

Journal View

Study Shows Racial Differences in Vitamin D–Binding Protein

Variations in the vitamin D–binding protein gene may help to explain differences in vitamin D levels and clinical vitamin D deficiency in black versus white individuals, according to a study in the *New England Journal of Medicine*.

The researchers analyzed data on total 25-hydroxyvitamin D, vitamin D–binding protein, parathyroid hormone, and bone mineral density in black and white adults from a United States population—based cohort study. The participants also underwent genotyping studies for the common rs7041 and rs4588 2 polymorphisms of the vitamin D–binding protein gene. The concentrations of bioavailable 25-hydroxyvitamin D were calculated in a subgroup of 1025 homozygous participants.

The black participants had a lower mean total 25-hydroxyvitamin D level: 15.6 ng/mL, compared with 25.8 ng/mL in white participants. The levels of vitamin D–binding protein were 168 and 337 µg/mL, respectively.

On adjusted analysis, the two polymorphisms accounted for close to 80 percent of the variation in vitamin D–binding protein levels and for 10 percent of the variation in total 25-hydroxyvitamin D. After genotype

was accounted for, race explained less than 0.1 percent of the variation in vitamin D–binding protein. Despite their lower vitamin D levels, the black participants had a higher mean bone mineral density.

Study participants with lower total and bioavailable 25-hydroxyvitamin D levels had higher parathyroid hormone levels. However, at each level of parathyroid hormone, total 25-hydroxyvitamin D was lower among black participants. In the homozygous subgroup analysis, levels of bioavailable 25-hydroxyvitamin D were similar by race, and within categories of parathyroid hormone level.

The new results confirm that black persons have lower total 25-hydroxyvitamin D than do their white counterparts. However, because black individuals also have lower levels of vitamin D–binding protein, the levels of bioavailable 25-hydroxyvitamin D are not significantly different. The authors discuss the implications for assessing racial and ethnic differences in vitamin D levels, including the potential role of vitamin D–binding protein measurement [Powe CE, et al. Vitamin D–binding protein and vitamin D status of black Americans and white Americans. *N Engl J Med* 2013; 369:1991–2000]. ●

Score Predicts Kidney Failure or Death in Rhabdomyolysis

A risk prediction score calculated with the use of routine admission data performs well in predicting the risk of renal replacement therapy (RRT) or mortality in patients with rhabdomyolysis, according to a study in *JAMA Internal Medicine*.

The researchers analyzed data from 2731 patients treated for rhabdomyolysis at two hospitals between 2000 and 2011. All had creatine phosphokinase levels greater than 5000 U/L within 3 days of admission. The risk prediction score was developed with the use of data from 1397 patients treated at one hospital and was validated by the use of data from 974 patients at the other hospital. The main outcome of interest was a composite of continuous RRT and in-hospital death.

Overall, 8.0 percent of patients required continuous RRT, 14.1 percent died in the hospital, and 19.0 percent met either outcome. Rates of the composite outcome were highest for patients with rhabdomyolysis associated with cardiac arrest (58.5 percent), compartment syndrome (41.2 percent), and sepsis (39.3 percent). Other independent risk factors included older age, female sex, and baseline creatinine, creatine phos-

phokinase, phosphate, calcium, and bicarbonate levels.

A risk score comprising these variables performed well in identifying rhabdomyolysis patients at high risk of RRT or death, with C statistics of 0.82 in the derivation cohort and 0.83 in the validation cohort. In the latter group, the composite outcome rates were 2.3 percent in patients with a risk score less than 5 versus 61.2 percent for those with a score greater than 10. For a risk score less than 5, the negative predictive value was 97.7 percent and the positive predictive value was 27.2 percent.

Patients with rhabdomyolysis are at risk of potentially life-threatening acute kidney injury. The new risk prediction score, based on readily accessible demographic, clinical, and laboratory variables, performs well in identifying patients at lower and higher risk of continuous RRT and in-hospital mortality. The authors believe their score will be most useful for triage of patients evaluated in the emergency department [McMahon GM, et al. A risk prediction score for kidney failure or mortality in rhabdomyolysis. *JAMA Intern Med* 2013; 173:1821–1827]. ●

Evidence Questions Benefits of ESAs for Anemia in Heart Disease

Erythropoiesis-stimulating agents (ESAs) are not beneficial—and may be harmful—in the treatment of mild to moderate anemia in patients with heart disease, according to a review in the *Annals of Internal Medicine*.

