BMJ

BMJ 2013;346:f3940 doi: 10.1136/bmj.f3940 (Published 22 July 2013)

PRACTICE

RATIONAL IMAGING

Investigating stable chest pain of suspected cardiac origin

This article describes how stable chest pain of suspected cardiac origin can be radiographically investigated according to the patient's risk of coronary artery disease

Declan P O'Regan *consultant radiologist*[1], Stephen P Harden *consultant radiologist*[2], Stuart A Cook *professor of cardiology*[1 3]

[1]Robert Steiner MRI Unit, MRC Clinical Sciences Centre, London W12 0NN, UK; [2]Department of Cardiothoracic Radiology, University Hospital Southampton NHS Foundation Trust, Southampton, UK; [3]Department of Cardiology, National Heart Centre Singapore, Singapore

This series provides an update on the best use of different imaging methods for common or important clinical presentations. The series advisers are Fergus Gleeson, consultant radiologist, Churchill Hospital, Oxford, and Kamini Patel, consultant radiologist, Homerton University Hospital, London. To suggest a topic for this series, please email us at practice@bmj.com

A 45 year old man, who was a non-smoker and did not have diabetes or hyperlipidaemia, presented to his doctor with chest discomfort after exercise. There were no relevant findings on clinical examination and resting electrocardiography (ECG) results were normal.

What is the next investigation?

Cardiovascular disease is a leading cause of death in the United Kingdom[1]; however, most first presentations with chest pain to primary care have a non-cardiac cause.[2] It is important to establish which patients' symptoms are caused by obstructive coronary artery disease, so that these patients can be optimally managed to control angina and reduce mortality.[3] To support clinical decision making, the National Institute for Health and Care Excellence (NICE) published guidance in 2010 on the assessment of patients with chest pain of suspected cardiac origin.[4] This advice proposed a major change in clinical practice by no longer recommending exercise ECG to investigate stable chest pain in patients without known coronary artery disease. Exercise ECG is limited by the need for an interpretable ECG, the ability of the patient to exercise adequately, and a wide variability in diagnostic accuracy compared with cardiac imaging.[5 6]

The assessment of patients with suspected stable chest pain begins with a full history, clinical evaluation, and resting ECG. Subsequent investigation is guided by calculating the pre-test probability of coronary artery disease using age, sex, risk factors, and symptom characteristics (see table⇓ and fig 1⇓). The NICE guidelines stratify patients into three risk groups and recommend a different strategy for cardiac investigations in each group. Most patients will have symptomatic coronary artery disease diagnosed or excluded on the basis of non-invasive cardiac imaging, with invasive angiography reserved for higher risk patients being considered for revascularisation.

With increasing use of cardiac computed tomography in lower risk populations, the effect of radiation dose is an important consideration, although this might be offset by fewer patients undergoing nuclear medicine studies. As newer imaging technology becomes available, radiation dose and diagnostic accuracy may continue to improve. Typical dose ranges are given below for tests that use ionising radiation and should be considered against the annual background dose of about 3 mSv.

Tests recommended for patients with a low pre-test risk (10-29%)

Computed tomography coronary artery calcium score

Calcium scoring (sensitivity 98%, specificity 40%) is a screening test for coronary artery disease that also has prognostic value for future cardiac events.[7] ECG-gated computed tomography of the heart is performed without contrast medium and a workstation is used to calculate the calcium (Agatston) score on the basis of the extent of calcified coronary plaque. Calcium scoring has a negative predictive value of 99% for obstructive coronary artery disease in low risk populations, and a normal study result predicts a 2% cardiac event rate over the next five years.[7 8] If the calcium score is zero then non-coronary causes of chest pain should be considered. However, obstructive

