Biopsy transcriptome expression profiling to identify kidney transplants at risk of chronic injury: a multicentre, prospective study

Summary

Background

Chronic injury in kidney transplants remains a major cause of allograft loss. The aim of this study was to identify a gene set capable of predicting renal allografts at risk of progressive injury due to fibrosis.

Methods

This Genomics of Chronic Allograft Rejection (GoCAR) study is a prospective, multicentre study. We prospectively collected biopsies from renal allograft recipients (n=204) with stable renal function 3 months after transplantation. We used microarray analysis to investigate gene expression in 159 of these tissue samples. We aimed to identify genes that correlated with the Chronic Allograft Damage Index (CADI) score at 12 months, but not fibrosis at the time of the biopsy. We applied a penalised regression model in combination with permutation-based approach to derive an optimal gene set to predict allograft fibrosis. The GoCAR study is registered with ClinicalTrials.gov, numberNCT00611702.

Findings

We identified a set of 13 genes that was independently predictive for the development of fibrosis at 1 year (ie, CADI-12 ≥2). The gene set had high predictive capacity (area under the curve [AUC] 0·967), which was superior to that of baseline clinical variables (AUC 0·706) and clinical and pathological variables (AUC 0·806). Furthermore routine pathological variables were unable to identify which histologically normal allografts would progress to fibrosis (AUC 0·754), whereas the predictive gene set accurately discriminated between transplants at high and low risk of progression (AUC 0·916). The 13 genes also accurately predicted early allograft loss (AUC 0·842 at 2 years and 0·844 at 3 years). We validated the predictive value of this gene set in an independent cohort from the GoCAR study (n=45, AUC 0·866) and two independent, publically available expression datasets (n=282, AUC 0·831 and n=24, AUC 0·972).

Interpretation

Our results suggest that this set of 13 genes could be used to identify kidney transplant recipients at risk of allograft loss before the development of irreversible damage, thus allowing therapy to be modified to prevent progression to fibrosis.

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