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New warning signs may predict kidney transplant failure

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Kidney transplants that show a combination of fibrosis (scarring) and inflammation after one year are at higher risk of long-term transplant failure, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology* (*JASN*).

To identify these abnormalities, doctors would need to perform routine biopsies on apparently normal kidney transplants—rather than waiting for problems to occur. "Even for some transplants that would be expected to have a very long graft survival, protocol biopsies performed in the first year may indicate the kidney is undergoing damaging inflammation, which is associated with increased risk for reduced function and graft survival," comments Mark D. Stegall, MD (Mayo Clinic, Rochester, MN).

As part of a project to explore the reasons for long-term kidney transplant failure, the Mayo Clinic transplant program has been performing routine biopsies at regular intervals after transplantation. The Mayo Clinic program was among the first to incorporate such "protocol" biopsies into the routine care of clinically stable transplants.

The researchers analyzed factors related to transplant survival in 151 patients who had no apparent problems after living-donor kidney transplantation. One-year biopsies showed no abnormalities in 57 percent of kidneys; another 30 percent had fibrosis (scarring) but no inflammation. In these two groups, the transplanted kidney continued to function normally from one to five years' follow-up.

However, in the remaining 13 percent of transplants, the biopsies showed fibrosis plus inflammation. These transplants had declining kidney function and a reduced long-term survival rate. Kidneys showing fibrosis plus inflammation also had increased numbers of immune cells as well as a "rejection-like" gene expression signature.

Thus, in apparently normal kidney transplants, biopsies showing fibrosis and inflammation signal kidney damage and an increased risk of long-term failure. "It is likely that the intragraft environment of patients with fibrosis and inflammation is damaging to the allograft," says Stegall.

Without routine "protocol" biopsies, these warning signs would go undetected until clinical abnormalities developed, according to Stegall. "The use of protocol biopsies allows for more detailed investigations of the intragraft environment," he says. "Such routine biopsies could provide a unique way to predict which kidney transplant recipients may be at increased risk for loss of kidney function, or to identify potential targets for early preventative treatment."

The study was limited to patients who received kidneys from living donors and who had no apparent complications during the first year. As a result, the findings may not apply to other groups of transplant recipients, including those who have complications such as delayed transplant function or acute rejection.

More information: The article, entitled "Fibrosis with Inflammation at One Year Predicts Transplant Functional Decline," will appear online on September 2, 2010, doi:10.1681/ASN.2010010049

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