Aim: This study aims to investigate the signaling pathway AMP-activated protein kinase (AMPK)- Peroxisome proliferator-activated receptor-gamma coactivator (PGC)1α-sirtuin (SIRT)3 in the human corpus cavernosum (HCC) between healthy individuals and those with cardiovascular disease risk factors (CVDRF).

Introduction: SIRT3 is a mitochondrial NAD+-dependent protein-deacetylase involved in the regulation of cellular metabolism. As a key factor in AMPK and PGC1α activation in stress, the decrease in SIRT3 expression or activity is associated with diverse pathologies and aging. Actually, SIRT3 expression was found decreased in HCC of aged individuals with CVDRF. CVDRF such as diabetes mellitus (DM), dyslipidemia, hypertension and obesity strongly associate to endothelial dysfunction, which early manifests as erectile dysfunction (ED).

Methods: HCC’s samples from individuals aged 40-60 years, submitted to programmed urological surgeries at Hospital São João-Porto, were divided in three groups (n = 4): (1)-controls without ED or CVDRF; (2)-DM patients; and (3)-patients with three or more CVDRF including DM. Dual immunolabelling of SIRT3 and superoxide dismutase (SOD)2 with alpha-actin was carried out. As well, levels of SIRT1, SIRT3, SOD2, PGC1α, NADPH oxidase (Nox1), phospho-AMPK and AMPK were assessed by Western blotting (WB).

Results: We observed SIRT3 and SOD2 expression in α-actin-labelled fusiform muscle cells in all groups. The semi-quantification by WB demonstrated a significant decrease in SOD2 expression in group 3 relatively to controls, as well as, an increased tendency of Nox1 and PGC1α and a decreasing trend in phospho-AMPK in groups 2 and 3. No differences in SIRT1 and SIRT3 were observed among groups.

Conclusion: This study suggests that CVRF including DM increase oxidative stress in HCC owning to a decrease in SOD2 expression and concomitant increment in Nox1. Further studies with an increased number of HCC samples will be necessary to elucidate the role of the AMPK-PGC1α-SIRT3 signaling pathway in the response to oxidative damage.

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References