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# Association of Height with Mortality in Patients Undergoing Maintenance Hemodialysis

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## Abstract

**Background and objectives** Body mass index (BMI), determined as kilograms in body weight divided by the square of the height in meters ($m^2$), is inversely associated with mortality in patients undergoing maintenance hemodialysis (MHD). It is commonly inferred that differences in the weight component of the BMI equation are responsible for this negative correlation. However, there are almost no data on the relationship between height and mortality in these patients. This study was conducted to examine the association between height and mortality in MHD patients and to evaluate the contribution of height to the BMI-mortality relationship.

**Design, setting, participants, & measurements** A prospective study conducted from July 1, 2001, through June 30, 2006, enrolled a nationally representative cohort of 117,644 MHD patients receiving treatment in DaVita, Inc. outpatient dialysis facilities with (*1*) known height and weight, (*2*) age ≥18 years, (*3*) dialysis vintage ≥90 days, and (4) nonoutlying BMI values (≥12 to ≤60 $kg/m^2$). The end date of follow-up was June 30, 2007, and median follow-up was 852 days (interquartile range, 504–1367 days). Mortality hazard ratios were computed within sex-standardized deciles of height and weight, and outcomes included all-cause mortality and cardiovascular, gastrointestinal, cancer, and infection mortality. Hazard models were unadjusted, adjusted for case-mix variables, or adjusted for case-mix variables plus laboratory variables.

**Results** Mean age was 61±15 years; 45% of patients were women and 57% had diabetes. In adjusted models, height, also adjusted for weight, was directly associated with all-cause mortality and cardiovascular, infection, and cancer mortality. Compared with the median height decile, mortality risk in the highest height decile was 1.18 (95% confidence interval, 1.14 to 1.23) in fully adjusted analyses ($P<0.001$). Receiver-operating characteristic curves indicated that in adjusted analyses the contribution of height to the relationship between BMI and mortality was almost identical to that of weight.

**Conclusions** In MHD patients, height is positively associated with mortality risk and contributes similarly to weight with regard to the negative BMI-mortality relationship.

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## Introduction

Many studies indicate that in patients undergoing maintenance hemodialysis (MHD), body mass index (BMI) is negatively correlated with mortality in a pattern that is essentially opposite (the mirror image) of that found in the general population, except when BMI is very low (1–3).This phenomenon is commonly thought to reflect the effect of body weight, adjusted for differences in height, on mortality. However, because BMI values are also determined by the square of body height, it is possible that variations in height also contribute to the BMI-mortality relationship. To this point, the relationship of height to mortality has been largely unexamined in adult MHD patients. This subject has been studied for decades in the general population, where greater height has often been associated with reduced all-cause mortality (4–7), cardiovascular mortality (4–8), and mortality due to other causes not related to cancer (4,5,7). However, several well designed studies of the general population report no association between height and these outcomes after adjustment for age and/or proxies of socioeconomic status (9–11).

Because of the lack of data on this relationship in patients with chronic kidney failure, we examined the relationship between height and mortality in a large cohort of MHD patients. As a result of the considerable discussion regarding the significance of the altered BMI-mortality relationship in these patients, we also examined the potential contribution of variations in height to this BMI-mortality relationship.

## Materials and Methods

### Patients

We examined the national database of DaVita, Inc., a large dialysis organization in the United States. A 5-year cohort was created using data collected from both incident (receiving treatment for <6 months) and prevalent MHD patients undergoing treatment between

July 1, 2001, and June 30, 2006, in DaVita outpatient dialysis facilities. The institutional review committees of Harbor–University of California, Los Angeles Medical Center and DaVita, Inc., approved the studies. Because of the large sample size studied, the anonymity of the patients studied, and the nonintrusive nature of the research, the requirement for a written consent form was waived.

### Clinical and Demographic Measures

Baseline values were used for up to 20 calendar quarters (q1–q20) for each laboratory and clinical measure for each patient over the 5-year cohort period. The first (baseline) quarter for each patient was the calendar quarter in which the patient's dialysis vintage was ≥90 days. Dialysis vintage was defined as the duration of time between the first day of dialysis treatment and the first day that the patient entered the cohort. Height was typically measured by a stadiometer at a patient's first dialysis treatment. In patients unable to stand, height was ascertained using a measuring tape. These measurements were recorded in inches and rounded to the nearest whole number. For the purposes of our study, this value was converted to meters and rounded to the nearest hundredth of a meter. No information was available regarding amputations; however, because amputations in both lower extremities that would shorten height probably would be very uncommon, particularly when patients were commencing MHD therapy, we inferred that this lack of information would not materially affect the results of this study.

The presence or absence of diabetes at baseline and race/ethnicity were obtained directly from the DaVita database. Histories of tobacco smoking and preexisting comorbid conditions were obtained by linking the DaVita database to Medical Evidence form 2728 of the US Renal Data System and were categorized into nine comorbid conditions: (*1*) cancer, (*2*) HIV infection, (*3*) peripheral vascular disease, (*4*) congestive heart failure, (*5*) hypertension, (*6*) cerebrovascular accident, (*7*) atherosclerotic heart disease, (*8*) other cardiac disease, and (*9*) chronic obstructive pulmonary disease. The recorded causes of death were obtained from the US Renal Data System. Cardiovascular death was defined as death due to myocardial infarction, cardiac arrest, heart failure, cerebrovascular accident, or other cardiac causes. Gastrointestinal (GI) death was defined as death due to liver failure, pancreatitis, perforated bowel, and other disorders of the GI tract, but excluding cancer death. Cancer death was defined as death due to any malignancy. Infection death was defined as death resulting from infections of the pulmonary, cardiovascular, or central nervous system or from septicemia, hepatitis, AIDS, peritonitis, or other infection-related causes.

