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Diagnostic value of cadmium-zinc-telluride myocardial perfusion imaging versus coronary angiography in coronary artery disease

A PRISMA-compliant meta-analysis

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Abstract

Background: Rapid progress has been made in research of cadmium-zinc-telluride (CZT) technology in the last few years, which might serve as a new method to diagnose coronary artery disease. However, compared with coronary angiography, the diagnostic value of CZT is still controversial. We aimed to evaluate diagnosis value of coronary angiography versus CZT in coronary artery disease.

Methods: We searched the database for eligible researches associated with CZT- myocardial perfusion imaging (MPI) and invasive coronary angiography, extracted the relevant data, and rigorously screened it according to the inclusion and exclusion criteria. The accuracy indicators included sensitivity, specificity, accuracy, positive and negative likelihood ratios.

Results: According to the inclusion and exclusion criteria, we finally found 20 studies containing 2350 patients in this search. Pooled results showed that sensitivity of CZT-MPI was 0.84% and 95% confidence interval (95% CI): 0.78 to 0.89, specificity was 0.72, 95% CI (0.62–0.76), the specificity was lower apparently. The positive likelihood ratio was 3.0, 95% CI (2.4–3.8), the negative likelihood ratio was 0.22, 95% CI (0.16–0.31), diagnostic odds ratio was 14, 95% CI (7.84–17.42).

Conclusion: This meta-analysis showed that CZT-MPI had satisfactory sensitivity and specificity for diagnosing coronary artery disease. Larger studies are required for further evaluation.

Abbreviations: BMI = body mass index, CAD = coronary artery disease, CAG= coronary angiography, CI = confidence interval, CZT = cadmium-zinc-telluride, MPI = myocardial perfusion imaging, PCI = percutaneous coronary intervention, SPECT = single-photon emission computed tomography, Tc = technetium.

Keywords: angiography, CZT-MPI, meta-analysis

1. Introduction

As we all know that the technological innovation has provided a great help for doctors to recognize and diagnose diseases. In 1939, Swedish physiologist Gordon Liljestrand first innovated nuclear cardiology technique, which promoted the progress of modern cardiology and created a noninvasive method for cardiovascular disease. [1] Nuclear myocardial perfusion imaging (MPI) can detect the underlying cardiovascular disease, such as stable ischemic heart disease, myocardial infraction, heart failure, and so on. However, because of blurred image and long examination time, the application of traditional single-photon emission computed tomography (SPECT) is still limited. [2] Scientists have paid attention to the emergence of cadmium-zinc-telluride (CZT) cameras with clinical application since 1996. They found that the scan time reduced and led to less radiation exposure to patients, meanwhile improving systemic sensitivity and spatial resolution. [3] Given to the restrictions on the clinical application of CZT-SPECT,[4] the gold standard for coronary artery disease is still coronary angiography (CAG).[5–7] On account of lack of enough evidence to recommend it for extensive clinical application in coronary artery disease, we conducted this meta-analysis containing all eligible studies to evaluate the diagnosis accuracy of CZT-SPECT compared with CAG. We hope our research will provide basic evidence and promote wide application.

Although there was a meta-analysis on the myocardial perfusion imaging with CZT technology in 2017, which contained 16 studies prior to 2017 and showed that CZT-MPI has satisfactory sensitivity, but specificity is suboptimal, they pointed that further research needs to be conducted to get a more believable result, several case-controls designed studies have investigated the diagnostic value of CZT-SPECT over the last 2 years. Given the conflicting evidence on this issue, we designed

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the updated meta-analysis of all available studies to arrive at a more reliable conclusion.

2. Methods

We performed our meta-analysis according to PRISMA proposal, which is recommended for reporting meta-analysis .[8] Our study was a meta-analysis based on published articles, and the included studies were published after ethics approval. Thus, ethical approval was not necessary in this study.

2.1. Search strategy

To identify eligible studies for this meta-analysis, 2 investigators (Y-QZ and LH) searched the PubMed, Embase, Web of Science, CNKI, and WanFang database in all languages which were published until March 2018, combined with a manual search of reference lists from identified studies. For the article search, the following combination of medical subject heading or suitable key words were used: coronary heart disease, coronary artery disease, ischemic heart disease or myocardial infraction and cadmium-zinc-telluride single-photon emission computed tomography or CZT-SPECT and coronary angiography or invasive coronary angiography. We have also searched individually to obtain more eligible studies and case-control studies which contained in the reference.

2.2. Selection and exclusion criteria

To present the selection for studies obtained in this meta-analysis, the inclusion criteria were pre-established: the objects of study experimented both CZT-SPECT and coronary angiography

Table 1

Characteristics of the studies included for meta-analysis.

Author	Year	Patients no.	Study type	Age	Male	DM	Obesity	HT	HCT	Smoking	BMI	Prior CAD	CAD type
Fiechter[14]	2011	66	RC	63	0.79	0.36	0.35	0.83	0.71	0.21	28	NA	Stable
Ben-Haim[15]	2010	5	PO	65	0.64	0.36	NA	0.6	0.56	NA	25	84%	Stable
Duvall[15]	2011	230	RC	64	0.69	0.4	NA	0.8	0.81	0.53	28	53%	Stable
Gimelli[16]	2012	137	PO	61	0.74	0.28	0.1	0.33	0.23	0.41	NA	NA	Stable
Ben-Haim[17]	2014	19	RC	62	49	0.39	1	0.67	0.57	0.42	36	35%	Stable
Chowdhury[18]	2014	165	RC	63	0.52	0.16	NA	NA	NA	NA	NA	33%	Stable
Duvall[19]	2014	115	RC	60	0.41	0.31	NA	0.66	0.56	0.5	29	16%	Acute chest pain
Goto[20]	2014	322	RC	69	0.73	0.41	NA	0.8	0.65	0.3	25	NA	Stable
Mouden[21]	2014	100	PO	66	0.5	0.31	NA	0.67	0.66	0.19	29	NA	Stable
Nishiyama[22]	2014	76	RC	69	0.63	0.42	NA	0.69	0.44	0.46	24	NA	Stable
Barone-Rochette[23]	2015	104	RC	65	0.7	0.38	0.32	0.57	0.56	0.41	27	51%	Stable
Liu[24]	2015	211	RC	59	NA	0.29	NA	0.71	0.59	0.36	NA	NA	Stable
Nakazato[25]	2015	67	RC	56	0.5	0.41	1	0.77	0.57	0.2	42	NA	Stable
Perrin[26]	2015	149	RC	62	0.8	0.31	0.3	0.63	0.58	NA	28	55%	Stable
Shiraishi[27]	2015	55	RC	75	0.25	0.4	NA	0.62	0.53	NA	24	NA	Stable
Sharir[28]	2016	271	RC	61	0.69	0.28	NA	0.52	0.6	NA	27	NA	Stable
Yu-Hua [29]	2017	102	RC	62	0.64	0.38	NA	0.76	0.47	0.25	26	0.73	Stable
Shimpei Ito[30]	2017	72	PO	72	0.82	0.39	0.08	0.76	0.56	0.65	24	0.31	Stable
Denis Agostini[31]	2017	30	PO	65	0.7	0.33	0.27	0.67	0.6	0.57	NA	0.5	Stable
Gilles Barone-Rochette[32]	2018	54	PO	65	0.41	0.16	NA	0.38	0.32	0.13	27	NA	Stable

