Calcium signalling in the human coronary microcirculation

Here we characterize the profile of Ca^{2+} signalling in response to pharmacological and physiological agonists in small arteries dissected from the right atrial appendage of patients undergoing elective surgery. Arterial segments (<200 μm in diameter) were either cannulated and pressurised or pinned in a chamber and in each case loaded with the calcium-sensitive indicator Cal-520 AM. Arteries were imaged using confocal microscopy and changes in smooth muscle cell (SMC) and endothelial (EC) Ca^{2+} simultaneously imaged at high frequency (30 Hz). SMCs generated spontaneous, localized Ca^{2+} events (Ca^{2+} sparks), which were potentiated by the opener of ryanodine receptors, caffeine (0.1 mM, n=5). At 0.5 mM, caffeine produced global Ca^{2+} oscillations (0.05 Hz, n=5) without affecting endothelial cell Ca^{2+}. High-K^+ (45 mM) induced homogenous increases in Ca^{2+} in all SMCs (n=3), consistent with the presence of voltage-dependent Ca^{2+} channels. Arterial SMCs were insensitive to the α_1-adrenoreceptor agonist phenylephrine (10 μM) but responded to the muscarinic agonist acetylcholine (0.1-1 μM) with an initial Ca^{2+} spike, seen as an intracellular propagating Ca^{2+} wave, followed by a plateau component superimposed by irregular Ca^{2+} oscillations. The frequency of ACh-induced Ca^{2+} oscillations was 0.09 ± 0.01 Hz in arteries ~100-200 μm in diameter and in smaller arterioles (<25 μm) 0.17 ± 0.02 Hz (n=3). Despite also stimulating Ca^{2+} oscillations in ECs (n=5), the only functional effect of ACh was vasoconstriction. In contrast, bradykinin (10 nM) stimulated Ca^{2+} oscillations only in ECs and vasodilation (n=5). Imaging both SMC and EC Ca^{2+} provides a method to characterize the receptor distribution in the human coronary microcirculation and potentially link this to functional responses. The challenge is to try to assess how these vessels from patients with coronary heart disease compare to healthy tissue.