GENE VS. LIFE STYLE: A 10-YEAR LONGITUDINAL STUDY DETERMINING MECHANISMS OF INDIVIDUAL DIFFERENCE IN AGE-RELATED ARTERIAL STIFFENING

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Introduction

Increased arterial stiffness is a strong cardiovascular disease (CVD) risk (Vlachopoulos et al. 2010). Previous cross-sectional and short-term intervention studies suggest large inter-individual differences in magnitude of age-related arterial stiffening as well as efficiency of regular physical activity on arterial destiffening (Iemitsu et al. 2006; Hayashi et al. 2008). To shed light on underlying mechanisms responsible for individual difference in age-related arterial stiffening, we examined contributions of polymorphisms in endothelin (ET) and estrogen-related genes and regular physical activity using a 10-year longitudinal study design.

Methods

We evaluated changes in blood pressure and brachial-ankle pulse wave velocity (baPWV), an index of arterial stiffness, in 90 volunteers (51 men, current age=63±14 yrs) who had participated other experiments including baPWV measurement in our laboratory approximately 10 years ago. We determined the gene single-nucleotide polymorphisms of 958A/G in exon 6 of ET-A receptor (ET-A), 831A/G in exon 4 of ET-B receptor (ET-B), and at -401T/C of intron 1 of the estrogen receptor (ER)- α gene. Average follow-up duration was 10±0.9 years. Subjects were divided into three groups based on current physical activity level (quantified by a questionnaire): less than 5 METs/week (LO, n=49), 5-15 METs/week (MID, n=23), and more than 15 METs/week (HI, n=18) of aerobic exercise.

Results

In pooled subjects, baPWV increased by +11.8% (from 13.4±2.6 to 14.9±3.1 m/sec). HI group exhibited significantly smaller increase in baPWV (+5.5±9.9%) compared with the other groups (LO: +13.4±10.7%; MID; +13.4±11.0%) after adjustment for confounding factors (e.g., current age, current blood pressure, and baseline baPWV level), irrespective of each genotype. Interestingly, physically inactive individuals (i.e., LO and MID groups) having G/G genotype of ET-B showed significantly and substantially greater increase in baPWV (19.1±12.9%) than the others having AA or A/G genotypes (12.2±9.0% and 11.4±9.9%, respectively) after adjustment for confounding factors. ET-A and ER- α genotype did not affect age-related increase in baPWV.

Discussion

The 10-year longitudinal observation establishes the attenuating effect of regular aerobic exercise on age-related arterial stiffening. In addition, our results suggest that ET-B polymorphism may influence extent of arterial stiffening with aging. Increased arterial stiffness has emerged as a strong predictor of future CVD events and all-cause mortality (Vlachopoulos et al. 2010). Therefore, to shed light on mechanisms responsible for divergent arterial stiffening with age is important to devise strategy of CVD prevention. The present study provides us important caution that specific polymorphisms of ET-related gene possibly facilitate arterial stiffening.

References

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