What Drives Early Dialysis Initiation and How Do We Optimize Timing of RRT?

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Timing of dialysis initiation has been in the spotlight in recent years (1). During the last decade, there has been a trend toward initiation of chronic dialysis at higher levels of eGFR (2). The reason for increased attention to the topic is accumulating evidence that early dialysis initiation does not improve patient outcomes and results in unwarranted costs. In observational studies, higher eGFR at dialysis initiation has been associated with higher mortality risk after initiation, independent of patient characteristics including nutritional status (1,3). The Initiating Dialysis Early and Late (IDEAL) trial recently reported that compared with a strategy of delayed dialysis initiation, earlier initiation in patients with advanced CKD was not associated with improved survival (4) or quality of life, but was associated with increased costs (5). The percentage of patients who initiate RRT at higher eGFR values continued to rise through 2009, both in the United States (6) as well as in Canada. Several factors have been hypothesized to contribute to the reported increase in eGFR at dialysis initiation, including greater acceptance of older and sicker patients with multiple comorbidities for dialysis intervention, a belief that of earlier dialysis initiation is associated with patient benefit, eGFR reporting and reliance on eGFR values to guide timing of dialysis initiation, misinterpretation of clinical practice guidelines, a desire to simplify management of CKD complications, and a greater financial reimbursement to providers associated with dialysis compared with CKD care (1,2).

Prior studies have evaluated both patient and provider characteristics associated with timing of dialysis initiation (2,7). In this issue of CJASN, Sood et al. aimed to determine how patient, facility, and geographic characteristics influence the variation of eGFR at dialysis initiation across Canada (8). The authors observed that patient-related factors accounted for >95% of the explained variability of eGFR at dialysis initiation (8). Many of the specific patient characteristics associated with earlier dialysis initiation are similar to those previously observed in United States cohorts (2,7,9), and include female sex and presence of comorbidities. Prior studies have also suggested that patients with congestive heart failure initiate dialysis at higher eGFR values, likely to assist in the management of the patient’s volume status (2,7). It is likely that in Canada, similar to the United States, acceptance of older and sicker patients for dialysis therapy has contributed to the trend of rising eGFR at dialysis initiation because these patients typically are unable to tolerate uremia to the same degree as younger patients and they may have artificially higher eGFR estimates from their reduced muscle mass.

The study by Sood et al. also demonstrated an association between lower phosphorus levels and earlier dialysis initiation (8). Although this may represent poor nutritional status, it may also represent residual confounding. Because phosphorus is renally cleared, it may be that patients with a greater eGFR have greater clearance of phosphorus and lower serum levels.

Use of peritoneal dialysis (PD) as the renal replacement modality was associated with higher eGFR at initiation compared with hemodialysis. In a subgroup analysis of the IDEAL trial limited to participants who planned to commence PD, rates of death, cardiovascular events, and peritonitis were not different between early and delayed start arms. However, the proportion of patients planning to commence PD who actually initiated dialysis with PD was higher in the early start group (80% versus 70%; \( P=0.01 \)) (10). The need for careful planning of PD catheter insertion and training for PD before urgent indications for dialysis arise likely pushes providers to initiate patients who desire to commence PD earlier. Because residual renal function is important for PD patient outcomes, avoidance of hemodialysis as the first dialysis modality is highly desirable. Further research is needed that would identify optimal timing for PD catheter placement and patient training, while avoiding unnecessary time on dialysis as well as missed PD opportunities.

Variability of eGFR at dialysis initiation in the Canadian cohort was largely explained by the patient characteristics, with minimal geographic variation. This finding is somewhat surprising. In a study of factors that influence the decision to start dialysis among European nephrologists, nephrologists from countries with a high incidence of treated ESRD chose higher eGFR values for dialysis initiation and were more likely to initiate their patients early in the presence of advanced age and chronic conditions (11). Similarly, in the United States, the incidence of treated ESRD, particularly among elderly patients and patients with multiple comorbid conditions, is highest in regions with the highest intensity of end-of-life care (12). Slinin et al. found a weak association between density of nephrologists and
eGFR at dialysis initiation: Patients living in areas with lower or higher nephrologist density were less likely to initiate dialysis earlier than patients living in areas with 1–1.5 nephrologists per 100 ESRD patients (7). Possibly, areas differ in their capacity to accommodate patients with ESRD, competition for patients, incentive to initiate patients at lower eGFRs, and health care intensity. Because Canada is potentially a more homogenous country with a single-payer healthcare system and fewer dialysis providers, it is possible that it has lower regional variability of medical practices.

