NT-proBNP assay may preclude the need for routine endomyocardial biopsy to detect cardiac allograft rejection, but not early after transplantation

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Background: Endomyocardial biopsy (EMB) remains the standard for the diagnosis of rejection after heart transplantation (HTx). Very high levels of the N-terminal fragment of B-type natriuretic peptide (NT-proBNP), an established marker for the diagnosis of heart failure, are common in the first 3 months after HTx. The aim of this study was to determine whether the NT-proBNP assay may detect or exclude cardiac allograft rejection.

Methods: From January 2003 to December 2008, we performed 678 EMB procedures in 81 HTx recipients. Immediately before EMB, a venous blood sample was drawn to determine the NT-proBNP level. Clinically significant rejection was defined as moderate-to-severe rejection or any rejection episode with accompanying hemodynamic compromise and requiring treatment. We related the NT-proBNP levels with the presence or absence of clinically significant rejection, before and after 90 days post HTx, and identified the NT-proBNP level that more accurately predicted rejection.

Results: Due to insufficient biopsy specimen, a histological diagnosis of rejection was not possible in 26 EMB. For the remaining 652 EMB, the median time between HTx and EMB was 7 (IQR: 2.3; 21.0) months. Overall, we recorded 36 clinically significant rejections, of which 27 occurred >90 days after HTx. We found a strong interaction between time after HTx and the diagnostic accuracy of NT-proBNP (interaction test P<0.001): NT-proBNP predicted clinically significant rejection only after 90 days post-HTx. An NT-proBNP level > 1231 pg/mL (best discriminatory value) was associated with clinically significant rejection >90 days after HTx (area under the ROC curve 0.79; 95% CI, 0.75-0.83). The criterion NT-proBNP > 1231 pg/mL, present in 92 of 446 EMB procedures >90 days after HTx, showed 70% sensitivity, 83% specificity, 21% positive predictive value, and 98% negative predictive value for the diagnosis of clinically significant rejection.

Conclusion: NT-proBNP levels relate with the histological findings of EMB specimens and have a high negative predictive value for the detection of clinically significant rejection after 90 days post-HTx.