Diagnostic and Interventional Imaging 102 (2021) 337–345

Guidelines/*Cardiac imaging*

Position paper on stress cardiac MRI in chronic coronary syndrome: Endorsed by the Société Française de Radiologie (SFR) the Société Française d'Imagerie CardioVasculaire (SFICV) and the Société Française de Cardiologie (SFC)

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ARTICLE INFO

Keywords:
Angina pectoris
Myocardial ischemia
Stable coronary artery disease
Cardiac MRI

ABSTRACT

This position paper was intended to update the former consensus between the French Societies of Radiology and Cardiology about the use of stress cardiac magnetic resonance imaging (MRI) in chronic coronary syndrome published in 2009. The Delphi method was used to build the present consensus. This expert panel consensus includes recommendations for indications, procedure with patient preparation, stress inducing drugs, acquisition protocol, interpretation and risk stratification by stress MRI.

Abbreviations: CAD, Coronary artery disease; COPD, Chronic obstructive pulmonary disease; CT, Computed tomography; CTA, Computed tomography angiography; ECG, Electrocardiogram; ESC, European Society of Cardiology; FFR, Fractional flow reserve; LGE, Late gadolinium chelate enhancement; LV, Left ventricle; MRI, Magnetic resonance imaging; PET, Positron emission tomography; PSIR, Phase-sensitive inversion recovery; PTP, Pre-test probability; SFC, French Society of Cardiology; SFR, French Society of Radiology.

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https://doi.org/10.1016/j.diii.2021.02.005
2211-5684/

1. Introduction

Cardiac magnetic resonance imaging (MRI) has become a key examination in routine clinical practice for assessing ventricular function, valvular regurgitation, extracellular volume and myocardial enhancement [1–3]. The goal of this opinion paper issued by a national expert committee from the French Society of Radiology (SFR) and the French Society of Cardiology (SFC) is to define how cardiac stress MRI should be positioned in the management of patients suspected of/or having chronic coronary artery disease (CAD). This consensus includes recommendations for indications, procedure with patient preparation, stress inducing drug, acquisition protocol, interpretation and risk stratification by stress MRI.

2. Indications of stress MRI in chronic coronary syndrome

This section mainly refers to the 2019 European Society of Cardiology (ESC) Guidelines for the diagnosis and management of chronic coronary syndromes [4]. Most common indications of stress MRI are summarized in Table 1.

2.1. In symptomatic patients

The preliminary stage in approaching the diagnosis of thoracic pain or dyspnea is to determine the probability of obstructive coronary artery disease. Patient assessment should first and foremost be based on clinical questions about patient's past history and risk factors, details of the characteristics of chest pain and presence of dyspnea, electrocardiogram (ECG), chest X-ray, and echocardiography. The initial examination should also be used to consider any possible differential diagnosis and research functional angina (anemia, hyperthyroidism, severe blood hypertension with left ventricular hypertrophy, valve disease and in particular aortic stenosis and hypertrophic cardiomyopathy or the possibility of rhythm disorders). If patient's condition is deemed unstable, the clinician must refer to guidelines on acute coronary syndromes, which are not covered in the present document [5,6].

The pre-test probability (PTP) of obstructive coronary artery disease is calculated considering, age, gender, presence of dyspnea, and the typical or atypical characteristics of the patient's angina pain. Typical angina pain is defined on the basis of three criteria:

i) the presence of chest pain suggesting angina;
ii) triggered by exercise or emotional stress
iii) that is rapidly alleviated when the patient stops exercising or has taken nitro-derivatives, usually via the sublingual route.

Angina pain is described as atypical when only two criteria are present; in most cases when chest pain is not triggered by exercise. If only one of these criteria is present, the pain is not considered to be angina. In agreement with the European Society of Cardiology we recommend the use of Diamond and Forrester's method in its version updated in 2019, which gives a more accurate assessment of the probability of obstructive coronary artery disease and can also be used for elderly patients (Fig. 1) [4,7–10].

Patients with PTPs > 15% of CAD, especially mid to high PTPs, are those who would benefit the most from functional non-invasive imaging testing, such as stress MRI, particularly if a revascularization procedure is likely, or if the patient has known obstructive coronary artery disease [4]. For patients with PTPs between 5–15%, testing for diagnosis may be considered after assessing the overall clinical likelihood based on the modifiers of PTPs presented in Fig. 2. There is no indication to perform a diagnostic test if PTP is under 5%.

Functional imaging for myocardial ischemia, such as stress MRI, is indicated when coronary computed tomography angiography (CTA) has shown CAD of uncertain functional significance or is not diagnostic.

