Kidney lesions associated with risk of heart disease in chronic kidney disease patients

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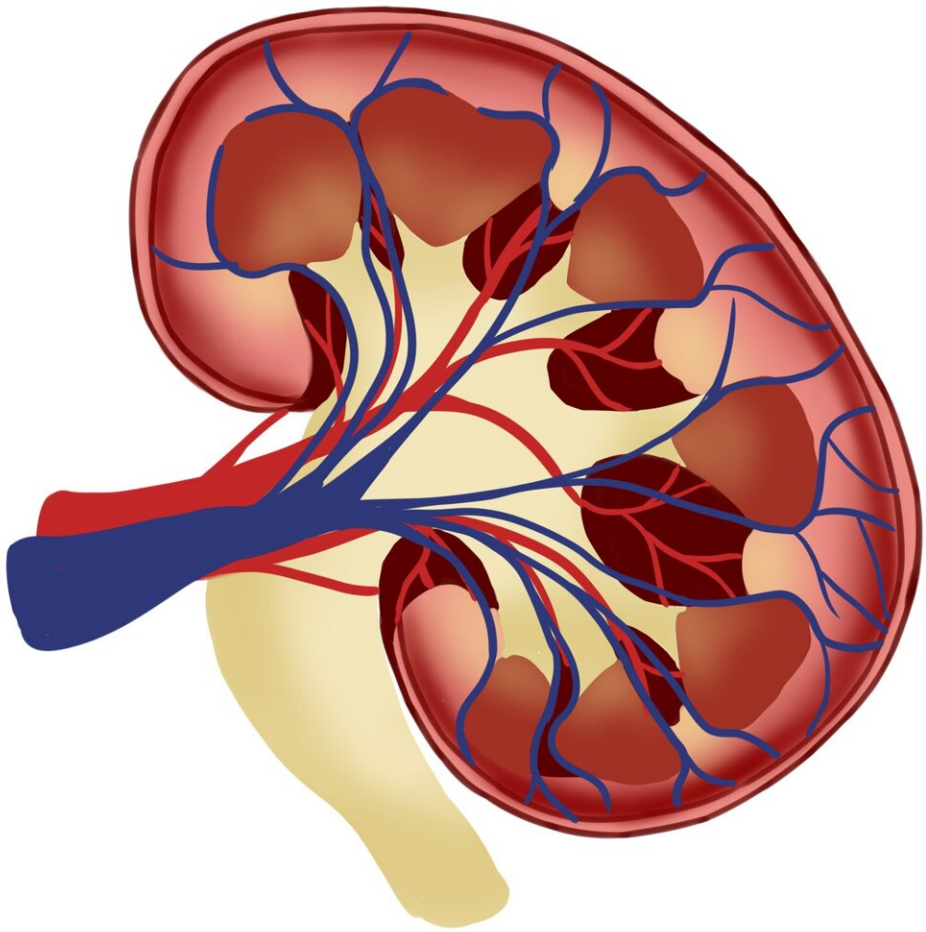

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Chronic kidney disease (CKD) is an independent risk factor for heart diseases, such as heart attacks, strokes or heart failure. A new study by investigators from Brigham and Women's Hospital, a founding member of the Mass General Brigham healthcare system, and Boston Medical Center (BMC) analyzed this relationship in greater detail by examining kidney tissue collected during clinically indicated biopsies. In a paper published in *JAMA Cardiology*, the team reports associations between different types of kidney lesions, markers of CKD progression, and heart disease based on 597 adults without any history of heart disease from the Boston Kidney Biopsy Cohort.

"The kidneys and the heart are organs that talk to each other extensively and directly," said lead author Leo F. Buckley, PharmD, of the Department of Pharmacy at Brigham. "Our study helps to illustrate more clearly how the kidney itself relates to the heart. We studied this directly by looking at a piece of tissue collected from the kidney to see if lesions on it are associated with different types of heart disease."

