AJKD
Original Investigation

Ultrafiltration Rate and Mortality in Maintenance Hemodialysis Patients

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Background: Observational data have demonstrated an association between higher ultrafiltration rates and greater mortality among hemodialysis patients. Prior studies were small and did not consider potential differences in the association across body sizes and other related subgroups. No study has investigated ultrafiltration rates normalized to anthropometric measures beyond body weight. Also, potential methodological shortcomings in prior studies have led to questions about the veracity of the ultrafiltration rate−mortality association.

Study Design: Retrospective cohort.

Setting & Participants: 118,394 hemodialysis patients dialyzing in a large dialysis organization, 2008 to 2012.

Predictors: Mean 30-day ultrafiltration rates were dichotomized at 13 and 10 mL/h/kg, separately and categorized using various cutoff points. Ultrafiltration rates normalized to body weight, body mass index, and body surface area were investigated.

Outcomes: All-cause mortality.

Measurements: Multivariable survival models were used to estimate the association between ultrafiltration rate and all-cause mortality.

Results: At baseline, 21,735 (18.4%) individuals had ultrafiltration rates $>$ 13 mL/h/kg and 48,529 (41.0%) had ultrafiltration rates $>$ 10 mL/h/kg. Median follow-up was 2.3 years, and the mortality rate was 15.3 deaths/100 patient-years. Compared with ultrafiltration rates $\leq$ 13 mL/h/kg, ultrafiltration rates $>$ 13 mL/h/kg were associated with greater mortality (adjusted HR, 1.31; 95% CI, 1.28-1.34). Compared with ultrafiltration rates $\leq$ 10 mL/h/kg, ultrafiltration rates $>$ 10 mL/h/kg were associated with greater mortality (adjusted HR, 1.22; 95% CI, 1.20-1.24). Findings were consistent across subgroups of sex, race, dialysis vintage, session duration, and body size. Higher ultrafiltration rates were associated with greater mortality when normalized to body weight, body mass index, and body surface area.

Limitations: Residual confounding cannot be excluded given the observational study design.

Conclusions: Regardless of the threshold implemented, higher ultrafiltration rate was associated with greater mortality in the overall study population and across key subgroups. Randomized controlled trials are needed to investigate whether ultrafiltration rate reduction improves clinical outcomes.

Am J Kidney Dis. 68(6):911-922.

INDEX WORDS: Hemodialysis; mortality; ultrafiltration rate (UFR); body size; body weight; body mass index (BMI); body surface area (BSA); anthropometric measures; metabolic mass; rapid fluid removal; end-stage renal disease (ESRD).

Hemodialysis (HD) patients have high rates of morbidity and mortality.[1] Fluid removal practices likely contribute to these poor outcomes. Existing data support an association between more rapid fluid removal during dialysis and greater mortality.[2-4] End-organ ischemia of the heart, brain, and gut from overt and subclinical hemodynamic instability plausibly underlie this association.[5-8] Ultrafiltration rate is quantifiable and represents a modifiable fluid-related aspect of the HD prescription that is potentially within dialysis facility control. Currently, the Centers for Medicare & Medicaid Services (CMS) is considering an ultrafiltration rate threshold of 13 mL/h/kg as a quality measure to assess dialysis facility fluid management, and such a threshold has been incorporated into the CMS 2016 End Stage Renal Disease Core Survey.[9,10]

Three observational investigations have demonstrated harm from greater ultrafiltration rates.[2-4] However, the studies are modestly sized, precluding robust analyses among key subgroups with plausibly different ultrafiltration rate−outcome associations. The ultrafiltration rate threshold delineating heightened risk may vary by patient type, which if true would make a single ultrafiltration rate benchmark inappropriate as a quality measure. Patient characteristics such as body size and composition influence

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Received February 24, 2016. Accepted in revised form June 14, 2016. Originally published online August 27, 2016.

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0272-6386
http://dx.doi.org/10.1053/j.ajkd.2016.06.020

total-body water distribution and plasma refill, making body size and its correlating factors of race and sex plausible modifiers of the ultrafiltration rate−outcome association. Additionally, ultrafiltration rates are typically normalized to body weight. However, ultrafiltration rate normalization to other anthropometric measures that may capture metabolic mass better has not been evaluated. Finally, potential shortcomings in prior analyses may have biased risk estimates. Investigators included interdialytic weight gain (IDWG), session duration, and weight, all ultrafiltration rate calculation components, in multivariable models. Such inclusion may obscure the true association between ultrafiltration rates and outcomes.[11] These uncertainties, along with the observational nature of the data, have led to reluctance by guideline bodies such as NKF-KDOQI (National Kidney Foundation−Kidney Disease Outcomes Quality Initiative) to issue firm ultrafiltration rate guidelines and questions about the appropriateness of a single weight-based ultrafiltration rate threshold for all patients.[12,13]

We undertook this study to further investigate the association of ultrafiltration rate and mortality in a large prevalent HD patient cohort. We examined the ultrafiltration rate−mortality association across body size, sex, race, dialysis vintage, and HD session duration subgroups. We also investigated the robustness of the ultrafiltration rate−mortality association across ultrafiltration rate calculations normalized to different anthropometric measures.

METHODS

Study Design

Data were obtained from a cohort of 337,863 patients receiving HD at a single large dialysis organization (LDO) from June 2008 through December 2012. Figure 1 displays study design. Patients were included if they were 18 years or older, received in-center HD, and had been on dialysis therapy for 90 days or longer at study entry. Exclusion criteria included the occurrence of death or censoring event during the exposure period, fewer than 7 in-center HD treatments during the exposure period, and missing ultrafiltration rate data. We identified all in-center HD patients who met study eligibility criteria as of June 1, 2008 (study start date). For patients entering the LDO database later in calendar time, eligibility criteria was assessed on the first outpatient HD treatment date in the data. This date was the study entry date for patients entering the cohort after June 1, 2008.

Demographic characteristics (age, sex, race, height, and dialysis vintage) and comorbid conditions (diabetes, heart failure, and coronary disease) were considered as of cohort entry. Laboratory and HD treatment data were captured in a 30-day baseline period. Laboratory covariates (urea reduction ratio, albumin, sodium, creatinine, hemoglobin, and phosphate) were considered as the last nonmissing values in the baseline period. Predialysis systolic blood pressure was considered as the mean of values in the baseline period. Ultrafiltration rates were assessed in a 30-day exposure period following the baseline period. Patients surviving the baseline and exposure periods (to study day 60) were followed forward in historical time to death, censoring event, or study end (December 31, 2013).

This study was approved by the University of North Carolina at Chapel Hill Institutional Review Board (IRB number 15-2100). Given the large cohort size, data anonymity, and nonintrusive research, informed consent requirements were exempted.

Data Collection

All data were obtained from the LDO's medical records. Demographics were recorded upon admission to an organization facility. Comorbid conditions were determined by a nephrologist at the time of patient entry to the LDO and updated based on clinical course. Laboratory results were measured biweekly or monthly. Dialysis treatment data including session duration and pre- and postdialysis weights were recorded on a treatment-to-treatment basis. IDWG was defined as predialysis weight (kg) minus postdialysis weight (kg) from the previous treatment. Based on review of relevant medical records and per standardized LDO protocol, death dates were recorded by facility personnel.

