Assessment of Myocardial Ischemia Using Stress Perfusion Cardiovascular Magnetic Resonance

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Coronary artery disease (CAD) is a major cause of mortality and morbidity throughout the world, and its prevalence is expected to increase worldwide. Myocardial ischemia is a strong predictor of future adverse outcomes in patients with suspected CAD. The detection of ischemia is an important part of the diagnostic strategy for patients with suspected CAD. Stress myocardial perfusion cardiovascular magnetic resonance (CMR) is a noninvasive diagnostic approach for the detection of myocardial ischemia. CMR offers several advantages over single-photon emission computed tomography, such as high spatial resolution and no radiation exposure. Stress perfusion CMR offers high diagnostic performance for the detection of CAD and prognostic value in patients with suspected CAD. In this review, we describe how to perform stress perfusion CMR and interpret its findings. We also discuss recent updates concerning the diagnostic and prognostic value of stress perfusion CMR in patients with suspected CAD.

Key words Magnetic resonance imaging · Myocardial perfusion imaging · Coronary artery disease · Myocardial ischemia.

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INTRODUCTION

Coronary artery disease (CAD) is a major cause of mortality and morbidity throughout the world, and its prevalence is expected to increase worldwide [1]. Myocardial ischemia is a strong predictor of adverse outcomes, such as future myocardial infarction and cardiac death [2]. The detection of ischemia is therefore an important part of the diagnostic strategy for patients with suspected CAD.

The noninvasive assessment of myocardial perfusion, such as via single-photon emission computed tomography (SPECT), is widely used for the detection of myocardial ischemia and risk stratification for patients with known or suspected CAD. Stress myocardial perfusion cardiovascular magnetic resonance (CMR) is a noninvasive diagnostic approach for the detection of myocardial ischemia. Stress perfusion CMR offers several advantages over SPECT, including a high spatial resolution and no radiation exposure. Stress perfusion CMR yields high diagnostic accuracy for the detection of CAD [3-13], and its prog-

nostic value has also been documented [14,15].

The purpose of this review is to describe how to obtain and interpret stress perfusion CMR images and to report its diagnostic and prognostic value in patients with suspected CAD.

HOW TO PERFORM STRESS PERFUSION CMR

Preparation of the magnetic resonance imaging environment

Performing CMR examinations requires the incorporation of additional physiological monitoring into general magnetic resonance (MR) equipment, such as electrocardiogram (ECG) monitoring, MR-compatible blood pressure monitoring with remote activation from the control room, and oxygen saturation monitoring [16]. Most MR systems currently use advanced triggering modules based on vector-cardiography (VCG). During positioning, the quality of the ECG trace should be checked. If the tracing is unsatisfactory, repositioning of ECG electrodes is required to obtain an optimum signal. An MR-compatible power injector and separate infusion pump are required to deliver an intravenous bolus of contrast agent and continuous infusion

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of adenosine (Fig. 1). A crash cart including a defibrillator and adequate expertise in basic and advanced cardio-respiratory life support must be available throughout the CMR examination to address any adverse events.

Patient preparation

Patients are instructed to abstain from substances containing caffeine 12–24 h prior to stress testing, as caffeine attenuates the coronary hyperemic response to pharmacologic stress agents by blocking the A_{2A} receptors [17]. Generally, 2 intravenous lines are placed in the antecubital vein in each arm: one for gadolinium and one for a stress agent. A blood pressure cuff is placed on either arm with care not to interfere with the injection of the gadolinium or stress agent. MR-compatible ECG electrodes and the receiver coil are placed on the chest. It is essential to explain the breath-hold commands to the patient and, if necessary, briefly practice these instructions.

