Abstract: P256

Telomere lengths and the rejuvenating factor GDF11 in coronary artery disease

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Background/Introduction: Telomeres are dynamic chromosome-end structures that protect DNA in our genome from deterioration. Throughout life, telomere lengths (TLs) become shorter, and the rate of this process has been associated with lifestyle and the onset of age-related diseases. Moreover, the aging-associated factor growth differentiation factor 11 (GDF11) has been suggested as a rejuvenating factor. Together, the interplay of these aspects that possibly modulate the aging process is of interest to explore.

Purpose: To investigate the associations between leukocyte TLs (LTLs) and chronological age, comorbidities and clinical outcome in patients with coronary artery disease (CAD). Potential covariations between LTL and GDF11 were further assessed.

Methods: 300 patients with stable CAD, 20% female, age range 36-81 yrs, were included. Within 2 years, a composite of new clinical events (unstable angina pectoris, myocardial infarction (MI), stroke and deaths) was recorded. DNA and RNA were isolated from whole blood for the analysis of LTLs and GDF11 gene expression, respectively. LTLs were measured by PCR using telomere-specific primers and determined relatively to a single copy gene (36B4). The amount of GDF11 was measured as relative quantification using PCR and the house-keeping gene β2M.

Results: We observed that patients with previously suffered MI presented with 20% shorter LTLs vs. patients without (p = 0.015), however, only in men (p = 0.009, n = 115). To further explore this association, LTLs were divided into quartiles (Qs) and further dichotomized at the distinctive cut-off level between Q3 and Q4. LTLs in the upper Q were associated with 60% lower frequency of having suffered a previous MI (p = 0.008, adjusted for age, treated hypertension, body mass index (BMI), triglycerides, HDL and fasting glucose). LTLs were not differently distributed according to sex or the presence of treated hypertension (52%), diabetes type 2 (25%), metabolic syndrome (35%) and clinical outcome (12%). In the total cohort, LTLs were further inversely correlated to age (r = - 0.17, p = 0.007), however, only in women (r = - 0.37, p = 0.006). In all subjects, GDF11 gene-expression was weakly and inversely correlated to age (r = - 0.16, p = 0.010). Overall, no correlation was observed between LTLs and gene-expression of GDF11. However, when dividing into subgroups, a strong correlation was observed in overweight women (BMI > 25), (r = 0.40, p = 0.028).

Conclusions: Although no association between LTLs and clinical outcome was observed, LTLs correlated to the severity of CAD in men, in this case previously suffered MI. In women, LTLs seem to be more associated with age. The results may indicate gender-related differences in regulatory mechanisms of TLs and a possible metabolically influenced association between LTLs and GDF11.