(NT-proBNP) protein was higher in patients with than in those without AF (6.23 ± 0.62 vs 4.72 ± 0.33 , $p = 0.012$, $n = 176$). We also performed an exploratory analysis only in patients without signs of coronary artery disease on CTCA (AF=27, SR=80). In this subgroup, NT-proBNP (6.478 ± 0.8442 vs 4.554 ± 0.4122 , $p = 0.023^*$), BNP (1.111 ± 0.083 vs 0.9713 ± 0.029 , $p = 0.0175^*$), Stem Cell Factor (SCF, 162.8 ± 7.860 vs 140.4 ± 5.127 , $p = 0.0097^{**}$) and VEGF-D (47.44 ± 2.708 vs 41.38 ± 1.694 , $p = 0.0389^*$) were higher in the 27 patients with AF.

Conclusion While NT-proBNP is mostly known as a marker for heart failure, NT-proBNP appears as a potential blood marker for AF in patients without history of stroke, hypertension, diabetes or heart failure. Further validation of these initial, hypothesis-generating results seems warranted.

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THE RELATIONSHIP BETWEEN CAROTID ARTERY INTIMAL-MEDIAL THICKNESS AND LEFT VENTRICULAR FUNCTION BY SPECKLE TRACKING ECHOCARDIOGRAPHY IN PATIENTS WITH CORONARY ARTERY DISEASE

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Background and aim of the work Since cardiovascular diseases are associated with high mortality and generally undiagnosed before the onset of clinical findings, there is a need for a reliable tool for early diagnosis. Carotid intima-media thickness (CIMT) is a non-invasive marker of coronary artery disease (CAD) and is widely used in practice as an inexpensive, reliable method. Left ventricular (LV) function can be accurately assessed by 2D speckle-tracking strain echocardiography (2D-STE). In our study, we aimed to investigate the relationship of CIMT and LV function assessed by 2D-STE in patients with stable (CAD) and the ability of 2D-STE and CIMT to predict significant CAD.

Methods Cross sectional study included 40 patients with history suspected stable angina pectoris, normal LV ejection fraction. All patients were examined by 2D-STE, carotid ultrasound, and coronary angiography (CA). 2D-STE was performed in the 3 apical projections. Peak regional longitudinal systolic strain was measured in 17 myocardial segments and averaged to provide global longitudinal peak systolic strain (GLS). LVGLS results were compared with CA findings in a receiver operating curve (ROC) to determine the cut-off for normal and abnormal strain values. The calculated optimal strain value was compared to mean CIMT measurements. The patients were divided into two groups according to the result of the CA: group 1 (29 patients) with significant coronary lesion $> 70\%$, and group 2 (11 patients) having at least one lesion more than 50% within the main branches of the coronary arteries.

Results GLS was significantly lower in patients with CAD+ (group 1) compared to patients without CAD- (group 2) [$-11.86 \pm 2.89\%$ versus $-18.65 \pm 0.79\%$] $P < 0.001$. ROC curve between GLS and CA showed cut-off value for LVGLS was less than -15.6% for prediction of significant CAD with AUC = 0.878; 95% CI 0.78–0.96 $p = 0.00$. The diagnostic performance of GLS for detecting severity of CAD was [sensitivity 93.1%, specificity 81.8% and accuracy 90%]. The mean

CIMT was 1.49 ± 0.35 mm in group 1, vs 0.75 ± 0.3 mm in group (2) ($p = 0.000$). ROC curve between mean CIMT and CA showed cutoff value for mean CIMT was > 1.1 mm for prediction of significant CAD with AUC= 0.871 (95% CI 0.79–0.97, $p = 0.00$). There was a significant, nearly linear correlation between IMT and GLS and advancing CAD ($p = 0.00$), as there was incremental significant increase in CIMT and decrease of GLS with increasing number of coronary vessels involved. Further analyses showed that GLS was highly significant negatively correlated with mean CIMT.

Conclusion GLS assessed by 2DSTE at rest was predictor of significant CAD; So 2DSE seems capable of identifying high-risk patients. Increased carotid IMT values were associated with decreased LV function assessed by 2D strain measurements and the presence and severity of CAD. So these findings support the use of carotid IMT measurements as marker of subclinical LV dysfunction and to predict risk and severity of coronary heart disease.

