AJKD
Editorial

On Being Better Kidney Doctors: Understanding Trajectories, Probabilities, Predictability, and People

Related Articles, p. 495, p. 504, and p. 513

In the last decade, chronic kidney disease (CKD) has become recognized as a more common condition than previously appreciated in the medical field: as a multiplier of risk and as an important prognostic factor for a number of health outcomes, such as cardiovascular disease, hospitalization, dialysis, and death.[1,2] Universally, it now is recognized as a public health problem, requiring attention from policy makers, administrators, primary care physicians, and specialists. The 2002 publication of the KDOQI (Kidney Disease Outcomes Quality Initiative) guidelines for the definition, classification, and evaluation of CKD was a catalyst for this increase in awareness,[3] giving some sensible structure and nomenclature to the condition. Since 2002, the number of publications and research studies describing improved understanding of the biology of the condition and the outcomes of people with CKD has increased exponentially.

In this issue of the *American Journal of Kidney Diseases*, 3 important articles are presented that help inform both research and clinical care in this area.[4-6] These reports focus on movement among CKD states: speed of the travel, shape of the path, and implications of uncertainty (lack of our understanding) of this journey. The main theme is the uncertainty and diversity evident in pathways to clinical outcomes of those with CKD, particularly with respect to progression of kidney disease. The authors all emphasize the need to better characterize and understand that heterogeneity. By so doing, we will not only be able to care better for patients, but will also be better able to design and execute clinical trials and generate evidence on which to base that clinical care.

The report by O'Hare et al[4] describes the trajectories of more than 5,000 persons within the Veterans Affairs system who started dialysis therapy between 2001 and 2003 and had at least 2 years of data prior to that start. Using the integrated laboratory and administrative database available through the Veterans Affairs system, they were able to capture patient characteristics and care practices to explore not only the trajectories, but also potential influences on those trajectories. While recognizing that this study examines only those who ultimately ended up on dialysis therapy (ie, the results are limited by survivor bias), there are important lessons here. First, although most people who initiated dialysis therapy within the 2-year follow-up were those with an estimated glomerular filtration rate (eGFR) <30 mL/min/1.73 m^2 (63%) and had relatively slower slopes of decrease, a significant proportion were patients with higher eGFRs who had faster rates of decrease (34%), whereas 3% of patients with eGFRs >60 mL/min/1.73 m^2 had catastrophic rates of decrease. Anchoring the outcome as time to dialysis therapy within 2 years, these findings are not unexpected given that to get to dialysis therapy within 2 years from a higher GFR, one would have to have a steep trajectory. Hospitalizations and episodes of acute kidney injury (AKI) were important associations seen in those with steeper eGFR trajectories. Those with the highest levels of kidney function were least likely to receive predialysis care, likely due to nonappreciation of their potential to progress. The report reminds us that those who arrive at dialysis therapy do so in various ways: the authors define 4 different patterns of eGFR decrease prior to dialysis therapy and note the need for more flexible approaches to preparation for renal replacement therapy initiation based on the knowledge of the heterogeneity of progression within populations of identified individuals.

Li et al,[5] using the African American Study of Kidney Disease (AASK) cohort, describe the trajectories of 846 African Americans who participated in both the clinical trial and subsequent longitudinal cohort follow-up study for a period of up to 12 years. They describe a 41% nonprogression rate, variability in trajectories with both acceleration and deceleration of slopes over time, and a significant deviation from linearity in GFR slopes within individuals during this extensive follow-up period. There are a number of important observations from this study that are pertinent to clinical care: nonlinearity is related to duration of follow-up. The longer one is followed up, the greater the opportunity to have events occur that change the trajectory. Although this is obvious to most clinicians, implications for the design of clinical studies are profound, as is the impact on planning for resource allocation. In clinical practice, we often predict trajectories based on the most recent values of kidney function and other clinical parameters, but given these results, clinicians would need to constantly readjust assessments based on the totality of data from a given patient and consider most recent values in the context of prior values. Seasoned clinicians may already do this implicitly, but those earlier in their career or less well-versed in

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CKD may have difficulty assimilating this into their decision making, especially in the absence of explicit models that describe complex clinical pathways of renal progression that do not follow steady linear models. Note that most predictive models use outcomes at 1, 3, or 5 years, which are relatively short-term outcomes in CKD. Li et al[5] use Bayesian smoothing techniques and describe a variety of patterns that deviate from linearity among individuals. They argue for the need for application of these more sophisticated analytic approaches to long-term follow-up and clinical study design. The demonstrated association of time varying factors changes in eGFR slope is important. The authors describe acute and chronic factors that explain the diversity observed in progression. These include episodes of AKI, hospitalization, infection, medication changes, and individual biomedical factors. Including these factors in studies using "within-person design" would allow evaluation of the single and cumulative effect of these factors within 2 discrete periods within and between individuals. This type of analysis will truly allow for a more personalized medicine approach in discussions with patients while still providing physicians and health administrators with robust information to guide prognosis and decision making.

The publication by Schell et al[6] offers a different dimension to these 2 reports and is complementary to them. These authors use a qualitative approach to understanding patient and physician perspectives regarding kidney disease trajectories and the effects of lack of predictability of disease progression in terms of speed and linearity on discussions between patients and physicians. The themes that recur are those of uncertainty and unpredictability from both the patient and physician perspective. This uncertainty leads to difficulties addressing preparation for dialysis therapy, frustration on the part of physicians, and emotional stress for patients. These in turn are barriers to understanding and communication and lead to the potential for adverse outcomes (lack of fistula creation, depression, and nonadherence to treatment recommendations). Although based on a relatively small number of interviews (11 physicians and 29 patients aged >65 years), the insights gleaned resonate with any of us involved in clinical care and with the key messages of the 2 reports cited previously. The authors offer some tools and methods by which to improve communication and the patient experience that need to be tested in clinical environments, with and without better knowledge of trajectories as described.

The need to understand the trajectory of CKD is immensely important to the individuals and families who live with this condition, to the medical care team providing care, and to administrators who are planning for resources to support them.

The recognition of the heterogeneity of outcomes and the different pathways to these outcomes in patients with CKD is not a novel concept, but applying scientific rigor to its understanding has become very important.[7] The use of sophisticated modeling techniques that take into account time-varying factors, changes in trajectories over discrete periods, and the influence of AKI with and without return to baseline are all methods that have been used to various degrees in different studies.[8-13] The challenge of the future is how to combine these more complex analytic methods, use the increasingly available information from predictive models for outcomes at different times, combine these with disease-specific novel biomarkers, and design clinical studies to evaluate the impact of different interventions on outcomes.[14-17]

Acknowledging the diversity of the progression of CKD within and between individuals and understanding it will improve communication between physicians and their patients and ultimately may improve the preparation of those individuals for renal replacement therapy or other clinical outcomes, with subsequent positive implications for resource use and health care systems. The 3 publications in the present issue of *AJKD* serve to remind us how the art and science of medicine work together to improve the care of patients with CKD: good communication integrating emotional and medical conditions of individuals based on scientifically rigorous data will certainly make us better kidney physicians.

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