Pharmacological stressors

Stress perfusion CMR is usually performed under pharmacologic stress. Various pharmacologic stress agents, such as ade-

nosine, dipyridamole and regadenoson, are used to induce vasodilation [18,19]. These pharmacologic stress agents relax the arteriolar tonus through the stimulation of A_{2A} receptors and are associated with a 3- to 5-fold increase in myocardial blood flow (MBF) in normal subjects [20] (Table 1). Adenosine is the most widely used stress agent for myocardial perfusion CMR. Adenosine activates A_1 , $A_{2A,B}$, and A_3 receptors non-selectively and has an extremely short half-life (<10 seconds) [18], allowing the side effects to be resolved quickly by termination of the adenosine infusion. Adenosine is administered at an infusion dose of 140 $\mu\text{g/kg/min}$ for 3–4 minutes [16]. In patients showing an inadequate hemodynamic response (heart rate increase <10 bpm or systolic blood pressure decrease <10 mm Hg) to the standard adenosine protocol, a high-dose adenosine protocol up to 210 $\mu\text{g/min/kg}$ should be considered [16]. Dipyridamole is an inhibitor of adenosine reuptake that acts indirectly by increasing the local concentration of endogenous adenosine and is activated by metabolism in the liver. The vasodilatory capacity of dipyridamole depends on the individual metabolic rate [18]. Side effects of dipyridamole can be resolved by administration of theophylline [18]. However, a prolonged duration of action for dipyridamole (approximately 30 minutes) makes it less controllable, and it is infrequently used today. Perfusion CMR with dipyridamole uses an infusion dose of 0.56 mg/kg for 4 minutes, with the peak of vasodilation reached at about 2 minutes after finishing the infusion [21]. Regadenoson (initial half-life 2–4 min) is a selective A_{2A} agonist given as an intravenous bolus at a fixed dose of 400 μg [19]. Owing to selective A_{2A} receptor stimulation, regadenoson has a lower incidence of significant side effects and less effect on blood pressure than adenosine [19]. The longer half-life of regadenoson brings the disadvantage of a longer persistence of side effects, although the adverse event rate is lower than that with adenosine or dipyridamole. Regadenoson is administered intravenously 1 minute before contrast injection, reducing the need for infusion pumps and 2 intravenous lines by giving a bolus injection at a fixed dose [16,19]. Table 1 summarizes the characteristics of the stress agents.

Adenosine 5'-triphosphate (ATP) is a precursor of endogenous adenosine with a very short half-life (<10 seconds) and

Fig. 1. Typical example of an MRI unit equipped with a power injector with a dual injection system (contrast agent and saline) (black arrow) and an MR-compatible infusion system for the administration of vasodilator agents (white arrow).

Table 1. Characteristics of stress agents

Stress agent	Dose and infusion rate	Mechanism of action	Half-life
Dipyridamole	0.56 mg/kg 4-min infusion	Inhibiting the adenosine reuptake	30 min
Adenosine	140–210 $\mu\text{g/kg/min}$ 3–5-min infusion	Activation of A_1 , $A_{2A,B}$, A_3 receptors	<10 sec
Adenosine 5'-triphosphate (ATP)	160 $\mu\text{g/kg/min}$ 3–5-min infusion	Same as adenosine	Same as adenosine
Regadenoson	0.4 mg Single bolus	Activation of A_{2A} receptor	2–4 min

effects similar to adenosine [22]. The main advantage of ATP is the reduced cost [23]. There are also fewer side effects with intravenous infusion ATP than adenosine, an important factor in the clinical setting [24,25]. Accordingly, ATP is widely used as a pharmacologic stress agent instead of adenosine for stress myocardial perfusion imaging, mainly in Asian countries [26-29] and some European countries [23,25]. ATP is administered intravenously at 0.16 mg/kg/min [22,24-29]. Watanabe et al. [26] found a similar diagnostic efficacy with dipyridamole (0.156 mg/kg/min) and ATP (0.16 mg/kg/min). Chun et al. [27] directly compared the effect of adenosine (0.14 mg/kg/min) and ATP (0.16 mg/kg/min) in the same subjects using Tl-201 SPECT and reported that the hemodynamic changes and degree of myocardial uptake were similar between adenosine and ATP.

Contra-indications for these stress agents include second- or third-degree atrioventricular block, systolic blood pressure <90 mm Hg, sinus bradycardia (heart rate <40 bpm), reactive airway

disease with regular use of inhalers and known hypersensitivity to these agents [16,30]. Side effects for these stress agents may include light flushing, mild chest discomfort and headache. More serious side effects include atrioventricular conduction block, bronchospasm, a rapid decrease in blood pressure or cerebral hypoperfusion with potential neurological symptoms in the presence of significant carotid stenosis [30].