Invasive coronary angiography is recommended as an alternative test to diagnose CAD in patients with a high clinical likelihood, severe symptoms refractory to medical therapy or typical angina at a low level of exercise, left ventricular dysfunction, and clinical evaluation that indicates high event risk.

Table 1
Indications and patient selection for cardiac stress MRI.

Common indications for stress MRI in chronic coronary syndrome
Initial test to diagnose CAD in symptomatic patients with PTP > 15%
Initial test to diagnose CAD in symptomatic patients with PTP between 5–15% after assessing overall clinical likelihood based on PTP modifiers (Fig. 1)
When coronary CTA has shown CAD of uncertain functional significance or is not diagnostic
In high-risk asymptomatic adults (with diabetes, a strong family history of CAD, or when previous risk-assessment tests suggest a high risk of CAD), functional imaging, such as stress MRI, may be considered for cardiovascular risk assessment
Should be considered when an adverse evolution of the patient's obstructive coronary artery disease is suspected: change in (the severity of the) symptoms and the ECG (onset of Q waves, change in repolarisation, onset of a left bundle branch block. . .), or deterioration of left ventricular function, if the site and extent of ischemia would influence clinical decision making
In stable patients with known CAD, reassessment of their prognosis can be discussed when the time elapsed since the last stress test considered to present a low risk has exceeded its period of validity (3 to 5 years)
Specific situations where stress MRI may be preferable to other imaging modalities
Female patients
Obese patients or poorly echogenic patients
Younger patients
Atrial fibrillation
Cardiac function and morphology information needed (*i.e.*, hypertrophic cardiomyopathy, precise LVEF evaluation before CRT)
Cardiac tissue characterization information needed (*i.e.*, fibrosis in hypertrophic cardiomyopathy, precise evaluation of viability in CAD)

CAD: coronary artery disease; CTA: computed tomography angiogram; CRT: cardiac resynchronization therapy; ECG: electrocardiogram; LVEF: left ventricular ejection fraction; PTP: pre-test probability.

2.2. In asymptomatic patients

Data are lacking on indications and how to manage positive test result in asymptomatic subjects. According to ESC guidelines [4], functional imaging or coronary CTA may be considered in "high-risk asymptomatic adults (with diabetes, a strong family history of CAD, or when previous risk-assessment tests suggest a high risk of CAD) for cardiovascular risk assessment".

2.3. Follow-up of patient with known CAD

The long-term prognosis for patients with CAD depends on the demographics and clinical features, on left ventricular function and angiographically defined coronary lesions and finally the results of stress imaging. The latter should be considered when an adverse evolution of the patient's obstructive coronary artery disease is suspected: change in (the severity of the) symptoms and the ECG (onset of Q waves, change in repolarization, onset of a left bundle branch block), or worsening of left ventricular function.

There is no randomized study focused on the value of monitoring of stable patients by periodical stress imaging. However, a reassessment of their prognosis can be discussed when the time elapsed since the last stress test considered to present a low risk has exceeded its period of validity. A period of 3 to 5 years was proposed in the 2019 ESC guidelines [4].

	Typical		Atypical		Non-angina		Dyspnea[a]	
Age (year)	Male	Female	Male	Female	Male	Female	Male	Female
30-39	3%	5%	4%	3%	1%	1%	0%	3%
40-49	22%	10%	10%	6%	3%	2%	12%	3%
50-59	32%	13%	17%	6%	11%	3%	20%	9%
60-69	44%	16%	26%	11%	22%	6%	27%	14%
≥70	52%	27%	34%	19%	24%	10%	32%	12%

Fig. 1. Pre-test probability (PTP) of obstructive coronary artery disease in 15,815 symptomatic patients according to age, gender and the type of symptoms (adapted from Ref. [4]). The patients who presented with isolated dyspnea, or had it as a predominant symptom were included in addition to the usual categories of Diamond and Forrester's algorithm [9]. The cells in dark green show the groups for which the non-invasive tests are the most relevant (PTP > 15%). Cells in pale green show the groups with a PTP between 5–15% for whom diagnostic tests should be considered after overall clinical probability has been assessed based on the modifiers shown in Fig. 2.

Pre-test probability based on gender, age and the type of symptoms

Decreases the probability	Increases the probability
Normal stress test*	Risk factors for cardiovascular disease
Absence of coronary calcification	(dyslipidemia, diabetes, tobacco use,
(Agatson score = 0) *	hypertension, family history)
	Abnormalities on the ECG at rest (Q waves,
	Changes in segment ST or in the T wave)
	Left ventricular dysfunction suggesting
	obstructive coronary artery disease
	Abnormal stress test*
	Presence of coronary calcifications on CT *

* indicates if available

Fig. 2. Figure shows determinants of the clinical likelihood of obstructive coronary artery disease (adapted from Ref [4]).