Author	Index test	Comparator	CZT-SPECT
Fiecher[14]	Stress/rest Tc MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 3 mo	Discovery NM/CT 570c
Ben-Haim[15]	Stress Tc/rest Tl dual-isotope MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 3 mo	D-SPECT
Duvall[15]	Stress-only, rest/stress, orstress/rest Tl or Tc MPI	Qualitative angiographic analysis (70% cutoff)–ICA within 2 mo	Discovery NM 530c
Gimelli[16]	Stress/rest Tc MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 1 mo	Discovery NM 530c
Ben-Haim[17]	Stress/rest Tc MPI	Qualitative angiographic analysis (70% cutoff)–ICA within 3 mo	D-SPECT
Chowdhury[18]	Stress/rest Tc MPI	Qualitative angiographic analysis (70% cutoff)–ICA within 2 mo	Discovery NM 530c
Duvall[19]	Stress-only, rest/stress,or stress/rest Tc MPI	Qualitative angiographic analysis (unspecified cutoff)–ICA up to 18 mo after MPI	Discovery NM 530c
Goto[20]	Stress/rest Tc MPI	Qualitative angiographic analysis (75% cutoff)–ICA within 2 mo	Discovery NM 530c
Mouden[21]	Stress/rest Tc MPI	Fractional flow reserve (75% cutoff)-ICA within 1 d	Discovery NM/CT 570c
Nishiyama[22]	Stress/rest Tc MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 3 mo	Discovery NM 530c
Barone-Rochette[23]	Stress Tl/rest Tc dual-isotope MPI	Quantitative angiographic analysis (70% cutoff)–ICA within 3 mo	Discovery NM 530c
Liu[24]	Stress/rest Tl MPI	Qualitative angiographic analysis (70% cutoff)–ICA within 6 mo	Discovery NM 530c
Nakazato[25]	Rest/stress or stress/rest Tl or Tc MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 2 mo	D-SPECT
Perrin[26]	Stress-only or stress/rest Tc MPI	Quantitative angiographic analysis (50% cutoff)–ICA within 3 mo	D-SPECT
Shiraishi[27]	Stress/rest Tl MPI	Qualitative angiographic analysis (75% cutoff)–ICA within 1 mo	Discovery NM 530c
Sharir[28]	Stress/rest Tc MPI	Qualitative angiographic analysis (70% cutoff)–ICA within 2 mo	Discovery NM 530c
Yu-Hua [29]	Stress/rest Tl MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 2 mo	Discovery NM 530c
ShimpeiIto[30]	Stress/rest Tc MPI	Qualitative angiographic analysis (75% cutoff)–ICA within 1 mo	Discovery NM 530c
Denis Agostini[31]	Stress/rest Tc MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 1 mo	D-SPECT
Gilles Barone-Rochette[32]	Stress/rest Tc MPI	Qualitative angiographic analysis (50% cutoff)–ICA within 14 d	Discovery NM 530c

BMI = body mass index, CAD = coronary artery disease, CZT-SPECT = cadmium-zinc-telluride single-photon emission computed tomography, DM = diabetes mellitus, HCT = hypercholesterolemia, HT = hypertension, ICA = invasive coronary angiography, MPI = myocardial perfusion imaging, NA = not available or applicable, Tc = technetium-99m, Tl = thallium-201.

Table 2

Features of diagnostic accuracy in included study.

Author	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	True positive	True negative	False positive	False negative
Fiechter[14]	0.86	0.66	2.49	0.22	44	10	5	7
Ben-Haim[15]	1.0	0.0	–	–	4	0	1	0
Duvall[15]	0.95	0.37	1.51	0.14	121	38	65	6
Gimelli[16]	0.91	0.58	2.16	0.16	103	14	10	10
Ben-Haim[17]	0.83	0.88	6.67	0.19	7	10	1	1
Chowdhury[18]	0.84	0.79	3.96	0.21	74	61	16	14
Duvall[19]	0.56	0.61	14.6	0.71	31	37	23	24
Goto[20]	0.82	0.72	2.9	0.25	51	187	73	11
Mouden[21]	0.6	0.76	2.47	0.53	12	61	19	8
Nishiyama[22]	0.85	0.8	4.32	0.19	46	18	4	8
Barone-Rochette[23]	0.93	0.5	1.86	0.14	73	13	13	5
Liu[24]	0.76	0.74	2.91	0.32	27	130	46	8
Nakazato[25]	0.79	0.81	4.15	0.26	31	23	5	8
Perrin[26]	0.87	0.6	2.2	0.21	93	26	17	13
Shiraishi[27]	0.83	0.77	3.68	0.22	12	32	9	2
Sharir[28]	0.89	0.83	5.1	0.14	122	111	23	15
Yu-Hua[29]	0.85	0.9	8.5	0.17	35	55	5	6
Shimpei Ito[30]	0.35	0.86	2.4	0.76	20	12	2	38
Denis Agostini[31]	0.67	0.89	6.1	0.37	12	10	6	2
Gilles Barone-Rochette[32]	0.93	0.69	3	0.1	26	18	8	2

within half a year; studies that provided sufficient data to extracted true positives, true negatives, false positives, and false negatives. If the studies provided more than 1 set of data, we selected data that were more suitable for inclusion to exclude the influence of obvious difference between studies. The criteria for exclusion were: studies that gave too limited data for extraction; laboratory or animal studies, not relevant to the coronary angiography and CZT in coronary artery disease diagnosis value; abstracts-only articles, reviews, meta-analysis, and unpublished studies; inclusion of data duplicated in other studies.