### Laboratory Measures

Blood samples were drawn in all of the DaVita dialysis clinics and were transported to the DaVita Laboratory in Deland, Florida, typically within 24 hours. All laboratory measurements were performed using automated and standard methods in the DaVita Laboratory. Most laboratory values were measured monthly, including serum creatinine, albumin, calcium, phosphorus, bicarbonate, and total iron-binding capacity. Serum ferritin was measured at least quarterly. Hemoglobin was measured at least monthly in essentially all patients and weekly to biweekly in most patients. Blood samples were collected immediately before dialysis. Serum urea nitrogen was collected immediately after dialysis in order to calculate urea kinetics. Baseline measures for each laboratory variable were used in all analyses.

### Statistical Analyses

The relationship of height with mortality outcomes was examined using Cox proportional hazards regression with baseline measures. Hazard models were analyzed within sex-standardized deciles of height. For example, the 5th height decile included men ranging from the 40.1th to the 50.0th percentile for all male heights, plus women ranging from the 40.1th to the 50.0th percentile for all female heights. The relationship of body weight to mortality endpoints was analyzed each sex separately in the same manner. Weight analyses were adjusted for height (and vice-versa) and additionally for case-mix variables and laboratory measurements. For each analysis, three models were examined based on the level of multivariate adjustment:

1. A minimally adjusted (referred to as unadjusted) model including height and weight categories and mortality endpoints, adjusted only for weight in analyses related to height (and for height in analyses related to weight) and cohort entry quarter (q1 through q20).
2. A case-mix–adjusted model that included all of the above plus age, sex, and race/ethnicity (self-identified blacks, Hispanics, Asians, non-Hispanic whites and other), presence of diabetes mellitus, the nine preexisting comorbid states, history of tobacco smoking, categories of dialysis vintage (<6 months, 6 months–2 years, 2–5 years, and ≥5 years), primary insurance (Medicare, Medicaid, private, and other), marital status (married, single, divorced, widowed, and other), dialysis dosage as indicated by Kt/Vurea (single pool), and residual renal function at entry quarter (*i.e.*, urinary urea clearance).
3. A case-mix plus laboratory-adjusted model that included all of the covariates in the unadjusted and the case-mix model and the following 11 laboratory variables in serum or blood, which are known to have an association with clinical outcomes in patients undergoing hemodialysis: (*1*) albumin, (*2*) total iron-binding capacity, (*3*) ferritin, (*4*) creatinine, (*5*) phosphorus, (6) calcium, (*7*) normalized protein nitrogen appearance (normalized protein catabolic rate), (*8*) bicarbonate, (*9*) white blood cell count, (*10*) lymphocyte percentage, and (*11*) hemoglobin.

To explore the effects of potential confounders, two additional models were examined where appropriate: An age-adjusted model and a model adjusted for age, sex, and race. These models were also adjusted for weight in analyses of height (and vice-versa) and for cohort entry quarter. We used a receiver-operating characteristic curve to assess the ability of height and weight, independently, to predict mortality in a case-mix model (adjusted for age, sex, and presence of diabetes mellitus). In these analyses, the height curve was not adjusted for weight, and the weight curve was not adjusted for height.

For all analyses, two-sided $P$ values are reported, and results are considered statistically significant if the $P$ value was $<0.05$. Unless otherwise stated, data are given as the mean, and variance is presented as SD. Missing covariate data (<1% for most laboratory and demographic variables) were imputed by the mean or median of the existing values. All statistical analyses were performed using Stata software, version 13 (Stata Corp., College Station, TX).

## Results

The original 5-year (July 1, 2001–June 30, 2006) national database of all DaVita patients included 164,789 patients. After exclusion of patients who did not receive in-center hemodialysis (such as patients undergoing peritoneal dialysis), had a dialysis vintage <90 days, whose reported age was <18 years or not verifiable, or whose BMI at baseline or at any time during follow-up was <12 or >60 kg/m$^2$, 117,644 MHD patients remained with known age, height, weight, BMI, and total follow-up time (Figure 1). These patients had a median follow-up time of 852 days (interquartile range, 504–1367). Table 1 shows the relevant demographic, clinical, and laboratory data for the study patients according to their sex-standardized height decile. The mean age was 61±15 years; 45% of patients were female and 57% had diabetes.

Tables 2 and 3 display mortality hazard ratios for sex-standardized height and weight deciles, respectively, in all 117,644 hemodialysis patients studied. These analyses were based on fixed covariates at baseline (non–time dependent) and case-mix plus laboratory-adjusted (fully adjusted) models, with the fifth decile serving as the reference group. To attain a more commensurate analysis, the associations of height and weight with mortality were compared across the deciles in two separate case-mix plus laboratory-adjusted, non–time-dependent models (Figure 2). In unadjusted analyses, height was inversely associated with mortality (Table 2). This relationship was reversed after adjustment for patient age. Indeed, in unadjusted analyses, height and age were inversely correlated at a low order of magnitude ($r=-0.13$; $P<0.001$), and age was strongly associated with mortality. For example, in comparison to the third quintile of age, the first age quintile mortality hazard ratio was 0.44 (95% confidence interval, 0.43 to 0.45) and the fifth age quintile mortality hazard ratio was 1.97 (95% confidence interval, 1.93 to 2.02; data not shown). In fully adjusted analyses, the relationship between patient height and patient weight with all-cause mortality was opposite because weight was inversely association with mortality (Figure 2, Tables 2 and 3). Cardiovascular, infection-related, GI, and cancer-related mortality were also examined (Figure 3, A–D). Patient height and weight were, respectively, directly and inversely associated with cardiovascular and infection- and cancer-related mortality. No clear associations between height and weight and GI mortality were apparent. Similarly, higher all-cause mortality risks of taller patients (>70th sex-standardized percentile of height) relative to shorter patients (≤70th sex-standardized percentile of height) were observed in various subgroup analyses in adjusted models, but were slightly attenuated after further adjustment for laboratory variables (Figure 4).

We also used a receiver-operating characteristic curve comparing the performance of height and weight, independently, in predicting mortality in a model adjusted for age, sex, and presence of diabetes mellitus (Figure 5). In this analysis, weight and height were not adjusted for each other. Compared with the height model (area under the curve, 0.70), the weight model had an area under the curve of 0.71, indicating that height contributes about the same as weight to the BMI-mortality relationship.

