

Selective activation and translocation of p-STAT3 and iNOS in human cardiac tissue in patients with type II diabetes mellitus after ischemia and reperfusion

The Problem

Cardiac surgery and ischemia reperfusion is more consequential in diabetic patients compared to non-diabetic patients.

The exact cellular mechanism of this effect is not known. Many kinases have been associated with ischemia reperfusion injury. Many kinases act on proteins within mitochondria by stabilizing the mitochondrial membrane and on cardiomyocytes activating pro-survival proteins in the cells. However, the upstream triggers for activation of these kinases and the sequence of their activation in multistep cascade is not clear, though several G-protein coupled receptors has been implicated.

Aim/Goal

The objective of the current study is to assess the impact of cardiopulmonary bypass and cardioplegia on activating signal transducer and activator of transcription (STAT3) and reperfusion injury salvage cascade (RISK) pathways in non-diabetic and controlled type II diabetic patients.

The activation of gp130 receptors NPY2 and NPY5 may lead to down stream activation of protective pathways, such as pSTAT3 pathway in controlled diabetic patients.

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The Interventions

Right atrial appendage was collected from patients before and after cardioplegia and cardiopulmonary bypass. The analysis was carried out on 20 patients [n=8 non-diabetic (ND), n=12 well controlled diabetes mellitus (DM)]. The tissues were analyzed for IL-6, leptin and NPY receptor regulation, the phosphorylation of STAT3, RISK and downstream pathways.

The Results

Immunoblotting revealed a significant up-regulation of leptin ob-receptors and anti-apoptotic factor BCL-2 in both diabetic and non-diabetic patients. There was significant phosphorylation of STAT3 transcription factor leading to up-regulation of iNOS, VEGF and MnSOD in both groups.

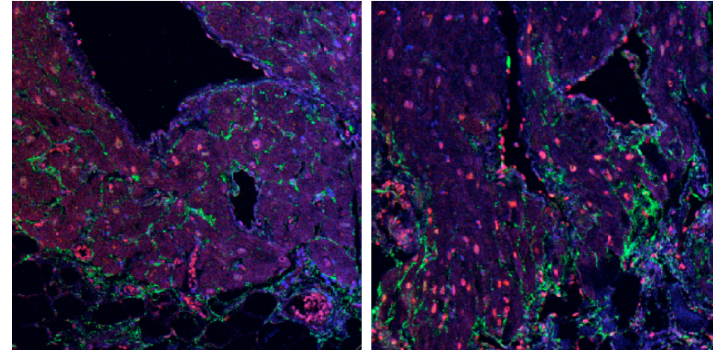


Figure 1: (Left) Immunohistochemistry slide of atrial tissue showing Pre cardioplegia and cardiopulmonary bypass expression of p-STAT3 in pink in cardiac muscle nuclei, leptin receptors (ob-r) in green. (Right) Post cardioplegia and cardiopulmonary bypass significantly increased expression of p-STAT3 and ob-r.

Lessons Learned

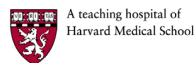
PSTAT3 and downstream pathway through gp130 receptors NPY2 and NPY5 activation leads to increased expression of cell survival proteins in controlled type II diabetes mellitus patients.

Next Steps/What Should Happen Next

- Examine and compare the activation of the pathway in non-controlled type II diabetes mellitus patients with our current data



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