Designation of Exposures and Outcome

In primary analyses, prescribed ultrafiltration rate normalized to body weight (mL/h/kg) was calculated as follows: IDWG (mL)/prescribed session duration (h)/post-HD weight (kg) for each exposure period HD treatment. Prescribed ultrafiltration rate was assumed constant during each treatment and was considered as a mean of ultrafiltration rate values over the 30-day exposure period. A 30-day exposure period was selected a priori to limit survivorship bias and mirror prior analyses.[3,4] Sixty- and 90-day periods were considered in sensitivity analyses, and results were analogous (Table S1, available as online supplementary material). Additional sensitivity analyses considered time-updated ultrafiltration rate and mortality.

In primary analyses, prescribed ultrafiltration rate was treated as binary (≤10 vs >10 mL/h/kg and ≤13 vs >13 mL/h/kg, separately) to mirror the dichotomized approach of quality measures.[14] Secondary analyses considered categorized ultrafiltration rates (<10, 10-13, and >13 mL/h/kg), consistent with prior studies,[2,4] and more granular ultrafiltration rate categories (<6, 6-<8,

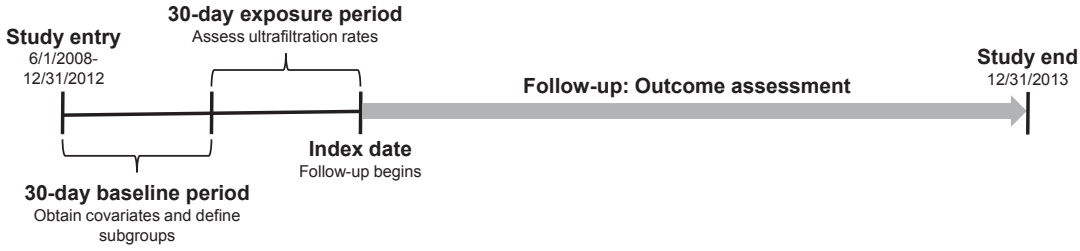

Figure 1. Study design schematic.

8-<10, 10-<12, 12-<14, and ≥14 mL/h/kg) and continuous ultrafiltration rates. To evaluate for a dose-response relationship, we constructed a frequency-based ultrafiltration rate exposure definition. We considered the proportion of HD treatments in the exposure period with ultrafiltration rates > 13 mL/h/kg: <25%, 25% to 50%, and >50% of treatments. We selected a threshold of 13 mL/h/kg to mirror the CMS surveyor tool cutoff point.[10] We conducted additional analyses considering delivered ultrafiltration rates. Delivered ultrafiltration rate normalized to body weight (mL/h/kg) was calculated as: ultrafiltration volume (mL)/delivered session duration (h)/post-HD weight (kg).

Secondary analyses were performed considering ultrafiltration rate normalized to body mass index (BMI; kg/m^2) and body surface area (BSA; m^2), separately. To mirror primary analyses, BMI and BSA were calculated based on post-HD weight. BSA was calculated according to Du Bois and Du Bois.[15] In these analyses, ultrafiltration rate normalized to BMI (mL/h/kg/m^2) and ultrafiltration rate normalized to BSA (mL/h/m^2) were dichotomized at the 80th percentiles. The 80th percentile threshold was selected to mirror the primary analysis because 13 mL/h/kg represented the 80th percentile of mL/h/kg rate normalized to body weight.

The outcome of interest was all-cause mortality. Patients were considered at risk for the study outcome following the exposure period and remained at risk until death or censoring for loss to follow-up or study end (December 31, 2013). Dialysis modality change and kidney transplantation were treated as competing risks.[16]

Statistical Analyses

Analyses were performed using SAS, version 9.4 (SAS Institute Inc). Baseline patient characteristics were described across ultrafiltration rate groups as count and proportion for categorical variables and mean ± standard deviation for continuous variables.

Time-to-event analyses were conducted using unadjusted and adjusted Fine and Gray proportional subdistribution hazards regression models to estimate hazard ratios (HRs). The proportionality assumption was confirmed by Schoenfeld residual testing. Missing values of laboratory variables were imputed using the Markov chain Monte Carlo method with 10 imputations (albumin, n = 2,184; creatinine, n = 7,473; phosphorus, n = 1,430; hemoglobin, n = 627; and urea reduction ratio, n = 1,642).[17] Implausible values of pre- and post-HD weight, session duration, and post-HD weight were considered missing. Collinearity of exposure and model covariates was evaluated by the variance inflation factor. IDWG, session duration, and post-HD weight demonstrated moderate collinearity with ultrafiltration rate and were excluded from the model (variance inflation factor ≥ 1.3 vs =1.0 for all other model variables).

Effect modification of the ultrafiltration rate−mortality association on the basis of sex, race (black vs nonblack), ethnicity (Hispanic vs non-Hispanic), body weight (<20th vs >80th percentile of post-HD weight), dialysis vintage (<4 vs ≥4 years), and session duration (<4 vs ≥4 hours) was explored through restriction subgroup analyses. Significance of interaction was assessed by the Wald test of nested models that did and did not include 2-way cross-product terms. Restricted analyses, using the same analytic methods as primary analyses, were performed in subgroups of interest (session duration ≥ 4 hours and dialysis vintage ≥ 4 years). In secondary analyses, the Vuong test was used to compare the relative mortality predictive value of ultrafiltration rates normalized to body weight (kg), mL/h/kg (vs BMI, mL/h/kg/m^2, and BSA, mL/h/m^2, separately) based on the cumulative incidence function of fully adjusted models.[18]

In sensitivity analyses, we assessed the association between time-updated ultrafiltration rate (milliliters per hour per kilogram) and mortality using marginal structural proportional hazards models. Marginal structural models estimate the effect of a time-varying exposure on an outcome by controlling for the effects of time-dependent confounders.[19,20] Table *a* and figure *a* of Item S1 provide detailed methods.

RESULTS

Cohort Characteristics

Figure 2 displays a flow chart of patient selection. Table 1 displays cohort characteristics across prescribed ultrafiltration rate groups. Compared with patients with ultrafiltration rates ≤ 13 mL/h/kg, patients with ultrafiltration rates > 13 mL/h/kg had smaller body sizes, were younger, and were more likely to be female, nonblack, and Hispanic and have comorbid heart failure, longer dialysis vintage, shorter session durations, and larger IDWGs. Table S2 displays comparisons of included and excluded patients.

Overall, 118,394 patients underwent 1,511,740 treatments during the exposure period. Of these, 69,865 (59.0%) patients had ultrafiltration rates < 10 mL/h/kg, 26,794 (22.6%) had ultrafiltration rates of 10 to 13 mL/h/kg, and 21,735 (18.4%) had ultrafiltration rates > 13 mL/h/kg. Median follow-up was 2.3 (interquartile range [IQR], 1.0-4.4) years, and there were 310,064 patient-years of total follow-up. Mortality occurred at a rate of 15.3 deaths/100 patient-years.

