

## Original Article

# The sensitivity and specificity of single photon emission computed tomography (SPECT) in the diagnosis of coronary artery disease (CAD): a meta-analysis

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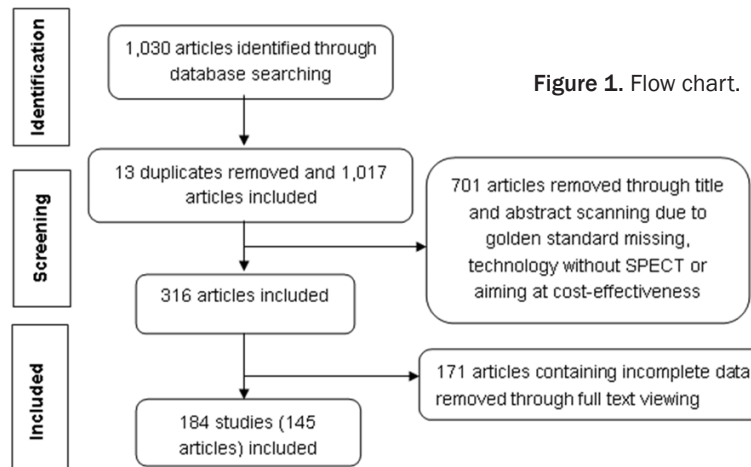
**Abstract:** Background: Coronary artery disease (CAD) is a serious threat to health with effective diagnostic methods significantly reducing its risk. While single photon emission computed tomography (SPECT), is an effective non-invasive diagnostic test with broad prospects for development, its sensitivity (SEN) and specificity (SPE) remain to be proven. Methods: All publications were searched through PubMed, Embase and Cochrane Library. Studies comparing SEN and false positive rate (FPR) of SPECT in the diagnosis of CAD were included. Data regarding relative outcomes in each study were extracted, based on SEN and FPR with 95% confidence intervals (CI). A meta-analysis was performed with several subgroup analyses. Further, the summary receiver operating characteristic (SROC) curve was plotted and its area under the curve (AUC) was calculated. Results: According to the results of meta-analysis, thallium-201 (TI-201) is regarded as the best radiotracer with the largest partial AUC 0.86, SEN and FPR 0.82 (0.79, 0.85) and 0.25 (0.21, 0.29). Technetium-99m (Tc-99m) performs closely to TI-201, as SEN of Tc-99m was 0.84 (0.82, 0.86), FPR 0.30 (0.27, 0.33), and partial AUC 0.85. However, there was no observed competitive advantage in combining TI-201 together with Tc-99m. Although dual labeled compounds have highest SEN (0.85 (0.77, 0.91)), it FPR is lowest with FPR of 0.32 (0.25 to 0.39), partial AUC only 0.80. Conclusion: TI-201 FPR was demonstrated to be the optimal radiotracer of SPECT in the diagnoses of CAD, and low-level exercise combined with pharmacologic agents was the preferable choice of SPECT stress inducer. To sum up, based on its SEN and FPR, SPECT can be widely used in CAD diagnosis.

**Keywords:** Coronary artery disease, single photon emission computed tomography, coronary angiography, technetium-99m, thallium-201, meta-analysis

## Introduction

Coronary artery disease (CAD), also known as ischemic heart disease, is caused by insufficient myocardial blood supply, leading to stable angina, unstable angina, myocardial infarction, and sudden coronary death [1]. Since coronary circulation consists of the blood-supply vessels of the heart muscle myocardium, as so-called "end circulation", there are no compensatory or secondary branch vessels, which causes serious problems when any blockage occurs. Hypertension, smoking, hyperlipidemia, diabetes and physical inactivity are considered to be high risk factors [2], while familial inheritance is also one of the main causes. Atherosclerosis of coronary artery is the direct catalyst leading to CAD [3]. According to previous studies [4, 5],

women are on served to be more vulnerable to CAD than men in similar conditions, and the risk of CAD increases with age. Meanwhile, ethnicity also plays an important role. Cardiovascular disease causes over 17 million worldwide deaths annually, and CAD accounts for the largest proportion of this [1]. According to Global Burden of Disease Study (GBD 2013), CAD was the primary cause of life loss in 2013 [6], although mortality in patients with CAD decreased between 1980 and 2010, a trend particularly strong in developed countries [7]. Another reason for such a high mortality rate is that CAD is difficult to diagnose as its initial primary symptom is chest pain after strenuous exercise or stress, which can dissipate after rest [8]. Therefore, an efficient, safe and accurate diagnostic method is necessary and at



present, based on the advice of National Heart, Lung, and Blood Institute, electrocardiogram (EKG), echocardiography, chest X-ray, single photon emission computed tomography (SPECT) and coronary angiography (CA) are the most common cardio logical diagnostic tests and procedures. All of the test methods can be classified into two groups: invasive (CA), and non-invasive, (EKG, X-ray, SPECT, etc). [9].

Since 1960, when the first CA was somewhat accidentally carried out by Mason Sones [10], it has developed gradually and been accepted as the golden standard in consideration of its accuracy. Both the main and branch of coronary artery are visible under X-ray for the detection of occlusion, stenosis, restenosis, or thrombosis with the help of special coronary catheter puncturing into the artery and injection of radio contrast. Even though it is convenient to diagnosis, not everyone can tolerate radio contrast, and due to its invasive, this does not seem to be the optimal choice for patients with suspected CAD.

SPECT, one of the non-invasive methods, is increasing in popularity due to its general applicability and relative harmlessness. Computed tomography images can be obtained by varying the intensity of  $\gamma$  rays from different organs or parts of the body. According to the distinction between images under stress and at rest, doctors can diagnose myocardial ischemia, evaluate the lesion range and assess the degree of CAD [11].

In addition, there is much research on the sensibility (SEN) and false positive rate (FPR) of

diagnosis of CAD, but the results vary significantly. For example, even using the same imaging isotope and stress inducer drug, the SPE in the study of Ogliby *et al.* turned out to be 100% [12], while Miller *et al.* suggests the SPE was only 27.5% [13]. Such difference was common in existing studies. Although there were several meta-analyses [14-16], most of the literatures were out of date or limited, and none of them considered the influence of ethnicity. To iron out these flaws,

this meta-analysis would involve updated credible studies, and discuss the potential influential factors including tracer atom, stress and ethnicity.

## Methods

### Literature identification

By searching on PubMed, Embase and Cochrane Library, relevant literature identification was completed without language restriction. Meanwhile, keywords such as “coronary artery disease”, “coronary angiography”, “single photon emission computed tomography” and their synonyms were combined to use as searching terms. Besides this, reference lists of relevant literatures were searched and examined in case of any omission. All the potential literatures were assessed by two reviewers separately.

### Inclusion criteria

Studies were included if they satisfied the following criteria: (i) all subjects included were suspected as CAD, with no limitation of patients' ethnicity; (ii) SPECT must be used as one of the diagnostic tools, irrespective of type of radioactive tracer or stress inducer; (iii) the gold standard must be CA, irrespective of interpretation; (iv) a comparison must be performed in the study between SPECT and CA.

