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Diagnostic and Prognostic Value of Stress Cardiovascular Magnetic Resonance Imaging in Patients With Known or Suspected Coronary Artery Disease
A Systematic Review and Meta-analysis

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Supplemental content

IMPORTANCE The clinical utility of stress cardiovascular magnetic resonance imaging (CMR) in stable chest pain is still debated, and the low-risk period for adverse cardiovascular (CV) events after a negative test result is unknown.

OBJECTIVE To provide contemporary quantitative data synthesis of the diagnostic accuracy and prognostic value of stress CMR in stable chest pain.

DATA SOURCES PubMed and Embase databases, the Cochrane Database of Systematic Reviews, PROSPERO, and the ClinicalTrials.gov registry were searched for potentially relevant articles from January 1, 2000, through December 31, 2021.

STUDY SELECTION Selected studies evaluated CMR and reported estimates of diagnostic accuracy and/or raw data of adverse CV events for participants with either positive or negative stress CMR results. Prespecified combinations of keywords related to the diagnostic accuracy and prognostic value of stress CMR were used. A total of 3144 records were evaluated for title and abstract; of those, 235 articles were included in the full-text assessment of eligibility. After exclusions, 64 studies (74 470 total patients) published from October 29, 2002, through October 19, 2021, were included.

DATA EXTRACTION AND SYNTHESIS This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

MAIN OUTCOMES AND MEASURES Diagnostic odds ratios (DORs), sensitivity, specificity, area under the receiver operating characteristic curve (AUROC), odds ratio (OR), and annualized event rate (AER) for all-cause death, CV death, and major adverse cardiovascular events (MACEs) defined as the composite of myocardial infarction and CV death.

RESULTS A total of 33 diagnostic studies pooling 7814 individuals and 31 prognostic studies pooling 67 080 individuals (mean [SD] follow-up, 3.5 [2.1] years; range, 0.9-8.8 years; 381 357 person-years) were identified. Stress CMR yielded a DOR of 26.4 (95% CI, 10.6-65.9), a sensitivity of 81% (95% CI, 68%-89%), a specificity of 86% (95% CI, 75%-93%), and an AUROC of 0.84 (95% CI, 0.77-0.89) for the detection of functionally obstructive coronary artery disease. In the subgroup analysis, stress CMR yielded higher diagnostic accuracy in the setting of suspected coronary artery disease (DOR, 53.4; 95% CI, 27.7-103.0) or when using 3-T imaging (DOR, 33.2; 95% CI, 19.9-55.4). The presence of stress-inducible ischemia was associated with higher all-cause mortality (OR, 1.97; 95% CI, 1.69-2.31), CV mortality (OR, 6.40; 95% CI, 4.48-9.14), and MACEs (OR, 5.33; 95% CI, 4.04-7.04). The presence of late gadolinium enhancement (LGE) was associated with higher all-cause mortality (OR, 2.22; 95% CI, 1.99-2.47), CV mortality (OR, 6.03; 95% CI, 2.76-13.13), and increased risk of MACEs (OR, 5.42; 95% CI, 3.42-8.60). After a negative test result, pooled AERs for CV death were less than 1.0%.

CONCLUSION AND RELEVANCE In this study, stress CMR yielded high diagnostic accuracy and delivered robust prognostication, particularly when 3-T scanners were used. While inducible myocardial ischemia and LGE were associated with higher mortality and risk of MACEs, normal stress CMR results were associated with a lower risk of MACEs for at least 3.5 years.

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Key Points

Question What is the diagnostic and prognostic value of stress cardiovascular magnetic resonance imaging (CMR) for the evaluation of stable chest pain?

Findings In this systematic review and meta-analysis pooling 74 470 patients with stable chest pain over 381 357 person-years of follow-up, stress CMR yielded high diagnostic accuracy and accurate risk stratification in patients with known or suspected coronary artery disease, particularly when 3-T imaging was used. The presence of stress-inducible ischemia and late gadolinium enhancement was associated with higher mortality and likelihood of cardiovascular events, while normal stress CMR results were associated with a lower likelihood of cardiovascular events for at least 3.5 years.

Meaning These findings suggest that combined assessment of inducible myocardial ischemia and late gadolinium enhancement by stress CMR is an accurate method to diagnose and risk stratify patients with stable chest pain and known or suspected coronary artery disease.

Coronary artery disease (CAD) is the leading cause of cardiovascular (CV) morbidity and mortality worldwide. Noninvasive imaging plays a central role in the 2019 European Society of Cardiology guidelines on chronic coronary syndromes[1] and the 2021 American Heart Association/American College of Cardiology (AHA/ACC) guidelines on chest pain.[2] Evaluation of stress-inducible myocardial ischemia by assessment of perfusion reserve or regional wall motion abnormalities is a key element in the diagnostic workup of patients with stable chest pain and intermediate to high pretest probability of CAD.[1,3]

New recommendations for the use of noninvasive imaging in coronary syndromes developed by a transatlantic intersociety task force[4] endorse the use of stress cardiovascular magnetic resonance imaging (CMR) to detect ischemia and guide clinical decision-making in patients with a high intermediate pretest clinical likelihood of CAD. Consistent with this endorsement, the 2021 AHA/ACC guidelines for the evaluation and diagnosis of chest pain delivered class 1 and 2A recommendations for stress CMR as first-line functional investigation for the evaluation of chest pain in patients with known or suspected CAD who are at intermediate risk.[2]

Coronary artery disease is one of the primary indications for CMR,[5,6] and the use of stress CMR has been steadily growing worldwide.[6] However, contemporary data on the diagnostic accuracy and prognostic value of stress CMR in patients with known or suspected CAD are currently lacking. After 20 years of clinical use and the completion of large multicenter observational studies[7,8] and randomized clinical trials,[9,10] which were not included in previous systematic reviews and meta-analyses,[11-14] we appraised the best available contemporary evidence to deliver an updated quantitative synthesis on the diagnostic accuracy and prognostic value of stress CMR for the assessment of chest pain.

Methods

This systematic review and meta-analysis was planned, conducted, and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline for design, analysis, and reporting of meta-analyses of randomized and observational studies[15] and the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy.[16] A review protocol was prospectively registered on PROSPERO (CRD42022299275).

Systematic Review

We searched PubMed and Embase databases, the Cochrane Database of Systematic Reviews, the PROSPERO database, and the ClinicalTrials.gov registry for potentially relevant articles from January 1, 2000, through December 31, 2021 (eFigure 1 in Supplement 1). We used 2 prespecified combinations of keywords related to the diagnostic accuracy of stress CMR (eMethods in Supplement 1). We also searched reference lists of all identified articles for additional relevant studies, including hand searching reviews and published meta-analyses.

Two authors (G.B. and A.D.C.) performed the screening of titles and abstracts, reviewed full-text articles, and determined their eligibility. Discrepancies were resolved by consensus with other reviewers (F.R., M.Y.K., and A.C.). The review process was not blinded to study results. Studies were eligible if they met the following criteria: (1) were published as a full-length article, (2) were written in the English language, (3) had a prospective or retrospective study design, (4) enrolled 100 or more patients aged 18 years or older, and (5) reported estimates of the diagnostic accuracy of stress CMR compared with invasive coronary angiography (ICA) or fractional flow reserve (FFR) as the reference test and/or reported raw data for all-cause death, CV death, and major adverse cardiovascular events (MACEs, defined as the composite of CV death and myocardial infarction [MI]) for study participants with either positive or negative stress CMR scans. Studies were eligible regardless of whether they included patients who were referred for suspected or known CAD and regardless of the technique used for evaluation of inducible ischemia (ie, wall motion analysis or perfusion; qualitative, semiquantitative, or fully quantitative).

Two investigators (G.B. and A.D.C.) abstracted relevant data of patient populations, study-level characteristics, and outcomes from original eligible sources. The ascertainment of clinical events was accepted as reported. The quality of eligible studies was evaluated using the Quality Assessment of Diagnostic Accuracy Studies, version 2 (QUADAS-2) tool[17] for diagnostic studies and the Newcastle-Ottawa Scale[18] for prognostic studies.

Statistical Analysis

Categorical variables were reported as percentages and continuous variables as means with SDs or medians with

IQRs, as appropriate. We used the inverse variance heterogeneity model for the meta-analysis of diagnostic studies, which proved superior to the standard bivariate model.[19] For each study, raw data of true-positive, true-negative, false-positive, and false-negative results were either extracted from the study or generated from reported diagnostic estimates. Diagnostic odds ratios (DORs), area under the receiver operating characteristic curve (AUROC), sensitivity, specificity, negative likelihood ratio (NLR), and positive likelihood ratio (PLR) were calculated. An ROC plot was used to summarize study-level findings. Pooled estimates of sensitivity and specificity for stress CMR derived from the meta-analysis were used to generate a leaf plot illustrating the association between pretest and posttest probability of CAD.

In the prognostic meta-analysis, summary effect sizes for all-cause death, CV death, and MI were calculated primarily for the presence or absence of inducible ischemia in addition to late gadolinium enhancement (LGE). A random-effects model was used, and study-specific odds ratios (ORs) were pooled using the Mantel-Haenszel method for each study outcome. The Hartung-Knapp adjustment[20] was applied to all analyses except for those with 3 or fewer studies per group. Mean effects were not calculated for outcomes reported by fewer than 3 studies. Interstudy heterogeneity was assessed using the I^2 statistic and represented as a Baujat plot.[21] Significant heterogeneity was defined as I^2 values of 50% or greater. The z statistic was computed for each end point of interest, and the results were considered statistically significant at 1-sided $P < .05$.

