

Predialysis Care and Cardiovascular Outcomes: Why the Lead Up to Dialysis Matters



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Kidney Int Rep (2019) 4, 635–637; <https://doi.org/10.1016/j.ekir.2019.03.010>

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Cardiovascular disease is common in advanced chronic kidney disease (CKD) and end-stage renal disease. In fact, cardiovascular disease accounts for approximately 50% of deaths among dialysis patients with the most common etiology being arrhythmia or cardiac arrest (40% of deaths).¹ Atrial fibrillation is an exceedingly common arrhythmia among patients with CKD, and in particular those with end-stage renal disease on dialysis in whom more than 10% have atrial fibrillation, a prevalence more than 10-fold higher than the general population.² The presence of atrial fibrillation in advanced CKD is associated with progression to end-stage renal disease, cardiovascular events, and death.³ Management of atrial fibrillation with anticoagulation in this population is complicated by both a decreased efficacy with regard to stroke prevention and a markedly increased risk for bleeding complications.⁴ Given the high burden of

cardiovascular disease, in particular atrial fibrillation, combined with a lack of efficacy from standard treatments in the advanced CKD population, preventive measures to reduce morbidity and mortality are sorely needed. In a recent observational study from Taiwan, early and more frequent outpatient predialysis nephrology care was associated with an approximate 10% reduction in risk for major adverse cardiovascular events (myocardial infarction, heart failure, stroke, and sudden death) over the first year on dialysis.⁵ This finding raises the question of whether outpatient interaction with nephrology care in the predialysis time frame may actually prevent adverse cardiovascular outcomes once a patient starts dialysis and if so, does timing (early in CKD care) and intensity (number of visits) matter?

In this issue of *Kidney International Reports*, Anumudu *et al.*⁶ address the following question: *Can early and more frequent outpatient predialysis nephrology care serve as a preventive measure to reduce the incidence of atrial fibrillation once a patient initiates dialysis?* This retrospective study used

the US Renal Data System to identify more than 300,000 older patients (67 to 99 years old) without a prior Medicare billing claim for atrial fibrillation who initiated dialysis in the United States between 1996 and 2013. Patients were subclassified based on whether they received any outpatient predialysis nephrology care (yes or no), the duration of predialysis nephrology care (≤ 6 months, 7–12 months, or ≥ 12 months), and the number of predialysis nephrology visits (1–4 visits, 5–9 visits, or ≥ 10 visits). The authors found that having any outpatient predialysis nephrology care was associated with a 14% reduction (adjusted hazard ratio 0.86; 95% confidence interval 0.84–0.87) in the risk of incident atrial fibrillation once a patient initiates dialysis. Interestingly, although the dichotomous exposure of any outpatient predialysis nephrology care was associated with a reduced risk of atrial fibrillation, there was no apparent signal with regard to a “dose-response” effect, as there was minimal difference in terms of the magnitude of risk for atrial fibrillation between early (≥ 12 months before dialysis) versus late (≤ 6 months before dialysis) outpatient nephrology care. In contrast, it appears that the total number of nephrology visits did show a modest “dose-response” effect with more predialysis nephrology visits associating with a slightly lower risk for future incident atrial fibrillation; however, the investigators did not have access to information regarding the rate of CKD progression. So in fact, what we may be observing is simply more visits due to a slower decline in estimated glomerular filtration rate over time, a factor that is

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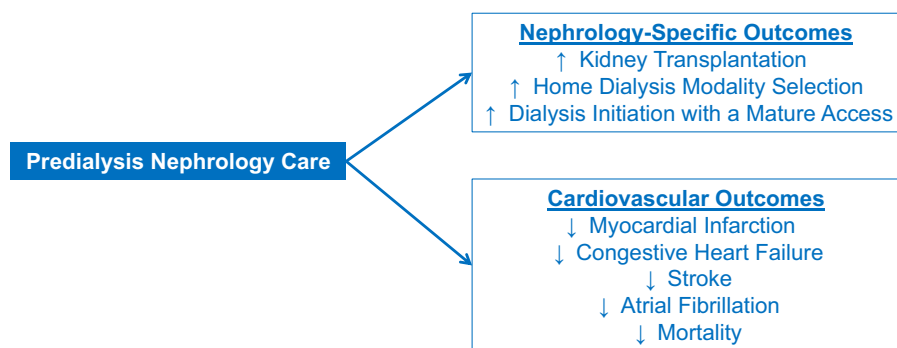


Figure 1. Beneficial effects of predialysis nephrology care in advanced chronic kidney disease. Up and down arrows refer to increased or decreased rates of each outcome.

associated with healthier patients and better outcomes overall.

