic kidney disease. *J Am Soc Nephrol*. 2009; 20(3):479–487. [PubMed: 19211716]
17. Stevens J, Cai J, Pamuk ER, Williamson DF, Thun MJ, Wood JL. The effect of age on the association between body-mass index and mortality. *N Engl J Med*. 1998; 338(1):1–7. [PubMed: 9414324]
18. Postorino M, Marino C, Tripepi G, Zoccali C. Abdominal obesity and all-cause and cardiovascular mortality in end-stage renal disease. *J Am Coll Cardiol*. 2009; 53(15):1265–1272. [PubMed: 19358939]
19. National Institutes of Health. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults--The Evidence Report. *Obes Res*. 1998; 6 (Suppl 2):51S–209S. [PubMed: 9813653]
20. Glanton CW, Hypolite IO, Hsieh PB, Agodoa LY, Yuan CM, Abbott KC. Factors associated with improved short term survival in obese end stage renal disease patients. *Ann Epidemiol*. 2003; 13(2):136–143. [PubMed: 12559673]
21. Miller JE, Kovesdy CP, Nissenson AR, Mehrotra R, Streja E, Van Wyck D, et al. Association of hemodialysis treatment time and dose with mortality and the role of race and sex. *Am J Kidney Dis*. 2010; 55(1):100–112. [PubMed: 19853336]
22. Miller JE, Kovesdy CP, Norris KC, Mehrotra R, Nissenson AR, Kopple JD, et al. Association of cumulatively low or high serum calcium levels with mortality in long-term hemodialysis patients. *Am J Nephrol*. 2010; 32(5):403–413. [PubMed: 20814200]
23. Kalantar-Zadeh K, Streja E, Kovesdy CP, Oreopoulos A, Noori N, Jing J, et al. The obesity paradox and mortality associated with surrogates of body size and muscle mass in patients receiving hemodialysis. *Mayo Clin Proc*. 2010; 85(11):991–1001. [PubMed: 21037042]
24. Kalantar-Zadeh K, Miller JE, Kovesdy CP, Mehrotra R, Lukowsky LR, Streja E, et al. Impact of race on hyperparathyroidism, mineral disarrays, administered vitamin D mimetic, and survival in hemodialysis patients. *J Bone Miner Res*. 2010; 25(12):2448–2458.
25. Molnar MZ, Lukowsky LR, Streja E, Dukkupati R, Jing J, Nissenson AR, et al. Blood pressure and survival in long-term hemodialysis patients with and without polycystic kidney disease. *J Hypertens*. 2010; 28(12):2475–2484. [PubMed: 20720499]
26. Kalantar-Zadeh K, McAllister CJ, Lehn RS, Lee GH, Nissenson AR, Kopple JD. Effect of malnutrition-inflammation complex syndrome on EPO hyporesponsiveness in maintenance hemodialysis patients. *Am J Kidney Dis*. 2003; 42(4):761–773. [PubMed: 14520627]
27. Longenecker JC, Coresh J, Klag MJ, Levey AS, Martin AA, Fink NE, et al. Validation of comorbid conditions on the end-stage renal disease medical evidence report: the CHOICE study.