Correspondence to: D P O'Regan declan.oregan@imperial.ac.uk

Learning points

- The National Institute for Health and Care Excellence (NICE) does not recommend exercise electrocardiography for investigating stable chest pain in patients without known coronary artery disease
- NICE guidance recommends that the sequence of imaging tests be determined by the patient's risk of coronary artery disease
- Patients with a pre-test probability of 10-29% for coronary artery disease are initially investigated with coronary artery calcium scoring using computed tomography
- Computed tomography coronary angiography is performed in patients with a calcium score of 1-400 to determine whether there are any coronary stenoses
- Patients with a 30-60% risk are initially investigated with functional cardiac imaging to diagnose flow limiting coronary disease
- Invasive coronary angiography, as a first line investigation, is reserved for symptomatic patients with a 61-90% pre-test probability of coronary artery disease when revascularisation is a treatment option

coronary artery disease may go undetected in younger patients in whom atherosclerotic plaque has not advanced to the stage of calcification.[8] If the calcium score is 1-400, computed tomography coronary angiography should be performed immediately afterwards to assess potential coronary stenoses. If the calcium score exceeds 400, non-invasive functional imaging or invasive coronary angiography should be considered as the next investigation.

Calcium scoring is associated with a relatively low dose of radiation (≤3 mSv), is rapid and easy to perform, and does not require heart rate control. Calcified plaques are often not flow limiting due to remodelling of the vessel wall but are a marker for the presence of non-calcified plaques elsewhere.[9] Around 17% of patients attending a rapid access chest pain clinic will be referred for calcium scoring. The test will effectively rule out symptomatic coronary artery disease in at least 70% of these patients.[10]

Computed tomography coronary angiography

Computed tomography coronary angiography (sensitivity 98%, specificity 92%) is used to determine whether patients with a calcium score of 1-400 have obstructive coronary artery disease.[11] Imaging is performed using an ECG-gated computed tomography scanner with at least 64 slices during a timed bolus of intravenous contrast medium. Three dimensional images of the angiogram are reconstructed on a workstation to visualise coronary stenoses caused by calcified or non-calcified plaque. The positive predictive value of this technique for detecting a coronary stenosis of 50% or more is 91%, with a negative predictive value of 83%.[12] In patients with a calcium score of less than 100, the negative predictive value rises to 93%.[13] If there is doubt about the importance of a stenosis then functional cardiac imaging can be considered.

Patients often require heart rate control with oral or intravenous cardioselective β blockers and may be given sublingual glyceryl trinitrate for coronary vasodilatation. β blockers should be used with caution in patients with severe asthma or decompensated heart failure. NICE recommends using next generation scanners for patients who are difficult to image with conventional 64 slice equipment because they offer higher image resolution with lower radiation exposure and are cost effective.[14 15] Radiation doses of less than 1 mSv are achievable with these scanners in non-obese patients with stable heart rates, but in clinical practice doses typically range between 2 and 12 mSv.[16]

Tests recommended for patients with a medium pre-test risk (30-60%)

Functional cardiac imaging

Functional cardiac imaging uses pharmacological agents to identify flow limiting coronary disease. It is the first line investigation for patients with a 30-60% pre-test probability of coronary artery disease. Functional imaging may be performed in several different ways and NICE recommends four commonly available methods. The choice of investigation will largely depend on local availability and patient suitability, but it should also be informed by diagnostic accuracy and any potential risks.

Perfusion imaging

In patients with flow limiting coronary disease, an intravenous vasodilator (such as adenosine, regadenoson, or dipyridamole) will increase the difference between perfusion of normal myocardium and that supplied by a stenosed artery. This can be visualised with myocardial perfusion scintigraphy (sensitivity 91%, specificity 78%), which uses a tracer taken up by cardiac myocytes and imaged with a gamma camera. Images acquired during vasodilator stress and at rest are compared to assess whether perfusion is impaired within a coronary artery territory.[17] Cardiac magnetic resonance imaging, where first pass contrast enhanced imaging of the heart is performed during a vasodilator infusion, can also be used to assess myocardial perfusion (sensitivity 90%, specificity 79%).[18] This test has a higher negative predictive value than myocardial perfusion scintigraphy (91% *v* 79%) and it avoids exposure to radiation (6-9 mSv).[19] Adenosine is contraindicated in severe asthma and in patients with second or third degree heart block. Cardiac magnetic resonance imaging is not suitable for patients with an incompatible pacemaker or claustrophobia. Patients should not ingest caffeine in the 24 hours before the test due to competitive inhibition of adenosine.

