Sickle Cell Trait

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treatment recommendations."

Twofold increase in ESRD for African Americans with SCT
Naik and colleagues analyzed the association between SCT and ESRD in a sample of 9909 self-reported African Americans from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. Sickle cell trait was present in 7.5% of the sample. Rates of other genetic variants associated with kidney disease were 12.8% for APOL1 high-risk genotypes and 2.5% for hemoglobin C trait.

There were some significant baseline differences among groups: SCT carriers had a lower estimated glomerular filtration rate and higher urine albumin-to-creatinine ratio. Chronic kidney disease (CKD) prevalence was 36.8% in the SCT group, compared to 25.9% for individuals with hemoglobin C, and 25.1% for those with neither trait.

At a median follow-up of 6.5 years, ESRD incidence was 8.5 per 1000 person-years for those with SCT, compared to 3.9 per 1000 for those with hemoglobin C trait, and 4.0 per 1000 for those with neither trait. On adjusted analysis, the hazard ratio for ESRD was 2.03 for individuals with SCT. Hemoglobin C trait was unrelated to ESRD incidence.

For individuals with APOL1 high-risk genotypes, ESRD incidence was 6.6 per 1000 person-years. There was no interaction between SCT and APOL1 status. The association between SCT and CKD was stronger among those without hypertension: odds ratio 2.94, compared to 1.63 in those with hypertension.

“Our study demonstrates that SCT is not only a significant genetic risk factor for the development of ESRD in African Americans, but also that it confers a similar degree of risk for ESRD as APOL1 high-risk genotypes, which are currently the most widely recognized genetic variant associated with kidney disease in this population,” Naik and colleagues write.

The findings suggest “an additional genetic basis” for the higher rate of advanced kidney disease among African Americans. While the mechanism of kidney damage is yet unclear, some evidence points to vascular damage and hypoxia in the renal medulla—the same pathway leading to nephropathy in patients with sickle cell disease.

SCT linked to lower HbA1c

Lacy, Wu, and colleagues analyzed data on 4620 African American participants from two community-based cohort studies: the CARDIA Study and the Jackson Heart Study. The participants, mean age 52.3 years, made up to three study visits including concurrent measures of fasting glucose and HbA1c.

These measures were analyzed for association with SCT, which was present in 7.9% of those studied. Participants with SCT were older, had lower kidney function, lower HbA1c, and a higher reported rate of diagnosed diabetes. On analysis using generalized estimating equations, mean HbA1c was 5.72% in those with SCT, compared to 6.01% in the non-SCT group. The average difference of 0.30% was present across a range of fasting or 2-hour glucose levels.

On adjusted analysis, SCT was associated with a mean 0.38% reduction in HbA1c at a given fasting glucose concentration. The difference was greater at higher fasting and 2-hour glucose concentrations.

The presence of SCT was associated with potentially missed cases of diabetes, defined as HbA1c of 6.5% or higher. Diabetes prevalence was 3.8% for participants with SCT versus 7.3% for those without. By comparison, rates of self-reported diabetes diagnosis were 17.2% and 14.7%, respectively.

The SCT group also had a lower prevalence of HbA1c of 5.7% to less than 6.5%, consistent with prediabetes: 29.2%, compared to 48.6% for those without SCT.

“These findings suggest that HbA1c may systematically underestimate past glycaemia in African American patients with SCT and may require further evaluation,” Lacy and colleagues write.

The authors discuss some ways in which SCT might affect the accuracy of HbA1c. Red blood cells may be shorter-lived in people with SCT, thus reducing the time available for hemoglobin glycation. It’s also possible that the presence of HbS might interfere with common HbA1c assays. (The authors note that their study used high-performance liquid chromatography techniques that have not shown clinically significant interference in those with HbA1c).

The most common hemoglobin variant in the US population, SCT is found in 8% to 10% of African Americans with SCT, compared to less than 1% of white Americans. The American Society of Hematology notes that SCT may be present in 1 to 3 million Americans, and in more than 100 million people worldwide.