In the Canadian study, facility characteristics explained only 3.1% of eGFR variability with increase in interfacility variation among hemodialysis patients compared with PD patients (8). It is no surprise that the dialysis facility has little influence over the timing of dialysis initiation. At least in the United States, there is little interaction between the facility at which patients will ultimately obtain dialysis and their predialysis care. The link between the facility and the patient’s timing of dialysis initiation is likely mediated through the provider. Unfortunately, in the study by Sood et al., there was no information available about the provider (8).

The provider is an understudied entity in the timing of dialysis initiation. In the United States, certain provider characteristics such as fewer years of experience and graduation from a foreign medical school have been associated with earlier dialysis initiation, independent of patient characteristics (7). In the study by Sood et al. (8), there are also footprints of the provider’s influence over timing of dialysis initiation. If patients were initiated on dialysis based solely on clinical features (symptoms, volume status, etc.), one would assume that their distance from a dialysis facility would not influence the timing of dialysis initiation. However, Sood et al. demonstrate in a multivariable model that greater distance from a dialysis unit is associated with delayed dialysis initiation. This implies that providers take patients’ circumstances into the decision to initiate dialysis. One could posit that if patients living a significant distance from a dialysis facility are able to tolerate later dialysis initiation presumably without adverse outcomes, then patients living closer to a dialysis facility could also tolerate waiting longer to start dialysis. The other factor linking the provider to timing of the initiation of dialysis is the provider’s observed association with predialysis nephrology care. Patients followed by a nephrologist before dialysis initiation for >30 days were 28% more likely to initiate dialysis with higher eGFRs than patients with predialysis care <30 days. This result is similar to that described by Slinin et al., who suggested that both predialysis care by a nephrologist or the presence of an arteriovenous (AV) fistula or AV graft was associated with higher eGFR at dialysis initiation (7). The observational nature of both of these studies does not allow for causal inference; it is possible that patients with no predialysis nephrology care are more likely to present with advanced CKD, or AKI, and low eGFRs resulting in a delayed initiation. An alternative explanation is that nephrologists might move dialysis initiation forward in time (i.e., early initiation), particularly when an AV access is in place, perhaps because of belief that early dialysis initiation is associated with improved patient outcomes, or to simplify management of CKD complications, or because of a financial incentive (given that payment for dialysis is greater, at least in the United States, than payment for clinic visits). Given these observations, it may be that the provider has a strong influence over when patients initiate dialysis, independent of patient characteristics or symptoms.

Timely initiation of dialysis is likely to improve patients’ well-being by decreasing the proportion of life spent undergoing dialysis, and is also likely to provide financial savings to society. There is some evidence that the trend for initiation of dialysis at higher eGFRs started to reverse in 2009 (13). This is also evident in Figure 2 in the article by Sood et al. (8), in which there is a steady upward trend in early dialysis initiation until 2010. Although the trend toward early dialysis initiation appears to have halted, there are limited data to determine whether these early changes are isolated events or sustained practice changes in response to the IDEAL trial. Continued temporal monitoring of timing of dialysis is warranted.

It is unclear how best to target optimal timing of dialysis initiation. Designing interventions targeting delayed dialysis initiation at the facility level might be difficult. In the United States, dialysis facilities do not usually participate in the decision to initiate dialysis. Furthermore, limiting the eGFR of the patients that they could accept for dialysis initiation would clash with the facilities’ financial interests. Despite this, we agree with the authors that making eGFR at dialysis initiation a quality pay-for-performance measure is premature. Without better defining optimal timing for dialysis initiation, these measures might result in an inadvertent delay in needed therapy for some patients, as well as an unintended decrease in PD use. As the body of evidence related to timing of dialysis initiation and outcomes develops, greater emphasis should be placed on disseminating these findings to practicing nephrologists. Although patient characteristics are important in the decision to initiate dialysis, the provider appears to be a strong, modifiable factor that greatly influences the decision of when patients should initiate RRT.

Disclosures
None.

References


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See related article, “Variation in the Level of eGFR at Dialysis Initiation across Dialysis Facilities and Geographic Regions,” on pages 1747–1756.