Kidney and Cardiovascular Disease Risk Genes Aren't the Same

For the most part, gene variants associated with kidney disease and cardiovascular disease are different from one another, according to a report in the American Journal of Kidney Diseases.

Two targeted single-nucleotide polymorphism (SNP) analyses were performed by the use of data from many thousands of participants enrolled in six different disease consortia. The first analysis looked for associations between 19 SNPs known to be associated with kidney function and a series of vascular phenotypes. The second analysis sought associations of 64 validated vascular SNPs with markers of kidney damage. One kidney disease–related SNP—rs653178 near the SH2B2 adaptor protein 3 gene (SH2B3)—was also associated with systolic and diastolic blood pressure and coronary artery disease, as previously reported. Otherwise, the kidney disease variants were not significantly associated with vascular phenotypes, with nonsignificant results in 127 out of 133 tests.

Likewise, most SNPs associated with vascular phenotypes were unrelated to kidney phenotypes, with nonsignificant results in 187 out of 192 tests. The only exceptions were two highly correlated SNPs at the SH2B3 locus.


Even After “Black Box” Warning, For-Profit Dialysis Centers Used More ESAs

After a “black box” warning to use the lowest possible dose of erythropoiesis-stimulating agents (ESAs), for-profit dialysis facilities continued to prescribe higher ESA doses, according to a report in JAMA Internal Medicine.

The researchers analyzed U.S. Renal Data System data on more than 275,000 patients receiving in-center hemodialysis before and after a 2007 black box warning on ESA use. This safety directive from the U.S. Food and Drug Administration called for use of the lowest possible ESA dose to avoid the need for blood transfusion and for withholding ESAs in patients with hemoglobin levels higher than 12 g/dL. The researchers analyzed the effects of the black box warning on ESA dosing and hematocrit for both for-profit and nonprofit dialysis facilities.

At both times and across hematocrit categories, for-profit dialysis facilities used higher doses of ESAs than did nonprofit facilities, after adjustment for case mix. At for-profit centers, the median weekly ESA dose was 9020 U before the black box warning and 8322 U afterward. At nonprofit centers, the figures were 5670 U and 5063 U, respectively.

The median weekly ESA dose increased 54.7 percent for patients who switched from a nonprofit to a for-profit facility from before to after the black box warning, and a 50.9 percent decrease for those who switched from a for-profit to a nonprofit facility. After the warning, for-profit dialysis centers performed no better than nonprofit centers in avoiding hematocrit levels below 30 percent.

The findings suggest that “financial considerations may have played a role” in ESA dosing at for-profit centers. The authors discuss the need for ongoing monitoring of dialysis care and outcomes since implementation of the bundled reimbursement system [Ishida JH, et al. Dialysis facility profit status and compliance with a black box warning. JAMA Intern Med 2013; May 13:1–2. doi:10.1001/jamainternmed.2013.979].

Tobacco Smoke Linked to Lower eGFR in Teens

Active or passive exposure to tobacco smoke is associated with decreased kidney function in adolescents, according to a study in Pediatrics.

The study included data on 7516 participants, aged 12 to 17 years, in the National Health and Nutrition Examination Survey from 1999 to 2010. All had available data on serum creatinine and cotinine. Active and secondhand smoking were assessed on the basis of self-report or serum cotinine levels above 10 ng/mL or at 0.05 ng/mL, respectively. The relationships between either type of smoking and estimated glomerular filtration rate (eGFR) were analyzed.

The adolescents had a median eGFR of 96.8 mL/min per 1.73 m2 and a median serum cotinine concentration of 0.07 ng/mL. With multivariable adjustment, each interquartile range increase in serum cotinine (0.03 to 0.59 ng/mL) was associated with a 1.1 mL/min per 1.73 m2 decrease in eGFR.

In comparison with unexposed adolescents, the mean differences in eGFR were −0.4 mL/min per 1.73 m2 in the first tertile of serum cotinine concentration, −0.9 mL/min per 1.73 m2 in the second tertile, and −2.2 mL/min per 1.73 m2 in the third tertile. Among active smokers, the differences by tertile were 0.2, −1.9, and −2.6 mL/min per 1.73 m2, respectively. The association between cotinine and eGFR appeared stronger in boys and in younger and lighter adolescents.

Active and passive smoking are demonstrated risk factors for kidney disease in adults. This cross-sectional study links tobacco smoke exposure to reduced eGFR in adolescents, suggesting that the adverse effects of smoking on kidney function may start in childhood. The authors note that although the associations are modest, they could have a major impact on kidney disease at the population level [Garcia-Esquinas E, et al. Kidney function and tobacco smoke exposure in US adolescents. Pediatrics 2013; 131:e1415–e1423].

Choice of Statins May Affect Diabetes Risk

Patients taking certain higher-potency statin drugs may be at increased risk for the development of diabetes, suggests a study in the British Medical Journal.

Using Ontario health data, the researchers identified a population of more than 470,000 nondiabetic patients aged 60 years or older who started statin therapy between 1997 and 2010. All were new users who had not been prescribed a statin for at least 1 year previously. The indication for statins was primary prevention in 48 percent of patients and secondary prevention in 52 percent. The use of individual statins was analyzed for association with the development of new-onset diabetes.

With pravastatin as the reference drug, three higher-potency statins—atorvastatin, rosuvastatin, and simvastatin—were associated with an increased risk of incident diabetes. The adjusted hazard ratios were 1.22, 1.18, and 1.10, respectively. Diabetes risk was not increased for users of fluvastatin or lovastatin.

The absolute increases in risk per 1000 person-years were 31 with atorvastatin and 36 with rosuvastatin, compared with 26 with simvastatin and 23 with pravastatin. The associations were similar in the primary and secondary prevention groups and when statins were grouped by potency. However, the increase in risk with rosuvastatin became nonsignificant after adjustment for dose.

Some studies have suggested that statin treatment may be associated with an increased incidence of new-onset diabetes. Amid conflicting results, few studies have compared the effects of different statins.

These population-based data suggest increased diabetes risk among older patients taking higher-potency statins—particularly atorvastatin and simvastatin. The risk associated with rosuvastatin may depend on dose. The authors acknowledge some important limitations of their study, including a lack of information on key diabetes risk factors [Carter AA, et al. Risk of incident diabetes among patients treated with statins: population based study. BMJ 2012; 346:f2610].

Long-Chain n-3 Fatty Acids Affect Sudden Cardiac Death Risk

During the first year of receiving hemodialysis, patients with higher levels of long-chain n-3 fatty acids are at lower risk of sudden cardiac death, reports a study in Kidney International.

The study included a nationally representative cohort of patients from more than 1000 hemodialysis units in 2004 to 2005. The researchers identified 100 cases of sudden cardiac death and 0.20 in the fourth quartile. The protective effect was apparent even during the first few months of dialysis, when the risk of sudden cardiac death is highest.

Experimental and clinical studies suggest that long-chain n-3 fatty acids may protect against sudden cardiac death, the leading cause of death in hemodialysis patients. The new analysis suggests that long-chain n-3 fatty acids are “strongly and independently” associated with risk of sudden cardiac death during the first year of hemodialysis. The authors call for a randomized controlled trial of long-chain n-3 fatty acid supplementation for hemodialysis patients [Friedman AN, et al. Inverse relationship between long-chain n-3 fatty acids and risk of sudden cardiac death in patients starting hemodialysis. Kidney Int 2013; 83:1130–1135].