

## Machine Learning Technique

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kidney disease. [This study is a step toward] trying to identify the heterogeneity underlying what we think are common forms of kidney disease.”

Each patient is unique, says the other lead author, Zihe Zheng, MBBS, MHS, a doctoral candidate in the department of biostatistics at the University of Pennsylvania Perelman School of Medicine: “Patients are different, and people with similar kidney function are still different. This heterogeneity is something we really want to highlight [in this study]. Our main focus is to classify patients to find out how they are different from each other in the expectation that that will shine some light on the underlying pathophysiology.”

### 72 baseline characteristics

The study used data from the CRIC project, an ongoing prospective cohort study of adults with CKD stage 2 to 4. Participants were recruited from 2003 through 2008 from clinical centers in seven U.S. cities. Since then, they have been followed through annual clinic visits during which investigators collect health information and urine and blood specimens for an extensive testing menu.

The researchers analyzed this database using a machine learning method called unsupervised consensus clustering. Consensus clustering refers to a process of using several algorithms to look for similarities that is “unsupervised” because researchers did not decide in advance how the groups should look. The algorithms looked at 72 baseline characteristics of the patients out of 822 variables measured in each patient at the CRIC study baseline. The 72 variables were selected based on a literature review for those most clinically relevant to CKD.

### Three clusters

“The algorithm revealed three unique CKD subgroups that best represented patients’ baseline characteristics,” the authors write. Cluster 1 included patients with “relatively favorable levels” of bone and mineral, cardiac, and kidney function markers; diabetes; and obesity. The patients used fewer medications than members of the other clusters. Patients in cluster 2 had a higher prevalence of diabetes, had greater markers of obesity, and used more medications. Patients in cluster 3 had even higher levels of diabetes and obesity, and had the least favorable levels of bone and mineral, cardiac, inflammation, and kidney function

markers.

The cluster membership was strongly associated with patients’ future risks of kidney disease progression, cardiovascular events, and death, with risks escalating from cluster 1 through 3. “We showed a strong independent association between the cluster membership and future adverse events, after controlling for the known CKD risk factors, such as eGFR, UACR, blood pressure and diabetes status, etc., to be at the same level,” the authors write. “The cluster membership provided a simple metric of summarizing the patient heterogeneity and comorbidity profiles encoded in the 72 baseline variables.”

Consensus clustering has been used as a phenotyping tool in other heterogeneous conditions such as heart disease, type 2 diabetes, and several forms of cancer, and the authors write that “identification of clinical meaningful subgroups among CKD patients provides an important step toward patient classification and precision medicine in nephrology. Being able to characterize this heterogeneity early is an important step towards individualizing follow-up strategies for these patients.”

“I think this is a step in the direction of using multi-dimensional data for risk prediction for chronic kidney disease,” Waikar said. It remains to be seen whether mining the data in electronic medical records will be an approach that clinicians will be able to use to identify the prognosis and tailor the treatment for individual patients who share certain characteristics. “Can we identify the patients in clinical practice who would benefit from more intensive therapy and more intensive monitoring?” he asks.

As an example of the kinds of clues about treatment targets the information could provide, the study notes that inflammatory mechanisms are involved in the development and progression of CKD and its comorbidities such as cardiovascular disease. “The identified clusters may represent different states of inflammation which could, in part, explain the differences in risks of developing adverse clinical events,” the authors write.

Girish N. Nadkarni, MD, MPH, assistant professor at Mount Sinai Health System in New York City, who was not involved in the study, said the study recognizes “that chronic kidney disease is quite a heterogeneous syndrome, and [the researchers] are trying to use data-driven techniques to tease out the heterogeneity. They are trying to show that this is not just one disease but a syndrome comprised of many different subtypes of different types of disease. There is great promise in this approach in order to discover unknown risk factors. This is the first step in a continuum of research trying to show that all chronic kidney diseases are not the same.” ■

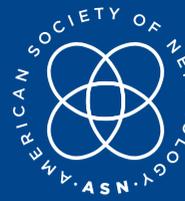
## Slower CKD Progression with RASIs versus CCBs

Patients taking renin-angiotensin system inhibitors (RASIs) have slower progression of kidney disease than those taking calcium channel blockers (CCBs), according to a “real-world” study in the *American Journal of Kidney Diseases*.

With the use of 2007–2017 data from the Swedish Renal Registry, researchers identified two groups: 2458 new users of RASIs and 2345 patients starting treatment with CCBs. At a median follow-up of 4.1 years, rates of KRT initiation, death from any cause, and major adverse cardiovascular events (MACEs) were compared between the two treatment groups. Patients with stage 3 CKD taking the same medications were

studied as positive controls.

“These findings suggest that RASi initiation might slow the progression of kidney disease compared with CCB in patients with advanced CKD, and offer similar cardiovascular protection,” the investigators conclude [Fu EL, et al. Comparative effectiveness of renin-angiotensin system inhibitors and calcium channel blockers in individuals with advanced CKD: A nationwide observational cohort study. *Am J Kidney Dis*, published online ahead of print November 24, 2020. doi: 10.1053/j.ajkd.2020.10.006; [https://www.ajkd.org/article/S0272-6386\(20\)31121-5/fulltext](https://www.ajkd.org/article/S0272-6386(20)31121-5/fulltext)]. ■



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