A prospective, multi-centre, randomized trial of 3 diagnostic strategies in suspected Coronary Heart Disease (CMR *vs*. UK NICE guidelines *vs*. MPS)

The CE-MARC 2 trial

John P. Greenwood, David P. Ripley, Colin Berry, Gerry P. McCann, Sven Plein, Chiara Bucciarelli-Ducci, Erica Dall'Armellina, Abhiram Prasad, Colin C. Everett, Linda D. Sharples, on behalf of the CE-MARC 2 Investigators

Disclosures:
Trial Sponsor – British Heart Foundation

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Background

- Invasive coronary angiography is commonly used early in diagnostic pathways in patients with suspected CHD
- A large US study reported that approximately 60% of elective cardiac catheterisations found no obstructive CHD[1]
- Current guidelines for investigation of stable chest pain advocate management based on the pre-test likelihood of CHD
- However, pre-test likelihood models can overestimate CHD risk, therefore paradoxically increasing the probability of invasive coronary angiography
- Reducing unnecessary angiography should reduce patient risk and provide significant financial savings

1. Patel MR, *N Engl J Med*. 2010;362(10):886-895

Purpose and key points about methods

- Purpose: in patients with suspected CHD, is CMR-guided care superior to national guidelines–directed care[1] and MPS-guided care, in reducing the occurrence of unnecessary invasive angiography occurring within 12m?

- CE-MARC 2 was a multi-centre, 3-parallel group, randomized clinical trial using a pragmatic comparative effectiveness design[1]
- Patients with suspected angina pectoris were eligible if they were ≥30 years, had a CHD pre-test likelihood (PTL) of 10-90%, and were suitable for revascularization
- Patients were randomised 2:2:1 to CMR or MPS or NICE guidelines-directed care
- Patients in the NICE group were scheduled for CCT, MPS or direct-to-cath dependent on their PTL of CHD (as per UK NICE guidelines)
- Primary EP: protocol-defined unnecessary coronary angiography occurring within 12 months, defined by a normal FFR value (or QCA) in all vessels 2.5 mm or more in diameter

1. Ripley et al, *Am Heart J*. 2015; 169(1): 17-24

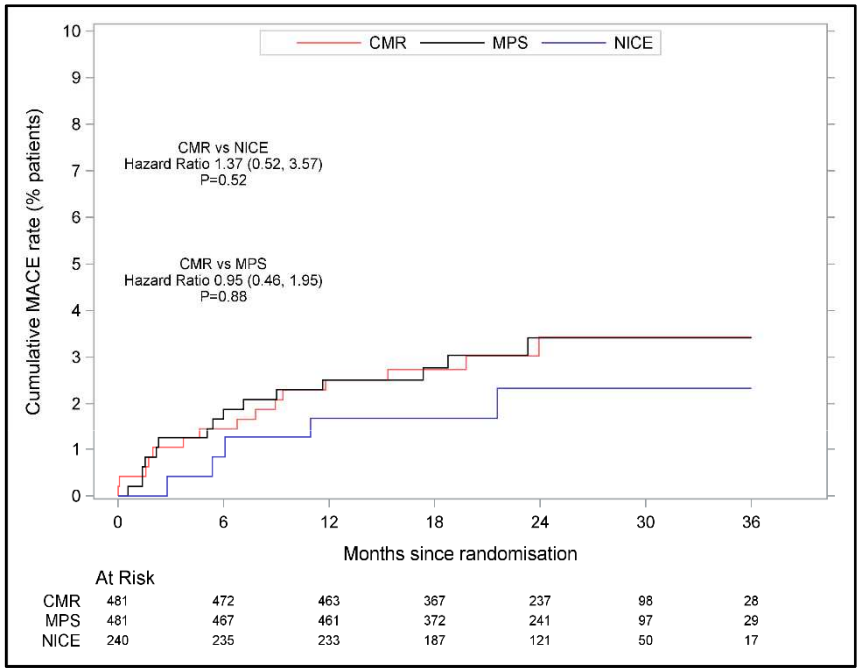
Results

- 1,202 patients (55% of eligible) were recruited (Nov 2012-Mar 2015)
- 265 (22.0%) patients underwent angiography within 12m:
  - NICE 42.5%; CMR 17.7%; MPS 16.2%