Wall motion imaging

The sympathomimetic drug dobutamine can be used to induce a regional wall motion abnormality within ischaemic myocardium during continuous imaging of the left ventricle. These abnormalities may be visualised using echocardiography (sensitivity 87%, specificity 84%) or cardiac magnetic resonance (sensitivity 91%, specificity 81%).[20 21] Image quality for echocardiography may be improved in patients who are difficult to image with intravenous contrast agents.[22] Contraindications to dobutamine include severe aortic stenosis and obstructive hypertrophic cardiomyopathy. Major complications occur in 1.7 per 1000 patients, with the most common serious event being sustained ventricular tachycardia.[23]

Tests recommended for patients with a high pre-test risk (61-90%)

Invasive catheter angiography

If the estimated likelihood of coronary artery disease is 61-90%, or if functional or anatomical coronary imaging is non-diagnostic, patients who would be considered for

revascularisation are offered invasive coronary angiography. A catheter is passed through the common femoral or radial artery and used to selectively visualise the coronary arteries with contrast medium during fluoroscopy. This is considered the gold standard investigation for assessing the lumen of the coronary arteries. As well as diagnosing coronary artery disease, patients may proceed to coronary stenting to relieve anginal symptoms if a suitable stenosis is identified. It may be difficult to define the importance of an intermediate stenosis on an angiogram, so the flow limiting effect can be assessed by using a pressure recording catheter.[24] The typical radiation dose for diagnostic coronary angiography is 3-6 mSv. The overall complication rate is 7.4 per 1000, with a mortality rate of 0.7 per 1000.[25] The most common complications are arrhythmias, vascular injury, and myocardial ischaemia.

Outcome

On the basis of age, sex, risk factors, and symptoms, the patient's pre-test probability of coronary artery disease was 21% and he was referred for calcium scoring. The calcium score was 11 (fig 2⇓) and he proceeded to computed tomography coronary angiography, which identified a 70% stenosis of the left anterior descending coronary artery (fig 3⇓). Adenosine stress perfusion cardiac magnetic resonance imaging showed reduced perfusion of the septum within the territory of the left anterior descending coronary artery. He was managed for stable angina on the basis of these findings (fig 4⇓).

Contributions: DPO'R prepared the manuscript and selected the patient and images. SPH and SAC helped edit the manuscript. DPO'R is guarantor.

Competing interests: We have read and understood the BMJ Group policy on declaration of interests and declare the following interests: None.

Provenance and peer review: Commissioned; externally peer reviewed.

Patient consent obtained.