### Data extraction

Independently, two reviewers screened the titles and abstracts of retrieved literatures, and in some cases, the full text was examined for

**Table 1.** Main results of meta-analysis

Study			Study Number	Sensitivity	False Positive Rate	AUC	Partial AUC
Overall			184	0.84 (0.82, 0.85)	0.28 (0.26, 0.31)	0.85	0.82
Thallium-201	Total		60	0.82 (0.79, 0.85)	0.25 (0.21, 0.29)	0.86	0.86
	Stress	Exercise	21	0.80 (0.73, 0.85)	0.30 (0.23, 0.39)	0.82	0.74
		Drug	26	0.83 (0.79, 0.87)	0.20 (0.16, 0.24)	0.88	0.72
		Dual	4	0.87 (0.78, 0.92)	0.39 (0.28, 0.51)	0.76	0.83
	Ethnicity	Caucasian	41	0.82 (0.79, 0.85)	0.26 (0.21, 0.31)	0.85	0.76
		Asian	19	0.83 (0.78, 0.87)	0.24 (0.18, 0.31)	0.87	0.76
Technetium-99m	Total		113	0.84 (0.82, 0.86)	0.30 (0.27, 0.33)	0.85	0.85
	Stress	Exercise	27	0.89 (0.86, 0.92)	0.34 (0.27, 0.41)	0.87	0.83
		Drug	47	0.83 (0.79, 0.86)	0.28 (0.24, 0.33)	0.84	0.79
		Dual	16	0.84 (0.80, 0.88)	0.27 (0.22, 0.33)	0.85	0.78
	Ethnicity	Caucasian	96	0.84 (0.82, 0.86)	0.31 (0.28, 0.34)	0.84	0.80
		Asian	17	0.88 (0.82, 0.92)	0.23 (0.18, 0.29)	0.88	0.72
Dual	Total		11	0.85 (0.77, 0.91)	0.32 (0.25, 0.39)	0.80	0.80
	Stress	Exercise	2	0.67 (0.30, 0.90)	0.29 (0.15, 0.50)	0.74	0.66
		Drug	3	0.88 (0.77, 0.94)	0.32 (0.22, 0.44)	0.82	0.83
		Dual	6	0.88 (0.79, 0.94)	0.34 (0.23, 0.48)	0.83	0.87

AUC: area under the curve. *FPR* (false positive rate) =  $1 - \text{SPE}$  (specificity). Note: Stress types of some studies are not clear, as a result summary of studies numbers of Exercise, Drug and Dual may not equal the total number.

more details. Any disagreements regarding inclusion were solved under discussion. The following information was extracted: author, year of publication, country, diagnosed disease, the diagnostic technique employed, isotope, stress inducer and interpretation of SPECT, inclusion of CA as gold standard, and finally outcomes which represented data as true positive, false positive, true negative and false negative, and these were obtained to fulfill the  $2 \times 2$  contingency table.

#### Statistical analysis

SEN and SPE of each test method were calculated, based on data showing in both true and false positives and negatives ( $2 \times 2$ ) contingency tables. Meanwhile, the heterogeneity among selected studies was tested through Cochran's Q, to find if the data could be pooled together. Usually, when  $P < 0.01$  there was significant heterogeneity, and it was necessary to perform subgroup analyses. Moreover, if primary subgroup did not work very well, the secondary subgroup was used.

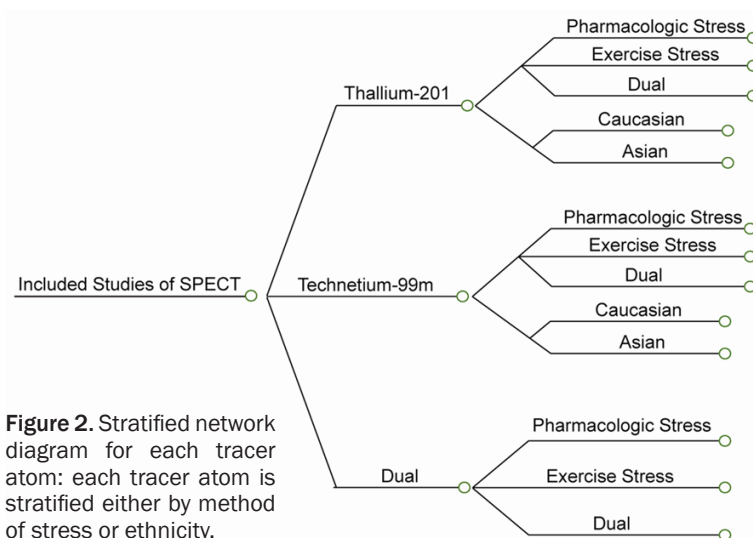
Furthermore, meta-analysis model of pooling all studies and of subgroup categorized by potential influencing factors were fitted for SEN and SPE with software R® version 3.2.1 (Ma-

thSoft, Cambridge, Massachusetts). The SEN and the SPE of SPECT compared with gold standard were expressed in the number less than 1 with 95% confidence intervals (CI). According to these data, a summary receiver operating characteristic (SROC) curve was performed, and the area under the SROC curve (AUC) was computed through the relative integral formula to reflect the SEN and SPE among different subgroups. The AUC values were in the range of 0 to 1, and if a diagnostic method was clearly superior, its AUC would be 1; and vice versa. Besides, to make our SROC curves more visible, instead of SPE, the FPR were used as abscissa. The conversion adopted was:  $\text{FPR} = 1 - \text{SPE}$ .

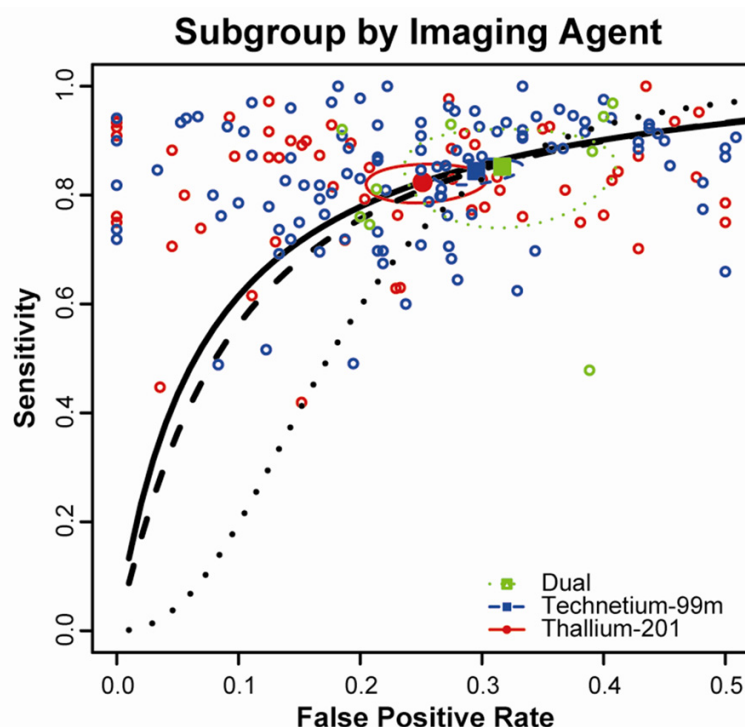
#### Results

##### Included studies

This meta-analysis involved 184 studies collected from 145 articles with 19,182 subjects [12, 13, 17-159], since these all satisfied the criteria mentioned above. At first, 1,017 literatures contained the searching terms were identified and retrieved, after eliminating 13 duplicates. By skimming the title and abstract of identified articles, 846 were selected and the full texts were reviewed. Among them, 701



**Figure 2.** Stratified network diagram for each tracer atom: each tracer atom is stratified either by method of stress or ethnicity.



**Figure 3.** The summary receiver operator characteristic (SROC) curves shows the diagnostic power of three imaging agents to coronary artery disease.

studies were excluded, since they did not mention the gold standard, or did not make explicit the technology of SPECT, or were aimed at cost-effectiveness (**Figure 1**).