2.3. Data extraction

According to the inclusion and exclusion criteria listed above, useful data in all eligible studies were extracted by 2 authors (Y-QZ and Y-FJ). Conflicts were discussed with a third investigator (Y-FZ). We extracted data including first author; publication year; study type; machine type of CZT-SPECT; patients number; index test; comparison with coronary angiography, and we extracted the true positive; false negative; true negative; false positive, besides we contained patient general condition, such as age, sex, hypertension, hyperlipemia, diabetes mellitus, smoking,

Table 3

Internal validity of included studies according to the quality assessment of diagnostic accuracy studies (QUADAS)-2 checklist*.

Study	Bias in patient selection	Bias in index test	Bias in reference standard	Bias in flow and timing	Applicability of patient selection	Applicability of index test	Applicability of reference standard
Fiechter (2011)	±	+	±	±	+	±	+
Ben-Haim (2010)	±	+	±	±	+	±	+
Duvall (2011)	±	+	±	±	+	±	+
Gimelli (2012)	±	+	±	±	+	±	+
Ben-Haim (2014)	±	+	±	±	±	±	+
Chowdhury (2014)	±	+	±	±	+	±	+
Duvall (2014)	±	+	±	–	+	±	+
Goto (2014)	±	+	±	±	+	±	+
Mouden (2014)	+	+	+	+	±	+	±
Nishiyama (2014)	±	+	±	±	+	±	+
Barone-Rochette (2015)	±	+	±	±	+	±	+
Liu (2015)	±	+	±	±	+	±	+
Nakazato (2015)	±	+	±	±	+	±	+
Perrin (2015)	±	+	±	±	+	±	+
Shiraishi (2015)	±	+	±	±	+	±	+
Sharir (2016)	±	+	±	±	+	±	+
Yu-Hua Dean Fang (2017)	±	+	±	±	+	±	+
Shimpei Ito (2017)	±	+	±	±	+	±	+
Denis Agostini (2017)	+	+	±	±	+	±	+
Gilles Barone-Rochette (2018)	±	+	±	±	+	±	+

* (+) indicates a favorable scenario (i.e., low risk of bias); (±) indicates a mixed scenario (i.e., moderate or uncertain risk of bias); (–) indicates an unfavorable scenario (i.e., high risk of bias).

body mass index, obesity, and type of coronary artery disease. When we found the data were incomplete or missing, we tried to contact the corresponding author for information in detail. Study quality was assessed according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2), which has more detailed evaluation criteria than QUADAS. Nowadays, QUADAS-2 is recommended to evaluate the quality of studies that are relevant to diagnosis.[9]

3. Statistical analysis

We performed a meta-analysis based on the recommended diagnostic methods.[10] All statistical tests were calculated with Stata version 14.0 (Stata Corporation, Texas). The diagnostic measures of this meta-analysis were according to random-effect model. Sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and diagnostic odds ratio (DOR) were used to assess the diagnosis accuracy of CZT-SPECT.[11] Besides, we conducted summary receiver-operating characteristic (SROC) curves to describe total studies diagnostic performance, the guidelines of area under curve in SROC are following: high for > 0.9 moderate for 0.7 to 0.9, and low for 0.5 to 0.7, [12] AS for heterogeneity of studies, we appraised I^2 statistic and Q test. *P* values less than.1 implied that sufficient heterogeneity existed. We also conducted meta regression to explore the source of heterogeneity. The following variables were used: study type (retrospective vs prospective), the type of CZT-SPECT machine (discovery NM 530c vs Discovery NM/CT 570c or D-SPECT), index-test 1 (stress/rest Tc MPI vs stress-only, rest/stress, or stress/rest Tl or Tc MPI), index-test 2 (stress-only vs rest/stress, or stress/rest Tl or Tc MPI) and the criterion of coronary angiography (qualitative angiographic analysis 50% cut off vs 70% or 75%).

