18F-Sodium fluoride positron emission tomography, aortic disease activity and ischaemic stroke risk

A. Fletcher[1], E. Tzolos[1], S. Joshi[1], J. Kwiecinski[1], R. Bing[1], M.K. Doris[1], A.J. Moss[1], E.J. Van Beek[2], N. Joshi[3], P. Adamson[4], W. Whiteley[5], J. Wardlaw[5], P. Slomka[6], D.E. Newby[1], M.R. Dweck[1]

[1]University of Edinburgh, Edinburgh, United Kingdom; [2]Queen's Medical Research Institute, Edinburgh Imaging Facility, Edinburgh, United Kingdom; [3]Bristol Heart Institute, Bristol, United Kingdom; [4]University of Otago Christchurch, Christchurch Heart Institute, Christchurch, New Zealand; [5]University of Edinburgh, Centre for Clinical Brain Science, Edinburgh, United Kingdom; [6]Cedars-Sinai Medical Center, Department of Imaging (Division of Nuclear Cardiology), Los Angeles, United States of America

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.

Objective: To investigate whether aortic 18F-NaF activity (AMA) predicts thoracic aortic atherosclerotic disease progression and subsequent ischaemic stroke or myocardial infarction in patients with established cardiovascular disease.

Methods: In a post-hoc observational cohort study, we evaluated AMA and CMA 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 or CMA and progression of calcified atherosclerotic plaque in both thoracic aortic and coronary territories on follow up CT, as well as subsequent ischaemic stroke or myocardial infarction.

Results: In 141 and 231 patients with repeat aortic and coronary CT imaging respectively at 12.7±2.7 months, AMA correlated with log progression of thoracic aortic calcium scores (r=0.21, p=0.011), volume (r=0.29, p<0.01) and mass (r=0.29, P<0.01) as well as log coronary calcium score progression (r=0.21, p=0.03). CMA correlated with log coronary (r=0.42, p<0.01), but not log aortic (p>0.80) calcium score progression. 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.
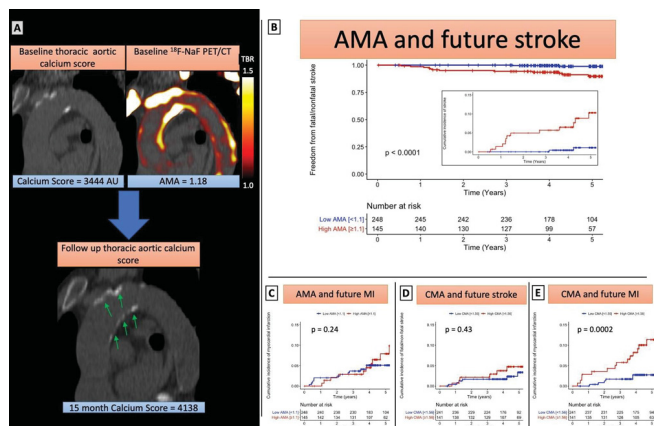
AMA, disease progression and outcomes

	No Stroke (n=381)	Stroke (n=16)	p-value
Clinical Factors			
Revised Framingham 10-year stroke risk (%)	15±9	17±8	0.37
Age (years)	69.6±8.4	71.4±7.4	0.41
Male Sex	308 (80)	15 (93)	0.313
Atrial fibrillation	17 (4.5)	1 (6.2)	1.00
Diabetes	74 (19.4)	3 (18.8)	1.00
Systolic blood pressure (mmHg)	146±19	149±24	0.56
Hypertension medication	345 (90.6)	12 (75.0)	0.11
Current smoker	45 (11.8)	2 (12.5)	1.00
Antiplatelet therapy	297 (78.0)	15 (93.8)	0.22
Anticoagulation therapy	26 (6.8)	2 (12.5)	0.72
Imaging Biomarkers			
Aortic microcalcification activity	1.08±0.09	1.14±0.04	<0.001
Ascending aorta	1.06±0.08	1.12±0.04	<0.001
Aortic arch	1.12±0.12	1.19±0.07	0.002
Thoracic Aortic calcium score (AU)	209 [13 - 866]	583 [276 - 948]	0.09
Ascending calcium score (AU)	0 [0 - 0]	0 [0 - 26]	0.14
Arch calcium score (AU)	207 [11 - 838]	531 [183 - 880]	0.28
Thoracic Aortic calcium volume (AU)	647 [80 - 2292]	1578 [695 - 2496]	0.10
Ascending calcium volume (AU)	0 [0 - 0]	0 [0 - 97]	0.16
Arch calcium volume (AU)	638 [73 - 2150]	1322 [534 - 2356]	0.28
Thoracic Aortic calcium mass (AU)	561 [54 - 2544]	1917 [755 - 2442]	0.09
Ascending calcium mass (AU)	0 [0 - 0]	0 [0 - 74]	0.16
Arch calcium mass (AU)	542 [53 - 2468]	1578 [545 - 2281]	0.25
Coronary microcalcification activity	0.60 [0 - 2.79]	1.4 [0 - 3.72]	0.36
Coronary calcium score (AU)	452 [112 - 1075]	1057 [197 - 1888]	0.15

AU, Agatston Units
n (%); mean ± standard deviation; median [interquartile interval]

Variables associated with stroke