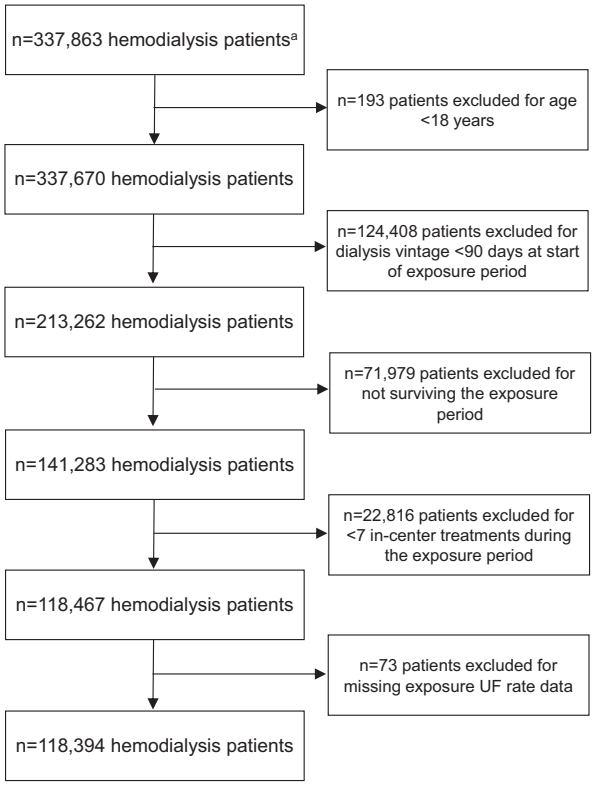

Figure 2. Flow chart of cohort selection. [a]Source cohort consisted of 337,863 in-center hemodialysis patients with complete age, sex, race, and ethnicity data. Abbreviation: UF, ultrafiltration.

Table 1. Baseline Characteristics Across Prescribed Ultrafiltration Rate Groups

		30-d Mean Prescribed UF Rate		
	Total (N = 118,394)[b]	<10 mL/h/kg (n = 69,865 [59.0%])[a]	10-13 mL/h/kg (n = 26,794 [22.6%])[a]	>13 mL/h/kg (n = 21,735 [18.4%])[a]
UF rate				
mL/h/kg	9.4 ± 4.3	6.6 ± 2.5	11.4 ± 0.9	16.0 ± 2.9
mL/h/kg/m^2	27.2 ± 13.2 (n = 118,215)	19.5 ± 8.5 (n = 69,743)	32.8 ± 6.4 (n = 26,765)	45.0 ± 10.8 (n = 21,707)
mL/h/m^2	377.2 ± 154.2 (n = 118,215)	286.3 ± 107.7 (n = 69,768)	451.1 ± 70.0 (n = 26,765)	578.3 ± 111.8 (n = 21,707)
Age, y	61 ± 15	62 ± 15	61 ± 15	58 ± 16
Female sex	53,307 (45.0)	30,964 (44.3)	11,554 (43.1)	10,789 (49.6)
Black race	45,289 (38.3)	28,584 (40.9)	9,713 (36.3)	6,992 (32.2)
Hispanic ethnicity	19,520 (16.5)	9,823 (14.1)	5,108 (19.1)	4,589 (21.1)
History of heart failure	31,534 (26.6)	16,775 (24.0)	7,911 (29.5)	6,848 (31.5)
History of CVD	66,988 (56.6)	37,999 (54.4)	15,864 (59.2)	13,125 (60.4)
History of diabetes	61,721 (52.1)	36,085 (51.6)	14,467 (54.0)	11,169 (51.4)
Dialysis vintage				
<1 y	25,283 (21.4)	16,874 (24.2)	4,963 (18.5)	3,446 (15.9)
1-2 y	39,411 (33.3)	23,995 (34.3)	8,788 (32.8)	6,628 (30.5)
3-4 y	22,718 (19.2)	12,842 (18.4)	5,404 (20.2)	4,472 (20.6)
≥5 y	30,982 (26.2)	16,154 (23.1)	7,639 (28.5)	7,189 (33.1)
Vascular access				
Graft	25,743 (21.7)	14,323 (20.5)	6,184 (23.1)	5,236 (24.1)
Fistula	61,991 (52.4)	35,226 (50.4)	14,784 (55.2)	11,981 (55.1)
Catheter	30,660 (25.9)	20,316 (29.1)	5,826 (21.7)	4,518 (20.8)
Post-HD weight, kg	79.2 ± 22.4	84.6 ± 23.7	75.6 ± 18.3	73.5 ± 6.5
IDWG, kg	2.9 ± 2.2	2.5 ± 2.1	3.3 ± 2.0	3.6 ± 2.2
BMI, kg/m^2	27.7 ± 7.3 (n = 118,215)	29.3 ± 7.8 (n = 69,743)	26.6 ± 6.1 (n = 26,765)	23.9 ± 5.1 (n = 21,707)
BSA, m^2	1.9 ± 0.3 (n = 118,215)	2.0 ± 0.3 (n = 69,768)	1.9 ± 0.2 (n = 26,765)	1.7 ± 0.2 (n = 21,707)
Prescribed session duration, min	218 ± 36	223 ± 39	214 ± 28	205 ± 28
Pre-HD SBP				
≤130 mm Hg	28,766 (24.3)	17,419 (24.9)	6,403 (23.9)	4,944 (22.7)
131-150 mm Hg	34,102 (28.8)	20,217 (28.9)	7,783 (29.0)	6,102 (28.1)
151-170 mm Hg	30,279 (25.6)	17,640 (25.2)	6,934 (25.9)	5,705 (26.2)
≥171 mm Hg	25,247 (21.3)	14,589 (20.9)	5,674 (21.2)	4,984 (22.9)
Missed sessions ≥ 3	23,590 (19.9)	13,590 (19.5)	5,183 (19.3)	4,817 (22.2)
Albumin[b]				
≤3.0 g/dL	6,390 (5.4)	3,932 (5.6)	1,216 (4.5)	1,242 (5.7)
3.1-3.5 g/dL	19,852 (16.8)	11,829 (16.9)	4,255 (15.9)	3,768 (17.3)
3.6-4.0 g/dL	56,005 (47.3)	33,335 (47.7)	12,785 (47.7)	9,885 (45.5)
>4.0 g/dL	36,147 (30.5)	20,769 (29.7)	8,538 (31.9)	6,840 (31.5)
Serum sodium, mEq/L[b]	138.2 ± 2.1	138.4 ± 2.0	138.2 ± 2.1	137.8 ± 2.3
Creatinine, mg/dL[b]	8.3 ± 3.1	8.1 ± 3.1	8.6 ± 3.1	8.6 ± 3.1
Phosphorus[b]				
≤4.0 mg/dL	23,431 (19.8)	14,849 (21.3)	4,815 (18.0)	3,767 (17.3)
4.1-5.0 mg/dL	33,958 (28.7)	20,981 (30.0)	7,553 (28.2)	5,424 (25.0)
5.1-6.0 mg/dL	29,464 (24.9)	17,376 (24.9)	6,754 (25.2)	5,334 (24.5)
>6.0 mg/dL	31,541 (26.6)	16,659 (23.8)	7,672 (28.6)	7,210 (33.2)

(Continued)

Primary Analyses

Unadjusted and adjusted associations between prescribed ultrafiltration rate normalized to body weight and mortality are presented in Table 2. Prescribed ultrafiltration rates > 13 (vs ≤13) mL/h/kg were associated with greater mortality (adjusted HR, 1.31; 95% confidence interval [CI], 1.28-1.34). At a lower threshold, prescribed ultrafiltration rates > 10 (vs ≤10) mL/h/kg were also associated with greater mortality (adjusted HR, 1.22; 95% CI, 1.20-1.24).