Height was inversely correlated with dialysis dose in unadjusted ($r=-0.27$; $P<0.001$) and age-, sex-, and race-adjusted analyses ($r=-0.14$; $P<0.001$). This inverse correlation persisted after further adjustment for body weight, although this association was weaker ($r=-0.07$; $P<0.001$) (data not shown).

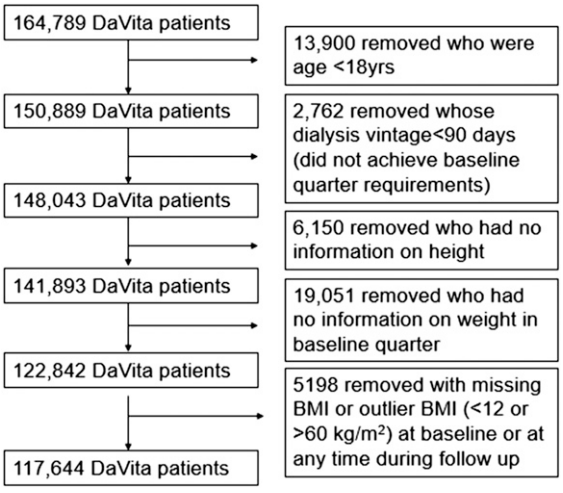


**Figure 1. | Algorithm summarizing the inclusion and exclusion criteria used to constitute the cohort for analysis.** BMI, body mass index.

## Discussion

The results of this study, carried out in a large cohort of 117,644 MHD patients who were followed for a median of 852 days (interquartile range, 504–1367 days), indicate that height was directly associated with all-cause mortality and with mortality due to cardiovascular events, cancer, and infection. In contrast, weight was inversely associated with these four outcomes as well as with GI-related mortality. GI mortality accounted for only 1061 (1.76%) of the 60,285 deaths in this cohort. Hence, a type 2 error may have obscured a relationship between height and GI mortality.

The positive correlation between height and mortality in this study has important implications with regard to the causes and interpretation of the well described inverse relationship between BMI and mortality in MHD patients. Almost all evaluations of this relationship have inferred that the weight component of the BMI is responsible for this inverse association. The putative causes of this relationship are focused on the possible survival advantages of increased body fat and skeletal muscle mass or lean body mass (1–3). Although we observed that weight has a modestly greater effect on mortality than does height, our

**Table 1. Demographic, clinical, and laboratory characteristics of 117,644 patients undergoing maintenance hemodialysis across deciles of height**

| Characteristic | Total Study Sample ($n$=117,644) | Height Decile | | | |
|---|---|---|---|---|---|
| | | 1 ($n$=13,477) W: 1.40–<1.52 M: 1.40–<1.64 | 2 ($n$=15,414) W: 1.52–<1.53 M: 1.64–<1.70 | 3 ($n$=18,608) W: 1.53–<1.60 M: 1.70–<1.71 | 4 ($n$=7,719) W: NA[a] M: 1.71–<1.75 |
| Age (yr) | 61±15 | 64±17 | 63±16 | 63±15 | 62±15 |
| Women (%) | 45 | 42 | 36 | 64 | 0 |
| Diabetes mellitus (%) | 57 | 59 | 58 | 58 | 54 |
| Weight (kg) | 75.3±20.3 | 63.2±15.6 | 68.6±16.0 | 69.6±17.2 | 78.1±17.2 |
| Mortality (%) | 51 | 56 | 52 | 52 | 51 |
| **Race (%)** | | | | | |
| White | 43 | 33 | 38 | 42 | 48 |
| Asian | 3 | 9 | 5 | 4 | 2 |
| Black | 32 | 18 | 23 | 27 | 28 |
| Hispanic | 14 | 29 | 25 | 18 | 14 |
| Other | 7 | 10 | 9 | 8 | 7 |
| **Dialysis vintage (%)** | | | | | |
| <6 mo | 53 | 52 | 54 | 54 | 54 |
| 6–<24 mo | 18 | 18 | 18 | 18 | 19 |
| 2–<5 yr | 18 | 18 | 17 | 18 | 17 |
| ≥5 yr | 11 | 12 | 11 | 10 | 10 |
| **Primary insurance (%)** | | | | | |
| Medicare | 63 | 64 | 64 | 64 | 63 |
| Medicaid | 5 | 8 | 6 | 4 | 4 |
| Private | 10 | 9 | 10 | 9 | 10 |
| Other | 14 | 11 | 13 | 12 | 15 |
| Missing | 8 | 8 | 8 | 8 | 8 |
| **Marital status (%)** | | | | | |
| Married | 40 | 40 | 42 | 37 | 49 |
| Divorced | 7 | 6 | 5 | 7 | 6 |
| Single | 23 | 23 | 21 | 21 | 21 |
| Widowed | 13 | 15 | 14 | 17 | 6 |
| Missing | 18 | 18 | 18 | 18 | 18 |
| Kt/V (dialysis dose) | 1.52±0.34 | 1.62±0.36 | 1.56±0.34 | 1.59±0.34 | 1.47±0.33 |
| KRU | 2.52±1.23 | 2.46±0.99 | 2.49±1.11 | 2.47±1.03 | 2.59±1.47 |
| **Comorbid conditions (%)** | | | | | |
| Hypertension | 79 | 78 | 79 | 79 | 80 |
| Cancer | 5 | 4 | 4 | 4 | 5 |
| AHD | 22 | 21 | 22 | 22 | 22 |
| Heart failure | 27 | 27 | 28 | 29 | 27 |
| Other cardiac disease | 5 | 5 | 6 | 5 | 6 |
| PVD | 11 | 10 | 11 | 11 | 11 |
| Cerebrovascular accident | 7 | 7 | 7 | 8 | 8 |
| HIV infection | 2 | 2 | 2 | 2 | 2 |
| COPD | 6 | 5 | 6 | 6 | 5 |
| Tobacco use | 6 | 3 | 4 | 4 | 4 |
| **Serum laboratory values** | | | | | |
| Albumin (g/dl) | 3.68±0.44 | 3.69±0.43 | 3.69±0.44 | 3.67±0.43 | 3.72±0.45 |
| Creatinine (mg/dl) | 8.07±3.14 | 7.82±3.02 | 8.01±3.13 | 7.65±2.96 | 8.44±3.25 |
| TIBC (mg/dl) | 208±43.4 | 206±42.6 | 208±43.2 | 208±43.8 | 211±42.7 |
| Carbon dioxide (mg/dl) | 22.3±2.87 | 22.3±2.89 | 22.2±2.90 | 22.3±2.89 | 22.3±2.83 |
| Calcium (mg/dl) | 9.19±0.68 | 9.14±0.69 | 9.14±0.68 | 9.20±0.69 | 9.15±0.66 |
| Phosphorus (mg/dl) | 5.59±1.43 | 5.51±1.44 | 5.52±1.43 | 5.51±1.41 | 5.58±1.46 |
| Ferritin (ng/ml) | 574±511 | 552±480 | 534±477 | 535±478 | 500±457 |
| nPCR (g/d) | 0.95±0.24 | 0.99±0.26 | 0.97±0.25 | 0.96±0.25 | 0.96±0.24 |
| Blood hemoglobin (g/dl) | 12.0±1.30 | 12.1±1.28 | 12.1±1.29 | 12.0±1.30 | 12.1±1.29 |
| WBC ($\times 10^3/\mu$l) | 7.43±1.39 | 7.48±2.32 | 7.50±2.44 | 7.51±2.36 | 7.45±2.48 |
| Lymphocytes (%) | 20.5±7.51 | 20.3±7.29 | 20.3±7.33 | 20.4±7.49 | 19.9±7.44 |

