Initiation of Dialysis at Higher Levels of Estimated GFR and Subsequent Withdrawal

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Over the last 10–15 years, there has been a pervasive trend toward initiation of chronic dialysis at higher levels of estimated GFR (eGFR) across a range of different patient groups and practice settings (1–5). This finding seems to suggest that on average patients are now initiating chronic dialysis substantially earlier in the course of their kidney disease than in previous years (3). In light of recent trial evidence demonstrating that earlier initiation of dialysis at higher levels of eGFR does not lead to improved outcomes (6), these findings have helped to focus a spotlight on contemporary dialysis initiation practices (7–9).

Over roughly the same time period, there has been a marked increase in the percentage of patients who eventually withdraw from dialysis (10), raising the question of whether parallel trends in these two critical treatment decisions may be more than coincidental. In this issue of CJASN, Ellwood and colleagues used patient-level data from the Canadian Organ Replacement Registry to evaluate the association between eGFR at initiation and subsequent withdrawal from chronic dialysis (11). Between 2001 and 2009, rates of withdrawal in Canada doubled from 1.5 to 3.0 per 100 patient-years, and withdrawal as a cause of death increased from 7.9% to 19.5%. Those patients who initiated dialysis at an eGFR >10.5 ml/min per 1.73 m² were 17% more likely to withdraw from dialysis, and patients who initiated dialysis in more recent years were more likely to withdraw from dialysis even after adjustment for eGFR at initiation. That dialysis patients have the option to discontinue treatment is often viewed as a blessing (12). In this conceptualization, dialysis is viewed as a life-sustaining treatment and discontinuation as a way for patients to exercise some control over the timing and circumstances of their own death. The experience of the novelist James Michener, who was on dialysis for 4 years before he died, exemplifies this perspective. Michener said: “A person on dialysis undergoes very heavy and irritating treatment and in time it seems more than you can bear... There’s always an easy out. Just don’t go to hospital. Then, after two weeks, you’re dead.” He discontinued dialysis a few days after his 90th birthday and died later the same month (13). Michener’s experience contrasts with that of Art Buchwald, another famous writer who also discontinued dialysis. Buchwald’s experience challenges the perception of dialysis as a life-sustaining treatment and exposes some of the uncertainty involved in decisions about both initiation and discontinuation (14). Buchwald had CKD, diabetes, nephrolithiasis, and a history of stroke. He initiated dialysis a few weeks after his 80th birthday during a hospital admission for critical limb ischemia. His doctors told him that if he didn’t have his leg removed he would die of gangrene, “a slow and painful death, that didn’t sound very pleasant.” When his renal function worsened after an angiogram, he was told that he needed to “begin dialysis immediately so as to make it possible to proceed with the amputation.” Buchwald agreed to initiate dialysis so that his foot and lower leg could be amputated. Within 5 weeks of surgery he decided to stop: “I don’t see a future in this and I don’t want to do it anymore!” Buchwald made his decision after seeing an advertisement for hospice in an elevator: “I had discovered the idea of hospice by then, and knew I had an alternative.” To everyone’s surprise, Buchwald went on to live another 11 months, long enough to be “kicked out” of hospice. Buchwald’s experience illustrates how decisions about dialysis initiation can be intertwined with other major treatment decisions (in this case amputation), and how discussions of treatment options can be framed in such a way that patients are left feeling that they have little choice but to proceed with dialysis (15). Buchwald’s experience also illustrates the large degree of uncertainty that often exists about prognosis, future illness trajectory, and optimal approaches to treatment for patients with advanced kidney disease (16). That Buchwald survived for 11 months after discontinuing dialysis raises the question of whether he really “needed” this treatment in the first place. At the time of discontinuation, he clearly had enough renal function to survive more than the 8-10 days expected for an anuric patient (10,17). Whether this was also true around the time of initiation or whether he had subsequently recovered some renal function is unclear. Trajectories of renal function leading up to initiation of chronic dialysis are quite heterogeneous, and it is not uncommon for patients with established kidney disease to initiate dialysis during an episode of AKI (18,19). While we often look for recovery of renal function in the setting of acute kidney injury, we usually don’t look quite so hard once patients are on “chronic” dialysis. One wonders whether Buchwald would have chosen to initiate dialysis at all had he been educated about more...
after dialysis initiation, and what the experience of being on conservative treatment options earlier in his illness trajectory. Or perhaps the experience of being on dialysis was instrumental in shaping his eventual decision to discontinue this therapy, making him more receptive to other options such as hospice? Especially in complex older patients, there is often substantial uncertainty about whether symptoms will improve after dialysis initiation, and what the experience of being on dialysis will actually be like.