Table 1 (Cont'd). Baseline Characteristics Across Prescribed Ultrafiltration Rate Groups

		30-d Mean Prescribed UF Rate		
	Total (N = 118,394)[b]	<10 mL/h/kg (n = 69,865 [59.0%])[a]	10-13 mL/h/kg (n = 26,794 [22.6%])[a]	>13 mL/h/kg (n = 21,735 [18.4%])[a]
Hemoglobin[b]				
<10.0 g/dL	12,805 (10.8)	7,373 (10.6)	2,713 (10.1)	2,719 (12.5)
10.0-11.9 g/dL	56,405 (47.6)	33,526 (48.0)	12,680 (47.3)	10,199 (46.9)
≥12.0 g/dL	49,184 (41.5)	28,966 (41.5)	11,401 (42.6)	8,817 (40.6)
Urea reduction ratio, %[b]	73.0 ± 6.8	72.8 ± 7.0	73.2 ± 6.5	73.5 ± 6.5

Note: Values for categorical variables are given as number (percentage); for continuous variables, as mean ± standard deviation.

Abbreviations: BMI, body mass index; BSA, body surface area; CVD, cardiovascular disease; HD, hemodialysis; IDWG, interdialytic weight gain; SBP, systolic blood pressure; UF, ultrafiltration.

[a]Total n except where noted.

[b]Imputed using Markov chain Monte Carlo method using 10 imputations when missing (n = 2,184 for albumin, n = 88,218 for serum sodium, n = 7,473 for creatinine, n = 1,430 for phosphorus, n = 627 for hemoglobin, and n = 1,642 for urea reduction ratio).

Because we lacked data on residual urine output, we performed analyses restricted to patients with dialysis vintages of 4 or more years (n = 40,706). Results were analogous to those of the full cohort (Table 2). We observed a dose-response association between ultrafiltration rate and mortality, with more frequent exposure to elevated ultrafiltration rates associated with increased harm. Compared with <25% of

Table 2. Associations Between Prescribed Ultrafiltration Rate and All-Cause Mortality Among All Patients and Patients With Longer Dialysis Vintage

	No. (%)	Unadjusted HR (95% CI)	Adjusted[a] HR (95% CI)
Full Cohort (N = 118,394)			
Mean UF rate dichotomized at 10 mL/h/kg			
≤10 mL/h/kg	69,865 (59.0)	1.00 (reference)	1.00 (reference)
>10 mL/h/kg	48,529 (41.0)	1.10 (1.08-1.12)	1.22 (1.20-1.24)
Mean UF rate dichotomized at 13 mL/h/kg			
≤13 mL/h/kg	96,659 (81.6)	1.00 (reference)	1.00 (reference)
>13 mL/h/kg	21,735 (18.4)	1.15 (1.12-1.17)	1.31 (1.28-1.34)
Mean UF rate categorized			
<10 mL/h/kg	69,865 (59.0)	1.00 (reference)	1.00 (reference)
10-13 mL/h/kg	26,794 (22.6)	1.05 (1.03-1.07)	1.12 (1.10-1.15)
>13 mL/h/kg	21,735 (18.4)	1.16 (1.14-1.19)	1.35 (1.32-1.39)
Restricted Cohort: Dialysis Vintage ≥4 y (n = 40,706)			
Mean UF rate dichotomized at 10 mL/h/kg			
≤10 mL/h/kg	21,470 (52.7)	1.00 (reference)	1.00 (reference)
>10 mL/h/kg	19,236 (47.3)	1.03 (1.00-1.06)	1.19 (1.15-1.23)
Mean UF rate dichotomized at 13 mL/h/kg			
≤13 mL/h/kg	31,488 (77.4)	1.00 (reference)	1.00 (reference)
>13 mL/h/kg	9,218 (22.6)	1.05 (1.02-1.09)	1.26 (1.21-1.30)
Mean UF rate categorized			
<10 mL/h/kg	21,470 (52.7)	1.00 (reference)	1.00 (reference)
10-13 mL/h/kg	10,018 (24.6)	1.00 (0.97-1.04)	1.10 (1.06-1.15)
>13 mL/h/kg	9,218 (22.6)	1.05 (1.02-1.10)	1.30 (1.25-1.35)

Note: Fine and Gray proportional subdistribution hazards regression models with kidney transplantation and dialysis modality change treated as competing risks were used to estimate the ultrafiltration rate and all-cause mortality association.

Abbreviations: CI, confidence interval; HR, hazard ratio; UF, ultrafiltration.

[a]Adjusted for baseline age (continuous), sex (female vs male), race (black vs nonblack), ethnicity (Hispanic vs non-Hispanic), dialysis vintage (1-2, 3-4, ≥5 vs <1 year), vascular access (graft, fistula vs catheter), history of heart failure (yes vs no), history of cardiovascular disease (yes vs no), history of diabetes (yes vs no), albumin (3.1-3.5, 3.6-4.0, >4.0 vs ≤3.0 g/dL), creatinine (continuous), phosphorus (4.1-5.0, 5.1-6.0, >6.0 vs ≤4.0 mg/dL), hemoglobin (10.0-11.9, ≥12.0 vs <10.0 g/dL), urea reduction ratio (continuous), prehemodialysis systolic blood pressure (131-150, 151-170, >170 vs ≤130 mm Hg), and missed sessions (≥3 vs <3). Subgroups of interest were excluded from the adjustments listed previously when applicable.

treatments above the threshold, incrementally greater proportions of treatments with ultrafiltration rates > 13 mL/h/kg were associated with incrementally greater mortality (adjusted HRs of 1.26 [95% CI, 1.23-1.29] for 25%-49% of treatments and 1.40 [95% CI, 1.36-1.43] for ≥50% of treatments).

Sensitivity Analyses Related to Exposure Specification

In secondary analyses considering more finely categorized ultrafiltration rates, mortality risk increased incrementally across successively greater ultrafiltration rate categories (Table 3). When ultrafiltration rate was considered continuously, mortality risk increased by 3% for every 1-mL/h/kg ultrafiltration rate increase.