A systematic review of the literature was performed to evaluate the benefits and harms of treatments for anemia in patients with heart disease. The analysis focused on studies of blood transfusion, iron, or ESAs for adults with anemia and congestive heart failure or coronary heart disease.

On the basis of six trials and 26 observational studies, there was “low-strength” evidence of improvement in short-term

mortality among patients treated with liberal transfusion protocols, compared with less aggressive protocols. The difference was not significant on meta-analysis. However, one small trial in patients with acute coronary syndrome reported lower mortality in patients treated with a liberal transfusion strategy: 1.8 versus 13.0 percent. Three trials of intravenous iron therapy provided “moderate-strength” evidence of improvements in short-term exercise tolerance and quality of life in anemic patients with heart failure.

The review identified 17 randomized trials of ESAs, most conducted in patients with heart failure. The studies provided

“high-strength” evidence that ESAs did not lead to reductions in mortality, cardiovascular events, or hospitalizations. There was also “moderate-strength” evidence that ESAs did not lead to improved quality of life. The review also identified moderately strong evidence linking ESAs to serious harms, including hypertension, venous thromboembolism, and possibly mortality, in patients with congestive heart failure.

The review analyzes the growing body of evidence on strategies for correcting anemia in patients with heart disease. The data provide no consistent evidence of reduced mortality with higher transfusion thresholds, but they do suggest sympto-

matic improvements with intravenous iron. Further studies of both treatments are warranted.

The authors conclude: “Erythropoiesis-stimulating agents do not seem to benefit patients with mild to moderate anemia and heart disease and may be associated with serious harms.” The review serves as the basis for a new American College of Physicians guideline on the treatment of anemia in patients with heart disease: <http://annals.org/article.aspx?articleid=1784292> [Kansagara D, et al. Treatment of anemia in patients with heart disease: a systematic review. *Ann Intern Med* 2013; 159:746–757]. ●

Can APOL1 Explain Higher Risk of ESRD in Black Patients?

Increased rates of kidney disease progression among black patients—regardless of cause—are at least partly related to variants of the apolipoprotein L1 gene (APOL1), suggests a study in the *New England Journal of Medicine*.

The researchers analyzed data from 693 black patients from the African American Study of Kidney Disease and Hypertension (AASK) who had chronic kidney disease (CKD) attributed to hypertension, and 2955 white or black patients with CKD from the Chronic Renal Insufficiency Cohort (CRIC) study,

about half of whom had diabetes. Both analyses compared outcomes in a “high-risk” group with two copies of high-risk APOL1 variants versus a “low-risk” group with zero or one copy.

In the AASK data, black participants with high-risk APOL1 status were more likely to meet a composite outcome of ESRD or doubling of serum creatinine: 58.1 percent versus 36.6 percent, hazard ratio 1.88. The association was unaffected by study interventions or baseline proteinuria.

Among CRIC participants, those

with two copies of APOL1 risk variants had a steeper decline in estimated GFR. The high-risk APOL1 group also had a higher rate of a composite outcome of ESRD or a 50 percent reduction in estimated GFR. Among black CRIC participants, the risk of the composite outcome was 46 percent higher in the high-risk APOL1 group than in the low-risk group. This was so regardless of the presence or absence of diabetes.

Previous research has linked APOL1 variants to increased rates of kidney diseases in black individuals, including

ESRD in patients without diabetes. On the basis of the new study, high-risk APOL1 genes appear to contribute to an elevated risk of ESRD and progressive CKD in black versus white patients, regardless of diabetes status. The researchers write that their study provides “direct evidence...that the APOL1 high-risk variants are associated with increased disease progression over the long term” [Parsa A, et al. APOL1 risk variants, race, and progression of chronic kidney disease. *N Engl J Med* 2013; 369:2183–2196]. ●