Gene expression test reduces need for invasive heart muscle biopsy

April 26 2010

Monitoring rejection in heart transplantation patients with a simple blood test co-developed by NewYork-Presbyterian Hospital/Columbia University Medical Center physician-scientist Dr. Mario Deng in 2005 can safely reduce their need for invasive heart-muscle biopsies, a new study has found.

The multicenter study called Invasive Monitoring Attenuation by Gene Expression (IMAGE) included research by Dr. Deng. Results were presented at the Annual Scientific Meeting of the International Society for Heart and Lung Transplantation in Chicago and are published online in the New England Journal of Medicine today.

Researchers looked at an FDA-cleared gene expression test called AlloMap molecular expression testing, which measures 11 genes from molecular pathways in white blood cells associated with heart transplant rejection. They found the approach was safe, resulted in significantly fewer biopsies compared with a traditional strategy of routine biopsies, and was preferred by patients.

"The genomics revolution initiated by the completion of the Human Genome Project has made possible what was only dreamed about before -- namely the ability to improve patient care by ruling out rejection without taking an invasive heart tissue sample," says Dr. Mario Deng, director of cardiac transplantation research at Columbia University Medical Center, associate professor of medicine at Columbia University College of Physicians and Surgeons and a cardiologist at NewYork-

Presbyterian Hospital/Columbia University Medical Center.

After the first year of transplant, heart transplant patients have an average risk of 3 to 5 percent for moderate or severe rejection. Rejection of a transplanted heart can lead to heart damage and eventual failure and loss of life. Consequently, for the rest of their lives, patients must be monitored for rejection to guide their immunosuppressant drug therapy.

Investigators randomly assigned 602 patients who were six months to five years since their heart transplantation to undergo rejection monitoring using either gene-expression profiling or routine endomyocardial biopsy, in addition to clinical and echocardiographic assessment of graft function. They compared the two groups for a composite primary outcome of rejection with heart function compromise, graft dysfunction due to other causes, death, or retransplantation. They found that during a median follow-up of 19 months, patients monitored with gene-expression profiling, as compared with those who underwent routine biopsies, had similar two-year cumulative rates of the composite primary outcome. The two-year rates of all-cause mortality were also similar in the gene-expression profiling and biopsy arms. Patients in the gene-expression profiling group underwent one-sixth the number of biopsies per person-year of follow-up compared with patients in the biopsy group. (For those in the gene expression test group, biopsies were performed when the test indicated an elevated risk for rejection, or if there were other clinical indications of rejection via cardiogram or symptoms.)

The new findings build on development and validation the Allomap blood test published in a research study called CARGO (Cardiac Allograft Rejection Gene Expression Observational Study) in 2005 (Deng et al, American Journal of Transplantation). The CARGO-study, whose lead author was Dr. Deng, showed that the blood test could detect

whether a chronic heart transplant patient is rejecting his heart, and reduce the need for invasive heart-muscle biopsies.

Beyond their instrumental role in the development of the original AlloMap molecular test and now its safe implementation into routine patient care, Dr. Deng's team has also spearheaded research into how this test works, specifically how the biological activity of white blood cell genes is linked to rejection in the transplanted heart. They found that the higher the rejection-related immunological activity in the white cell of the heart recipient, the slower the transplanted heart's electrical activity is spreading and the weaker the muscle is pumping. This research is in print in the Journal of Heart and Lung Transplantation and will be presented at the ISHLT meeting in Chicago by Dr. Deng's postdoctoral scientist Dr. Khurram Shahzad of Columbia University Medical Center.

Based on this groundbreaking translational research, NewYork-Presbyterian/Columbia is offering AlloMap blood test monitoring as an alternative to invasive biopsy to all heart transplant patients who are stable. The AlloMap test is the first transplantation test cleared by the U.S. Food and Drug Administration in the novel category of In Vitro Diagnostic Multivariate Index Assay (IVDMIA) category. More than 1,000 of these AlloMap blood tests have been done since inception of the program in 2006 at NYP/Columbia, and more than 20,000 tests in most U.S. heart transplantation centers.

"As the country's largest heart transplant program, our Hospital is taking the lead in offering our patients this cutting-edge tool to improve patients' quality of life," says Dr. Deng.

Provided by New York- Presbyterian Hospital