Delivered and prescribed ultrafiltration rates were highly correlated ($r = 0.96$; $P < 0.005$). Results from analyses considering the delivered ultrafiltration rate−mortality association were analogous to primary prescribed ultrafiltration rate results (Table S3). To investigate the association of ultrafiltration rates and mortality without influence from risk incurred during the long interdialytic interval, we performed analyses excluding HD treatments following the 72-hour interdialytic interval. Results were consistent with full cohort findings (Table S4). Results from models investigating time-updated prescribed ultrafiltration rate and mortality were also analogous to primary findings (Item S1).

Subgroup Analyses

Table 4 displays results from subgroup analyses. Higher prescribed ultrafiltration rate (across all specifications) was associated with significantly greater mortality in all subgroups studied. When ultrafiltration rate was dichotomized at 13 mL/h/kg, this association was more pronounced in blacks versus nonblacks, non-Hispanics versus Hispanics, patients with dialysis vintage of 4 or more years versus less than 4 years, patients with session durations of 4 or more hours versus less than 4 hours, and heavier versus lighter patients (P for interaction < 0.05 for all, indicating that subgroup effect size differences were significant). Similarly, prescribed ultrafiltration rate considered continuously (per 1 mL/h/kg) was associated with greater mortality across all subgroups. Effect sizes were significantly greater among females versus males, non-Hispanics versus Hispanics, patients with a dialysis vintage less than 4 years versus 4 or more years, and heavier versus lighter patients (P for interaction < 0.05 for all).

Body Size Influence

When prescribed ultrafiltration rate was normalized to BMI, ultrafiltration rates > 37 (vs ≤37 [the 80th percentile]) mL/h/kg/m^2 were associated with increased mortality (adjusted HR, 1.27; 95% CI, 1.24-1.30). When normalized to BSA, ultrafiltration rates > 500 (vs ≤500 [the 80th percentile]) mL/h/m^2 were associated with increased mortality (adjusted HR, 1.23; 95% CI, 1.20-1.26). Using the Vuong test, modeling ultrafiltration rate normalized to weight (compared to BMI and BSA, separately) was most predictive of mortality ($P < 0.001$ for both).[18]

To further explore the ultrafiltration rate−mortality association across body sizes, we categorized body size as <20th, 20th to 80th, and >80th percentile of post-HD body weight, BMI, and BSA (separately). Again, ultrafiltration rates > 13 (vs ≤13) mL/h/kg were associated with greater death risk in each subgroup. The association was strongest among patients with higher versus lower body weights and at higher

Table 3. Associations Between Continuous and Finely Categorized Prescribed Ultrafiltration Rate and All-Cause Mortality

		HR (95% CI)	
	No. (%)	Unadjusted	Adjusted[a]
Mean UF rate, per 1-mL/h/kg	118,394 (100.0)	1.01 (1.01-1.02)	1.03 (1.02-1.03)
Mean UF rate			
<6 mL/h/kg	23,813 (20.1)	1.00 (reference)	1.00 (reference)
6-<8 mL/h/kg	21,729 (18.4)	0.99 (0.96-1.02)	1.03 (1.00-1.07)
8-<10 mL/h/kg	24,323 (20.5)	1.01 (0.98-1.04)	1.09 (1.06-1.12)
10-<12 mL/h/kg	19,457 (16.4)	1.04 (1.01-1.07)	1.15 (1.12-1.19)
12-<14 mL/h/kg	13,086 (11.1)	1.08 (1.05-1.12)	1.23 (1.18-1.27)
≥14 mL/h/kg	15,986 (13.5)	1.19 (1.15-1.23)	1.43 (1.39-1.48)

Note: Fine and Gray proportional subdistribution hazards regression models with kidney transplantation and dialysis modality change treated as competing risks were used to estimate the ultrafiltration rate and all-cause mortality association.

Abbreviations: CI, confidence interval; HR, hazard ratio; UF, ultrafiltration.

[a]Adjusted for baseline age (continuous), sex (female vs male), race (black vs nonblack), ethnicity (Hispanic vs non-Hispanic), dialysis vintage (1-2, 3-4, ≥5 vs <1 year), vascular access (graft, fistula vs catheter), history of heart failure (yes vs no), history of cardiovascular disease (yes vs no), history of diabetes (yes vs no), albumin (3.1-3.5, 3.6-4.0, >4.0 vs ≤3.0 g/dL), creatinine (continuous), phosphorus (4.1-5.0, 5.1-6.0, >6.0 vs ≤ 4.0 mg/dL), hemoglobin (10.0-11.9, ≥12.0 vs <10.0 g/dL), urea reduction ratio (continuous), prehemodialysis systolic blood pressure (131-150, 151-170, >170 vs ≤130 mm Hg), and missed sessions (≥3 vs <3).

Table 4. Associations Between Prescribed Ultrafiltration Rate and Mortality Within Subgroups of Interest

Sex	Female (n = 53,307)	Male (n = 65,087)	*P* for Interaction[a]
Mean UF rate dichotomized at 10 mL/h/kg			<0.001
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)	
>10 mL/h/kg	1.26 (1.23-1.30)	1.18 (1.15-1.21)	
Mean UF rate dichotomized at 13 mL/h/kg			0.2
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)	
>13 mL/h/kg	1.33 (1.29-1.37)	1.29 (1.25-1.33)	
Mean UF rate continuous, per 1-mL/h/kg	1.03 (1.03-1.03)	1.02 (1.02-1.03)	0.004
Race	Nonblack (n = 73,105)	Black (n = 45,289)	*P* for Interaction[a]
Mean UF rate dichotomized at 10 mL/h/kg			0.6
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)	
>10 mL/h/kg	1.21 (1.19-1.24)	1.23 (1.19-1.27)	
Mean UF rate dichotomized at 13 mL/h/kg			0.004
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)	
>13 mL/h/kg	1.28 (1.24-1.31)	1.38 (1.32-1.43)	
Mean UF rate continuous, per 1-mL/h/kg	1.03 (1.02-1.03)	1.03 (1.03-1.03)	0.2
Ethnicity	Non-Hispanic (n = 98,874)	Hispanic (n = 19,520)	*P* for Interaction[a]
Mean UF rate dichotomized at 10 mL/h/kg			0.1
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)	
>10 mL/h/kg	1.23 (1.20-1.25)	1.17 (1.12-1.23)	
Mean UF rate dichotomized at 13 mL/h/kg			0.002
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)	
>13 mL/h/kg	1.33 (1.29-1.36)	1.20 (1.14-1.27)	
Mean UF rate continuous, per 1-mL/h/kg	1.03 (1.02-1.03)	1.02 (1.01-1.03)	0.03
Dialysis Vintage	<4 y (n = 77,688)	≥4 y (n = 40,706)	*P* for Interaction[a]
Mean UF rate dichotomized at 10 mL/h/kg			<0.001
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)	
>10 mL/h/kg	1.17 (1.13-1.21)	1.25 (1.22-1.28)	
Mean UF rate dichotomized at 13 mL/h/kg			<0.001
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)	
>13 mL/h/kg	1.23 (1.19-1.28)	1.37 (1.33-1.41)	
Mean UF rate continuous, per 1-mL/h/kg	1.03 (1.02-1.03)	1.02 (1.02-1.03)	0.007
Session Duration	<4 h (n = 78,504)	≥4 h (n = 39,890)	*P* for Interaction[a]
Mean UF rate dichotomized at 10 mL/h/kg			0.9
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)	
>10 mL/h/kg	1.22 (1.20-1.25)	1.23 (1.19-1.27)	
Mean UF rate dichotomized at 13 mL/h/kg			0.02
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)	
>13 mL/h/kg	1.30 (1.26-1.33)	1.39 (1.32-1.46)	
Mean UF rate continuous, per 1-mL/h/kg	1.03 (1.02-1.03)	1.03 (1.02-1.03)	0.09