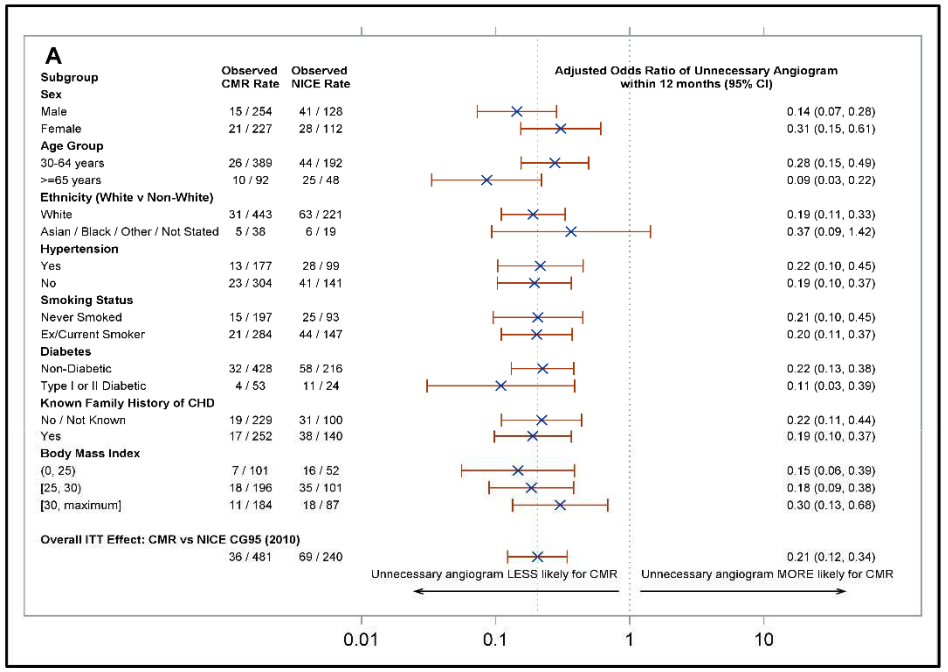
- The primary endpoint (unnecessary angiography) occurred in:
  - NICE 28.8%; CMR 7.5%; MPS 7.1%
- Adjusted OR (95%CI) of unnecessary angiography:
  - CMR vs NICE 0.21 (0.12 to 0.34; P<0.001)
  - CMR vs MPS 1.27 (0.79 to 2.03; P=0.32)

- Positive angiography observed in:
  - NICE 29(12.1%); CMR 47(9.8%); MPS 42(8.7%) [P=0.36]

Results



Time to first MACE after a minimum of 12-month follow-up from randomization (median, 16 months)

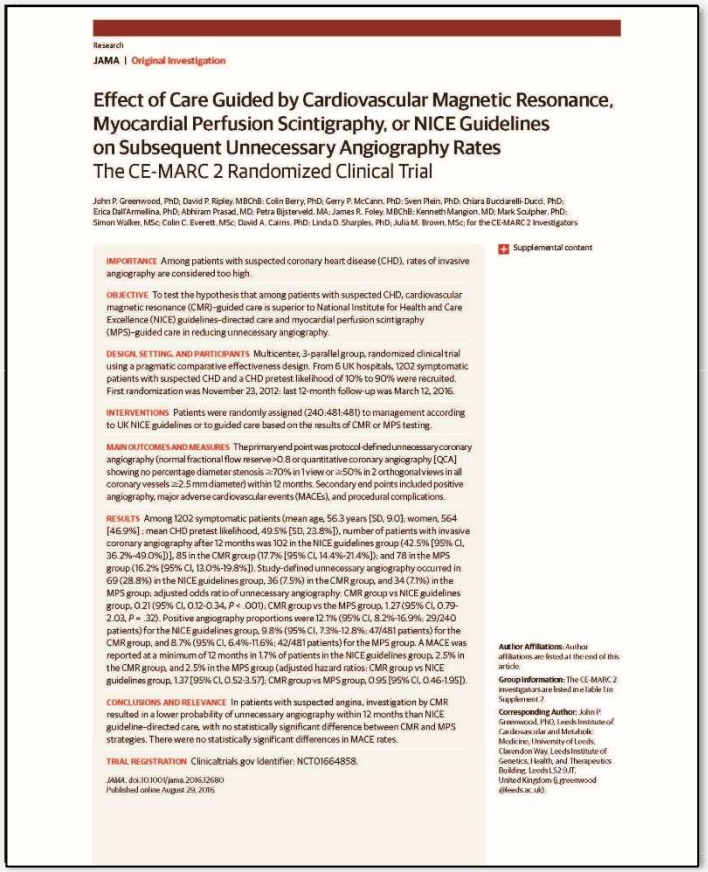


Effect of patient characteristics on results for CMR-guided care vs NICE guidelines-directed care

Conclusions

- In patients with suspected angina, investigation by CMR produced a lower probability of unnecessary angiography within 12 months than NICE guidelines–directed care
- There was no statistically significant difference between CMR and MPS strategies
- There were no statistically significant differences between the three groups in terms of MACE rates at 12 months after randomization

