Inflammation and clotting abnormality in aneurysmal coronary artery disease

Coronary artery aneurysms and ectasia (CAEA) are defined as localized or diffuse coronary artery dilations that exceed diameter of the adjacent segment by at least 50%. CAEA are present in ≈2-5% of all-comer patients undergoing coronary angiography (CAG). They may cause both chronic myocardial ischemia and acute coronary syndromes (ACS).

Some, but not all, CAEA are associated with adjacent coronary artery stenosis, and the atherosclerotic obstructive coronary artery disease (O-CAD) may partly contribute to the increased clinical risk in relation to CAEA. There is circumstantial, indirect evidence that CAEA may be associated with a prothrombotic state. Recent studies patients showed a major adverse cardiovascular event rate of over 10% per year. CAEA presence markedly increases the risk of an acute myocardial infarction (AMI) in comparison to CAEA-free patients with OCAD; there is also a greater risk of developing another cardiac event afterwards. Mechanisms underlying these prothrombotic tendencies in CAEA remain undetermined. In a recent computed tomography angiography study, clinically silent intraluminal thrombus was present in some 60% of CAEAs; this is in contrast to the aneurysmatic disease of the aorta (AAA) that shows a higher (up to 90-100%) incidence of perimural thrombus. Indeed, the AAA disease is known to be associated with a prothrombotic state manifested by significantly altered fibrin clot properties. The fibrinogen level, that is usually increased in CAEA, is the key factor determining fibrin clot properties. Increased fibrinogen and/or thrombin concentration may be related to a more compact and resistant to lysis thrombus structure. Such clot phenotype has been postulated to be a risk factor of thrombosis. In the Project we will analysis if CAEA are related to a prothrombotic state in relation to unfavorably modified fibrin properties. Another key research line in the study is inflammation in relation to CAEA. Several lines of data suggest potential relationships between inflammation and CAEA. In addition, there is recent, unquestionable evidence for the role of inflammation in atherosclerosis (CANTOS trial). In addition, coagulation and inflammation are intricately related processes that exhibit crosstalk at numerous levels. Inflammatory mechanisms shift the haemostatic balance to favor the activation of coagulation, clotting can increase the inflammatory response causing a vicious cycle. The oxidative stress is postulated as a factor that promotes fibrinogen oxidation leading to fibrinogen secondary structure modifications that make it more resistant to lysis. Oxidative stress activity has been suggested to be increased in CAEA patients. In the Project we will analysis if 8-isoprostane, the established oxidative stress maker, levels are increased in CAEA patients in relation altered fibrin clot properties. Interestingly, some studies suggest that the chronic inflammation process in CAEA patients with is different, and it may be significantly more severe, than the one in O-CAD. Some inflammation markers correlate both with the number of CAEA-affected coronary vessels and/or a slow coronary flow. Similar relationship has been recently postulated for metaloproteinase-3 (MMP-3). This Project will investigate relationships between MMPs and several other inflammatory molecules levels with the CAEA volume using a novel, accurate and feasible for routine use, tool that we have recently introduced.

This Project addresses an issue with major implications to human health. A prothrombotic clot phenotype has been implicated in CAEA in absence of any systematic research data. In particular, today there is no consensus among physicians regarding antiplatelet and oral anticoagulation therapy in CAEA patients.