(Continued)

Table 4 (Cont'd). Associations Between Prescribed Ultrafiltration Rate and Mortality Within Subgroups of Interest

Post-HD Weight	<20th percentile[b] (n = 23,524)	>80th percentile[b] (n = 23,646)	*P* for Interaction[a]
Mean UF rate dichotomized at 10 mL/h/kg			0.2
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)	
>10 mL/h/kg	1.14 (1.10-1.19)	1.22 (1.16-1.29)	
Mean UF rate dichotomized at 13 mL/h/kg			<0.001
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)	
>13 mL/h/kg	1.15 (1.11-1.20)	1.36 (1.22-1.51)	
Mean UF rate continuous, per 1-mL/h/kg	1.01 (1.01-1.02)	1.02 (1.02-1.03)	<0.001

Note: Except where indicated, values shown are adjusted HR (95% CI). In particular, Fine and Gray proportional subdistribution hazards regression models with kidney transplantation and dialysis modality change treated as competing risks were used to estimate the ultrafiltration rate and all-cause mortality association. Adjusted for age (continuous), sex (female vs male), race (black vs nonblack), ethnicity (Hispanic vs non-Hispanic), dialysis vintage (1-2, 3-4, ≥5 vs <1 year), vascular access (graft, fistula vs catheter), history of heart failure (yes vs no), history of cardiovascular disease (yes vs. no), history of diabetes (yes vs no), albumin (3.1-3.5, 3.6-4.0, >4.0 vs ≤3.0 g/dL), creatinine (continuous), phosphorus (4.1-5.0, 5.1-6.0, >6.0 vs ≤ 4.0 mg/dL), hemoglobin (10.0-11.9, ≥12.0 vs <10.0 g/dL), urea reduction ratio (continuous), pre-HD systolic blood pressure (131-150, 151-170, >170 vs ≤130 mm Hg), and missed sessions (≥3 vs <3). Effect modifiers of interest were excluded from the adjustments listed above.

Abbreviations: CI, confidence interval; HD, hemodialysis; HR, hazard ratio; UF, ultrafiltration.

[a]Significance of interaction terms was determined using the Wald test.

[b]Post-HD weight 20th percentile = 60.9 kg and 80th percentile = 95.3 kg. The 20th to 80th percentile was included in the model but is not shown.

versus lower BMI. The magnitude of association was similar across BSA strata (Fig 3).

Ultrafiltration Rate Quality Measure Considerations

Because the proposed CMS Quality Incentive Program ultrafiltration rate measure excludes patients with prescribed session durations of 4 or more hours from the metric numerator, we performed analyses restricted to patients with prescribed session durations of 4 or more hours (n = 39,890). Among patients with session durations of 4 or more hours, prescribed ultrafiltration rates > 13 (vs ≤13) mL/h/kg and prescribed ultrafiltration rates > 10 (vs ≤10) mL/h/kg were associated with greater mortality regardless of body size. These associations were more pronounced in heavier patients (>80th percentile of body weight) versus lighter patients (Table 5).

DISCUSSION

Prior studies have shown associations between rapid fluid removal and mortality among HD patients, but questions about study design and potential differences across subpopulations remain. In the largest to date observational cohort, we demonstrated an association between greater ultrafiltration rate and mortality, showing incrementally greater harm from ultrafiltration rates starting at 6 mL/h/kg. Our results suggest that notable ultrafiltration-related harm begins before 10 mL/h/kg, substantially lower than the proposed quality measure threshold of 13 mL/h/kg. The ultrafiltration rate−mortality association was significant across all body sizes, with larger patients having greater mortality risk from higher ultrafiltration rates. Ultrafiltration rate normalized to body weight had a stronger association with mortality (vs normalization to BMI or BSA). Findings were robust across key subpopulations.

To date, 3 observational studies have examined the ultrafiltration rate−mortality association. There have been no randomized controlled trials. In a DOPPS (Dialysis Outcomes Practice Patterns Study) analysis, Saran et al[2] demonstrated a modest association between ultrafiltration rates > 10 mL/h/kg and all-cause mortality. In an Italian cohort, Movilli et al[3] identified an ultrafiltration rate threshold of 12.4 mL/h/kg as the most predictive cutoff point of mortality. In a post hoc analysis of the Hemodialysis (HEMO) Study, Flythe et al[4] found that ultrafiltration rates > 13 mL/h/kg (vs <10 mL/h/kg) were associated with greater mortality. Effect modification on the basis of heart failure was observed, suggesting that risk may occur at rates of 10 mL/h/kg in some populations. Spline analyses showed that ultrafiltration rate risk began to increase at 10 mL/h/kg among all patients.[4] Mechanistic studies evaluating intradialytic echocardiography, troponin, and endotoxin have established hemodynamic-induced end-organ ischemia as a potential mediator of the ultrafiltration rate−mortality association.[5,6,8,21]

Despite consistent findings across existing epidemiologic studies, the methodological shortcomings of these investigations have tempered enthusiasm for ultrafiltration rate clinical guidelines.[22-24] We sought to address these uncertainties. IDWG