Values expressed with a plus/minus sign are mean±SD. W, women; M, men; NA, not applicable; KRU, residual renal function; AHD, atherosclerotic heart disease; PVD, peripheral vascular disease; COPD, chronic-obstructive pulmonary disorder; TIBC, total iron-binding capacity; nPCR, normalized protein ctabolic rate expressed as normalized protein nitrogen appearance; WBC, white blood cell.

[a]Height ranges for the 3rd and 4th deciles of female height were not different because of large statistical representation of heights in this range. This was similarly observed in men in the 5th and 6th deciles of male heights. Thus, no female patients or male patients were represented in the 4th or 6th height deciles, respectively.

[b]A nonparametric test for trend was used to compare demographic and clinical variables among the 10 height deciles.

**Table 1. (Continued)**

| Height Decile | | | | | | |
|---|---|---|---|---|---|---|
| 5 (*n*=13,340) W: 1.60–<1.61 M: 1.75–<1.76 | 6 (*n*=7044) W: 1.61– <1.64 M: NA[a] | 7 (*n*=12,427) W: 1.64–<1.66 M: 1.76–<1.80 | 8 (*n*=10,151) W: 1.66– <1.70 M: 1.80– <1.81 | 9 (*n*=11,514) W: 1.70–<1.73 M: 1.81–<1.88 | 10 (*n*=7950) W: 1.73–2.00 M: 1.88–2.00 | *P* Value[b] |
| 62±15 | 62±15 | 61±15 | 60±15 | 59±15 | 57±15 | <0.001 |
| 48 | 100 | 44 | 43 | 25 | 48 | <0.001 |
| 57 | 61 | 57 | 56 | 55 | 54 | <0.001 |
| 75.4±18.9 | 72.2±18.6 | 79.4±19.5 | 81.7±20.3 | 87.0±21.3 | 90.0±23.8 | <0.001 |
| 51 | 50 | 50 | 51 | 49 | 46 | <0.001 |
| 45 | 41 | 50 | 47 | 49 | 43 | <0.001 |
| 2 | 1 | 1 | <1 | <1 | <1 | <0.001 |
| 35 | 40 | 35 | 40 | 41 | 48 | <0.001 |
| 12 | 10 | 8 | 6 | 5 | 3 | <0.001 |
| 6 | 7 | 5 | 5 | 4 | 4 | <0.001 |
| 53 | 52 | 53 | 53 | 53 | 50 | 0.88 |
| 18 | 18 | 19 | 19 | 19 | 18 | 0.004 |
| 18 | 19 | 17 | 18 | 18 | 19 | 0.74 |
| 11 | 11 | 11 | 11 | 10 | 12 | 0.001 |
| 64 | 64 | 63 | 62 | 61 | 61 | <0.001 |
| 4 | 6 | 4 | 4 | 4 | 4 | <0.001 |
| 10 | 9 | 10 | 10 | 10 | 10 | <0.001 |
| 14 | 13 | 15 | 15 | 17 | 16 | <0.001 |
| 8 | 9 | 8 | 9 | 8 | 9 | <0.001 |
| 40 | 31 | 41 | 40 | 43 | 37 | <0.001 |
| 7 | 8 | 7 | 8 | 7 | 8 | 0.79 |
| 23 | 23 | 23 | 25 | 25 | 29 | <0.001 |
| 13 | 21 | 11 | 11 | 8 | 9 | <0.001 |
| 17 | 17 | 18 | 17 | 17 | 17 | <0.001 |
| 1.53±0.34 | 1.58±0.32 | 1.50±0.33 | 1.47±0.32 | 1.43±0.21 | 1.43±0.31 | <0.001 |
| 2.54±1.32 | 2.44±0.87 | 2.55±1.32 | 2.56±1.38 | 2.61±1.45 | 2.60±1.32 | <0.001 |
| 79 | 80 | 79 | 80 | 79 | 80 | 0.95 |
| 5 | 4 | 5 | 5 | 5 | 4 | <0.001 |
| 21 | 17 | 22 | 21 | 21 | 17 | <0.001 |
| 27 | 25 | 28 | 27 | 26 | 25 | <0.001 |
| 5 | 5 | 6 | 5 | 6 | 5 | <0.001 |
| 11 | 11 | 12 | 11 | 11 | 11 | <0.001 |
| 7 | 6 | 8 | 7 | 7 | 7 | 0.03 |
| 2 | 2 | 2 | 2 | 2 | 2 | <0.001 |
| 6 | 5 | 6 | 6 | 6 | 5 | <0.001 |
| 6 | 6 | 5 | 6 | 6 | 6 | <0.001 |
| 3.68±0.44 | 3.64±0.42 | 3.68±0.44 | 3.68±0.44 | 3.71±0.45 | 3.68±0.45 | <0.001 |
| 8.04±3.12 | 7.49±2.72 | 8.11±3.13 | 8.28±3.24 | 8.60±3.36 | 8.62±3.30 | <0.001 |
| 209±44.1 | 205±43.7 | 209±43.5 | 208±43.0 | 210±43.2 | 207±42.9 | <0.001 |
| 22.3±2.85 | 22.3±2.89 | 22.3±2.85 | 22.3±2.88 | 22.2±2.84 | 22.3±2.84 | 0.92 |
| 9.21±0.69 | 9.26±0.69 | 9.21±0.68 | 9.22±0.68 | 9.21±0.68 | 9.25±0.68 | 0.003 |
| 5.57±1.41 | 5.54±1.40 | 5.61±1.41 | 5.67±1.45 | 5.73±1.45 | 5.75±1.42 | <0.001 |
| 515±446 | 534±459 | 503±444 | 506±460 | 493±441 | 508±437 | <0.001 |
| 0.94±0.24 | 0.93±0.24 | 0.94±0.24 | 0.93±0.23 | 0.93±0.23 | 0.91±0.23 | <0.001 |
| 12.0±1.31 | 12.0±1.29 | 12.0±1.29 | 12.0±1.32 | 12.0±1.31 | 12.0±1.33 | <0.001 |
| 7.41±2.34 | 7.51±2.42 | 7.42±2.48 | 7.38±2.54 | 7.29±2.25 | 7.28±2.32 | <0.001 |
| 20.6±7.55 | 20.9±7.51 | 20.6±7.59 | 20.6±7.58 | 20.8±7.68 | 21.2±7.75 | 0.02 |

