Impact of pulmonary stenosis vs. regurgitation on strain and strain rate using cardiac magnetic resonance feature tracking in a porcine model

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Background: Pulmonary stenosis (PS) is common in congenital heart disease and an integral finding in Tetralogy of Fallot (TOF). Pulmonary regurgitation (PR) is more commonly found following surgery in repaired TOF. We aimed to evaluate the haemodynamic effects of PS and PR on cardiac physiology in a porcine model using cardiac magnetic resonance-based feature tracking (CMR-FT) deformation imaging.

Methods: CMR-FT was performed in 14 pigs before and 10-12 weeks after surgery. Surgery included either pulmonary artery banding to simulate PS (n = 7), or an incision to the pulmonary valve to simulate PR (n = 7). CMR-FT assessment included left and right ventricular global longitudinal (LV/RV GLS) and LV circumferential (GCS) strain and strain rates (SR) as well as left and right atrial reservoir/conduit/booster pump (LA/RA Es, Ee, Ea) strain and SR.

Results: RV GLS was significantly reduced following PS compared to PR induction (PS -7.51 vs. PR -23.84, $p < 0.001$). RV GLS improved after induction of PR (before -20.50 vs. after -23.84, $p = 0.018$) as opposed to PS (before -11.73 vs. after -7.51, $p = 0.128$). Similarly, RA Es (PS 14.22 vs. PR 27.34, $p = 0.017$) and Ee (PS 8.65 vs. PR 20.51, $p = 0.004$) were decreased in PS compared to PR with detrimental impact of PS (Es before 23.20 vs. after 14.22, $p = 0.018$, Ee before 15.04 vs. after 8.65, $p = 0.028$) but not PR (Es before 31.65 vs. after 27.34, $p = 0.176$, Ee before 20.63 vs. after 20.51, $p = 0.499$).

Conclusion: In a porcine model of RV pressure vs. volume overload, increased after- but not preload shows detrimental impact on RV and RA physiology.

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A pragmatic approach to the investigation of stable chest pain: A UK, multi-centre, randomised trial to improve patient outcomes, quality of life and cost effectiveness (CE-MARC 3)

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Background: There remains uncertainty and debate about the optimal non-invasive diagnostic imaging strategy for patients with suspected coronary artery disease (CAD). Computed Tomography Coronary Angiography (CTCA) and functional imaging are both guideline-recommended, although comparative evidence in patients with intermediate-high pre-test likelihood (PTL) of CAD is limited.

Methods: CE-MARC3 aims to establish if a personalised investigation strategy compared to CTCA-first approach for all, leads to improved patient outcomes. 4,000 patients newly referred for the investigation of suspected cardiac chest pain will be recruited and randomised 1:1 to either personalised care (first line CTCA or functional imaging based on PTL), or CTCA first line for allcomers. Inclusion/exclusion criteria shown in Figure 1.

The primary endpoint is a composite of cardiovascular death, myocardial infarction, or unobstructed coronary arteries on invasive angiography, at 12 months. Remote follow up will occur at 6 and 12 months for symptoms, quality of life, and guideline directed medical therapy usage (Figure 2).

A cost-effectiveness analysis will be performed based on EQ-5D-5L, capturing impacts on health, measured in quality adjusted life years (QALYs), and costs (including investigations, procedures, procedural complications, medical treatment costs and any future hospital admissions).

The trial protocol has been designed to be pragmatic to capture real world practice and minimise hospital visits and inconvenience to patients. Novelly, it will be possible for the whole trial pathway to be conducted remotely with the option to perform non-face-to-face consent, randomisation, and data collection including EQ-5D-5L.

Results: This is a large-scale, pragmatic, multi-centre randomised trial at 20 UK hospitals with well-established clinical services for both CTCA and functional cardiac imaging. Centres with geographical spread and with ethnically diverse populations have been selected. The main trial is funded by the charity Heart Research UK (TRP13/19) and the Quality-of-Life Sub-study by the British Heart Foundation (PG/21/10724).

As of August 2024, the trial remains open to recruitment, having randomised >2,500 patients (1st patient randomised 26/04/2022), with an original planned recruitment closure date of end of April 2025 (Figure 3).