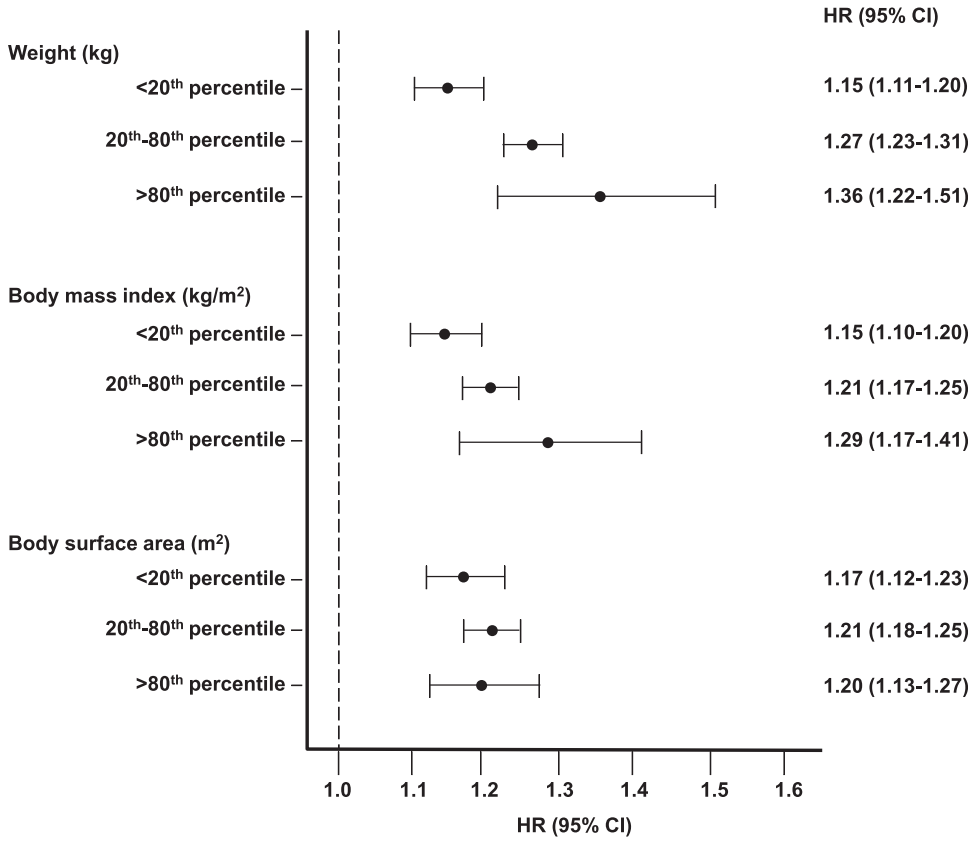

Figure 3. Associations between prescribed ultrafiltration rate and mortality by percentile of postdialysis weight, body mass index (BMI), and body surface area (BSA). Fine and Gray proportional subdistribution hazards regression models with kidney transplantation and dialysis modality change treated as competing risks were used to estimate the ultrafiltration rate and all-cause mortality association comparing mean ultrafiltration rates > 13 mL/h/kg with those ≤13 mL/h/kg within strata of body weight, BMI, and BSA (separately). Models were adjusted for age (continuous), sex (female vs male), race (black vs nonblack), ethnicity (Hispanic vs non-Hispanic), dialysis vintage (1-2, 3-4, ≥5 vs <1 year), vascular access (graft, fistula vs catheter), history of heart failure (yes vs no), history of cardiovascular disease (yes vs no), history of diabetes (yes vs no), albumin (3.1-3.5, 3.6-4.0, >4.0 vs ≤3.0 g/dL), creatinine (continuous), phosphorus (4.1-5.0, 5.1-6.0, >6.0 vs ≤ 4.0 mg/dL), hemoglobin (10.0-11.9, ≥12.0 vs <10.0 g/dL), urea reduction ratio (continuous), prehemodialysis systolic blood pressure (131-150, 151-170, >170 vs ≤130 mm Hg), and missed sessions (≥3 vs <3). Postdialysis weight was used to calculate normalized ultrafiltration rates for weight, BMI, and BSA. The 20th/80th percentile for postweight = 60.9/95.3 kg; 21.8/32.8 kg/m^2 for BMI; 1.66/2.10 m^2 for BSA. The 80th percentile for ultrafiltration rate normalized to BMI = 37 mL/h/(kg/m^2); ultrafiltration rate normalized to BSA = 500 mL/h/m^2. The 80th percentile selected for BMI and BSA based on 13 mL/h/kg being the 80th percentile of ultrafiltration rate when normalized to post-HD weight. Abbreviations: CI, confidence interval; HR, hazard ratio.

(or ultrafiltration volume), session duration, and post-HD weight all contribute to the ultrafiltration rate calculation and were included in prior multivariable models, potentially introducing effect size inaccuracies. In our new analyses, we did not adjust for these factors because controlling for these variables obscures interpretation of findings. Stated otherwise, accepting that high ultrafiltration rate must result from high IDWG, low session duration, low body weight, or some combination thereof, we did not artificially constrain these factors analytically but accepted their inherent contributions to ultrafiltration rate. Additionally, concern for confounding from residual kidney function has led to scrutiny of prior studies because urine output is a critical confounder.[23] To address this, we performed analyses restricted to patients on dialysis therapy for 4 or more years, a population with generally low urine output.

Our present analyses demonstrate that prescribed (and delivered) ultrafiltration rates > 10 mL/h/kg are associated with greater mortality. This finding is consistent with Saran et al[2] and the Flythe et al[4] spline analysis showing a steep increase in ultrafiltration rate−related mortality risk at 10 mL/h/kg. An ultrafiltration rate threshold of 13 mL/h/kg, as instituted in the Core Survey and as proposed for the 2019 CMS Quality Incentive Program, is likely conservative.[9,10] Additionally, the National Quality Forum−endorsed ultrafiltration rate measure includes a session length restriction. The metric numerator includes only patients with ultrafiltration rates ≥ 13 mL/h/kg and delivered session durations less than 4 hours. Although this restriction may be in line with patient preference data showing aversion to longer session lengths,[25] our data demonstrate that patients with longer session durations incur greater mortality risk at

Table 5. Associations Between Prescribed Ultrafiltration Rate and Mortality Overall and by Percentile of Post-HD Weight in Patients With Prescribed Session Durations of 4 or More Hours

		Post-HD Weight		
	All	<20th Percentile: <70.9 kg	20th-80th Percentile: 70.9-110.2 kg	>80th Percentile: >110.2 kg
No. of patients	39,890	7,925	24,009	7,956
IDWG, kg	3.5 ± 2.3	2.8 ± 2.2	3.4 ± 2.2	4.3 ± 2.4
Prescribed session duration, min	253 ± 34	247 ± 31	250 ± 31	265 ± 42
Associations[a]				
Mean UF rate dichotomized at 10 mL/h/kg				
≤10 mL/h/kg	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
>10 mL/h/kg	1.23 (1.18-1.27)	1.08 (1.01-1.16)[b]	1.18 (1.13-1.24)[b]	1.39 (1.24-1.55)[b]
Mean UF rate dichotomized at 13 mL/h/kg				
≤13 mL/h/kg	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
>13 mL/h/kg	1.38 (1.31-1.45)	1.21 (1.12-1.31)[b]	1.32 (1.23-1.43)[b]	1.76 (1.41-2.18)[b]
Mean UF rate categorized				
<10 mL/h/kg	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
10-13 mL/h/kg	1.14 (1.09-1.18)	0.98 (0.90-1.06)[b]	1.12 (1.06-1.18)[b]	1.31 (1.16-1.48)[b]
>13 mL/h/kg	1.42 (1.35-1.50)	1.20 (1.11-1.31)[b]	1.36 (1.26-1.48)[b]	1.81 (1.45-2.25)[b]

Note: Unless otherwise indicated, values are given as mean ± standard deviation.

Abbreviations: CI, confidence interval; HD, hemodialysis; HR, hazard ratio; IDWG, interdialytic weight gain; UF, ultrafiltration.