1 Office for National Statistics. Deaths Registered in England and Wales, 2011. www.ons.gov.uk/ons/rel/vsob1/mortality-statistics--deaths-registered-in-england-and-wales--series-dr-/2011/stb-deaths-registered-in-england-and-wales-in-2011-by-cause.html .
2 Nilsson S, Scheike M, Engblom D, Karlsson LG, Molstad S, Akerlind I, et al. Chest pain and ischaemic heart disease in primary care. *Br J Gen Pract* 2003;53:378-82.
3 National Institute for Health and Care Excellence. The management of stable angina. CG126. 2011. www.nice.org.uk/CG126.
4 National Institute for Health and Care Excellence. Chest pain of recent onset: assessment and diagnosis of recent onset chest pain or discomfort of suspected cardiac origin. CG95. 2010. http://publications.nice.org.uk/chest-pain-of-recent-onset-cg95/guidance.
5 Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2012;60:e44-164.
6 Gianrossi R, Detrano R, Mulvihill D, Lehmann K, Dubach P, Colombo A, et al. Exercise-induced ST depression in the diagnosis of coronary artery disease. A meta-analysis. *Circulation* 1989;80:87-98.
7 Sarwar A, Shaw LJ, Shapiro MD, Blankstein R, Hoffman U, Cury RC, et al. Diagnostic and prognostic value of absence of coronary artery calcification. *JACC Cardiovasc Imaging* 2009;2:675-88.
8 Villines TC, Hulten EA, Shaw LJ, Goyal M, Dunning A, Achenbach S, et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography: results from the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry. *J Am Coll Cardiol* 2011;58:2533-40.
9 Sangiorgi G, Rumberger JA, Severson A, Edwards WD, Gregoire J, Fitzpatrick LA, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using nondecalcifying methodology. *J Am Coll Cardiol* 1998;31:126-33.
10 National Institute for Health and Clinical Excellence. Chest pain of recent onset: calcium scoring factsheet. 2010. www.nice.org.uk/nicemedia/live/12947/47987/47987.pdf.
11 Janne d'Othee B, Siebert U, Cury R, Jadvar H, Dunn EJ, Hoffmann U. A systematic review on diagnostic accuracy of CT-based detection of significant coronary artery disease. *Eur J Radiol* 2008;65:449-61.
12 Miller JM, Rochitte CE, Dewey M, Arbab-Zadeh A, Niinuma H, Gottlieb I, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med* 2008;359:2324-36.
13 Arbab-Zadeh A, Miller JM, Rochitte CE, Dewey M, Niinuma H, Gottlieb I, et al. Diagnostic accuracy of computed tomography coronary angiography according to pre-test probability of coronary artery disease and severity of coronary arterial calcification. The CORE-64 (Coronary Artery Evaluation Using 64-Row Multidetector Computed Tomography Angiography) international multicenter study. *J Am Coll Cardiol* 2012;59:379-87.
14 National Institute for Health and Clinical Excellence. Computed tomography (CT) scanners for cardiac imaging—Somatom Definition Flash, Aquilion One, Brilliance iCT and Discovery CT750. 2012. http://guidance.nice.org.uk/DT/3.
15 Westwood M, Al M, Burgers L, Redekop K, Lhachimi S, Armstrong N, et al. A systematic review and economic evaluation of new-generation computed tomography scanners for imaging in coronary artery disease and congenital heart disease: Somatom Definition Flash, Aquilion ONE, Brilliance iCT and Discovery CT750 HD. *Health Technol Assess* 2013;17:1-243.
16 Achenbach S, Marwan M, Ropers D, Schepis T, Pflederer T, Anders K, et al. Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur Heart J* 2010;31:340-6.
17 Jaarsma C, Leiner T, Bekkers SC, Crijns HJ, Wildberger JE, Nagel E, et al. Diagnostic performance of noninvasive myocardial perfusion imaging using single-photon emission computed tomography, cardiac magnetic resonance, and positron emission tomography imaging for the detection of obstructive coronary artery disease: a meta-analysis. *J Am Coll Cardiol* 2012;59:1719-28.
18 Hamon M, Fau G, Nee G, Ehtisham J, Morello R, Hamon M. Meta-analysis of the diagnostic performance of stress perfusion cardiovascular magnetic resonance for detection of coronary artery disease. *J Cardiovasc Magn Resonance* 2010;12:29.
19 Greenwood JP, Maredia N, Younger JF, Brown JM, Nixon J, Everett CC, et al. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. *Lancet* 2012;379:453-60.
20 Sicari R, Nihoyannopoulos P, Evangelista A, Kasprzak J, Lancellotti P, Poldermans D, et al. Stress echocardiography expert consensus statement—executive summary: European Association of Echocardiography (EAE) (a registered branch of the ESC). *Eur Heart J* 2009;30:278-89.
21 Nandalur KR, Dwamena BA, Choudhri AF, Nandalur MR, Carlos RC. Diagnostic performance of stress cardiac magnetic resonance imaging in the detection of coronary artery disease: a meta-analysis. *J Am Coll Cardiol* 2007;50:1343-53.
22 Mulvagh SL, DeMaria AN, Feinstein SB, Burns PN, Kaul S, Miller JG, et al. Contrast echocardiography: current and future applications. *J Am Soc Echocardiogr* 2000;13:331-42.
23 Geleijnse ML, Krenning BJ, Nemes A, van Dalen BM, Soliman OII, ten Cate FJ, et al. Incidence, pathophysiology, and treatment of complications during dobutamine-atropine stress echocardiography. *Circulation* 2010;121:1756-67.
24 Pijls NHJ, van Schaardenburgh P, Manoharan G, Boersma E, Bech J-W, van't Veer M, et al. Percutaneous coronary intervention of functionally nonsignificant stenosis 5-year follow-up of the DEFER study. *J Am Coll Cardiol* 2007;49:2105-11.
25 West R, Ellis G, Brooks N. Complications of diagnostic cardiac catheterisation: results from a confidential inquiry into cardiac catheter complications. *Heart* 2006;92:810-4.

