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SYSTEMATIC REVIEW AND META-ANALYSIS

Cardiac Computed Tomography Versus Transesophageal Echocardiography for the Detection of Left Atrial Appendage Thrombus: A Systemic Review and Meta-Analysis

Shandong Yu, MD, PhD; Heping Zhang, MD; Hongwei Li, MD, PhD

BACKGROUND: Transesophageal echocardiography (TEE) has been considered the gold standard for left atrial appendage (LAA) thrombus detection. Nevertheless, TEE may sometimes induce discomfort and cause complications. Cardiac computed tomography has been studied extensively for LAA thrombus detection. We performed this systemic review and meta-analysis to assess the diagnostic accuracy of cardiac computed tomography for LAA thrombus detection compared with TEE.

METHODS AND RESULTS: A systemic search was conducted in the PubMed, Embase, and Cochrane Library databases from January 1977 to February 2021. Studies performed for assessment diagnostic accuracy of cardiac computed tomography on LAA thrombus compared with TEE were included. Summary sensitivity, specificity, and posterior probability of LAA thrombus was calculated by using bivariate random-effects model. The Quality Assessment of Diagnostic Accuracy Studies-2 tool was used for the quality assessment. A total of 27 studies involving 6960 patients were included in our study. The summary sensitivity of early imaging studies was 0.95 (95% CI, 0.79–0.99), and the specificity was 0.89 (95% CI, 0.85–0.92). The positive posterior probability was 19.11%, and the negative posterior probability was 0.16%. The summary sensitivity of delayed imaging studies was 0.98 (95% CI, 0.92–1.00), and the specificity was 1.00 (95% CI, 0.98–1.00). The positive posterior probability was 95.76%, and the negative posterior probability was 0.12%. The delayed imaging method significantly improved the specificity (1.00 versus 0.89; $P<0.05$) and positive posterior probability (95.76% versus 19.11%; $P<0.05$).

CONCLUSIONS: Cardiac computed tomography with a delayed imaging is a reliable alternative to TEE. It may save the patient and health care from an excess TEE.

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Key Words: cardiac computed tomography ■ diagnostic accuracy ■ left atrial appendage thrombus ■ systemic analysis and meta-analysis ■ transesophageal echocardiogram

Left atrial appendage (LAA) thrombus, which may present in conditions resulting in left atrial flow stasis, especially in atrial fibrillation, is an important source of cardioembolic stroke. Transesophageal echocardiography (TEE) is currently considered the gold standard for the detection of LAA thrombus, based on 2 large prospective studies.[1,2] However, TEE is a semi-invasive and time-consuming procedure. Although generally safe when performed by experienced operators, TEE carries physical discomfort for

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CLINICAL PERSPECTIVE

What Is New?

- This updated meta-analysis demonstrated that compared with transesophageal echocardiography, cardiac computed tomography showed a high diagnostic accuracy for left atrial appendage thrombus detection when delayed imaging was used.

What Are the Clinical Implications?

- Cardiac computed tomography with a delayed imaging method is a reliable alternative tool for left atrial appendage thrombus detection.
- Doing a delayed computed tomography scan adds nominal radiation exposure (<1 millisievert) and allows a single test to perform both tasks (pulmonary vein assessment and rule out left atrial thrombus), saving the patient and health care from an excess transesophageal echocardiography before pulmonary vein isolation.

Nonstandard Abbreviations and Acronyms

CCT	cardiac computed tomography
LAA	left atrial appendage
PVI	pulmonary vein isolation

some patients and is associated, although rarely, with potentially life-threatening complications.[3]

In the past 2 decades, cardiac computed tomography (CCT) has been studied extensively for LAA thrombus detection. Almost all of the studies reported that CCT has a high sensitivity for LAA thrombus detection, whereas the specificity has been reported variable. Studies using delayed imaging method reported higher specificity than studies using early imaging method. Moreover, it only takes a few minutes for CCT scan, far less than that of TEE. This will reduce time cost for examiners and patients. Some researchers have assessed the diagnostic accuracy of CCT by conducting meta-analyses.[4–8] The results of these studies have reported that CCT has good diagnostic accuracy for LAA thrombus detection,[4–8] especially when the delayed imaging method is used.[4,5] However, there are reasons to conduct a new meta-analysis. First, all studies included in these meta-analyses were conducted before the year of 2014, and studies using delayed imaging method were relative few. Second, the pooled sensitivity and specificity of 2 meta-analyses[7,8] were relatively low. Third, 2 meta-analyses[4,5] included 1 study[9] that did not meet the criteria because CCT was used for cardiogenic embolus detection, not LAA thrombus detection. In this study, CCT was used for cardiogenic thrombus but not LAA thrombus detection.[9] Moreover, there have been some new studies (at least 10) on LAA thrombus detection using CCT in recent years, some of which reported higher specificity and narrower CIs.[10–12] We therefore conducted this systematic review and meta-analysis to determine the diagnostic accuracy of CCT versus TEE for LAA thrombus detection.

METHODS

Authors declare that they will make the data, methods used in the analysis, and materials used to conduct the research available to any researcher for purposes of reproducing the results or replicating the procedure. The data that support the findings of this study are available from the first author on reasonable request.

This meta-analysis was performed on the basis of guidelines from the Preferred Reporting Items for a Systematic Review and Meta-Analysis of Diagnostic Test Accuracy Studies statement (Tables S1 and S2).[13] The literature search, article screening, study selection, quality assessment, and data extraction were performed by 2 authors (S.Y. and H.Z.) independently. Disagreements were resolved by discussion, and a consensus was reached in the selection of the articles for analysis.

Search Strategy

PubMed, Embase, and Cochrane Library databases were searched from January 1977 to February 2021. The search terms are shown in Table S3. In addition, we searched relevant studies from references of the retrieved articles.

Study Selection

Studies fulfilling the following criteria were included: (1) assessment of left atrial thrombus; (2) patients who underwent both CCT and TTE; and (3) sensitivity, specificity, positive predictive value, and negative predictive value data were provided or could be calculated.

Data Extraction and Quality Assessment

Data extraction was performed by 2 authors (S.Y. and H.Z.) independently. We extracted demographics of patients, indications of left atrial thrombus, and CCT method (eg, electrocardiogram (ECG) gated versus non–ECG gated).

Quality Assessment of Diagnostic Accuracy Studies-2 was used for the quality assessment of the included studies.[14] Two authors (S.Y. and H.Z.)

assessed the risk of bias and applicability concerns independently. The following domains were used to assess bias risk and applicability concerns: patient selection, performance of the index test, performance of the reference standard, and flow and timing (the interval between index test and standard reference, for risk of bias assessment only).[14]

Data Synthesis and Statistical Analysis

Metandi and midas commands in Stata 15.0 (StataCorp, College Station, TX) were used for data synthesis and analysis.[15,16] The analysis was implemented mainly by midas, and metandi was used to construct hierarchical summary receiver operating characteristic curve. Sensitivity, specificity, and likelihood ratio (LR), along with 95% CIs, were calculated from the contingency 2×2 tables of true-positive, false-positive, false-negative, and true-negative results using a bivariate random-effects model estimation. Random effects model was selected because heterogeneity is expected in meta-analysis of diagnostic accuracy studies.[17]

Primarily, midas uses an exact binomial rendition[18] of the bivariate mixed-effects regression model developed by Van Houwelingen[19] for treatment trial meta-analysis and modified for synthesis of diagnostic test data.[17] It fits a 2-level model, with independent binomial distributions for the true positives and true negatives conditional on the sensitivity and specificity in each study and a bivariate normal model for the logit transforms of sensitivity and specificity between studies. The standard output of the bivariate model includes the following: mean logit sensitivity and specificity with their SEs and 95% CIs; and estimates of the between-study variability in logit sensitivity and specificity and the covariance between them. On the basis of these parameters, we can calculate other measures of interest, such as the likelihood ratio for positive and negative test results, the diagnostic odds ratio (OR), and the correlation between logit sensitivity and specificity. Summary sensitivity, specificity, and the corresponding positive likelihood, negative likelihood, and diagnostic ORs are derived as functions of the estimated model parameters. The derived logit estimates of sensitivity, specificity, and respective variances are used to construct a hierarchical summary ROC curve to display the variation in diagnostic accuracy among studies.[20]

