TELOMERE SHORTENING AND HIGH-RESOLUTION RESPIROMETRY IN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH MORBID OBESITY

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Introduction: Obesity is a chronic disorder frequently associated to mitochondrial dysfunction. Mitochondrial-dependent production of reactive oxygen species (ROS) cause damage to mitochondrial components and initiate degradative cellular processes that significantly contributes to cellular senescence. Correlations between ROS production and accelerated telomere shortening are already established in different clinical settings. However, there is no data regarding mitochondrial respiration parameters as an integrative measure of the dynamics of coupled metabolic pathways and their contribution to telomere shortening in peripheral mononuclear cells (PBMC) from patients with morbid obesity. In this regard, the aim of this work is to evaluate telomere shortening in PBMC from patients with morbid obesity and correlate with mitochondrial parameters. Material and Methods: Thirty-nine patients with morbid obesity (BMI ≥ 35 kg/m²) and 27 healthy eutrophic controls (BMI 20.0 - 24.9) were recruited and gave informed written consent. Demographic data and clinical history was recorded. Relative mean telomere length (T/S) from PBMC was measured by real time qPCR. Activity of mitochondrial respiration in intact fresh PBMC was achieved through high-resolution respirometry (HRR, Oxygraph-2k; Oroboros Instruments).

Results and Discussion: Telomere length (TL) was significantly shorter in patients when compared to controls (mean = 0.49 95% CI (0.37 – 1.80) versus mean = 1.57 95% CI (0.50 – 1.67), P = 0.004), and remained so after adjustment for age as covariate in a linear regression analysis (P = 0.026). There was a significant inverse correlation between TL and age (r = -0.4108, P = 0.0116) or BMI (r = -0.4174, P = 0.0005) in patients with morbid obesity. Preliminary data from HRR also suggest mitochondrial dysfunction in patients with morbid obesity. Conclusions: Telomere length is diminished in patients with morbid obesity and inversely correlated with age and BMI. Further studies are underway to confirm if telomere shortening could be a consequence of mitochondrial dysfunction.

Key words: Telomere shortening, morbid obesity, qPCR
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