Cite this as: *BMJ* 2013;346:f3940

Table

Table 1| Proportion of people estimated to have coronary artery disease according to typicality* of symptoms, age, sex, and risk (high or low).[4] Values are proportion of people at each mid-decade age with clinically relevant CAD†

Age (years)	Non-anginal chest pain‡				Atypical angina				Typical angina			
	Men		Women		Men		Women		Men		Women	
	Low risk§	High risk§	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk
35	3	35	1	19	8	59	2	39	30	88	10	78
45	9	47	2	22	21	70	5	43	51	92	20	79
55	23	59	4	25	45	79	10	47	80	95	38	82
65	49	69	9	29	71	86	20	51	93	97	56	84

*Typical angina pain is constricting discomfort in the front of the chest, neck, shoulders, jaw, or arms, which is precipitated by physical exertion and relieved by rest or glyceryl trinitrate within about 5 minutes. Atypical angina pain has two of the features of typical angina. Non-angina pain has none or one of the features of typical angina pain.

†If there are resting ST-T changes or Q waves on electrocardiography, the likelihood of CAD is higher in all patient groups; for men over 70 years with atypical or typical symptoms assume a risk estimate of >90%; for women over 70 years, assume an estimate of 61-90% unless the woman is at high risk and has typical symptoms, in which case a risk of >90% should be assumed.

‡These patients are not routinely investigated for CAD unless there is a high clinical suspicion.

A diagnosis is made by clinical assessment alone in patients with a pre-test probability of <10% or >90%.

§High risk=diabetes, smoking or hyperlipidaemia (total cholesterol >6.47 mmol/L; 1 mmol/L=38.61 mg/dL); low risk=none of the above three risk factors.

CAD=coronary artery disease.

Figures

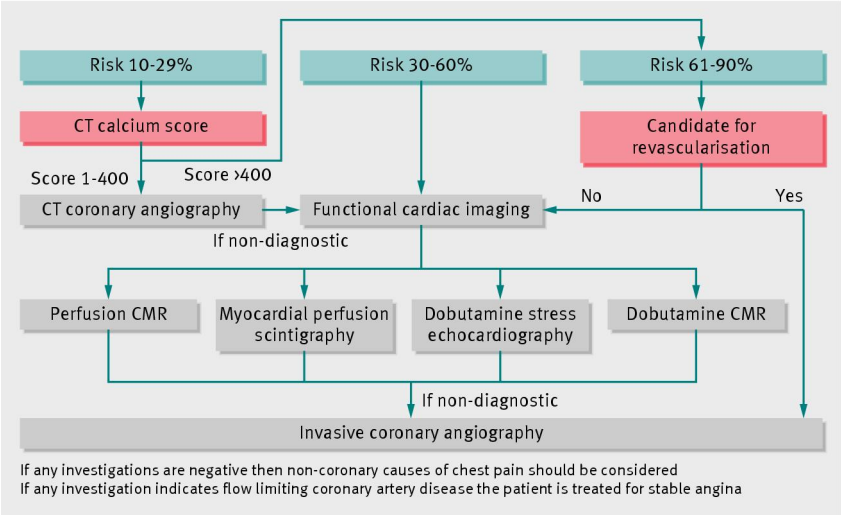

Fig 1 Diagnostic pathways for the investigation of stable chest pain in patients without known coronary artery disease based on pre-test probability.[4] CT=computed tomography; CMR=cardiac magnetic resonance imaging

Fig 2 Computed tomography calcium scoring showing calcified plaque that has been highlighted in the left anterior descending coronary artery (arrow)