**Table 2. All-cause mortality hazard ratio by sex-standardized height decile**

| Height Decile | Mortality (%) (Frequency) | Hazard Ratio (95% Confidence Interval) | | | | |
|---|---|---|---|---|---|---|
| | | Unadjusted[a] | Age Adjusted[a] | Age, Sex, Race Adjusted[a] | Case-Mix Adjusted[b] | Fully Adjusted[c] |
| 1 | 52 (7059) | 0.98 (0.95 to 1.02) | 0.90 (0.87 to 0.93) | 0.95 (0.92 to 0.99) | 0.88 (0.85 to 0.91) | 0.91 (0.88 to 0.94) |
| 2 | 53 (8224) | 1.03 (0.99 to 1.07) | 0.96 (0.93 to 0.99) | 1.00 (0.97 to 1.03) | 0.94 (0.91 to 0.98) | 0.97 (0.94 to 1.00) |
| 3 | 52 (9657) | 1.01 (0.98 to 1.04) | 0.95 (0.92 to 0.98) | 0.97 (0. 94 to 1.00) | 0.94 (0.91 to 0.97) | 0.95 (0.92 to 0.98) |
| 4 | 51 (3940) | 1.01 (0.97 to 1.05) | 1.00 (0.96 to 1.04) | 0.99 (0.95 to 1.03) | 0.98 (0.94 to 1.02) | 0.97 (0.94 to 1.01) |
| 5[d] | 52 (6905) | 1 | 1 | 1 | 1 | 1 |
| 6 | 53 (3705) | 1.04 (0.99 to 1.08) | 1.02 (0.98 to 1.06) | 1.04 (1.00 to 1.08) | 1.05 (1.01 to 1.10) | 1.06 (1.02 to 1.11) |
| 7 | 52 (6410) | 1.04 (1.01 to 1.08) | 1.07 (1.03 to 1.10) | 1.05 (1.02 to 1.09) | 1.08 (1.05 to 1.12) | 1.07 (1.03 to 1.11) |
| 8 | 50 (5039) | 0.98 (0.95 to 1.02) | 1.05 (1.01 to 1.09) | 1.04 (1.00 to 1.08) | 1.09 (1.05 to 1.13) | 1.06 (1.02 to 1.10) |
| 9 | 49 (5637) | 0.97 (0.94 to 1.01) | 1.10 (1.06 to 1.13) | 1.07 (1.03 to 1.11) | 1.15 (1.11 to 1.20) | 1.14 (1.10 to 1.18) |
| 10 | 47 (3709) | 0.93 (0.89 to 0.96) | 1.11 (1.07 to 1.16) | 1.11 (1.06 to 1.15) | 1.24 (1.19 to 1.29) | 1.18 (1.14 to 1.23) |

[a]Adjusted for weight and cohort entry quarter.
[b]Further adjusted for age, sex, race/ethnicity, diabetes mellitus, nine pre-existing comorbidities (cancer, HIV infection, peripheral vascular disease, congestive heart failure, hypertension, cerebrovascular accident, atherosclerotic heart disease, other cardiac disease, and chronic obstructive pulmonary disease), tobacco smoking, dialysis vintage, insurance status, marital status, dialysis dose, and residual renal function.
[c]Additionally adjusted for 11 serum or blood laboratory variables (albumin, total iron-binding capacity, ferritin, creatinine, phosphorus, calcium, normalized protein catabolic rate expressed as normalized protein nitrogen appearance, bicarbonate, white blood cell count, lymphocyte percentage, and hemoglobin).
[d]The fifth height decile was considered the decile of reference for calculations of all-cause mortality.

study suggests that the patient's height has approximately the same effect as weight on the BMI-mortality relationship because the BMI calculation includes the square of height. Thus, it is not entirely correct to interpret the BMI-mortality relationship in MHD patients as indicating that obesity and possibly increased muscle mass exclusively account for the lower mortality in these individuals. Short height also contributes to this statistically protective relationship of large BMI and lower mortality.