#### Characteristics of included studies

Among these 184 studies, 36 were targeted on Asian patients, while other studies were targeted on Caucasian ethnicities. Three types of ra-

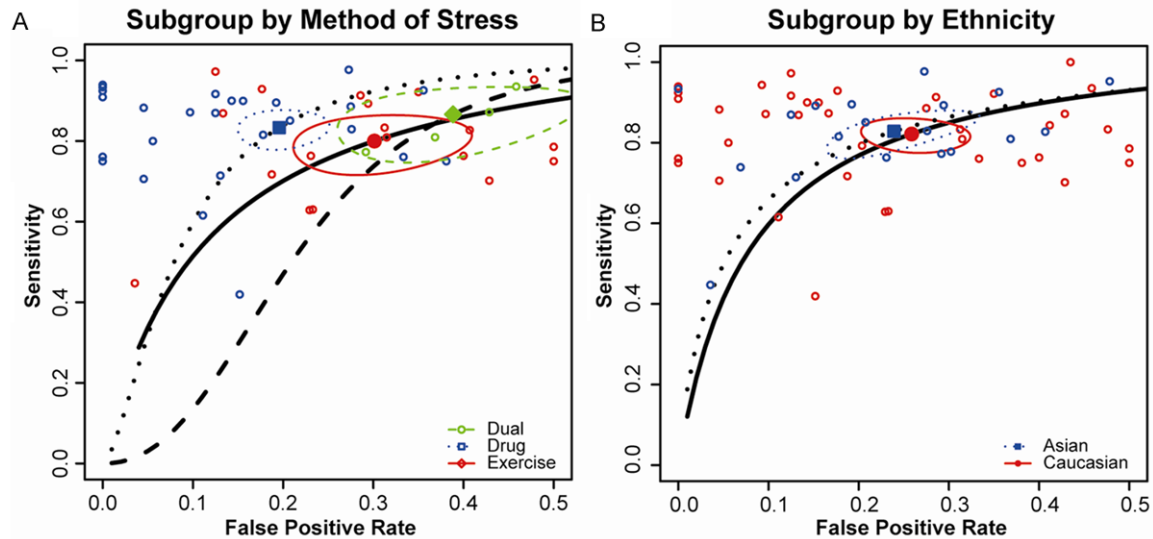
diotracer were involved, with technetium-99m (Tc-99m) the most common. Besides this, thallium-201 (Th-201) and Tc-99m plus Th-201 (Dual) were also used in some studies. Pharmacologic agents, exercise and both (Dual) were used to produce cardiac load. Adenosine, dipyridamole and dobutamine were employed as pharmacologic stress inducer. In addition, all the studies took CA as gold standard reference. Details of selected studies were shown in [Table S1](#). The quality of included studies using QUADAS-2 was shown in [Table S2](#).

#### Total SPECT

SEN and SPE of SPECT were compared with CA in all included studies. Pooling all data together, the overall SEN turned out to be 0.84 (0.82, 0.85), while the FPR was 0.28 (0.26, 0.31), and its partial AUC was 0.82, seen in **Table 1**.

Meanwhile, heterogeneity among all kinds of SPECT was calculated individually, as well as to SEN and SPE with *P* values less than 0.01, which could be deemed as existing significant heterogeneity. Considering the potential differences generated by various radiotracers, subgroup analysis was performed. Nevertheless, the heterogeneity was still extant between studies using same isotope. The secondary subgroup analyses were then conducted, in terms of stress inducer and ethnicity.

Therefore, in this meta-analysis, to reduce error between different SPECT equipment and patients' race, two-class subgroup analyses were used, which meant all the studies were divided into three first-class subgroups, first with Tc-99m, TI-201 and dual, and after that each primary subgroup was classified as pharmacologic stress inducer, exercise and both, or as Asian and Caucasian, as shown in **Figure 2**.



**Figure 4.** The summary receiver operator characteristic (SROC) curves based on subgroup analysis of Thallium-201. A. Method of Stress; B. Ethnicity.

#### Thallium-201

There were 60 studies related to TI-201 included with SEN 0.82 (0.79, 0.85), lower than the overall SEN. But the SPE of TI-201 was higher than the pooled data average, with FPR 0.25 (0.21, 0.29). Additionally, based on the SROC curve for total TI-201 shown in **Figure 3**, its partial AUC was calculated as 0.86.

With regards to the SEN of secondary subgroup (stress inducer), exercise was 0.80 (0.73, 0.85), drug was 0.83 (0.79, 0.87), and combination of both components was 0.87 (0.78, 0.92). FPR for exercise was 0.30 with 95% CI 0.23 to 0.39, for drug 0.20 (0.16, 0.24), and for dual 0.39 (0.28, 0.51). According to SROC curve demonstrated in **Figure 4A**, the partial AUC for each inducer was 0.74, 0.71 and 0.83.

As for ethnicity, SEN was 0.82 with 95% CI ranging from 0.79 to 0.85, and 0.83 with 95% CI from 0.78 to 0.87 respectively for Caucasian and Asian respectively. FPR was 0.26 with 95% CI 0.21 to 0.31 for Caucasian, and 0.24 with 95% CI 0.18 to 0.31 for Asian. The partial AUC of the two ethnicities were both 0.76 as shown in **Figure 4B**.

#### Technetium-99m

Tc-99m was the most common isotope atom used as radiotracer, so 113 studies with 10,746

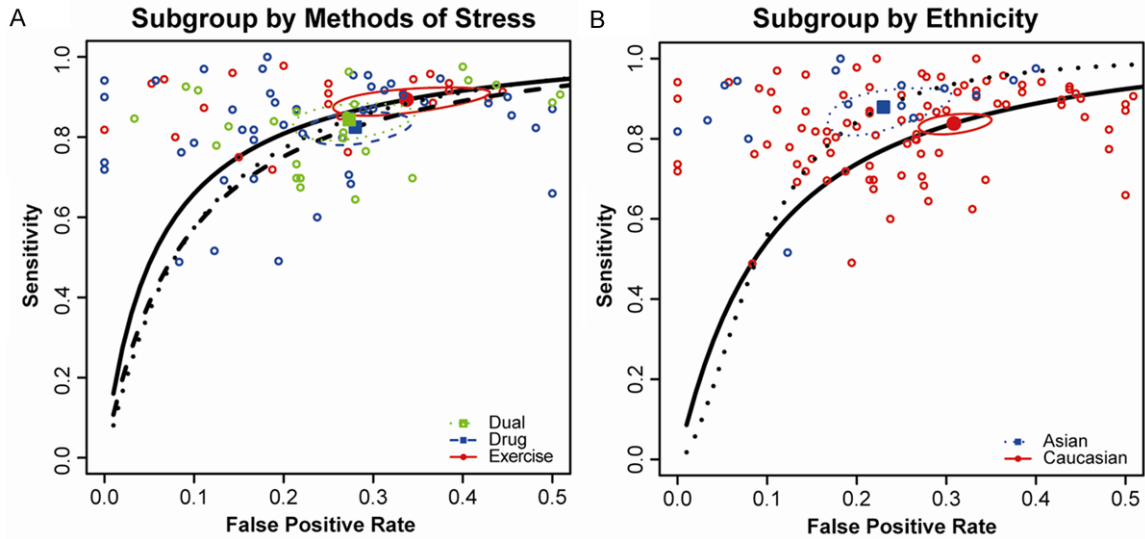
patients were involved. The SEN and FPR of total data were 0.84 with narrow 95% CI from 0.82 to 0.86, 0.30 with 95% CI from 0.27 to 0.33. Partial AUC shown in **Figure 3** was 0.85.

Categorized by stress inducer, exercise had the best SEN 0.89 with 95% CI from 0.86 to 0.92, but the worst SPE, since it FPR was 0.34 with 95% CI from 0.27 to 0.41. Additional, SEN and SPE of dual were both better than drug alone, since SEN of drug was 0.83 with 95% CI 0.79 to 0.86, of dual was 0.84 with 95% CI 0.80 to 0.88; FPR of drug was 0.28 with 95% CI 0.24 to 0.33, and of dual was 0.27 with 95% CI 0.22 to 0.33. However, considering these two aspects and after correction, the order was exercise, drug and dual, with partial AUC 0.83, 0.79 and 0.78 respectively, as shown in **Figure 5A**.