Splenic switch-off is a novel sign in the assessment of stress adequacy during adenosine myocardial stress perfusion CMR [31]. The spleen has an abundant blood flow in the resting state. However, splanchnic vasoconstriction is induced by the administration of adenosine. Therefore, the spleen has reduced signal intensity during stress compared with the resting state on perfusion imaging (Fig. 2). Failed splenic switch-off with adenosine is an observation that identifies understressed patients who are at risk of having false-negative findings on stress perfusion CMR (Fig. 3). Using splenic switch-off as the assessment

Fig. 2. A case with splenic switch-off. In this 81-year-old woman with chest oppression, the spleen exhibits reduced signal intensity during stress (A and B) compared with the resting state (C and D) on perfusion imaging (dotted circles). CAG reveals significant stenosis in the RCA (white arrow) (E). In this patient, stress-induced ischemia due to significant stenosis in the RCA is accurately detected by stress perfusion cardiovascular magnetic resonance in the inferior wall (arrowheads) (A). CAG: coronary angiography, RCA: right coronary artery.

Fig. 3. A case with failed splenic switch-off. In this 73-year-old man with dyspnea on exertion, the spleen signal intensity on perfusion CMR was not reduced during stress (A and B) compared with perfusion CMR at rest (C and D) (dotted circles). In this patient, stress perfusion CMR failed to detect stress-induced ischemia despite the presence of significant stenosis in the proximal left anterior descending artery on CAG (arrow) (E). CMR: cardiovascular magnetic resonance, CAG: coronary angiography.

for adequate pharmacological response may improve the test sensitivity of stress perfusion magnetic resonance imaging (MRI). However, pharmacologic stress perfusion CMR acquired after the administration of regadenoson shows no attenuation of splenic blood flow. Therefore, splenic switch-off as the assessment for adequate pharmacological response cannot apply to stress perfusion imaging with regadenoson.

Perfusion CMR imaging

An extracellular gadolinium-based contrast agent is used for first-pass myocardial perfusion CMR. It is recommended that CMR be performed according to the standardized CMR protocols proposed by the Society for Cardiovascular Magnetic Resonance [16]. Stress perfusion CMR is generally performed as part of a comprehensive CMR protocol including cine MRI, perfusion MRI, and late gadolinium-enhanced (LGE) imaging. After obtaining a true short axis view of the left ventricle and before starting pharmacological stress, a “test” perfusion sequence without contrast should be acquired to assess the presence of artifacts, satisfactory VCG triggering and patient compliance with breathing commands. The patients are instructed to begin holding their breath at the start of image acquisition and to continue breath-holding for as long as possible followed by shallow breathing in order to minimize respiratory artifacts. It is important to obtain data every heart beat with at least 3 slices per beat during 40–50 RR intervals. Immediately after perfusion CMR acquisition is started, the contrast agent is injected as a bolus into a peripheral vein at a dose of 0.05–0.10 mmol/kg and a rate of 3–7 mL/s, followed by a 30-mL saline flush using the same injection rate to facilitate a compact bolus passage [3,16].

HOW TO INTERPRET STRESS PERFUSION CMR

Myocardial perfusion CMR can be evaluated by visual, semi-quantitative and quantitative analyses [5,32]. Semi-quantitative and quantitative analyses rely on time intensity curves measured from regions of interest in the left-ventricular (LV) blood and myocardium. A widely available post-processing software program is lacking at present for quantitative analysis. Furthermore, performing a quantitative analysis can be difficult because the MR signal from the LV blood pool is no longer proportional to the gadolinium concentration during the first pass [32]. Consequently, semi-quantitative and quantitative analyses of perfusion CMR are largely restricted to research applications. Accordingly, we will focus on the visual assessment of stress perfusion CMR in this review.