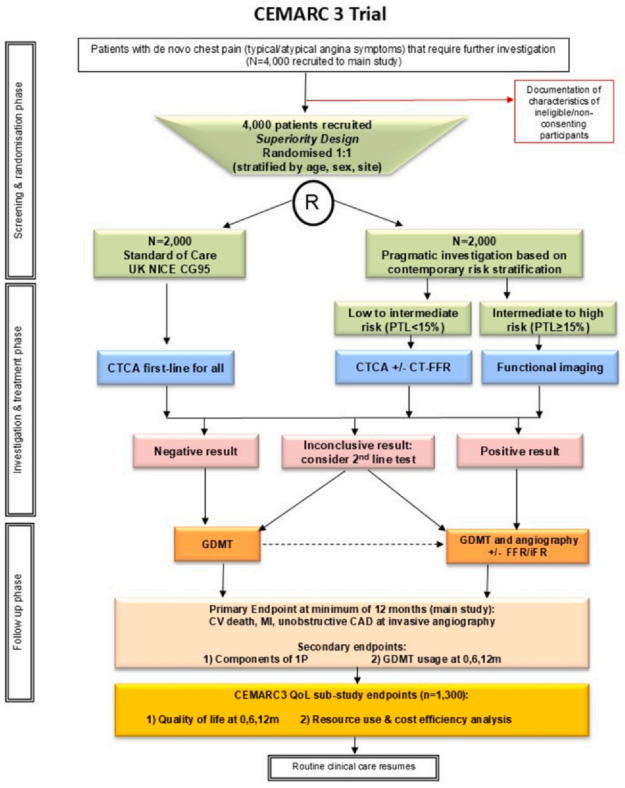
Currently, of the randomised population, ~43% are female, ~75% have a PTL of 15% or more and ~12% are non-white. In the functional arm, ~1/4 patients have had stress CMR, potentially providing adequate power to investigate stress CMR as a co-variate.

Conclusion: This trial will address whether, in patients with suspected cardiac chest pain, a strategy of personalised investigation according to PTL compared to CTCA for allcomers, leads to improved patient outcomes, quality of life and cost-effectiveness.

Trial entry criteria

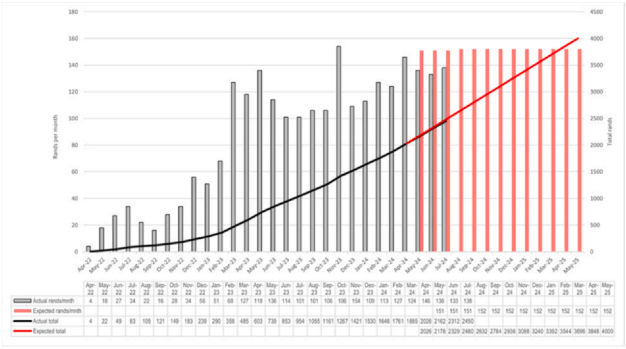
Inclusion Criteria
• Male ≥45 years, female ≥50 years
• Typical or atypical angina (chest pain)
• At least one major cardiovascular risk factor (diabetes, peripheral arterial disease, cerebrovascular disease, current or past tobacco use, hypertension, dyslipidaemia, or family history of premature CAD)
• Suitable for coronary revascularisation if required, as determined by clinician/shared decision making
• Given written informed consent to participate in the trial
Exclusion Criteria
• Prior normal CTCA within the last 2-years or any prior CTCA with extensive calcification (CAC>400)
• Clinically unstable cardiac symptoms (clinician discretion)
• Known obstructive CAD (including previous MI, ACS or coronary revascularisation)
• Absolute contraindication to CTCA or functional cardiac imaging
• Pregnancy and/or breast feeding
• Chronic kidney disease (i.e. eGFR <30mL/min/1.73m2)

Trial protocol flow chart



GDMT, guidelines directed medical therapy; PTL, Pre-Test Liklihood

Predicted vs actual recruitment



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Preliminary baseline CEST CMR measurements of cardiac energetics in healthy subjects

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Background: Cardiovascular disease remains a leading cause of death worldwide, but novel cardiac MRI technologies may present a way to noninvasively evaluate cardiac function, improving diagnoses and subsequent therapeutic options. Chemical Exchange Saturation Transfer (CEST) is a CMR technique that allows for the measurement of in vivo metabolites of interest. Previous human studies using myocardial samples from heart transplants and ^{31}P CMR spectroscopy of phosphocreatine have implicated creatine levels in heart failure. This study aims to preliminarily establish a baseline CEST-CMR measured creatine in healthy individuals as an assessment of metabolic activity in the heart.

Methods: 44 subjects (23 males and 21 females of mean ages 33.8 and 27.4, respectively) were screened against chronic diseases, including hypertension, hyperlipidemia, and cardiovascular disease. Cardiac CEST images were taken using Siemens PRISMA (13 females and 8 males) and CIMA (8 females and 15 males) scanners. From each subject, 31 images at varying ppm shifts were obtained. ImageJ was used to segment the interventricular septum of the heart for each image, from which mean gray values were measured. These values were fitted to a Z-spectrum curve. A creatine MTR asymmetry curve was created from the Z-spectrum and used to quantify creatine levels. An unpaired two-tailed t-test was used to analyze for differences between males and females. On the CIMA, a rigorous phantom scan was done with known creatine concentrations of 0 mmol to 50 mmol in increments of 10 mmol to validate the CEST protocol.