BS12 IGM AND IGG ANTI-OXIDISED LOW-DENSITY LIPOPROTEIN ANTIBODIES PREDICT PROTECTIVE ATHEROSCLEROTIC CHARACTERSTICS ON CARDIAC CT: A SUBSTUDY OF THE SCOTTISH COMPUTED TOMOGRAPHY OF THE HEART (SCOT-HEART) TRIAL

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Background CT coronary angiography (CTCA)-derived low attenuation plaque has recently been identified as the strongest predictor of future myocardial infarction. Antibodies against oxidized low-density lipoprotein (oxLDL)/ malondialdehyde-modified LDL (MDA-LDL) are related to freedom from cardiovascular events.

Objectives To investigate possible relationships between CTCA-derived atherosclerotic plaque subtypes and anti-oxLDL antibodies.

Methods In a post-hoc analysis of the multicentre randomised controlled SCOT-HEART trial (Scottish COmputed Tomography of the HEART), we investigated the association between quantitatively assessed atherosclerotic plaque types on CTCA and IgM/ IgG anti-MDA-LDL or oxLDL. Serological biomarkers were measured using laboratory-developed enzyme-linked immunosorbent assays, and assessed versus imaging parameters.

Results In 830 patients (52.8% male, 57.6±9.8 years), IgM anti-MDA-LDL was significantly inversely associated with coronary artery calcium score (p=0.0099) and obstructive coronary artery disease (OR 0.63 ([95% CI, 0.42-0.95], p=0.028). IgG anti-MDA-LDL strongly indicated protection from greater number of obstructed coronary arteries (OR 0.20 [95% CI 0.07-0.62], p=0.0048). Increasing tertiles of IgG anti-MDA-LDL related to less low attenuation plaque (p value for trend; unadjusted, p=0.021; adjusted for cardiovascular risk score, p=0.023). When using a predefined threshold of low attenuation plaque burden >4%, the highest tertile of IgG anti-MDA-LDL was significantly associated with low attenuation plaque at a threshold that confers a reduced likelihood of fatal or non-fatal myocardial infarction, withstanding adjustment for cardiovascular risk score (OR 0.58 [95% CI 0.34-0.96], p=0.037), p=0.027 for trend.

Conclusions Both IgM and IgG anti-MDA-LDL antibodies are associated with protection from various atherosclerotic plaque characteristics. For the first time we provide evidence linking IgG anti-MDA-LDL antibodies with protection from low attenuation plaque, which is the strongest predictor of future fatal and non-fatal myocardial infarction.

Conflict of Interest None

BS13 INTRAVITAL INVESTIGATIONS OF THE ROLE OF IL-36 IN MEDIATING AGE AND GENDER SPECIFIC CHANGES IN THE INJURED BEATING CORONARY MICROCIRCULATION

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Introduction Whilst blood flow restoration is critical following myocardial infarction (MI), ischemia-reperfusion injury (IRI) accounts for ~50% of the final infarct size. We have previously shown intravitally that myocardial IRI induces thromboinflammation and reduces functional capillary density (FCD) in adult mouse beating heart microcirculation in vivo. [1] The newly discovered and inflammatory cytokine, interleukin-36 (IL-36), could potentially mediate these disturbances. However, its role in myocardial IRI is not known. This study aimed to determine whether coronary microcirculatory disturbances and infarct size post-IRI were modified by age and gender. Secondly, we investigated if IL-36 (α/β) and its receptor (IL-36R) were present in the heart, and whether their expression varied in an injury and age-related manner. Lastly, we investigated whether an IL-36 receptor antagonist (IL-36Ra) could confer vasculoprotection and reduce myocardial infarction.

Methods Myocardial IRI was induced in adult (3-months) and aged (>18-months) female mice, with gender differences assessed in adult male and female mice. Beating heart coronary microcirculation was imaged intravitally and also ex vivo using multiphoton microscopy. IL-36R/α/β, and VCAM-1 expression were investigated immunohistochemically or using western blots. In some studies, recombinant mouse IL-36Ra (15ug/mouse) was injected intra-arterially at 5 minutes pre-reperfusion and 60 minutes post-reperfusion. Infarct size was measured using dual TTC/Evans Blue staining.

Results Significantly increased basal (p<0.0001) and IRI-induced (p<0.0001) neutrophil recruitment, and greater decreases in FCD, was observed in aged mice compared to adults. Neutrophils primarily adhered within coronary capillaries although in aged hearts remarkable venular adhesion was also identified. These events were mirrored in deeper myocardial layers when imaged using multiphoton microscopy. Interesting gender-dependent perturbations were noted. Neutrophil recruitment dominated in injured female hearts whilst male hearts demonstrated a greater presence of occlusive platelet microthrombi. IL-36R/α/β were expressed predominantly on vasculature of murine hearts, with cardiomyocyte and intercalated disc expression being observed. Expression of IL-36R/α/β and VCAM-1 significantly increased with injury and age (see table 1). Interestingly, increased injury and age- related vascular expression of IL-36R/α/ß was observed specifically on micro- and not macro-vessels. IL-36Ra significantly reduced inflammation (p<0.0001) and infarct size (p<0.0001) in both adult and aged mice.

Conclusion Our novel findings of enhanced coronary microcirculatory perturbations associated with age may explain the poorer outcomes in elderly MI patients. Furthermore, the cellular nature of the thromboinflammatory response may explain the gender-related differences in outcome after MI. Importantly, we are the first to demonstrate that targeting IL-36 may be a potential novel therapy for treatment of myocardial IRI.

Conflict of Interest No

Abstract BS13 Table 1

	Young sham vs Young IRI	Young sham vs Aged sham	Young IRI vs Aged IRI	Aged sham vs Aged IRI
IL-36	**	****	****	*
Il-36	**	****	***	*
IL-36R	*	****	****	-
VCAM-1	**	****	*	*

*p<0.05; **p<0.01; ***p<0.001; ****p<0.0001 when compared using an unpaired student t-test; N=4 mice for each group.

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