P27 OXIDATION OF LDL BY FERRITIN IN LYSOSOMES INCREASES OXIDATIVE STRESS IN MACROPHAGES

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We have shown previously that LDL can be oxidised by iron in the lysosomes of macrophages. Some of the iron in lysosomes might be delivered to them by the autophagy of ferritin, the main iron-storage protein in the body. Ferritin oxidises LDL at lysosomal pH (pH 4.5) much faster than at pH 7.4. We have now investigated the effects of LDL oxidation by ferritin in lysosomes on macrophage function. Lysosomal lipid peroxidation was measured in human THP-1 macrophage-like cells by flow cytometry using the lysosome-targeted probe Foam-LPO. Pre-incubating the cells with ferritin for 24 h, to allow its endocytosis and delivery to lysosomes, followed by treatment with LDL or LDL aggregated by sphingomyelinase caused a significant increase in lysosomal lipid peroxidation compared to cells that were not pre-incubated with ferritin. LDL oxidised by ferritin at pH 4.5 and then incubated with cells increased the formation of intracellular reactive oxygen species, measured by microscopy using the fluorescent probe dihydroethidium. The reactive oxygen species were reduced considerably by the antioxidant cysteamine. Incubation of cells with ferritin-oxidised LDL increased apoptosis, measured using annexin V and propidium iodide. These results suggest that ferritin can increase oxidative stress in lysosomes and that LDL oxidised by ferritin in lysosomes, if released from dead macrophages, might cause apoptosis in neighbouring macrophages.

We thank Tertiary Education Trust Fund (TETFund) for supporting this work.

P28 DOES MILD CORONARY ARTERY ATHEROSCLEROSIS PROGRESS AT SERIAL ANGIOGRAPHY?

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Serial Angiography?

Methodology: Coronary angiography records of >25,000 patients over a 10-year period were reviewed. We identified those with a repeat angiogram >1 year after the first, whose baseline angiography showed >1 coronary segment categorised as mildly diseased, and <5 mild disease in other segments. Demographics and risk factors for CAD were recorded. Angiograms were reassessed by a panel of cardiologists, in 13 segments, categorising each into normal (0% stenosis, score 0); mildly (1-49%, 1), moderately (50-74%, 2), or severely diseased (75-99%, 3) or totally occluded (100%, 4).

Results: We identified 86 patients (53 males, 33 females; mean ± SD age 60.7±9.1 years), yielding 1118 coronary segments for analysis. Time to follow-up angiography was 4.0±1.8 years. 29% mild CAD segments were seen at baseline (26%). Patient aggregate scores increased from yielding 1118 coronary segments for analysis. Time to follow-up angiography was 4.0 years.

Summary: Mild CAD progresses modestly over four years; in this cohort, 29% of cases became moderate and 4.7% severe.

Acknowledgements: This work was funded by the Wellcome Trust (104492/Z/14/Z) and supported by the Cambridge NHMRC Biomedical Research Centre and the Cambridge BHF Centre for Cardiovascular Research Excellence.

Rationale: Dysregulated inflammation post myocardial infarction (MI) hinders myocardial salvage and the recovery of left ventricular function after percutaneous coronary intervention.

Methods: We previously confirmed that 48Ga-DOTATATE, a somatostatin receptor subtype-2 positron emission tomography (PET) ligand, could accurately identify pro-inflammatory macrophages within atherosclerotic plaques. Here, we tested the hypothesis that 48Ga-DOTATATE could also detect persistent post-infarct myocardial inflammation. Patients with MI within 3 months (n=6), and patients with a remote history of MI (n=6), underwent 48Ga-DOTATATE and 18F-fluorodeoxyglucose (FDG) PET imaging as previously described (1).

Poster Presentations