Meta-analysis results were presented using classic forest plots with point estimates of the effect size and 95% CIs, with square area indicating study weight. A jackknife sensitivity analysis was performed for each outcome to evaluate the robustness of the results and the effect of each study on the summary estimate of effect. The likelihood of publication bias was assessed using funnel plots by displaying individual study ORs with 95% CIs for the end points of interest, with the addition of the nonparametric trim-and-fill procedure to adjust for funnel plot asymmetry by generating hypothetical missing studies; for all models including more than 10 studies, funnel plot asymmetry was also evaluated using tests proposed by Deeks et al[22] for diagnostic studies and Egger et al[23] for prognostic studies (with 1-sided $P < .10$ indicating significant publication bias).

Subgroup analyses were performed to investigate possible sources of heterogeneity and to assess the effect of selected variables, including sample size, sex, CAD prevalence, thresholds of diameter stenosis, year of publication, magnetic field strength, and stressor agent. Annualized event rates (AERs) for studies were calculated by dividing the number of events by the follow-up duration. The low-risk period was defined as the mean interval during which the patient group with a negative test remained lower than the threshold of 1% of the cumulative MACE rate.[24] All statistical analyses were performed using R software, version 4.1.0. (R Foundation for Statistical Computing) (R packages and functions are detailed in the eMethods in Supplement 1).

Results

Of 3144 records (1152 diagnostic studies and 1992 prognostic studies) identified and retrieved for title and abstract evaluation, 2909 (1038 diagnostic studies and 1871 prognostic studies) were excluded, resulting in 235 potentially relevant articles (114 diagnostic studies and 121 prognostic studies) included in the full-text assessment of eligibility. After exclusions, 64 studies,[7-10,25-83] including 33 diagnostic studies[8,10,25-55] pooling 7814 individuals and 31 prognostic studies[7,9,25,56-83] pooling 67 080 individuals, published between October 29, 2002, and October 19, 2021, were included in the meta-analysis (eFigure 1 in Supplement 1). The study-level prevalence of CAD ranged between 11% and 83% in diagnostic studies. The mean (SD) follow-up was 3.5 (2.1) years (range, 0.9-8.8 years), for a total of 381 357 person-years among 74 470 total patients. The overall quality of included studies was high (eFigure 2 and eTable 3 in Supplement 1). The main characteristics of studies included in the diagnostic[8,10,25-55] and prognostic[7,9,25,56-83] meta-analyses are summarized in eTables 1 and 2 in Supplement 1.

Diagnostic Meta-analysis

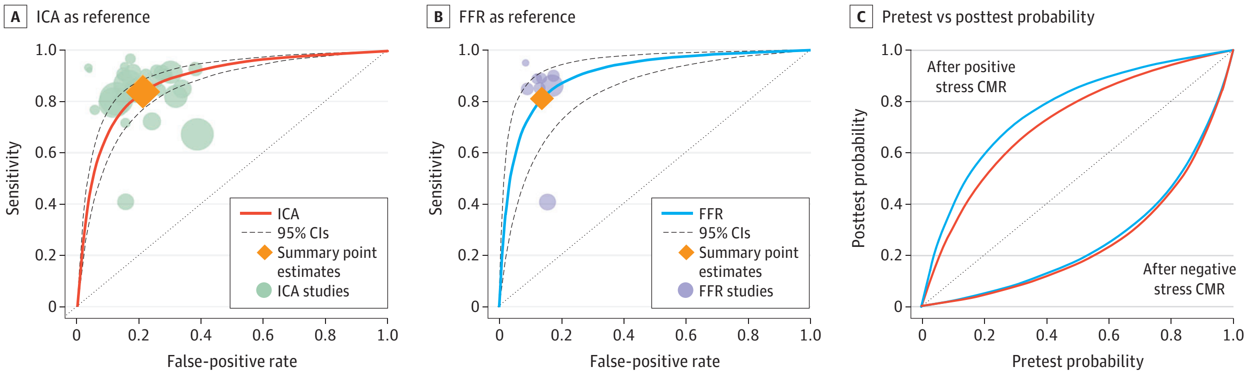
Stress CMR vs ICA

The diagnostic accuracy of stress CMR compared with ICA as the reference test was reported in 30 studies[8,10,25-52] pooling 7496 symptomatic patients, of whom 537 had known CAD and 2825 had suspected CAD. In the per-patient analysis, stress CMR yielded a pooled DOR of 19.1 (95% CI, 12.6-29.1), a sensitivity of 84% (95% CI, 79%-88%), a specificity of 79% (95% CI, 73%-84%), a PLR of 4.0 (95% CI, 3.0-5.3), an NLR of 0.2 (95% CI, 0.2-0.3), and an AUROC of 0.81 (95% CI, 0.78-0.84) for the detection of anatomically obstructive CAD (**Figure 1**A). In the per-vessel analysis, stress CMR yielded a pooled DOR of 21.0 (95% CI, 10.2-43.4), a sensitivity of 72% (95% CI, 61%-81%), a specificity of 89% (95% CI, 82%-94%), a PLR of 6.7 (95% CI, 3.8-11.8), an NLR of 0.3 (95% CI, 0.2-0.5), and an AUROC of 0.82 (95% CI, 0.76-0.87).

Stress CMR vs Invasive FFR

The diagnostic accuracy of stress CMR compared with invasive FFR as the reference test was reported in 8 studies[10,27,37,44,45,53-55] pooling 1196 symptomatic patients, of whom 354 had known CAD and 593 had suspected CAD. In the per-patient analysis, stress CMR yielded a pooled DOR of 26.4 (95% CI, 10.6-65.9), a sensitivity of 81% (95% CI, 68%-89%), a specificity of 86% (95% CI, 75%-93%), a PLR of 5.8 (95% CI, 3.0-11.4), an NLR of 0.2 (95% CI, 0.1-0.4), and an AUROC of 0.84 (95% CI, 0.77-0.89) for the detection of functionally obstructive CAD (Figure 1B). In the per-vessel analysis, stress CMR yielded a pooled DOR of 24.1 (95% CI, 5.5-105.4), a sensitivity of 70% (95% CI, 46%-86%), a specificity of 91% (95% CI, 74%-97%), a PLR of 8.0 (95% CI, 2.4-26.5), an NLR of 0.3 (95% CI, 0.1-0.8), and an AUROC of 0.83 (95% CI, 0.70-0.91).

Figure 1. Diagnostic Yield of Stress Cardiovascular Magnetic Resonance Imaging (CMR) in Stable Chest Pain



FFR indicates fractional flow reserve; ICA, invasive coronary angiography.

Prognostic Meta-analysis

All-Cause Mortality

A total of 11 studies[9,56-65] pooling 51 166 individuals reported all-cause mortality. The presence of inducible ischemia was associated with a 2-fold increased mortality (OR, 1.97; 95% CI, 1.69-2.31; *P* = .002) (**Figure 2**A). The presence of LGE was associated with 2-fold increased mortality (OR, 2.22; 95% CI, 1.99-2.47; *P* < .001) (**Figure 3**A). Pooled AERs for all-cause mortality were 2.97% in patients with inducible ischemia vs 1.40% in patients without inducible ischemia (*P* < .001) and 4.46% in patients with LGE vs 2.30% in patients without LGE (*P* < .001) (**Figure 4**A).

Cardiovascular Mortality

A total of 14 studies[9,62,65-76] pooling 12 252 individuals reported CV death data. The presence of inducible ischemia detected by stress CMR was associated with 6-fold increased CV mortality (OR, 6.40; 95% CI, 4.48-9.14; *P* < .001) (Figure 2B). The presence of LGE was associated with 6-fold increased CV mortality (OR, 6.03; 95% CI, 2.76-13.13; *P* < .001) (Figure 3B). Pooled AERs for CV death were 2.51% in patients with inducible ischemia vs 0.59% in patients without inducible ischemia (*P* < .001) and 2.51% in patients with LGE vs 0.71% in patients without LGE (*P* < .001) (Figure 4B).

MACEs

A total of 22 studies[7,9,25,59,60,65-68,71-83] pooling 17 084 individuals reported MACE data. The presence of inducible ischemia was associated with a 5-fold higher likelihood of incident MACEs (OR, 5.33; 95% CI, 4.04-7.04; *P* < .001) (**Figure 5**). The presence of LGE was associated with a 5-fold higher likelihood of MACEs (OR, 5.42; 95% CI, 3.42-8.60; *P* < .001) (Figure 3C). Pooled AERs for MACEs were 4.31% in patients with ischemia vs 0.98% in patients without ischemia (*P* < .001) and 2.90% in patients with LGE vs 0.78% in patients without LGE (*P* < .001) (Figure 4A).

Combining ischemia and LGE information, we documented the highest AER when both were present and the lowest AER when both were absent (Figure 4B). At a mean follow-up of 3.5 years, normal stress CMR results featuring the absence of both inducible ischemia and LGE were associated with a pooled AER of 0.58%, while the presence of both ischemia and LGE yielded a pooled AER of 4.24% (*P* < .001).

Study Quality and Publication Bias

According to the QUADAS-2 tool, risk of bias was low in 29[27-55] of 33 diagnostic studies[8,10,25-55] (eFigure 2 in Supplement 1). Of 31 prognostic studies,[7,9,25,56-83] 15 studies[7,9,25,56,60,62-64,66,68,73,74,76,78,80] scored 9 stars and 16 studies[57-59,61,65,67,69-72,75,77,79,81-83] scored 8 stars according to the Newcastle-Ottawa Scale (eTable 3 in Supplement 1). In ICA studies,[8,10,25-52] the Deeks test[22] ruled out small study bias and publication bias (*P* = .34) (eFigure 3 in Supplement 1). The Deeks test was not performed in FFR studies[10,27,37,44,45,53-55] because the number of studies was insufficient. With regard to prognostic studies,[7,9,25,56-83] we ruled out publication bias by visual inspection of funnel plots and the Egger test[23] of intercept, which was nonsignificant for each outcome (eFigure 4 in Supplement 1).