2.4. Patients selection for stress MRI in chronic coronary syndrome

The most exhaustive meta-analysis reveals that MRI stress testing and positron emission tomography (PET)/CT are the most sensitive and specific imaging modalities when invasive coronary angiography shows that the patient's stenosis is > 50% or the fractional flow reserve (FFR) is positive [27]. A strategy guided by MRI has the advantage of decreasing the number of invasive coronary angiography without compromising the patients' prognosis [12]. The British healthcare system considers that an MRI guided strategy for exploring patients referred for angina yields the best cost efficacy ratio compared to the other alternatives. A recent study has demonstrated that the use of stress MRI compared to invasive FFR in patients who present with stable angina decreased the number of invasive coronary angiography without compromising the patients' prognosis [11].

Despite the higher diagnostic performance of stress MRI, the type of imaging to use mostly depends on availability, local expertise, contraindications and patient's choice. However, MRI should be considered as the most appropriate choice in some clinical situations (Table 1). MRI does not produce ionizing radiation, is not sensitive to breast or diaphragm attenuation and shows no gender-based differences in accuracy [11]. Because of its safety, stress MRI is especially useful in young and female patients. In obese patients, stress echocardiography is limited by poor

echogenicity, and single-photon emission computed tomography can be limited by attenuation, with a higher incidence of false-positive results. Coronary computed tomographic angiography is hampered by patient morphology and higher radiation. Stress perfusion MRI is feasible, safe and has accurate discriminative prognostic value even in morbidly obese patients (BMI ≥ 40 kg/m^2) [12]. Both single-photon emission computed tomography and stress echocardiography have reduced diagnostic accuracy in patients with left bundle branch block. Dobutamine stress MRI may have greater diagnostic accuracy than dobutamine echocardiography thanks to comprehensive examination with the addition of perfusion and late gadolinium chelate enhancement [13]. Nevertheless, data on accuracy of stress MRI using vasodilators in left bundle branch patients is limited and cannot be recommended over another imaging modality to those patients. Stress MRI is feasible in patients with atrial arrythmia and has good discriminative prognostic value [14]. Finally, the main advantage of stress MRI is the ability to accurately evaluate cardiac morphology, function and tissue characteristics during the same test. For instance, this modality should be considered if a stress imaging is indicated for a patient with hypertrophic cardiomyopathy to identify focal or diffuse fibrosis, or for a patient with heart failure to measure left ventricular ejection fraction (before cardiac resynchronization therapy and/or defibrillator implantation) and right ventricle function. Stress MRI also offers a precise evaluation of myocardial viability thanks to high spatial resolution and excellent correlation with histology, which provide valuable information with regard to revascularization.

3. Procedure

3.1. Safety of MRI stress tests

Abundant literature shows that myocardial ischemia-inducing tests (dobutamine) or coronary reserve tests (adenosine, regadenoson, dipyridamole) can be performed with MRI in perfectly acceptable conditions for the patient [15]. Vasodilators should be preferred to dobutamine that carries a higher complication rate in clinical practice. Dobutamine can be used at a low dose to research contractile reserve and to explore the viability of the myocardium. Our group regrets that vasodilators have not been granted a visa for MRI stress tests. In France their use is justified by many articles in the literature, European recommendations, several randomized studies and meta-analyses and the recommendations from international societies [16–22].

MRI stress tests require strict safety measures:

- the hospital must have a cardiology intensive care unit;
- the patient must be duly informed of how the examination will be performed, the fact that the drug is being used off-label and the risks entailed. An informed consent form must be signed;
- the medical staff should respect the contraindications, dosage and routes of administration of the pharmacological products and contrast agents involved, be aware of their side-effects and the withdrawal criteria;
- contraindications for provoked myocardial ischemia testing must be respected (Table 2).

Table 2
Stress MRI contraindications.

