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Association of age, BMI and smoking habits with leukocyte telomere length dynamics

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Telomeres are nucleoprotein structures at the ends of chromosomes. They have functions in maintaining chromosomal stability and integrity. Telomeres shorten with each cell division due to incomplete replication of their terminal single-stranded section. Hence, they shorten progressively with cell division. Critically short telomeres can drive cells into senescence or even death. The replicative capacity of cells is reduced with decreasing telomere length (TL), thus the regenerative ability of the body. Progressively increasing number of senescent cells in tissues leads to reduced tissue function which eventually leads to functional deterioration in organs and finally organ failure and death. Hence, it is hypothesised that the TL-induced senescence is one of the driving forces of human ageing and TL has been proposed as a candidate biomarker of ageing.
A number of epidemiological studies found associations between TL in leukocytes (LTL) and lifespan, diseases and lifestyle-related factors. However the evidence from highly heterogeneous studies with contradictory results remains equivocal. To evaluate the value of LTL as a potential biomarker of ageing, more detailed investigations of associations of LTL with lifestyle factors, age-related health outcomes and mortality are needed. Therefore, in this dissertation it was aimed to provide a detailed investigation of the relationship of obesity and smoking habits with leukocyte telomere dynamics.
Two systematic literature reviews were performed to provide an overview on the evidence on the relationship between age and LTL, and obesity and LTL. The associations of obesity, duration of obesity, weight changes during adulthood and smoking habits with LTL and rate of LTL change per year among older adults (≥50 years) were evaluated in a large population-based cohort from Germany.
In the literature, negative correlations between mean age and LTL were consistently observed. The majority of identified studies (124 out of 129) had cross-sectional design and reported telomere loss rates in the range of 20-30 BP/year. However, the quantitative summarisation and comparability of studies was limited due to their diversity and lack of standardisation of reported data.
The systematic review of the literature for the association between adiposity and LTL was focused on BMI as the adiposity measure due to the scarcity of data on other measures. 29 studies were identified, 16 of which reported correlation and/or regression coefficients between BMI and LTL, and could be meta-analysed. The majority of published studies found statistically significant inverse associations between BMI and LTL. The pooled correlation and regression coefficients showed a consistent inverse association.

The association of BMI, weight changes and smoking behaviour with LTL was analysed in 3600 participants of the ESTHER study, whereas their association with rate of telomere change per year was analysed in 1000 participants after 8-year of follow-up. Age was inversely associated with LTL and women had around 80 BP longer LTL than men. Age and sex remained as independent predictors of LTL and rate of LTL change in the multivariate adjusted regression analyses. BMI, weight gain and smoking was inversely associated with LTL. The associations of BMI and weight gain with LTL varied according to age and appeared to be stronger in those younger than 60 years. Although ever smoking was associated with shorter LTL, no clear dose-response relationship was observed with amount of smoking. No clear patterns or trends were observed between any of BMI-related variables and rate of LTL change. Ever smokers had slower LTL loss rates per year than never smokers.

Reviewing the literature revealed the heterogeneity of studies in the field with regards to their designs, populations, sample sizes, and LTL measurement methods; measurement errors limit the comparability of findings and establishment of magnitude of the exact quantitative associations of age and lifestyle-related factors with LTL and LTL change rates. Although BMI was inversely associated with LTL and this observation is biologically plausible, the associations were of rather small magnitude indicating that only a very small proportion of LTL is statistically explained by BMI. The results from the ESTHER study was overall consistent with the literature and provided supportive evidence for a potential role of obesity and smoking in premature ageing as reflected in more pronounced LTL shortening. They also point to potential important interactions of the association between obesity and BMI by age, and to the possibility of potential confounding of the smoking-LTL association by (subclinical) malignancies. The reasons of null findings in the longitudinal analysis for obesity and the slower LTL attrition rates observed in smokers should be further elucidated in further research.

Overall, this comprehensive investigation document that telomere dynamics are complex and LTL has high inter-individual variability, which could only be partially explained by lifestyle-related factors. Together with the increasing evidence showing that LTL is determined a large degree by genetic factors and early life exposure, the present findings indicate that adulthood LTL provides only partial information about LTL dynamics. Further research should cover the entire lifespan of individuals with repeated LTL measurements and consider genetic factors and early childhood exposures simultaneously when evaluating potential roles of adulthood determinants of LTL such as obesity and smoking habits.