Estimating Residual Kidney Function With and Without Urine Clearance Measures: A Useful Tool for Incremental Dosing of Dialysis

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Residual kidney function (RKF) is associated with better outcomes among dialysis patients. Although RKF is routinely assessed in peritoneal dialysis in the United States and RKF data are incorporated into the peritoneal dialysis prescription, RKF seldom is assessed in hemodialysis (HD). Accordingly, insufficient attention may be paid to strategies to preserve RKF and incorporate knowledge of RKF into the HD prescription, strategies that could result in more patient-centered care and better outcomes.

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In 1972, President Richard Nixon and the US Congress enacted legislation allowing qualified individuals with end-stage kidney disease younger than 65 years to enroll in the federal Medicare program,[1] launching what would become widespread availability of dialysis in the United States. The standard thrice-weekly in-center HD regimen was instituted without any randomized controlled trial comparing outcomes of 3 times a week with other frequencies, such as twice-weekly HD for incident dialysis patients,[2] and in contrast to many other industrialized nations, very few patients received peritoneal dialysis.[3] The consequences of this historical choice have become more apparent as the dialysis population has grown to more than half a million US residents.[4]

The care of patients with advanced chronic kidney disease, particularly at the time of transition to kidney replacement therapy, is complex and costly.[5,6] Compared with twice-weekly HD, the current standard of initiating HD patients with thrice-weekly sessions results in substantially higher costs for HD. Furthermore, there may be other untoward consequences for incident patients, including accelerated loss of RKF and poor survival upon abrupt and outright transition to thrice-weekly HD therapy.[7] In contrast, initiation of HD through a twice-weekly HD regimen, also known as "incremental dialysis," appears more consistent with patient-centered care, particularly when targeted to specific patient characteristics.[7] Given that dialysis patient outcomes in the United States may lag behind some other industrialized nations,[8] there is a pressing urgency to test the benefits of an incremental HD initiation strategy, focusing on key outcomes such as preservation of RKF and first-year mortality,[2,9] particularly given that dialysis often is initiated at fairly high estimated glomerular filtration rates (GFRs) in the United States.[10]

Maintained RKF, on transition to dialysis, provides an additional level of autoregulation of electrolyte clearance, volume removal, and sodium homeostasis, which may be superior to that of dialysis therapy.[11,12] Further, middle-molecule clearance is more effective in native kidneys than with standard in-center HD.[11-15] Given these benefits, it is important to be able to assess RKF to allow for more patient-centered dialysis prescriptions and to help guide necessary and timely changes in HD regimens, including potential increased frequency from 2 to 3 times weekly.

The current standard for assessment of RKF is a 24- to 48-hour interdialytic urine collection, with measurement of urine urea nitrogen excretion to conform to measures of dialysis clearance and creatinine to estimate creatinine clearance as a better proxy of GFR than urea nitrogen clearance. This 24- to 48-hour assessment is an inconvenient process with considerable room for error, suggesting a critical unmet need for equations to estimate RKF in HD patients when urine volume and/or other urinary measures are not available, similar to current GFR estimating equations. In this issue of *Kidney Medicine*, Chin et al[16] examine different strategies for efficient quantification of RKF in incident HD patients.

Chin et al note the logistic difficulties surrounding the collection and analysis of 24-hour urine samples to calculate native kidney urea clearance (K_{RU}). The difficulty obtaining data for RKF through K_{RU} is a central reason why these tests are not performed more often in HD patients. To state the obvious, if data for RKF are not collected, the HD prescription cannot be adjusted to account for RKF. This may undermine the successful implementation of the incremental dialysis protocols and compel patients to receive more dialysis than is necessary. The focus on HD clearance (Kt/V) measures without adjustment for RKF may also hinder an incremental dialysis strategy. Given these logistic challenges, Chin et al[16] endeavor to model K_{RU} using markers such as β_2-microglobulin and serum cystatin C values in patients who make >100 mL of urine per day. The retrospective study used corrected K_{RU} measurements from 24-hour urine collections, adjusted with Daugirdas correction factors (0.92-0.98) for the time since last dialysis as the reference test for comparison.[17]

