TRANSPLANTATION

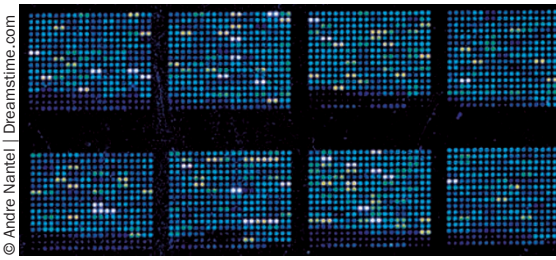
A noninvasive strategy to monitor rejection in patients with a heart transplant

Heart-transplant recipients typically undergo multiple biopsies in the first year following transplantation. These invasive procedures enable histological evaluation to monitor for rejection, but are associated with discomfort, inconvenience, and an infrequent but potentially serious risk of complications. Pham *et al.* report that a noninvasive strategy, which involves gene-expression profiling, is not inferior to standard biopsy as a method for detecting rejection of a cardiac transplant.

The IMAGE investigators randomly assigned 602 patients who had undergone cardiac transplantation at least 6 months previously to the AlloMap® Molecular Expression test (XDx, Brisbane, CA, USA), or endomyocardial biopsies. The composite primary outcome of the study was first occurrence of rejection with hemodynamic compromise, graft dysfunction resulting from other causes, death, or retransplantation.

Median follow-up was 19 months. As expected, patients monitored with gene-expression profiling underwent fewer biopsies during follow-up than patients in the biopsy group (0.5 versus 3 per patient-year). Gene-expression profiling was not associated with an increased risk of serious adverse outcomes. The gene-profiling and biopsy groups had similar 2-year cumulative rates of the composite primary outcome (14.5% and 15.3%, respectively) and death (6.3% and 5.5%, respectively).

The authors acknowledge a number of study limitations. First, the selected patients were at low risk of rejection, as they had undergone transplantation at least 6 months previously. Furthermore, only 20% of potentially eligible patients were enrolled, owing to patient or physician preference, which might also indicate the inclusion of mostly low-risk patients. Second, the noninferiority margin was wide, and the 95% CI did not exclude the possibility of a 68% increase in primary events in the gene-profiling group, although it also did not exclude a 33% decrease in primary event rates compared with the biopsy group. Finally, only six of the 34 rejection episodes in the gene-profiling group were detected solely with the use of the gene-expression test; however, these cases would have gone undetected by clinical assessment. Despite these limitations, this study is important for the future management of patients who have undergone a heart transplant.



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Original article Pham, M. X. *et al.* Gene-expression profiling for rejection surveillance after cardiac transplantation. *N. Engl. J. Med.* **362**, 1890–1900 (2010)