Subgroup Analysis

Results of the subgroup analysis are summarized in eTables 4 and 5 in Supplement 1. Stress CMR yielded higher diagnostic performance for the detection of anatomically and functionally obstructive CAD in 2 scenarios: suspected CAD (DOR, 53.4; 95% CI, 27.7-103.0) and 3-T imaging (DOR, 33.2; 95% CI, 19.9-55.4). In FFR studies,[10,27,37,44,45,53-55] higher diagnostic accuracy was observed when women were assessed or when the FFR cutoff was lowered to 0.75. In ICA studies,[8,10,25-52] quantitative assessment yielded higher DORs and specificity compared with visual assessment, and dipyridamole achieved higher accuracy overall compared with adenosine.

Sensitivity Analysis

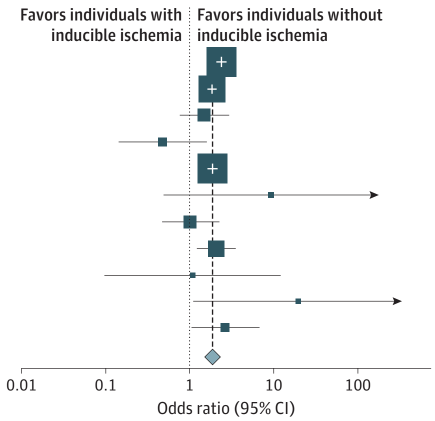
Two diagnostic studies[10,51] were visually and quantitatively identified as outliers in the ICA analysis[8,10,25-52] (eFigure 3 in Supplement 1). Removal of the 2 outliers[10,51] increased diagnostic accuracy, with a pooled DOR of 25.2 (eFigure 5 in Supplement 1). In the FFR analysis,[10,27,37,44,45,53-55] removal of the

Figure 2. Prognostic Value of Inducible Ischemia in Stable Chest Pain for All-Cause Death and Cardiovascular Death

A All-cause death

Study	Ischemic (+) Events	Ischemic (+) Total No.	Ischemic (-) Events	Ischemic (-) Total No.	Odds ratio (95% CI)	Weight, %
Pezel et al,[64] 2021	489	2940	2190	28822	2.43 (2.18-2.70)	27.9
Marcos-Garces et al,[63] 2020	393	2582	324	3807	1.93 (1.65-2.26)	24.3
Knott et al,[61] 2020	14	266	28	783	1.50 (0.78-2.89)	4.8
Esteban-Fernández et al,[57] 2020	4	45	11	65	0.48 (0.14-1.61)	1.6
Heitner et al,[58] 2019	510	2388	855	6763	1.88 (1.66-2.12)	26.9
Nagel et al,[9] 2019	4	221	0	224	9.29 (0.50-173.57)	0.3
Catalano et al,[56] 2018	9	82	41	383	1.03 (0.48-2.21)	3.7
Shah et al,[65] 2013	28	210	40	582	2.08 (1.25-3.48)	7.2
Klumpp et al,[60] 2013	2	143	1	77	1.08 (0.10-12.08)	0.4
Macwar et al,[62] 2013	8	240	0	264	19.34 (1.11-336.89)	0.3
Hundley et al,[59] 2002	11	93	9	186	2.64 (1.05-6.61)	2.6
Total (95% CI)		**9210**		**41956**	**1.97 (1.69-2.31)**	**100**

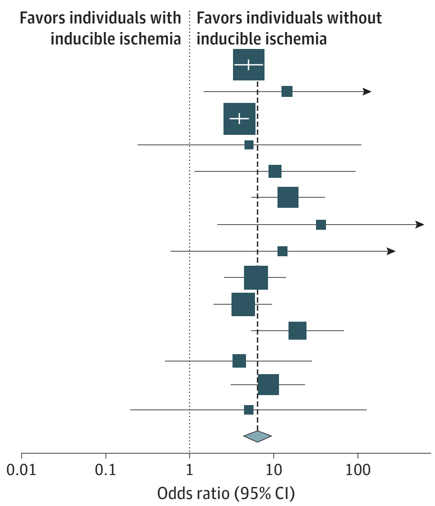
Heterogeneity: $\tau^2 = 0.0197$; $\chi^2 = 25.38$; $df = 10$; $P = .01$; $I^2 = 61\%$



B Cardiovascular death

Study	Ischemic (+) Events	Ischemic (+) Total No.	Ischemic (-) Events	Ischemic (-) Total No.	Odds ratio (95% CI)	Weight, %
Pezel et al,[64] 2021	57	267	93	1791	4.96 (3.46-7.10)	19.8
Ng et al,[72] 2021	3	38	1	170	14.49 (1.46-143.37)	2.2
Pezel et al,[73] 2021	140	738	165	2926	3.92 (3.08-4.99)	22.3
Nagel et al,[9] 2019	2	221	0	224	5.11 (0.24-107.13)	1.3
Pontone et al,[75] 2016	4	223	1	570	10.39 (1.16-93.50)	2.4
Shah et al,[65] 2013	24	210	5	582	14.89 (5.60-39.58)	8.7
Macwar et al,[62] 2013	15	240	0	264	36.36 (2.16-611.10)	1.5
Freed et al,[69] 2013	2	43	0	106	12.83 (0.60-272.97)	1.3
Bodi et al,[67] 2012	29	712	7	1010	6.08 (2.65-13.97)	10.6
Bingham and Hachamovitch,[66] 2011	20	298	10	610	4.32 (1.99-9.34)	11.5
Coelho-Filho et al,[68] 2011	18	109	3	296	19.32 (5.56-67.07)	6.2
Lo et al,[71] 2011	2	43	2	160	3.85 (0.53-28.19)	2.8
Wallace et al,[76] 2009	15	60	6	161	8.61 (3.16-23.48)	8.4
Kuijpers et al,[70] 2004	1	68	0	112	5.00 (0.20-124.49)	1.2
Total (95% CI)		**3270**		**8982**	**6.40 (4.48-9.14)**	**100**

Heterogeneity: $\tau^2 = 0.1331$; $\chi^2 = 18.17$; $df = 13$; $P = .15$; $I^2 = 28\%$



Study-specific odds ratios were pooled using the Mantel-Haenszel method. The dashed vertical line represents the pooled effect estimate. Squares represent weighted point estimates of the effect of each study. The diamond size is proportional to the overall weight in the random-effects model.

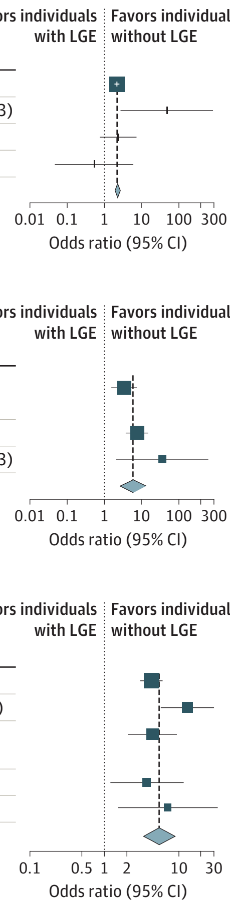
single outlier[10] improved diagnostic summary estimates, attaining a pooled DOR of 41.3 (eFigure 6 in Supplement 1). No single prognostic study changed the pooled OR for each end point of interest.

Discussion

The current systematic review and meta-analysis covered the last 20 years of clinical research in the field of stress CMR using state-of-the-art statistical methods for quantitative data synthesis. We provided the largest summary evidence available by pooling 74 470 patients and 381 357 person-years of follow-up. Our findings reaffirmed that stress CMR yields high diagnostic accuracy, robust cardiac prognostication, and accurate risk stratification in patients with stable chest pain and known or suspected CAD. Our analysis was focused on symptomatic patients, consistent with current international guideline indications on deferring or eliminating unnecessary testing when the diagnostic yield is low or when individuals are asymptomatic.[1,2]

Stress CMR consistently delivered high diagnostic accuracy across multiple clinical scenarios and temporal pattern analyses. This accuracy was particularly evident with regard to the detection of functionally obstructive lesions assessed by FFR, which was found to provide optimum balance between myocardial revascularization and medical treatment in the FAME (Fractional Flow Reserve Versus Angiography in Multivessel Evaluation) trials.[84,85] In addition to results from previous meta-analyses,[86,87] our findings provide evidence that stress CMR has better diagnostic performance in the setting of suspected CAD or when using 3-T imaging due to improved contrast resolution[88-90] and quantitative perfusion assessment, which can be advantageous to better identify the extent of disease or peri-infarction ischemia in multivessel CAD compared with visual assessment alone and can more accurately detect microvascular disease and the effectiveness of the stressor agents.[91] The signal of dipyridamole out-

Figure 3. Prognostic Significance of Late Gadolinium Enhancement (LGE) in Stable Chest Pain



A All-cause death

Study	LGE (+) Events	LGE (+) Total No.	LGE (-) Events	LGE (-) Total No.	Odds ratio (95% CI)	Weight, %
Heitner et al,[58] 2019	870	3445	755	5706	2.22 (1.99-2.47)	98.7
Macwar et al,[62] 2013	14	201	0	303	46.94 (2.78-791.53)	0.1
Catalano et al,[56] 2018	4	22	39	443	2.30 (0.74-7.14)	0.9
Klumpp et al,[60] 2013	1	107	2	113	0.52 (0.05-5.86)	0.2
Total (95% CI)		**3775**		**6565**	**2.22 (1.99-2.47)**	**100**

Heterogeneity: $\tau^2 < .0001$; $\chi^2 = 5.86$; $df = 3$; $P = .12$; $I^2 = 49\%$