After the intravenous bolus administration of contrast agents, there is pronounced signal enhancement in the right-ventricular

(RV) cavity, followed by the LV cavity and, finally, the LV myocardium. When coronary arteries are narrowed by atherosclerotic disease, coronary autoregulation attempts to normalize the MBF by reducing the resistance of distal perfusion beds to preserve adequate myocardial oxygen supply [33,34]. Since autoregulation already causes compensatory maximal dilation at rest in the stenosis-dependent myocardium, these vessels cannot be dilated any further. Thus, pharmacologic vasodilation induces an increase in the blood flow in myocardial areas supplied by normal coronary arteries, whereas no changes are found in areas supplied by stenotic coronary arteries [33,34]. As a result, normal myocardium will show a homogenous increase in the signal intensity, followed by contrast washout. Conversely, the area supplied by coronary arteries with significant stenosis will show a delayed signal intensity increase. This manifests as a darker area, known as a perfusion defect, in the poorly perfused myocardium (Fig. 4). A true perfusion defect is characterized by being most prominent in the subendocardium, occurring in segments that anatomically correlate to a particular coronary artery distribution and persisting for several RR intervals [35].

Perfusion images are generally assessed using the American Heart Association (AHA) 16-segment model. Rest and stress perfusion images are displayed side by side on a workstation and visually evaluated by manually paging the images. In addition, corresponding slices of LGE images are presented. Table 2 summarizes how to interpret stress perfusion CMR using LGE. First, LGE images are reviewed to obtain information regarding the presence or absence of myocardial infarction (MI), and then the stress and rest perfusion CMR images are evaluated for ischemia [35] (Fig. 5). Ischemia is considered present if a myocardial perfusion defect is present during stress that was not observed at rest in the absence of MI. If a myocardial perfusion defect is seen in both rest and stress perfusion CMR images and there is no evidence of scarring on LGE images, the defect is considered an artifact or resting ischemia.

Several important pitfalls should be acknowledged when interpreting perfusion CMR. The most common and annoying artifact is dark rim artifact (DRA) [36], which typically occurs at the interface between the LV cavity and subendocardial border and can be mistaken for a true perfusion defect. It may mimic a subendocardial perfusion defect in its location but has characteristics that allow it to be differentiated from a true perfusion defect. DRA often appears darker than the non-enhanced myocardium before contrast arrival and thus darker than a true perfusion defect (Fig. 6). It tends to occur before the start of myocardial enhancement and lasts for only a few heart beats before rapidly decreasing in severity and disappearing during the washout phase of contrast. Myocardial hypointensities that do not correspond to an artery distribution territory may be a clue in distinguishing DRA from true perfusion defects [37]. Arti-

Fig. 4. First-pass myocardial perfusion CMR images during ATP stress (A) and in the resting state (B) in a patient with chest pain. The stress perfusion CMR image shows an area of hypoperfusion in the anteroseptal wall (arrows) that is not depicted in the rest perfusion image, indicating ischemic myocardium due to significant stenosis in the LAD artery. The corresponding LGE image shows the absence of myocardial infarction (C). CAG shows significant coronary artery stenosis (arrowhead) in the LAD artery (D). CMR: cardiovascular magnetic resonance, ATP: adenosine 5'-triphosphate, LAD: left anterior descending, LGE, late gadolinium-enhanced MRI, CAG: coronary angiography.

Table 2. Visual analysis of cardiac perfusion images

Stress	Rest	LGE	Interpretation
Negative	Negative	Negative	Normal
Negative	Negative	Positive	Infarction
Positive	Negative	Negative	Ischemia
Positive	Positive	Positive	Infarction
Positive	Positive	Negative	Artifacts, resting ischemia, delayed contrast arrival

LGE: late gadolinium-enhanced MRI

fact mechanisms that may lead to DRA include Gibbs artifact caused by limited resolution, susceptibility artifacts from the passage of the contrast and cardiac motion during data acquisition [36]. The prominence of such artifacts can be reduced by increasing spatial resolution in the phase-encoding direction, as this minimizes Gibbs artifact, which is thought to play an important role in the appearance of DRA [36].