Posterior probability of LAA thrombus was also calculated to assess the diagnostic accuracy. The formula is as follows: posterior probability=pretest probability (LAA thrombus incidence)×LR/(pretest probability×LR+1). I^2 index was used to assess the heterogeneity.[21] Heterogeneity sources among studies was investigated by using multiple univariable meta-regression and subgroup analysis. Publication bias was assessed by the Deek method.[22]

RESULTS

Search Results

We identified 588 potentially eligible articles. In total, 555 articles were excluded by reviewing the titles and abstracts. The remaining 33 articles were evaluated in detail. Finally, 27 articles that met the inclusion criteria were identified (Figure 1). Six studies were excluded because not all patients underwent TEE,[23–25] no thrombus was found,[26] the sensitivity and specificity could not be calculated because the reference test was surgical finding,[27] and one study was not limited to LAA thrombus detection.[9]

Baseline Characteristics of the Included Studies

The baseline characteristics of the included studies are shown in Table 1.[28–51] Seventeen studies (63%) had a prospective design, and 10 studies (37%) had a retrospective design. Nineteen studies (70%) were performed with patients scheduled for pulmonary vein isolation (PVI), 4 studies (15%) were performed with patients recently experiencing stroke, 1 study was performed with patients scheduled to direct current cardioversion, and the remaining 3 studies had mixed populations. The ECG-gated method was used in 16 studies (59%). CCT with delayed imaging was performed in 11 studies (41%). The incidence of LAA thrombus was 3.68% (251/6960).

Quality Assessment

The results of the quality assessment are summarized in Table S4. In total, 3.70% (1/27) of the studies showed an unclear risk of bias in the patient selection domain, 7.41% (2/27) of the studies showed an unclear risk of bias in the index test domain, 33.33% (9/27) of the studies showed an unclear risk of bias in the reference standard domain, and 7.41% (2/27) of the studies showed a high or unclear risk of bias in the flow and timing domain.

Main Analysis

Analysis was based on study design (prospective or retrospective), imaging methods (early or delayed imaging; ECG gated or non–ECG gated), indication (PVI or not PVI), and sample size (patient number >100 or ≤100). The results are shown in Table 2. Sensitivity and negative LR (LR–) were not influenced by any factors, but the delayed imaging method had a significant impact on specificity and positive LR (LR+). The pooled sensitivity and specificity of the early and delayed

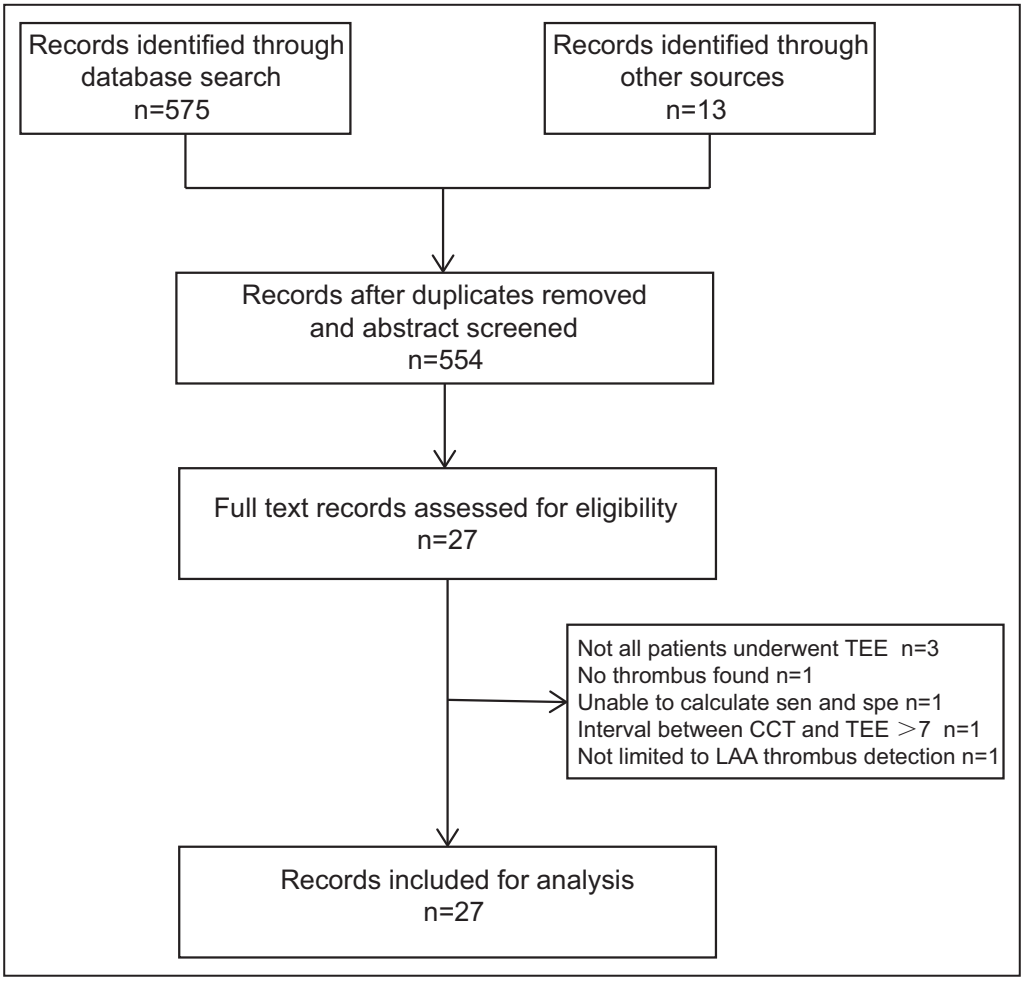

Figure 1. Flowchart of selection of studies.
CCT indicates cardiac computed tomography; LAA, left atrial appendage; sen, sensitivity; spe, specificity; and TEE, transesophageal echocardiography.

imaging subgroups are also shown in Figures 2A and 2B and 3A and 3B.

The incidence of LAA thrombus in the early imaging subgroup and delayed imaging group was 2.56% (120/4695) and 5.78% (131/2265), respectively. The positive posterior probability of the early imaging subgroup was 18.70%, and the negative posterior probability of the early imaging subgroup was 0.15% (Figure 2C). *P*=0.11 suggests no strong evidence of publication bias has been found (Figure 2D). The positive posterior probability of the delayed imaging subgroup was 95.51%, and the negative posterior probability of the delayed imaging subgroup was 0.12% (Figure 3C). *P*=0.14 suggests no strong evidence of publication bias has been found (Figure 3D).

Compared with the early imaging group, the delayed imaging method had a significantly higher LR+ and similar LR–, meaning that the delayed imaging method significantly improved the diagnostic accuracy. The positive posterior probability of the delayed imaging group was significantly higher than that of the early imaging group.

The hierarchical summary receiver operating characteristic curves of the early imaging group and delayed imaging group are shown in Figure 4A and 4B. The 95% prediction region and confidence region of the delayed imaging group (Figure 4A) were smaller than those of the early imaging group (Figure 4B), indicating that the diagnostic accuracy of the delayed imaging group was better than that of the early imaging group.