B Cardiovascular death

Study	LGE (+) Events	LGE (+) Total No.	LGE (-) Events	LGE (-) Total No.	Odds ratio (95% CI)	Weight, %
Bingham and Hachamovitch,[66] 2011	20	341	10	567	3.47 (1.60-7.51)	44.0
Bodi et al,[67] 2012	17	193	19	1529	7.68 (3.92-15.04)	49.1
Macwar et al,[62] 2013	11	201	0	303	36.64 (2.15-625.43)	6.9
Total (95% CI)		**735**		**2399**	**6.03 (2.76-13.13)**	**100**

Heterogeneity: $\tau^2 = 0.2039$; $\chi^2 = 3.99$; $df = 2$; $P = .2$; $I^2 = 50\%$

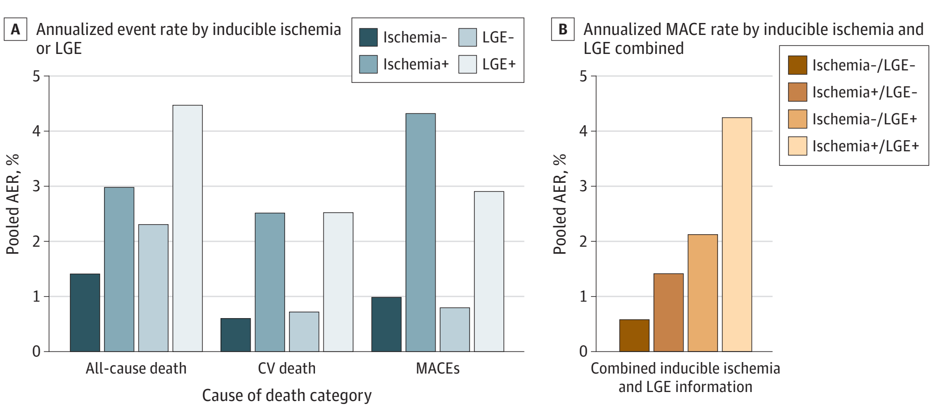
C Major adverse cardiac events

Study	LGE (+) Events	LGE (+) Total No.	LGE (-) Events	LGE (-) Total No.	Odds ratio (95% CI)	Weight, %
Kwong et al,[7] 2019	84	572	69	1777	4.26 (3.05-5.95)	39.0
Bodi et al,[67] 2012	15	193	10	1529	12.80 (5.67-28.92)	19.4
Bingham and Hachamovitch,[66] 2011	25	341	10	567	4.41 (2.09-9.29)	21.5
Shah et al,[83] 2014	9	88	5	167	3.69 (1.20-11.38)	12.5
Klumpp et al,[60] 2013	12	107	2	113	7.01 (1.53-32.11)	7.7
Total (95% CI)		**1301**		**4153**	**5.42 (3.42-8.60)**	**100**

Heterogeneity: $\tau^2 = 0.1130$; $\chi^2 = 6.54$; $df = 4$; $P = .16$; $I^2 = 39\%$

Study-specific odds ratios were pooled using the Mantel-Haenszel method. The dashed vertical line represents the pooled effect estimate. Squares represent weighted point estimates of the effect of each study. The diamond size is proportional to the overall weight in the random-effects model.

Figure 4. Pooled Annualized Event Rate (AER) by Stress Cardiovascular Magnetic Resonance Imaging Findings in Stable Chest Pain



P < .001 for all comparisons.
AER indicates annualized event rate; CV, cardiovascular; LGE, late gadolinium enhancement.

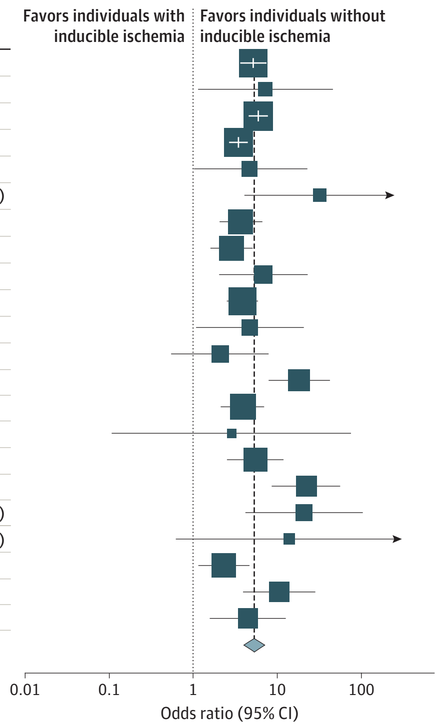
performing adenosine was intriguing and possibly reflected the incremental diagnostic value of combined perfusion and wall motion assessment.[75] This finding requires careful interpretation and prospective verification in regadenoson studies and needs to be weighed against the cost, potential tolerability, and benefit of the stressor agents.[92]

In our diagnostic meta-analysis, 2 studies[10,51] were identified as outliers that had a diagnostic yield lower than the mean for stress CMR. The Dan-NICAD (Danish Study of Non-Invasive Diagnostic Testing in Coronary Artery Disease) randomized clinical trial[10] enrolled patients with a low to intermediate pretest probability of CAD and an abnormal coronary computed tomography (CT) angiographic scan before CMR and found low sensitivity for second-line perfusion investigations. However, the specific study design could have led to selection bias and potentially impacted diagnostic estimates.[93]

Figure 5. Prognostic Value of Inducible Ischemia in Stable Chest Pain for Major Adverse Cardiac Events

	Ischemic (+)		Ischemic (−)			
Study	Events	Total No.	Events	Total No.	Odds ratio (95% CI)	Weight, %
Pezel et al,[64] 2021	75	267	128	1791	5.08 (3.68-7.00)	8.1
Ng et al,[72] 2021	3	38	2	170	7.20 (1.16-44.70)	1.8
Pezel et al,[73] 2021	245	738	227	2926	5.91 (4.82-7.25)	8.7
Kwong et al,[7] 2019	60	405	93	1944	3.46 (2.45-4.88)	8.0
Nagel et al,[9] 2019	9	221	2	224	4.71 (1.01-22.06)	2.4
Heydari et al,[79] 2016	20	79	1	94	31.53 (4.12-241.16)	1.5
Pontone et al,[75] 2016	30	223	23	570	3.70 (2.10-6.52)	6.6
Becker et al,[25] 2015	41	184	22	240	2.84 (1.62-4.97)	6.6
Shah et al,[83] 2014	10	75	4	180	6.77 (2.05-22.34)	3.4
Bikiri et al,[78] 2014	65	256	51	628	3.85 (2.58-5.75)	7.6
Abbasi et al,[77] 2014	5	93	3	253	4.73 (1.11-20.22)	2.6
Klumpp et al,[60] 2013	11	143	3	77	2.06 (0.56-7.60)	3.0
Shah et al,[65] 2013	38	210	7	582	18.15 (7.96-41.37)	5.0
Bodi et al,[67] 2012	44	712	17	1010	3.85 (2.18-6.79)	6.6
Lubbers et al,[82] 2012	0	14	1	125	2.86 (0.11-73.55)	0.7
Bingham and Hachamovitch,[66] 2011	25	298	10	610	5.49 (2.60-11.60)	5.5
Coelho-Filho et al,[68] 2011	34	109	6	296	21.91 (8.87-54.12)	4.6
Lo et al,[71] 2011	9	43	2	160	20.91 (4.32-101.16)	2.3
Kelle et al,[81] 2009	2	34	0	89	13.77 (0.64-294.48)	0.8
Wallace et al,[76] 2009	19	60	27	161	2.30 (1.16-4.55)	5.9
Jahnke et al,[80] 2007	9	45	10	428	10.45 (3.99-27.37)	4.3
Hundley et al,[59] 2002	12	93	6	186	4.44 (1.61-12.26)	4.1
Total (95% CI)		**4340**		**12 744**	**5.33 (4.04-7.04)**	**100**

Heterogeneity: $\tau^2 = 0.2200$; $\chi^2 = 50.42$; $df = 21$; $P < .01$; $I^2 = 58\%$



Study-specific odds ratios were pooled using the Mantel-Haenszel method. The dashed vertical line represents the pooled effect estimate. Squares represent weighted point estimates of the effect of each study. The diamond size is proportional to the overall weight in the random-effects model.

The MR-IMPACT II (Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial II) study[51] compared stress CMR with single-photon emission CT in a population with intermediate CAD prevalence (49%). However, this study[51] had a fairly high number of patients with previous MI (27%); in these patients, it can be more difficult to discriminate myocardial scarring and residual ischemia, and the expected higher prevalence of microvascular disease in this population can inflate the number of false-positive findings. This multicenter study[51] enrolling participants from 33 different institutions aimed to frame a realistic clinical environment not restricted to high-volume leading centers. In both studies,[10,51] measurements were performed by an independent core laboratory with readers fully blinded to additional patient information and results, limiting the bias of the clinical context when reporting stress CMR studies.

When interpreting these findings, we should remember that myocardial ischemia exists on a continuum, and binary categorizations have inherent limitations. Furthermore, shortcomings in the accuracy of established invasive gold standards must be carefully considered. Notably, FFR was first calibrated against noninvasive tests,[94] including bicycle exercise testing, thallium scintigraphy, and stress echocardiography with dobutamine, which were themselves validated against ICA as the reference test, resulting in problematic circular thinking.[95,96] An FFR threshold of 0.80 or lower has been adopted into clinical practice guidelines[97] as an actionable value to guide revascularization despite robust evidence supporting larger treatment benefit at lower FFR values[98,99]; our findings indicate better agreement at an FFR threshold of 0.75.