Chin et al calculated K_{RU} values using data collected from 604 incident in-center HD patients at 5 local facilities and, in conjunction with serum creatinine, serum urea nitrogen, and demographic data, derived and validated equations to predict the observed K_{RU}. Three models were evaluated, as described in Table 1. The mathematical models are complex and available in the full article,[16] but a simplified table describes their inputs and performance

Table 1. Comparison of Models Used to Determine Native K_{RU}

Model Type	Components (equation inputs)	Requires 24-h Urine Collection?	Performance
Chin model 1[16]	24-h urine volume	Yes	Second best performing
Chin model 2[16]	24-h urine volume; demographic data; serum creatinine and urea nitrogen	Yes	Best performing
Chin model 3[16]	Demographic data; serum creatinine	No	Performed poorly
UCI/Daugirdas equation[17]	Demographic data; pre- and postdialysis SUN; and calculated URR	Yes	Estimated K_{RU} comparable with urea kinetic modeling

Abbreviations: K_{RU}, native kidney urea clearance; SUN, serum urea nitrogen; UCI, University of California Irvine; URR, urea reduction ratio.

compared with that of the University of California Irvine/Daugirdas equation.[17]

Models that used 24-hour urine volume performed well (models 1 and 2), whereas model 3, which relied only on serum tests and demographic characteristics, performed similarly to the calculated GFR. Although model 3 is more easily used and can be calculated quickly, models 1 and 2 offer improved diagnostic accuracy, and electronic medical record platforms could be programed to calculate K_{RU} results using these routinely obtained laboratory data. Urine volume can easily be tracked serially, removing the logistical difficulty with patients bringing urine samples to clinics, clinics sending collections for laboratory analysis with optimal times pre– and post–serum testing, and following up the chemical analysis results in a busy HD clinic setting. The equations combined with computing power available today provide a utilitarian approach to estimate K_{RU} with very little work involved for the physician. Only urine volume collection quantification is needed by the patient.[16]

An important contribution of this study is that it allows a simple, cost-effective, and less labor-intensive approach to estimating RKF in a way that can be taken into account to make recommendations for dialysis prescription transition and initiation. Further, the trending of these equations (estimated K_{RU}) can be used to assess when a patient could need escalation of dialysis therapy according to the incremental dialysis protocols. Removing logistical barriers will lead to greater acceptance by providing data for K_{RU}/RKF to guide dosing recommendations of HD when starting twice-weekly HD. This will also facilitate future pragmatically designed trials that can test incremental versus non-incremental HD approaches.[16] The result of these data will be the potential to start a significant percentage of incident dialysis patients on incremental dialysis protocols with less than 3 sessions per week. In this way, kidney replacement therapy can be provided on a "sliding scale" rather than with the currently inflexible standard prescription approach intended to optimize Kt/V and urea reduction ratio.[14]

In conclusion, preservation of RKF upon transition is an invaluable goal. To achieve this goal, providers need to be aware of RKF and prescribe dialysis in such a way to limit RKF loss while remaining prepared to increase the dialysis prescription in a timely manner when RKF diminishes. Key applications of the work by Chin et al, which facilitates efficient and easy monitoring of RKF, could include larger scale implementation of incremental and twice-weekly HD therapy.[18] Having the estimated K_{RU} data available while using incremental HD to transition a patient into kidney replacement therapy can be invaluable for supporting prompt decision making and patient-centered care. This has the potential to ease the existing debate about early versus late dialysis initiation by emphasizing that dialysis can be incremental rather than all or none.[19,20] The key aspect to this potential paradigm shift in HD prescribing is RKF, and work that allows easier assessment of RKF is key to shifting care in the future.

ARTICLE INFORMATION

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