Background Arterial 18F-sodium fluoride (18F-NaF) activity on positron emission tomography (PET) is a marker of active microcalcification and atherosclerosis. Coronary 18F-NaF activity (CMA) predicts coronary artery disease progression and subsequent myocardial infarction. We aimed to investigate whether aortic 18F-NaF activity (AMA) predicts thoracic aortic atherosclerotic disease progression and subsequent ischaemic stroke in patients with established cardiovascular disease.

Methods In a post-hoc observational cohort study, we evaluated AMA in patients with stable coronary artery disease (n=239) or aortic stenosis (n=158) who had underwent thoracic 18F-NaF PET and computed tomography (CT). We assessed the associations between AMA and progression of thoracic aortic calcification on follow up CT and subsequent ischaemic stroke or myocardial infarction.

Results In 141 patients with repeat CT imaging at 12.7±2.7 months, AMA correlated with progression of thoracic aortic calcium scores (r=0.21, p=0.011). In 397 patients, 16 had an ischaemic stroke and 25 had a myocardial infarction after 4.7±1.6 years. After adjusting for clinical risk factors, CMA and calcium scoring, AMA was associated with stroke (hazard ratio, 1.71 [95% confidence interval 1.00-2.90], p=0.048). AMA was superior to clinical risk and calcium scores in identifying patients with stroke (c-statistic 0.76 versus 0.58 versus 0.63 respectively, p<0.05). Survival analysis demonstrated that AMA was associated with ischaemic stroke (p<0.001) but not myocardial infarction (p=0.45), whereas CMA was associated with myocardial infarction (p<0.001) but not stroke (p=0.39).

Conclusions In patients with established cardiovascular disease, AMA is associated with progression of aortic atherosclerosis and future ischaemic stroke. Arterial 18F-NaF identifies localised areas of atherosclerotic disease activity that relate to regional atherothrombotic events.

Conflict of Interest None to declare.

Introduction Atherosclerosis is an insidious disease where the accumulation of low-density lipoprotein in the arterial walls generates plaques, which may rupture leading to an untimely death or loss of quality of life. A key barrier for the treatment of atherosclerosis is identifying and predicting those plaques which are most vulnerable to rupture. This project aimed to bridge this diagnostic gap by using monoclonal antibodies for targeted imaging of malondialdehyde-low density lipoprotein (MDA-LDL), a component of vulnerable plaques.

Method A humanised monoclonal antibody (LO1-huFab) was expressed in human embryonic kidney cells (HEK)-293 cells with an unpaired sulphydryl group for site-specific maleimide conjugation. The purified protein was site-specifically conjugated to a near-infrared fluorophore (LO1-huFab-750) and co-injected with fluorophores targeting matrix metalloproteinases (MMPSense) and integrin a5b3 (IntegrinSense). Non-invasive fluorescence molecular tomography imaging was
performed four hours post-injection with the amount of the
three different tracers in the aortic arch quantified.

Results LO1-huFab demonstrated in vivo targeting in LDLR--
mouse model with the ability to distinguish animals with and
without disease (63.16 ± 12.64 pmol vs 23.92 ± 4.35 pmol,
p=0.045, n=4 per group). Multiplexing with MMPSense and
IntegriSense revealed LO1-huFab-750 to be the first probe to
distinguish between disease states. Ex vivo fluorescence reflect-
tance imaging validated the focal signal of LO1-huFab-750
observed in the aortic root and abdominal aorta. Rapid clear-
ance of LO1-huFab-750 through the glomerular filtration
system was evident through ex vivo quantification of fluo-
rescence in the kidneys.

Conclusion Site-specific near-infrared labeling of antibodies
allowed for non-invasive imaging of atherosclerosis demon-
strating its potential in identifying critical components of vul-
nerable plaques. These promising results have prompted the
conjugation of LO1 antibody fragments with nanoparticles for
targeted therapeutics of atherosclerosis.

Conflict of Interest N/A

Background Uraemic cardiomyopathy is present in >70% of
patients with end-stage renal disease (ESRD). Myocardial fia-
rosis is a hallmark of uraemic cardiomyopathy and is associ-
ated with an increased risk of heart failure and sudden
cardiac death. Coronary microvascular dysfunction (CMD) is
common in ESRD and is an adverse prognostic marker that
may contribute to this increased mortality. In hypertrophic car-
diomyopathy (HCM), a condition that shares phenotypical
similarities with uraemic cardiomyopathy including hypertro-
phy, cellular disarray and fibrosis, a negative correlation exists
between myocardial fibrosis and CMD, raising the possibility
that fibrosis is the result of microvascular ischaemia. This
study aimed to determine whether a similar relationship exists
in ESRD.

Methods 15 patients with ESRD underwent transthoracic echo-
cardiography, coronary flow velocity reserve (CFVR) assess-
ment by Doppler echocardiography and 3Tesla cardiac
magnetic resonance imaging. Subjects with known coronary
t coronary artery disease, moderate/severe valvular heart disease, diabetes