CHRNA5-ADAMTS7 HAPLOTYPE PREDICTS MORTALITY FOLLOWING ACUTE MYOCARDIAL INFARCTION

Moderated Poster Contributions
Hall C
Monday, March 31, 2014, 10:00 a.m.-10:15 a.m.

Session Title: Genetic Risk Markers in ACS
Abstract Category: 1. Acute Coronary Syndromes: Clinical
Presentation Number: 1273M-359B

Authors: Edward Coverstone, Petra Lenzini, LiShiun Chen, Laura Bierut, John Spertus, Richard Bach, Sharon Cresci, Washington University School of Medicine, St. Louis, MO, USA, Saint Luke’s Mid America Heart Institute and the University of Missouri-Kansas City, Kansas City, MO, USA

Background: Genetic variants in ADAMTS7 have previously been associated with coronary calcification and the angiographic extent of coronary disease. Variants in a nearby gene encoding the nicotinic alpha-5 cholinergic receptor, CHRNA5, have been associated with increased smoking dependence, more extensive peripheral vascular disease, and lung cancer. We sought to investigate the association of regional CHRNA5-ADAMTS7 haplotypes with mortality in patients following myocardial infarction (MI).

Methods: Caucasian subjects (N=2054) hospitalized with MI enrolled in the prospective multi-center TRIUMPH study were genotyped for polymorphisms in CHRNA5 and ADAMTS7. After adjusting for sex, GRACE score, and smoking status, stratified proportional hazards models were used to estimate independent contribution of haplotype and 1-year mortality.

Results: Seven CHRNA5-ADAMTS7 haplotypes represented 98.6% of the regional haplotypes. Although individual variants forming the haplotype had an association with mortality (unadjusted p values 0.04 to 2E-04), one CHRNA5-ADAMTS7 haplotype, present in 21.3% of the population, was significantly and strongly associated with decreased mortality at one year (p = 8E-05). After adjusting for sex, GRACE score, and smoking status, carriers of this haplotype had significantly decreased mortality compared to non-carriers (adjusted HR = 0.42, 95% CI 0.26, 0.68; p = 4.1E-04). This association remained significant at two-year follow-up (adjusted HR = 0.55, 95% CI 0.39, 0.78; p = 9.4E-04). None of the other 6 regional haplotypes was significantly associated with 1- or 2-year mortality.

Conclusion: To our knowledge, this is the first description of a common CHRNA5-ADAMTS7 haplotype that is strongly associated with improved mortality after MI. This novel observation suggests that attention to the full regional haplotype for CHRNA5-ADAMTS7 is important for risk prediction and underscores the need for further research into the mechanisms by which these genetic markers confer increased risk of mortality following MI.