

Scaled Ultrafiltration Rate in Hemodialysis—Time for a Change?



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In this issue of *KI Reports*, Raimann *et al.*¹ examined the rate and association between ultrafiltration rate (UFR) and mortality in their clinical research article, Ultrafiltration Rate Thresholds Associated with Increased Mortality Risk in Hemodialysis, Unscaled or Scaled to Body Size.

Ultrafiltration-induced hypotension causes ischemia in the heart, brain, and gut, which results in consequences, such as myocardial stunning, dementia, translocation of gut bacteria into the bloodstream, and mortality.² Because brisk volume removal leads to more intradialytic hypotension, an examination of the effect of UFR on mortality is important. Beginning in 2006, the association between mortality and ultrafiltration was examined with by Saran *et al.*³ At the time of its publication, it was known that excessive interdialytic weight gain (IDWG) was an independent predictor of mortality and a state requiring a higher UFR. Saran *et al.*³ studied the relationship between treatment time and UFR and

patient outcomes in the Dialysis Outcomes and Practice Patterns Study. A UFR >10 ml/kg/h was shown to be associated with a higher risk of mortality (risk ratio = 1.09) and a higher chance of intradialytic hypotension. A year later, Movilli *et al.*⁴ found that a UFR <12.37 ml/kg/h was associated with better survival in hemodialysis patients compared with a higher UFR. In 2011, Flythve *et al.*⁵ showed that UFR >13 ml/kg/h was associated with increased all-cause and cardiovascular-related mortality compared with a UFR up to 10 ml/kg/h. Subsequent literature confirmed the association of high UFR, scaled to bodyweight, with mortality. As a result, the Centers for Medicaid and Medicare Services established a quality measure to a UFR not to exceed 13 ml/kg/h and alignment to this threshold has become standard practice.

The difficulty with the above studies has been their observational nature and the many confounding variables in the association between UFR and mortality. At its core, UFR during a particular dialysis session is primarily determined by IDWG and treatment time. Multiple factors affect these 2 variables. First,

greater amounts of interdialytic weight are associated with increased all-cause and cardiovascular mortality.⁶ Greater IDWG naturally results in higher UFR in the setting of fixed treatment times in outpatient dialysis units. Conversely, longer treatment time is associated with reduced mortality.³ Second, fluid intake as well as residual kidney function both influence the degree of IDWG. Fluid intake may be increased by noncompliance with fluid restriction or decreased due to poor nutritional intake, both of which lead to poor outcomes. On the contrary, residual kidney function allows for continuous fluid excretion via urine output, which decreases IDWG. In addition, residual kidney function itself is associated with decreased mortality. Lastly, prescribed time is laden with confounding variables because shorter times may be prescribed to those with a history of early dialysis treatment terminations.

Although the above issues pose formidable obstacles to creating reasonable observational studies, scaling ultrafiltration to body mass adds yet another layer of complexity. Improved nutrition leads to a higher body mass, and to increased sodium intake followed by increased IDWG. Conversely, malnourished patients could have low IDWG resulting in a low UFR, but also a low body mass which affects scaled UFR in a complex way. In sum, multiple layers of complexity exist when evaluating something as seemingly straightforward as the association between UFR and mortality. Although past literature has attempted to minimize the effect of confounding factors on UFR and mortality, no publication to date has examined

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the association between mortality and UFR, which is not scaled to body mass. The current publication by Raimann *et al.*¹ addresses this issue.

This publication was an observational cohort study of 2542 adult patients who were on thrice-weekly maintenance hemodialysis between January 1, 2014 and October 31, 2018. The mean age of patients was 61.9 ± 15 years. Of these patients, 42% were female, 40% were African American, and 38.8% had a history of diabetes mellitus. A total of 494 patients died during the study period. Unscaled UFRs were evaluated for an association with mortality, and UFRs scaled to body mass were evaluated over a range of body mass. Raimann *et al.* showed that a UFR >1000 ml/h was associated with a mortality hazard ratio of 1.5. This relationship was independent of postdialysis body weight in between a body mass of 80 to 140 kg. In addition, the mortality hazard ratio was shown to vary depending on body mass. The mortality hazard ratio for UFRs exceeding 13 ml/kg/h was 1.2 for a body mass of 60 kg, 1.45 with a body mass of 80 kg, and >2.0 for a body mass of 100 kg. The general trend is that a single UFR, scaled to body mass, is associated with a higher mortality in heavier patients.

To date, Raimann *et al.*¹ is the first publication to examine the association between unscaled UFR and mortality. It showed that higher UFR is associated with increased mortality. It also showed that a high UFR of >13 ml/kg/h is associated with a higher risk of mortality in patients of higher body mass as compared with those of a lower body mass. In summary, this research paper calls into question the suitability of UFRs scaled to bodyweight. It suggests that unscaled UFRs may be more applicable to the outpatient dialysis setting, and the authors recommend that an agreement of an unscaled UFR to a particular mortality hazard ratio be the accepted. The currently accepted UFR of 13 ml/kg/h may be a disadvantage to heavier patients and the authors note that more research needs to be done in defining an optimal upper ceiling of UFR. Given the number of factors that compound observational studies, randomized prospective trials will be needed. This is an important study which brings into question long-held assumptions about safe UFRs.

DISCLOSURE

The author declared no competing interests.

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