Both multi-vessel disease and microvascular dysfunction have been reported to show a similar entire subendocardial

perfusion defect during stress perfusion CMR [38]. With a visual analysis of the images, it is sometimes difficult to distinguish between multi-vessel disease and microvascular dysfunction. The addition of coronary morphology imaging, such as whole-heart coronary MR angiography or coronary CT angiography, to perfusion CMR can help distinguish between multi-vessel disease and microvascular dysfunction (Fig. 7).

Coronary tortuosity and ectasia are phenomena often encountered and caused by age or arteriosclerosis [39]. Contrast agents passing through a tortuous coronary artery must travel a longer distance to the myocardium than when passing through normal coronaries. Tortuosity and ectasia of the coronary artery may lead to delayed regional contrast arrival, resulting in an increased number of false positive results (Fig. 8). The delay caused by the longer distance of the bolus to reach the myocardium should be transmural, while with a true perfusion defect, hypoenhancement is non-transmural in the majority of cases.

DIAGNOSTIC PERFORMANCE OF STRESS PERFUSION CMR

Stress perfusion CMR vs. SPECT

SPECT, commonly used worldwide for the assessment of myocardial ischemia, may have suboptimal diagnostic accuracy in patients with multi-vessel CAD because of equilibration of

ischemia [40]. Stress perfusion CMR imaging yields high diagnostic accuracy for the detection of CAD, especially at the sub-endocardial level, due to its inherent high spatial resolution [3-5]. Many comparative studies with SPECT suggest that stress perfusion CMR can realistically be used as an alternative modality with superior performance relative to that of SPECT. In our single-center studies that directly compared stress perfusion

Fig. 5. Interpretation of stress perfusion CMR in relation to LGE CMR. When interpreting a stress CMR study, myocardial perfusion CMR images during stress (A) and at rest (B) and corresponding LGE CMR images (C) are displayed side-by-side. The top and bottom rows represent the same images with and without markers. In the LGE images (C), subendocardial MI is noted in the anteroseptal wall (white circle). The stress and rest images are evaluated for ischemia in the area outside of the MI region, indicated by the white circle. A myocardial perfusion defect is present during stress that was not observed at rest in the absence of MI (dotted circle), indicating stress-induced myocardial ischemia. CMR: cardiovascular magnetic resonance, LGE: late gadolinium-enhanced MRI, MI: myocardial infarction.

Fig. 6. DRA. ATP stress (A) and rest (B) perfusion CMR images show a DRA at the interface between the left ventricular cavity and subendocardial border of the septum (black arrows). True ischemia can be seen in the anterior wall of the stress perfusion CMR image (white arrowheads) in this case. DRA: dark rim artifact, ATP: adenosine 5'-triphosphate, CMR: cardiovascular magnetic resonance.

Fig. 7. A 64-year-old woman with chest pain and hypertension. Subendocardial hypoperfusion is observed in the entire circumference of the left ventricle on stress perfusion magnetic resonance imaging (arrows) (A and B) and no myocardial infarction was evident on LGE image (C), suggesting that this patient might have multi-vessel disease or microvascular dysfunction. Multi-vessel disease was excluded by coronary magnetic resonance angiography (D). Note that this patient has a thickened left-ventricular wall. Subendocardial hypoperfusion is frequently observed in patients with left-ventricular hypertrophy, including those with hypertrophic cardiomyopathy and a hypertensive heart. LGE: late gadolinium-enhanced MRI, RCA: right coronary artery, LAD: left anterior descending artery, LCX: left circumflex artery.

