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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☆

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ABSTRACT

Aims: This study aimed to compare the diagnostic accuracy of stress myocardial perfusion imaging between cardiac magnetic resonance (CMR) and nuclear medical imaging, including single-photon emission computed tomography (SPECT) and positron emission tomography (PET), for the diagnosis of hemodynamically significant coronary artery disease (CAD) with fractional flow reserve (FFR) as the reference standard.

Methods and results: We searched PubMed and Embase for all published studies that evaluated the diagnostic accuracy of stress myocardial perfusion imaging modalities, including CMR, SPECT, and PET, to diagnose hemodynamically significant CAD with FFR as the reference standard. A total of 28 articles met the inclusion criteria and were included in the meta-analysis: 14 CMR, 13 SPECT, and 5 PET articles. The results demonstrated a pooled sensitivity of 0.88 (95% confidence interval [CI]: 0.80–0.93), 0.69 (95% CI: 0.56–0.79), and 0.83 (95% CI: 0.70–0.91), and a pooled specificity of 0.89 (95% CI: 0.85–0.93), 0.85 (95% CI, 0.80–0.89), and 0.89 (95% CI, 0.86–0.91) for CMR, SPECT, and PET, respectively. The area under the curve (AUC) of CMR, PET, and SPECT was 0.94 (95% CI, 0.92–0.96), 0.92 (95% CI, 0.89–0.94), and 0.87 (95% CI, 0.83–0.89), respectively.

Conclusions: CMR and PET both have high accuracy and SPECT has moderate accuracy to detect hemodynamically significant CAD with FFR as the reference standard. Furthermore, the diagnostic accuracy of CMR at 3.0 T is superior to 1.5 T.

1. Introduction

CAD is still a main cause of death in large parts of the world, and the prevalence of CAD is expected to increase worldwide [1,2]. Accurate assessment of myocardial ischemia caused by epicardial coronary artery stenosis is very essential for the treatment and prognosis. Traditionally, invasive coronary angiography (ICA) is considered as the reference standard for the detection and evaluation of the severity of CAD, but this invasive procedure only provides coronary morphological information and has limited capability in determine the functional significance of coronary artery stenosis [3–5]. FFR is a well-established and accurate method to assess the hemodynamic significance of coronary artery stenosis [6,7], however, the measurement of FFR is also an invasive procedure with possible complications and radiation exposure. Stress myocardial perfusion imaging modalities, such as CMR, SPECT, and PET, are well-recognized noninvasive diagnostic methods to detect hemodynamically significant CAD in patients with suspected or known CAD with FFR as the reference standard [8–19]. As we know, CMR has a number of advantages compared with nuclear medical imaging, including high spatial and temporal resolution, free of ionizing radiation, and no attenuation or scatter artifacts. However, articles that directly compared the diagnostic accuracy between CMR and nuclear medical imaging were very scarce. Therefore, this meta-analysis was performed to compare the diagnostic accuracy for detecting hemodynamically significant CAD between CMR and nuclear medical imaging (SPECT and PET), using stress myocardial perfusion imaging with FFR as the reference standard.

Abbreviations and acronyms: AUC, area under the curve; CAD, coronary artery disease; CCTA, coronary computed tomography angiography; CI, confidence interval; CMR, cardiac magnetic resonance; DOR, diagnostic odds ratio; FFR, fractional flow reserve; ICA, invasive coronary angiography; MI, myocardial infarction; NLR, negative likelihood ratio; PET, positron emission tomography; PLR, positive likelihood ratio; SPECT, single-photon emission computed tomography; SROC, summary receiver operation characteristic.

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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2. Methods

We pre-specified objectives and methods, and reported the results in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [20].

2.1. Data sources and searches

We searched PubMed and Embase databases for all published studies in the English language evaluating the diagnostic accuracy of stress myocardial perfusion imaging for the diagnosis of hemodynamically significant CAD with FFR as the reference standard. We used the following Medical Subject Headings and search terms: "magnetic resonance imaging or MRI", "single photon emission computed tomography or SPECT", "positron emission tomography or PET", "fractional flow reserve or FFR" and "coronary artery disease or CAD". The exact search syntax was provided in the supplementary materials (Supplementary Table S1). The bibliographies of selected articles and relevant reviews were also screened for potentially suitable references.

2.2. Study selection

Studies were included if: ① stress myocardial perfusion imaging using CMR, SPECT, or PET was used as a diagnostic test for hemodynamically significant CAD; ② FFR served as the reference standard and FFR < 0.75 or 0.8 was considered hemodynamically significant CAD; ③ studies were prospective; ④ results were reported in absolute numbers of true positive, false positive, true negative, and false negative results, or sufficiently detailed data, such as sensitivity, specificity, and positive number detected by reference standard, were provided to derive these numbers. A study was eligible regardless of whether patients were referred for suspected or known CAD. Studies were excluded if they were: ① animal studies; ② phantom studies; ③ retrospective studies; ④ posters; ⑤ letter to the editors. If multiple papers came from the same research group, we only include the paper with the largest sample size.

2.3. Quality assessment

The quality assessment of included studies had to conform to the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) criteria [21]. The QUADAS-2 tool consists of 4 key domains, including patient selection, index test, reference standard, and flow and timing, and 10 questions to appraise the quality of diagnostic accuracy studies.