The 2019 MR-INFORM (MR Perfusion Imaging to Guide Management of Patients With Stable Coronary Artery Disease) trial[9] randomized 918 symptomatic patients at high pretest probability of CAD to undergo ICA plus FFR vs stress CMR-guided assessment. The MACE rate and percentage of patients free of angina were similar for both strategies at 1 year; however, the use of stress CMR was associated with a lower incidence of downstream ICA and coronary revascularization than the use of FFR.[9] Similar findings have been reported in the setting of low-risk acute coronary syndromes by a network meta-analysis of diagnostic randomized clinical trials,[100] which found that stress CMR was associated with fewer referrals to downstream ICA than coronary CT angiography or other noninvasive imaging modalities and without obvious consequences for the subsequent risk of MI.

This evidence translates into a distinctly favorable cost-effectiveness profile for stress CMR compared with its relevant comparators.[101] According to a cost-effectiveness analysis[102] comparing different first-line diagnostic approaches for stable chest pain and a decision-analytic model estimating lifetime health care costs and quality-adjusted life-years derived from the multicenter SPINS (Stress CMR Perfusion Imaging in the United States) study,[103] stress CMR strongly dominated single-photon emission CT and coronary CT angiography strategies when considering either all MACEs or CV mortality alone. Thus, having access to CMR is a beneficial situation for patients and may lead to substantial cost savings by reducing the need for additional unnecessary tests and revascularization procedures.[104,105]

The prognostic value of noninvasive cardiac assessments was the objective of a previous meta-analysis[13] raising the possibility of clinical equipoise for estimation of CV death and MI. While the message that any negative test conveys excellent prognosis may be reassuring to patients and challenges the need for further downstream testing, the posttest probability of disease needs to be adjusted for baseline population event risk and should always be carefully interpreted in the context of pretest probability and prevalence of disease and according to the clinical scenario. In our analysis, the presence of inducible ischemia on stress CMR was a robust estimator of increased mortality and MACEs, further heightened by the presence of LGE. Conversely, normal stress CMR results were associated with a low incidence of MACEs, yielding a low-risk posttest period of at least 3.5 years. Our data were consistent with the results of previous meta-analyses[106,107] and findings of the European Cardiovascular Magnetic Resonance (EuroCMR) registry,[5] in which patients with suspected CAD and a negative stress CMR result experienced an AER for aborted sudden cardiac death and nonfatal MI of less than 1%.

Ultimately, the prognostic value of stress CMR, either performed with vasodilators or dobutamine, provides incremental risk stratification in patients with stable chest pain.[65,80] Further studies are needed to establish the optimal CMR method for absolute quantification of myocardial blood flow and the optimal ischemic threshold associated with larger treatment effect, which would be useful to identify patients who would most benefit from myocardial revascularization vs safe deferral.

Strengths and Limitations

This study has several strengths. We summarized the largest evidence available, making use of the best methods for quantitative synthesis, and we provide robust estimates of the diagnostic and prognostic value of stress CMR. We provide new information on the duration of the low-risk period for MACEs after a normal stress CMR result. This knowledge has the potential to inform future clinical guidelines about ideal intervals for repeat imaging and to provide useful guidance for subsequent management of assessment strategies among symptomatic patients with initial normal imaging results or subclinical disease.[108] Results of the subgroup analyses also suggest better diagnostic performance of stress CMR in the setting of suspected CAD, especially when using 3-T imaging and fully quantitative approaches.

This study also has limitations. First, we did not compare the yield of stress CMR with other imaging modalities because it was beyond the scope of the current work, and literature specifically addressing these topics already exists.[109-111] Second, our results are mostly derived from observational studies reflecting different guideline recommendations across 2 decades of practice. Within this time span, thresholds for coronary stenosis have changed,[112] methods for estimation of pretest probabilities of obstructive CAD have been updated and recalibrated,[1,2] and CMR protocols have been implemented, including quantitative perfusion assessment,[61] new tools for evaluation of stress adequacy,[113-115] more widespread use of regadenoson,[116] and other disruptive technical innovations.[117-119] Third, we recognize there is a lack of information about medical therapy, completeness of myocardial revascularization, extent of inducible ischemia, degree of myocardial fibrosis, and prevalence of microvascular dysfunction. Despite the intrinsic challenges and limitations of study-level meta-analysis, including limited adjustment for confounding factors and susceptibility to the ecological fallacy, we attempted to synthesize the results in a robust manner that addressed potential bias.

Conclusions

This systematic review and meta-analysis found that in patients with stable chest pain and known or suspected CAD, stress CMR yielded high diagnostic accuracy to detect both anatomically and functionally significant CAD, with 3-T and quantitative perfusion approaches delivering higher diagnostic performance. Stress CMR also provided robust prognostic information and accurate risk stratification. While the presence of ischemia and LGE were associated with higher CV risk and mortality, normal stress CMR results were associated with a lower likelihood of MACEs for at least 3.5 years. These findings suggest that combined assessment of inducible myocardial ischemia and LGE by stress CMR is an accurate method to diagnose and risk stratify patients with known or suspected CAD.

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REFERENCES

1. Knuuti J, Wijns W, Saraste A, et al; ESC Scientific Document Group. 2019 ESC guidelines for the diagnosis and management of chronic coronary syndromes. *Eur Heart J*. 2020;41(3):407-477. doi:10.1093/eurheartj/ehz425

2. Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/SCMR guideline for the evaluation and diagnosis of chest pain: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation*. 2021;144(22):e368-e454. doi:10.1161/CIR.0000000000001029

3. Patel AR, Salerno M, Kwong RY, Singh A, Heydari B, Kramer CM. Stress cardiac magnetic resonance myocardial perfusion imaging: JACC review topic of the week. *J Am Coll Cardiol*. 2021;78(16):1655-1668. doi:10.1016/j.jacc.2021.08.022

4. Edvardsen T, Asch FM, Davidson B, et al. Non-invasive imaging in coronary syndromes: recommendations of the European Association of Cardiovascular Imaging and the American Society of Echocardiography, in collaboration with the American Society of Nuclear Cardiology, Society of Cardiovascular Computed Tomography, and Society for Cardiovascular Magnetic Resonance. *Eur Heart J Cardiovasc Imaging*. 2022;23(2):e6-e33. doi:10.1093/ehjci/jeab244

5. Bruder O, Wagner A, Lombardi M, et al. European Cardiovascular Magnetic Resonance (EuroCMR) registry—multi national results from 57 centers in 15 countries. *J Cardiovasc Magn Reson*. 2013;15(1):9. doi:10.1186/1532-429X-15-9

6. Kwong RY, Petersen SE, Schulz-Menger J, et al; Global Cardiovascular Magnetic Resonance Registry (GCMR) Investigators. The Global Cardiovascular Magnetic Resonance Registry (GCMR) of the Society for Cardiovascular Magnetic Resonance (SCMR): its goals, rationale, data infrastructure, and current developments. *J Cardiovasc Magn Reson*. 2017;19(1):23. doi:10.1186/s12968-016-0321-7

7. Kwong RY, Ge Y, Steel K, et al. Cardiac magnetic resonance stress perfusion imaging for evaluation of patients with chest pain. *J Am Coll Cardiol*. 2019;74(14):1741-1755. doi:10.1016/j.jacc.2019.07.074

8. Arai AE, Schulz-Menger J, Berman D, et al; GadaCAD Investigators. Gadobutrol-enhanced cardiac magnetic resonance imaging for detection of coronary artery disease. *J Am Coll Cardiol*. 2020;76(13):1536-1547. doi:10.1016/j.jacc.2020.07.060

9. Nagel E, Greenwood JP, McCann GP, et al; MR-INFORM Investigators. Magnetic resonance perfusion or fractional flow reserve in coronary disease. *N Engl J Med*. 2019;380(25):2418-2428. doi:10.1056/NEJMoa1716734

10. Nissen L, Winther S, Westra J, et al. Diagnosing coronary artery disease after a positive coronary computed tomography angiography: the Dan-NICAD open label, parallel, head to head, randomized controlled diagnostic accuracy trial of cardiovascular magnetic resonance and myocardial perfusion scintigraphy. *Eur Heart J Cardiovasc Imaging*. 2018;19(4):369-377. doi:10.1093/ehjci/jex342

11. Haberkorn SM, Haberkorn SI, Bönner F, Kelm M, Hopkin G, Petersen SE. Vasodilator myocardial perfusion cardiac magnetic resonance imaging is superior to dobutamine stress echocardiography in the detection of relevant coronary artery stenosis: a systematic review and meta-analysis on their diagnostic accuracy. *Front Cardiovasc Med*. 2021;8:630846. doi:10.3389/fcvm.2021.630846

12. Danad I, Szymonifka J, Twisk JWR, et al. Diagnostic performance of cardiac imaging methods to diagnose ischaemia-causing coronary artery disease when directly compared with fractional flow reserve as a reference standard: a meta-analysis. *Eur Heart J*. 2017;38(13):991-998. doi:10.1093/eurheartj/ehw095

13. Smulders MW, Jaarsma C, Nelemans PJ, et al. Comparison of the prognostic value of negative non-invasive cardiac investigations in patients with suspected or known coronary artery disease—a meta-analysis. *Eur Heart J Cardiovasc Imaging*. 2017;18(9):980-987. doi:10.1093/ehjci/jex014

14. El Aidi H, Adams A, Moons KGM, et al. Cardiac magnetic resonance imaging findings and the risk of cardiovascular events in patients with recent myocardial infarction or suspected or known coronary artery disease: a systematic review of prognostic studies. *J Am Coll Cardiol*. 2014;63(11):1031-1045. doi:10.1016/j.jacc.2013.11.048

15. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *Syst Rev*. 2021;10(1):89. doi:10.1186/s13643-021-01626-4

