Mitochondrial Function In Post-Angioplasty Intimal Hyperplasia And Hypoxia.

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Introduction:

Intimal hyperplasia (IH) is a complication of coronary intervention. Intimal injury happens after balloon angioplasty. This leads to neo-intimal formation which increases in thickness. This leads to further complications of restenosis, atherosclerosis and thrombosis. The thick intimal layer creates regions of hypoxia in the layers of the vessel. The aim of the study was to investigate the mitochondrial function in the IH.

Hypothesis:

Intimal hyperplasia following coronary intervention compromises the oxygen flow leading to hypoxia with altered mitochondrial function

Methods:

Female Yucatan swine were recruited to study. The study protocol was approved by the Institutional Animal Care and Use Committee (IACUC). High fat (45%) and high fructose diet (20%) was given to the swine. The swine were placed on the diet for around a period of 12 months. Coronary intervention was done on these swine. Angioplasty was performed on the coronary arteries. These swine were euthanized after 5-8 months of performing angioplasty on them. The normal swine was recruited into study at 6-7 weeks of age. Experimental diet was initiated and the swine was euthanized at 17-20 weeks. Histology of the Coronary vasculature is studied. The Vascular smooth muscle cells were obtained from the swine and cultured in the lab. Mitochondrial marker- Peroxisome proliferator-activates receptor γ coactivator (PGC1α) which is the key regulator for mitochondrial biogenesis is studied in the cells after induction of hypoxia in the hypoxia inducing chamber.

Results:

The results show that there is a significant decrease in the expression of mitochondrial biogenesis marker, PGC-1α in swine with IH ($p=0.006$: 95%CI: -48.8 to -27.4). PGC-1α expression was also decreased under influence of hypoxia to VSMCs ($p=0.03$, 95%CI: 4.6 to 110.3). Hypoxia significantly elevated reactive oxygen species (ROS) levels expression ($p=0.0001$, 95% CI: -157.48 to -136.9)

Conclusion:

These findings demonstrate that there could be an association between decreased expression of mitochondrial biogenesis marker PGC-1α with IH. Hypoxia induced decrease in PGC-1α expression and increased ROS expression could be associated with IH in coronary artery.

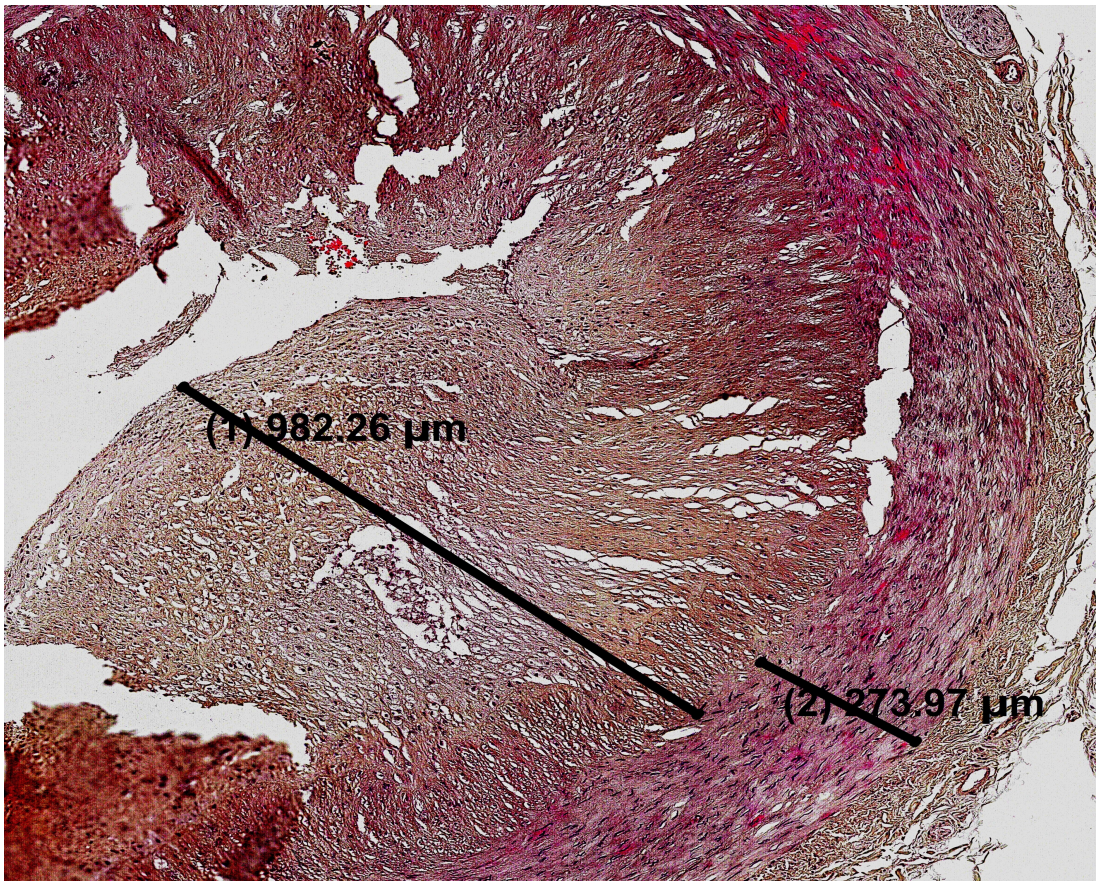
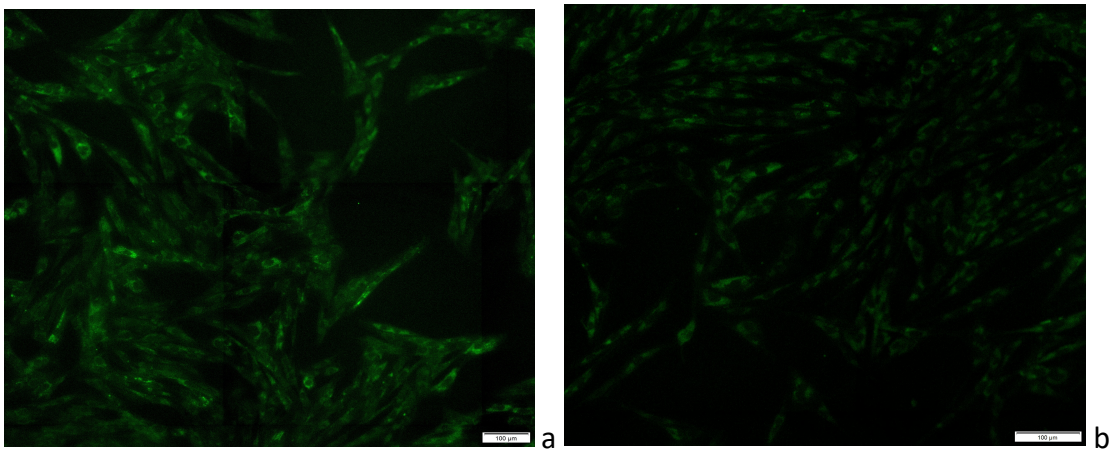


Figure 1. Coronary section showing Intimal Hyperplasia.



a b

Figure 2. Showing decreased expression of PGC-1 α in VSMCs under hypoxia in Fig. b compared to Normoxia Fig. a.