Analysis Based on Indications

Most patients in these studies were patients scheduled for PVI or patients experiencing stroke. Because these 2 indications have different LAA thrombus incidence (pretest probability), the posterior probability may be different. The incidence of LAA thrombus in the PVI with delayed imaging subgroup was 3.44% (52/1511). And the incidence of LAA thrombus in the stroke subgroup was 13.92% (77/553). Because the

Table 1. Baseline Characteristics of Included Studies

Study	Year	Design	No. of patients	Men, %	Age, y	Indication	CT type	Slice thickness, mm	Diagnostic criteria for TEE
Achenbach[28]	2004	Prospective	52	64	66±10	DCCV	ECG-gated EBCT; early phase	1.5	LAT/LAAT
Kim[29]	2007	Retrospective	223	82	57±10	PVI	ECG-gated 16-, 40-, 64-slice MDCT; early phase	1.2, 0.75, 0.6	LAAT+SEC
Shapiro[30]	2007	Retrospective	21	N/A	N/A	No restrict	ECG-gated 64 slice; MDCT; early phase	0.6	LAAT
Feuchtner[31]	2008	Prospective	64	68	58±13	PVI/valve surgery	ECG-gated 64 slice; MDCT	0.6	LAT/LAAT
Tang[32]	2008	Prospective	170	72	56±12	PVI	Non–ECG-gated 64 slice; MDCT; early phase	N/A	LAT/LAAT
Hur[33]	2008	Retrospective	101	62	67	Stroke	ECG-gated 64-section CCTA; early phase	0.6	LAAT
Patel[34]	2008	Prospective	72	69	56±10	PVI	ECG-gated 64 slice; MDCT; early phase	0.625	LAAT+SEC
Martinez[35]	2009	Prospective	402	76	56±10	PVI	64 Slice; MDCT; early phase	0.6	LAAT
Hur[36]	2009	Prospective	55	65	61	Stroke	ECG-gated 64-section CCTA; late phase	0.6	LAAT
Kim[37]	2010	Prospective	314	59	65±13	Stroke	ECG-gated 64-slice MDCT; late phase	0.625	LAAT
Kapa[38]	2010	Prospective	255	78	59±11	PVI	ECG-gated DSCT; early phase	0.6	LAAT
Maltagliati[39]	2011	Prospective	171	83	60±11	PVI	64-Slice MDCT; early phase	N/A	LAA/LAAT
Hur[40]	2011	Prospective	83	67	63±10	Stroke	ECG-gated DSCT; late phase	0.6	LAAT+SEC
Swait[41]	2012	Retrospective	70	N/A	N/A	PVI	ECG-gated (patient in sinus rhythm) and nongated (patients in AF) 256-, 128-, and 64-slice CCT; late phase	N/A	LAT+LAAT
Hur[42]	2013	Prospective	101	70	62±10	PVI	ECG-gated 128-, 64-slice CCT; late phase	0.6	LAT+LAAT
Dorenkamp[43]	2013	Prospective	329	65	62±10	PVI	ECG-gated 64-slice MDCT; early phase	0.625	LAT+LAAT
Budoff[44]	2014	Retrospective	86	81	66	PVI	64-Slice CCTA; late phase	N/A	LAAT
Hong[45]	2014	Retrospective	678	78	57±11	PVI	ECG-gated 64-slice MDCT; early phase	0.6	LA/LAAT+SEC
Homsi[46]	2016	Prospective	124	83	58±12	AF/stroke	64-Slice MDCT; early phase	0.9	LAAT+SEC
Lazoura[11]	2016	Retrospective	122	78	60	PVI	ECG-gated DSCT; late phase	0.5	LAAT
Wang[47]	2016	Retrospective	831	75	61±10	PVI	Non–ECG-gated 64 slice; MDCT; early phase	0.625	LAAT+SEC
Zhai[48]	2017	Retrospective	783	72	55±11	PVI	ECG-gated 64 slice; MDCT; late phase	0.625	
Kottmaier[49]	2019	Prospective	622	69	60±10	PVI	ECG-gated (patient in sinus rhythm) and nongated (patients in AF) 64-slice DSCT early phase image	0.6	LAT
Kuronuma[12]	2019	Prospective	81	75	68±11	PVI	ECG-gated CCT; late phase	N/A	LAAT
Li[50]	2019	Prospective	302	54	64±7	PVI	64-Slice DSCT; late phase	0.6	LAAT
Guha[51]	2020	Retrospective	480	66	63	PVI	64-Slice MDCT; early phase	0.63	LAAT
Spagnolo[10]	2020	Prospective	260	77	59±11	PVI	ECG-gated 64-slice CCT; late phase	N/A	LAAT

AF indicates atrial fibrillation; CCT, cardiac CT; CCTA, coronary CT angiography; CT, computed tomography; DCCV, direct current cardioversion; DSCT, dual-source CT; ECG, electrocardiogram; EBCT, electron-beam CT; LAAT, left atrial appendage thrombus; LAT, left atrial thrombus; MDCT, multidetector CT; N/A, not available; PVI, pulmonary vein isolation; SEC, spontaneous echo contrast; and TEE, transesophageal echocardiography.

Table 2. Sensitivity and Specificity of Each Subgroup

Subgroup	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR– (95% CI)	Incidence of thrombus
Prospective	0.97 (0.82–1.00)	0.97 (0.93–0.99)	29.91 (13.36–66.96)	0.03 (0.00–0.20)	169/3467
Retrospective	0.98 (0.85–1.00)	0.92 (0.82–0.97)	12.63 (5.30–30.12)	0.02 (0.00–0.19)	82/3493
Early	0.95 (0.79–0.99)	0.89 (0.85–0.92)*	8.99 (6.61–12.21)*	0.06 (0.01–0.26)	120/4695
Delayed	0.99 (0.92–1.00)	1.00 (0.98–1.00)*	368.27 (41.94–3233.86)*	0.01 (0.00–0.08)	131/2265
ECG gated	0.98 (0.87–1.00)	0.97 (0.93–0.99)	36.30 (12.99–101.46)	0.02 (0.00–0.14)	158/3604
Non–ECG gated	0.97 (0.73–1.00)	0.91 (0.85–0.95)	11.32 (6.61–19.39)	0.03 (0.00–0.36)	93/3356
PVI	0.98 (0.84–1.00)	0.95 (0.91–0.97)	19.69 (10.13–38.3)	0.03 (0.00–0.19)	134/6146
Non-PVI	0.99 (0.76–1.00)	0.96 (0.86–0.99)	28.11 (6.75–117.02)	0.01 (0.00–0.30)	117/814
PVI delayed	0.99 (0.79–1.00)	1.00 (0.93–1.00)	302.20 (14.3–6386.8)	0.01 (0.00–0.25)	52/1511
Stroke	0.99 (0.87–1.00)	0.99 (0.93–1.00)	172.40 (13.8–2151.4)	0.01 (0.00–0.14)	77/553
Small sample	0.99 (0.70–1.00)	0.94 (0.83–0.98)	17.56 (5.47–56.43)	0.01 (0.00–0.44)	84/592
Large sample	0.98 (0.85–1.00)	0.96 (0.92–0.98)	23.98 (11.61–49.54)	0.03 (0.00–0.17)	167/6368

ECG, electrocardiogram; LR indicates likelihood ratio; and PVI, pulmonary vein isolation.
*indicates a statistical difference.

early imaging method has a low LR+ value, we mainly analyzed data from the delayed imaging group. The results are shown in Table 2 and Figures 5 and 6. The pooled sensitivity and specificity were similar between the 2 subgroups (Table 2 and Figures 5A and 5B and 6A and 6B). Although the estimated LR+ of the stroke subgroup was lower than that of the PVI subgroup, the positive posterior probability of the stroke subgroup was higher (96.00% versus 91.22%) because of the higher LAA thrombus incidence (Figures 5C and 6C). P=0.71 and P=0.09 suggested no strong evidence of publication bias has been found (Figures 5D and 6D). Meta-regression was performed to explore the source of heterogeneity. The results showed that the delayed imaging method, ECG-gated method, and PVI may be the source of heterogeneity (Figure S1). When the delayed imaging method was defined as the interval between contrast injection and image capture of >1 minute, the heterogeneity of the delayed imaging subgroup decreased significantly (Figure S2).

DISCUSSION

In this comprehensive meta-analysis of 27 studies, we assessed the diagnostic accuracy of CCT compared with TEE. The results demonstrated that CCT showed a high diagnostic accuracy for LAA thrombus detection when delayed imaging was used. In the delayed imaging subgroup, the positive posterior probability was 95.76%, and the negative posterior probability was 0.12%. Accurate identification of LAA thrombi is important for patients with atrial fibrillation and suspected cardiogenic stroke. For patients with atrial fibrillation, it can change the subsequent treatment strategy; for patients with suspected cardiogenic stroke, it can clarify a diagnosis. In the subgroup analysis based on these 2 indications, the positive posterior probabilities of PVI with delayed imaging and stroke subgroups were 91.22% and 96%, respectively. The negative posterior probabilities of these 2 subgroups were 0.34% and 0.14%, respectively. In the stroke subgroup, the LR+ value of the study with the early imaging method[33] was 25. This relatively low LR+ value underestimated the positive posterior probability. Therefore, the actual positive posterior probability would be higher. If the LR+ value of PVI with the delayed imaging subgroup was used, the positive posterior probability would be 98%. This means that CCT with delayed imaging method has a better diagnostic accuracy for LAA thrombus detection in patients with stroke.

