

Reduced HO1 and Adiponectin Levels in Diabetic Patients May Cause Vascular and Cardiac Dysfunction

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Nuclear factor Erythroid-derived 2-like 2 (Nrf2) is a transcription factor that protects cells from oxidative stress by activating protective antioxidant and detoxifying enzymes, including heme oxygenase 1 (HO1). HO1 and adiponectin are cardioprotective. Our objective was to determine the correlation between Nrf2 genes and adiponectin in visceral fat, serum inflammatory cytokines and endothelial progenitor cells (EPCs) level and function in diabetic patients undergoing coronary artery bypass grafting surgery (CABG).

Control (n=15) and diabetic (n=28) patients undergoing CABG were examined. The level of EPCs (flow cytometry) and function (colony forming units and MTT) were measured in peripheral blood before surgery. Adipose tissue was collected during surgery.

The levels of Nrf2 mRNA (quinine oxidoreductase, glutathione S-transferase and Thioredoxin1) in adipose tissue increased in the diabetic group compared with controls together with a significant decrease in HO1 and adiponectin protein expression. Higher levels of inflammatory cytokines (TNF alpha, MCP1, IL6, p<0.05) and ROS p<0.01, were found in diabetic patients. The proportion of cells co-expressing VEGFR-2, CD133, and CD34 was lower in the diabetic group, p<0.05. The viability of diabetic EPCs was lower compared to controls and correlated inversely with HbA1c levels (p<0.01).

Epicardial visceral fat adipocytes expressed elevated levels of Nrf2 genes and decreased HO1 and adiponectin suggesting that a rise in redox stress and ROS contribute to the increased in inflammatory cytokines and the impairment of EPCs functions in diabetic patients. Recruitment of HO1 and adiponectin shown to be cardioprotective in models of ischemia injury suggest that these factors play a pivotal role in cardiac and vascular protection. HO1 and adiponectin deficiency may be a factor in a weakened redox homeostasis and vasculogenesis and may serve as targets for therapeutic intervention in diabetic patients with coronary diseases.