16. Higgins J, Thomas J, Chandler J, et al, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 6.3. The Cochrane Collaboration; 2022. Accessed May 2, 2023. https://training.cochrane.org/handbook/current

17. Whiting PF, Rutjes AWS, Westwood ME, et al; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011;155(8):529-536. doi:10.7326/0003-4819-155-8-201110180-00009

18. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Ottawa Hospital Research Institute. 2021. Accessed November 11, 2021. https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp

19. Furuya-Kanamori L, Kostoulas P, Doi SAR. A new method for synthesizing test accuracy data outperformed the bivariate method. *J Clin Epidemiol*. 2021;132:51-58. doi:10.1016/j.jclinepi.2020.12.015

20. Hartung J, Knapp G. A refined method for the meta-analysis of controlled clinical trials with binary outcome. *Stat Med*. 2001;20(24):3875-3889. doi:10.1002/sim.1009

21. Baujat B, Mahé C, Pignon JP, Hill C. A graphical method for exploring heterogeneity in meta-analyses: application to a meta-analysis of 65 trials. *Stat Med*. 2002;21(18):2641-2652. doi:10.1002/sim.1221

22. Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. *J Clin Epidemiol*. 2005;58(9):882-893. doi:10.1016/j.jclinepi.2005.01.016

23. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315(7109):629-634. doi:10.1136/bmj.315.7109.629

24. Hachamovitch R, Hayes S, Friedman JD, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: what is the warranty period of a normal scan? *J Am Coll Cardiol*. 2003;41(8):1329-1340. doi:10.1016/S0735-1097(03)00125-6

25. Becker M, Hundemer A, Zwicker C, et al. Detection of coronary artery disease in postmenopausal women: the significance of integrated stress imaging tests in a 4-year prognostic study. *Clin Res Cardiol*. 2015;104(3):258-271. doi:10.1007/s00392-014-0780-5

26. Bernhardt P, Spiess J, Levenson B, et al. Combined assessment of myocardial perfusion and late gadolinium enhancement in patients after percutaneous coronary intervention or bypass grafts: a multicenter study of an integrated cardiovascular magnetic resonance protocol. *JACC Cardiovasc Imaging*. 2009;2(11):1292-1300. doi:10.1016/j.jcmg.2009.05.011

27. Bettencourt N, Chiribiri A, Schuster A, et al. Cardiac magnetic resonance myocardial perfusion imaging for detection of functionally significant obstructive coronary artery disease: a prospective study. *Int J Cardiol*. 2013;168(2):765-773. doi:10.1016/j.ijcard.2012.09.231

28. Biglands JD, Ibraheem M, Magee DR, Radjenovic A, Plein S, Greenwood JP. Quantitative myocardial perfusion imaging versus visual analysis in diagnosing myocardial ischemia: a CE-MARC substudy. *JACC Cardiovasc Imaging*. 2018;11(5):711-718. doi:10.1016/j.jcmg.2018.02.019

29. Chen MY, Bandettini WP, Shanbhag SM, et al. Concordance and diagnostic accuracy of vasodilator stress cardiac MRI and 320-detector row coronary CTA. *Int J Cardiovasc Imaging*. 2014;30(1):109-119. doi:10.1007/s10554-013-0300-0

30. Doesch C, Seeger A, Hoevelborn T, et al. Adenosine stress cardiac magnetic resonance imaging for the assessment of ischemic heart disease. *Clin Res Cardiol*. 2008;97(12):905-912. doi:10.1007/s00392-008-0708-z

31. Doyle M, Fuisz A, Kortright E, et al. The impact of myocardial flow reserve on the detection of coronary artery disease by perfusion imaging methods: an NHLBI WISE study. *J Cardiovasc Magn Reson*. 2003;5(3):475-485. doi:10.1081/JCMR-120022263

32. Gebker R, Frick M, Jahnke C, et al. Value of additional myocardial perfusion imaging during dobutamine stress magnetic resonance for the assessment of intermediate coronary artery disease. *Int J Cardiovasc Imaging*. 2012;28(1):89-97. doi:10.1007/s10554-010-9764-3

33. Gebker R, Jahnke C, Manka R, et al. Additional value of myocardial perfusion imaging during dobutamine stress magnetic resonance for the assessment of coronary artery disease. *Circ Cardiovasc Imaging*. 2008;1(2):122-130. doi:10.1161/CIRCIMAGING.108.779108

34. Gebker R, Jahnke C, Paetsch I, et al. Diagnostic performance of myocardial perfusion MR at 3 T in patients with coronary artery disease. *Radiology*. 2008;247(1):57-63. doi:10.1148/radiol.2471070596

35. Greenwood JP, Maredia N, Younger JF, 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(9814):453-460. doi:10.1016/S0140-6736(11)61335-4

36. Greulich S, Steubing H, Birkmeier S, et al. Impact of arrhythmia on diagnostic performance of adenosine stress CMR in patients with suspected or known coronary artery disease. *J Cardiovasc Magn Reson*. 2015;17:94. doi:10.1186/s12968-015-0195-0

37. Hamada S, Gotschy A, Wissmann L, et al. Multi-centre study of whole-heart dynamic 3D cardiac magnetic resonance perfusion imaging for the detection of coronary artery disease defined by fractional flow reserve: gender based analysis of diagnostic performance. *Eur Heart J Cardiovasc Imaging*. 2017;18(10):1099-1106. doi:10.1093/ehjci/jex160

38. Husser O, Bodí V, Sanchís J, et al. Additional diagnostic value of systolic dysfunction induced by dipyridamole stress cardiac magnetic resonance used in detecting coronary artery disease. *Rev Esp Cardiol*. 2009;62(4):383-391. doi:10.1016/S0300-8932(09)70895-4

39. Ishida N, Sakuma H, Motoyasu M, et al. Noninfarcted myocardium: correlation between dynamic first-pass contrast-enhanced myocardial MR imaging and quantitative coronary angiography. *Radiology*. 2003;229(1):209-216. doi:10.1148/radiol.2291021118

40. Klem I, Greulich S, Heitner JF, et al. Value of cardiovascular magnetic resonance stress perfusion testing for the detection of coronary artery disease in women. *JACC Cardiovasc Imaging*. 2008;1(4):436-445. doi:10.1016/j.jcmg.2008.03.010

41. Klumpp B, Miller S, Seeger A, et al. Is the diagnostic yield of myocardial stress perfusion MRI impaired by three-vessel coronary artery disease? *Acta Radiol*. 2015;56(2):143-151. doi:10.1177/0284185114523758

42. Kotecha T, Chacko L, Chehab O, et al. Assessment of multivessel coronary artery disease using cardiovascular magnetic resonance pixelwise quantitative perfusion mapping. *JACC Cardiovasc Imaging*. 2020;13(12):2546-2557. doi:10.1016/j.jcmg.2020.06.041

43. Manka R, Jahnke C, Kozerke S, et al. Dynamic 3-dimensional stress cardiac magnetic resonance perfusion imaging: detection of coronary artery disease and volumetry of myocardial hypoenhancement before and after coronary stenting. *J Am Coll Cardiol*. 2011;57(4):437-444. doi:10.1016/j.jacc.2010.05.067

44. Manka R, Paetsch I, Kozerke S, et al. Whole-heart dynamic three-dimensional magnetic resonance perfusion imaging for the detection of coronary artery disease defined by fractional flow reserve: determination of volumetric myocardial ischaemic burden and coronary lesion location. *Eur Heart J*. 2012;33(16):2016-2024. doi:10.1093/eurheartj/ehs170

45. Manka R, Wissmann L, Gebker R, et al. Multicenter evaluation of dynamic three-dimensional magnetic resonance myocardial perfusion imaging for the detection of coronary artery disease defined by fractional flow reserve. *Circ Cardiovasc Imaging*. 2015;8(5):e003061. doi:10.1161/CIRCIMAGING.114.003061

46. Merkle N, Wöhrle J, Nusser T, et al. Diagnostic performance of magnetic resonance first pass perfusion imaging is equally potent in female compared to male patients with coronary artery disease. *Clin Res Cardiol*. 2010;99(1):21-28. doi:10.1007/s00392-009-0071-8

47. Min JY, Ko SM, Song IY, Yi JG, Hwang HK, Shin JK. Comparison of the diagnostic accuracies of 1.5T and 3T stress myocardial perfusion cardiovascular magnetic resonance for detecting significant coronary artery disease. *Korean J Radiol*. 2018;19(6):1007-1020. doi:10.3348/kjr.2018.19.6.1007

48. Motwani M, Maredia N, Fairbairn TA, et al. High-resolution versus standard-resolution cardiovascular MR myocardial perfusion imaging for the detection of coronary artery disease. *Circ Cardiovasc Imaging*. 2012;5(3):306-313. doi:10.1161/CIRCIMAGING.111.971796

49. Pilz G, Bernhardt P, Klos M, Ali E, Wild M, Höfling B. Clinical implication of adenosine-stress cardiac magnetic resonance imaging as potential gatekeeper prior to invasive examination in patients with AHA/ACC class II indication for coronary angiography. *Clin Res Cardiol*. 2006;95(10):531-538. doi:10.1007/s00392-006-0422-7

50. Schwitter J, Wacker CM, van Rossum AC, et al. MR-IMPACT: comparison of perfusion-cardiac magnetic resonance with single-photon emission computed tomography for the detection of coronary artery disease in a multicentre, multivendor, randomized trial. *Eur Heart J*. 2008;29(4):480-489. doi:10.1093/eurheartj/ehm617

51. Schwitter J, Wacker CM, Wilke N, et al; MR-IMPACT Investigators. MR-IMPACT II: Magnetic Resonance Imaging for Myocardial Perfusion Assessment in Coronary Artery Disease Trial: perfusion-cardiac magnetic resonance vs. single-photon emission computed tomography for the detection of coronary artery disease: a comparative multicentre, multivendor trial. *Eur Heart J*. 2013;34(10):775-781. doi:10.1093/eurheartj/ehs022