In view of the influence of ethnicity, the secondary subgroup was performed as Caucasian and Asian, and SEN was 0.84 with 95% CI from 0.82 to 0.86, 0.88 with 95% CI from 0.82 to 0.92, and FPR was 0.31 with 95% CI between 0.28 and 0.34, 0.23 with 95% CI between 0.18 and 0.29. Referring to SROC curve **Figure 5B**, the partial AUC was 0.80 for Caucasian and 0.72 for Asian.

#### Combination

The subgroup analysis of combination, which used both Tc-99m and TI-201, included only 11



**Figure 5.** The summary receiver operator characteristic (SROC) curves based on subgroup analysis of Technetium-99m. A. Method of Stress; B. Ethnicity.

studies, and all subjects were Caucasian, with only second-class stress inducer being conducted. The merged data of dual showed that SEN was 0.85 and its 95% CI with limitation of 0.77 to 0.91, and FPR was 0.32, and 95% CI was 0.25 to 0.39. As illustrated in **Figure 3**, the partial AUC was 0.80.

In the secondary subgroup, both drug and dual stress inducers showed good performance in SEN, as their SEN was 0.88 with 95% CI 0.77 to 0.94, and 0.88 with 95% CI 0.79 to 0.94. FPR of each was 0.32 with 95% CI 0.22 to 0.44, and 0.34 with 95% CI 0.23 to 0.48. Although the SEN of exercise was 0.67 with wide 95% CI from 0.30 to 0.90, much lower than drug and dual, its FPR was 0.29 with 95% CI 0.15 to 0.50. To sum up, drug performed better than exercise, but worse than combination, as their partial AUC was 0.83, 0.66, and 0.87 in SROC curve.

### Discussion

This meta-analysis gathered data from 184 studies of 145 articles with 19,182 total subjects, who were suspected to suffer from CAD, and all studies involved assessed the SEN and SPE of SPECT, compared with golden reference CA. Three types of radiotracers, three kinds of stress inducer, and two different ethnicities were tested and to minimize the probable influence generated by different SPECT equipment

and races, they were categorized into two-class subgroups. The primary subgroup was Tc-99m, TI-201 and dual, and the secondary subgroup was pharmacologic agent, exercise and both, or Asian and Caucasian. Due to non-invasiveness of ultrasound, this analysis was designed to investigate if the SEN and SPE of SPECT were high enough to be used widely in CAD diagnosis with isotope and stress inducer being the optimal choices. Additionally, this meta-analysis tried to assert in whether the performance of SPECT had a significant difference among various ethnicities.

According to partial AUC of SROC curve for TI-201, Tc-99m, and combination shown in **Figure 2**, TI-201 seems to be the optimal radio-tracer with partial AUC of 0.86, larger than overall AUC 0.82. Tc-99m was slightly behind TI-201, of which the partial AUC was 0.85. Although combination had best performance in SEN, this constituted the lowest SPE and partial AUC 0.80 still indicated its lower performance. TI-201 showed no significant difference in various ethnic groups, however, the partial AUC of Caucasian was 0.80 higher than 0.72 of Asian with reference to Tc-99m.

Radiotracers were crucial to SPECT performance, since it determined the SEN and SPE of SPECT directly, and currently TI-201 and Tc-99m, including Tc-99m sestamibi and Tc-99m tetrofosmin, were quite common in the studies.

Tl-201, a radioactive isotope with 81 protons and 201 neutrons, was widely used as a radio-tracer in the field of medicine. The half-life of Tl-201 is 74 hours, gamma decay with 80 keV emission energy. As for Tc-99m, a meta stable nuclear isomer of Tc-99, its half-life was around 6 hours, and it decays and emits 140 keV gamma rays. Both isotopes can be extracted by normally functional myocardial cells selectively. The first-pass extraction of Tl-201 can reach nearly 85%, while the first-pass extraction of Tc-99m was less. Besides this, due to the lack of redistribution, two injections at stress and rest separately were required when Tc-99m was served as radiotracer [160]. To avoid the interference on second test of standard one-day single-isotope SPECT and shorten diagnostic time [56], some studies used dual-isotope, which meant Tl-201 for rest and Tc-99m for stress. However, this protocol did not work successfully. Probably due to immature dual-isotope SPECT technique and equipment, it had the highest SEN with lowest SPE and wide confidential interval leading to its smallest partial AUC.

As for stress inducing method, exercise, pharmacologic agent and combination were frequently used to raise heartbeat and blood pressure to an adequate level. In consideration of side-effect and cost-efficiency, exercise was a convenient choice. But in some cases, as patients had certain concomitants, like high-risk unstable angina, uncontrolled hypertension. In conditions such as these where exercise is inadvisable, pharmacologic agents must be used. Common medicines used as stress inducer include adenosine, dipyridamole and dobutamine. Different drugs have different mechanisms, so medicine choice depends on patients' condition. In general, a combination of low-level exercise with drug infusion can decrease the drug side-effects and improve image quality [160]. Therefore, using the same radiotracer, dual stress inducers combined had better performance.

The diversities among isotope extraction, absorption of background tissues and organs, and clearance of organism of different ethnicities can all influence the performance of SPECT.

This meta-analysis compared SPECT with gold standard CA and indicated the SEN and SPE of three radiotracers and stress inducers applied

to SPECT, and of two ethnicities in diagnosing CAD. However there were still some limitations: (i) to guarantee the quantity of selected studies, all the studies which met the criteria were included, so some data might have seen restriction from any accidental error, such as the influence of cell extraction generated by myocardial disease, and  $\gamma$  ray decay caused by excess fat or breast tissue, both of these factors can lead to misdiagnosis and increase false positive rate; (ii) the sample size of selected studies were varied. The smallest studies had just 16 subjects [150], while the largest one involved 785 patients [28]. So the small sample studies was easily diluted, which meant the large-size studies were dominant; (iii) although two-class subgroup analyses were performed, heterogeneity among each group was still extant, which might be resultant from the technique of SPECT, such as ECG-gated SPECT and attenuation correction SPECT, or method of SPECT image interpretation, as visual, semi-quantitative and quantitative.

## Conclusions

Based on the present studies, Tl-201 seemed the optimal SPECT radiotracer aimed at myocardial perfusion scintigraphy with highest SPE, and combined low-level exercise with pharmacologic agent was the preferable choice of stress inducer. However, the application of stress inducer of SPECT in practical clinical diagnosis needs to adequately consider the patient's condition. Additionally, extant studies were not enough to state the explicit connection between ethnicity and SPECT performance. Although SPECT was performed well in both SEN and SPE and can be widely used in CAD diagnosis, whether it can take the place of CA requires further research.

## Disclosure of conflict of interest

None.

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**Table S1.** Main characteristics of included studies

