Polycystic Kidney Disease: MRI Provides An Early Alert To Progression

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A new method using magnetic resonance imaging (MRI) accurately tracks structural changes that predict functional changes earlier than standard blood and urine tests in people with autosomal dominant polycystic kidney disease (PKD), according to a study funded by the National Institutes of Health (NIH). PKD is a common inherited condition characterized by cysts that grossly distort the kidneys and liver and by high blood pressure and brain aneurysms (bulges in arteries). Findings are in the May 18 issue of the New England Journal of Medicine.

Researchers found that both small and large cysts and both kidneys grew continuously at steady rates, seemingly tailored to the individual with PKD, regardless of patient age. These structural changes correlate with losses in kidney function, suggesting that MRI can be used to track the major contributor to the progression of PKD, an advance that could speed the discovery of new therapies.

"There is so much variability in the loss of kidney function among PKD patients, even within families with the same altered gene, that it was assumed that cysts and kidneys must grow at variable rates. So it's quite remarkable to find cysts and kidneys in individuals growing at uniform and predictable rates," said Catherine M. Meyers, M.D., a kidney specialist at the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). "Our experience is still limited, but this method appears very promising."

The Consortium for Radiological Imaging Studies of Polycystic Kidney Disease (CRISP) enrolled 241 patients, ages 15 to 46 years, with autosomal dominant PKD and normal to mild losses in kidney function (stage 1 or 2). The researchers developed MRI techniques to reliably and accurately produce 3-dimensional images from which cysts and kidneys, and the proportion of the kidneys occupied by cysts, could be measured. Changes in cyst and kidney volume were compared to standard blood and urine tests of kidney function and to a specialized test measuring how fast the kidneys filtered a substance called iothalamate from the blood.

"Being able to predict how quickly a disease will progress--rather than waiting years for it to actually happen--should speed up trials of potential therapies. Up to now we had to observe patients for years before we could tell if a therapy was working," said lead author Jared J. Grantham, M.D., a kidney specialist at the University of Kansas School of Medicine in Kansas City and long-time advocate for PKD patients. "It should now be possible to test potential therapies earlier in the disease, when therapies are more likely to prevent kidney failure."

Already, the new MRI method is receiving closer scrutiny. CRISP patients have been asked to stay for another 4 years of MRI monitoring, and about 100 of them are planning to join NIDDK's HALT-PKD trial (www.pkd.wustl.edu/pkd-tn), the first intervention trial to use the MRI method along with standard tests of kidney function. HALT-PKD enrolled its first patient in January 2006 to learn if careful blood pressure control and ACE-inhibitors or angiotensin receptor blockers (ARBs) can prevent progression of PKD.

CRISP clinical centers are at the University of Kansas Medical Center in Kansas City, Emory University in Atlanta, Mayo Clinic in Rochester, Minn., and the University of Alabama at Birmingham. Washington University in St. Louis analyzed the MRI images and study data.

As many as half a million people in the United States and 4 to 6 million world-wide are estimated to have PKD. In autosomal dominant PKD, the most common form, symptoms usually appear between the ages of 30 and 40 and include back and side pain and headaches. Half of patients develop kidney failure, on average around age 54; 23,000 were on dialysis or had a transplant for kidney failure in 2003, making it this country's fourth leading cause of kidney failure. More information about PKD is available from NIDDK at www.niddk.nih.gov and from the PKD Foundation at http://www.pkdcure.org and 1-800-PKD-CURE.

There is no cure and no specific treatment for PKD, but careful blood pressure control and using ACE-inhibitors or ARBs, types of blood pressure medicines, significantly delays or prevents kidney disease and failure from diabetes and other causes by reducing protein in the urine and preventing damage to the small blood vessels in the kidneys. Earlier trials of these treatments in PKD were not definitive, possibly because a small number of patients were involved.

NIDDK's National Kidney Disease Education Program (http://www.nkdep.nih.gov) aims to raise awareness of the seriousness of kidney disease, the importance of testing those at high risk, and the availability of treatment to prevent or slow kidney failure.

The National Institutes of Health (NIH) -- The Nation's Medical Research Agency -- includes 27 Institutes and Centers and is a component of the U.S. Department of Health and Human Services. It is the primary federal agency for conducting and supporting basic, clinical and translational medical research, and it investigates the causes, treatments, and cures for both common and rare diseases.

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