TELOMERES LENGTH IN GENETICALLY DIAGNOSED FAMILIAL HYPERCHOLESTEROLEMIA

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Introduction: Telomere Length Shortening (TLS) reflects cellular senescence and associates with multiple chronic diseases, including cardiovascular disease (CVD). Effects on TLS by CVD risk factors have been demonstrated, despite that elevated LDL cholesterol (LDL-C) has been not investigated. Familial Hypercholesterolemia (FH), characterized by genetically elevated LDL-C and premature CVD, calls for in depth investigation on its relation with TLS.

Materials and methods: We measured Leukocytes Telomere Length (LTL) on mononuclear cells-derived genomic DNA from 206hypercholesterolemic patients from the lipid clinic of Bassini Hospital (Milan). Genome sequencing identified 135heterozygous hypercholesterolemia patients (HeFH) (mutations on LDLR) and 71hypercholesterolemic non-HeFH (non-FH HC) patients. Clinical history, Dutch Lipid Clinic Network Score (DLCNS) were collected and biochemical parameters were determined. Clinical parameters and LTL were compared that of 320 subjects from the PLIC Study (136.37±35.58mg/dL, mean LDL-C), age-matched with hypercholesterolemic patients.

Results: As compared to controls LTL of HeFH was shorter, although a younger age (37±18y vs 49±15y, $p<0.001$). This difference was significant both in HeFH below 35years-old and in those over 50 years-old and it was still consistent in HeFH vs controls free from statin (1.22±0.08vs 1.58±0.04, $p= 0.001$).
Only when pairing for LDL-C, LTL were shorter in HeFH vs non-FH HC (1.33±0.05vs 1.55±0.08, $p=0.019$), independently from DLCNS score, previous CVD as well as statin treatment (1.27±0.06vs 1.54±0.06, $p= 0.005$).

Discussion and conclusions: Genetically elevated LDL-C results in shorter LTL, thus indicating early cellular senescence and perhaps contributing to premature cardiovascular morbidity in FH patients.