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HIGHLY SELECTIVE TROPONIN T (HSTNT) AND HEART-TYPE FATTY ACID-BINDING PROTEIN (H-FABP) AS MARKERS OF TYPE 4A MYOCARDIAL INFARCTION AND ADVERSE EVENTS IN ELECTIVE PERCUTANEOUS CORONARY INTERVENTION (PCI)

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Introduction Heart-type Fatty Acid-Binding Protein (H-FABP) may be useful for early diagnosis of ACS1,2 and has been associated with increased cardiovascular events. Type 4a procedural myocardial infarction (MI) may occur after percutaneous coronary intervention (PCI).³ Little is known about the use of early biomarkers as predictors of cardiovascular events following elective PCI.

Methods We prospectively evaluated highly sensitive troponin T (hsTnT), H-FABP, troponin I (TnI), creatine kinase MB type (CKMB), myoglobin, glycogen phosphorylase BB (GPBB) and carbonic anhydrase III (CAIII) at 0, 4, 6 and 24 h following elective PCI. Baseline demographic and cardiac risk factors were recorded. The primary endpoint was type 4a MI, diagnosed as a rise of $> 5 \times 99^{\text{th}}$ upper reference limit (URL) of 14 ng/L (i.e. rise of > 70 ng/L) at 6 h if hsTnT was normal at baseline or $> 20\%$ from 0 to 6 hrs if hsTnT was > 14 ng/L at baseline.³ Patients were followed up at 1 year to assess for

Median hsTnT release in type 4a MI and no type 4a MI

Abstract 219 Figure 1 hsTnT release between type 4a MI ($n = 37$) and no type 4a MI ($n = 172$)

Median H-FABP release in type 4a MI and no type 4a MI

Abstract 219 Figure 2 H-FABP release between type 4a MI (n = 37) and no type 4a MI (n = 172)

major adverse clinical events (MACE); MI, target vessel revascularisation, heart failure, stroke and death.

Results We enrolled 241 patients of whom 32 were excluded due to withdrawal of consent or PCI being cancelled after angiography. A cohort of 209 patients was included in analysis, of whom 144 (68.9%) were male, mean age was 68.8 years, 28 (13.4%) were smokers, 31 (14.8%) were diabetic, 199 (95.2%) had hypercholesterolaemia and 138 (66.0%) had hypertension. Type 4a MI was observed in 37 (17.7%) patients. Comparing those with and without type 4a MI, there was no statistical difference in risk factors ($p > 0.05$) except for age, ($p = 0.015$). Median troponin at 6 h was 90.24 ng/L (95% CI 76.56–186.41) versus 14.43 ng/L (95% CI 16.37–21.26) in the type 4a / non type 4a groups respectively, $p < 0.001$, Figure 1. Median H-FABP at 4 h was most predictive of type 4a MI (followed by CKMB and myoglobin) with levels of 6.23 mg/L (95% CI 4.38–18.96), versus 2.05 mg/L (95% CI 2.23–2.74), $p < 0.001$, AUC 0.91, Table 1, Figure 2. Results for TnI, CKMB, myoglobin, GBPP and CAIII are shown in Table 1. Multivariate logistic regression (stepwise elimination) showed H-FABP to be most predictive of type 4a MI, $p < 0.001$. Sensitivity of 4 h H-FABP (> 6.32 mg/L) for type 4a MI was 51.5%, specificity 96.1%, positive predictive value (PPV) 73.9%, negative predictive value (NPV) 90.3%, odds ratio (OR) 26.39, relative risk (RR) 7.62. MACE was noted in 6 (2.9%) patients (three MI, two death and one stroke), 3 of which had type 4a MI at index PCI, $p = 0.036$. Table 2 compares median change in H-FABP and hsTnT from 0–6 h in patients who developed MACE at 1 year with CAIII performing best, $p = 0.02$.