52. Takase B, Nagata M, Kihara T, et al. Whole-heart dipyridamole stress first-pass myocardial perfusion MRI for the detection of coronary artery disease. *Jpn Heart J*. 2004;45(3):475-486. doi:10.1536/jhj.45.475

53. Ebersberger U, Makowski MR, Schoepf UJ, et al. Magnetic resonance myocardial perfusion imaging at 3.0 Tesla for the identification of myocardial ischaemia: comparison with coronary catheter angiography and fractional flow reserve measurements. *Eur Heart J Cardiovasc Imaging*. 2013;14(12):1174-1180. doi:10.1093/ehjci/jet074

54. Ramos V, Bettencourt N, Silva J, et al. Noninvasive anatomical and functional assessment of coronary artery disease. *Rev Port Cardiol*. 2015;34(4):223-232. doi:10.1016/j.repc.2014.10.008

55. Watkins S, McGeoch R, Lyne J, et al. Validation of magnetic resonance myocardial perfusion imaging with fractional flow reserve for the detection of significant coronary heart disease. *Circulation*. 2009;120(22):2207-2213. doi:10.1161/CIRCULATIONAHA.109.872358

56. Catalano O, Moro G, Mori A, et al. Cardiac magnetic resonance in stable coronary artery disease: added prognostic value to conventional risk profiling. *Biomed Res Int*. 2018;2018:2806148. doi:10.1155/2018/2806148

57. Esteban-Fernández A, Bastarrika G, Castanon E, et al. Prognostic role of stress cardiac magnetic resonance in the elderly. *Rev Esp Cardiol (Engl Ed)*. 2020;73(3):241-247. doi:10.1016/j.rec.2019.02.007

58. Heitner JF, Kim RJ, Kim HW, et al. Prognostic value of vasodilator stress cardiac magnetic resonance imaging: a multicenter study with 48 000 patient-years of follow-up. *JAMA Cardiol*. 2019;4(3):256-264. doi:10.1001/jamacardio.2019.0035

59. Hundley WG, Morgan TM, Neagle CM, Hamilton CA, Rerkpattanapipat P, Link KM. Magnetic resonance imaging determination of cardiac prognosis. *Circulation*. 2002;106(18):2328-2333. doi:10.1161/01.CIR.0000036017.46437.02

60. Klumpp B, Seeger A, Bretschneider C, et al. Is myocardial stress perfusion MR-imaging suitable to predict the long term clinical outcome after revascularization? *Eur J Radiol*. 2013;82(10):1776-1782. doi:10.1016/j.ejrad.2013.06.003

61. Knott KD, Seraphim A, Augusto JB, et al. The prognostic significance of quantitative myocardial perfusion: an artificial intelligence–based approach using perfusion mapping. *Circulation*. 2020;141(16):1282-1291. doi:10.1161/CIRCULATIONAHA.119.044666

62. Macwar RR, Williams BA, Shirani J. Prognostic value of adenosine cardiac magnetic resonance imaging in patients presenting with chest pain. *Am J Cardiol*. 2013;112(1):46-50. doi:10.1016/j.amjcard.2013.02.054

63. Marcos-Garces V, Gavara J, Monmeneu JV, et al. Vasodilator stress CMR and all-cause mortality in stable ischemic heart disease: a large retrospective registry. *JACC Cardiovasc Imaging*. 2020;13(8):1674-1686. doi:10.1016/j.jcmg.2020.02.027

64. Pezel T, Unterseeh T, Garot P, et al. Long-term prognostic value of stress cardiovascular magnetic resonance-related coronary revascularization to predict death: a large registry with >200 000 patient-years of follow-up. *Circ Cardiovasc Imaging*. 2021;14(10):e012789. doi:10.1161/CIRCIMAGING.121.012789

65. Shah R, Heydari B, Coelho-Filho O, et al. Stress cardiac magnetic resonance imaging provides effective cardiac risk reclassification in patients with known or suspected stable coronary artery disease. *Circulation*. 2013;128(6):605-614. doi:10.1161/CIRCULATIONAHA.113.001430

66. Bingham SE, Hachamovitch R. Incremental prognostic significance of combined cardiac magnetic resonance imaging, adenosine stress perfusion, delayed enhancement, and left ventricular function over preimaging information for the prediction of adverse events. *Circulation*. 2011;123(14):1509-1518. doi:10.1161/CIRCULATIONAHA.109.907659

67. Bodi V, Husser O, Sanchis J, et al. Prognostic implications of dipyridamole cardiac MR imaging: a prospective multicenter registry. *Radiology*. 2012;262(1):91-100. doi:10.1148/radiol.11110134

68. Coelho-Filho OR, Seabra LF, Mongeon FP, et al. Stress myocardial perfusion imaging by CMR provides strong prognostic value to cardiac events regardless of patient's sex. *JACC Cardiovasc Imaging*. 2011;4(8):850-861. doi:10.1016/j.jcmg.2011.04.015

69. Freed BH, Narang A, Bhave NM, et al. Prognostic value of normal regadenoson stress perfusion cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2013;15(1):108. doi:10.1186/1532-429X-15-108

70. Kuijpers D, van Dijkman PRM, Janssen CHC, Vliegenthart R, Zijlstra F, Oudkerk M. Dobutamine stress MRI. part II. risk stratification with dobutamine cardiovascular magnetic resonance in patients suspected of myocardial ischemia. *Eur Radiol*. 2004;14(11):2046-2052. doi:10.1007/s00330-004-2426-x

71. Lo KY, Leung KF, Chu CM, Loke KL, Chan CK, Yue CS. Prognostic value of adenosine stress myocardial perfusion by cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease. *QJM*. 2011;104(5):425-432. doi:10.1093/qjmed/hcq238

72. Ng MY, Chin CY, Yap PM, et al. Prognostic value of perfusion cardiovascular magnetic resonance with adenosine triphosphate stress in stable coronary artery disease. *J Cardiovasc Magn Reson*. 2021;23(1):75. doi:10.1186/s12968-021-00770-z

73. Pezel T, Garot P, Kinnel M, et al. Long-term prognostic value of ischaemia and cardiovascular magnetic resonance–related revascularization for stable coronary disease, irrespective of patient's sex: a large retrospective study. *Eur Heart J Cardiovasc Imaging*. 2021;22(11):1321-1331. doi:10.1093/ehjci/jeab186

74. Pezel T, Unterseeh T, Kinnel M, et al. Long-term prognostic value of stress perfusion cardiovascular magnetic resonance in patients without known coronary artery disease. *J Cardiovasc Magn Reson*. 2021;23(1):43. doi:10.1186/s12968-021-00737-0

75. Pontone G, Andreini D, Bertella E, et al. Prognostic value of dipyridamole stress cardiac magnetic resonance in patients with known or suspected coronary artery disease: a mid-term follow-up study. *Eur Radiol*. 2016;26(7):2155-2165. doi:10.1007/s00330-015-4064-x

76. Wallace EL, Morgan TM, Walsh TF, et al. Dobutamine cardiac magnetic resonance results predict cardiac prognosis in women with known or suspected ischemic heart disease. *JACC Cardiovasc Imaging*. 2009;2(3):299-307. doi:10.1016/j.jcmg.2008.10.015

77. Abbasi SA, Heydari B, Shah RV, et al. Risk stratification by regadenoson stress magnetic resonance imaging in patients with known or suspected coronary artery disease. *Am J Cardiol*. 2014;114(8):1198-1203. doi:10.1016/j.amjcard.2014.07.041

78. Bikiri E, Mereles D, Voss A, et al. Dobutamine stress cardiac magnetic resonance versus echocardiography for the assessment of outcome in patients with suspected or known coronary artery disease: are the two imaging modalities comparable? *Int J Cardiol*. 2014;171(2):153-160. doi:10.1016/j.ijcard.2013.11.038

79. Heydari B, Juan YH, Liu H, et al. Stress perfusion cardiac magnetic resonance imaging effectively risk stratifies diabetic patients with suspected myocardial ischemia. *Circ Cardiovasc Imaging*. 2016;9(4):e004136. doi:10.1161/CIRCIMAGING.115.004136

80. Jahnke C, Nagel E, Gebker R, et al. Prognostic value of cardiac magnetic resonance stress tests: adenosine stress perfusion and dobutamine stress wall motion imaging. *Circulation*. 2007;115(13):1769-1776. doi:10.1161/CIRCULATIONAHA.106.652016

81. Kelle S, Egnell C, Vierecke J, et al. Prognostic value of negative dobutamine-stress cardiac magnetic resonance imaging. *Med Sci Monit*. 2009;15(10):MT131-MT136.

82. Lubbers DD, Rijlaarsdam-Hermsen D, Kuijpers D, et al. Performance of adenosine "stress-only" perfusion MRI in patients without a history of myocardial infarction: a clinical outcome study. *Int J Cardiovasc Imaging*. 2012;28(1):109-115. doi:10.1007/s10554-010-9775-0

83. Shah RV, Heydari B, Coelho-Filho O, et al. Vasodilator stress perfusion CMR imaging is feasible and prognostic in obese patients. *JACC Cardiovasc Imaging*. 2014;7(5):462-472. doi:10.1016/j.jcmg.2013.11.011

84. Tonino PAL, Fearon WF, De Bruyne B, et al. Angiographic versus functional severity of coronary artery stenoses in the FAME study fractional flow reserve versus angiography in multivessel evaluation. *J Am Coll Cardiol*. 2010;55(25):2816-2821. doi:10.1016/j.jacc.2009.11.096

85. De Bruyne B, Fearon WF, Pijls NHJ, et al; FAME 2 Trial Investigators. Fractional flow reserve–guided PCI for stable coronary artery disease. *N Engl J Med*. 2014;371(13):1208-1217. doi:10.1056/NEJMoa1408758

86. Jaarsma C, Leiner T, Bekkers SC, 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(19):1719-1728. doi:10.1016/j.jacc.2011.12.040

87. Yang K, Yu SQ, Lu MJ, Zhao SH. Comparison of diagnostic accuracy of stress myocardial perfusion imaging for detecting hemodynamically significant coronary artery disease between cardiac magnetic resonance and nuclear medical imaging: a meta-analysis. *Int J Cardiol*. 2019;293:278-285. doi:10.1016/j.ijcard.2019.06.054

88. Cheng ASH, Pegg TJ, Karamitsos TD, et al. Cardiovascular magnetic resonance perfusion imaging at 3-Tesla for the detection of coronary artery disease: a comparison with 1.5-Tesla. *J Am Coll Cardiol*. 2007;49(25):2440-2449. doi:10.1016/j.jacc.2007.03.028

89. Bernhardt P, Walcher T, Rottbauer W, Wöhrle J. Quantification of myocardial perfusion reserve at 1.5 and 3.0 Tesla: a comparison to fractional flow reserve. *Int J Cardiovasc Imaging*. 2012;28(8):2049-2056. doi:10.1007/s10554-012-0037-1

90. Walcher T, Ikuye K, Rottbauer W, Wöhrle J, Bernhardt P. Is contrast-enhanced cardiac magnetic resonance imaging at 3 T superior to 1.5 T for detection of coronary artery disease? *Int J Cardiovasc Imaging*. 2013;29(2):355-361. doi:10.1007/s10554-012-0099-0

91. Sharrack N, Chiribiri A, Schwitter J, Plein S. How to do quantitative myocardial perfusion cardiovascular magnetic resonance. *Eur Heart J Cardiovasc Imaging*. 2022;23(3):315-318. doi:10.1093/ehjci/jeab193

92. Vasu S, Bandettini WP, Hsu LY, et al. Regadenoson and adenosine are equivalent vasodilators and are superior than dipyridamole: a study of first pass quantitative perfusion cardiovascular magnetic resonance. *J Cardiovasc Magn Reson*. 2013;15(1):85. doi:10.1186/1532-429X-15-85

93. Lijmer JG, Mol BW, Heisterkamp S, et al. Empirical evidence of design-related bias in studies of diagnostic tests. *JAMA*. 1999;282(11):1061-1066. doi:10.1001/jama.282.11.1061

94. Pijls NH, De Bruyne B, Peels K, et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. *N Engl J Med*. 1996;334(26):1703-1708. doi:10.1056/NEJM199606273342604

95. van de Hoef TP, Meuwissen M, Escaned J, et al. Fractional flow reserve as a surrogate for inducible myocardial ischaemia. *Nat Rev Cardiol*. 2013;10(8):439-452. doi:10.1038/nrcardio.2013.86

96. Soares A, Brown DL. The fallacies of fractional flow reserve. *Int J Cardiol*. 2020;302:34-35. doi:10.1016/j.ijcard.2019.12.040

97. Neumann FJ, Sousa-Uva M, Ahlsson A, et al; ESC Scientific Document Group. 2018 ESC/EACTS guidelines on myocardial revascularization. *Eur Heart J*. 2019;40(2):87-165. doi:10.1093/eurheartj/ehy394

98. Mohdnazri SR, Keeble TR, Sharp AS. Fractional flow reserve: does a cut-off value add value? *Interv Cardiol*. 2016;11(1):17-26. doi:10.15420/icr.2016:7:2

99. Johnson NP, Tóth GG, Lai D, et al. Prognostic value of fractional flow reserve: linking physiologic severity to clinical outcomes. *J Am Coll Cardiol*. 2014;64(16):1641-1654. doi:10.1016/j.jacc.2014.07.973

100. Siontis GC, Mavridis D, Greenwood JP, et al. Outcomes of non-invasive diagnostic modalities for the detection of coronary artery disease: network meta-analysis of diagnostic randomised controlled trials. *BMJ*. 2018;360:k504. doi:10.1136/bmj.k504

101. Pandya A, Yu YJ, Ge Y, et al. Evidence-based cardiovascular magnetic resonance cost-effectiveness calculator for the detection of significant coronary artery disease. *J Cardiovasc Magn Reson*. 2022;24(1):1. doi:10.1186/s12968-021-00833-1

102. Ge Y, Pandya A, Steel K, et al. Cost-effectiveness analysis of stress cardiovascular magnetic resonance imaging for stable chest pain syndromes. *JACC Cardiovasc Imaging*. 2020;13(7):1505-1517. doi:10.1016/j.jcmg.2020.02.029

103. Ge Y, Steel K, Antiochos P, et al. Stress CMR in patients with obesity: insights from the Stress CMR Perfusion Imaging in the United States (SPINS) registry. *Eur Heart J Cardiovasc Imaging*. 2021;22(5):518-527. doi:10.1093/ehjci/jeaa281

104. Greenwood JP, Walker S. Stress CMR imaging for stable chest pain syndromes: underused and undervalued? *JACC Cardiovasc Imaging*. 2020;13(7):1518-1520. doi:10.1016/j.jcmg.2020.04.006

105. Schwitter J. The SPINS trial: building evidence and a consequence? *J Am Coll Cardiol*. 2019;74(14):1756-1759. doi:10.1016/j.jacc.2019.07.075

106. Gargiulo P, Dellegrottaglie S, Bruzzese D, et al. The prognostic value of normal stress cardiac magnetic resonance in patients with known or suspected coronary artery disease: a meta-analysis. *Circ Cardiovasc Imaging*. 2013;6(4):574-582. doi:10.1161/CIRCIMAGING.113.000035

107. Lipinski MJ, McVey CM, Berger JS, Kramer CM, Salerno M. Prognostic value of stress cardiac magnetic resonance imaging in patients with known or suspected coronary artery disease: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2013;62(9):826-838. doi:10.1016/j.jacc.2013.03.080

108. Jukema R, Maaniitty T, van Diemen P, et al. Warranty period of coronary computed tomography angiography and [15O]H2O positron emission tomography in symptomatic patients. *Eur Heart J Cardiovasc Imaging*. 2023;24(3):304-311. doi:10.1093/ehjci/jeac258

109. Xu J, Cai F, Geng C, Wang Z, Tang X. Diagnostic performance of CMR, SPECT, and PET imaging for the identification of coronary artery disease: a meta-analysis. *Front Cardiovasc Med*. 2021;8:621389. doi:10.3389/fcvm.2021.621389

110. Pontone G, Guaricci AI, Palmer SC, et al. Diagnostic performance of non-invasive imaging for stable coronary artery disease: a meta-analysis. *Int J Cardiol*. 2020;300:276-281. doi:10.1016/j.ijcard.2019.10.046

111. Knuuti J, Ballo H, Juarez-Orozco LE, et al. The performance of non-invasive tests to rule-in and rule-out significant coronary artery stenosis in patients with stable angina: a meta-analysis focused on post-test disease probability. *Eur Heart J*. 2018;39(35):3322-3330. doi:10.1093/eurheartj/ehy267

112. Jeremias A, Kirtane AJ, Stone GW. A test in context: fractional flow reserve: accuracy, prognostic implications, and limitations. *J Am Coll Cardiol*. 2017;69(22):2748-2758. doi:10.1016/j.jacc.2017.04.019

113. Manisty C, Ripley DP, Herrey AS, et al. Splenic switch-off: a tool to assess stress adequacy in adenosine perfusion cardiac MR imaging. *Radiology*. 2015;276(3):732-740. doi:10.1148/radiol.2015142059

114. Kotecha T, Monteagudo JM, Martinez-Naharro A, et al. Quantitative cardiovascular magnetic resonance myocardial perfusion mapping to assess hyperaemic response to adenosine stress. *Eur Heart J Cardiovasc Imaging*. 2021;22(3):273-281. doi:10.1093/ehjci/jeaa252

115. Burrage MK, Shanmuganathan M, Masi A, et al. Cardiovascular magnetic resonance stress and rest T1-mapping using regadenoson for detection of ischemic heart disease compared to healthy controls. *Int J Cardiol*. 2021;333:239-245. doi:10.1016/j.ijcard.2021.03.010

116. Cerqueira MD, Nguyen P, Staehr P, Underwood SR, Iskandrian AE; ADVANCE-MPI Trial Investigators. Effects of age, gender, obesity, and diabetes on the efficacy and safety of the selective A2A agonist regadenoson versus adenosine in myocardial perfusion imaging integrated ADVANCE-MPI trial results. *JACC Cardiovasc Imaging*. 2008;1(3):307-316. doi:10.1016/j.jcmg.2008.02.003

117. Steen H, Montenbruck M, Kelle S, et al. Fast-strain encoded cardiac magnetic resonance during vasodilator perfusion stress testing. *Front Cardiovasc Med*. 2021;8:765961. doi:10.3389/fcvm.2021.765961

118. Zhou R, Huang W, Yang Y, et al. Simple motion correction strategy reduces respiratory-induced motion artifacts for k-t accelerated and compressed-sensing cardiovascular magnetic resonance perfusion imaging. *J Cardiovasc Magn Reson*. 2018;20(1):6. doi:10.1186/s12968-018-0427-1

119. Foley JRJ, Richmond C, Fent GJ, et al. Rapid cardiovascular magnetic resonance for ischemic heart disease investigation (RAPID-IHD). *JACC Cardiovasc Imaging*. 2020;13(7):1632-1634. doi:10.1016/j.jcmg.2020.01.029