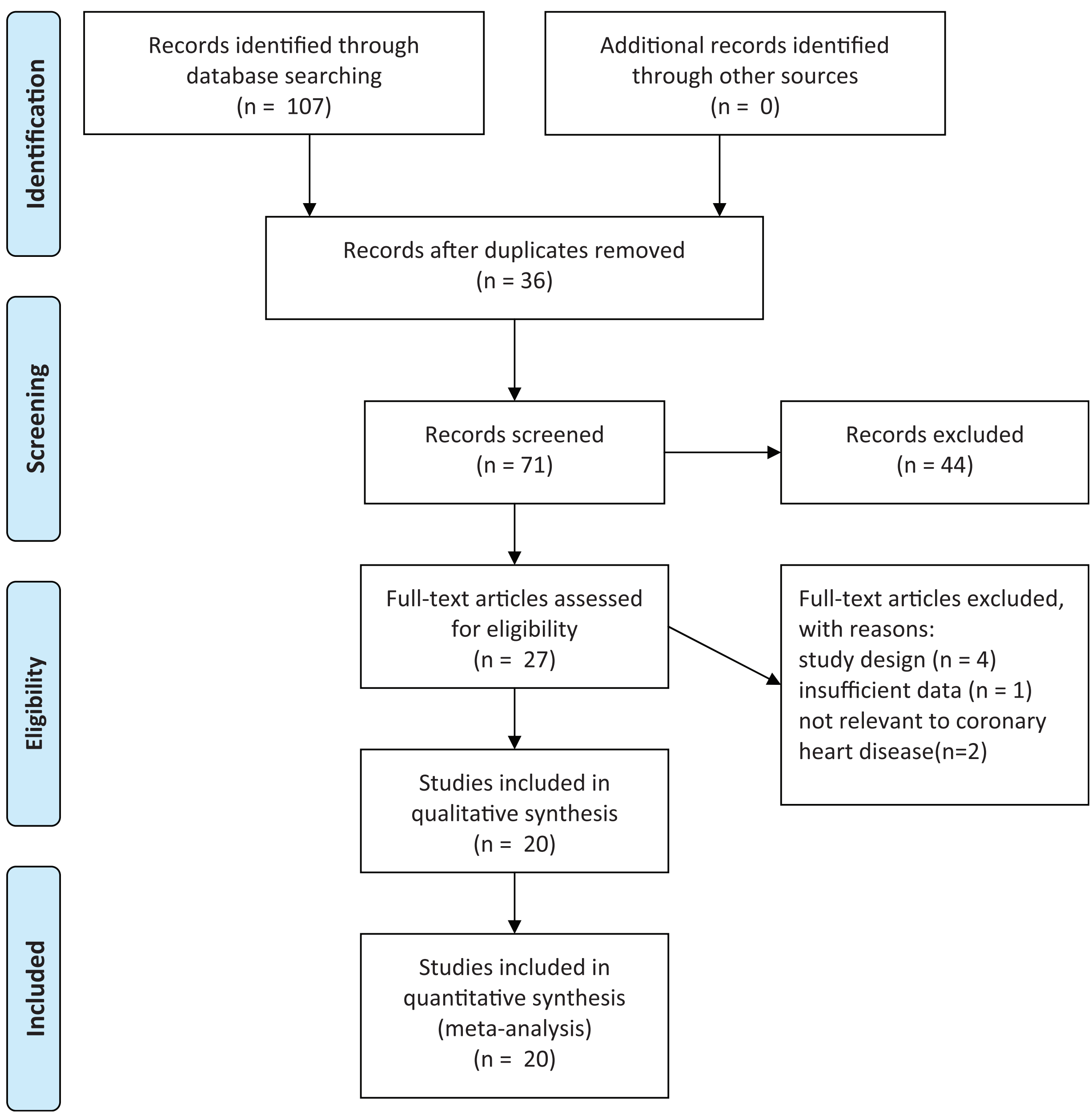

Figure 1. The complete procedure of the study selection and exclusion. Twenty studies were ultimately included.

Funnel plot for evaluating publication bias among the 20 studies was included in the meta-analysis.[13] Further, subgroup analyses were performed by sample size.

4. Results

4.1. Study characteristics

One hundred seven records in total were identified in initial article search via databases, 36 records were removed because they are duplicated studies, review articles or not related to the current study. There were 71 articles left for screening and 44 of articles were eliminated. We have read 27 studies by full-text, and 7 of full-text articles were excluded due to in-apposite study design (n=4), inadequate supply of data (n=1), and not relevant to coronary heart disease (n=2). Eventually, there were 20 studies [14–32] containing 2350 eligible patients for this meta-analysis, which were published between 2010 and 2018 and associated with the CZT diagnosis accuracy compared with the method of CAG. The sample size ranged from 5 to 322 of all eligible studies and the machine type of CZT-SPECT including Discovery NM/CT 570c, Discovery NM 530c, and D-SPECT. 6 [15,16,21,30–32] studies are prospective studies and 14 [14,15,17–20,22–29] studies are retrospective studies. There are 13 [14,16–18,20–23,27,28,30–32] researches which index test are Stress/rest Tc MPI. Characteristics of the studies included for meta-analysis are shown in Table 1. Features of Diagnostic Accuracy in included study and studies characteristics and Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) results are presented in Tables 2 and 3. Figure 1 shows the complete procedure of the study selection and exclusion.

4.2. Meta-analysis results

We pooled sensitivity, specificity, PLR, NLR, and DOR to estimate the diagnostic accuracy of CZT-SPECT. The pooled sensitivity was 0.84% and 95% confidence interval (95% CI): 0.78 to 0.89, specificity was 0.72, 95% CI (0.62–0.76), the PLR was 3.0, 95% CI (2.4–3.8), the NLR was 0.22, 95% CI (0.16–0.31), DOR was 14, 95% CI (7.84–17.42). Conspicuously, the specificity is significant lower than sensitivity. We also found that Q test is meaningful both in sensitivity and specificity. Besides, we implemented SROC curves for all individual studies which showed the accuracy of CZT-SPECT is 0.85 (0.81–0.88), and the graph indicated that the sensitivity and specificity are both variable. The forest plot to estimate the sensitivity and specificity of CZT-SPECT in diagnosis of coronary artery disease (Fig. 2). SROC curves are presented in Fig. 3.