Provoked ischemia testing contraindications
Myocardial infarction or recent acute coronary syndrome (less than 5 days)
Uncontrolled rhythm disorder
Serious conduction disorders (atrioventricular block ≥ 2)
Known significant untreated stenosis of the left main artery
Non-controlled heart failure, severe aortic stenosis, obstructive cardiomyopathy
Patient's refusal
Vasodilators (dipyridamole, adenosine, regadenoson) contraindications
2nd or 3rd degree atrioventricular block or sinus dysfunction
Systolic pressure < 90 mmHg
Severe systemic arterial hypertension (> 220/120 mmHg)
Sinusal bradycardia (heart rate < 40 bpm)
Hypersensitivity to the active principle or one of the excipients
Known hypersensitivity to stress agent
Active bronchostrictive or bronchospastic disease with regular use of inhalers*
Dobutamine contraindications
Severe systemic arterial hypertension (≥ 220/120 mmHg)
Unstable angina pectoris
Severe aortic valve stenosis
Complex cardiac arrhythmias including uncontrolled atrial fibrillation
Hypertrophic obstructive cardiomyopathy
Myocarditis, endocarditis, or pericarditis
Uncontrolled heart failure
Atropine contraindications
Narrow-angle glaucoma
Myasthenia gravis
Obstructive uropathy
Obstructive gastrointestinal disorders
MRI absolute contra-indications
Incompatible cardiac implantable electronic device (PM, ICD and CRT)
Metallic intraocular foreign bodies
Implantable neurostimulation systems
Cochlear implants/ear implant
Drug infusion pumps
Catheters with metallic components
Metallic fragments such as bullets, shotgun pellets, and metal shrapnel
Cerebral artery aneurysm clips
Magnetic dental implants, tissue expander, artificial limb, hearing aid, piercing

bpm: beats per minute; CRT: cardiac resynchronization therapy; ICD: implantable cardioverter defibrillators; PM: pacemaker.
* Regadenoson has been demonstrated to be safe to use in patients with mild to moderate chronic obstructive pulmonary disease and asthma (see text for details).

3.2. Before stress test

A physician specialized in cardiovascular imaging should practice cardiac stress MRI in cooperation with a physician trained in cardiorespiratory resuscitation able to take care of the patient immediately if necessary [23]. The paramedical team should include two operators, one trained in the use of the emergency trolley and a radiology technician. An area located beside the MRI suite must be available and equipped with all items required for emergency procedures: oxygen and suction drainage, emergency trolley equipped with all drugs and antidotes (aminophylline, beta-blockers, salbutamol, adrenalin, nitrates). Naso-tracheal intubation equipment and a defibrillator must be available. The different emergency procedures, useful phone numbers and names of the different operators should be displayed in the room. The patient should be given a 12-channel reference ECG before being installed in the room. Twelve to 24 h before a stress MRI the patient must not take any medication or food that is likely to inhibit drugs or change the interpretation. For dobutamine, beta blockers and nitro-derivatives are prohibited. For dipyridamole, adenosine and regadenoson, caffeine (coffee, tea, chocolate or drinks containing these, food or drugs containing caffeine) aminophylline, dipyridamole and nicotine are contraindicated. Fasting is not mandatory; a light meal is advised before the examination. Vasodilators frequently induce side effects that must be explained to the patient.

3.3. During stress test

Two venous lines (flexible 16- or 20-gauge catheters) are made available, one for injecting the stress-inducing product and the other for the gadolinium-based contrast medium

(except for regadenoson for which a single venous line is sufficient).

Patients' monitoring (amagnetic device mandatory) should include: continuous 3-channel ECG, arterial pressure, digital oximeter. An alarm button is placed in the patient's hand. Oral contact with the technician is allowed via microphones. Headphones are placed on patient's ears to reduce noise.

If urgent care or resuscitation is required, the patient must be removed from the examination room immediately.

3.4. At the end of the test

- Care should be taken when the patient stands up due to the risk of orthostatic hypotension;
- Twelve-channel ECG should be performed to check return to baseline;
- The patient should remain under surveillance till ECG returns to baseline, with no chest pain and recovery of side effect;
- Aminophylline injection is not given systematically when stress agent is dipyridamole, the half-life of aminophylline being much longer than that of dipyridamole. It can be helpful if the patient suffers from unpleasant side effects. Aminophylline is not indicated after administration of adenosine. Aminophylline is not advised after injection of regadenoson in epileptic patients, both drugs having pro-convulsive effect;
- The patients can leave the department after a period of surveillance if no intercurrent clinical event has occurred.

4. Stress inducing drugs; precautions and contraindications

A study suggested that dipyridamole is less sensitive and specific than adenosine or regadenoson for MRI stress testing [24]. Adenosine or regadenoson should therefore be preferred and dipyridamole should only be used if adenosine or regadenoson are not available in the hospital. In addition, regadenoson is a drug that is easier to use as there is only one dosage for adults. The likelihood of dosage errors is therefore decreased. Regadenoson specifically targets the cardiac receptors thus mitigating the benign side effects connected to this vasodilator. This group of experts estimates that regadenoson is currently the most suitable vasodilator to be used in cardiac stress MRI.