Author	Year	Country	Ethnicity	Imaging Agent	Stress	Sample Size	Outcome				Sensitivity	Specificity
							TP	FP	FN	TN		
Abramson [17]	2000	Canada	Caucasian	Tc	Or	19	9	8	0	2	100.0%	20.0%
Acampa [18]	1998	Italy	Caucasian	Tc	Exercise	32	24	1	1	6	96.0%	85.7%
Aggeli [19]	2007	Greece	Caucasian	TI	Drug	48	24	1	6	17	80.0%	94.4%
Aksut [20]	1995	USA	Caucasian	TI	Drug	443	358	7	40	38	89.9%	84.4%
Amanullah [21]	1993	Sweden	Caucasian	Tc	Drug	40	32	0	2	6	94.1%	100.0%
Amanullah [22]	1997	USA	Caucasian	Dual	Drug	222	159	14	12	37	93.0%	72.5%
Astarita [23]	2001	Italy	Caucasian	TI	Exercise	53	23	16	0	14	100.0%	46.7%
Avakian [24]	2001	Brazil	Caucasian	TI	Drug	110	13	12	18	67	41.9%	84.8%
Banzo [25]	2003	Spain	Caucasian	Tc	Dual	99	47	26	4	22	92.2%	45.8%
Banzo [25]	2003	Spain	Caucasian	Tc	Dual	99	39	14	12	34	76.5%	70.8%
Becker [26]	2015	Germany	Caucasian	Tc	Drug	424	127	59	30	208	80.9%	77.9%
Benoit [27]	1996	Belgium	Caucasian	Tc	Exercise	72	55	1	8	8	87.3%	88.9%
Berman [28]	2006	USA	Caucasian	Tc	Exercise	365	251	40	24	50	91.3%	55.6%
Berman [28]	2006	USA	Caucasian	Tc	Drug	420	252	77	28	63	90.0%	45.0%
Berman [28]	2006	USA	Caucasian	Tc	Dual	785	503	117	52	113	90.6%	49.1%
Berman [28]	2006	USA	Caucasian	Tc	Dual	290	186	9	39	56	82.7%	86.2%
Beygui [29]	2000	France	Caucasian	TI	Exercise	179	44	25	26	84	62.9%	77.1%
Blankstein [30]	2009	USA	Caucasian	Tc	Or	34	23	3	2	6	92.0%	66.7%
Bokhari [31]	2008	USA	Caucasian	Dual	Exercise	218	116	16	27	59	81.1%	78.7%
Boomsma [32]	1998	Netherlands	Caucasian	Tc	Exercise	65	34	10	2	19	94.4%	65.5%
Borges-Neto [33]	1988	USA	Caucasian	Tc	Drug	100	77	5	7	11	91.7%	68.8%
Chammas [34]	2002	Lebanon	Asian	Tc	Exercise	58	30	6	4	18	88.2%	75.0%
Ciavolella [36]	1993	Italy	Caucasian	Tc	Exercise	197	178	3	4	12	97.8%	80.0%
Cramer [37]	1996	Netherlands	Caucasian	Tc	Drug	35	23	1	6	5	79.3%	83.3%
Daou [38]	2002	France	Caucasian	TI	Exercise	338	167	17	98	56	63.0%	76.7%
DiBello [39]	1996	Italy	Caucasian	Tc	Drug	45	33	1	5	6	86.8%	85.7%
Dondi [40]	2004	Italy	Caucasian	Tc	Dual	130	104	6	4	16	96.3%	72.7%
Dondi [40]	2004	Italy	Caucasian	Tc	Dual	130	100	2	8	20	92.6%	90.9%
Elhendy [43]	1998	Netherlands	Caucasian	Tc	Dual	70	29	7	16	18	64.4%	72.0%
Elhendy [44]	2000	Netherlands	Caucasian	Tc	Drug	50	27	9	3	11	90.0%	55.0%
Elhendy [45]	2001	Netherlands	Caucasian	Tc	Exercise	332	183	25	57	67	76.3%	72.8%
Elhendy [42]	2006	Netherlands	Caucasian	Tc	Drug	88	44	7	9	28	83.0%	80.0%
Elhendy [41]	2006	Netherlands	Caucasian	Tc	Or	92	39	7	12	34	76.5%	82.9%
Emmett [46]	2002	Canada	Caucasian	Tc	Exercise	100	62	11	8	19	88.6%	63.3%
Esteves [47]	2014	USA	Caucasian	Tc	Or	55	36	7	3	9	92.3%	56.3%
Esteves [47]	2014	USA	Caucasian	Tc	Or	55	31	9	8	7	79.5%	43.8%
Esteves [47]	2014	USA	Caucasian	Tc	Or	55	33	4	6	12	84.6%	75.0%
Fagret [48]	1995	France	Caucasian	Tc	Drug	25	14	0	5	6	73.7%	100.0%
Ficaro [49]	1996	USA	Caucasian	Dual	Dual	60	38	6	11	5	77.6%	45.5%
Ficaro [49]	1996	USA	Caucasian	Dual	Dual	60	41	6	8	5	83.7%	45.5%
Forster [50]	2009	Germany	Caucasian	Tc	Or	72	26	10	7	29	78.8%	74.4%
Fragasso [51]	1999	Italy	Caucasian	Tc	Exercise	101	56	28	1	16	98.2%	36.4%
Gallowitsch [52]	1998	Austria	Caucasian	TI	Exercise	68	30	10	6	22	83.3%	68.8%
Gallowitsch [52]	1998	Austria	Caucasian	TI	Exercise	68	35	4	1	28	97.2%	87.5%
Gallowitsch [52]	1998	Austria	Caucasian	TI	Drug	39	12	1	5	21	70.6%	95.5%
Gallowitsch [52]	1998	Austria	Caucasian	TI	Drug	39	15	1	2	21	88.2%	95.5%
Gallowitsch [52]	1998	Austria	Caucasian	TI	Or	107	42	11	11	43	79.2%	79.6%
Gallowitsch [52]	1998	Austria	Caucasian	TI	Or	107	50	5	3	49	94.3%	90.7%
Gentile [53]	2001	Italy	Caucasian	TI	Dual	132	101	11	7	13	93.5%	54.2%
George [54]	2014	USA	Caucasian	Tc	Or	381	143	50	86	102	62.4%	67.1%
Gonzalez [55]	2005	Chile	Caucasian	TI	Dual	145	102	12	15	16	87.2%	57.1%
Grossman [56]	2004	USA	Caucasian	Tc	Exercise	74	38	25	1	10	97.4%	28.6%
Grossman [56]	2004	USA	Caucasian	Tc	Exercise	74	35	15	4	20	89.7%	57.1%
Groutars [57]	2003	Netherlands	Caucasian	Dual	Dual	123	102	6	6	9	94.4%	60.0%
Groutars [57]	2003	Netherlands	Caucasian	Dual	Dual	123	93	11	3	16	96.9%	59.3%