Conclusions/implications Median 4 h H-FABP was most predictive of a 6 h hsTnT rise as a consequence of type 4a MI

Abstract 219 Table 1 Summary of biomarker results at 4 h

4 hr biomarker	Type 4a MI		No type 4a MI		AUC	p value
	Median	IQR	Median	IQR		
H-FABP (µg/L)	6.23	6.22	2.05	1.45	0.91	<0.001
TnI (µg/L)	<0.18	0.07	<0.18	0.01	0.62	0.004
CKMB (µg/L)	3.54	3.37	2.01	1.25	0.75	<0.001
Myoglobin (ng/ml)	72.75	55.68	35.82	38.91	0.72	<0.001
GPBB (pg/L)	3.37	3.50	3.45	2.48	0.50	0.889
CAIII (µg/L)	28.76	23.67	25.25	26.41	0.60	0.168

H-FABP: heart-type fatty acid-binding protein; hsTnT: highly sensitive troponin T; TnI: troponin I; CKMB: creatine kinase MB; GPBB: glycogen phosphorylase; CAIII: carbonic anhydrase III; IQR: interquartile range; AUC: area under curve

Abstract 219 Table 2 Summary of biomarker change from 0–6 h in 1 year MACE and non-MACE patients

Biomarker	MACE		No MACE		AUC	p value
	Median change	IQR	Median change	IQR		
hsTnT (ng/L)	38.32	135.61	7.07	23.49	0.94	0.06
H-FABP (µg/L)	3.73	21.36	0.56	2.45	0.91	0.04
TnI (µg/L)	0.47	0.01	0.09	0.22	0.97	0.11
CK-MB (µg/L)	0.45	4.01	0.18	1.14	0.89	0.29
Myoglobin (ng/ml)	15.47	185.49	2.80	36.55	0.94	0.07
GPBB (pg/L)	-0.86	8.08	1.75	5.13	0.71	0.31
CAIII (µg/L)	24.13	18.23	1.08	20.91	0.91	0.02

H-FABP: heart-type fatty acid-binding protein; hsTnT: highly sensitive troponin T; TnI: troponin I; CKMB: creatine kinase MB; GPBB: glycogen phosphorylase; CAIII: carbonic anhydrase III; IQR: interquartile range; AUC: area under curve

in elective PCI, followed by CKMB and myoglobin. H-FABP and CAIII were independently predictive of MACE at 1 year and MACE was associated with type 4a MI at index PCI.

Young Investigators Prize 2016

A THE CORONARY ARTERY DISEASE ASSOCIATED GENE HHIPL1 PROMOTES ATHEROSCLEROSIS

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Genome-wide association studies have identified chromosome 14q32 as a locus for coronary artery disease in humans. The disease associated variants fall in a gene called *Hedgehog interacting protein-like 1 (HHIPL1)*, which encodes an uncharacterised sequence homolog of a Hedgehog protein antagonist. Here, we present our investigation of HHIPL1 function and its role in atherosclerosis.

Epitope tagged HHIPL1 protein is present in the media of HHIPL1 transfected cells and immunoprecipitates with GFP tagged Sonic Hedgehog (SHH) protein, demonstrating that HHIPL1 is a secreted interactor of SHH. We measured HHIPL1 gene expression in different cardiovascular cell types and found that it is primarily expressed in aortic smooth muscle cells (AoSMCs). We performed siRNA knock-down of HHIPL1 in AoSMCs and observed a reduction of 32% (+/-11%) in proliferation ($p = 0.002$ at 72 h) and a reduction of 27% (+/-4%) in migration ($p = 0.02$ at 12 h). We went on to examine the role of Hhipl1 in atherosclerosis *in vivo*. In atherosclerotic mouse aortas Hhipl1 expression increased with disease progression (~2-fold increase at 6 weeks vs 32 weeks of age, $p = 0.001$). We crossed Hhipl1^{-/-} mice onto Apoe^{-/-} and Ldlr^{-/-} atherosclerosis prone backgrounds. Hhipl1^{-/-} mice displayed a reduction of 57% (+/-28%) in lesion area compared with controls on an Ldlr^{-/-} background (*en face* aorta, n = 10 Hhipl1^{+/+}; Ldlr^{-/-} vs n = 19 Hhipl1^{-/-}; Ldlr^{-/-}, t-test $p = 0.00007$) and 49% (+/-28%) reduction on an Apoe^{-/-} background (*en face* aorta, n = 9 Hhipl1^{+/+}; Apoe^{-/-} vs n = 17 Hhipl1^{-/-}; Apoe^{-/-}, t-test $p = 0.0004$).

Our data represent the first experimental investigation of HHIPL1. We find that HHIPL1 is a proatherogenic protein that regulates smooth muscle cell proliferation and migration,