4.1. Dose

- Dobutamine: the expert group does not advise to research myocardial ischemia with dobutamine and suggests that vasodilators would be preferred. However, it is possible to use dobutamine to research contractile reserve and assess myocardial viability. The maximum dose is 15 μg/kg/min that should be reached by steps of 2.5 to 5 μg/kg/min. The duration of each step should be in between 2 to 3 min starting from an initial dose of 5 μg/kg/min;
- Adenosine: 140 μg/kg/min. The dose can be increased to 210 μg/kg/min if after 2–3 min, the patient's heart rate does not increase of 10 beats per minute or if systolic blood pressure does not decrease by at least 10 mm Hg;
- Regadenoson: a single dose is used in adults without considering size or weight: 0.4 mg in intravenous injection;
- Dipyridamole: 0.56 to 0.82 mg/kg via slow intravenous administration over a period of 3 min.

4.2. Contraindications

Contraindications of stress agents are reported in Table 2. All three vasodilators (Dipyridamole, Adenosine, Regadenoson) share common contraindications. However according to available data from observational studies as well as controlled clinical trials, the use of regadenoson in patients with mild to moderate asthma and mild to moderate chronic obstructive pulmonary disease (COPD) is safe [25–29]. Regadenoson should be used very cautiously in patients with severe COPD, in patients who require 24-hour/day home oxygen administration, have previously been intubated for respiratory failure, have had recent exacerbations or required uptitration of their medication regimen within a 1-month period, because data in these populations are limited. Regadenoson should be avoided in patients with severe bronchial asthma.

4.3. Potential side-effects

At low doses dobutamine rarely causes complications; on the contrary, higher doses (20–40 μg/kg/min) can induce chest pain and palpitations.

More serious complications are rare. They include myocardial infarction, ventricular fibrillation and ventricular tachycardia.

Adenosine, regadenoson and dipyridamole can induce hot flushes, headaches, precordial pain, palpitations and dyspnea. These side effects occur frequently (in around 30% of patients), but they are usually benign and rapidly reversible.

The more serious side effects are rarer. They included transient conduction disorders, hypotension, sinusal tachycardia and bronchospasm.

The side effects described for adenosine occur less frequently with regadenoson, but the half-life of regadenoson is longer, so that the patient should be monitored a bit longer with regadenoson than with adenosin.

5. Acquisition protocol

Cine MRI sequences associated with first pass-perfusion and late enhancement ones form the basis of any stress cardiac MRI. Examples of acquisition protocols with approximate timeline are proposed in Fig. 3.

5.1. Cine-MRI

This part is based on fast acquisition cine sequences using steady-state free precession (slice thickness 6–8 mm, with or without 2–4 mm interslice gaps (to make a total of 10 mm), temporal resolution ≤ 45 ms between phases to optimize evaluation of wall motion [30]. Parallel imaging shortens the acquisition process. These pulse sequences should include at least:

- slices covering the whole left ventricle (LV) in its short axis from base to apex. The most basal slice must be immediately proximal to the position of the mitral valve;
- three long-axis slices of the LV including 2-chamber, 4-chamber and left ventricular outflow tract views.

5.2. Stress test using vasodilators: myocardial perfusion imaging

Perfusion MRI is based on a qualitative (visual) analysis of the enhancement of the myocardial signal during the first pass of a bolus injection of gadolinium chelate. The temporal resolution of perfusion sequences should allow the acquisition of 3–5 slices within an R-R space. Saturation-recovery is used as pre pulse.

The following should be performed:

- at least 3 slices in the short axis of the LV and most often a slice in the vertical plane of the long axis and another in the horizontal plane of the long axis;

