„Medizinische Doktorarbeit“ in Stem Cell Biology

(Institute of Neurophysiology, Medical Faculty, University of Cologne, Germany)

Project:
Inducing signals of endogenous cardiac regenerative processes through pressure-controlled intermittent coronary sinus occlusion (PICSO) in Pork heart failure

Subject:
Test of **Porcine** blood sera **after** PICSO **treatment in acute experimental coronary occlusion** on fibroblasts and cardiomyocytes Proliferation

Description of Project:

Cardiac repair has steered clinical attention for decades and is an unmet need since available regenerative therapies lack robust mechanistic evidence. Pressure-controlled intermittent coronary sinus occlusion (PICSO) may activate endogenous regenerative processes in a failing myocardium **according to a hypothesis “embryonic recall” using a mechanochemical feedback loop. This thesis is in c**ooperation with our partner in Wien, **Animal research has been performed previously and tissue and blood samples are now available for future analysis. This is in continuation with previous joint publications:** We investigated molecular consequences of PICSO in animals with induced heart failure as well as in patients with advanced heart failure in a non-randomized controlled trial.

Technique:

PICSO is a trans-coronary sinus catheter intervention developed decades ago to prevent and treat myocardial ischemia, based on a physiologically adapted alternative to the concept of retroperfusion and early clinical experience gathered with the Beck´s procedure. The intermittent occlusion of the main coronary venous drainage system redirects blood flow towards ischemic areas and subsequent washout clears the ischemic and reperfused microcirculation potentially inducing salvage.
The interventional technology is based on a simple venous catheterization accessing the coronary sinus and temporarily occluding the coronary venous outflow. Whereas sensing the systolic pressure peaks via mechano-sensation and transduction is believed to be the source of the activation of the cytoskeleton of endothelial and perivascular cells, the periodic action of coronary sinus occlusion is necessary to achieve optimal effectiveness. The mechanochemical feedback loop acting in the coronary venous circulation is estimated to induce a pattern of micro RNA normally functioning in cardiac development inducing a

chain of regenerative steps in the adult heart. Normally PICSO needs five to 20 heartbeats according to the amount of cardio venous flow to reach a systolic pressure plateau indicative for a complete filling of the cardio venous compartment and therefore the time to permit normal drainage (see Figure 1).

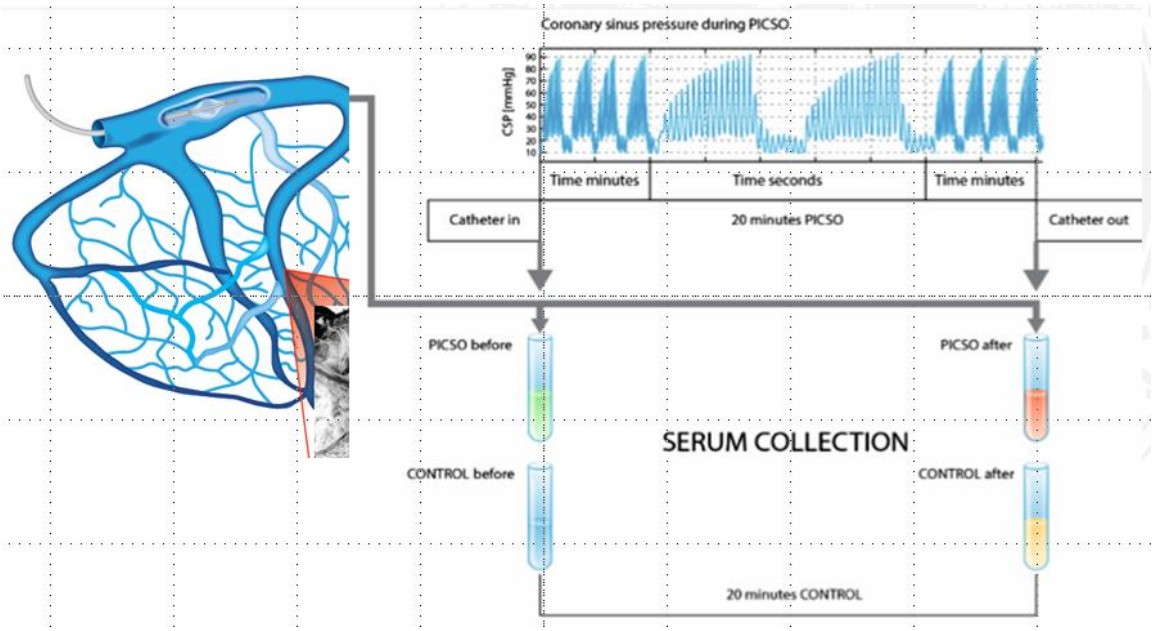

Figure 1: Study protocol and serum collection. After advancement of a coronary sinus catheter and temporary pressure controlled occlusion (PICSO) of a major portion of outflow from coronary veins pressures are increased, systolic pressures peaks are thought to be the driving force to activate venous endothelium. Serum was collected pre and post intervention or from the coronary sinus and immediately frozen to -80.

Our group is engaged in the exploration of mechanisms involved in cardiac repair and regeneration after PICSO by using several techniques including cell and molecular biology (e.g: Affymetrix Microarray Technology) associated to immunohistochemistry, electrophysiological and imaging techniques. The objective of this work is to decipher molecular pathways of regeneration.

Working language: English and German.

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