

Endomyocardial Biopsy Microscopic Molecular Profiling Correlates with Donor Derived Cell Free DNA

Background: Cardiac allograft rejection (AR) diagnosis has relied on endomyocardial biopsy (EMBx) and histopathology (HP). Quantifying donor-derived cell free DNA (ddcfDNA) has recently offered a non-invasive alternative for detecting graft injury (1). EMBx mRNA analysis via molecular microscope profiles (MMP) quantifies AR probability not subject to HP interpretation (2). Our aim was to evaluate the clinical role of MMP in cardiac transplant recipients (HTx) with positive ddcfDNA.

Methods: We identified 30 patients with ddcfDNA testing and subsequent EMBx for HP and MMP analysis. MMP was conducted by the molecular microscope diagnostic system (MMDX™). Patients with multi-organ transplantation or coronary allograft vasculopathy were excluded. MMP, HP, echo and ddcfDNA association were assessed using logistical regression (SPSS™).

Results: Average time post-transplant was 1540 ± 1544 days, average LVEF 55%, and average ddcfDNA 0.78 ± 1.1 . Donor specific antibodies were present in 33% of patients. MMP was abnormal in 13/30 patients and correlated with ddcfDNA levels ($p=0.014$). MMP abnormalities included 7 antibody mediated rejection (AMR), 3 acute cellular rejection (ACR), and 3 injury patterns. By HP, biopsies were abnormal in 14/27 patients; 13 ACR (grade 1) and 1 AMR (grade 2). Abnormal HP did not correlate with ddcfDNA levels ($p= 0.08$). HP and MMP are often discordant, Table 1.

Conclusion: Elevated values of ddcfDNA correlate with AR as defined by MMP and not with HP or echocardiography. Large prospective clinical trials are needed to define clinical outcomes from treatment strategies based on biopsy results. Multi-modality testing may be necessary to monitor cardiac transplant patients for rejection and avoid misclassification.

Table 1.

		Molecular Microscope Profile		
		Normal	Abnormal	Total
Histopathology	Normal	9	5	14
	Abnormal	5	8	13
	Total	14	13	27

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References:

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2. Alam A, Van Zyl J, Paul Milligan G, Michelle McKean S, Patel R, Anne Hall S. Evolving the surveillance and workup of heart transplant rejection: A real-world analysis of the Molecular Microscope Diagnostic System. *Am J Transplant* 2022.