[a]Values given as adjusted HR (95% CI). In particular, Fine and Gray proportional subdistribution hazards regression models with kidney transplantation and dialysis modality change treated as a competing risks were used to estimate the ultrafiltration rate and all-cause mortality association. Models are adjusted for age (continuous), sex (female vs male), race (black vs nonblack), ethnicity (Hispanic vs non-Hispanic), dialysis vintage (1-2, 3-4, ≥5 vs <1 year), vascular access (graft, fistula vs catheter), history of heart failure (yes vs no), history of cardiovascular disease (yes vs no), history of diabetes (yes vs no), albumin (3.1-3.5, 3.6-4.0, >4.0 vs ≤3.0 g/dL), creatinine (continuous), phosphorus (4.1-5.0, 5.1-6.0, >6.0 vs ≤ 4.0 mg/dL), hemoglobin (10.0-11.9, ≥12.0 vs <10.0 g/dL), urea reduction ratio (continuous), pre-HD systolic blood pressure (131-150, 151-170, >170 vs ≤130 mm Hg), and missed sessions (≥3 vs <3). Subgroups of interest were excluded from the adjustments listed above. Significance of interaction terms was determined using Wald $\chi 2$ (type 3) tests.

[b]Interaction term significant at $P < 0.01$.

higher ultrafiltration rates. We also observed a dose-response association between ultrafiltration rate and mortality: more frequent exposure to higher ultrafiltration rates is associated with an incrementally higher death risk. Frequency-based definitions of ultrafiltration rates may better capture risk than single-treatment or mean-based ultrafiltration rate definitions. Reassuringly, we observed the ultrafiltration rate−mortality association to be robust across subgroups, rendering a single mean-based threshold approach reasonable. We also observed similar associations between prescribed and delivered ultrafiltration rates and mortality, providing reassurance regarding the proposed quality measure's capture of delivered ultrafiltration rates. Together, these data provide strong observational evidence supporting an association between greater ultrafiltration rates and mortality.

Fluid removal−related harm occurs when the ultrafiltration rate exceeds the plasma refill rate and subclinical or clinical hemodynamic compromise occurs. Vascular refill is influenced by many factors, including body size, sex, nutritional status, total-body volume status and distribution, and blood flow distribution.[26] It is plausible that the ultrafiltration rate−outcome association varies across body types. Therefore, we considered fluid removal normalized to body weight, BMI, and BSA. Ultrafiltration rate normalized to weight had the strongest association with mortality, but when ultrafiltration rate was modeled continuously, the effect size varied across sex and body size, with females (vs males) and heavier (vs lighter) patients having greater mortality risk. Similar effect size differences were observed when ultrafiltration rate was normalized to BMI. Normalizing ultrafiltration rate to BSA produced more stable effect estimates across BSA strata. The ideal indexing method might yield similar strengths of association across body sizes as observed with BSA. However, the effect size differences across body sizes when ultrafiltration rate was normalized to both weight and BMI were modest, and all 3 normalization methods revealed significantly greater mortality with higher ultrafiltration rates across all body sizes. Because body weight is readily available for ultrafiltration rate calculation in the clinic and effect sizes only modestly different across body size strata, ultrafiltration rate normalization to body weight is reasonable.

Several limitations of our study should be acknowledged. This is an observational analysis and may contain uncontrolled confounding. To minimize

confounding from difficult-to-measure factors such as health status, we controlled for variables including albumin, phosphate, creatinine, albumin, and weight. Related, we performed analyses restricted to patients of advanced dialysis vintage to minimize confounding from residual urine output. Nevertheless, we cannot rule out the possibility of confounding from these factors or other unconsidered factors. For example, body size, clearance, and session duration are closely related. Despite including urea reduction ratio and body size (by ultrafiltration rate) in our models, we cannot rule out residual confounding from clearance and body size–related factors. We also lacked data for dialysate and dietary sodium, potential confounders of the ultrafiltration rate−mortality association. Reassuringly, the addition of serum sodium level to multivariable models did not substantially alter ultrafiltration rate−mortality effect estimates (Table S5), but residual confounding from these and other factors cannot be excluded. Prospective study of ultrafiltration rate and outcomes is warranted. Second, we were unable to investigate cause-specific mortality due to a lack of adjudicated death causes in our database. Third, we were unable to consider intradialytic symptoms due to a lack of symptom data. Fourth, our data were derived from a single LDO and may not be representative of other dialysis providers. Finally, our study included adult in-center maintenance HD patients with dialytic vintage of 90 or more days. Results should not be extrapolated to excluded populations such as incident HD patients.

In conclusion, we demonstrated an association between ultrafiltration rates $>$ 10 mL/h/kg (vs $\leq$10 mL/h/kg) and all-cause mortality and showed an incremental increase in ultrafiltration-related risk beginning at a ultrafiltration rate of 6 mL/h/kg. Additionally, we found the ultrafiltration rate−outcome association to be robust across body size, sex, and racial subgroups and provided evidence supporting normalization of ultrafiltration rate to weight versus other anthropometric metrics. The richness of the ultrafiltration rate−outcome observational evidence base and the regulatory interest in adoption of an ultrafiltration rate quality measure calls for a randomized controlled trial investigation of ultrafiltration rates and outcomes.

ACKNOWLEDGEMENTS

The authors thank DaVita Clinical Research for providing data for this study. DaVita Clinical Research had no role in the design or implementation of this study or the decision to publish. The authors thank Alan Brookhart for data access and insightful comments on analyses and Diane Reams for data and contract management assistance.

Support: Dr Assimon is supported by National Institute of Diabetes and Digestive and Kidney Diseases training grant T32 DK007750.

Financial Disclosure: Dr Flythe has received speaking honoraria from Dialysis Clinic Inc, Renal Ventures, American Renal Associates, American Society of Nephrology, and Baxter. Drs Flythe and Assimon have received research funding for research unrelated to this study from the Renal Research Institute, a subsidiary of Fresenius Medical Care, North America.

Contributions: Research idea and study design: MMA, JBW, JEF; data acquisition: MMA, JBW, LW, JEF; data analysis/interpretation: MMA, JBW, LW, JEF; statistical analysis: JBW, LW; supervision or mentorship: JEF. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. JEF takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted, and that any discrepancies from the study as planned have been explained.

Peer Review: Evaluated by 2 peer reviewers, a Statistical Editor, a Co-Editor, and the Editor-in-Chief.

SUPPLEMENTARY MATERIAL

Table S1: Associations between prescribed ultrafiltration rate and all-cause mortality using 60- and 90-d exposure.

Table S2: Comparison of baseline characteristics of included and excluded patients.

Table S3: Associations between delivered ultrafiltration rate and all-cause mortality.

Table S4: Associations between prescribed ultrafiltration rate and all-cause mortality excluding Mon and Tues treatments.

Table S5: Associations between prescribed ultrafiltration rate and all-cause mortality in models with and without serum sodium adjustment.

Item S1: Detailed methods of marginal structural model analyses.

Note: The supplementary material accompanying this article (http://dx.doi.org/10.1053/j.ajkd.2016.06.020) is available at www.ajkd.org

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