GLP-1 receptor expression in epicardial adipose tissue is associated with genes involved in fatty acid oxidation and white-to-brown fat differentiation

Elena Dozio1, Elena Vanello2, Alexis E. Malavazos3, Lorenza Tacchini4, Gertrud Schmitz5, Gianluca Iacobellis6, Massimiliano M. Corsi Romanelli5

1Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy; Laboratory of Molecular Pathology, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy
2Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy
3High Specialty Center for Diabetology, Nutritional Education and Cardiometabolic Prevention, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy
4Institute for Clinical Chemistry and Laboratory Medicine, University of Regensburg, Regensburg, Germany
5Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, University of Miami, Miller School of Medicine, Miami, FL, USA
6Department of Biomedical Sciences for Health, Università degli Studi di Milano, Milan, Italy; Service of Laboratory Medicine - Clinical Pathology, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy

INTRODUCTION: Epicardial adipose tissue (EAT) is a risk factor for cardiovascular diseases. Glucagon-like peptide 1 analogs (GLP-1A) were reported to induce beneficial cardiovascular effects and reduce EAT, possibly through targetting GLP-1 receptor (GLP-1R). Nevertheless, the role of EAT GLP-1R, GLP-2R and their interplay with EAT genes involved in adipogenesis and fatty acid (FA) metabolism are unknown. We aimed to analyze whether EAT transcriptome is related to GLP-1R and GLP-2R gene expression, and GLP-1 and GLP-2 plasma levels in coronary artery disease patients (CAD).

METHODS: EAT was collected from 17 CAD patients undergoing coronary artery bypass grafting for microarray analysis of GLP-1R, GLP-2R and genes involved in FA metabolism and adipogenesis. EAT thickness was measured by echocardiography. GLP-1 and GLP-2 levels were quantified by enzyme-linked immunosorbent assay in CAD and healthy subjects (CTR).

RESULTS: EAT GLP-1R was directly correlated with genes promoting beta-oxidation and white-to-brown adipocyte differentiation, and inversely with pro-adipogenic genes. GLP-2R was positively correlated with genes involved in adipogenesis and lipid synthesis, and inversely with genes promoting beta-oxidation. GLP-1 and GLP-2 levels were higher in CAD than CTR and in patients with greater EAT thickness.

CONCLUSION: GLP-1 analogs may target EAT GLP-1R and therefore reduce local adipogenesis, improve fat utilization and induce brown fat differentiation. As EAT lies in direct contiguity to myocardium and coronary arteries, the beneficial effects of GLP-1 activation may extend to the heart. The increased levels of circulating GLP-1 and GLP-2 and EAT GLP-2R may be compensatory mechanisms related to CAD and also EAT expansion, but the meaning of these observations needs to be further investigated.

1. Conflict of interest: None
2. Funding: The study was supported by funding from Fondazione E. A. Fiera Internazionale di Milano to Università degli Studi di Milano and Ricerca Corrente funding from Italian Ministry of Health to IRCCS Policlinico San Donato.

Keywords: Epicardial adipose tissue, GLP-1 receptor, GLP-2 receptor, fatty acid oxidation, white-to-brown fat differentiation