2.4. Data extraction

Firstly, identifying information about the study was extracted, such as first author and year of publication. Further extracted variables consisted of patient characteristics, technical information and absolute number of true positive, true negative, false positive and false negative test results. If available, data were recorded at the patient and vessel level. Studies used >1 cutoff value for hemodynamically significant CAD or different scanner brands and magnet field strength, as a consequence, reported >1 pair of sensitivity and specificity, these data were all recorded separately for further analysis or subgroup analysis. It is noteworthy that the study with the highest accuracy was selected in each analysis or subgroup analysis, for example, if the diagnostic accuracy was 0.9 at the patient level, but 0.8 at the vessel level in a study, then the former would be chosen for further analysis regardless of patient or vessel level; however, if analysis was performed at the patient and vessel level, this pair of sensitivity and specificity would be both chosen for analysis. If a study included ≥2 diagnostic tests for detecting hemodynamically significant CAD, each test was considered separately. Two investigators (K Yang and SQ Yu) extracted data independently, and discrepancies were resolved by consensus.

2.5. Data synthesis and statistical analysis

On the basis of the results from the (derived) 2×2 contingency tables, the bivariate meta-analysis model was employed to calculate the pooled parameters with their corresponding 95% CIs, including sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR) and diagnostic odds ratio (DOR). The pooled DOR for each imaging modality was used for the construction of summary receiver operating characteristic (SROC) curves, and the area under the SROC curve (AUC) was calculated, which is an all-dimensional evaluation for the accuracy of diagnosis. The following guidelines have been suggested for interpretation of AUC values: low ($0.5 \le AUC < 0.7$), moderate ($0.7 \le AUC < 0.9$), high ($0.9 \le AUC \le 1$) accuracy [22]. The Cochran-Q test and measured inconsistency (I^2) were used to evaluate the heterogeneity between studies. Possible publication bias was assessed by Deeks' funnel plots. MIDAS module [22] for STATA software version 14.0 (College station, Texas, USA) and Review Manager (RevMan) version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) were applied to perform the analysis and construct the graphs. Two-tailed P value of <0.05 was considered to be significant.

Besides, additional analyses, such as sensitivity or subgroup analysis and meta-regression, were also performed in this meta-analysis. The sensitivity analysis was assessed by Cook's distance and outlier detection. We also performed subgroup analyses in patients with multivessel disease between CMR and SPECT (PET was not available), and subgroup analyses based on magnetic field strength (3.0 T or 1.5 T) and FFR threshold (0.8 or 0.75) for CMR. Finally, we conducted meta-regression analyses on sensitivity and specificity in the bivariate model to identify predefined sources of heterogeneity, such as prevalence of CAD, multivessel disease, hypertension, diabetes mellitus and methodological parameters.

3. Results

3.1. Study selection and characteristics

Systematic search resulted in 963 potentially relevant articles. After duplicate removal and title and abstract screening, 90 full articles were retrieved for further evaluation. The flowchart of article search and selection process was shown in Fig. 1. A total of 28 articles with a total of 2665 patients ($n = 2665$) met the study criteria and were included in the meta-analysis, including 14 CMR ($n = 979$), 13 SPECT ($n = 1045$), and 5 PET ($n = 641$) articles (Supplementary references 1–28). It is noteworthy that 4 articles investigated multimodality imaging in each single study (e.g., CMR vs. SPECT) [17–19,28]. Detailed characteristics of the included studies in this meta-analysis were presented in the Supplementary Table S2–4, more detailed information see Supplementary Excel S1. Quality assessment of the included studies was shown in Supplementary Fig. S1, the result revealed that the overall quality of included studies was generally high.

3.2. Pooled diagnostic accuracy of three imaging modalities

Firstly, regardless of patient or vessel level, the pooled estimates of sensitivity of CMR, SPECT and PET were 0.88 (95% CI: 0.80–0.93), 0.69 (95% CI: 0.56–0.79), 0.83 (95% CI: 0.70–0.91) and specificity were 0.89 (95% CI: 0.85–0.93), 0.85 (95% CI: 0.80–0.89), 0.89 (95% CI: 0.86–0.91), respectively. SROC curves showed that the AUCs of CMR, SPECT and PET were 0.94 (95% CI: 0.92–0.96), 0.87 (95% CI: 0.83–0.89) and 0.92 (95% CI: 0.89–0.94), respectively (Fig. 2a–c, Supplementary Table S5). Forest plots for sensitivity and specificity of CMR, SPECT and PET were shown in Fig. 3a–c.

Further analyses at the patient and vessel level were also performed in this meta-analysis. At the vessel level, the pooled sensitivity and specificity of CMR, SPECT and PET were summarized in Table 1. These 3 imaging modalities had similar specificity, however, SPECT had the lowest sensitivity (0.64, 95% CI: 0.47–0.77) compared with CMR and PET (0.85, 95% CI: 0.75–0.92 and 0.83, 95% CI: 0.68–0.92, respectively). At the patient level, the pooled sensitivity and specificity were only available for CMR and SPECT, and also summarized in Table 1. CMR had higher sensitivity and specificity (0.87, 95% CI: 0.73–0.94 and 0.87, 95% CI: 0.82–0.90, respectively) compared with SPECT (0.72, 95% CI: 0.52–0.86 and 0.79, 95% CI: 0.71–0.85, respectively). SROC curves and forest plots are provided in the supplementary materials (Supplementary Figs. S2–S5).