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Grover-Mckay [58]	1994	USA	Caucasian	TI	Drug	18	10	0	1	7	90.9%	100.0%
Hacker [59]	2005	Germany	Caucasian	Tc	Drug	50	12	9	5	24	70.6%	72.7%
Hambye [60]	2004	Belgium	Caucasian	Tc	Dual	100	60	3	26	11	69.8%	78.6%
Hambye [60]	2004	Belgium	Caucasian	Tc	Dual	100	63	3	23	11	73.3%	78.6%
Hannoush [61]	2003	Lebanon	Asian	Tc	Dual	51	40	4	1	6	97.6%	60.0%
He [62]	1997	USA	Caucasian	Tc	Drug	59	41	5	7	6	85.4%	54.5%
He [63]	2002	China	Asian	Tc	Drug	51	33	3	1	14	97.1%	82.4%
He [64]	2003	China	Asian	Tc	Exercise	26	18	0	4	4	81.8%	100.0%
Hecht [65]	1993	USA	Caucasian	TI	Exercise	71	47	7	4	13	92.2%	65.0%
Heiba [66]	1997	Kuwait	Asian	Tc	Exercise	34	28	1	2	3	93.3%	75.0%
Hida [67]	2009	Japan	Asian	Tc	Drug	119	32	7	30	50	51.6%	87.7%
Ho [68]	1995	Taiwan	Asian	TI	Drug	54	42	3	1	8	97.7%	72.7%
Ho [69]	1997	Taiwan	Asian	TI	Exercise	51	29	3	9	10	76.3%	76.9%
Huang [70]	1997	Taiwan	Asian	TI	Drug	93	60	5	7	21	89.6%	80.8%
Huang [71]	1998	Taiwan	Asian	TI	Drug	110	53	8	12	37	81.5%	82.2%
Hung [72]	2006	Taiwan	Asian	TI	Drug	126	75	16	6	29	92.6%	64.4%
Iftikhar [73]	1996	USA	Caucasian	Tc	Drug	38	22	1	6	9	78.6%	90.0%
Isaaz [74]	2008	France	Caucasian	Dual	Exercise	149	22	40	24	63	47.8%	61.2%
Iskandrian [75]	1991	USA	Caucasian	TI	Drug	148	121	2	11	14	91.7%	87.5%
Jeetley [76]	2006	UK	Caucasian	Tc	Drug	123	79	13	17	14	82.3%	51.9%
Johansen [77]	2005	Denmark	Caucasian	Dual	Dual	357	94	48	32	183	74.6%	79.2%
Kajinami [78]	1995	Japan	Asian	TI	Exercise	251	110	48	23	70	82.7%	59.3%
Katayama [79]	2008	Japan	Asian	TI	Dual	46	17	7	5	17	77.3%	70.8%
Khattar [80]	1997	UK	Caucasian	Tc	durg	39	30	2	0	7	100.0%	77.8%
Khattar [81]	1998	UK	Caucasian	Tc	Drug	100	41	11	19	29	68.3%	72.5%
Kisacik [82]	1996	Turkey	Caucasian	Tc	Exercise	69	45	8	2	14	95.7%	63.6%
Korosoglou [83]	2006	Germany	Caucasian	Tc	-	89	48	13	14	14	77.4%	51.9%
Kupari [84]	1992	Finland	Caucasian	TI	Or	44	21	10	0	13	100.0%	56.5%
Lancellotti [85]	2001	Belgium	Caucasian	Tc	Drug	75	48	1	21	5	69.6%	83.3%
Lima [86]	2002	USA	Caucasian	Tc	Dual	255	187	12	25	31	88.2%	72.1%
Lin [87]	2006	Taiwan	Asian	Dual	Drug	40	19	3	6	12	76.0%	80.0%
Lipiec [88]	2008	Poland	Caucasian	Tc	Drug	103	79	5	10	9	88.8%	64.3%
Liu [89]	1998	Taiwan	Asian	TI	Exercise	90	50	10	6	24	89.3%	70.6%
Mahmorian [90]	1990	USA	Caucasian	TI	Exercise	296	192	10	29	65	86.9%	86.7%
Mak [91]	1995	Singapore	Asian	Tc	Exercise	139	110	6	11	12	90.9%	66.7%
Marwick [92]	1992	USA	Caucasian	TI	Drug	50	35	0	11	4	76.1%	100.0%
Marwick [93]	1993	Belgium	Caucasian	TI	Drug	217	108	25	34	50	76.1%	66.7%
Masood [94]	2005	USA	Caucasian	Tc	Dual	118	80	14	6	18	93.0%	56.3%
Masood [94]	2005	USA	Caucasian	Tc	Dual	118	81	13	5	19	94.2%	59.4%
Masood [94]	2005	USA	Caucasian	Tc	Dual	118	60	11	26	21	69.8%	65.6%
Masood [94]	2005	USA	Caucasian	Tc	Dual	118	67	4	19	28	77.9%	87.5%
Masood [94]	2005	USA	Caucasian	Tc	Dual	118	58	7	28	25	67.4%	78.1%
Masood [94]	2005	USA	Caucasian	Tc	Dual	118	60	7	26	25	69.8%	78.1%
Matsymoto [95]	2006	Japan	Asian	Tc	Dual	56	22	1	4	29	84.6%	96.7%
McClellan [96]	1996	USA	Caucasian	TI	Exercise	303	193	12	82	16	70.2%	57.1%
Melikian [97]	2010	Belgium	Caucasian	Tc	Drug	67	31	10	16	10	66.0%	50.0%
Michaelides [98]	1999	Greece	Caucasian	TI	Exercise	245	196	6	15	28	92.9%	82.4%
Miller [13]	1997	USA	Caucasian	Tc	Drug	243	185	29	18	11	91.1%	27.5%
Mohiuddin [99]	1996	USA	Caucasian	TI	Drug	202	144	6	16	36	90.0%	85.7%
Montz [100]	1996	Spain	Caucasian	Tc	Exercise	142	113	13	8	8	93.4%	38.1%
Mouden [101]	2014	Netherlands	Caucasian	Tc	Drug	100	12	19	8	61	60.0%	76.3%
Nallamothu [102]	1995	USA	Caucasian	TI	Exercise	321	216	17	51	37	80.9%	68.5%
Nguyen [103]	1990	USA	Caucasian	TI	Drug	60	49	0	4	7	92.5%	100.0%
Nishimura [104]	1991	USA	Caucasian	TI	Drug	101	61	3	9	28	87.1%	90.3%
Nishiyama [105]	2014	Japan	Caucasian	Tc	Drug	76	47	11	7	11	87.0%	50.0%
Ogilby [106]	1992	USA	Caucasian	TI	Drug	45	31	0	2	12	93.9%	100.0%
Ogilby [12]	1998	USA	Caucasian	Tc	Drug	26	18	0	2	6	90.0%	100.0%
Palmas [107]	1995	USA	Caucasian	Tc	Exercise	70	60	1	6	3	90.9%	75.0%

