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ACCEPTED MANUSCRIPT

EARLY PCR DETECTION OF CHAGAS DISEASE REACTIVATION IN HEART-TRANSPLANTED PATIENTS

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ABSTRACT

BACKGROUND: Heart transplantation is an important therapeutic option for chagasic patients with severe cardiomyopathy. During patient follow-up, the differential diagnosis between cardiac transplant rejection and Chagas disease infection reactivation remains a challenging task, which hinders the rapid implementation of the appropriate treatment. Herein we investigate whether PCR strategies could facilitate early detection of *Trypanosoma cruzi* (*T. cruzi*) in transplanted endomyocardial biopsies (EMB).

METHODS: We analyzed 500 EMB specimens obtained from 58 chagasic cardiac transplanted patients, using PCR approaches targeted to nuclear (rDNA 24Sα) and mitochondrial (kDNA) markers, and compared the efficiency of these approaches with that of other tests routinely used. **RESULTS:** *T. cruzi* DNA was detected in 112 EMB specimens derived from 39 patients (67.2%), and the first positive result had a median time of 1.0-month post-transplant. Conventional histopathological, blood smear, and hemoculture analyses showed lower sensitivity and higher median time to the first positive result. Patient follow-up revealed that 31/39 PCR-positive cases presented clinical reactivation of Chagas disease at different times after transplantation. PCR techniques showed considerable sensitivity (0.82) and specificity (0.60), with area under the receiver operating characteristic (ROC) curves of 0.708 (P=0.001). Moreover, PCR techniques anticipated the clinical signs of Chagas disease reactivation by up to 36 months, with a median time of 6 months and an average of 9.1 months. **CONCLUSION:** We found a good association between the PCR diagnosis and the clinical signs of the disease, indicating that PCR

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