- Choices for Healthy Outcomes in Caring for ESRD. *J Am Soc Nephrol*. 2000; 11(3):520–529. [PubMed: 10703676]
28. bureau USC. Available from: <http://www.census.gov>
 29. Budget OoMa. Available from: <http://www.whitehouse.gov/omb/>
 30. Kilpatrick RD, McAllister CJ, Kovesdy CP, Derose SF, Kopple JD, Kalantar-Zadeh K. Association between Serum Lipids and Survival in Hemodialysis Patients and Impact of Race. *J Am Soc Nephrol*. 2007; 18(1):293–303. [PubMed: 17167113]
 31. Kopple JD. How to reconcile conventional and altered risk factor patterns in dialysis patients. *Seminars in dialysis*. 2007; 20(6):602–605. [PubMed: 17991211]
 32. Kalantar-Zadeh K. What is so bad about reverse epidemiology anyway? *Seminars in dialysis*. 2007; 20(6):593–601. [PubMed: 17991210]
 33. Kalantar-Zadeh K, Abbott KC, Salahudeen AK, Kilpatrick RD, Horwich TB. Survival advantages of obesity in dialysis patients. *Am J Clin Nutr*. 2005; 81(3):543–554. [PubMed: 15755821]
 34. Molnar MZ, Streja E, Kovesdy CP, Bunnapradist S, Sampaio MS, Jing J, et al. Associations of Body Mass Index and Weight Loss with Mortality in Transplant-Waitlisted Maintenance Hemodialysis Patients. *Am J Transplant*. 2011 in press.
 35. Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Woo MA, Tillisch JH. The relationship between obesity and mortality in patients with heart failure. *J Am Coll Cardiol*. 2001; 38(3):789–795. [PubMed: 11527635]
 36. Mohamed-Ali V, Goodrick S, Bulmer K, Holly JM, Yudkin JS, Coppack SW. Production of soluble tumor necrosis factor receptors by human subcutaneous adipose tissue in vivo. *Am J Physiol*. 1999; 277(6 Pt 1):E971–975. [PubMed: 10600783]
 37. Weber MA, Neutel JM, Smith DH. Contrasting clinical properties and exercise responses in obese and lean hypertensive patients. *J Am Coll Cardiol*. 2001; 37(1):169–174. [PubMed: 11153733]
 38. Rauchhaus M, Coats AJ, Anker SD. The endotoxin-lipoprotein hypothesis. *Lancet*. 2000; 356(9233):930–933. [PubMed: 11036910]
 39. Kalantar-Zadeh K, Kovesdy CP. Clinical outcomes with active versus nutritional vitamin D compounds in chronic kidney disease. *Clin J Am Soc Nephrol*. 2009; 4(9):1529–1539. [PubMed: 19661219]
 40. Macleod J, Davey Smith G. Psychosocial factors and public health: a suitable case for treatment? *J Epidemiol Community Health*. 2003; 57(8):565–570. [PubMed: 12883057]
 41. Kalantar-Zadeh K, Block G, Humphreys MH, Kopple JD. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. *Kidney Int*. 2003; 63(3):793–808. [PubMed: 12631061]
 42. Noori N, Kovesdy CP, Dukkipati R, Kim Y, Duong U, Bross R, et al. Survival predictability of lean and fat mass in men and women undergoing maintenance hemodialysis. *Am J Clin Nutr*. 2010; 92(5):1060–1070. [PubMed: 20844076]
 43. Kovesdy CP, George SM, Anderson JE, Kalantar-Zadeh K. Outcome predictability of biomarkers of protein-energy wasting and inflammation in moderate and advanced chronic kidney disease. *Am J Clin Nutr*. 2009; 90(2):407–414. [PubMed: 19535427]
 44. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. *Am J Kidney Dis*. 1998; 32(5 Suppl 3):S112–119. [PubMed: 9820470]
 45. Fouque D, Kalantar-Zadeh K, Kopple J, Cano N, Chauveau P, Cuppari L, et al. A proposed nomenclature and diagnostic criteria for protein-energy wasting in acute and chronic kidney disease. *Kidney Int*. 2008; 73(4):391–398. [PubMed: 18094682]
 46. Kalantar-Zadeh K, Kopple JD. Relative contributions of nutrition and inflammation to clinical outcome in dialysis patients. *Am J Kidney Dis*. 2001; 38(6):1343–1350. [PubMed: 11728973]
 47. Kalantar-Zadeh K, Kopple JD, Block G, Humphreys MH. A malnutrition-inflammation score is correlated with morbidity and mortality in maintenance hemodialysis patients. *Am J Kidney Dis*. 2001; 38(6):1251–1263. [PubMed: 11728958]
 48. Molnar MZ, Czira ME, Rudas A, Ujszaszi A, Lindner A, Fornadi K, et al. Association of the Malnutrition-Inflammation Score With Clinical Outcomes in Kidney Transplant Recipients. *Am J Kidney Dis*. 2011

