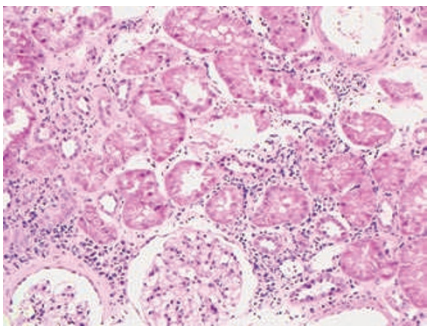
TRANSPLANTATION

Fibrosis with inflammation is associated with reduced graft function and survival

New research in kidney transplantation shows that the combination of fibrosis and inflammation (confirmed by 1-year protocol biopsy) is associated with reduced graft survival and a decline in kidney function. "Molecular profiling [of these grafts] suggest that this subclinical inflammation with fibrosis is mechanistically similar to acute cellular rejection," states first author Walter Park.

Surveillance biopsies are routinely performed to monitor kidney function after transplantation and can help establish the underlying pathological causes of graft loss. In an extension of previous work, Park and colleagues studied protocol biopsy samples from 151 kidney transplant recipients who were not at overt risk of reduced graft function at 1 year after transplantation and followed these individuals for a further 4 years on average. Grafts were classified according to Banff scores as having normal histology, fibrosis alone or fibrosis and inflammation (that is, presence of cellular infiltrates in nontrophic areas). Kidney transplants with normal histology or fibrosis alone had stable function for up to 5 years after transplantation. By contrast, grafts with fibrosis and inflammation not only had a decline in glomerular filtration rate after 1 year (with progressive functional decline during the next 3 years of follow-up), but also had reduced graft survival compared to 'normal' grafts.

Courtesy of L. D. Cornell, Mayo Clinic, Rochester, MN, USA



Moreover, immunohistochemical staining of biopsy samples confirmed high numbers of inflammatory cells in the cortical interstitium of these grafts. Additionally, analyses of gene expression profiles of the different graft groups showed that gene expression was substantially altered—with overexpression of genes associated with innate and adaptive immunity as well as acute rejection—in the grafts with fibrosis and inflammation.

The researchers hope that future work will help to develop new therapies to prevent the decline in function of grafts with inflammation and fibrosis, as well as to determine if subclinical inflammation is a common feature in kidney transplants.

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Original article Park, W. D. *et al.* Fibrosis with inflammation at one year predicts transplant functional decline. *J. Am. Soc. Nephrol.* **21**, 1987–1997 (2010)