A strength of the investigators' evaluation of predialysis medical care is including care beyond just nephrology. In addition to evaluating the association between predialysis nephrology care and the risk of incident atrial fibrillation, the authors also evaluate the association between both predialysis primary care and predialysis cardiology care and the risk of incident atrial fibrillation. As opposed to the protective association of nephrology care, predialysis primary care showed no protective association (adjusted hazard ratio 1.00; 95% confidence interval 0.97–1.03), whereas predialysis cardiology care was associated with a 5% higher risk of incident atrial fibrillation (adjusted hazard ratio 1.05; 95% confidence interval 1.03–1.07). Although the finding of a higher risk of incident atrial fibrillation among those patients receiving predialysis cardiology care suggests that there may be some degree of selection or detection bias that cannot be completely accounted for through statistical modeling (i.e., it is unlikely that simply seeing a cardiologist would increase one's risk for atrial fibrillation if all other competing risk factors were equal), incorporating rates of medical care with other medical subspecialties beyond nephrology strengthens the overall message of this study of

the beneficial effect of predialysis nephrology care. In particular, these interspecialty trends argue against better access to health care or an overall healthier population being the reasons for the study finding of the beneficial effects of predialysis nephrology care.

This study adds to the mounting evidence of the beneficial impact to overall health, beyond just atrial fibrillation, that outpatient nephrology care has on the patient with advanced CKD who is approaching dialysis (Figure 1). Prior studies have demonstrated that predialysis nephrology care improves both nephrology-specific outcomes (e.g., increased rates of transplantation, home dialysis modality selection, and dialysis initiation with a mature fistula or graft),^{7,8} as well as cardiovascular outcomes (e.g., myocardial infarction, stroke, heart failure, and mortality).^{5,9} These studies beg the question: *What specific routine intervention(s) provided by nephrologists is/are responsible for these improved outcomes, including atrial fibrillation, that persist even after a patient starts dialysis?* A variety of potential interventions could be hypothesized, including improved management of blood pressure, volume overload, hyperkalemia, anemia, acid-base disturbances, mineral bone disease, and nutritional deficiencies. It is likely that a variety of these interventions are responsible for the long-term

benefit in predialysis nephrology care as highlighted by these studies; however, the existing studies on predialysis care have not been designed in such a manner as to address which specific interventions provided by nephrologists are responsible for this long-term benefit. Thus, future studies are needed to further dissect the intricacies of predialysis nephrology care to highlight which specific predialysis interventions are responsible for this sustained beneficial effect to maximize the impact and efficiency of future predialysis care.

The more we learn about the beneficial effect of nephrology care in advanced CKD, particularly in those approaching dialysis, the stronger the case becomes for adopting a more standardized approach for this patient population. These recent studies reveal the wide spectrum of exposure these patients can have with nephrologists that is likely a product of nonuniform health care approaches. One alarming result from this article by Anumudu *et al.*⁶ is that 33.1% of older patients in the United States have no outpatient nephrology exposure before initiating dialysis. Clearly, this lack of nephrology exposure has adverse cardiovascular consequences, but likely also limits patients' education and options regarding dialysis modality, access creation, transplantation, and conservative care. These critical discussions leading up to dialysis are never had with at least one-third of the dialysis population. Among the remaining two-thirds of patients who do receive outpatient nephrology care before dialysis initiation, this study shows that there is clearly no standard in terms of how early or how often these patients are seen by nephrologists. Whether early versus late nephrology referral or more

frequent versus less frequent nephrology care is superior in advanced CKD remains largely unknown. Future studies addressing these knowledge gaps may help reshape the future of how advanced CKD should be managed by providing a blueprint on how nephrologists in particular and the medical community as a whole can best serve patients approaching dialysis.

DISCLOSURE

All the authors declared no competing interests.

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