- Quality of life and cost-effectiveness analyses will be important for understanding the patient-centred perspectives and payer/policy implications of these findings; these data are currently being analysed



Research

JAMA | Original Investigation

Effect of Care Guided by Cardiovascular Magnetic Resonance, Myocardial Perfusion Scintigraphy, or NICE Guidelines on Subsequent Unnecessary Angiography Rates
The CE-MARC 2 Randomized Clinical Trial

John P. Greenwood, PhD; David P. Ripley, MBChB; Colin Berry, PhD; Gerry P. McCann, PhD; Sven Plein, PhD; Chiara Bucciarelli-Ducci, PhD; Erica Dall'Armellina, PhD; Abhiram Prasad, MD; Petra Bijsterveld, MA; James R. Foley, MBChB; Kenneth Mangion, MD; Mark Sculpher, PhD; Simon Walker, MSc; Colin C. Everett, MSc; David A. Cairns, PhD; Linda D. Sharples, PhD; Julia M. Brown, MSc; for the CE-MARC 2 Investigators

Supplemental content

IMPORTANCE Among patients with suspected coronary heart disease (CHD), rates of invasive angiography are considered too high.

OBJECTIVE To test the hypothesis that among patients with suspected CHD, cardiovascular magnetic resonance (CMR)–guided care is superior to National Institute for Health and Care Excellence (NICE) guidelines–directed care and myocardial perfusion scintigraphy (MPS)–guided care in reducing unnecessary angiography.

DESIGN, SETTING, AND PARTICIPANTS Multicenter, 3-parallel group, randomized clinical trial using a pragmatic comparative effectiveness design. From 6 UK hospitals, 1202 symptomatic patients with suspected CHD and a CHD pretest likelihood of 10% to 90% were recruited. First randomization was November 23, 2012; last 12-month follow-up was March 12, 2016.

INTERVENTIONS Patients were randomly assigned (240:481:481) to management according to UK NICE guidelines or to guided care based on the results of CMR or MPS testing.

MAIN OUTCOMES AND MEASURES The primary end point was protocol-defined unnecessary coronary angiography (normal fractional flow reserve >0.8 or quantitative coronary angiography [QCA] showing no percentage diameter stenosis ≥70% in 1 view or ≥50% in 2 orthogonal views in all coronary vessels ≥2.5 mm diameter) within 12 months. Secondary end points included positive angiography, major adverse cardiovascular events (MACEs), and procedural complications.

RESULTS Among 1202 symptomatic patients (mean age, 56.3 years [SD, 9.0]; women, 564 [46.9%]; mean CHD pretest likelihood, 49.5% [SD, 23.8%]), number of patients with invasive coronary angiography after 12 months was 102 in the NICE guidelines group (42.5% [95% CI, 36.2%-49.0%]), 85 in the CMR group (17.7% [95% CI, 14.4%-21.4%]), and 78 in the MPS group (16.2% [95% CI, 13.0%-19.8%]). Study-defined unnecessary angiography occurred in 69 (28.8%) in the NICE guidelines group, 36 (7.5%) in the CMR group, and 34 (7.1%) in the MPS group; adjusted odds ratio of unnecessary angiography: CMR group vs NICE guidelines group, 0.21 (95% CI, 0.12-0.34, $P < .001$); CMR group vs the MPS group, 1.27 (95% CI, 0.79-2.03, $P = .32$). Positive angiography proportions were 12.1% (95% CI, 8.2%-16.9%; 29/240 patients) for the NICE guidelines group, 9.8% (95% CI, 7.3%-12.8%; 47/481 patients) for the CMR group, and 8.7% (95% CI, 6.4%-11.6%; 42/481 patients) for the MPS group. A MACE was reported at a minimum of 12 months in 1.7% of patients in the NICE guidelines group, 2.5% in the CMR group, and 2.5% in the MPS group (adjusted hazard ratios: CMR group vs NICE guidelines group, 1.37 [95% CI, 0.52-3.57]; CMR group vs MPS group, 0.95 [95% CI, 0.46-1.95]).

CONCLUSIONS AND RELEVANCE In patients with suspected angina, investigation by CMR resulted in a lower probability of unnecessary angiography within 12 months than NICE guideline–directed care, with no statistically significant difference between CMR and MPS strategies. There were no statistically significant differences in MACE rates.

TRIAL REGISTRATION Clinicaltrials.gov Identifier: NCT01664858.

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Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The CE-MARC 2 investigators are listed in eTable 1 in Supplement 2.

Corresponding Author: John P. Greenwood, PhD, Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, Clarendon Way, Leeds Institute of Genetics, Health, and Therapeutics Building, Leeds LS2 9JT, United Kingdom (j.greenwood@leeds.ac.uk).

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