Outcomes in Diabetic Patients With Heart Failure: Impact of ACE D/I Polymorphism

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Background: Diabetes adversely affects outcomes in patients with heart failure and may interact with genetic risk. We have previously demonstrated that the Angiotensin-converting enzyme deletion allele (ACE D) worsens survival in heart failure; however, its impact specifically in diabetics has not been investigated. We sought to evaluate ACE D genetic risk in patients with diabetes mellitus (DM) and heart failure.

Methods: The GRACE study, a prospective single center study of genetic risk of heart failure events, enrolled 478 patients at the University of Pittsburgh between 1996 and 2001. Of the 479 patients, 122 (77% male, 84% Caucasian, 57±10 years, 60% ischemic, LVEF <25%) had DM at baseline. Blood was obtained for DNA isolation and genotyped by standard PCR based techniques. Transplant free survival was compared in patients with diabetes based on the ACE (D/I/DI) genotype.

Results: Patients with DM were predominantly ischemic (66% vs 45%, p<0.001) and had worse NYHA scores (class 3, 63% vs 52%, p=0.03). Event odds ratio was 2.1(p=0.001) for DM. Transplant free survival was significantly worse in patients with DM (1 year: 77%±8%, p<0.001). In the subset with DM, transplant free survival was worse in the patients with the D allele (I/D/I:D: 1 year: 88%/75%/74%, 2 year: 77%/56%/46%, p=0.03, figure)

Conclusion: In diabetics, the D allele was associated with poorer transplant free survival. The ACE genotype may play a role in the modulation of endohedral dysfunction in patients with DM.

Transcardiac gradient of H-FABP correlated with left ventricular end-diastolic volume index (r=0.734, p<0.0001), but did not correlate with left ventricular ejection fraction and left ventricular end-diastolic pressure. Plasma levels of H-FABP, one of the cardiac specific proteins, increases in patients with DCM suggest sustained ongoing myocardial damage and myocardial loss in these patients. Therefore, the increase of H-FABP may be a more sensitive marker of left ventricular remodeling (LVEDVI) than BNP in patients with DCM.