Repeat Kidney Transplant Patients with Active Rejection Have Elevated Donor-Derived Cell-Free DNA

S. Mehta,1 J. Chang,2 T. Hailey,1 D. Hiller,3 M. Grskovic,3 J. Yee,1 R. Mannon1

1University of Alabama School of Medicine, Birmingham, AL
2Columbia University Medical Center, New York, NY
3CareDx, Brisbane, CA

Introduction

Many (13% in 2015) kidney transplant patients receive repeat transplants.1 The survival of repeat transplants are inferior to that of primary allografts.1 Recipients of kidney repeat transplants are at high immunological risk for rejection and complications of immunosuppression,1 and therefore these patients have high potential benefits from access to new biomarkers to monitor the status of the allograft. Donor-derived cell-free DNA test (dd-cfDNA, AllSure®) has established performance characteristics to diagnose the probability of active rejection in de novo kidney transplant recipients.2 dd-cfDNA is significantly higher (median 1.6%) in association with biopsy-based diagnosis of active rejection as compared to dd-cfDNA levels in cases of histology findings of no rejection (median 0.3%)1. Here we characterize dd-cfDNA in patients who have received a repeat kidney transplant where the prior graft remains in situ.

Methods

Plasma dd-cfDNA was collected from patients enrolled in the 14-center Circulating Donor-Derived Cell-free DNA in Blood for Diagnosing Acute Rejection in Kidney Transplant Recipients study (DIART, Clinical Trials Identifier NCT02424227)3. The DART study included 34 patients with more than one renal allograft in situ (repeat transplants). Patients from the repeat transplant group who began dd-cfDNA surveillance testing within 2 months post-transplant (≤ 75 dp) and had no clinically indicated biopsy at the first visit and no rejection anytime while on the study (n=12, repeat transplant surveillance cohort) and those who met the same conditions but had single kidney transplant (n=202, single transplant surveillance cohort) were included in the surveillance groups. Patient demographics and dd-cfDNA distribution were compared between the repeat and single transplant surveillance cohorts. A cohort with clinically indicated biopsy of the most recent allograft, the median dd-cfDNA at the time of a clinically indicated biopsy was 1.4%, significantly higher than the median 0.4% (P=0.009) in five repeat transplant patients negative for rejection at a clinically indicated biopsy. These dd-cfDNA values are comparable to single transplant patients: those with active rejection had a median dd-cfDNA of 1.6%, and those with no biopsy findings of rejection had a median of 0.3%.4

Results

In six repeat transplant patients with a diagnosis of active rejection of the most recent allograft, the median dd-cfDNA at the time of a clinically indicated biopsy was 1.4%, significantly higher than the median 0.4% (P=0.009) in five repeat transplant patients negative for rejection at a clinically indicated biopsy. These dd-cfDNA values are comparable to single transplant patients: those with active rejection had a median dd-cfDNA of 1.6%, and those with no biopsy findings of rejection had a median of 0.3%.4

Table 1. Repeat and single transplant surveillance patients share similar demographic and clinical correlates.

Table 2. Distribution of dd-cfDNA levels in repeat and single transplant surveillance patients.

Conclusion

In the small cohort of surveillance patients with no biopsy-proven rejection, repeat kidney transplant patients had slightly higher, but clinically similar dd-cfDNA levels (median 0.29%) compared to single allograft patients (median 0.19%). The dd-cfDNA levels in repeat transplant patients with no rejection by biopsy are significantly lower than dd-cfDNA levels in either single or repeat transplant patients with biopsy-proven rejection. The dd-cfDNA levels in repeat transplant patients with biopsy-proven rejection are significantly higher than dd-cfDNA levels in either single or repeat transplant patients without biopsy rejection.

This dd-cfDNA test has the potential to be used to identify active rejection and related injury as well as monitor rejection treatment in patients with repeat kidney transplants.

References


Disclosures

The DART study was sponsored by CareDx. DAI, CL, TH, and RRK have no commercial plant to report from CareDx. DAI, MB, and RL are employees of CareDx.