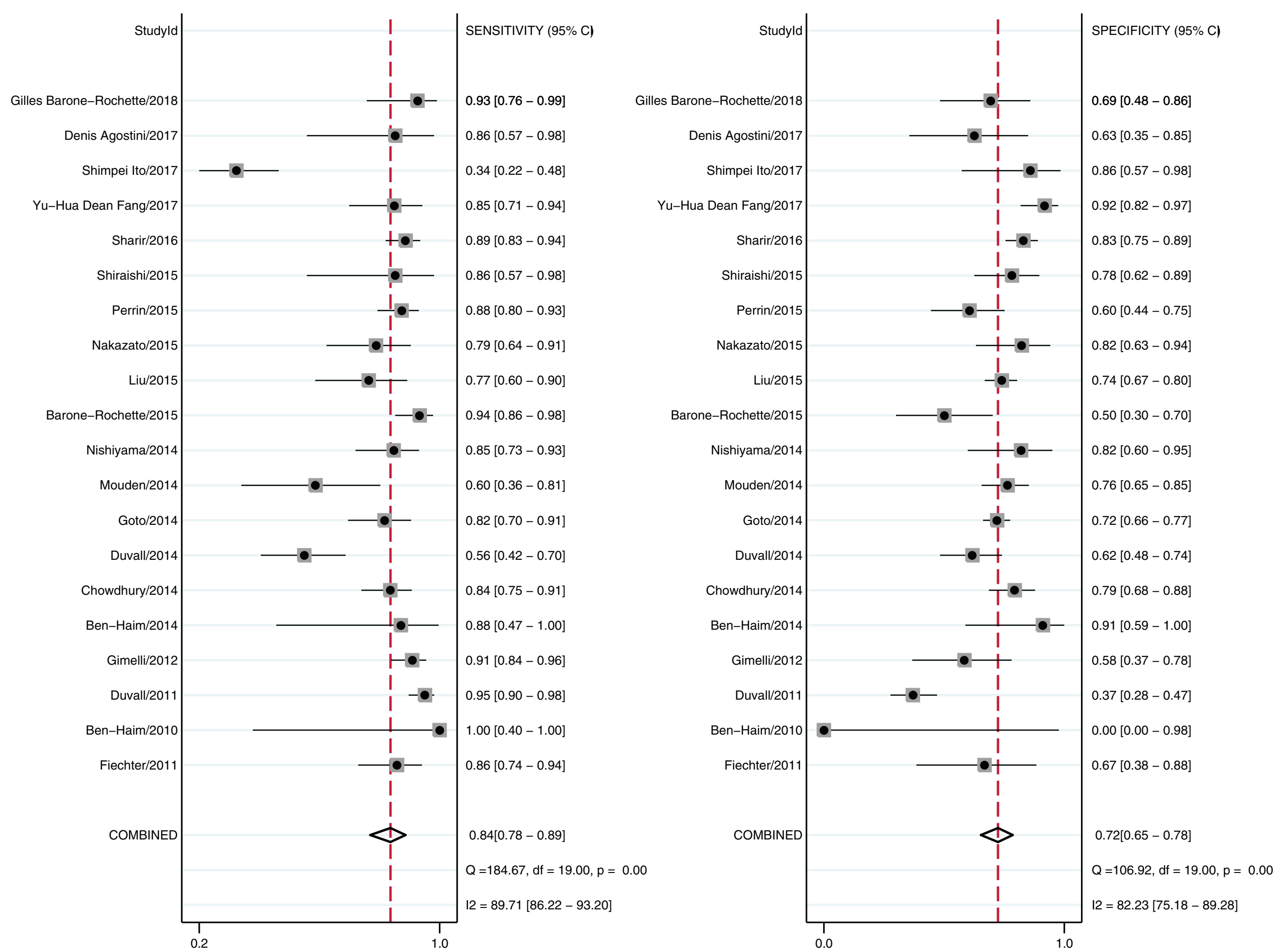

Figure 2. Forest plot of univariate analysis for sensitivity and specificity. Heterogeneity was appraised using the χ^2 test, with corresponding degrees of freedom (df) and *P* value. CI=confidence interval.