3.3. Publication bias

Deeks' funnel plot asymmetry tests were only performed for CMR and SPECT, which suggested statistically nonsignificant publication bias ($P = 0.18$ and 0.25, respectively) (Supplementary Fig. S6). Publication bias assessment was not performed for PET because it had fewer than 10 included studies.

3.4. Sensitivity analysis

Influence analysis and outlier detection identified two outliers of CMR [17,23] (Supplementary Fig. S7), after we excluded these two outliers, the pooled sensitivity and specificity didn't change significantly, but the degree of heterogeneity (I^2) decreased from 93.39 to 0 for sensitivity and 85.93 to 53.43 for specificity (Supplementary Fig. S8 and Table S6). Same analyses were also performed for SPECT and PET, one outlier of SPECT [24] and no outlier of PET was identified, respectively (Supplementary Figs. S9–10), the detailed results of SPECT were listed in Supplementary Table S6 after the outlier was excluded.

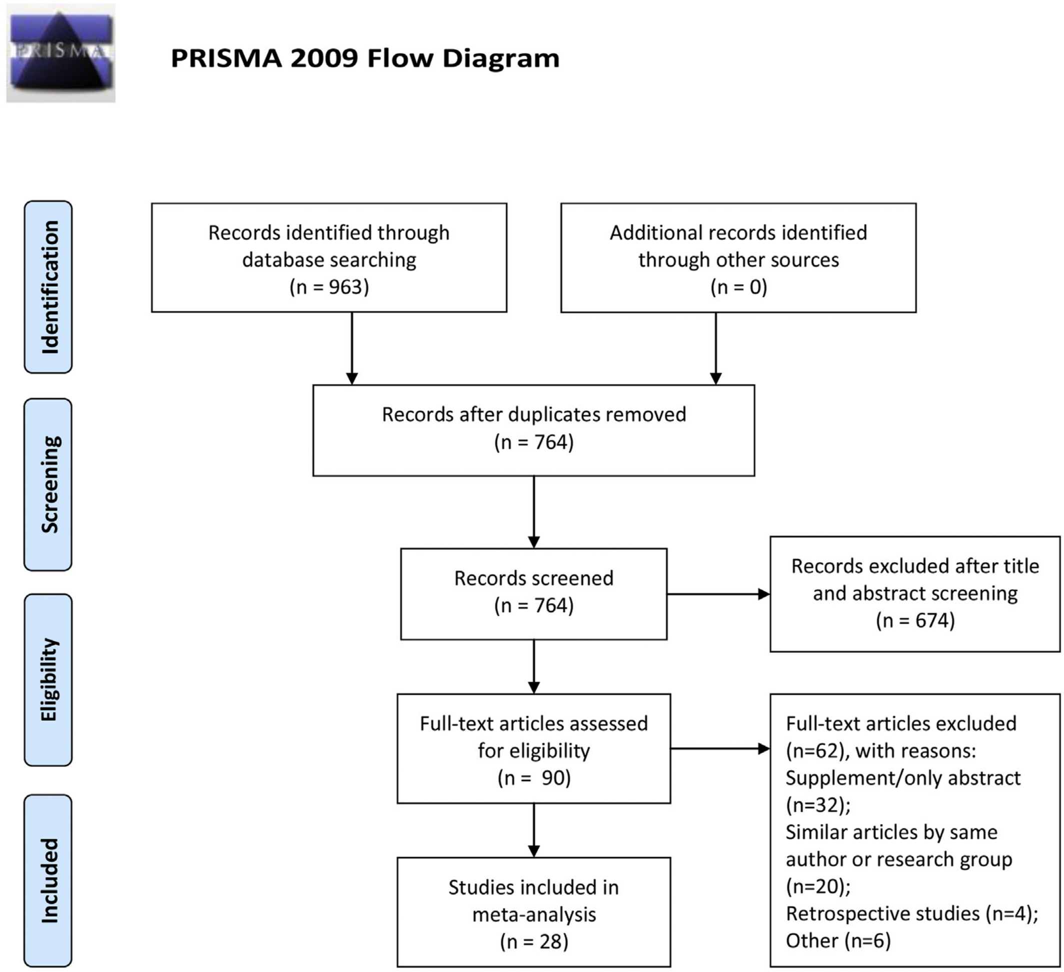


Fig. 1. Flow chart showing the process of literature search and selection algorithm. Of 963 potentially relevant studies, 28 articles met our inclusion criteria and were included in the meta-analysis. Of note, there were 4 studies that included multiple imaging modalities. CMR = cardiac magnetic resonance; SPECT = single-photon emission computed tomography; PET = positron emission tomography.

3.5. Subgroup analysis

Subgroup analyses based on the multivessel disease were performed between CMR and SPECT. The results indicated that SPECT had stable specificity in different percentage of patients with multivessel disease, but had a trend towards decreasing sensitivity with increasing percentage of patients with multivessel disease. CMR had similar specificity, but higher sensitivity compared with SPECT (Supplementary Table S7). For example, when there were >20% patients with multivessel disease, CMR and SPECT had similar specificity (0.88 vs. 0.87,respectively), but CMR had higher sensitivity and AUC compared with SPECT (0.87 vs. 0.68, and 0.93 vs. 0.88, respectively) (Supplementary Fig. S11). Besides, subgroup analyses based on the magnetic field strength (3.0 T or 1.5 T) and threshold of FFR (0.8 or 0.75) were performed for CMR. The results showed that diagnostic accuracy at 3.0 T was superior to 1.5 T (Supplementary Fig. S12), and the diagnostic performance, using a FFR cut-off value of 0.8 as reference, had higher specificity, but lower sensitivity compared with FFR cut-off value of 0.75, and the overall diagnostic accuracy of FFR = 0.8 was slightly higher than FFR = 0.75 (Supplementary Fig. S13).

