The impact of fasting and postprandial blood glucose increments on atherosclerosis via lipid composition and oxidative stress in patients with type 2 diabetes mellitus and coronary heart disease

Djindjic Boris, Sokolovic Dusan, Djindjic Natasa and Sokolovic Danka
University of Nis, Serbia

Objectives: Impact of fasting and postprandial blood glucose increments on atherosclerosis through changes of apolipoproteins and oxidative stress in patients with diabetes mellitus (T2DM) and Coronary Heart Disease (CHD) was evaluated.

Methodology: Ninety T2DM patients (60 with CHD and 30 without CHD) treated with metformin and/or sulphonylureas were enrolled in cross-sectional nested case-control clinical study. The areas under the six-point daily glucose curve above the fasting glucose concentrations (AUCpp) and over 5.5 mmol/L (AUCbg) were calculated to determine postprandial (AUCpp) and fasting (AUCbg-AUCpp) glucose increments. Apolipoproteins AII and B (ApoAII and ApoB), serum lipids and malondialdehyde (MDA) were determined.

Results: AUCbg-AUCpp 58.2 (95% CI 40.6-75.8) was higher in CHD group compared to non-CHD 36.9 (95% CI 23.5-50.2) mmol*h/L. They had similar Apo AII (mean±SD) 1.630±0.69 vs. 1.55±0.55 mg/dl and Apo B 1.48±0.48 vs. 1.43±0.62 mg/dl (CHD vs. non-CHD). The MDA was significantly higher in CHD 16.47±4.5 compared to non-CHD patients 13.42±4.01 μmol/g plasma proteins. The values of PCO were similar in both groups as well as serum lipids (HDL, LDL, total cholesterol and triglycerides). AUCpp positively correlates with MDA (r=0.45) and Apo B (r=0.49) in presence of CHD, AUCbg-AUCpp negatively correlate with Apo AII (r=−0.44) in absence of CHD. The analysis revealed that AUCpp over turning point of 0 mmol*h/L was associated with high MDA and Apo B in CHD.

Conclusion: In T2DM patients with stable CHD, AUCpp at any point significantly contributes to increasing of Apo B and MDA. Serum lipids did not show significant difference according to presence of CHD.

Molecular characterization and functional properties of induced pluripotent stem cells-derived cardiomyocytes from healthy and diseased individuals. Models for investigating inherited cardiac diseases

Ofer Binah
Technion – Israel Institute of Technology, Israel

In view of the therapeutic potential of cardiomyocytes derived from human induced pluripotent stem cells (iPSC-CM), our overall goal is to investigate their molecular characteristics, functional properties related to the excitation-contraction coupling (e.g., [Ca^{2+}] handling), pacemaker function and underlying ion currents, the effects of β-adrenergic stimulation, and responsiveness to common modifiers of cardiac function (e.g. β blockers). The iPSC clones we investigate are derived from human dermal fibroblasts or hair keratinocytes, and reprogramming is accomplished by infecting the cells with four human genes: OCT4, Sox2, Klf4 and C-Myc. Our major findings show that iPSC-CM: express cardiac specific RNA and proteins; exhibit regular pacemaker activity; exhibit key features of the excitation contraction coupling machinery; respond to ryanodine and caffeine (though less than adult cardiomyocytes), and express the SR-Ca^{2+} handling proteins ryanodine receptor and calsequestrin; respond to autonomic agonists and antagonists. Hence, our work demonstrates that iPSC-CM exhibit features resembling the adult myocardium, and thus constitute a potential source for cardiac regeneration. Concomitantly, in order to decipher the pathological mechanisms of inherited cardiac arrhythmias and cardiomyopathies, we are investigating iPSC-CM generated from skin biopsies/keratinocytes obtained from patient's catecholaminergic polymorphic ventricular tachycardia (CPVT), laminopathies, WPW and Duchenne muscular dystrophy (DMD). Our research shows that the mutated iPSC-CM feature key clinical phenotype of the disease, thus establishing the foundation for developing novel drug modalities.