How should we interpret the finding reported by Ellwood and colleagues of an association between eGFR at initiation of dialysis and time to withdrawal? Does this study suggest that we have become more likely to recommend dialysis in patients for whom the burdens outweigh the benefits? Although this study raises this provocative question, source data are insufficiently detailed to provide a definitive answer. In the absence of information about factors driving the decision to initiate dialysis at higher levels of eGFR, about the circumstances of dialysis withdrawal, and about the experiences of individual patients, it is difficult to hypothesize why withdrawal might be more common in those who initiated dialysis at higher levels of eGFR.

While the trend toward initiation of dialysis at higher levels of eGFR is widely thought to reflect a liberalization of dialysis initiation practices over time, exactly how these trends have changed is not well understood. Although registry data include information on underlying comorbidities and causes of kidney disease, they do not capture information on a range of other factors that may influence the timing of initiation. These include the presence and severity of clinical indications for dialysis (19), the severity of underlying comorbid conditions, the presence of conditions such as functional impairment (19) and frailty (20), the trajectory of renal function (18), and patient preferences. Multiple studies have now reported higher mortality rates in patients who initiate dialysis at higher levels of eGFR (21). In light of trial evidence that eGFR at initiation does not affect survival (6), these results probably indicate that such patients are somehow “sicker” than those who initiate dialysis at lower levels of eGFR. Perhaps members of this cohort who initiated dialysis at higher levels of eGFR had (or were believed to have) an urgent indication for dialysis? Perhaps they had an acute and unexpected deterioration in renal function at the time of initiation, as commonly occurs in the setting of acute illness? Perhaps they had more rapidly progressive kidney failure and/or more severe comorbid conditions? In all of these situations, it is easy to imagine how the decision to initiate dialysis might have been guided by considerations not captured in registry data.

Secular trends in dialysis withdrawal are also poorly understood. One challenge to interpretation is that the circumstances of withdrawal can vary widely (22), and, as the authors point out, detailed information about these is lacking in source data. Like Michener, some patients will have made a conscious decision to discontinue dialysis when the burdens of treatment exceeded the benefits, with the expectation of dying of uremia within 1–2 weeks. Although patients who discontinued dialysis due to recovery of renal function were not included in the outcome, there may have been some patients like Buchwald who survived unexpectedly for longer periods of time after withdrawal. This might help to explain why roughly a quarter of patients who withdrew from dialysis in this study were missing a date of death. Still other patients may have discontinued dialysis in the setting of a serious life-threatening illness or failure to thrive. The decision to discontinue dialysis may perhaps have been made by a surrogate decision maker and tied to broader decisions about desired treatment intensity at the end of life. In these circumstances, “withdrawal from dialysis” or “uremia” may not have been listed as a cause of death (22). The very high levels of end-of-life intensity of care among older US dialysis patients suggest that this may be a common context for decisions about dialysis discontinuation (23). In this setting, withdrawal from dialysis might be more of a “marker” for death than a true treatment “choice” of the sort made by Michener and Buchwald (24).

Which of these different scenarios occurred more frequently in cohort members who initiated dialysis at higher levels of eGFR is unclear. What is perhaps most striking about the results presented here is that there was an association between eGFR at initiation and subsequent withdrawal, but that this and other clinical measures were far less strongly associated with time to discontinuation than factors such as state of residence and race. Compared with the national average, these patients living in Alberta were 59% less likely and those living in Nova Scotia 67% more likely to discontinue dialysis. Compared with white patients, black and Asian patients were 69% and 62% less likely to discontinue dialysis, respectively. These findings match those of prior studies reporting geographic and racial differences in rates of dialysis discontinuation and hospice use among US dialysis patients (25–27) and intensity of end-of-life care among older US adults (28,29). Collectively, the strong associations of geography and race with patterns of dialysis withdrawal reported here and elsewhere seem to suggest that larger societal forces may be at work (24).

Ultimately, decisions about whether and when to initiate and discontinue chronic dialysis are dynamic treatment decisions that must often be made in the context of substantial uncertainty about prognosis, illness trajectory, and the expected benefits and burdens of alternative treatment options. These decisions may be intertwined with one another, with other major treatment decisions, and with broader decisions about desired level of intensity of care at the end of life. The more effectively we engage patients and their families in these decisions, the better we educate them about relevant treatment options, and the more we prepare them for what might lie ahead, the better equipped they will be to make choices that are right for them.

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References
3. O’Hare AM, Choi AI, Boscardin WJ, Clinton WL, Zawadzki I, Hebert PL, Kurella Tamura M, Taylor L, Larson EB: Trends in...

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Correction

The approved editorial contained the following reference errors:

- Citation 15 refers to reference 24 in the reference list.
- Citation 16 refers to reference 15 in the reference list.
- Citation 17 refers to reference 16 in the reference list.
- Citation 19 refers to reference 17 in the reference list.