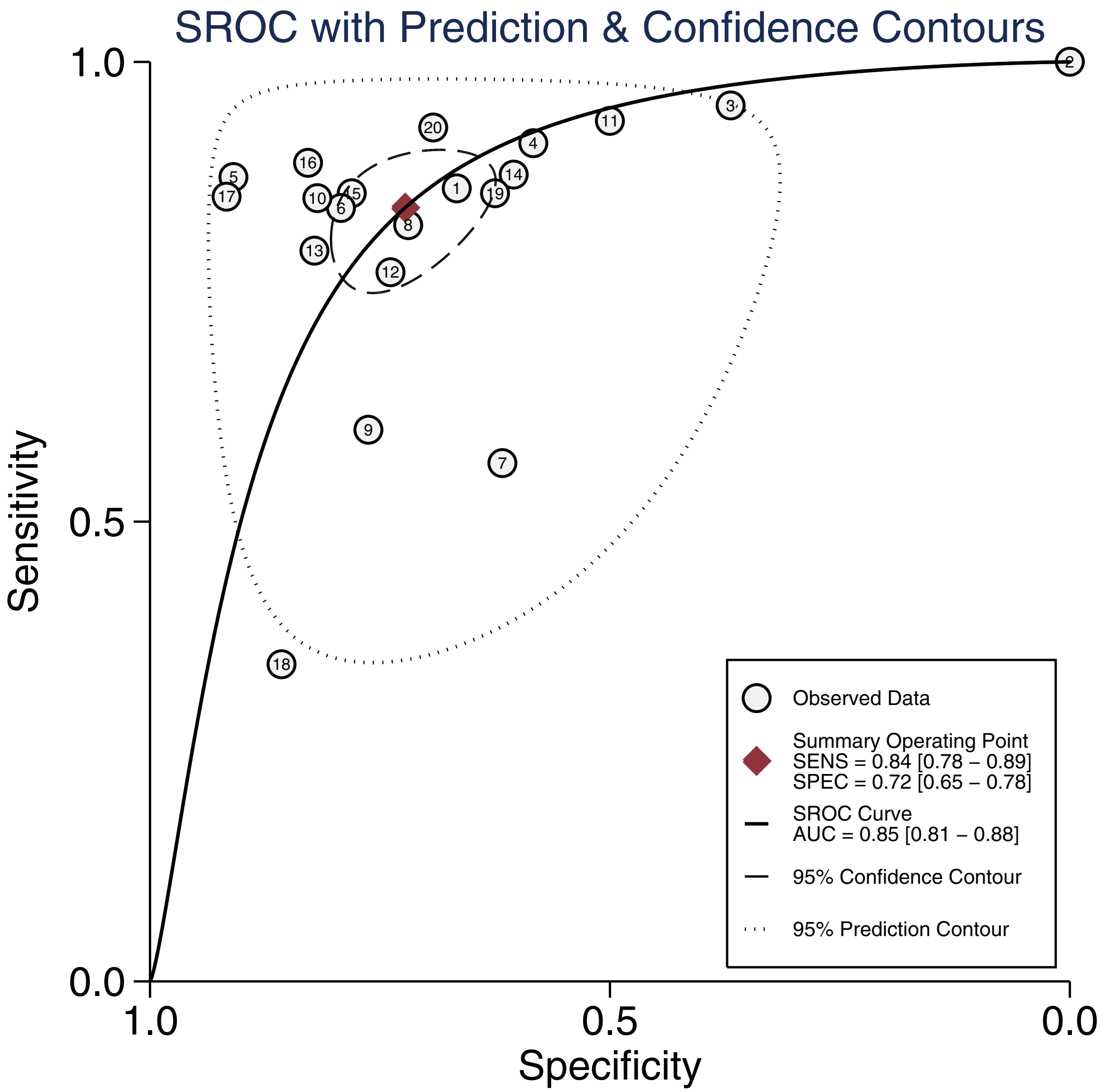

Figure 3. SROC curves. SROC = summary receiver-operating characteristic.

4.3. Meta-regression analysis

However, according to the results of I^2 and Q test, the heterogeneity of this study was significant. Then we conducted meta-regression analysis to explore the source of heterogeneity and found the index test with Stress/rest Tc MPI is meaningful in sensitivity and the index test with stress-only would influence the diagnostic specificity. Besides, we also implemented subgroup analysis to detect potential heterogeneity, for example we excluded the study of the sample size more than 200, and the results were shown by the forest plot. Figure 4 indicated the results of meta-regression, besides Table 4. showed the *P* value of meta-regression, which seems more significant, and the forest plot about subgroup analysis just containing the small sample size in Fig. 5.

4.4. Publication bias

To evaluate the publication bias of literatures, we performed the Deeks test, there is no apparent asymmetry in the shape of the Deeks funnel plots (Fig. 6) with *P* value = .54, suggesting that there is no significant publication bias in our study.

5. Discussion

Coronary artery disease (CAD) is one of the most important reasons of morbidity and mortality all over the world. [33] The diagnostic gold standard for coronary heart disease is still invasive CAG, which is not only used to diagnose CAD, but also can treat severe coronary stenosis during percutaneous coronary intervention (PCI). [4] However, CAG is invasive with many complications, for example, intraoperative and postoperative hemorrhage, hematoma, vascular endothelial injury, and so on. [34] New methods are required in diagnostic in potential CAD especially for sudden chest pain, atypical angina, and stable angina, the methods need to be more accurate and quicker.

The imaging principle of the CZT detector is to directly convert gamma rays into electrical signals. When the collected γ-rays interact with the CZT crystal, electrons and hole pairs are generated inside the crystal, and the number is proportional to the incident photons. Negatively charged electrons and positively charged holes move toward different electrodes, and the resulting charge pulse undergoes preamplification into voltage pulses. The preamplified output signal is processed by the subsequent circuit

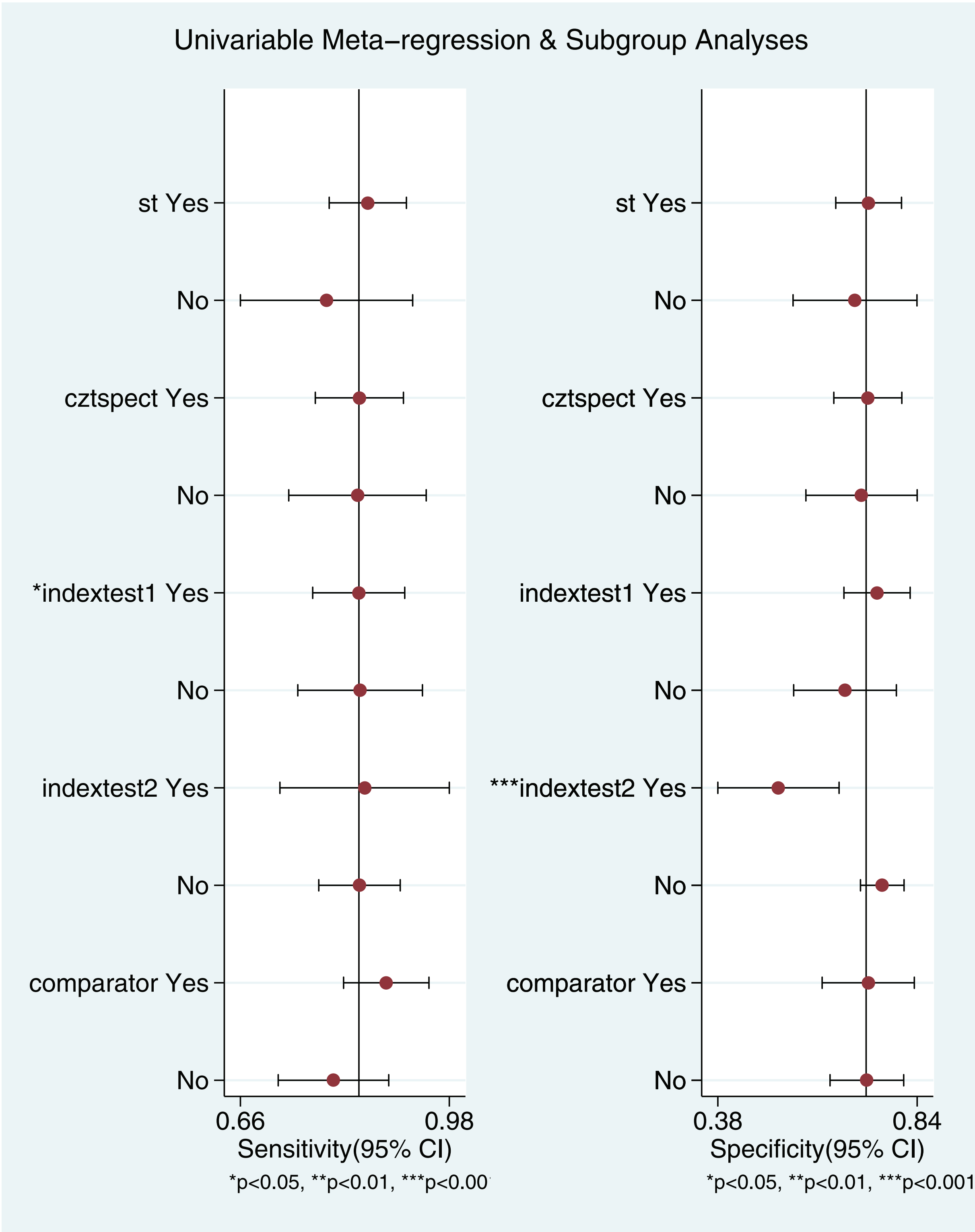

Figure 4. Subgroup analysis using meta regression. Results for meta regression.