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Patil [108]	2014	USA	Caucasian	Tc	Or	64	34	4	14	12	70.8%	75.0%
Patsilnakos [109]	2004	Greece	Caucasian	TI	Drug	75	31	11	4	29	88.6%	72.5%
Peltier [110]	2004	Belgium	Caucasian	Tc	Drug	35	18	2	4	11	81.8%	84.6%
Previtali [111]	1999	Italy	Caucasian	TI	Exercise	43	29	2	9	3	76.3%	60.0%
Psirropoulos [112]	2002	Greece	Caucasian	TI	Exercise	301	33	136	26	106	55.9%	43.8%
Rieber [113]	2004	Germany	Caucasian	Tc	Drug	43	9	4	4	26	69.2%	86.7%
Roach [114]	1996	Australia	Caucasian	TI	Exercise	69	38	3	15	13	71.7%	81.3%
Rollan [115]	2002	Spain	Caucasian	Tc	Drug	54	23	12	3	16	88.5%	57.1%
Rosenkranz [116]	2001	Germany	Caucasian	Tc	Drug	40	14	8	1	17	93.3%	68.0%
Rubello [117]	1995	Italy	Caucasian	Tc	Exercise	120	98	5	9	8	91.6%	61.5%
Rubello [117]	1995	Italy	Caucasian	Tc	Exercise	120	100	5	7	8	93.5%	61.5%
Sahiner [118]	2013	Turkey	Caucasian	TI	Drug	58	8	5	5	40	61.5%	88.9%
Sakuma [119]	2005	Japan	Asian	TI	Dual	40	17	7	4	12	81.0%	63.2%
San Roman [120]	1998	Spain	Caucasian	Tc	Drug	92	54	9	8	21	87.1%	70.0%
Santana-Boado [121]	1998	Spain	Caucasian	Tc	Dual	163	88	7	8	60	91.7%	89.6%
Santoro [122]	1998	Italy	Caucasian	Tc	Drug	60	32	3	1	24	97.0%	88.9%
Santoro [122]	1998	Italy	Caucasian	Tc	Drug	60	30	5	3	22	90.9%	81.5%
Schaap [123]	2013	Netherlands	Caucasian	Tc	Or	98	52	9	4	33	92.9%	78.6%
Schepis [124]	2007	Switzerland	Caucasian	Tc	Drug	77	32	3	10	32	76.2%	91.4%
Schillaci [125]	1997	Italy	Caucasian	Tc	Drug	40	21	5	1	13	95.5%	72.2%
Senior [126]	1994	UK	Caucasian	Tc	Drug	61	42	5	2	12	95.5%	70.6%
Senior [127]	2004	USA	Caucasian	Tc	Drug	55	21	1	22	11	48.8%	91.7%
Senior [128]	2013	UK	Caucasian	Tc	Drug	516	79	69	82	286	49.1%	80.6%
Shelley [129]	2003	India	Asian	Tc	Drug	108	64	8	0	36	100.0%	81.8%
Shin [130]	2009	USA	Caucasian	Dual	Drug	246	140	34	19	53	88.1%	60.9%
Shirai [131]	2002	Japan	Asian	TI	Exercise	603	106	13	131	353	44.7%	96.4%
Slavich [132]	1996	Italy	Caucasian	Tc	Drug	46	18	4	4	20	81.8%	83.3%
Slomaka [133]	2006	USA	Caucasian	Tc	Dual	174	115	7	22	30	83.9%	81.1%
Slomaka [133]	2006	USA	Caucasian	Tc	Dual	174	117	10	20	27	85.4%	73.0%
Smanio [134]	2007	Brazil	Caucasian	Tc	Drug	104	32	4	2	66	94.1%	94.3%
Smart [135]	2000	USA	Caucasian	Tc	Drug	183	95	17	24	47	79.8%	73.4%
Soman [136]	1997	UK	Caucasian	Tc	Drug	27	21	2	0	4	100.0%	66.7%
Soman [136]	1997	UK	Caucasian	Tc	Drug	27	19	2	2	4	90.5%	66.7%
Srimahachota [137]	2001	Thailand	Asian	Tc	Exercise	46	23	5	4	14	85.2%	73.7%
Stewart [138]	1991	USA	Caucasian	TI	Or	81	50	10	10	11	83.3%	52.4%
Suzuki [139]	2008	USA	Caucasian	Dual	Dual	90	58	5	5	22	92.1%	81.5%
Tadehara [140]	2008	Japan	Asian	Tc	Drug	101	50	14	4	33	92.6%	70.2%
Taillefer [141]	1997	Canada	Caucasian	TI	Exercise	48	24	8	8	8	75.0%	50.0%
Taillefer [141]	1997	Canada	Caucasian	Tc	Exercise	48	23	3	9	13	71.9%	81.3%
Taillefer [141]	1997	Canada	Caucasian	TI	Drug	37	24	0	8	5	75.0%	100.0%
Taillefer [141]	1997	Canada	Caucasian	Tc	Drug	37	23	0	9	5	71.9%	100.0%
Taillefer [141]	1997	Canada	Caucasian	TI	Exercise	48	22	10	6	10	78.6%	50.0%
Taillefer [141]	1997	Canada	Caucasian	Tc	Exercise	48	21	3	7	17	75.0%	85.0%
Taillefer [141]	1997	Canada	Caucasian	TI	Exercise	37	21	4	2	10	91.3%	71.4%
Taillefer [141]	1997	Canada	Caucasian	Tc	Drug	37	20	3	3	11	87.0%	78.6%
Taillefer [141]	1997	Canada	Caucasian	TI	Drug	85	48	8	16	13	75.0%	61.9%
Taillefer [141]	1997	Canada	Caucasian	Tc	Or	85	46	3	18	18	71.9%	85.7%
Taillefer [141]	1997	Canada	Caucasian	TI	Or	85	43	14	8	20	84.3%	58.8%
Taillefer [141]	1997	Canada	Caucasian	Tc	Or	85	41	6	10	28	80.4%	82.4%
Taillefer [142]	1999	USA	Caucasian	Tc	Or	53	28	2	10	13	73.7%	86.7%
Takeishi [143]	1998	Japan	Asian	Tc	Drug	65	39	4	5	17	88.6%	81.0%
Takeuchi [144]	1993	Japan	Asian	TI	Or	120	66	7	8	39	89.2%	84.8%
Takeuchi [145]	1995	Japan	Asian	TI	Or	52	17	2	6	27	73.9%	93.1%
Takeuchi [146]	1996	Japan	Asian	TI	Or	61	14	13	4	30	77.8%	69.8%
Thompson [147]	2005	USA	Caucasian	Tc	Dual	116	78	14	10	14	88.6%	50.0%
Thompson [147]	2005	USA	Caucasian	Tc	Dual	116	76	6	12	22	86.4%	78.6%
Tsai [148]	2002	Taiwan	Asian	TI	Exercise	86	60	11	3	12	95.2%	52.2%
Wang [149]	1995	USA	Caucasian	TI	Or	75	55	2	8	10	87.3%	83.3%

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Warner [150]	1993	China	Asian	Tl	Drug	16	14	0	1	1	93.3%	100.0%
Watanabe [151]	1997	Japan	Asian	Tl	Drug	70	34	8	7	21	82.9%	72.4%
Watanabe [151]	1997	Japan	Asian	Tl	Drug	70	40	3	6	21	87.0%	87.5%
Watanabe [151]	1997	Japan	Asian	Tl	Drug	140	74	11	13	42	85.1%	79.2%
Wolak [152]	2008	USA	Caucasian	Tc	Dual	114	55	12	14	33	79.7%	73.3%
Wolak [153]	2008	USA	Caucasian	Tc	Dual	114	56	12	13	33	81.2%	73.3%
Wolak [153]	2008	USA	Caucasian	Tc	Drug	188	124	13	19	32	86.7%	71.1%
Wu [154]	2009	Taiwan	Asian	Tc	Drug	218	123	33	7	55	94.6%	62.5%
Yao [155]	1997	China	Asian	Tc	Exercise	51	34	1	2	14	94.4%	93.3%
Yao [156]	2000	China	Asian	Tc	Exercise	64	42	1	3	18	93.3%	94.7%
Yao [157]	2004	China	Asian	Tc	Exercise	73	28	3	7	35	80.0%	92.1%
Yeih [158]	2007	Taiwan	Asian	Tl	Drug	51	20	3	8	20	71.4%	87.0%
Yoon [159]	2009	USA	Caucasian	Tc	Drug	344	191	83	28	42	87.2%	33.6%

TP: true positive, FP: false positive, FN: false negative, TN: true negative; Tc: technetium-99m, Tl: thallium-201, Dual: technetium-99m + thallium-201. There are 145 articles with 184 studies included in this meta-analysis.

**Table S2.** QUADAS-2

QUADAS-2 studid	Risk of Bias				Applicability			Qscore
	(1) subjbias	(2) testbias	(3) refbias	(4) diagbias	(5) subjapp	(6) testapp	(7) refapp	
Abramson, 2000	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Acampa, 1998	Yes	Unclear	Yes	Unclear	Yes	Yes	Yes	5
Aggeli, 2007	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Aksut, 1995	Yes	Yes	Yes	Yes	No	Yes	Yes	6
Amanullah, 1993	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	5
Amanullah, 1997	Yes	No	Yes	No	Yes	Yes	Yes	5
Astarita, 2001	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Avakian, 2001	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	6
Banzo, 2003	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Banzo, 2003	Yes	No	Yes	Unclear	Yes	Yes	Yes	5
Becker, 2015	Unclear	Yes	Yes	Yes	Yes	Unclear	Yes	5
Benoit, 1996	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	6
Berman, 2006	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	6
Berman, 2006	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Berman, 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Berman, 2006	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	5
Beygui, 2000	Yes	Yes	Yes	Yes	Yes	No	Yes	6
Blankstein, 2009	unclear	Yes	Yes	No	Yes	Yes	Yes	5
Bokhari, 2008	Yes	Unclear	Yes	Yes	No	Yes	No	4
Boomsma, 1998	Yes	Yes	Yes	Unclear	Yes	Yes	Unclear	5
Borges-Neto, 1988	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Chammas, 2002	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	6
Ciavolella, 1993	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	5
Cramer, 1996	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	5
Daou, 2002	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
DiBello, 1996	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Dondi, 2004	Unclear	Yes	Unclear	Yes	Unclear	Yes	Yes	4
Dondi, 2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Elhendy, 1998	Yes	Unclear	Yes	Unclear	Yes	Unclear	Yes	4
Elhendy, 2000	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Elhendy, 2001	Yes	Yes	Yes	Yes	No	No	Unclear	4
Elhendy, 2006	Unclear	Unclear	Yes	Yes	Yes	Yes	Unclear	4

