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Risk of Progression to ESKD or Death in Adults With CKD: Three Paths Identified

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Kidney Int Rep (2021) **6,** 1492–1493; https://doi.org/10.1016/j.ekir.2021.04.028

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> "Trajectories from the past
> are taking their toll…"
> The Beastie Boys[1]

Chronic kidney disease (CKD) represents one of the most impactful medical conditions from both a clinical toll and resource utilization perspective.[2] The burden of CKD increases hospitalization risk, increased risk of end-stage kidney disease (ESKD), and death. Furthermore, CKD enhances the impact of other chronic conditions, such as heart failure, diabetes, and cancer.[3] These epidemiological observations derive from a population-based assessment approach, but do not identify risk factors over time that delineate groups of patients with CKD at differing risks of progression to ESKD or death. Elucidation of reliable longitudinal prediction groups could hold promise to assign risk of these poor outcomes at the individual patient level, especially if the number of groups is not too large and the attribute defining the groups is discrete, easily identifiable, and not overly granular.

In this issue of *Kidney International Reports*, Sirvastava and colleagues[4] assess if hospitalization number after CKD diagnosis can serve as this defining attribute. The authors used data from the Chronic Renal Insufficiency Cohort to test their hypothesis, drawing from a subset of patients who did not progress to ESKD and did not die in the first 4 years after CKD diagnosis. They then applied latent trajectory analysis to determine if patients could be segregated into specific hospitalization, nonoverlapping patterns. Each pattern would then serve as the exposure variable, with subsequent progression to ESKD or mortality as the primary outcome variables.

Indeed, the authors identified 3 discrete hospitalization trajectories, low utilization, intermediate utilization, and high utilization, which corresponded to 0 (reference), 2.2 ± 1.5 and 6.3 ± 4.3 hospitalizations over the 4-year exposure period, respectively. Importantly, in this Bayesian analysis, the posterior probability of an individual subject being assigned correctly in their group was 1, 0.98, and 0.89 for the 3 groups. This high level of correct grouping into only 3 cohorts, based on a single attribute in a large population of patients with the heterogeneity of conditions associated with CKD, is quite surprising and remarkable. If these 3 utilization groups predict progression to ESKD or death, then these past trajectories would indeed be taking their toll.

Although the hospitalization densities remained stable for the overall Chronic Renal Insufficiency Cohort study subjects, those participants who progressed to ESKD or died had increasing densities in the years before these outcomes. Over a mean follow-up of 5 years, the risk for ESKD was approximately 50% greater for the intermediate utilizer group and 75% greater for the high utilizer group compared with the low utilizer group. With respect to mortality, the risk was 50% greater for the intermediate utilizer group, and 250% greater for the high utilizer group compared with the low utilizer group. The authors performed important sensitivity analyses, including those that exclusion of hospitalization duration of 1 day or fewer, accounting for a 1-year time lag to account for hospitalizations for dialysis initiation, and repeating the primary trajectory analysis for patients who did not progress to ESKD or die within 2 years of CKD diagnosis. In all additional assessments, the incremental association between utilization status and ESKD or ESKD-censored death remained. Strikingly, this association persisted even when adjusting for other strong predictors of progression to ESKD and mortality, such as kidney function (estimated glomerular filtration rate), proteinuria, and

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diabetes, as well as important social determinants of health, including income and education levels, health insurance status, and ethnicity.[5–7]

The investigators should be commended for this unique study, as it provides actionable information for the medical community that cares for patients with CKD. Hospitalizations are relatively easy to track, especially in integrated health care systems. Although the Chronic Renal Insufficiency Cohort data assessed hospitalizations in 6-month blocks, the observation that just 2 hospitalizations in a 4-year period increases risk for CKD progression or death, one could imagine an alert for a patient who experiences their second hospitalization after CKD diagnosis and not needing to wait 4 years. Such a process would be quite easy to operationalize and is supported by the additional analysis demonstrating the association between utilization group assignment at 2 years and outcomes. The observed associations between utilization groups and social determinants of health can allow for resource focus to be placed on the most at-risk groups. Finally, and obviously, our goal should be to slow CKD progression and reduce mortality risk. The utilization groups not only identify patients who may require more clinical attention but can enrich the CKD population to direct novel interventions to the most at-risk patient.

The retrospective analysis of this prospective Chronic Renal Insufficiency Cohort study has many strengths: a very well characterized longitudinal cohort, a long duration of follow-up, and a novel Bayesian approach to this population. The authors acknowledge the limitations of their work, including the low number of patients in the high utilization group, and the fact that 2- and 4-year hospitalization data may not be available to all health care providers. But, as noted previously, these limitations can be overcome with current electronic health record abstraction.

In summary, these past trajectories do take a serious toll on patients with CKD. The investigators have provided us with a simple and feasible method to identify that trajectory and hopefully to reduce that toll.

DISCLOSURE

The author declared no competing interests.

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