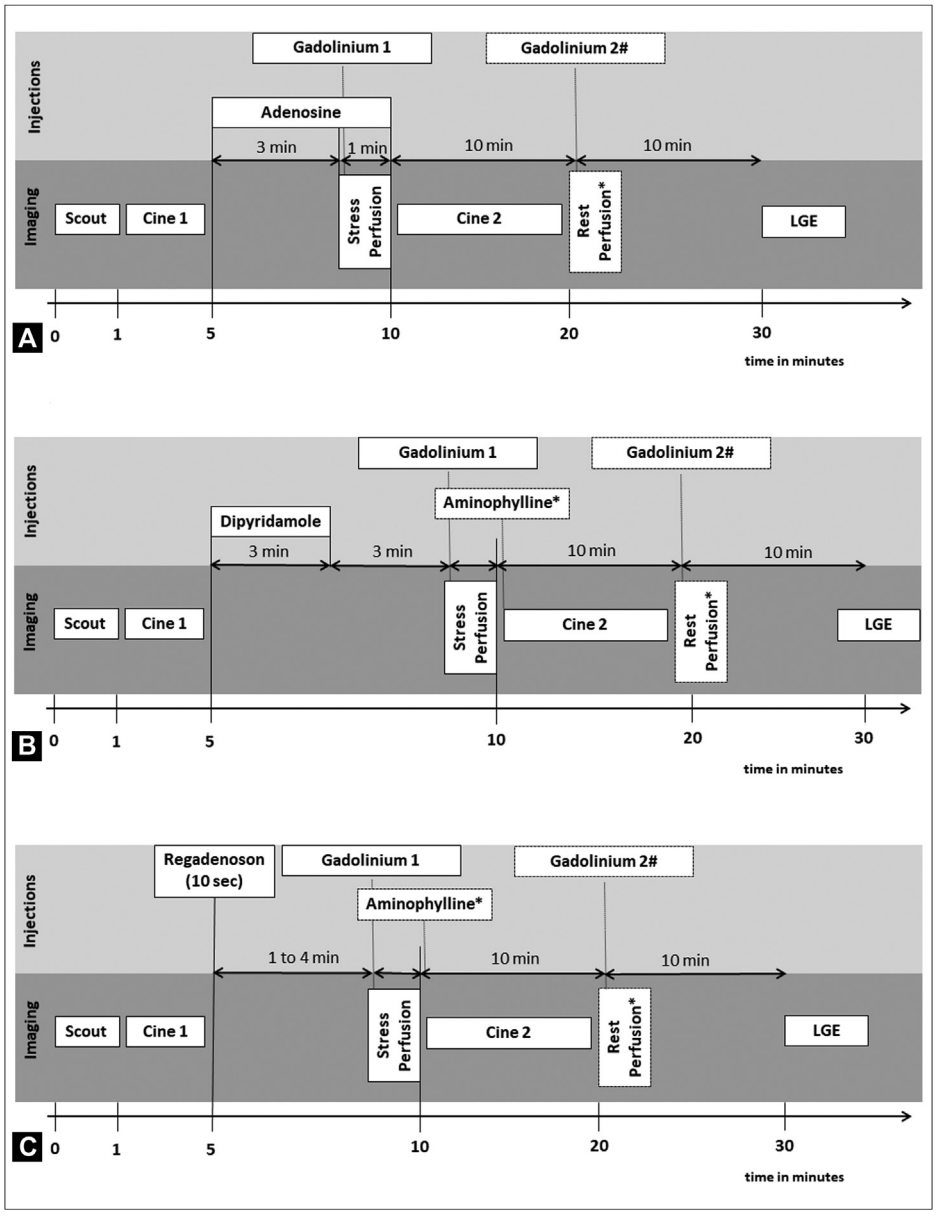

Fig. 3. Examples of stress MRI protocols according to vasodilator agent used: A: Adenosine; B: Dipyridamole; C: Regadenoson. *optionnal; #It might be reasonable to reinject gadolinium chelate to obtain good quality late gadolinium chelate enhancement (LGE) images after stress perfusion (if rest perfusion was not performed). LGE: Late gadolinium chelate enhancement.

- after intravenous administration of a bolus of 0.05 to 0.1 mmol/kg of gadolinium chelate (4–5 mL/s using an automatic injector);
- these slices are acquired on each R-R interval during the minute after injection of the bolus of gadolinium chelate;
- the acquisitions are performed under pharmacological stimulation:
  - during the last minute of the adenosine injection,
  - 3–5 min after the end of the slow intravenous administration of dipyridamole,
  - between 1 and 4 min after the intravenous bolus of regadenoson;
- pulse sequences must be adapted to the drug-induced tachycardia;
- a perfusion acquisition at rest after injection of the vasodilators is optional. It could be superfluous if the result of the stress perfusion is unequivocal (normal, ischemia). Aminophylline could also be injected after the first perfusion acquisition (minimum of 1 min after gadolinium chelate administration), to reverse vasodilation effect if dipyridamole or regadenoson is used as stress agent.

5.3. Late gadolinium chelate enhancement (LGE)

Two- or three-dimensional phase-sensitive inversion recovery (PSIR) sequences can be used.