The new studies suggest that the presence of SCT may signal some important clinical associations.

“These findings raise the possibility of benefit from incorporating information on hemoglobin in clinical risk stratification algorithms for interpreting HbA1c values for screening and diagnosis of prediabetes and diabetes,” Lacy and colleagues write. They call for further studies to assess whether delays in recognizing prediabetes and diabetes could account for the reduced kidney function in African Americans with SCT.

In a previous study (J Am Med Assoc 2014; 312:2115-2125), Naik and colleagues found an increased risk of CKD, lower kidney function, and higher albuminuria in African Americans with SCT. The authors note that, in contrast to APOL1 genotype, testing for SCT is routinely performed in newborn screening, athletic examinations, and pregnancy counseling.

“Genetic counseling about ESRD risks could allow for early CKD screening and risk factor modification such as smoking cessation, weight loss, hypertension/glucose control, and avoiding nephrotoxic agents,” Naik and coauthors write. They also raise the possibility that early intervention—including renal protective medications and disease-modifying sickle cell therapies—might be beneficial for African American patients at high risk for SCT-related kidney disease.

Findings

Osteoporosis Drugs for CKD Patients—Jury’s Still Out

Currently available data cannot establish the safety and efficacy of osteoporosis medications for patients with chronic kidney disease (CKD), concludes a meta-analysis in Annals of Internal Medicine.

A systematic review identified 13 randomized trials, including a total of 9850 patients, evaluating the clinical benefits and safety outcomes of osteoporosis medications in CKD patients. The medications studied were bisphosphonates, teriparatide, raloxifene, and denosumab. Outcomes of interest were bone mineral density (BMD), fractures, mortality, and adverse events. Kidney transplant recipients were enrolled in six trials, postmenopausal women with CKD in four, and patients with CKD stage 3 to 5 on dialysis in three.

There was moderately strong evidence that bisphosphonates slow BMD loss of the lumbar spine in kidney transplant patients. However, the effects in the femoral neck and other areas were unclear. There were conflicting or insufficient data on the effects of bisphosphonates on BMD in CKD patients who had not received a transplant. Bisphosphonates’ effects on fracture risk and safety outcomes were unclear.

There was low strength of evidence that raloxifene prevents vertebral fractures, but not that it increased BMD. Evidence on the effectiveness of teriparatide and denosumab was weak, with some data suggesting an increased risk of adverse outcomes.

Bone weakening and fractures are potential complications of CKD, leading to recommendations for treatment with medications for osteoporosis. But the new review shows an overall weak body of evidence for the safety and effectiveness of osteoporosis medications across the spectrum of CKD.


High Rate of AKI in Children with Diabetic Ketoacidosis

Nearly two-thirds of children with type 1 diabetes hospitalized for diabetic ketoacidosis (DKA) will develop acute kidney injury (AKI), suggests a study in JAMA Pediatrics.

The researchers reviewed all DKA admissions at a Canadian children’s hospital from 2008 to 2013. Complete medical records were available for 165 patients. The median age was 10.6 years; 54% were female. Three-fourths of patients were newly diagnosed with type 1 diabetes. Fifty-five percent were transferred from another hospital and nearly one-fourth were admitted to the ICU. Median initial pH was 7.1 and serum bicarbonate level 7.0 mEq/L.

Based on Kidney Disease/Improving Global Outcomes criteria, 64.2% of patients developed AKI while in the hospital. Of affected children, 34.9% had AKI stage 1, 45.3% had AKI stage 2, and 19.8% had AKI stage 3. Two patients required hemodialysis.

On adjusted analysis, factors associated with the development of stage 2 or 3 AKI were serum bicarbonate less than 10 mEq/L, adjusted odds ratio (OR) 5.22; and higher initial heart rate, OR 1.22 per increase of 5 beat/min. Odds of stage 1 AKI were increased for children with an initial corrected sodium level of 145 mEq/L or greater, OR 1.92. There were no deaths in children with or without AKI.

The study documents a high prevalence of AKI among children with DKA admitted to a tertiary care children’s hospital.