49. U.S. Renal Data System. USRDS 2006 Annual Data Report: Atlas of End-Stage Renal Disease in the United States. Bethesda, MD: NIH/NIDDK; 2008.
50. Agodoa L, Eggers P. Racial and ethnic disparities in end-stage kidney failure-survival paradoxes in African-Americans. *Semin Dial.* 2007; 20(6):577–585. [PubMed: 17991208]
51. United States Renal Data System. Excerpts from the USRDS 2005 Annual Data Report: Atlas of End-Stage Renal Disease in the United States, National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases. *Am J Kid Dis.* 2006; 47(Supplement 1):1–286. [PubMed: 16377379]
52. United States Renal Data System. Excerpts from the USRDS 2004 Annual Data Report. *Am J Kid Dis.* 2005; 45 (suppl 1):S1–S280.
53. United States Renal Data System. Annual Report and Atlas of Chronic Kidney Disease & End-Stage Renal Disease. USRDS Report. 2009
54. United States Renal Data System. United States Renal Data System 2006 Annual Data Report Atlas of Chronic Kidney Disease & End-Stage Renal Disease in the United States. *Am J Kidney Dis.* 2007; 49(Supplement 1):1–296. [PubMed: 17185139]
55. United States Renal Data System. US Department of Public Health and Human Services, Public Health Service. National Institutes of Health; Bethesda: 2002.
56. Morbidity and mortality of dialysis. NIH Consensus Statement. 1993; 11(2):1–33.
57. Mortality patterns--United States, 1997. *MMWR Morb Mortal Wkly Rep.* 1999; 48(30):664–668. [PubMed: 10488783]
58. Asher CR, Topol EJ, Moliterno DJ. Insights into the pathophysiology of atherosclerosis and prognosis of black Americans with acute coronary syndromes. *Am Heart J.* 1999; 138(6 Pt 1): 1073–1081. [PubMed: 10577437]
59. Davey Smith G, Neaton JD, Wentworth D, Stamler R, Stamler J. Mortality differences between black and white men in the USA: contribution of income and other risk factors among men screened for the MRFIT. MRFIT Research Group. Multiple Risk Factor Intervention Trial. *Lancet.* 1998; 351(9107):934–939. [PubMed: 9734939]
60. Wolf M, Betancourt J, Chang Y, Shah A, Teng M, Tamez H, et al. Impact of Activated Vitamin D and Race on Survival among Hemodialysis Patients. *J Am Soc Nephrol.* 2008
61. Volkova N, McClellan W, Soucie JM, Schoolwerth A. Racial disparities in the prevalence of cardiovascular disease among incident end-stage renal disease patients. *Nephrol Dial Transplant.* 2006; 21(8):2202–2209. [PubMed: 16522661]
62. Benabe JE, Rios EV. Kidney disease in the Hispanic population: facing the growing challenge. *J Natl Med Assoc.* 2004; 96(6):789–798. [PubMed: 15233489]
63. Pugh JA, Stern MP, Haffner SM, Eifler CW, Zapata M. Excess incidence of treatment of endstage renal disease in Mexican Americans. *Am J Epidemiol.* 1988; 127(1):135–144. [PubMed: 3276155]
64. Tareen N, Zadshir A, Martins D, Pan D, Nicholas S, Norris K. Chronic kidney disease in African American and Mexican American populations. *Kidney Int Suppl.* 2005; (97):S137–140. [PubMed: 16014092]
65. Perez-Luque E, Malacara JM, Olivo-Diaz A, Alaez C, Debaz H, Vazquez-Garcia M, et al. Contribution of HLA class II genes to end stage renal disease in mexican patients with type 2 diabetes mellitus. *Hum Immunol.* 2000; 61(10):1031–1038. [PubMed: 11082516]
66. Pugh JA. Diabetic nephropathy and end-stage renal disease in Mexican Americans. *Blood Purif.* 1996; 14(4):286–292. [PubMed: 8873954]
67. Frankenfield DL, Rocco MV, Roman SH, McClellan WM. Survival advantage for adult Hispanic hemodialysis patients? Findings from the end-stage renal disease clinical performance measures project. *J Am Soc Nephrol.* 2003; 14(1):180–186. [PubMed: 12506150]
68. Noori N, Kopple JD, Kovesdy CP, Feroze U, Sim JJ, Murali SB, et al. Mid-arm muscle circumference and quality of life and survival in maintenance hemodialysis patients. *Clin J Am Soc Nephrol.* 2010; 5(12):2258–2268. [PubMed: 20947789]
69. Bross R, Chandramohan G, Kovesdy CP, Oreopoulos A, Noori N, Golden S, et al. Comparing body composition assessment tests in long-term hemodialysis patients. *Am J Kidney Dis.* 2010; 55(5):885–896. [PubMed: 20346558]

70. Schutte JE, Townsend EJ, Hugg J, Shoup RF, Malina RM, Blomqvist CG. Density of lean body mass is greater in blacks than in whites. *J Appl Physiol.* 1984; 56(6):1647–1649. [PubMed: 6735823]
71. Calle EE, Thun MJ, Petrelli JM, Rodriguez C, Heath CW Jr. Body-mass index and mortality in a prospective cohort of U.S. adults. *N Engl J Med.* 1999; 341(15):1097–1105. [PubMed: 10511607]

Figure 1.
Unadjusted or crude mortality rate in different races across body mass index (BMI) categories

Figure 2.