- between 10 and 15 min (min) after intravenous administration of 0.1 to 0.15 mmol/kg of gadolinium chelate (dose depending on medical staff choice). It might be reasonable to reinject gadolinium chelate to obtain good quality LGE images after stress perfusion (if rest perfusion was not performed);
- inversion time is optimized for each patient so that the signal for healthy myocardium is zero at the time of acquisition;

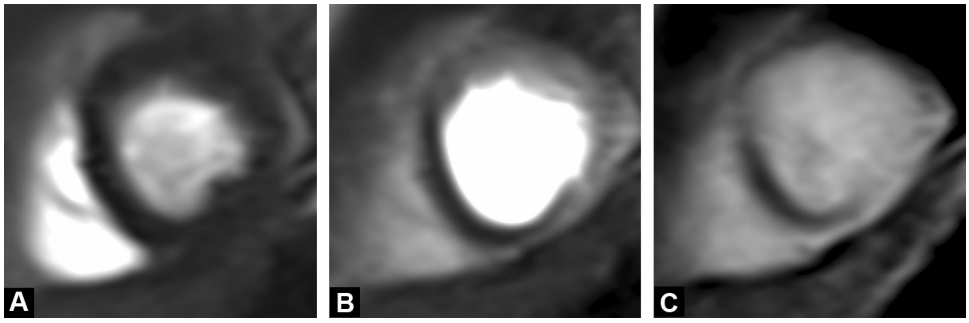

Fig. 4. Stress MRI imaging under regadenoson in a young adult with stenosis of the left anterior descending artery. Three sequential images are shown. A. Gadolinium chelate just reached the left ventricle cavity and no myocardial uptake of contrast material is visible. B. While normal myocardium enhances, septum and posterior wall perfusion is obviously decreased. C. Hypointensity, indicating ischemia, persisted during several cardiac cycles.

- slice thickness must be between 6- and 8-mm, in plane spatial resolution must be lower than ~1.4–1.8 mm.

6. Interpretation

Interpreting stress cardiac MRI is a synthesis that is not restricted to the analysis of first pass perfusion under vasodilators. The clinical, electrical and angiographic data (invasive coronary angiography or coronary CT) must be considered together with all features of MRI examination (hypokinesia, late enhancement). Therefore, in addition to experience in cardiac MRI, stress MRI should only be performed by teams with clinical competence in CAD.

6.1. Diagnosis of ischemia

The semiology of first pass perfusion sequence is fairly unequivocal. After intravenous administration, the gadolinium chelate appears successively in right heart chambers, pulmonary parenchyma then in the myocardium. Normal myocardium picks up the contrast clearly and evenly. Sometimes a perfusion gradient is observed from the epicardium to the endocardium; this feature must be fleeting to be considered as normal. In the case of coronary reserve deficit, persistent hypo perfusion is found in a segmental area (Fig. 4). This hypo perfused area is researched by browsing (slowly) through the first-pass sequence image by image. Going through the images using fast cine mode could mislead the observer then fleeting hypo perfusion could be missed. The perfusion images should be classified using the American Heart Association 17 segments model [31]. The number of diseased segments is used to assess the risk of adverse cardiovascular events. Hypo perfusion ≥ 2 segments is a sign of significant ischemia and carries a high risk of cardiovascular events.

The presence of ischemia is univocal when acquisitions and injections are correctly performed in a patient who has been previously vasodilated. Interpretation is facilitated when using motion compensation algorithms. When rest perfusion images are acquired it is important to make sure that the vasodilators are no longer effective; this is one of the advantages of adenosine, which has a very short half-life and thus does not require the use of an antagonist. When ischemia is detected, the first pass perfusion should be compared with cine sequences (wall motion abnormality and myocardial thinning are searched) and above all with the LGE:

- if the resting perfusion is normal and no LGE is visible, the hypo perfusion is reversible. Revascularization is a possible solution if at least 2 adjacent segments appear as hypo perfused during stress imaging;
- if hypo perfused segments are perfectly superimposable with LGE, the diagnosis is that of ischemic heart disease with necrotic sequalae. Occasionally, especially when infarct size is small, hypo perfused segments may not be identified during first pass perfusion sequence although typical ischemic LGE pattern is present [19];
- if hypo perfused area is wider than the LGE, peri-lesional stress hypo perfusion is present. It means that a revascularization procedure could be discussed according to the invasive coronary angiography findings.

6.2. Viability assessment

Stress cardiac MRI test must be completed by an analysis of myocardial viability using late enhancement after gadolinium chelate injection. A segmental hypersignal with < 25% of transmural extension indicates a strong probability of functional recovery after revascularization, whereas if > 75% is affected, no improvement can be expected [32]. A meta-analysis of 331 patients showed that less than 50% of transmural extension is predictive of functional recovery with 95% sensitivity and 51% specificity [33]. The contractile reserve test can be useful when the necrotic scar involves 25–50% of the thickness of the wall. The contractile reserve test consists of injecting a low dose of dobutamine (maximum 15 μg/kg/min in consecutive steps of 2.5–5 μg/kg/min every 2 to 3 min) analyzing the kinetics of the segment during the injection [34]. The thickness of the myocardium is not sufficient to assess myocardial viability because a thickness of less than 5 mm is not specific of non-viability [35].