In the general population, greater height is often associated with reduced all-cause mortality (4–7) and mortality due to cardiovascular events (4–8) or with such specific causes of death as stroke, diabetes, respiratory diseases, or external factors (*e.g.*, accidents, suicides, homicides) (4,5,7,12,13). Our findings essentially indicate the opposite relationship in adults receiving MHD with the exception of the direct association between height and total cancer mortality that we observed, which has also been reported in some studies of the general population (8,14,15). To our knowledge, no study in the general population has demonstrated a direct association between height and all-cause mortality or cardiovascular mortality as we observed in MHD patients.

It is relevant that many of the preceding studies examining the height-mortality relationship in the general population have important limitations that include (*1*) lack of adjustment for age and/or socioeconomic status, (*2*) small sample sizes, (*3*) exclusively male or female cohorts, and (*4*) self-reporting of height (7). Indeed, after adjustment for important confounding variables, some well conducted studies in the general population observed no relationship between height and all-cause or cause-specific mortality, including cancer mortality (4,8,9,13). The Framingham heart study described an inverse relationship between height and both all-cause mortality and cardiovascular mortality, but this association was extinguished after adjustment for age (10) because older people are shorter than normal younger adults (16,17). The National Health and Nutrition Examination Survey (NHANES) study, one of the largest studies to examine height-mortality relationships in the general population, also found an inverse relation between unadjusted height and mortality (9). No relationship between height and mortality was observed after adjustment for age and socioeconomic status. In contrast to the Framingham and NHANES studies, we found that the height-mortality relationship became significantly positive after adjustment for age.

The rationale for statistical adjustment for age is based on an increase in adult height that has occurred in recent generations. This presumably might be due to better nutrition and health care and reduced shrinkage in height with age due to less bone demineralization, disk compression, spinal deformities, and changes in posture (10). However, decreased height with age is also consistent with taller people dying at younger ages. It is emphasized that the direct relationship between height and mortality described in the present study was observed after adjustments for age and types of health insurance; the latter may be an indicator of socioeconomic status. Almost all studies of the relationship of BMI to mortality in MHD patients adjusted for age. Therefore, our findings that shorter height contributes to the reduced mortality associated

**Table 3. All-cause mortality hazard ratio by sex-standardized weight decile**

| Weight Decile | Mortality (%) (Frequency) | Hazard Ratio (95% Confidence Interval) | | | |
|---|---|---|---|---|---|
| | | Unadjusted[a] | Age, Sex, Race Adjusted[a] | Case-Mix Adjusted[b] | Fully Adjusted[c] |
| 1 | 65 (7608) | 1.38 (1.33 to 1.43) | 1.49 (1.44 to 1.55) | 1.75 (1.69 to 1.81) | 1.48 (1.43 to 1.53) |
| 2 | 58 (6910) | 1.17 (1.13 to 1.21) | 1.20 (1.16 to 1.25) | 1.33 (1.28 to 1.37) | 1.21 (1.17 to 1.25) |
| 3 | 57 (6652) | 1.10 (1.06 to 1.14) | 1.11 (1.08 to 1.15) | 1.18 (1.14 to 1.22) | 1.13 (1.09 to 1.17) |
| 4 | 54 (6372) | 1.02 (0.99 to 1.06) | 1.04 (1.04 to 1.08) | 1.07 (1.03 to 1.10) | 1.05 (1.01 to 1.08) |
| 5[d] | 50 (6264) | 1 | 1 | 1 | 1 |
| 6 | 47 (5923) | 0.94 (0.91 to 0.97) | 0.95 (0.92 to 0.99) | 0.92 (0.89 to 0.96) | 0.93 (0.90 to 0.97) |
| 7 | 46 (5566) | 0.86 (0.83 to 0.90) | 0.90 (0.87 to 0.93) | 0.84 (0.81 to 0.87) | 0.88 (0.85 to 0.91) |
| 8 | 46 (5359) | 0.82 (0.79 to 0.85) | 0.88 (0.84 to 0.91) | 0.80 (0.77 to 0.83) | 0.84 (0.81 to 0.87) |
| 9 | 43 (5067) | 0.77 (0.74 to 0.80) | 0.87 (0.84 to 0.90) | 0.76 (0.73 to 0.79) | 0.80 (0.78 to 0.84) |
| 10 | 39 (4564) | 0.67 (0.64 to 0.70) | 0.87 (0.84 to 0.90) | 0.71 (0.68 to 0.74) | 0.76 (0.73 to 0.79) |

[a] Adjusted for weight and cohort entry quarter.
[b] Further adjusted for age, sex, race/ethnicity, diabetes mellitus, nine pre-existing comorbidities (cancer, HIV infection, peripheral vascular disease, congestive heart failure, hypertension, cerebrovascular accident, atherosclerotic heart disease, other cardiac disease, and chronic obstructive pulmonary disease), tobacco smoking, dialysis vintage, insurance status, marital status, dialysis dose, and residual renal function.
[c] Additionally adjusted for 11 serum or blood laboratory variables (albumin, total iron-binding capacity, ferritin, creatinine, phosphorus, calcium, normalized protein catabolic rate expressed as normalized protein nitrogen appearance, bicarbonate, white blood cell count, lymphocyte percentage, and hemoglobin).
[d] The fifth height decile was considered the decile of reference for calculations of all-cause mortality.

with larger BMIs should apply to at least most published findings in MHD patients concerning this matter.

To our knowledge, only one other study has examined the relationship of height to all-cause mortality in adults with ESRD (18). Takenaka *et al.* described an inverse association between height and all-cause mortality in diabetic and nondiabetic MHD patients. Limitations of that study included its small cohort (104 patients) and lack of adjustment for such confounders of the height-mortality relationship as age or proxies for socioeconomic status, including insurance status. In the present study, there was also a slightly inverse relationship between height and mortality in unadjusted analyses. After adjustment for case-mix or case-mix plus laboratory variables, the association between height and mortality in our patients became clearly positive, owing primarily to the confounding effects of patient age (Table 2).