CMR and SPECT, the area under the receiver operating characteristic curve (AUC) for the detection of significant CAD [defined as >50% luminal narrowing on quantitative coronary angiography (QCA)] was 0.91 for perfusion CMR, which was significantly higher than that for SPECT (0.75, $p < 0.001$) in a vessel-based analysis [5]. In the previous multicenter, multi-vendor prospective MR-IMPACT trial, the diagnostic performance of stress perfusion CMR ($\text{AUC } 0.86 \pm 0.06$) was better than that of stress perfusion SPECT (0.67 ± 0.05 , $p = 0.013$), particularly in patients with 2- and 3-vessel disease [3]. Recently, the CE-MARC study, a prospective study comparing stress CMR and SPECT in a large real-world population, demonstrated that stress perfusion CMR ($\text{AUC } 0.89$) significantly out-performed stress SPECT ($\text{AUC } 0.74$, $p < 0.0001$) with higher sensitivity (CMR, 87%; SPECT, 67%) and higher negative predictive values (CMR, 91%; SPECT, 79%) than SPECT in a patient-based analysis [4]. The CE-MARC study also revealed that stress perfusion CMR performed better than SPECT not only in patients with multi-vessel CAD ($\text{AUC: CMR } 0.91$, $\text{SPECT } 0.77$, $p < 0.0001$) but also in those with single-vessel CAD ($\text{AUC: CMR } 0.87$, $\text{SPECT } 0.71$, $p < 0.0001$) (Table 3) [4]. In a previous meta-analysis

comparing the diagnostic accuracy of perfusion CMR, SPECT, and positron emission tomography (PET) using QCA as the reference standard, the patient-based analysis per imaging modality demonstrated pooled sensitivities of 88, 89, and 84% and specificities of 61, 76, and 81% for SPECT, CMR, and PET, respectively. CMR showed a significantly higher diagnostic accuracy than SPECT [6].

Diagnostic accuracy of stress perfusion CMR against QCA and FFR

QCA is a well-established technique for the anatomic assessment of CAD [41]. Multiple studies have assessed the ability of perfusion CMR to detect myocardial ischemia with QCA or a visual estimation of stenosis severity as a reference standard, and the high diagnostic accuracy of stress perfusion CMR has been proven [7-9]. A meta-analysis by Nandalur et al. [9] showed that stress perfusion CMR provides a sensitivity of 0.91 and a specificity of 0.81 on a patient level (disease prevalence=57.4%) when compared with QCA as a reference standard.

However, anatomical narrowing of the coronary artery does not always correlate with the functional significance of CAD.

Although QCA reveals anatomical narrowing of the coronary artery, it may not reliably detect whether or not stenosis leads to ischemia. At present, the fractional flow reserve (FFR), a meth-

od of assessing hyperemic pressure differences across coronary artery stenosis, is considered the gold standard for the diagnosis of ischemia-causing CAD [42]. Watkins et al. [10] compared

Fig. 8. A transmurial perfusion defect without subendocardial predominance is seen on both stress (A) and rest (B) perfusion CMR without evidence of myocardial infarction on late gadolinium-enhanced CMR (not shown). The X-ray coronary angiogram shows normal coronary arteries without atherosclerotic changes (C). Contrast agent passing through a tortuous RCA must travel a longer distance to the myocardium than through a normal LCA, which may lead to delayed regional contrast arrival. CMR: cardiovascular magnetic resonance, RCA: right coronary artery, LCA: left coronary artery.

Table 3. Stress perfusion CMR vs. SPECT

First author (reference no.)	Study	All/single vessel disease/ multi-vessel disease	AUC		p value
			CMR	SPECT	
Ishida et al. [5]	Single-center (n=69)	All*	0.91	0.75	<0.001
Schwitter et al. [3]	Multi-center (n=241)	All*	0.86	0.67	0.013
		Multi-vessel disease*	0.89	0.70	0.006
Greenwood et al. [4]	Single-center, randomized (n=676)	All†	0.89	0.74	<0.0001
		Single-vessel disease†	0.87	0.71	<0.0001
		Multi-vessel disease†	0.91	0.77	<0.0001

*>50% diameter stenosis on QCA, †>70% (>50% left main coronary trunk) diameter stenosis on QCA. CMR: cardiovascular magnetic resonance, SPECT: single-photon emission computed tomography, AUC: area under the receiver operating characteristic curve, QCA: quantitative coronary angiography