6.3. Artifacts and hypoperfusion without epicardial coronary stenosis

When linear hypo signal is visible on a single slice, typically on the septum (Fig. 5), this can suggest a truncation artifact (or Gibbs artifact). True myocardial hypo perfusion is characterized by a front wave shaped hypo signal persisting during several R-R intervals (at least 3). A resting acquisition can be performed and compared image by image with the stress acquisition. The truncation artifact is generally visible and unchanged in both series (stress and rest). It is restricted to the subendocardium.

Perfusion anomalies can be observed on the first pass perfusion images even if the patient does not have significant epicardial coronary artery stenosis, and should not always be considered as “false positive”:

- if the patient’s heart is hypertrophic, a sub-endocardial hypo signal can be observed and could be the substrate of functional angina;

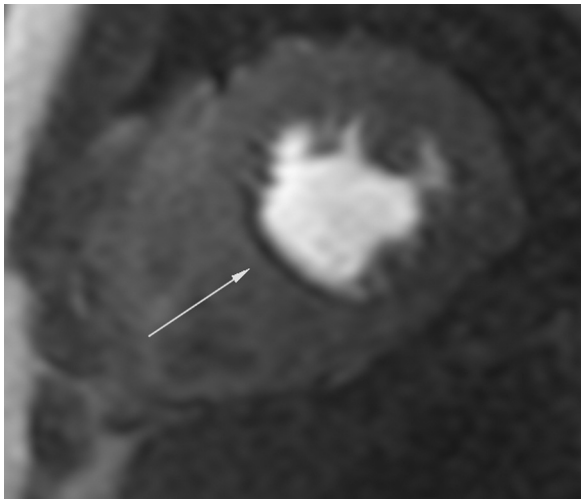

Fig. 5. Gibbs artifact in a young patient with hypertension. Hypointensity is visible in the phase encode direction when hyperintense gadolinium chelate appears in the left ventricle (arrow). The hyposignal, usually septal, is transient and limited to the endocardium. No ischemia was present in this patient.

- endothelial dysfunction may lead to sub-endocardial ischemia. Hypo signal is often circumferential and observed in the context of hypertension and/or diabetes mellitus.

7. Risk stratification by stress MRI

In line with the recommendations of the European Society of Cardiology, the expert group considers that an ischemia threshold ≥ 2 segments is the most relevant. A negative (perfusion or dobutamine) MRI stress test is associated with an annualized event rate $\leq 1\%$ for a follow-up period of over 2 years [36,37]. This "guarantee" period is assessed on the basis of a heterogeneous population and should thus be adapted according to the clinical risk factors such as age, female gender, presence of diabetes or the severity of coronary lesions [38].

In practice:

- in patient with unknown obstructive CAD, a positive MRI stress test indicates that an invasive coronary angiography should be performed to confirm the diagnosis and possibly treat the involved vessel. A non-conclusive MRI stress test requires an alternative method such as a CTA or an invasive coronary angiography according to the degree of clinical probability;
- in patient with known obstructive CAD, an invasive coronary angiography should only be performed if the MRI stress test shows ischemia in ≥ 2 segments, which is a sign of a high likelihood of events or if there are other criteria of severity such as the onset of symptoms at a low threshold of exercise, also a sign of a high risk of events, or if the patient remains symptomatic despite an optimal anti-angina treatment, or if LV function is compromised.

8. Conclusion

Cardiac stress testing by MRI has become the high-performance technology of choice for the diagnosis and classification of risk in patients with chronic coronary syndrome. Although vasodilators are the preferred products to carry out these procedures, because they are simple and safe to use, their administration in the MRI suite remains off-label in France. This group promotes the use of regadenoson for cardiac stress MRI. The latest recommendations issued by the European Society of Cardiology encourage the use of non-invasive imaging when obstructive coronary artery disease is suspected to the detriment of conventional treadmill test. This change in practice will stimulate the development of MRI stress tests that offer the advantages of a relatively low cost and no radiation exposure while offering a detailed analysis of the heart's morphology, function and viability of the myocardium during the same examination.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

The authors declare that the work described does not involve patients or volunteers.

Funding

This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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Project administration: Supervision; Alexis Jacquier, Alain Furber.

Review and editing: Martine Gilard, Louis Boyer.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.diii.2021.02.005.

Disclosure of interest

The authors declare that they have no competing interest.

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