and then the image is reconstructed. The CZT detector can handle 1 million photons / (s · mm^2) [3–5] at room temperature, thus guaranteeing a very high system sensitivity for gamma ray detection by the CZT detector. In recent years, with the continuous development of CZT-SPECT, the techniques have been advocated due to noninvasive and decrease exposure under radiation time for patients [35]. We conducted this meta-analysis to evaluate diagnosis value: coronary angiography and CZT-SPECT in coronary artery disease.

The results showed that the sensitive is 0.84 and specificity is 0.72, we can extrapolate that less than one-third of patients will be foreclosed. The data thus infer that further researches can be

Table 4

The results of meta-regression.

Parameter	Category	Sensitivity	P1	Specificity	P2
St (study type)	Retrospective	0.85[0.80–0.91]	.29	0.73[0.65–0.80]	.26
	Prospective	0.79[0.66–0.92]		0.70[0.56–0.84]	
cztspect	Discovery NM 530c	0.84[0.78–0.91]	.07	0.73[0.65–0.80]	.15
	Discovery NM/CT 570c or D-SPECT	0.84[0.73–0.94]		0.71[0.58–0.84]	
Index test1	Stress/rest Tc MPI	0.84[0.77–0.91]	.04	0.75[0.67–0.82]	.30
	others	0.84[0.75–0.94]		0.67[0.56–0.79]	
Index test2	Stress-only	0.85[0.72–0.98]	.22	0.52[0.38–0.66]	.00
	others	0.84[0.78–0.90]		0.76[0.71–0.81]	
Comparator	50% cut off	0.88[0.82–0.95]	.19	0.73[062–0.83]	.07
	70% or 75% cut off	0.80[0.72–0.89]		0.72[0.64–0.81]	

considered potential strategy to improve specificity. It's worth noting that Shinmei study focused on the point that whether the supine or prone positions will influence the diagnosis of CZT cameras. In their study, the time of injection was early and the liver could extremely affect the results, which may have decreased sensitivity in the supine position. Compare with another meta-analysis about CZT-SPECT and coronary angiograph, which showed sensitive is 0.86 and specificity is 0.70.[36] The pooled results are similar, both higher sensitives and lower specificities, which need further validation in larger populations.

However, the heterogeneity is prominent, which may be influenced by inconsistent characteristic of machine type, criteria for diagnosis of CAG, index test, and study populations. It is difficult to ascertain the clearly factors that influence heterogeneity, although the meta regression had been conducted.