The mechanisms responsible for the direct association between height and all-cause and cause-specific mortality in MHD patients are unclear. One possibility is that tall patients may not be as well dialyzed as shorter patients. Men and women of various heights and body types generally undergo hemodialysis for approximately the same amounts of time in individual long-term hemodialysis centers (19). Because taller individuals tend to have increased body mass, dialysis sessions of equal duration may predispose this group to a lower dialysis dose per unit body mass (*i.e.,* Kt/Vurea). Indeed, a recent report found that big men more frequently received lower dialysis doses, when adjusted for body mass, than did smaller, normal-sized people (20). In observational studies, dialysis dose is inversely associated with mortality in dialysis patients (21–23); thus, greater height might place a patient at greater risk for a less-than-optimal dialysis dose.

Height might also be more important than weight *per se* as the greater determinant of the needed dialysis dose. For a given height, greater body weight is probably determined more by fat mass than muscle mass. Because adipocytes contain only 5%–7% water (24), the additional dialysis needed to remove dialyzable toxins might be smaller in people with greater fat mass. In contrast, for a given weight, greater height may indicate greater lean body mass (25), and hence a larger pool of dialyzable toxins. Thus, taller people with ESRD may have a greater exposure to uremic toxins because they may have increased numbers of nonadipocyte cells and more dialyzable toxins due to increased muscle mass, for the same weight on average, as compared with shorter persons (26). Thus, these individuals might benefit more from a greater dose of dialysis than shorter individuals of the same weight. Although our analyses included statistical adjustment for baseline dialysis dose (Kt/V), such an adjustment demonstrates only whether inadequate dialysis dose is responsible for the observed direct height-mortality association if taller patients are indeed receiving sufficiently greater doses than shorter individuals after adjustment for body weight. Of note, we found that taller patients tended to receive slightly lower dialysis doses than shorter patients in models adjusted for weight.

An additional possible explanation for the association of height with higher mortality in MHD patients is that the

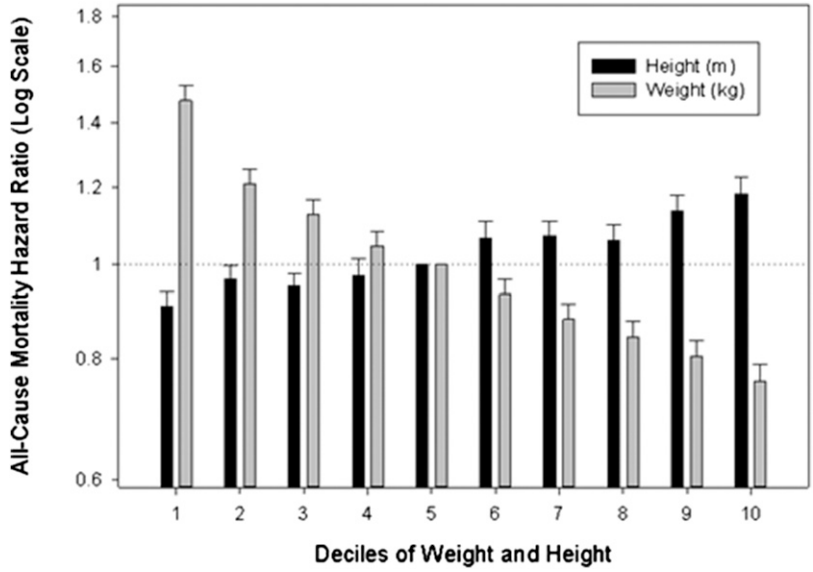


**Figure 2.** | **Case-mix plus laboratory-adjusted mortality hazard ratios by sex-standardized decile of height and weight.** Error bars represent 95% confidence intervals of hazard ratios.