The association between kidney disease biopsy lesions and risk of heart disease and death has not been studied outside of small cohort studies in the past. These prior studies also relied on traditional measures of kidney disease such as estimated glomerular filtration rate (eGFR) that quantifies how well the kidney is working or albuminuria, the amount of protein in the urine as a result of kidney damage. Using information from the biopsy provided further insight into the association between kidney disease and heart disease that was separate from the insight provided by eGFR and albuminuria.

"We have known for years that patients with kidney failure are at high risk of dying from heart disease and that patients with heart disease often have underlying kidney dysfunction. Our study tried to understand this bidirectional relationship by looking directly at the kidney abnormalities as seen under the microscope by expert pathologists and

linking them to important clinical outcomes that matter to our patients," said senior author Sushrut Waikar, MD, Chief of Nephrology at Boston Medical Center and the Norman G. Levinsky Professor of Medicine at Boston University Chobanian and Avedisian School of Medicine.

To conduct their study, Buckley, Waikar and colleagues used tissue collected from the Boston Kidney Biopsy Cohort, which includes samples provided by three hospitals in Boston: Massachusetts General, Brigham and Women's Hospital, and the Beth Israel Deaconess Medical Center. Two kidney pathologists, blinded to the original biopsy diagnosis, provided semi quantitative scores for abnormalities in the kidney that were observed through the microscope. Then, these findings were analyzed alongside the clinicopathological diagnosis of CKD from the patients' medical records. Two researchers also identified cardiovascular events by retrospectively reviewing all inpatient and outpatient hospital encounters and medical records.

Researchers found that over a median 5.5 years of follow-up, major adverse cardiovascular events, such as heart failure, stroke, heart attack and death, occurred in 126 participants. Two kidney anatomical abnormalities stood out: excess buildup of substances in the kidney filtration unit's mesangium ("mesangial expansion") and thickening of the walls of small blood vessels ("arteriolar sclerosis") were both linked with increased risk of heart disease. In addition, people with diagnoses of vascular kidney disease, a diagnosis of diabetic kidney disease, or greater severity of chronic kidney lesions were each associated with an increased risk of cardiovascular events.

"We found that people who had diabetes that was severe and long enough to lead to kidney damage also had a high risk of heart disease," Buckley said. "We really connected the heart, the kidneys and diabetes together."

These associations were independent of other clinical risk factors, like high blood pressure and diabetes, as well as the traditional measure of kidney filtration, eGFR and proteinuria, or levels of protein in urine. The eGFR was calculated using the creatinine-based, race-dependent equation that was used clinically at the time that patients were enrolled; this equation is now increasingly being replaced by less biased estimates that do not rely on race.

"Our purpose wasn't to tackle the issue of race and kidney function head on, but our findings do illustrate the problems associated with race-based equations," Buckley said. "We get around the issues with eGFR and go straight to the kidneys. Rather than estimating how well a patient's kidneys are functioning based on how old they are, what gender they are, and their race, we just look at their kidneys and identify the damage there."

Limitations of the study include that, compared to the U.S. population with CKD, the study included more autoimmune and glomerular disease and less diabetic kidney disease and hypertensive nephrosclerosis. Researchers did not adjust for post-biopsy treatments or history of diabetes or hypertension in their analysis. Future studies are needed to untangle the specific kidney-heart connections that give rise to mesangial expansion and arteriolar sclerosis and examine whether kidney lesions can be therapeutically targeted to reduce the risk of heart disease.

"We didn't study specifically whether people should be getting a biopsy or not. But when a doctor has already decided to do the biopsy, our results could provide a framework for interpreting results in terms of the patients' heart disease risk," Buckley said. "When doctors are considering management of kidney disease, they could also be thinking about the patient's heart disease."

More information: Associations between Kidney Histopathologic

Lesions and Incident Cardiovascular Disease in Adults with Chronic Kidney Disease, *JAMA Cardiology* (2023). DOI: 10.1001/jamacardio.2023.0056