Smoking and Diabetes Mellitus alter in vitro contractility of vascular smooth muscle cells derived from abdominal aortic aneurysm patients

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Introduction: Abdominal aortic aneurysms (AAA) are defined as a progressive weakening of the aortic wall, leading to gradual dilatation. Risk factors for AAA include aging, male sex and smoking. In contrast, there is a negative association between patients with diabetes mellitus (DM) and AAA development. We hypothesize that dysfunction of vascular smooth muscle cells (vSMC), the major cell type within the aortic wall, plays a paramount role in AAA pathophysiology. The aim of this study is to investigate the in vitro contractility of human AAA vSMC compared to non-pathologic vSMC, and correlate these findings to risk factors of the patients.

Methods: vSMC were isolated from aortic tissue obtained during open aneurysm repair from AAA patients. vSMC isolated from AAA patients (n=29) and controls (n=10, vSMC derived from non-dilated aortas of post-mortal kidney transplant donors) were included. Contractility was measured using Electric Cell-substrate Impedance Sensor (ECIS). ECIS is a technique used to quantify adherent cell behavior in real time, by generating an impedance value based on the coverage of electrodes embedded in a cell culture plate. Contractility can then be measured as a factor of change of the surface covered by the cells. vSMC were stimulated with ionomycin (Ca²⁺ ionophore which induces a contractile response in adherent vSMC induced by the influx of extracellular Ca²⁺) after 48 hours.

Results: vSMC contractility of AAA patients showed more variability compared to control vSMC. To define the normal vSMC contractility range, mean contractility including ±2 standard deviations (2SD) of the control cell lines was determined (83.51% ± 5.38%). We divided the AAA patients’ vSMC into subgroups based on their clinical characteristics focused on known risk factors for AAA (gender, BMI, smoking, DM), and especially looked at patients with vSMC contractility ±2SD of mean control vSMC contractility. Using this approach, we identified two groups of patients with altered vSMC contractility: smoking patients whose vSMC contract below the 2SD range of the controls (Smoking: median response: 79%, range: 67-91% vs. not smoking: median response: 87%, range: 71-95%, p = 0.13) and patients with DM whose vSMC contract above the 2SD range of the control contractility (DM: median response: 93%, range: 88-95% vs. no DM: median response: 83%, range: 67-91%, p = 0.013).

Conclusion: vSMC contractility is affected in certain clinically relevant subgroups of AAA patients and might therefore play a role in AAA pathophysiology. The mechanism behind this clinical correlation is still unclear and therefore we aim to tackle the underlying mechanism behind altered vSMC contractility by looking at proteins and pathways involved in the contractile cascade.