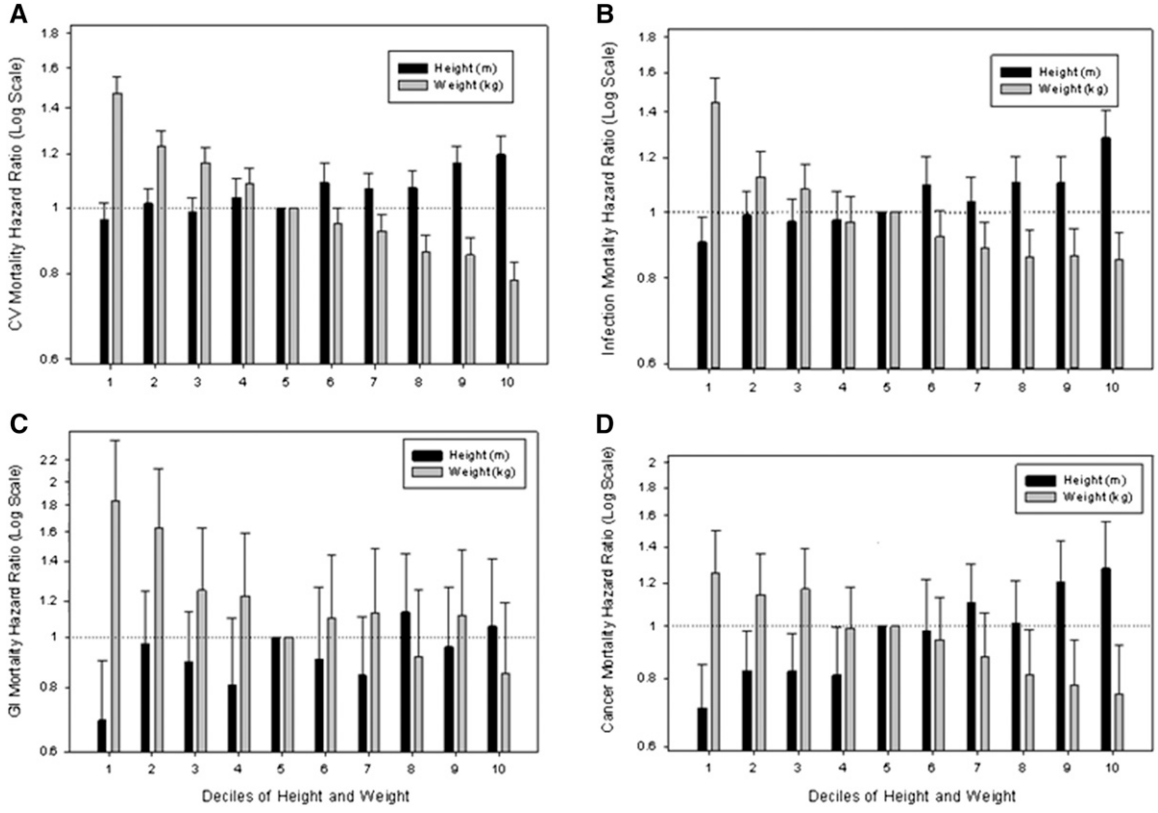


**Figure 3.** | **Case-mix plus laboratory-adjusted mortality hazard ratios by sex-standardized decile of height and weight.** (A) cardiovascular (CV), (B) infection, (C) gastrointestinal (GI), and (D) cancer mortality outcomes. Error bars represent 95% confidence intervals of hazard ratios.

total body burden of some uremic toxins may increase mortality, independent of the concentration of the toxins in the body. If this were the case, then taller people, who again for the same weight should have greater lean body mass, might be at greater risk for certain water-soluble uremic toxins. Some uremic toxins may have apoptotic, inflammatory, oxidative, or coagulative effects on the cardiovascular system and other organ systems (27,28), and are directly associated with cardiovascular morbidity and mortality in the CKD population (27,29,30).

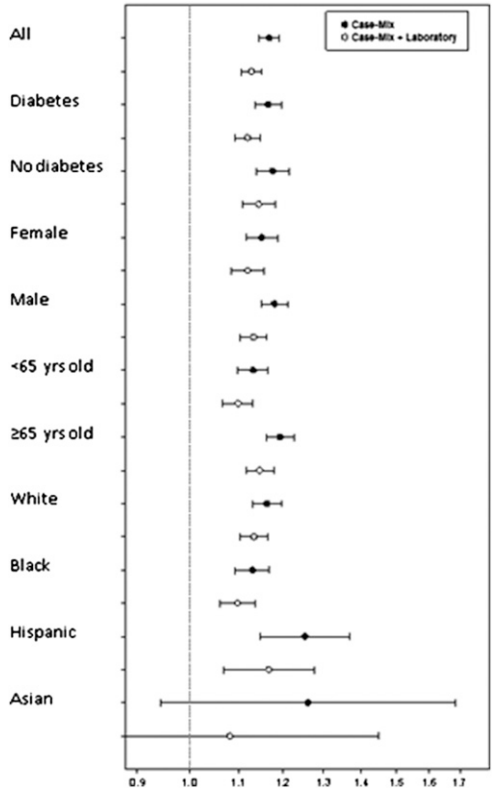


**Figure 4. | All-cause mortality risks of taller patients (>70th sex-standardized percentile of height) relative to shorter patients (≤70th sex-standardized percentile of height), adjusted for case-mix plus laboratory variables, in subgroup analyses.** A hazard ratio >1.0 indicates higher mortality risk in these taller patients compared with shorter patients.

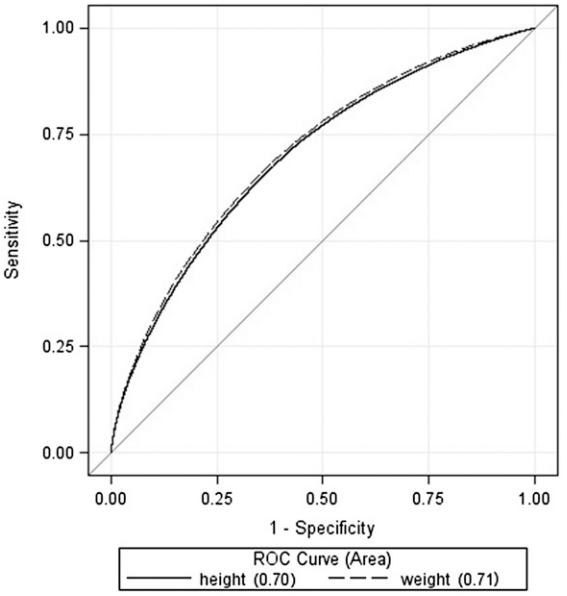


**Figure 5. | Receiver-operating characteristic (ROC) curve assessing the performance of height (unadjusted for weight) and weight (unadjusted for height) in predicting mortality in a case-mix model (adjusted for age, sex, and presence of diabetes).**

Aortic atherosclerosis with calcification is commonly associated with increased aortic pulse wave velocity after cardiac systole (31). Increased aortic pulse wave velocity is thought to be injurious to the cardiovascular system and is associated with increased cardiovascular and all-cause mortality in several populations (32), including MHD patients (33). Some but not all studies suggest that aortic pulse wave velocity may be elevated in taller MHD patients and in taller normal individuals (34–37). These findings, if confirmed, might explain the increased cardiovascular and all-cause mortality risk we observed in taller MHD patients.

People with advanced kidney disease and ESRD have an increased incidence of cancer compared with the general population (38). As in the general population (39,40), we observed a direct association between height and cancer-related mortality. It has been speculated that hereditary factors and early nutrition may be responsible for this relationship between height and cancer mortality in normal adults. However, it has been recently postulated that taller individuals may be at greater risk because of their greater number of cells (41), perhaps particularly when they are exposed to uremic toxins that engender oxidative, inflammatory, or carbonyl stress (42–44).

This study has several strengths. The cohort size was quite large—117,644 MHD patients—particularly compared with studies of height versus mortality in the general population or the one other published study involving 104 adults undergoing MHD. Our study population was national and diverse, and substantial amounts of clinically and demographically relevant data were available for characterizing the study cohort and for adjustment for many potential confounders of the height or BMI versus mortality relationships. The study also had limitations. We examined patients from 2001 to 2006, and mortality trends in this population may have changed. Information on the patients' medical history and other aspects of their lives before they began long-term dialysis treatment was also limited.

## Disclosures

None.

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