Although TEE is currently considered the gold standard for LAA thrombus detection, it is time-consuming.[52] In the past 2 decades, an increasing number of studies on the diagnostic accuracy of CCT for the detection of LAA thrombi have been performed. Most of these studies reported a high sensitivity and negative predictive value. LAA thrombus detection by CCT relies on filling defects. However, low blood flow velocity may also present as filling defects. It may be difficult to differentiate thrombi from low blood flow for early imaging method because the interval between contrast arrival and LAA image capture is too short. The delayed imaging method helps to differentiate thrombi and low blood flow. Our results showed that the delayed imaging method significantly improved the positive posterior probability compared with the early imaging method. In the subgroup analysis based on indications, our results showed that CCT with delayed imaging method has good diagnostic accuracy for LAA thrombus detection in patients with PVI and stroke. According to our results, we believe that CCT with a delayed imaging method is a reliable alternative tool for LAA thrombus detection. Furthermore, CCT has been recommended to assess left atrial and pulmonary vein

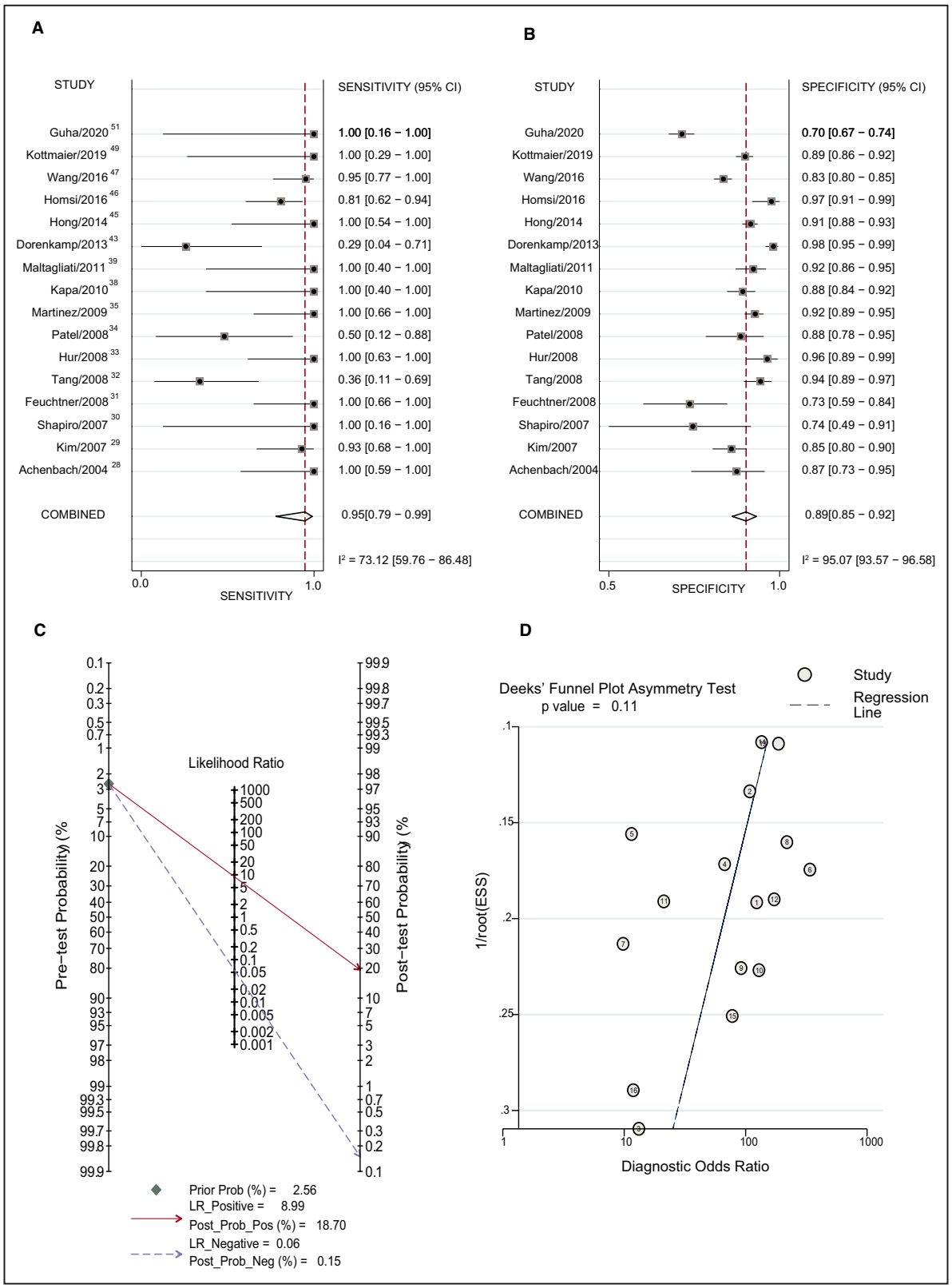

Figure 2. Forest plot of diagnostic accuracy of cardiac computed tomography (CCT) with early imaging method vs transesophageal echocardiography (TEE).

A, Sensitivity of CTT with the early imaging method vs TEE. **B**, Specificity of CCT with the early imaging method vs TEE. **C**, Posterior probability of CCT with the early imaging method vs TEE. **D**, The Deek method for assessment of publication bias. ESS, effective sample size; LR indicates likelihood ratio; Post Prob Neg, negative posterior probability; Post Prob Pos, positive posterior probability; and Prob, probability.