Table 4. Diagnostic accuracy of stress perfusion CMR against QCA and FFR

First author (reference no)	Study	Sensitivity (%)	Specificity (%)	AUC	Reference
Ishida et al. [5]	Single-center (n=69)	90	85	0.91	QCA
Greenwood et al. [4]	Single-center (n=676)	86.5	83.4	0.89	QCA
Watkins et al. [10]	Single-center (n=103)	95	91	NA	FFR
Lockie et al. [11]	Single-center (n=42)	82	94	0.92	FFR
Jaarsma et al. [6]	Meta-analysis studies (n=27) Patients (n=2841)	89	76	0.90	QCA
Nandalur et al. [9]	Meta-analysis studies (n=14) Patients (n=1183)	91	81	NA	QCA
Li et al. [12]	Meta-analysis studies (n=14) Patients (n=650)	90	87	0.95	FFR
Takx et al. [13]	Meta-analysis studies (n=15) Patients (n=798)	89	87	0.94	FFR

CMR: cardiovascular magnetic resonance, QCA: quantitative coronary angiography, FFR: fractional flow reserve, AUC: area under the receiver operating characteristic curve

the diagnostic accuracy of perfusion CMR versus FFR (a value <0.75 denoting significant stenosis). In a per-patient analysis, the sensitivity and specificity of perfusion CMR for the detection of functionally significant CAD were 95% and 91%, respectively, with respective positive and negative predictive values of 97% and 84% [10]. Lockie et al. [11] also compared perfusion CMR against FFR (a value <0.75 denoting significant stenosis). The sensitivity and specificity of visual CMR analysis to detect significant stenosis by FFR were 0.82 and 0.94, respectively, with an AUC of 0.92 [11]. Thus, stress perfusion CMR can detect functionally significant CAD with excellent diagnostic accuracy. In a meta-analysis reported by Li et al. [12], perfusion CMR allowed for the accurate detection of ischemic CAD with FFR as the reference standard. The pooled sensitivity, specificity, and AUC were 0.90, 0.87, and 0.95 at the patient level and 0.89, 0.86, and 0.93 at the vessel level, respectively. Another recent meta-analysis comparing stress perfusion CMR with other myocardial perfusion imaging modalities such as PET, SPECT, perfusion computed tomography and perfusion echocardiography, using FFR as a reference, concluded that stress perfusion CMR (sensitivity 89%, specificity 87%) has better diagnostic performance than SPECT (sensitivity 74%, specificity 79%) or echocardiography (sensitivity 69%, specificity 84%) and achieves similar high diagnostic performance compared with perfusion PET (sensitivity 84%, specificity 87%) and perfusion computed tomography (sensitivity 88%, specificity 80%) (Table 4) [13].

PROGNOSTIC VALUE OF PERFUSION CMR

Over the past several years, multiple studies have demonstrated that stress perfusion CMR has excellent prognostic characteristics and may help guide risk stratification of patients

with known or suspected CAD [14,15]. According to a recent meta-analysis of 19 intermediate-term follow-up studies using stress CMR, including 15 studies with vasodilator stress perfusion CMR, patients with ischemia had a higher incidence of nonfatal MI [odds ratio (OR): 5.4], cardiovascular death (OR: 5.9) and the combined endpoint (OR: 6.5) than those with a negative stress perfusion CMR study [14]. In addition, patients without evidence of ischemia on stress perfusion CMR have an annual event rate of <1% for either cardiovascular death or nonfatal MI, whereas patients with ischemia on stress perfusion CMR have a 5% annual event rate [14].

SPECT has excellent prognostic value for risk stratification and guiding therapeutic decision-making in patients with known or suspected CAD [43]. Recently, the prognostic value of CMR was compared with that of SPECT in patients with suspected CAD in a 5-year follow-up of the CE-MARC study [15]. The data indicated that CMR is a stronger predictor of risk for major adverse cardiac events (MACEs) than SPECT, independent of cardiovascular risk factors, angiography results, or initial patient treatment, although abnormal findings on CMR (hazard ratio, 2.77; $p<0.001$) and SPECT (hazard ratio, 1.62; $p=0.014$) were both strong and independent predictors of MACEs [15].

SUMMARY

With adequate imaging and interpretation skills, stress myocardial perfusion CMR provides an accurate assessment of myocardial ischemia and allows for risk stratification and prognostic evaluation in patients with known or suspected CAD.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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