Genetic Polymorphisms of the Angiotensin II Type 1 Receptor Gene and Diastolic Heart Failure

Wu, Genetic polymorphisms and diastolic heart failure
Cho-Kai Wu, MD,* Chia-Ti Tsai, MD, PhD,† Yi-Cheng Chang, MD,* Jing-Ling Luo, MD,† Yi-Chih Wang, MD,† Juey-Jen Hwang, MD, PhD,‡ Jiunn-Lee Lin, MD, PhD,† Chuen-Den Tseng, MD, PhD,† and Fu-Tien Chiang, MD, PhD†,‡

*Department of Internal Medicine, National Taiwan University College of Medicine and Hospital Yun-Lin Branch, Yun-Lin, Taiwan
†Division of Cardiology, Department of Internal Medicine, National Taiwan University College of Medicine and Hospital, Taipei, Taiwan
‡Department of Laboratory Medicine, National Taiwan University Hospital, Taipei, Taiwan

Background. The aim of the study was to investigate the association between Angiotensin II type 1 receptor (AGTR1) gene polymorphisms and diastolic heart failure (DHF) in a case controlled study.

Methods and Results. Of 1752 consecutive patients analyzed, 176 diagnosed with DHF confirmed by echocardiography were recruited. Controls were matched 1-to-1 by age, sex, hypertension, diabetes, renal function and medication use. We genotyped 11 single nucleotide polymorphisms (SNPs) according to HapMap Han Chinese Beijing databank across the AGTR1 gene to capture 96% of haplotype variance in all SNPs with minor allele frequencies ≥ 5%. We also genotyped A1166C (rs5186) SNP with known associations with cardiovascular disease and analyzed associations of SNPs and haplotypes with DHF and linkage disequilibrium (LD) structure of the AGTR1 gene.

In a single locus analysis, SNP rs16860760, rs389566, rs5186 were associated with DHF (allele-specific \( p = 0.004, 0.002, 0.002 \), respectively; permuted \( p = 0.045, 0.022, 0.027 \), respectively). SNP rs389566 with a minor allele frequency of 20.17%, had an odds ratio 2.03 for the autosomal dominant model (AA+AT : TT, 95% CI 1.29-3.19; \( p = 0.0012 \)) and 1.73 for the additive model (95% CI 1.21-2.48; \( p = 0.0018 \)), corresponding to a population attributable risk fraction of 27.21%. The haplotypes in a LD block of rs389566 (T-A-G and A-A-G) were also significantly associated with DHF (permuted \( p = 0.0125 \) and 0.0105 respectively).

Conclusions. We identified risk-conferring genetic variants of AGTR1 gene for DHF in a Chinese population.

Keywords: diastolic heart failure; polymorphism; genetics; Angiotensin II type 1 receptor