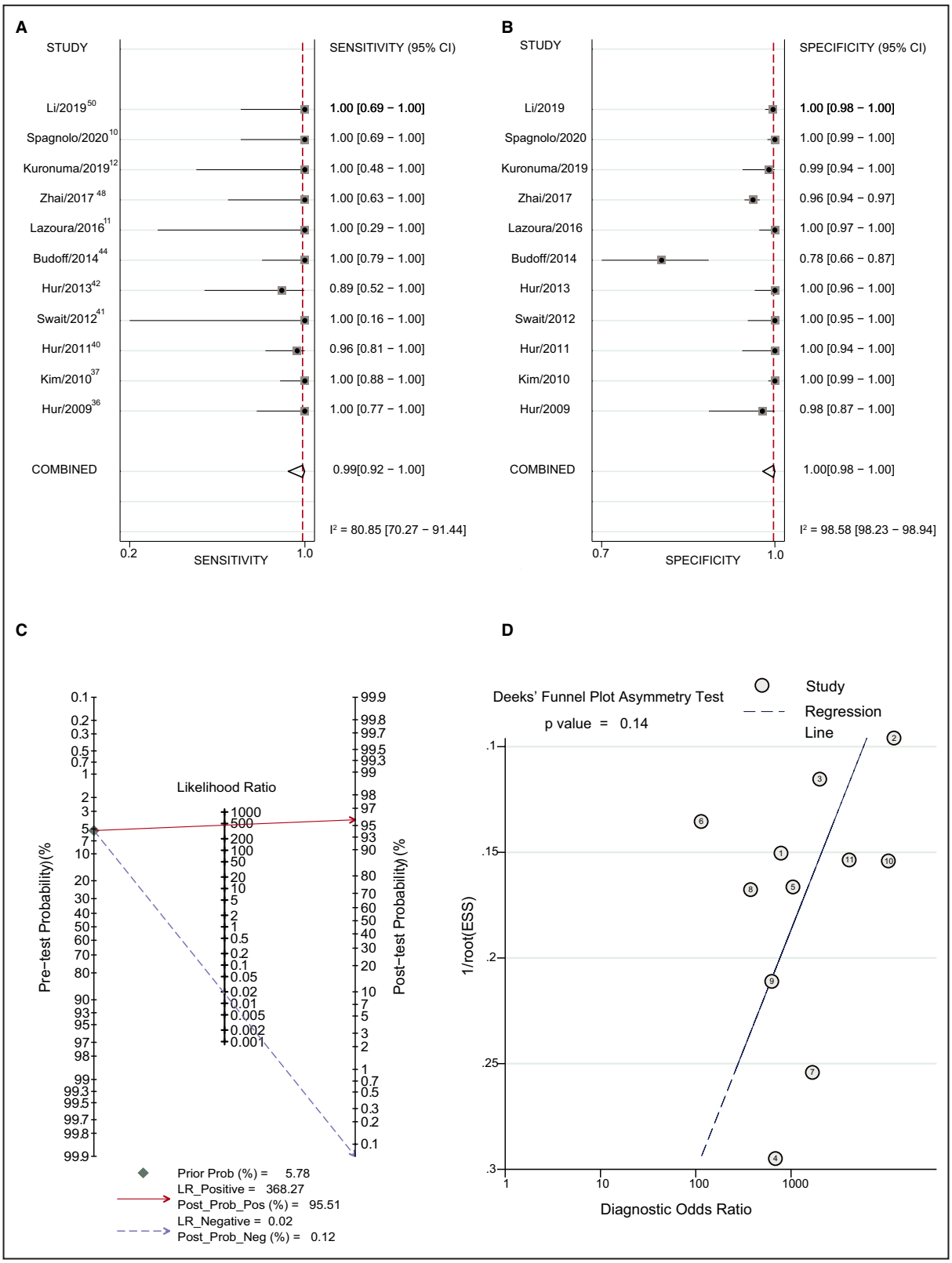

Figure 3. Forest plot of the diagnostic accuracy of cardiac computed tomography (CCT) with the delayed imaging method vs transesophageal echocardiography (TEE).

A, Sensitivity of CTT with the delayed imaging method vs TEE. **B**, Specificity of CCT with the delayed imaging method vs TEE. **C**, Posterior probability of CCT with the delayed imaging method vs TEE. **D**, The Deek method for assessment of publication bias. ESS, effective sample size; LR indicates likelihood ratio; Post Prob Neg, negative posterior probability; Post Prob Pos, positive posterior probability; and Prob, probability.

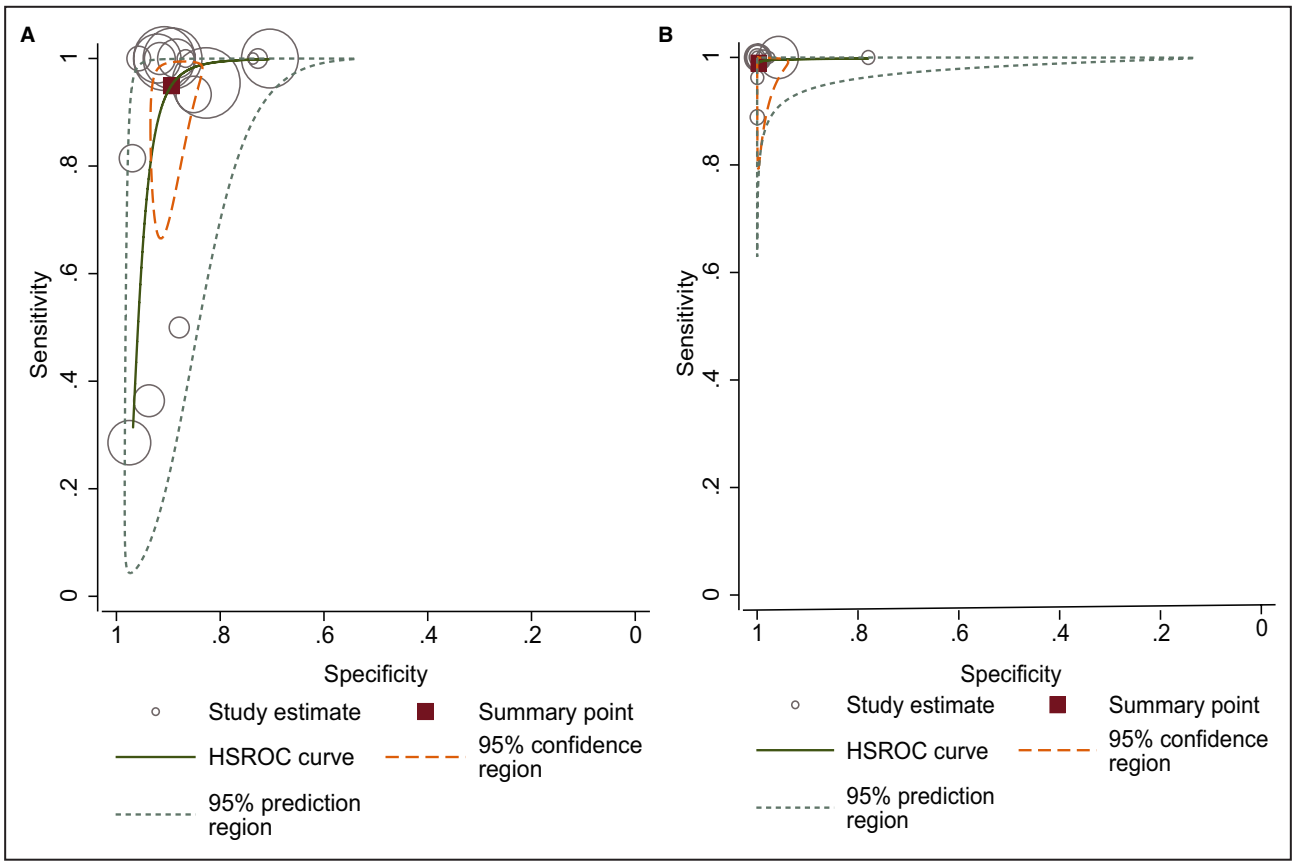

Figure 4. Hierarchical summary receiver operating characteristic (HSROC) curve of studies using the early imaging method (A) and delayed imaging method (B).

anatomical features before PVI.[53] In addition, the cost of CCT is only a few minutes. So, doing a delayed scan at the same time adds nominal radiation exposure (<1 millisievert) and allows a single test to perform both tasks (pulmonary vein assessment and rule out left atrial thrombus), saving the patient and health care from an excess TEE. TEE can be reserved for those with positive CCT to confirm the diagnosis of clot when needed. Given the high diagnostic accuracy and efficiency for LAA thrombus detection, TEE may be prevented in patients before PVI or in patients with stroke.

In previous studies,[4–7] the diagnostic accuracy of CCT was assessed by sensitivity, specificity, positive predictive value, and negative predictive value. However, the diagnostic accuracy of a test not only depends on sensitivity, specificity, positive predictive value, and negative predictive value but also depends on disease prevalence. The diagnostic accuracy of a test may vary in different populations because of different disease prevalence. The posterior probability calculated on the basis of disease prevalence may be more accurate. In our study, diagnostic accuracy was assessed by calculating the positive posterior probability and negative posterior probability based on the prevalence of LAA thrombi in each group. Our results did show the difference in posterior probability between patients before PVI and patients with stroke. Moreover, all studies included in previous meta-analyses were conducted before 2014, and studies using delayed imaging method were relatively few. In this study, we included studies published until February 2021, including 11 studies using delayed imaging method.

There are some disadvantages in the use of CCT for the detection of LAA thrombi. First, the contrast agent used during CCT examination may cause contrast-induced nephropathy and anaphylaxis. The risk of contrast-induced nephropathy is relatively low in patients with normal renal function. Although the risk may increase in patients with chronic kidney disease, most kidney injuries are reversible.[54] Second, patients are exposed to radiation. Currently, however, as technology has advanced, the level of radiation exposure is relatively low. CCT is most often done in <3 millisieverts, a marked reduction from early reports of ≥15 millisieverts in earlier studies.[55]

There are some limitations to our study. First, the heterogeneity was high, and the results of the meta-regression showed that the heterogeneity was from

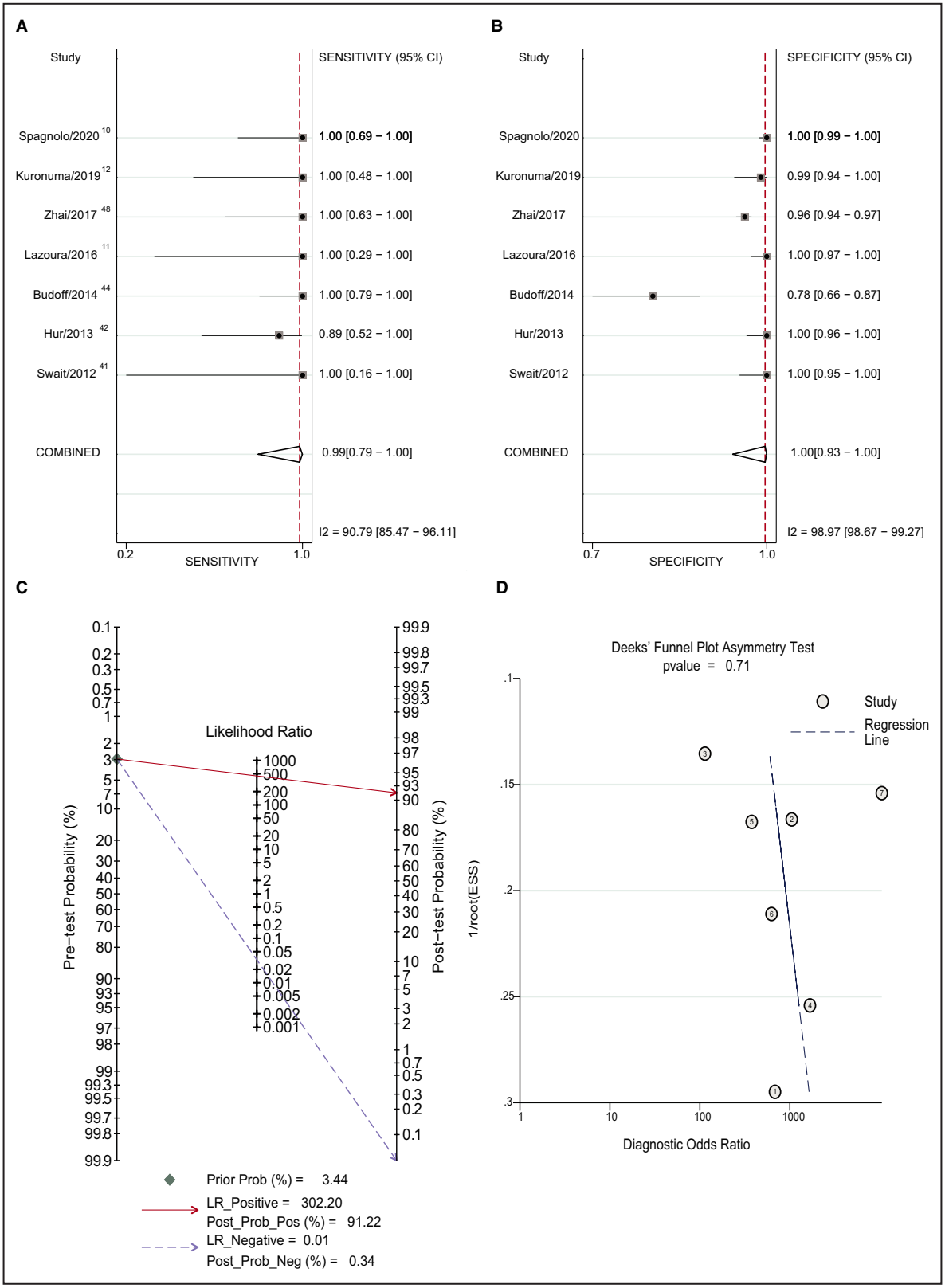

Figure 5. Forest plot of the diagnostic accuracy of cardiac computed tomography (CCT) in patients with pulmonary vein isolation (PVI) using delayed imaging method vs transesophageal echocardiography (TEE).
A, Sensitivity of CCT in patients with PVI using the delayed imaging method vs TEE. **B**, Specificity of CCT in patients with PVI using the delayed imaging method vs TEE. **C**, Posterior probability of CCT in patients with PVI using the delayed imaging method vs TEE. **D**, The Deek method for assessment of publication bias. ESS, effective sample size; LR indicates likelihood ratio; Post Prob Neg, negative posterior probability; Post Prob Pos, positive posterior probability; and Prob, probability.

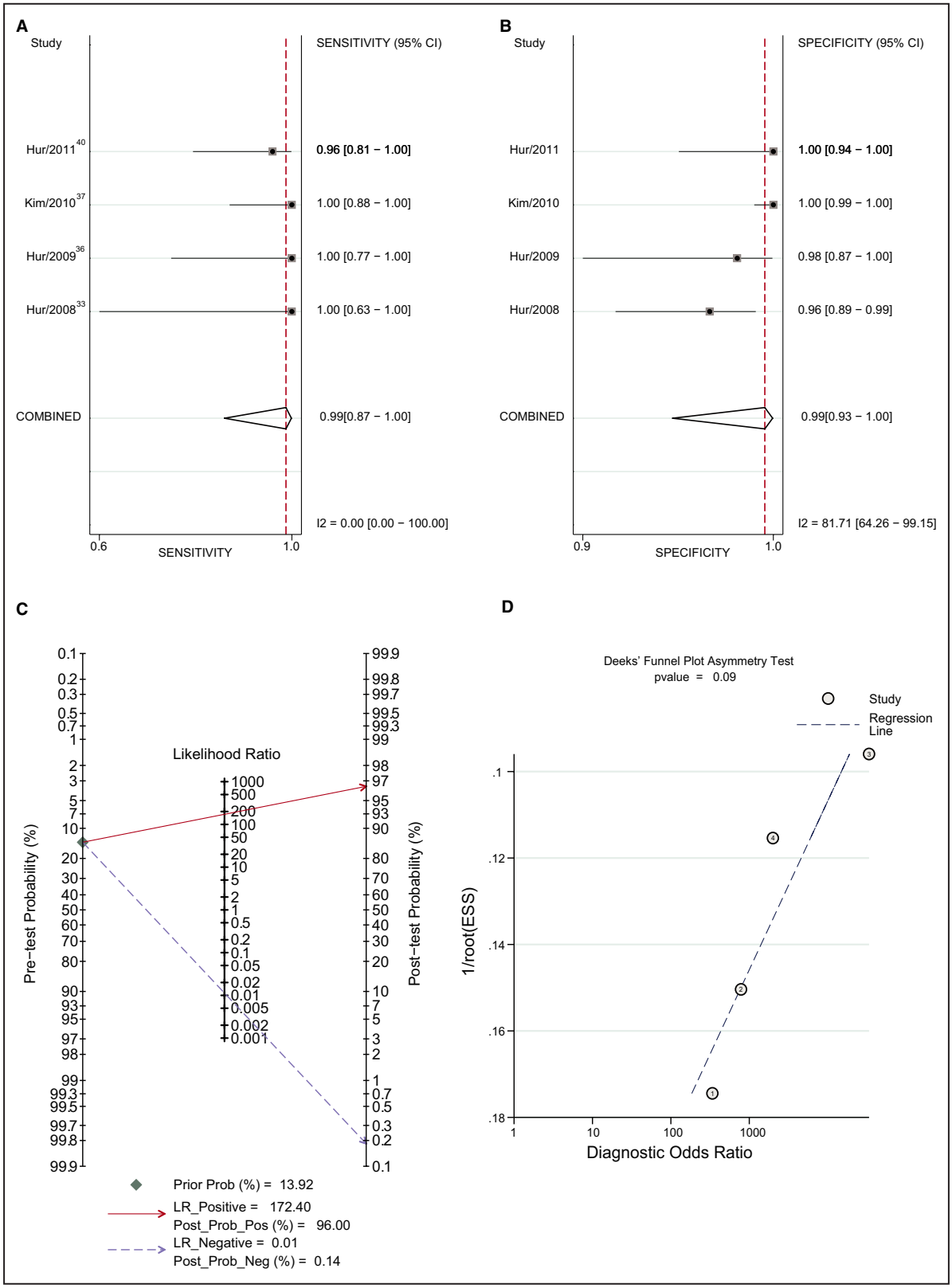

Figure 6. Forest plot of the diagnostic accuracy of cardiac computed tomography (CCT) in patients with stroke using delayed imaging method vs transesophageal echocardiography (TEE).

A, Sensitivity of CCT in patients with stroke using the delayed imaging method vs TEE. **B**, Specificity of CCT in patients with stroke using the delayed imaging method vs TEE. **C**, Posterior probability of CCT in patients with stroke using the delayed imaging method vs TEE. **D**, The Deek method for assessment of publication bias. ESS, effective sample size; LR indicates likelihood ratio; Post Prob Neg, negative posterior probability; Post Prob Pos, positive posterior probability; and Prob, probability.

the delayed imaging method, ECG-gated method, and PVI. Second, the reference standard was TEE, not surgical validation.

CONCLUSIONS

CCT with a delayed imaging method is superior to CCT with an early imaging method for LAA thrombus detection. It is a reliable alternative to TEE.

ARTICLE INFORMATION

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Disclosures

None.

Supplementary Material

Tables S1–S4
Figures S1–S2

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Supplemental Material

Table S1. PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on Page Number	Reported on Section/Paragraph
TITLE/ABSTRACT				
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	Page 1	Title
Abstract	2	Abstract: See PRISMA-DTA for abstracts (Table S4).	Page2	Abstract/ Paragraph 1-3
INTRODUCTION				
Rationale	3	Describe the rationale for the review in the context of what is already known.	Page 3	Introduction/ Paragraph 1
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	Page 3	Introduction / Paragraph 2
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	Page 4	Introduction / Paragraph 2
METHODS				
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Page 2	Registration
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Page 4	Methods/ Paragraph 3-4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Page 4	Methods/ Paragraph 3
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	Page 4	Methods/ Paragraph 3
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Page 4	Methods/ Paragraph 4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Page 5	Methods/ Paragraph 5
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	Page 5	Methods/ Paragraph 5

Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	Page 5	Methods/ Paragraph 6
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	Page 5-6	Methods/ Paragraph 7
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	Page 5-6	Methods/ Paragraph 7
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	Page 5-6	Methods/ Paragraph 7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Page 5-6	Methods/ Paragraph 7
RESULTS				
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	Page 6	Results/ Paragraph 1
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	Page 6-7	Results/ Paragraph 2
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	Page 7	Results/ Paragraph 3
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	Page 6	Results/ Paragraph 1
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	Page 7-8	Results/ Paragraph 4-6
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	Page 7-8	Results/ Paragraph 7-8
DISCUSSION				
Summary of evidence	24	Summarize the main findings including the strength of evidence.	Page 9	Discussion/ Paragraph 1
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	Page 10	Discussion/ Paragraph 2

Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	Page 11	Conclusion
FUNDING				
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	Page 11	Funding

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

Table S2. PRISMA-DTA for Abstracts Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on Page Number	Reported on Section/Paragraph
TITLE and PURPOSE				
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	Page 1	Title
Objectives	2	Indicate the research question, including components such as participants, index test, and target conditions.	Page2	Abstract/ Paragraph 1
METHODS				
Eligibility criteria	3	Include study characteristics used as criteria for eligibility.	Page2	Abstract/ Paragraph 2
Information sources	4	List the key databases searched and the search dates.	Page2	Abstract/ Paragraph 2
Risk of bias & applicability	5	Indicate the methods of assessing risk of bias and applicability.	Page2	Abstract/ Paragraph 2
Synthesis of results	A1	Indicate the methods for the data synthesis.	Page2	Abstract/ Paragraph 2
RESULTS				
Included studies	6	Indicate the number and type of included studies and the participants and relevant characteristics of the studies (including the reference standard).	Page2	Abstract/ Paragraph 2
Synthesis of results	7	Include the results for the analysis of diagnostic accuracy, preferably indicating the number of studies and participants. Describe test accuracy including variability; if meta-analysis was done, include summary results and confidence intervals.	Page2	Abstract/ Paragraph 2

DISCUSSION				
Strengths and limitations	9	Provide a brief summary of the strengths and limitations of the evidence	Page2	Abstract/ Paragraph 3
Interpretation	10	Provide a general interpretation of the results and the important implications.	Page2	Abstract/ Paragraph 3
OTHER				
Funding	11	Indicate the primary source of funding for the review.	NA	NA
Registration	12	Provide the registration number and the registry name	Page2	Registration

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.

Table S3. Search Strategy

PubMed	**EMBASE**	**Cocharane Library**
#1 “computed tomography” OR “CT” OR “cardiac CT” OR “echocardiography” OR “transesophagel echocardiography” OR “TEE” OR “imaging” #2 “left atrial” #3 “thrombus” OR “thrombosis” #4 “detection” OR “diagnosis” OR “assessment” #5 “cohort” OR “observational” OR “prospective” OR “retrospective” OR “trial” OR “epidemiology” # 6 #1 AND #2 AND #3 AND #4 AND #5	#1 “computed tomography” OR “CT” OR “cardiac CT” OR “echocardiography” OR “transesophagel echocardiography” OR “TEE” OR “imaging” #2 “ left atrial thrombus” OR “left atrial thrombosis” #3 “detection” OR “diagnosis” OR “assessment” #4 “cohort” OR “observational” OR “prospective” OR “retrospective” OR “trial” OR “epidemiology” #5 1# AND #2 AND #3 AND #4	#1 “computed tomography” OR “CT” OR “cardiac CT” OR “echocardiography” OR “transesophagel echocardiography” OR “TEE” OR “imaging” #2 “ left atrial thrombus” OR “left atrial thrombosis” #3 “detection” OR “diagnosis” OR “assessment” #4 “cohort” OR “observational” OR “prospective” OR “retrospective” OR “trial” OR “epidemiology” #5 1# AND #2 AND #3 AND #4

Table S4. Summary of QUADAS-2 Assessment of Included Studies

Study, Year	Risk of Bias				Applicability Concerns		
	Patient Selection	Index Test	Reference Standard	Flow and Timing	Patient Selection	Index Test	Reference Standard
Achenbach 2004	Low	Low	Low	Low	Low	Low	Low
Kim 2007	Low	Low	Low	Low	Low	Low	Low
Shapiro 2007	Low	Low	Low	High	Low	Low	Low
Feuchtner 2008	Low	Low	Unclear	Low	Low	Low	Low
Tang 2008	Low	Low	Low	Low	Low	Low	Low
Hur 2008	Low	Low	Unclear	Low	Low	Low	Low
Patel 2008	Low	Unclear	Unclear	Low	Low	Low	Low
Martinez 2009	Low	Low	Low	Low	Low	Low	Low
Hur 2009	Low	Low	Unclear	Low	Low	Low	Low
Kim 2010	Low	Low	Low	Low	Low	Low	Low
Kapa 2010	Low	Low	Low	Low	Low	Low	Low
Maltagliati 2011	Unclear	Unclear	Unclear	Low	Low	Low	Low
Hur 2011	Low	Low	Unclear	Low	Low	Low	Low
Swait 2012	Low	Low	Low	Low	Low	Low	Low
Hur 2013	Low	Low	Low	Low	Low	Low	Low
Dorenkamp 2013	Low	Low	Low	Low	Low	Low	Low
Budoff 2014	Low	Low	Low	Low	Low	Low	Low
Hong 2014	Low	Low	Unclear	Low	Low	Low	Low
Hosmi 2016	Low	Low	Low	Low	Low	Low	Low
Lazoura 2016	Low	Low	Low	Low	Low	Low	Low
Wang 2016	Low	Low	Low	Low	Low	Low	Low
Kottmaier 2018	Low	Low	Unclear	Low	Low	Low	Low
Kuronuma 2019	Low	Low	Low	Low	Low	Low	Low
Li 2019	Low	Low	Unclear	Low	Low	Low	Low
Spagnolo 2020	Low	Low	Low	Low	Low	Low	Low
Guha 2020	Low	Low	Low	Low	Low	Low	Low
Zhai 2017	Low	Low	Low	Low	Low	Low	Low

QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies 2

Figure S1.

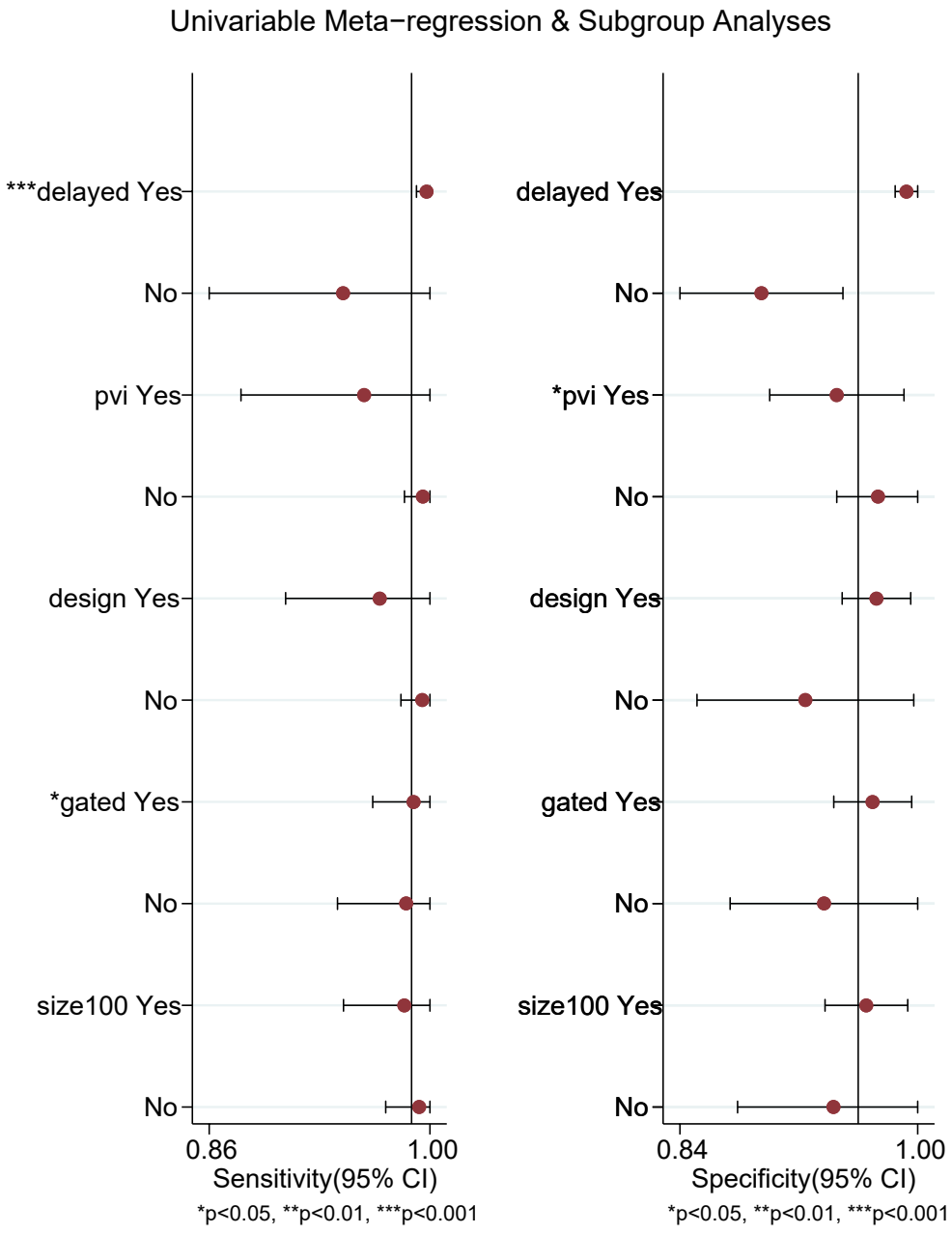
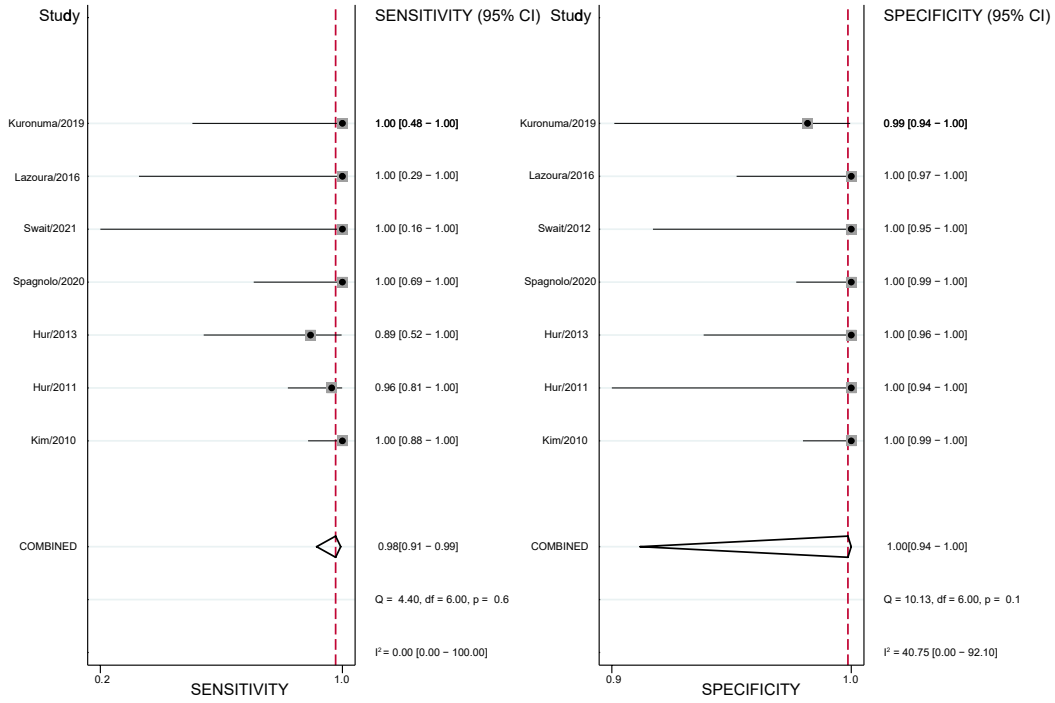

Univariable Meta−regression & Subgroup Analyses
***delayed Yes
No
pvi Yes
No
design Yes
No
*gated Yes
No
size100 Yes
No
0.86
1.00
Sensitivity(95% CI)
*p<0.05, **p<0.01, ***p<0.001
delayed Yes
No
*pvi Yes
No
design Yes
No
gated Yes
No
size100 Yes
No
0.84
1.00
Specificity(95% CI)
*p<0.05, **p<0.01, ***p<0.001

Figure S2.


Study
SENSITIVITY (95% CI)
Kuronuma/2019
1.00 [0.48 − 1.00]
Lazoura/2016
1.00 [0.29 − 1.00]
Swait/2021
1.00 [0.16 − 1.00]
Spagnolo/2020
1.00 [0.69 − 1.00]
Hur/2013
0.89 [0.52 − 1.00]
Hur/2011
0.96 [0.81 − 1.00]
Kim/2010
1.00 [0.88 − 1.00]
COMBINED
0.98[0.91 − 0.99]
Q = 4.40, df = 6.00, p = 0.6
I² = 0.00 [0.00 − 100.00]
0.2
1.0
SENSITIVITY
Study
SPECIFICITY (95% CI)
Kuronuma/2019
0.99 [0.94 − 1.00]
Lazoura/2016
1.00 [0.97 − 1.00]
Swait/2012
1.00 [0.95 − 1.00]
Spagnolo/2020
1.00 [0.99 − 1.00]
Hur/2013
1.00 [0.96 − 1.00]
Hur/2011
1.00 [0.94 − 1.00]
Kim/2010
1.00 [0.99 − 1.00]
COMBINED
1.00[0.94 − 1.00]
Q = 10.13, df = 6.00, p = 0.1
I² = 40.75 [0.00 − 92.10]
0.9
1.0
SPECIFICITY