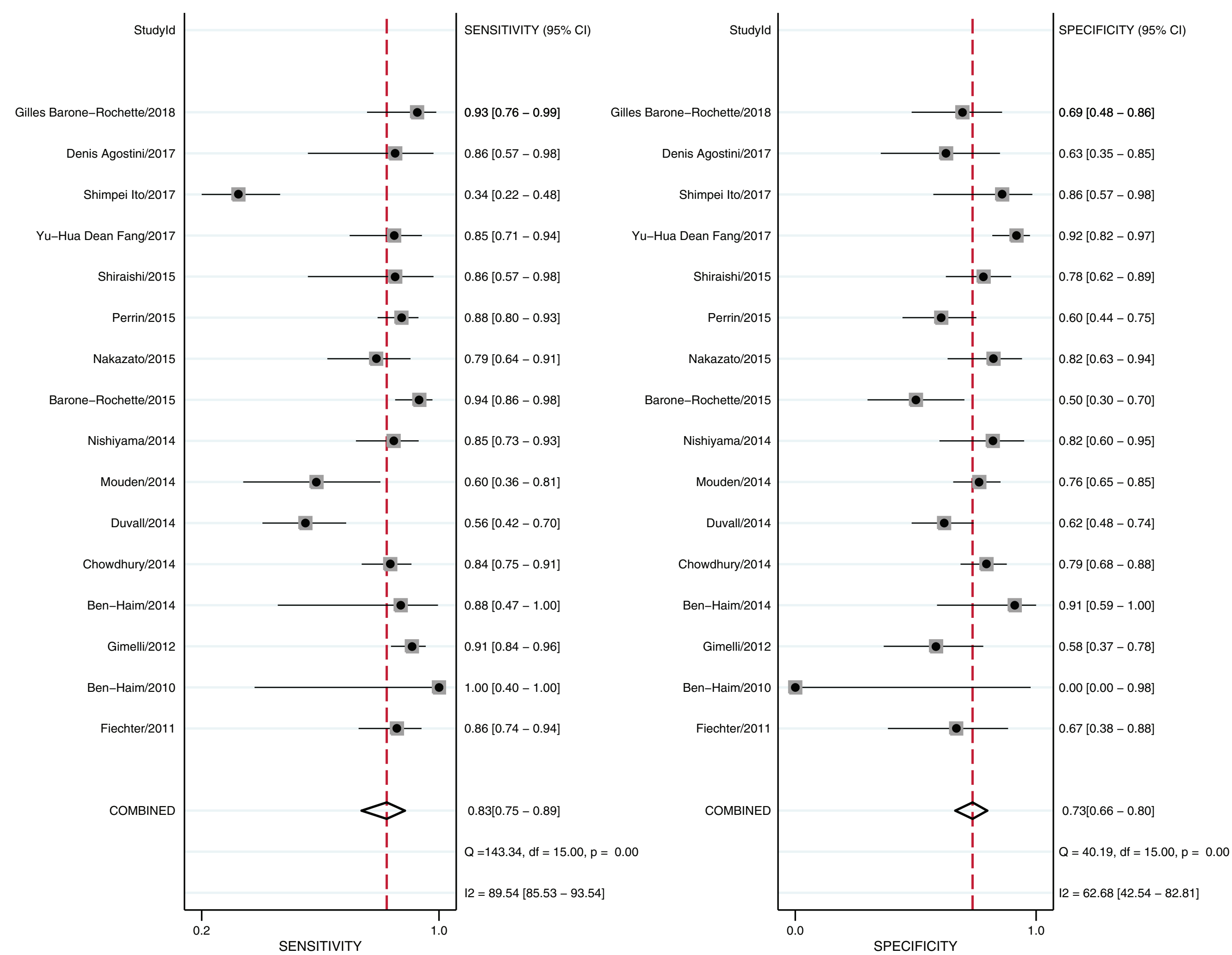

Figure 5. Sensitivity analysis. The forest plot about subgroup analysis just containing the small sample size.

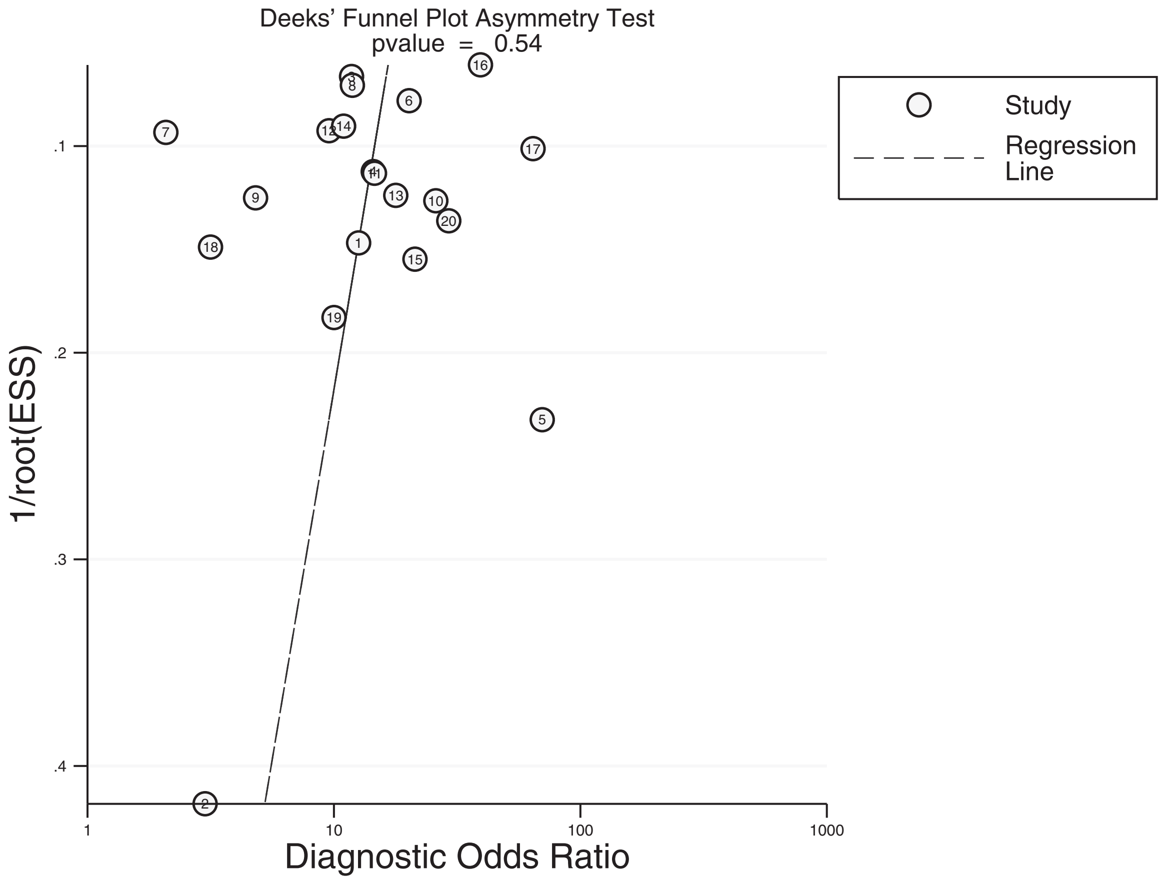

Figure 6. Test for publication analysis. The Deeks funnel plots.

Furthermore, it must be noted that Stress/rest Tc MPI of index test is distinctive which is meaningful in sensitive and index test with stress-only would influence the diagnostic specificity. To eliminate the influence of sample size, we excluded the study of the sample size greater than 200 and implemented meta-analysis, but the results showed no significant distinction in subgroup. At present, the CZT-SPECT machine mainly consists of 2 types: multipinhole collimation (Discovery NM 530c and Discovery NM/CT 570c) and parallel-hole collimation (D-SPECT), and our study revealed that there is no difference in machine types. [35,37]

However, some limitations did exist. First, the containing studies just come from a few databases, maybe many non-English research with high-quality will be excluded. Secondly, in spite of the significant results, there is no possible way to determine heterogeneity. The covariates data such as obesity, the type of coronary artery disease, index test and comparator standard of coronary angiograph that may contribute to the heterogeneity and cannot extracted available data from all eligible studies. Meanwhile, the control cases are different in elected study, some included patients with history of ischemic heart disease [13], but other patients with very low pretest likelihood of CAD .[24] Third, other potential factors contributed to the pooled result, for instance previous history of myocardial infarction, body position changes during examination and obesity, because of the limited of information, these features cannot be precisely explained. Image quality is very important for new diagnostic methods, and due to insufficient information about the image quality of CZT-SPECT, we cannot provide more details

Our study showed that although the diagnostic accuracy of CZT-SPECT is satisfactory, there still remain plenty of pitfalls in false-positive and false-negative lesions; it cannot replace the CAG.

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