Dialysis Should Be Started When Absolutely Necessary, Not Early and Incrementally

To the Editor: The commentary by Obi and Kalantar–Zadeh[1] and clinical paper by Chin *et al*.[2] on incremental dialysis deserves further scrutiny. The first issue is which patients, if any, are "optimal" for the incremental dialysis approach? Patients who are dialyzed early, at an estimated glomerular filtration rate (EGFR) >10 ml/min per 1.73 m^2, may not have a better survival with incremental dialysis versus waiting to initiate standard dialysis at lower eGFR levels.[3] Increasing urea clearance with 3 times per week dialysis, although used for assessing dialysis adequacy, has not been shown to have a survival benefit. Thus, the incremental increase in small molecule/urea clearance above endogenous renal clearance, does not justify starting dialysis in these patients with significant residual renal function, especially when considering the potential harms of dialysis. In contrast, maximizing diuretic therapy for patients with intractable fluid overload may be a good approach to delay dialysis initiation. Patients in whom diuretic management fails are not candidates for twice weekly incremental dialysis with limited weekly ultrafiltration, but may be appropriate candidates for conventional hemodialysis with an "early start" in some cases. Nephrologists who want to consider twice weekly hemodialysis for palliative care need to consider the high 3- and 6-month mortality rates in many of these high-risk patients.[4] Twice weekly hemodialysis may be used in 25% of patients dialyzed in China, a country where few patients initiate dialysis early.[5] This approach makes good sense in countries with limited resources for dialysis and may have the added benefit of preserving residual endogenous renal function with its potential survival benefit.

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2. Chin AI, Appasamy S, Carey RJ, et al. Feasibility of incremental 2-times weekly hemodialysis in incident patients with residual kidney function. *Kidney Int Rep*. 2017;2:933–942.
3. Rosansky SJ, Cancarini G, Clark WF, et al. Dialysis initiation: what's the rush? *Semin Dial*. 2013;26:650–657.
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The Authors Reply: We thank Dr. Rosansky for his comments.[1] First, we are in full agreement that dialysis should not be started until the patient requires renal replacement therapy. Patients in our study[2] were started on conventional hemodialysis (HD) 3 times per week, not on incremental HD, by their nephrologists who believed that initiation of dialysis was clinically needed, although we could not determine the exact reason for each dialysis initiation due to the retrospective nature of our study. Moreover, our study patients (based on 386 of the 410 study patients in whom immediate predialysis start serum creatinine values were available) had a mean modification of diet in renal disease estimated glomerular filtration rate (eGFR) of 9.7 ml/min per 1.73 m^2 (SD of 4.5), and 38% of the study cohort initiated dialysis with eGFR ≥10 ml/min per 1.73 m^2. These statistics are similar to those reported in the most recent United States Renal Data System report,[3] in which the mean eGFR at initiation of dialysis in 2014 was 10.2 ml/min per 1.73 m^2 and 39% of incident end-stage renal disease cases started with eGFR ≥10 ml/min per 1.73 m^2. Therefore, our study group did not appear to have been started on dialysis any earlier than what was observed nationally.

Our study aim was to assess the proportion of a clinically stable incident HD cohort who could have theoretically started dialysis on a twice weekly

regimen. For each of the subjects, we determined twice weekly HD clearance needed to "complement" the residual renal function, not to suggest that twice weekly HD be initiated to "supplement" the renal function of individuals who might not have required dialysis initiation. In addition, the basis for clearance calculations did not exceed the standard weekly urea clearance target of 2.3 that is generally recommended in clinical guidelines for HD.[4] Notably, our theoretical ideal twice weekly dialysis group had a measured standard weekly urea clearance of 1.02 volumes, which is approximately one-half of desired weekly clearance, and therefore, this group needed HD.

Second, although we agree with Dr. Rosansky that failure to control volume with diuretics might be a reason to initiate dialysis, we disagree that all patients in this scenario should start conventional thrice weekly treatments. Our calculations suggested that the volume removed on twice weekly HD, even with a tight upper limit of dialysis ultrafiltration rate <13 ml/kg per hour, may allow adequate weekly fluid control in many patients with residual renal function. Optimization of diuretic use in such patients, even when dialysis is initiated, may further aid in decreasing the ultrafiltration needs.

Finally, we agree that preserving residual kidney function is important and perhaps not emphasized enough in the care of HD patients. To that end, twice weekly HD in patients where it is feasible, may allow for greater native renal function longevity. We also hope that our study provides insight to incremental HD, so that it can be a real option for the appropriate patient, rather than just a default prescription for patients with limited resources.

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Re: Further Evidence Supporting the Accuracy of Quantitative Magnetic Resonance Imaging for Evaluating Iron Load in Dialysis Patients

To the Editor: In his editorial accompanying our article, Daniel Coyne raises important issues regarding the validity of magnetic resonance imaging (MRI) for quantifying iron load in dialysis patients.[1,2] We are disappointed that he did not analyze our article devoted to this topic, published in January 2017.[3] There is indeed a need to validate these MRI techniques in dialysis patients, notably by comparison with liver biopsy.[3] However, liver biopsy is an invasive and risky procedure, especially in frail patients with end-stage renal disease, and such studies therefore raise ethical concerns.[3]

In a pilot study, on the advice of ethicists, we compared the classic Scheuer score and Deugnier and Turlin histological classification of iron overload (Perls staining of hemosiderin deposits) with signal-intensity-ratio MRI values obtained with the Rennes University algorithm in 11 hemodialysis patients in whom liver biopsy was formally indicated for their medical follow-up.[3] For Scheuer's histological classification, the Wilcoxon matched-pairs test showed no significant difference in the ranking of iron overload by histology and MRI (summary of ranks $= 1.5$; $P = 1$) (Figure 1).[3] The MRI and Scheuer histological classifications were strongly correlated (rho $= 0.866$, $P = 0.0035$, Spearman coefficient), as were the absolute liver iron concentrations on MRI (rho $= 0.860$, $P = 0.0013$,