Hazard ratios (95% confidence intervals) of mortality across the body mass index (BMI) categories, obtained from Cox regression analyses of combined data on all three racial/ethnic groups in unadjusted (A), case-mix (B) and case-mix and MICS adjusted model (C). The case-mix model we adjusted for: age, gender, 10 pre-existing co-morbid states, categories of dialysis vintage, primary insurance, marital status, and residual urinary urea clearance during the entry quarter. MICS-adjusted models include all the case-mix covariates plus nPNA, serum levels of albumin, total iron-binding capacity, ferritin, creatinine, phosphorus, calcium, bicarbonate, blood white blood cell count, lymphocyte percentage and hemoglobin.

Figure 3.

Coefficient estimates and standard errors obtained from Cox regression model using body mass index (BMI) as a continuous variable among different races. Estimates have been adjusted for age, gender, and 10 pre-existing co-morbid states, categories of dialysis vintage, primary insurance, marital status, and residual urinary urea clearance during the entry quarter; nPNA, serum levels of albumin, total iron-binding capacity, ferritin, creatinine, phosphorus, calcium, bicarbonate, blood white blood cell count, lymphocyte percentage and hemoglobin.

Table 1

Basic characteristics of 109,605 maintenance hemodialysis patients

Variable	All Patients (N=109,605)	Blacks (n=39,090)	Non-Hispanic Whites (n=53,098)	Hispanics (n=17,417)
Age (year),	62±16	58±15	66±15	59±15
Gender (% female)	45	49	42	46
Diabetes mellitus (%)	45	43	43	57
Dialysis Vintage category				
0–6 months	12	9	15	10
6–24 months	31	26	35	30
2–5 years	35	35	34	37
>5 years	22	30	16	23
Medicare as primary insurance (%)	64	65	65	56
Marital Status category				
Married	40	29	46	43
Divorced	7	8	7	6
Single	23	34	16	22
Widowed	13	12	15	10
Other	17	17	16	19
Delivered single-pool Kt/V	1.5±0.36	1.5±0.3	1.5±0.4	1.6±0.4
KRU	0.5±1.5	0.3±1.1	0.6±1.8	0.4±1.4
Dialysis Catheter (%)	78	78	77	81
Serum albumin (g/dL)	3.67±0.47	3.70±0.47	3.65±0.46	3.69±0.47
Creatinine (mg/dL)	8.0±3.3	9.4±3.6	6.9±2.7	8.1±3.2
Total Iron-binding capacity (mg/dL)	208±46	202±44	212±47	209±44
Bicarbonate (mg/dL)	22.3±3.0	22.4±3.0	22.3±3.1	22.0±3.0
Phosphorus (mg/dL)	5.6±1.5	5.6±1.5	5.5±1.5	5.7±1.5
Calcium (mg/dL)	9.19±0.72	9.25±0.75	9.2±0.69	9.1±0.69
Ferritin (ng/mL)	510±487	559±530	479±457	495±467
Protein Catabolic Rate (g/kg/day)	0.94±0.25	0.92±0.75	0.93±0.25	1.0±0.26
Blood hemoglobin (g/dL)	12±1.4	12±1.4	12±1.4	12±1.3

Variable	All Patients (N=109,605)	Blacks (n=39,090)	Non-Hispanic Whites (n=53,098)	Hispanics (n=17,417)
WBC count ($\times 10^3/\mu\text{l}$)	7.5 $\pm$ 2.6	6.9 $\pm$ 2.3	7.8 $\pm$ 2.8	7.6 $\pm$ 2.3
Lymphocyte (% of total WBC)	20.5 $\pm$ 8.0	23.2 $\pm$ 8.2	18.4 $\pm$ 7.4	20.9 $\pm$ 7.2
Weight (kg)	76.1 $\pm$ 20.4	78.3 $\pm$ 21.3	76.4 $\pm$ 20.4	70.4 $\pm$ 17.1

Note: Race/ethnic groups are mutually exclusive. Continuous variables are shown as mean $\pm$ SD; categorical variables as percentage. Conversion factors for units: serum creatinine in mg/dL to mol/L, $\times 88.4$; serum albumin in g/dL to g/L, $\times 10$; blood hemoglobin in g/dL to g/L, $\times 10$; serum calcium in mg/dL to mmol/L, $\times 0.2495$; serum phosphorus in mg/dL to mmol/L, $\times 0.3229$. No conversion necessary for ferritin in ng/mL and $\mu\text{g/L}$ and WBC count in $10^3/\mu\text{L}$ and $10^9/\text{L}$.

Abbreviation: WBC, white blood cell