Published in final edited form as:

Semin Dial. 2017 May ; 30(3): 282–283. doi:10.1111/sdi.12602.

Ultrafiltration rate scaling in hemodialysis patients

Jennifer E. Flythe, MD, MPH^{1,3}, Magdalene M. Assimon, PharmD, MS^{1,2}, and Lily Wang, PhD^{2,3}

¹University of North Carolina Kidney Center, Division of Nephrology and Hypertension, Department of Medicine, UNC School of Medicine, Chapel Hill, NC

²Department of Epidemiology, UNC Gillings School of Global Public Health, Chapel Hill, NC

³Cecil G. Sheps Center for Health Services Research, University of North Carolina, Chapel Hill, NC

Over the last several years, data supporting an association between higher ultrafiltration (UF) rates and increased mortality among individuals receiving maintenance hemodialysis has accumulated.^{1–4} These observational findings are supported by mechanistic studies showing that intradialytic end-organ ischemic injury may occur in response to aggressive fluid removal.^{5–7} As a result of these studies and others, there has been heightened interest in improving clinic-level fluid management across the dialysis community,⁸ ultimately leading to the approval of an UF rate reporting measure for the 2020 Centers for Medicare and Medicaid (CMS) End Stage Renal Disease (ESRD) Quality Incentive Program (QIP).⁹ The CMS measure and its supporting data specify the dialytic UF rate in terms of mL/h/kg. Said differently, the selected UF rate metric is “scaled” to body weight (body mass).

In the January 2017 issue of *Seminars in Dialysis*, Daugirdas and Schneditz provided commentary on considerations for the appropriate scaling of hemodialysis UF rates.¹⁰ In their editorial, Daugirdas and Schneditz suggested that it may be more appropriate to scale UF rates to body surface area rather than to body weight. Relying on data from the Hemodialysis (HEMO) Study, the authors proposed that body surface area might better reflect vascular refilling capacity than body weight. They hypothesized that body surface area’s correlation with both blood volume and extracellular volume render it more relevant to refilling capacity than body weight on its own.¹⁰ Then, citing data from an observational analysis of UF rates (considered scaled to body weight, body mass index and body surface area) and all-cause mortality by Assimon *et al*, they noted that: 1) the rapid UF rate—mortality association may be more pronounced in patients of greater body weight, and 2) the UF rate—mortality association may be more consistent when scaled to body surface area than when scaled to body weight.⁴ Daugirdas and Schneditz appropriately pointed out that

Corresponding Author: Jennifer E. Flythe MD, MPH, University of North Carolina Kidney Center, 7024 Burnett-Womack CB #7155, Chapel Hill, NC 27599-7155, jflythe@med.unc.edu, (tel) 919-445-2656, (fax) 919-966-4251.

DISCLOSURES

Dr. Flythe has received speaking honoraria from Dialysis Clinic, Incorporated, Renal Ventures, American Renal Associates, American Society of Nephrology, Baxter, and multiple universities. Drs. Flythe and Assimon have received investigator initiated research funding from the Renal Research Institute, a subsidiary of Fresenius Medical Care, North America.

the Assimon *et al.* analyses were not stratified by sex, potentially obscuring important information that could shed light on the optimal approach to UF rate scaling.¹⁰

To provide additional insight into the UF rate scaling dilemma, we provide the results of updated UF rate—outcome analyses stratified by both sex and body size. In a previously described cohort of over 118,000 adult individuals who had received center-based hemodialysis for at least 90 days at study start, and using previously described methods,⁴ we estimated the associations of average delivered UF rates and all-cause mortality across strata of sex and body size (Table 1). When stratified by sex, the association between higher UF rates and increased mortality remained statistically significant across all body size strata. Although we observed some variation in the magnitude of risk across strata of sex and body size, such differences were not sufficiently pronounced to necessitate, in our opinion, stratum-specific UF rate goals.

The data suggest that risk from greater UF rates is higher among individuals of larger body sizes; however, the risk from greater UF rates remains significant among individuals of smaller body sizes. Since smaller patients do incur risk from more rapid fluid removal, it is reasonable to counsel either treatment time extension or interdialytic weight gain reduction in this subgroup to mitigate UF-related risk. However, like all clinical recommendations, counseling should be patient-specific. Individuals with poor nutritional status who would benefit from enhanced caloric intake should not be counseled to decrease sodium intake to a level that could be detrimental to their nutritional status. Furthermore, the data do not show a consistent rise in UF rate associated risk across categories of increasing body weight, suggesting that the UF rate—mortality association does not consistently vary by body size, rendering size-specific UF rate recommendations unnecessary based on the current published evidence.