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Elhendy, 2006	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Emmett, 2002	Unclear	Yes	Unclear	Yes	Yes	Yes	Yes	5
Esteves, 2014	Yes	No	Yes	Yes	Yes	Yes	Unclear	5
Esteves, 2014	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Esteves, 2014	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	6
Fagret, 1995	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	6
Ficaro, 1996	Yes	Yes	Yes	No	Yes	Yes	Yes	6
Ficaro, 1996	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	5
Forster, 2009	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Fragasso, 1999	Yes	Yes	Unclear	Yes	Unclear	Yes	Yes	5
Gallowitsch, 1998	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	5
Gallowitsch, 1998	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Gallowitsch, 1998	Yes	Yes	Yes	Yes	Unclear	Unclear	Yes	5
Gallowitsch, 1998	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Gallowitsch, 1998	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Gallowitsch, 1998	Yes	Yes	No	No	No	Yes	Yes	4
Gentile, 2001	Yes	Yes	No	Unclear	Yes	Unclear	Yes	4
George, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Gonzalez, 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Grossman, 2004	unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Grossman, 2004	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Groutars, 2003	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Groutars, 2003	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	6
Grover-Mckay, 1994	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Hacker, 2005	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Hambye, 2004	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	5
Hambye, 2004	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Hannoush, 2003	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	6
He, 1997	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
He, 2002	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
He, 2003	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Hecht, 1993	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Heiba, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Hida, 2009	Yes	Yes	Yes	No	Yes	Yes	Yes	6
Ho, 1995	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Ho, 1997	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Huang, 1997	Yes	Yes	Yes	Yes	Yes	No	Yes	6
Huang, 1998	Yes	Yes	Yes	No	Yes	Yes	Yes	6
Hung, 2006	Unclear	Unclear	Yes	Yes	Unclear	Yes	Yes	4
Iftikhar, 1996	Yes	Unclear	Yes	Yes	Yes	Unclear	Unclear	4
Isaaz, 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Iskandrian, 1991	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	6
Jeetley, 2006	Unclear	Yes	Yes	No	Yes	Unclear	Yes	4
Johansen, 2005	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Kajinami, 1995	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Katayama, 2008	Yes	Yes	Unclear	Yes	No	Yes	Yes	5
Khattar, 1997	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	6
Khattar, 1998	Yes	Yes	No	Yes	Yes	Yes	Yes	6
Kisacik, 1996	Yes	No	Yes	Yes	Unclear	Yes	Yes	5
Korosoglou, 2006	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7

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Kupari, 1992	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Lancellotti, 2001	Yes	Yes	Unclear	Unclear	Yes	Yes	Unclear	4
Lima, 2002	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Lin, 2006	Yes	No	Yes	Unclear	No	Yes	Yes	4
Lipiec, 2008	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Liu, 1998	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	6
Mahmorian, 1990	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Mak, 1995	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Marwick, 1992	Yes	Yes	Yes	Yes	Yes	No	Unclear	5
Marwick, 1993	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Masood, 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Masood, 2005	Unclear	Yes	Yes	Yes	Yes	Yes	Unclear	5
Masood, 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Masood, 2005	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Masood, 2005	Unclear	Yes	No	Yes	Yes	Yes	Yes	5
Masood, 2005	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Matsymoto, 2006	Yes	Yes	Yes	Yes	Yes	No	Yes	6
McClellan, 1996	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	6
Melikian, 2010	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Michaelides, 1999	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Miller, 1997	Yes	Yes	Yes	Yes	Yes	No	Yes	6
Mohiuddin, 1996	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Montz, 1996	Yes	No	Yes	Yes	Unclear	Yes	Yes	5
Mouden, 2014	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Nallamotheu, 1995	Yes	Yes	Yes	Yes	Yes	No	Yes	6
Nguyen, 1990	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Nishimura, 1991	Unclear	No	Yes	Yes	Yes	Yes	Yes	5
Nishiyama, 2014	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	6
Ogilby, 1992	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	6
Ogilby, 1998	Yes	Yes	No	Yes	Yes	Yes	Yes	6
Palmas, 1995	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	6
Patil, 2014	Yes	Yes	Yes	Yes	Unclear	Yes	Yes	6
Patsilinafos, 2004	Unclear	Yes	Yes	Yes	No	Yes	Yes	5
Peltier, 2004	Yes	Yes	Unclear	Yes	Yes	Yes	Unclear	5
Previtali, 1999	unclear	Yes	Yes	Yes	No	Yes	Yes	5
Psirropoulos, 2002	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Rieber, 2004	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes	5
Roach, 1996	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Rollan, 2002	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	6
Rosenkranz, 2001	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Rubello, 1995	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Rubello, 1995	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Sahiner, 2013	unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Sakuma, 2005	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	6
San Roman, 1998	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Santana-Boado, 1998	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Santoro, 1998	Yes	No	Yes	Unclear	Yes	Unclear	Yes	4
Santoro, 1998	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Schaap, 2013	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	6
Schepis, 2007	Yes	Yes	Yes	Yes	No	Yes	Yes	6
Schillaci, 1997	Unclear	Yes	Yes	Yes	No	Yes	Yes	5

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Senior, 1994	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Senior, 2004	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Senior, 2013	No	Yes	Yes	Yes	Yes	Yes	Yes	6
Shelley, 2003	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Shin, 2009	Yes	Yes	Yes	Unclear	Unclear	Yes	Yes	5
Shirai, 2002	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Slavich, 1996	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Slomaka, 2006	Yes	Yes	Yes	Yes	No	Yes	Yes	6
Slomaka, 2006	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Smanio, 2007	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	6
Smart, 2000	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	5
Soman, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Soman, 1997	Yes	Yes	Yes	Unclear	Yes	Yes	Yes	6
Srimahachota, 2001	Yes	Unclear	Yes	Yes	No	Unclear	Yes	4
Stewart, 1991	Yes	Yes	Yes	Yes	unclear	Yes	Yes	6
Suzuki, 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Tadehara, 2008	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Taillefer, 1997	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Taillefer, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Taillefer, 1997	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	5
Taillefer, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Taillefer, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Taillefer, 1997	No	No	Yes	Yes	Yes	Yes	Yes	5
Taillefer, 1997	Yes	No	Yes	Yes	Yes	Yes	Yes	6
Taillefer, 1997	Yes	No	Yes	Yes	No	Yes	Yes	5
Taillefer, 1997	Yes	Yes	Yes	No	Yes	Yes	Yes	6
Taillefer, 1997	No	Unclear	Yes	Yes	Yes	Yes	Yes	5
Taillefer, 1997	Yes	Yes	No	Yes	Yes	No	Yes	5
Taillefer, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Taillefer, 1999	Yes	Yes	Yes	Yes	No	Yes	Yes	6
Takeishi, 1998	Yes	Yes	Yes	No	Yes	Yes	No	5
Takeuchi, 1993	Unclear	Yes	Yes	Yes	Yes	No	Yes	5
Takeuchi, 1995	Yes	Yes	Unclear	No	Yes	Yes	Unclear	4
Takeuchi, 1996	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Thompsons, 2005	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	6
Thompsons, 2005	No	Unclear	No	Yes	Unclear	Yes	Yes	3
Tsai, 2002	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Wang, 1995	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Warner, 1993	Yes	No	Yes	No	Yes	Yes	Yes	5
Watanabe, 1997	Yes	Yes	Yes	Yes	No	Yes	No	5
Watanabe, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Watanabe, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Wolak, 2008	Yes	Yes	Yes	Yes	Yes	Yes	Yes	7
Wolak, 2008	Yes	No	Yes	Yes	No	Yes	Yes	5
Wolak, 2008	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Wu, 2009	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Yao, 1997	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	6
Yao, 2000	Yes	Yes	Yes	Yes	No	Yes	Yes	6
Yao, 2004	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	6
Yeih, 2007	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	6
Yoon, 2009	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	6