ASSOCIATION BETWEEN IL-2 AND HUMAN HEAT SHOCK PROTEIN 60 WITH CORONARY ARTERY CALCIUM SCORE

Background: Human heat shock protein 60 (HHSP60) functions as a major mitochondrial molecular chaperone. Based upon evidence suggesting that higher IL-2 levels and HHSP60 autoimmunity contribute to atherogenesis, we tested the hypothesis that IL-2 and HHSP60 associates with coronary artery calcium (CAC) score, using cross-sectional entry data from a large prospective population study.

Methods: We evaluated 998 asymptomatic adults, age 45-84 years, without known coronary artery disease enrolled in the Multi-Ethnic Study of Atherosclerosis (MESA), who had HHSP60 measured at baseline. Tertiles of serum levels of HHSP60 were evaluated. The independent association between IL-2 and HHSP60 with CAC were assessed using univariate and multivariate logistic regression analyses, with adjustments for coronary risk factors (Framingham Risk Score) and inflammatory variables (CRP, TNF, IL-6, and IL-2). The first serum tertile of HHSP60 levels was used as reference group.

Results: The logarithmic transformation of IL-2 and HHSP60 levels in serum had a normal distribution. There were no differences in age, gender, or race by tertiles of serum HHSP60 levels. Patients with diabetes, hypertension, obesity, or dyslipidemia did not show any difference in levels of HHSP60. The median Framingham risk score was 11 [5, 22], 8 [5, 16], and 9 [5, 18] for the first, second, and third tertiles respectively (p-value=0.043). In a univariable logistic regression analysis, tertile of serum HHSP60 was not associated with CAC. IL-2 and TNF-a were associated with increased CAC (IL-2: OR 3.69, p<0.001, TNF-a: OR 3.76, p<0.001). In multivariate logistic regression, the highest tertiles of HHSP60 and IL-2 were associated with increased risk of CAC even after adjusting for Framingham risk score and other inflammatory markers (HHSP60 T3: OR 1.41, p=0.05, IL-2: OR 2.27, p<0.001).

Conclusions: Increased serum levels of inflammatory markers (IL-2 and HHSP60) are associated with an increased CAC in asymptomatic adults, possibly reflecting an association with early development of atherosclerosis in healthy asymptomatic individuals.