3.6. Heterogeneity and meta-regression

Differences in the distribution of study characteristics, such as study methodology and patient characteristics, may potentially affect the diagnostic performance of CMR, SPECT and PET, and significant heterogeneity was detected in all 3 imaging modalities (Fig. 3a–c). Meta-regression analyses were performed to evaluate the potential covariates of heterogeneity for these 3 imaging modalities. We found that, for CMR and SPECT, the prevalence of multivessel disease ($P < 0.001$), prior myocardial infarction (MI) ($P < 0.001$), CAD ($P < 0.001$) and hypertension ($P < 0.001$) were significant predictors; besides, analysis at the patient or vessel level ($P = 0.01$) was also a significant predictor for SPECT. As for PET, the year of publication ($P = 0.02$), the prevalence of CAD ($P < 0.001$), hypertension ($P = 0.01$) and multivessel disease ($P < 0.001$) were significant predictors. Other covariates did not influence the diagnostic performance, more detailed information see Supplementary Table S8.

4. Discussion

Nuclear medical imaging modalities are well-validated and most widely used perfusion imaging techniques, other noninvasive myocardial perfusion imaging, such as CMR, is increasingly being performed to detect hemodynamically significant CAD, guide therapy, and provide prognostic information. This meta-analysis was performed to compare the diagnostic performance for detecting hemodynamically significant CAD between CMR and nuclear techniques, including SPECT and PET. In general, the results indicated that CMR and PET both had high accuracy and SPECT had moderate accuracy for detecting hemodynamically significant CAD using FFR as the reference standard.