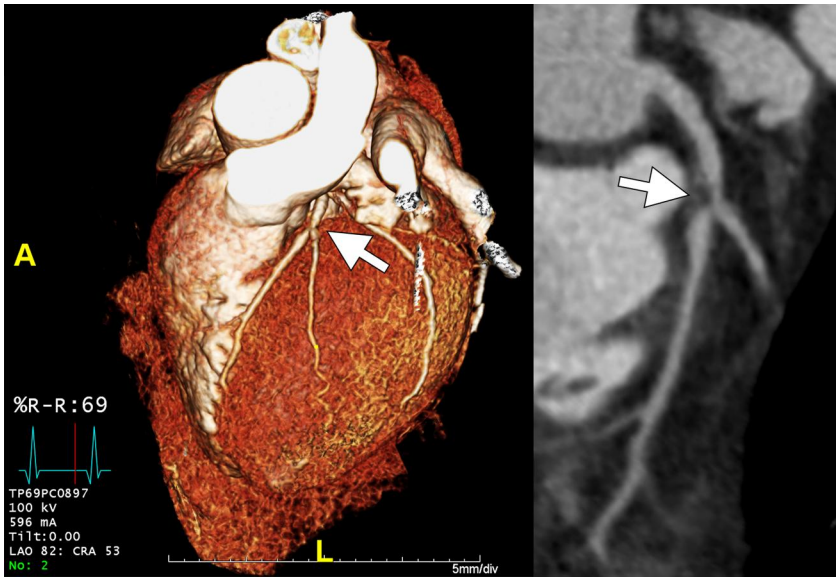

Fig 3 Computed tomography coronary angiography showing stenosis of the left anterior descending coronary artery (arrows) near the origin of the first diagonal branch on a whole heart image (left) and a curved reconstruction (right)

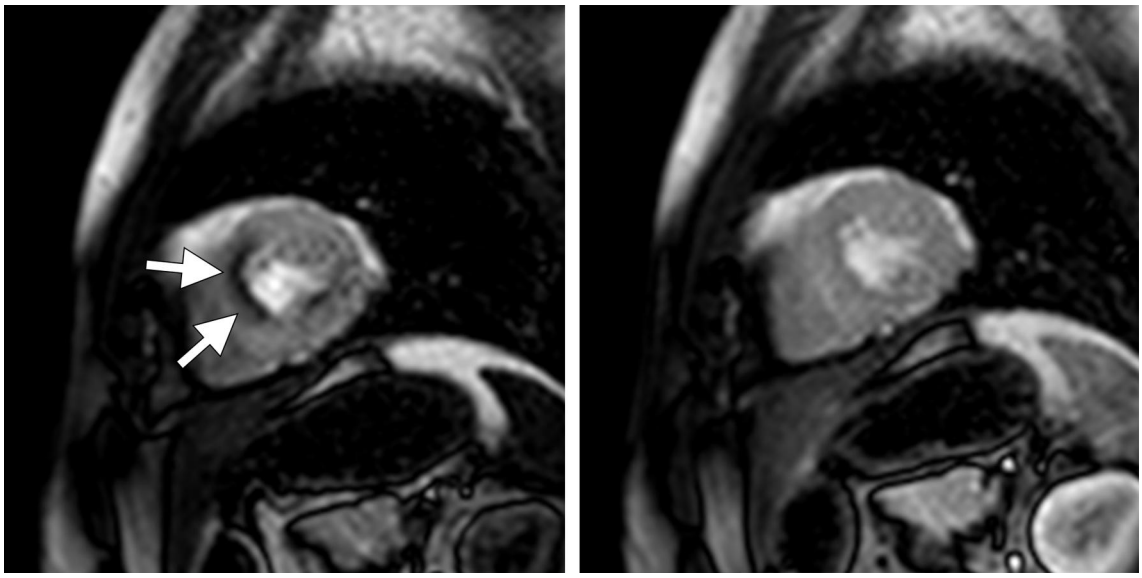

Fig 4 First pass perfusion cardiac magnetic resonance imaging performed during and after an adenosine infusion. An inducible perfusion defect is present during stress (left) within the territory of the left anterior descending coronary artery (arrows) compared with normal perfusion at rest (right)