RATE OF TELOMERE SHORTENING AND CARDIOVASCULAR PHENOTYPES

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doi:10.1136/heartjnl-2013-304019.125

Introduction Cross-sectional adult studies report associations between short leukocyte telomere length (LTL) and measures of vascular and cardiac damage. However, due to high inter-individual differences in LTL at birth and thereafter, it is unclear whether this relationship is due to inherited short telomere length or a higher rate of LTL shortening through life. In this study we explored whether the baseline LTL or the rate of LTL shortening could predict cardiovascular (CV) phenotypes during 10 year follow up in the MRC National Survey of Health and Development (NSHD, also known as 1946 birth cohort) study.

Methods 689 participants with measures of LTL and CV risk factors at 52 and 62 years underwent measurements of right common carotid intima-media thickness (cIMT), cardiac mass and left ventricular ejection fraction at 62 years. LTL was measured by real time PCR.

Results At both time points a negative association was found between LTL and age ($p < 0.01$), with longer LTL detected in females than males ($p < 0.01$). The rate of LTL shortening was faster in subjects with longer LTL at baseline ($p < 0.001$), in males ($p < 0.01$ vs females) and in those with carotid plaques ($p < 0.05$). The measure of LTL at 52 years did not predict CV phenotypes at 62 years. However, a faster rate of LTL shortening between 52 to 62 years was associated

with increased values of cIMT at 62 years ($r=0.01$; $p<0.01$) leading to a cross-sectional negative association between LTL and cIMT observed at 62 years ($r=-0.075$; $p<0.05$). At both time points, no associations were detected between levels of CV risk factors and cross-sectional and longitudinal measures of LTL. Cardiac measurements were not associated with 52 and 62 year LTL measures, nor with the rate of LTL shortening. Similar trends were observed in male and females and adjustments for CV risk factors, treatments and history of CV disease did not materially affect the results (table 1).

Conclusions/implications This is the first study showing an association between rate of LTL attrition and final vascular phenotype. These findings suggest that the rate of progression of cellular aging in late midlife (reflected by the rate of LTL attrition) influences predisposition to vascular damage, over and above the contribution of CV risk factors. Therefore, current results identified a possible novel pathway associated to an increased risk of CV disease. This can possibly improve the CV risk stratification of the patients. Furthermore, a better understanding of the factors influencing the rate of LTL has the potential to identify novel therapeutic targets and lead to a more effective CV disease prevention.