Finally, there does not appear to be significant advantages to scaling UF rate to either body surface area or body mass index as opposed to body weight. Scaling UF rate to body mass index or body surface area (vs. body weight) did not greatly enhance hazard ratio stability across strata of sex and body size. Our findings suggest that the current approach of scaling UF rates to body size as reflected by body weight without weight stratum-specific thresholds is reasonable.

When implementing clinical quality measures, population-level and individual-level risks and benefits must be weighed. Generally, ideal quality measures are simple and relevant to diverse subgroups so that they both minimize implementation-associated error and facilitate health of the broader population. We believe the current approach of specifying target UF rate thresholds scaled to body weight achieves these goals. However, in both the research and clinical care arenas, it is paramount that we question and re-examine accepted standards, never allowing ourselves to become complacent that existing standards equate with truth. Therefore, ongoing inquiry into the scaling issue is warranted as are randomized controlled clinical trials testing the causality of the observed UF rate—outcome associations.

Acknowledgments

The authors thank DaVita Clinical Research for providing data for this analysis. DaVita Clinical Research had no role in the design or implementation of this analysis or the decision to publish.

FUNDING SOURCES

Dr. Assimon is supported by grant F32 DK109561 and Dr. Flythe by grant K23 DK109401, both awarded by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health.

References

1. Movilli E, Gaggia P, Zubani R, Camerini C, Vizzardi V, Parrinello G, Savoldi S, Fischer MS, Londrino F, Cancarini G. Association between high ultrafiltration rates and mortality in uraemic patients on regular haemodialysis. A 5-year prospective observational multicentre study. *Nephrol Dial Transplant*. 2007; 22:3547–3552. [PubMed: 17890254]
2. Saran R, Bragg-Gresham JL, Levin NW, Twardowski ZJ, Wizemann V, Saito A, Kimata N, Gillespie BW, Combe C, Bommer J, Akiba T, Mapes DL, Young EW, Port FK. Longer treatment time and slower ultrafiltration in hemodialysis: associations with reduced mortality in the DOPPS. *Kidney Int*. 2006; 69:1222–1228. [PubMed: 16609686]
3. Flythe JE, Kimmel SE, Brunelli SM. Rapid fluid removal during dialysis is associated with cardiovascular morbidity and mortality. *Kidney Int*. 2011; 79:250–257. [PubMed: 20927040]
4. Assimon MM, Wenger JB, Wang L, Flythe JE. Ultrafiltration Rate and Mortality in Maintenance Hemodialysis Patients. *Am J Kidney Dis*. 2016; 68:911–922. [PubMed: 27575009]
5. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced cardiac injury: determinants and associated outcomes. *Clin J Am Soc Nephrol*. 2009; 4:914–920. [PubMed: 19357245]
6. Burton JO, Jefferies HJ, Selby NM, McIntyre CW. Hemodialysis-induced repetitive myocardial injury results in global and segmental reduction in systolic cardiac function. *Clin J Am Soc Nephrol*. 2009; 4:1925–1931. [PubMed: 19808220]
7. Eldehni MT, Odudu A, McIntyre CW. Randomized Clinical Trial of Dialysate Cooling and Effects on Brain White Matter. *J Am Soc Nephrol*. 2014; 24(4):957–965.
8. Weiner DE, Brunelli SM, Hunt A, Schiller B, Glasscock R, Maddux FW, Johnson D, Parker T, Nissenson A. Improving Clinical Outcomes Among Hemodialysis Patients: A Proposal for a “Volume First” Approach From the Chief Medical Officers of US Dialysis Providers. *Am J Kidney Dis*. 2014; 64:685–695. [PubMed: 25156305]
9. Department of Health and Human Services, Centers for Medicare and Medicaid Services. Federal Register. Nov 4.2016 81(214) [Accessed March 8, 2017] Rules and Regulations. Available at: <https://www.gpo.gov/fdsys/pkg/FR-2016-11-04/content-detail.html>.
10. Daugirdas JT, Schneditz D. Hemodialysis Ultrafiltration Rate Targets Should Be Scaled to Body Surface Area Rather than to Body Weight. *Semin Dial*. 2017; 30:15–19. [PubMed: 28043081]

