Endomyocardial Biopsy – A Source of Heartache

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BACKGROUND/PURPOSE

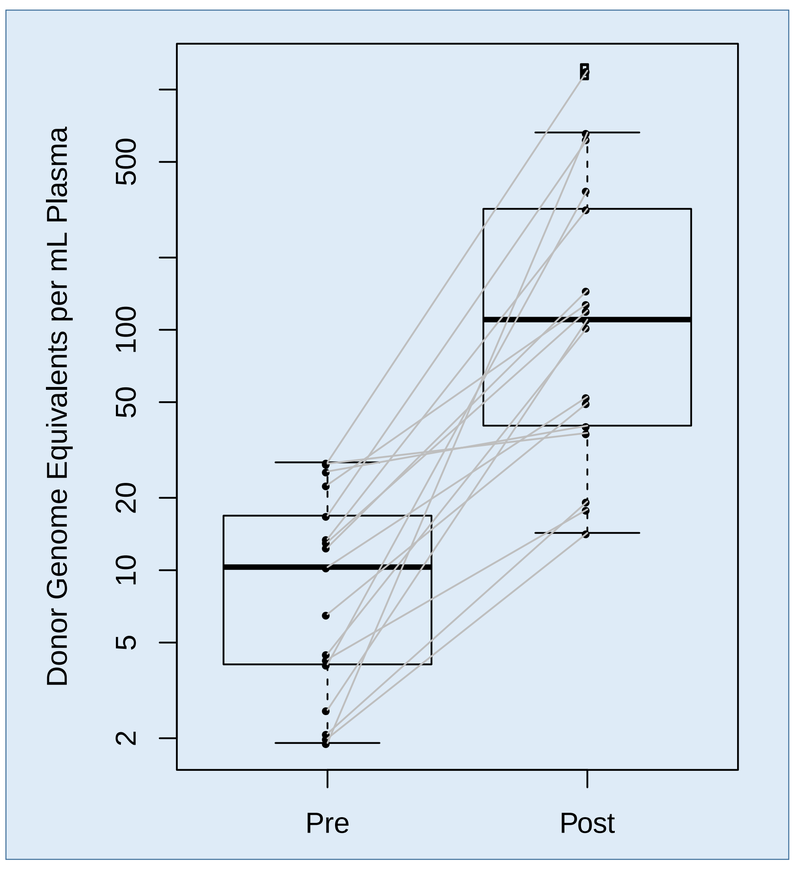
There is a tremendous need for a reliable non-invasive surveillance tool to detect rejection in heart transplant recipients. We sought to investigate the utility of donor specific cell free DNA (ds-cfDNA) as a marker for rejection. In the early phases of study design, blood samples for analysis were by protocol scheduled to be drawn at the time of endomyocardial biopsy. We hypothesized that the timing of the blood draw as it relates to the timing of the biopsy could be critically important if in fact, the biopsy itself were to produce an increase in ds-cfDNA. We performed this substudy to answer this question.

METHODS

Paired blood samples from 21 asymptomatic patients were drawn pre and post surveillance bx. Quantity of ds-cfDNA was determined using the myTAI-HEART™ test (a proprietary quantitative genotyping assay from TAI Diagnostics, Wauwatosa, WI). Excluding patients with known graft vasculopathy, cancer, mechanical circulatory support, or any cellular rejection with grade >1, 17 sample pairs were available. Bioptome size, number of bx samples and time between biopsy and sample draw were recorded and analyzed.

RESULTS

Quantity of ds-cfDNA was reported as donor genomic equivalents (GE) and ranged from 1.9 (med 12) pre-bx through 1200 (med 136) post-bx. Paired samples are shown in the figure. The GE of ds-cfDNA increased post-bx in all patients ($p<0.02$), with a median increase of 8.2x (range 0.34x - 345x). Patient ages ranged from 4 to 32 years (med 12). Patient weights ranged from 17 to 90 kg (med 49). Both age and weight are associated with GE change ($p<0.01$). Pts <17 years of age had an average GE increase of 29x versus pts >23 with an average GE increase of 1.1x. Age and weight are correlated, thus similar effects are seen by weight at time of draw. GE change did not correlate with bioptome size ($p=0.4$). The time between bx and the second blood draw ranged from 1 to 36 minutes and increased time correlated to increased total cell free DNA ($p=0.037$). Initial ds-cfDNA in GE is indicative of organ health before bx. Patients with elevated GE (>20, n=4) pre-biopsy saw less GE increase post-bx ($p<0.01$).



CONCLUSIONS

Standard endomyocardial bx induces a significant and measurable injury to the transplanted heart, influenced strongly by patient body size and pre-bx level of ds-cfDNA. As commercial quantitative assessment of ds-cfDNA becomes increasingly available as a biomarker to identify patients at low risk for rejection, it will be essential that practitioners are aware of the effect of sample timing as it relates to endomyocardial biopsy. Longer time between biopsy and blood sample correlated with increased total cell free DNA suggesting the procedure itself is pro-inflammatory. The relationship between endomyocardial biopsy and ds-cfDNA levels serves as evidence of the tremendous sensitivity of this technology to serve as a marker of cardiac injury.

Disclosure:
Assays performed by TAI Diagnostics
Dr. Zangwill – Consultant – TAI Diagnostics
Other authors – Relationships with TAI Diagnostics as reported (See Full Disclosure Notice on Poster Board)