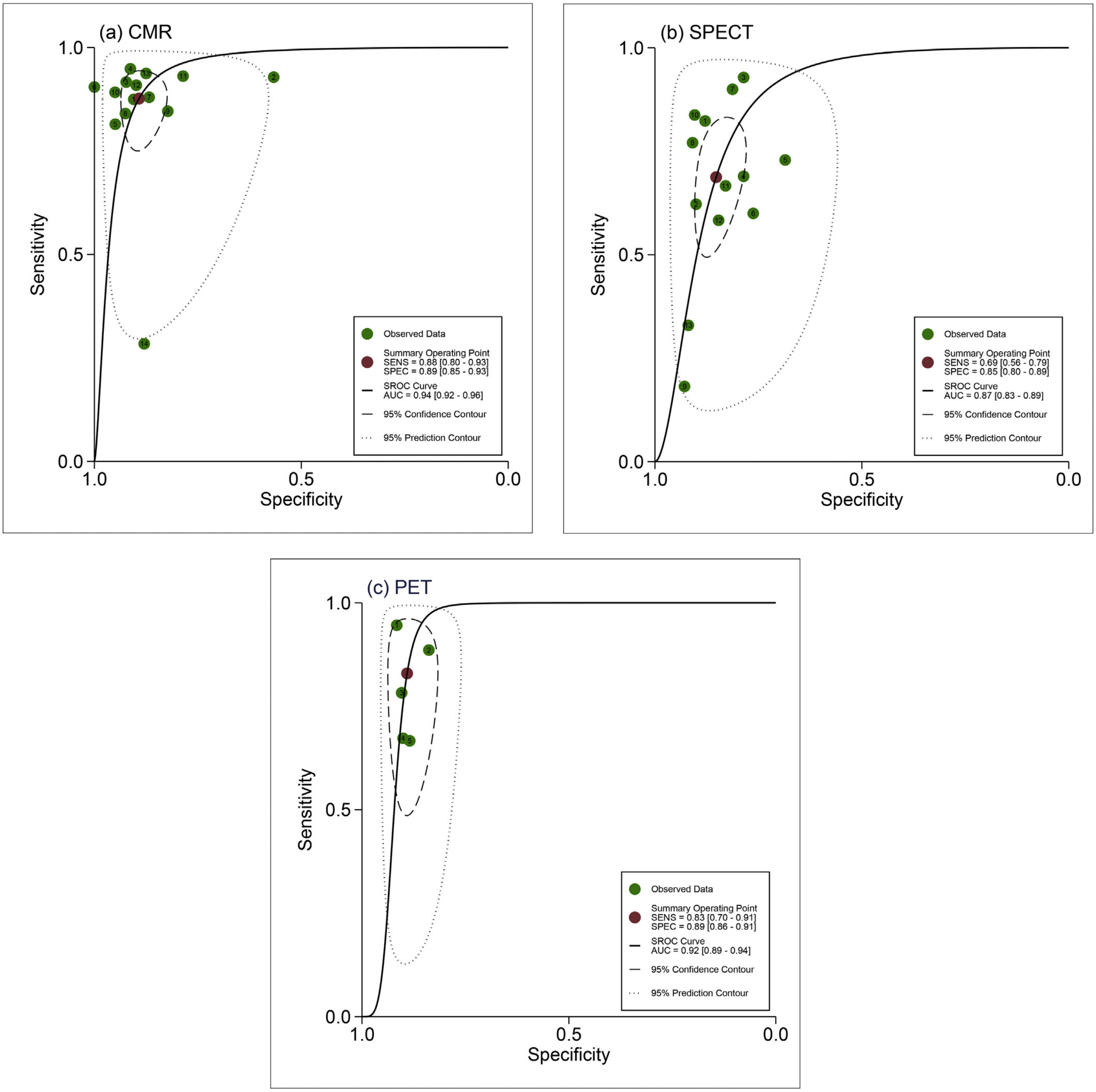
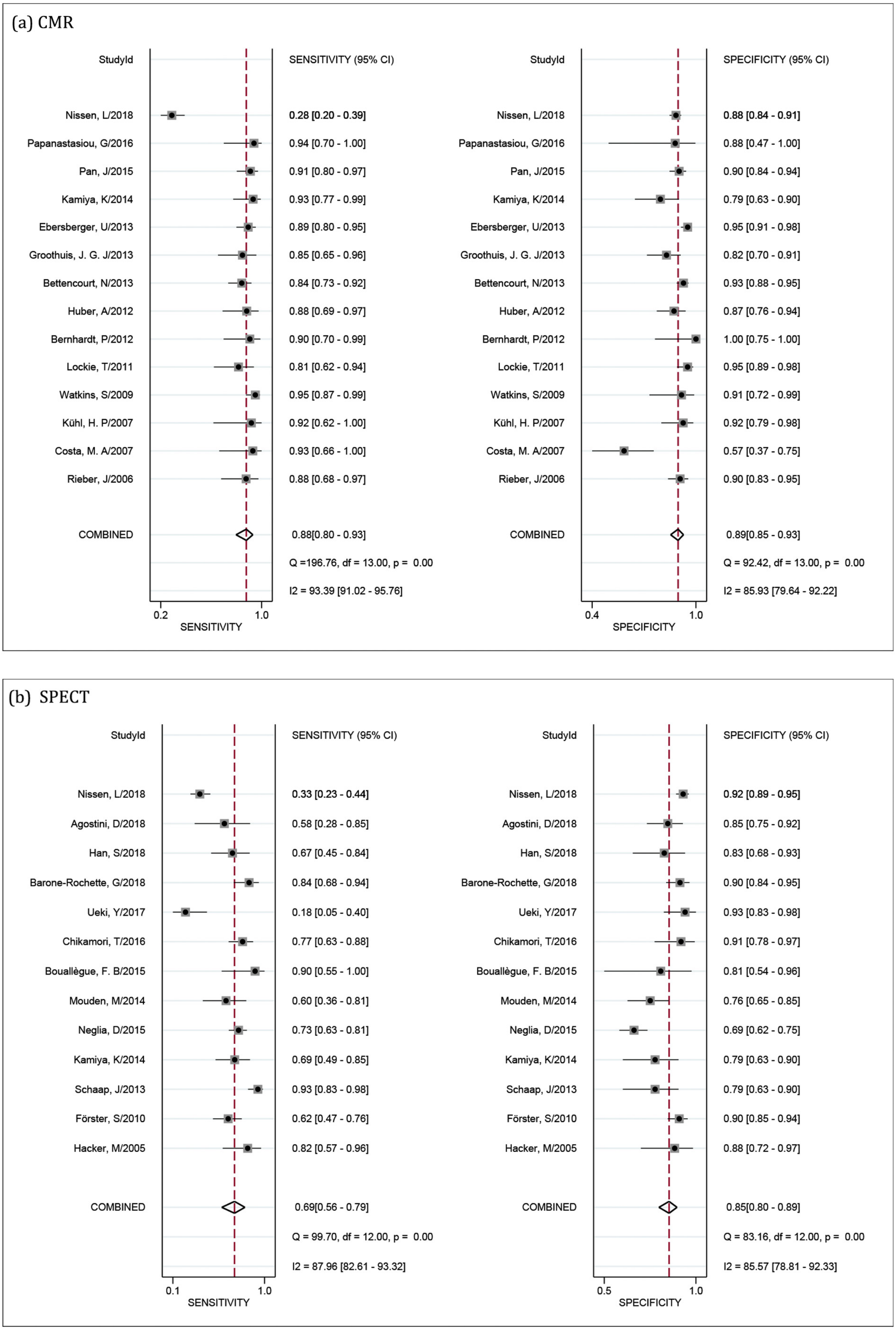


Fig. 2. SROC curves for diagnostic accuracy of CMR (a), SPECT (b) and PET (c). The AUCs of CMR, SPECT and PET were 0.94, 0.87 and 0.92, respectively.

In previous meta-analysis with coronary angiography as the reference standard (≥50% diameter stenosis) by Jaarsma et al. [25], the results showed that CMR, SPECT, and PET all yield a high sensitivity, but a broad range of specificity, and PET had the highest diagnostic performance. In the present meta-analysis, FFR was used as the reference standard, the specificity was slightly increased and CMR had the highest diagnostic accuracy, these differences may be because of the use of a hemodynamic reference standard instead of an anatomic reference standard. In another previous meta-analysis assessing the diagnostic accuracy of stress myocardial perfusion imaging by Takx et al. in 2014 [26], same reference standard was used and it reported similar diagnostic accuracy compared with our meta-analysis. But in the meta-analysis by Takx et al., NLR was chosen as the most important diagnostic test characteristic, and it put an emphasis on the accuracy for ruling out the hemodynamically significant CAD and the value of being gatekeeper for invasive revascularization. Besides, the evaluation of heterogeneity and subgroup analyses were not performed, for example, subgroup analysis based on the multivessel disease and magnetic field strength, which we were interested in, were not performed in this meta-analysis. In the current meta-analysis, it provided a considerable update on evaluating the diagnostic performance of noninvasive myocardial perfusion imaging for detecting hemodynamically significant CAD, including CMR, SPECT, and PET. Besides, an important strength of this meta-analysis was that subgroup analyses based on multivessel disease, magnetic field strength, and threshold of FFR were performed, which was not fully described before.

In patients with multivessel disease, there are still some limitations in the evaluation of balanced myocardial ischemia when morphological


(a) CMR
StudyId
SENSITIVITY (95% CI)
Nissen, L/2018 0.28 [0.20 - 0.39]
Papanastasiou, G/2016 0.94 [0.70 - 1.00]
Pan, J/2015 0.91 [0.80 - 0.97]
Kamiya, K/2014 0.93 [0.77 - 0.99]
Ebersberger, U/2013 0.89 [0.80 - 0.95]
Groothuis, J. G. J/2013 0.85 [0.65 - 0.96]
Bettencourt, N/2013 0.84 [0.73 - 0.92]
Huber, A/2012 0.88 [0.69 - 0.97]
Bernhardt, P/2012 0.90 [0.70 - 0.99]
Lockie, T/2011 0.81 [0.62 - 0.94]
Watkins, S/2009 0.95 [0.87 - 0.99]
Kühl, H. P/2007 0.92 [0.62 - 1.00]
Costa, M. A/2007 0.93 [0.66 - 1.00]
Rieber, J/2006 0.88 [0.68 - 0.97]
COMBINED 0.88[0.80 - 0.93]
Q =196.76, df = 13.00, p = 0.00
I2 = 93.39 [91.02 - 95.76]
0.2
1.0
SENSITIVITY
StudyId
SPECIFICITY (95% CI)
Nissen, L/2018 0.88 [0.84 - 0.91]
Papanastasiou, G/2016 0.88 [0.47 - 1.00]
Pan, J/2015 0.90 [0.84 - 0.94]
Kamiya, K/2014 0.79 [0.63 - 0.90]
Ebersberger, U/2013 0.95 [0.91 - 0.98]
Groothuis, J. G. J/2013 0.82 [0.70 - 0.91]
Bettencourt, N/2013 0.93 [0.88 - 0.95]
Huber, A/2012 0.87 [0.76 - 0.94]
Bernhardt, P/2012 1.00 [0.75 - 1.00]
Lockie, T/2011 0.95 [0.89 - 0.98]
Watkins, S/2009 0.91 [0.72 - 0.99]
Kühl, H. P/2007 0.92 [0.79 - 0.98]
Costa, M. A/2007 0.57 [0.37 - 0.75]
Rieber, J/2006 0.90 [0.83 - 0.95]
COMBINED 0.89[0.85 - 0.93]
Q = 92.42, df = 13.00, p = 0.00
I2 = 85.93 [79.64 - 92.22]
0.4
1.0
SPECIFICITY
(b) SPECT
StudyId
SENSITIVITY (95% CI)
Nissen, L/2018 0.33 [0.23 - 0.44]
Agostini, D/2018 0.58 [0.28 - 0.85]
Han, S/2018 0.67 [0.45 - 0.84]
Barone-Rochette, G/2018 0.84 [0.68 - 0.94]
Ueki, Y/2017 0.18 [0.05 - 0.40]
Chikamori, T/2016 0.77 [0.63 - 0.88]
Bouallègue, F. B/2015 0.90 [0.55 - 1.00]
Mouden, M/2014 0.60 [0.36 - 0.81]
Neglia, D/2015 0.73 [0.63 - 0.81]
Kamiya, K/2014 0.69 [0.49 - 0.85]
Schaap, J/2013 0.93 [0.83 - 0.98]
Förster, S/2010 0.62 [0.47 - 0.76]
Hacker, M/2005 0.82 [0.57 - 0.96]
COMBINED 0.69[0.56 - 0.79]
Q = 99.70, df = 12.00, p = 0.00
I2 = 87.96 [82.61 - 93.32]
0.1
1.0
SENSITIVITY
StudyId
SPECIFICITY (95% CI)
Nissen, L/2018 0.92 [0.89 - 0.95]
Agostini, D/2018 0.85 [0.75 - 0.92]
Han, S/2018 0.83 [0.68 - 0.93]
Barone-Rochette, G/2018 0.90 [0.84 - 0.95]
Ueki, Y/2017 0.93 [0.83 - 0.98]
Chikamori, T/2016 0.91 [0.78 - 0.97]
Bouallègue, F. B/2015 0.81 [0.54 - 0.96]
Mouden, M/2014 0.76 [0.65 - 0.85]
Neglia, D/2015 0.69 [0.62 - 0.75]
Kamiya, K/2014 0.79 [0.63 - 0.90]
Schaap, J/2013 0.79 [0.63 - 0.90]
Förster, S/2010 0.90 [0.85 - 0.94]
Hacker, M/2005 0.88 [0.72 - 0.97]
COMBINED 0.85[0.80 - 0.89]
Q = 83.16, df = 12.00, p = 0.00
I2 = 85.57 [78.81 - 92.33]
0.5
1.0
SPECIFICITY

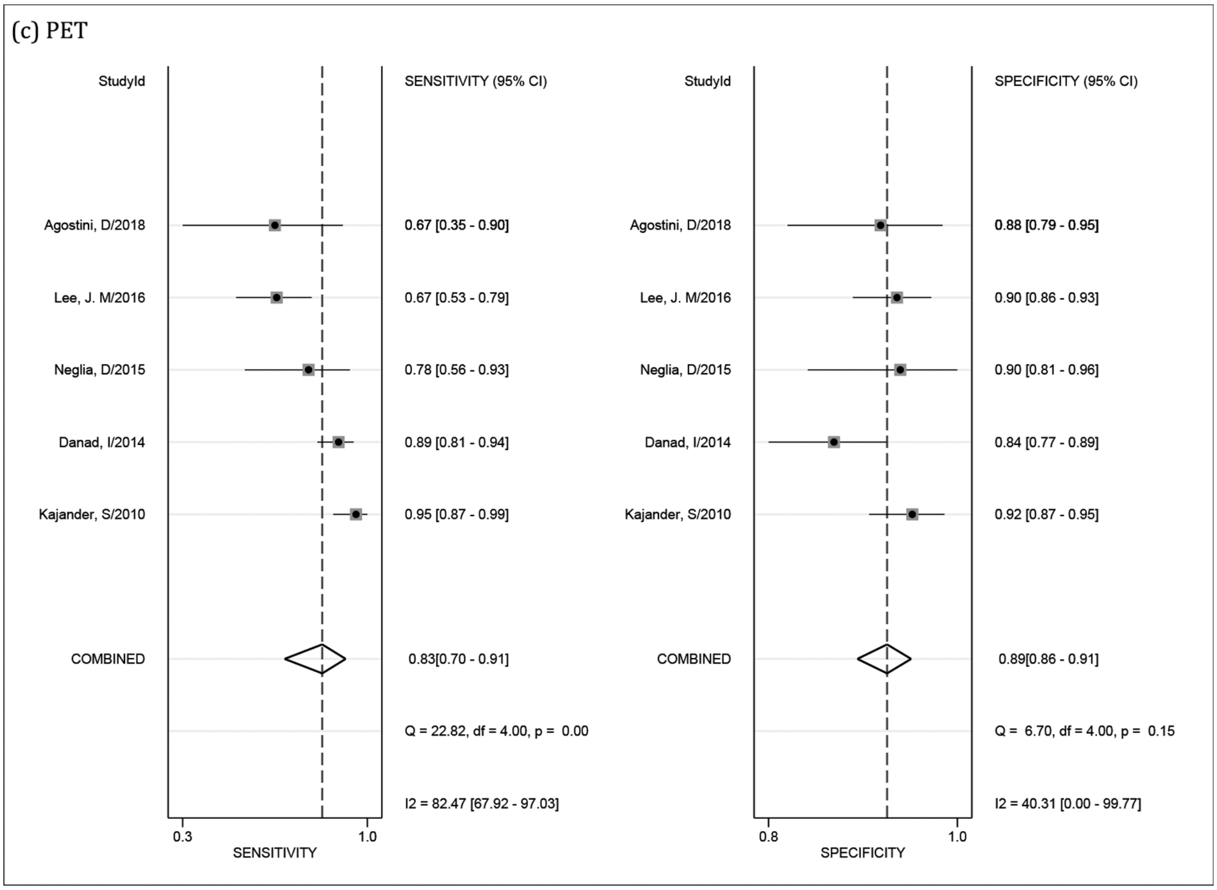


Fig. 3. Forest plots for sensitivity and specificity of CMR (a), SPECT (b) and PET (c). The combined sensitivity of CMR, SPECT and PET was 0.88, 0.69 and 0.83, respectively; and specificity was 0.89, 0.85 and 0.89, respectively.

correlation is not available [27]. In the present meta-analysis, we made a comparison of diagnostic accuracy in patients with multivessel disease between CMR and SPECT. We found that SPECT had stable specificity, but a trend towards decreasing sensitivity with increasing percentage of patients with multivessel disease, CMR had similar specificity and possibly higher sensitivity compared with SPECT. However, it is noteworthy that, for example, when there were >20% patients with multivessel disease, the mean prevalence of multivessel disease in SPECT was higher than that in CMR (59% vs. 40%, respectively), thus although the results indicated that diagnostic accuracy of CMR was superior to SPECT, the results might be not very powerful and the lower sensitivity and AUC of SPECT was likely due to the higher prevalence of multivessel disease, but this also confirmed that SPECT still had good specificity even in patients with higher prevalence of multivessel disease. In the article by Kamiya et al. [28] that directly compared the diagnostic performance between CMR and SPECT, the results showed that these two imaging modalities had the same specificity (79%), but CMR had higher sensitivity than SPECT (93% vs. 69%, respectively) in the prevalence of 56% patients with multivessel disease. However, analysis only performed in those patients with multivessel disease showed that CMR had higher sensitivity than SPECT (93% vs. 53%, respectively), while SPECT had higher specificity than CMR (100% vs. 60%, respectively). In another article by Nissen et al. [17] that also directly compared the diagnostic accuracy between CMR and SPECT, the results indicated that the sensitivity and specificity of CMR was slightly lower than that of SPECT (28% vs. 33% and 88% vs. 92%, respectively), both CMR and SPECT had low sensitivity due to patient population based on the coronary computed tomography angiography (CCTA) findings. These discrepancies may indicate that further studies should be performed to evaluate the diagnostic accuracy between CMR and SPECT in the same patient population.

Besides, comparison of diagnostic accuracy of CMR at 3.0 T and 1.5 T was performed in this meta-analysis. We found that the diagnostic accuracy at 3.0 T was higher than 1.5 T. To the best of our knowledge,

Table 1
Diagnostic performance of CMR, SPECT, and PET myocardial perfusion imaging at the patient and vessel level.

	No. of studies	Sensitivity (%)	Specificity (%)	PLR	NLR	DOR	AUC
Patient level							
CMR	7	87(73–94)	87(82–90)	6.6(4.6–9.4)	0.15(0.07–0.33)	45(15–128)	0.89(0.86–0.91)
SPECT	8	72(52–86)	79(71–85)	3.5(2.5–4.7)	0.35(0.20–0.63)	10(5–21)	0.83(0.79–0.86)
Vessel level							
CMR	12	85(75–92)	89(85–93)	7.9(5.4–11.5)	0.17(0.10–0.28)	48(22−102)	0.94(0.91–0.96)
SPECT	9	64(47–77)	89(86–91)	5.7(4.5–7.3)	0.41(0.27–0.62)	14(8–25)	0.89(0.86–0.92)
PET	4	83(68–92)	89(85–91)	7.2(5.2–10.0)	0.19(0.09–0.39)	38(15–97)	0.92(0.89–0.94)

Abbreviations: PLR = positive likelihood ratio; NLR = negative likelihood ratio; DOR = diagnostic odds ratio; AUC = area under the curve.

only one article by Bernhardt et al. [29] that directly compared the diagnostic accuracy between 3.0 T and 1.5 T using FFR as reference standard, the results showed that 3.0 T had higher sensitivity and specificity compared with 1.5 T (90.5% vs. 61.9%, 100% vs. 76.9%, respectively), and the AUC of 3.0 T was significantly higher than that of 1.5 T (0.96 vs. 0.65, $p < 0.001$). Significant increases in signal- and contrast-to-noise ratios at 3.0 T were probable explanations for the increased diagnostic accuracy [30,31]. Furthermore, the diagnostic accuracy of CMR using a FFR cut-off value of 0.8 or 0.75 was also compared in the present meta-analysis, the results indicated that a higher sensitivity when a FFR cut-off value of 0.75 was used, and a higher specificity when a FFR cut-off value of 0.8 was used. Articles by Watkins et al. [32] and Bettencourt et al. [33] that directly compared the diagnostic accuracy of CMR using a FFR cut-off value of 0.8 or 0.75 in the same patient population also reported the same results at the patient or vessel level. This is not hard to understand because a higher FFR cut-off value used as reference standard, a higher rate of false-negative and lower rate of false-positive numbers would be reported.

5. Study limitations

Several limitations should be taken into consideration for a comprehensive interpretation. Firstly, FFR measurement was not performed in all coronary arteries. In some articles, FFR was only measured in lesions of intermediate severity (diameter stenosis 50–75%), the reference standard was a combination of angiographic diameter stenosis measurements with or without corresponding FFR measurements. However, hemodynamically significant stenosis with a diameter reduction of <50% by coronary angiography cannot be fully ruled out. Similarly, stenosis of higher grade (>75%) was not always functionally significant according to FFR measurements [4]. Secondly, only studies using ICA with FFR as the reference standard were eligible for inclusion. Therefore, only 5 PET studies were included in this meta-analysis. Subgroup analyses, such as the diagnostic accuracy at the patient level and patients with multivessel disease, cannot be achieved in this meta-analysis. Thirdly, high degree of heterogeneity was observed in all these three imaging modalities, differences in study methodology and patient characteristics likely account for this observation, and meta regression analyses were performed to evaluate potential sources of heterogeneity, but random effects model provided an accurate summary diagnostic accuracy estimate largely unachievable by standalone studies. Fourthly, the percentage of patients with multivessel disease was different in each study, thus comparison between CMR and SPECT in a certain percentage of patients with multivessel disease (e.g. >20%) may introduce a lot of bias, so the results should be interpreted with caution. Finally, in this meta-analysis, we compared a state of the art technology (CMR) versus an “archeological” one (SPECT), this may be unfair and not comparable, but this due to the fact that SPECT is a well-established and most widely used imaging modality for the diagnosis of myocardial ischemia, so SPECT was chosen as an object to compare with CMR.

6. Conclusions

In this meta-analysis, CMR and PET both have high accuracy to diagnose hemodynamically significant CAD with FFR as the reference standard, and the diagnostic accuracy of CMR at 3.0 T is superior to 1.5 T. SPECT has moderate accuracy for the diagnosis of hemodynamically significant CAD.

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Declaration of Competing Interest

None.

Appendix A. Supplementary data

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