Table 1

Adjusted associations between delivered UF rate and mortality by sex and body size.^a

Body Size Measure	Female			Male		
	n	Percentile	HR (95% CI)	n	Percentile	HR (95% CI)
Post-dialysis weight						
	10,633	<20 (55.6 kg)	1.20 (1.13– 1.27)	12,983	<20 (65.8 kg)	1.10 (1.04– 1.17)
	10,708	20–39 (55.7 – 65.1 kg)	1.13 (1.06– 1.21)	13,074	20–39 (65.9 – 74.5 kg)	1.18 (1.11– 1.26)
	10,642	40–59 (65.2 – 75.7 kg)	1.32 (1.22– 1.43)	12,998	40–59 (74.6 – 84.0 kg)	1.24 (1.14– 1.34)
	10,699	60–79 (75.8 – 90.7 kg)	1.31 (1.18– 1.45)	13,055	60–79 (84.1 – 98.5 kg)	1.17 (1.06– 1.30)
	10,623	80 (90.8 kg)	1.28 (1.08– 1.51)	12,976	80 (98.6 kg)	1.41 (1.22– 1.63)
Body mass index						
	10,643	<20 (21.7 kg/m ²)	1.20 (1.13– 1.28)	12,992	<20 (21.9 kg/m ²)	1.13 (1.06– 1.19)
	10,651	20–39 (21.8 – 25.1 kg/m ²)	1.14 (1.07– 1.22)	13,006	20–39 (22.0 – 24.6 kg/m ²)	1.12 (1.05– 1.20)
	10,648	40–59 (25.2 – 28.9 kg/m ²)	1.36 (1.26– 1.47)	13,000	40–59 (24.7 – 27.4 kg/m ²)	1.25 (1.15– 1.35)
	10,643	60–79 (29.0 – 34.4 kg/m ²)	1.29 (1.17– 1.42)	12,998	60–79 (27.5 – 31.6 kg/m ²)	1.24 (1.13– 1.37)
	10,643	80 (34.5 kg/m ²)	1.37 (1.18– 1.59)	12,991	80 (>31.7 kg/m ²)	1.36 (1.19– 1.56)
Body surface area						
	10,642	<20 (1.56 m ²)	1.18 (1.11– 1.25)	12,999	<20 (1.77 m ²)	1.10 (1.04– 1.17)
	10,656	20–39 (1.57 – 1.69 m ²)	1.22 (1.14– 1.30)	13,009	20–39 (1.78 – 1.89 m ²)	1.23 (1.15– 1.31)
	10,657	40–59 (1.70 – 1.81 m ²)	1.29 (1.19– 1.39)	12,992	40–59 (1.90 – 2.01 m ²)	1.26 (1.17– 1.36)
	10,639	60–79 (1.82 – 1.97 m ²)	1.29 (1.17– 1.43)	13,000	60–79 (2.02 – 2.18 m ²)	1.20 (1.09– 1.33)
	10,648	80 (1.98 m ²)	1.38 (1.18– 1.60)	12,999	80 (2.19 m ²)	1.33 (1.15– 1.53)

^aFine 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 UF rates >13 mL/h/kg to those <13 mL/h/kg across strata of sex and body weight; mean UF rates >37 mL/h/(kg/m²) to those <37 mL/h/(kg/m²) across strata of sex and body mass index (BMI); and mean UF rates >500 mL/h/m² to those <500 mL/h/m² across strata of sex and body surface area (BSA). Models were adjusted for age (continuous), race (black vs. non-black), ethnicity (Hispanic vs. non-Hispanic), time on dialysis (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), phosphorous (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-dialysis systolic blood pressure (131–150, 151–170, >170 vs. <130 mmHg), and missed treatments (<3 vs. ≥3). Post-dialysis weight was used to calculate normalized UF rates for weight, BMI and BSA. In the overall study population, a UF rate of 13 mL/h/kg corresponded to the 80th percentile when UF rate was scaled to body weight (kg). Thus, analogous 80th percentile thresholds for UF rates scaled to BMI and BSA were evaluated, where the 80th percentile of UF rate scaled to BMI = 37 mL/h/(kg/m²) and the 80th percentile of UF rate scaled to BSA = 500 mL/h/m².

Abbreviations: HR=hazard ratio, CI=confidence interval, HD=hemodialysis

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript