87 YOUNG PEOPLE WITH HYPERTENSION HAVE CEREBRAL VASCULAR ABNORMALITIES THAT COULD IMPAIR CEREBRAL AUTOREGULATION SUPPORTING THE SELFISH BRAIN HYPOTHESIS

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Background High blood pressure (BP) in childhood is the strongest predictor of hypertension later in life suggesting that the mechanisms responsible are apparent early in life.

The selfish brain hypothesis postulates that impaired cerebral auto-regulation in susceptible individuals results in relative hypoperfusion of the brain-stem. The brain responds by activating the sympathetic nervous system to raise BP. Cerebral vascular anomalies such as vertebral artery hypoplasia or incomplete Circle of Willis would make the brain-stem more vulnerable to this hypo-perfusion. It is unclear whether these vascular anomalies are the cause of the hypertension or a consequence of vascular re-modelling due to hypertension.

We speculated that if these cerebral vascular anomalies were causative, they should have a high prevalence in young onset hypertensives. Conversely, if these cerebral vascular anomalies were secondary to hypertension, we would expect a low prevalence of cerebral arterial remodelling in a group of people with mild hypertension and a short duration of high BP.

Methods We undertook a retrospective analysis of all patients under the age of 40 years referred to our Hypertension Clinic between November 2011 and June 2016. As recommended by NICE, we looked for secondary causes and evidence of end organ damage in this population. Our routine protocol for young onset hypertension is to perform biochemical and anatomic screening (using MRI) for secondary causes of hypertension. We collected MRI data on cerebral vascular anomalies in addition to imaging the heart, aorta, adrenals and kidneys.

Results 65 patients, mean age 30 years (42M, 23F) were included. Mean clinic BP was 147/90 mmHg. 62 underwent comprehensive MRI scanning. A clear anatomical cause for the hypertension was found in 2 people (1 coarctation and 1 hypoplastic kidney). LVH was seen in 15 (24%).

Interestingly, cerebral artery anatomical variants (vertebral artery hypoplasia and/or incomplete Circle of Willis) were detected in 26 people (42%).

Discussion/Implications Cerebral vascular anomalies were common in this population of young people with mild hypertension and only a short duration of high blood pressure. This supports the concept that brain-stem hypo-perfusion might have a pathophysiological role in the aetiology hypertension. This would have important consequences highlighting the need to investigate possible causes of cerebral vascular anomalies in utero or during childhood. Longitudinal studies will help establish whether this causative role is plausible.

The selfish brain hypothesis also suggests that a low target BP may not be appropriate in some people where the initial cause of the hypertension is sympathetic activation due to brain-stem hypo-perfusion. It might explain the "foggy brain" that many hypertensive patients describe when their BP drops after medication.

88 THE HAEMODYNAMIC EFFECTS OF AN ILIAC ARTERIOVENOUS FISTULA TO TREAT HYPERTENSION ASSESSED USING CPET AND ECHO PARAMETERS

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Introduction A central stent derived arterio-venous iliac fistula using the ROX Coupler reduces blood pressure (BP) in patients (pts) with resistant and/or uncontrolled hypertension (HTN). We performed detailed stress echocardiograms (echos) during concurrent cardiopulmonary exercise testing (CPET) pre and post insertion of a ROX Coupler for HTN. We evaluated the pre and post ROX Coupler characteristics of pts who might progress to cardiac decompensation.

Methods 8 pts aged 46–78 (75% male) underwent CPET echos at baseline and between 1 and 6 months following ROX Coupler insertion. 1 pt had evidence of late decompensation with persistent ankle swelling not associated with venous stenosis and IVC>2.5 cm

Results Interim analysis suggests there were no significant differences for any CPET parameter before and after coupler insertion. However TR Vmax, a surrogate for pulmonary artery systolic pressure, significantly increased from 1.96 $\pm$0.94 m/s to 2.08$\pm$0.94 m/s, p=0.01. Meanwhile, lateral E/E, a marker of left ventricular filling pressure, significantly decreased from 12.7$\pm$7.2 to 10.7$\pm$3.8, p=0.005.

Conclusions A lower E/E lateral post ROX suggests the left ventricular filling pressure is reduced and the heart is working at a more efficient match of preload and afterload resulting in reduced cardiac oxygen consumption and reduced myocyte stress. An ongoing study is assessing the effect of the ROX Coupler upon AF outcomes by reversing the structural and electrical effects induced by longstanding HTN. These findings may support this hypothesis.

89 DEVELOPMENT AND EXTERNAL VALIDATION OF A MULTIVARIABLE MODEL OF PRE-TEST LIKELIHOOD OF CORONARY ARTERY DISEASE BASED ON A CONTEMPORARY UK POPULATION, WITH COMPARISON TO EXISTING RISK MODELS

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Introduction Pre-test likelihood models recommended in current UK and US guidelines have been shown to overestimate the probability of coronary artery disease(CAD). We aimed to develop a UK population-based multivariable risk model from CE-MARC(a contemporary study of stable CAD where all patients underwent X-ray coronary angiography) and validate it prospectively in the CE-MARC 2 trial population.

Methods CE-MARC (development population) enrolled patients between 2006–9 with suspected angina. Multivariable logistic regression modelled presence of significant stenosis

(QCA≥70% in epicardial arteries or ≥50% in Left Main Stem) as a function of baseline demographic and clinical characteristics. The validation population were from the CE-MARC 2 trial (2012–16) that underwent angiography, plus additional low and high-risk patients from Leeds General Infirmary (2014–2016) to ensure adequate numbers across the full risk spectrum. Discrimination and calibration were assessed and compared to existing CAD consortium models(ESC 2013 guidelines) and the Duke Score(NICE CG95 2010 and US 2012 guidelines).

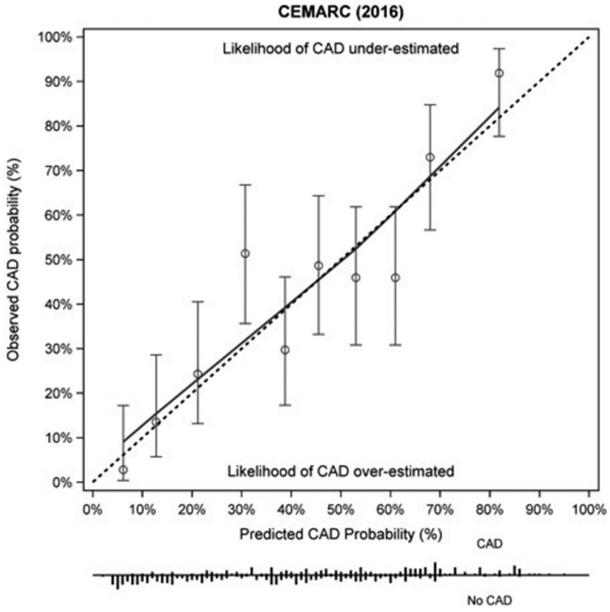
Results There were 675 patients in the development population, and 369 patients in the validation population(Table 1). A multivariable model was developed that included age, sex, angina type, smoking, diabetes, dyslipidaemia, hypertension, ECG Q-waves and ST segment abnormalities.The validation population had a similar CV risk profile. The new CE-MARC model discriminated well (c-statistic: 0.78 (95%CI 0.73–0.82)) and was well-calibrated (Table 2, Figure 1). In comparison, the Duke clinical model was very poorly calibrated (−1.016; −1.265 to −0.766; p<0.001) indicating substantial overestimation of pre-test likelihood compared to the average in the two populations (Figure 2, Table 2). The models used in the ESC 2013 guidelines under-estimated risk (0.74, 95% CI 0.51–0.97; p<0.001), but performed well once adjusted for different baseline risk levels (Table 2).

Abstract 89 Table 1 Demographics

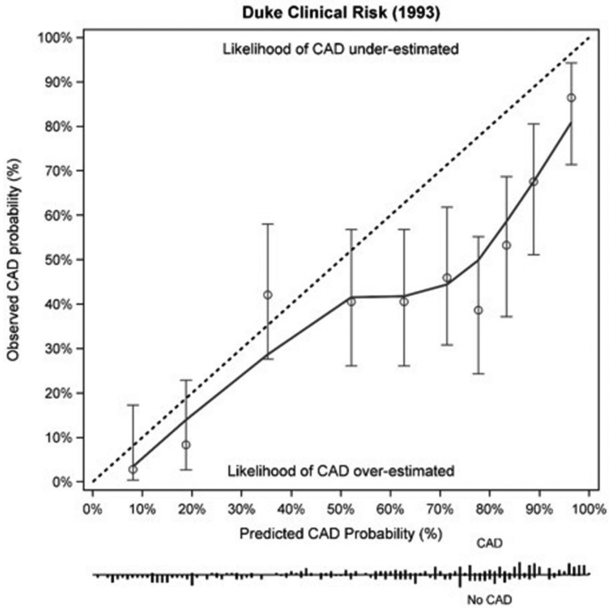
	Development population (n=675)	Validation population (n=369)
Age/years (mean/SD)	59.4 (9.66)	59.6 (10.10)
Male (n/%)	417 (61.8)	160 (43.4)
Typical pain (n/%)	145 (21.5)	182 (49.3)
Atypical pain (n/%)	497 (73.6)	154 (41.7)
Non-anginal pain (n/%)	32 (4.7)	33 (8.9)
Hypertension (n/%)	354 (52.4)	165 (44.7)
Current Smoker (n/%)	126 (18.7)	77 (20.9)
Dyslipidaemia (n/%)	358 (53.0)	170 (46.1)
Diabetes Mellitus (n/%)	76 (11.3)	61 (16.5)

Abstract 89 Table 2 Model performance statistics

Model	Discrimination (c-statistic)	Calibration in the large (alpha)	Logistic miscalibration (beta)
Development population			
Duke model (1993)	0.763 (0.725–0.800)	−1.108 (-1.305, 0.911); p<0.001	−0.298 (-0.416,–0.180); p<0.001
Genders *et al* (2012) Basic	0.770 (0.733–0.806)	0.713 (0.532, 0.893); p<0.001	−0.015 (-0.131, 0.101); p=0.803
Genders *et al* (2012) Clinical	0.762 (0.725–0.7995)	0.822 (0.639, 1.005); p<0.001	−0.051 (-0.159, 0.057); p=0.354
Validation population			
CEMARC	0.777 (0.731–0.824)	0.045 (-0.190, 0.280); p=0.709	0.028 (-0.214, 0.269); p=0.823
Pryor *et al* (1993)	0.752 (0.704–0.801)	−1.016 (-1.265,–0.766); p<0.001	−0.207 (-0.363,–0.050); p=0.010
Genders *et al* (2012) Basic	0.755 (0.706–0.803)	0.738 (0.507, 0.969); p<0.001	−0.007 (-0.182, 0.169); p=0.940
Genders *et al* (2012) Clinical	0.752 (0.703–0.800)	0.866 (0.629, 1.103); p<0.001	−0.054 (-0.121, 0.105); p=0.507



Abstract 89 Figure 1 Calibration plot showing relation between predicted PTL of CAD and observed rates of CAD by decile in validation population for CEMARC model



Abstract 89 Figure 2 Calibration plot showing the relation between predicted PTL of CAD and observed rates of CAD by decile in validation population for Duke model

Conclusion The CE-MARC risk model, developed from a large contemporary UK population undergoing angiography, performed very well in the independent validation sample, without needing any adjustment for different risk prevalence or for miscalibration. In contrast, the earlier Duke risk score substantially over-predicted CAD risk, and remained poorly-

calibrated even when this was corrected. The CAD consortium model (ESC 2013 guidelines), slightly under-estimated average CAD risk, but performed well once this was accounted for lower margin presents histogram of number of patients with each predicted risk score

90 HEAD-TO-HEAD COMPARISON SHOWS POOR PERFORMANCE OF BOTH DIAMOND-FORRESTER AND PRYOR MODELS IN PREDICTING CORONARY ARTERY DISEASE IN CHEST PAIN PATIENTS: A SINGLE CENTRE EXPERIENCE IN A LARGE COHORT OF PATIENTS

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Background An optimal investigation strategy for patients with suspected angina pectoris (AP) remains elusive. UK and ESC guidelines use historical prediction models to guide management after the likelihood of coronary artery disease (CAD) is estimated by symptoms, demographics and risk factors profile (NICE UK guidelines – Pryor model) or by demographics and symptoms only (ESC guidelines – Diamond Forrester model). Data are accumulating suggesting that these prediction models grossly overestimate CAD prevalence in today patients. This is a prospective study to assess the actual CAD prevalence in patients referred to a chest pain clinic, as defined by either obstructive CAD or a positive functional test and the comparative performance of the two models in predicting CAD in these patients.

Methods 1376 consecutive patients (age: 58±12 years) were reviewed in a dedicated chest pain clinic. Patients were assigned to five estimated CAD likelihood groups: **<10%, 10%–29%, 30%–60%, 61%–90% and>90%** using the NICE model and to three CAD likelihood groups: **<15%, 15%–85%** and **>85%** using the ESC model. Patients were diagnosed as having CAD when either obstructive (>70%) coronary stenoses were demonstrated by invasive angiogram or CTCA or a functional test was positive. The observed CAD prevalence was compared with the predicted one by the two models. Investigation strategies concordance between the NICE and ESC pathways was checked with kappa statistics and comparative diagnostic performance was assessed with ROCs.

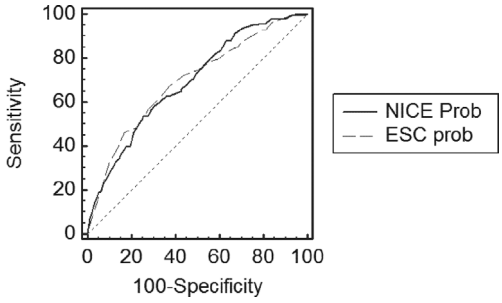
Results 652 pts. (47%) had non-anginal CP, 412 pts. (30%) had atypical AP and 312 (23%) had typical AP. 417 pts (30%) were not investigated for CAD due to non-anginal symptoms and/or low CAD probability. Investigations were completed in 858/959 pts. The actual CAD prevalence was **21%** vs. a NICE (Pryor) model predicted one of 53% and an ESC (Diamond-Forrester) model predicted one of 36% ($p<0.001$). There was poor agreement (*kappa*=0.07) between the two pathways as to investigations strategies, with the NICE pathway directing a much higher proportion of patients to invasive angiography when compared with the ESC one: 498/1386 (36%) vs. 51/1386 (4%), $p<0.0001$, respectively. Both models had modest predictive abilities with AUCs of 0.695 and 0.693, respectively (p=ns) – Figure 1: Comparison of ROCs for CAD likelihood scores by the NICE and the ESC models.

Conclusions 1. The overall prevalence of CAD in patients referred for suspected AP is significantly lower than expected by using either NICE or ESC endorsed historical model.

2. The use of risk factors profile in addition to demographics and symptoms characteristics does not improve diagnostic accuracy and increases the degree of overestimation.

3. The present NICE pathway directs a much higher proportion of patients to invasive angiography than the ESC one

4. The present results emphasise the need to develop updated prediction models.



Abstract 90 Figure 1

91 HOW USEFUL ARE RECENT STUDIES USING THE DIAMOND-FORRESTER RISK MODEL TO ASSESS CHEST PAIN?

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Background The conventional method to assess stable chest pain of recent onset is to classify the nature of the chest pain, and then apply a risk model to predict the probability that it is caused by obstructive coronary artery disease (CAD), as recommended in American, European and NICE guidelines. The European and NICE guidelines are derived from the 1979 Diamond-Forrester risk model (DFRM), although this has been criticised for overestimating the risk of CAD. We hypothesised that recent studies would be more consistent and useful than earlier studies in diagnosing CAD.

Methods We performed a systematic literature search on studies published on MEDLINE and EMBASE until Nov 2016. Searched terms were *Diamond Forrester* and *coronary artery disease*. Overlapping studies and review articles were excluded. Data on the nature of chest pain and presence of CAD was independently extracted by both authors. Crude relative risks (CRR) of CAD were calculated by comparing typical angina and atypical angina respectively to non-anginal chest pain or pain free as the reference, and not taking into account demographics or cardiovascular risk factors.

Results 10 studies (n=31,528) were eligible for analysis (mean age 59±10, 54% male), as shown in Table 1; these used a variety of different methods to diagnose CAD. Table 2 shows that compared to the original DFRM, more recent studies tended to use cohorts that had larger of patients with atypical angina and non-anginal chest pain with positive diagnoses of CAD varying dramatically; such as of those with typical angina the%age with CAD ranged from 9%–88%. There was