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Diagnostic performance of CT and its key signs for COVID-19: A systematic review and meta-analysis

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Diagnostic performance of CT and its key signs for COVID-19: A systematic review and meta-analysis

Abstract

Purpose: To evaluate the diagnostic value of chest CT in 2019 novel coronavirus disease (COVID-19), using the reverse transcription polymerase chain reaction（RT-PCR）as a reference standard. At the same time, the imaging features of CT in confirmed COVID-19 patients would be summarized.

Methods: A comprehensive literature search of 5 electronic databases was performed. The pooled sensitivity, specificity, positive predictive value, and negative predictive value were calculated using the random-effects model and the summary receiver operating characteristic (SROC) curve. We also conducted a meta-analysis to estimate the pooled incidence of the chest CT imaging findings and the 95% confidence interval (95%CI). Meta-regression analysis was used to explore the source of heterogeneity.

Results: Overall, 25 articles comprising 4,857 patients were included. The pooled sensitivity of CT was 93% (95% CI, 89-96%) and specificity was 44% (95% CI, 27-62%). The area under the SROC curve was 0.94 (95% CI, 0.91-0.96). For the RT-PCR assay, the pooled sensitivity of the initial test and the missed diagnosis rate after the second-round test were 76% (95% CI: 59-89%; I^2=96%) and 26% (95% CI: 14-39%; I^2=45%), respectively. According to the subgroup analysis, the diagnostic sensitivity of CT in Hubei was higher than that in other regions. Besides, the most

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common patterns on CT imaging finding was ground glass opacities (GGO) 58% (95% CI: 49-70%), followed by air bronchogram 51% (95% CI: 31-70%). Lesions were inclined to distribute in peripheral 64% (95% CI: 49-78%), and the incidence of bilateral lung involvement was 69% (95% CI: 58-79%).

Conclusions: There were still several cases of missed diagnosis after multiple RT-PCR examinations. In high-prevalence areas, CT could be recommended as an auxiliary screening method for RT-PCR.

Key points:

1. Taking RT-PCR as the reference standard, the pooled sensitivity of CT was 93% (95% CI, 89-96%) and the specificity was 44% (95% CI, 27-62%). The area under the SROC curve was 0.94 (95% CI, 0.91-0.96).

2. For the RT-PCR assay, the pooled sensitivity of the initial test and the missed diagnosis rate after the second-round test were 76% (95% CI: 59-89%) and 26% (95% CI: 14-39%), respectively.

3. GGO was the key sign of the CT imaging, with an incidence of 58% (95% CI: 49-70%) in patients with SARS-CoV-2 infection. Pneumonia lesions were inclined to distribute in peripheral 64% (95% CI: 49-78%) and bilateral 69% (95% CI: 58-79%) lung lobes.

Keywords:

COVID-19; chest CT; diagnostic performance; imaging features; RT-PCR.

Abbreviations:

COVID-19= 2019 novel coronavirus disease

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RT-PCR= reverse transcription polymerase chain reaction

SROC= summary receiver operating characteristic

GGO= ground glass opacities

TP= true positive

FP= false positive

FN= false negative

TN= true negative

AUC= area under the curves

1. Introduction

Since December 2019, an unidentified pneumonia with fever, cough, and myalgia as clinical presentations emerged in some hospitals in Hubei, China [1]. Deep sequencing detection and analysis of respiratory samples revealed a species of novel coronavirus, known as acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2]. The disease, named COVID-19, can progress to acute respiratory distress syndrome in severe cases, that requires intensive care unit admission and oxygen therapy [3]. As of April 23, 2020, the Corona Virus has been spreading rapidly around the world, with more than 2475723 clinical-confirmed cases and 169151 confirmed death [4]. In the absence of a clear vaccine and specific antiviral treatments, early diagnosis and interrupting transmission became essential in dealing with the new emerging SARS-CoV-2.

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The current recommendations for the diagnosis of COVID-19 are laboratory examinations such as nasopharyngeal and oropharyngeal swab tests. However, the problem of the false-negative RT-PCR assay for detecting SARS-CoV-2 was exposed in clinical work. It may be related to various aspects of nucleic acid detection experiments, such as sample collection, laboratory error, and so on. Until now, there are a variety of PCR kits available, with sensitivity ranging from 45% to 60%; thus, in the early stage of the disease, repeated tests may be required to obtain a definite diagnosis [5]. It is not easy to implement in global resource-limited settings. Since it mainly involved the respiratory system, a chest CT examination was strongly recommended for the preliminary assessment and follow-up of suspicious COVID-19 patients [6]. As a conventional imaging tool for diagnosing pneumonia, CT is relatively easier to operate and can quickly obtain diagnostic results. However, CT findings regarding these points showed variable diagnostic performance. For example, numerous cases had noteworthy CT findings despite a preliminary false-negative RT-PCR analysis results [7, 8]. Furthermore, several studies reported that CT had high sensitivity for COVID-19 [7, 9, 10], but a recent study including 121 cases found 56% of patients had a normal CT finding in the early stage of infection [11]. Hope et al. [12] described that CT did not add value to the diagnosis, while medical staff and CT scanners might also become infection vectors for other vulnerable patients who needed imaging.

Considering the inconsistency of the existing literature, we conducted a systematic review regarding the diagnostic performance of CT for COVID-19. At the

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same time, with the increasing global attention to COVID-19 outbreaks, a better understanding of chest CT imaging features is critical to ensuring patient management and treatment effectiveness. Therefore, we compiled the information to summarize the key signs of CT in patients with COVID-19.

2. Methods

This systematic review was conducted according to the guidelines of Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA). The protocol was registered on PROSPERO (CRD42020179689) [13].

2.1 literature searches

Searches were conducted in five medical databases including three English databases (PubMed, Embase, and Web of Science) and two Chinese databases (China Biology Medicine disc, and China National Knowledge Infrastructure). The search terms used: “COVID-19”, “2019 novel coronavirus disease”, “COVID-19 pandemic”, “COVID-19 virus infection”, “coronavirus disease-19”, “2019 novel coronavirus infection”, “2019-nCoV infection”, “coronavirus disease 2019”, “2019-nCoV disease”, “COVID-19 virus disease”, and “CT”, “Computed Tomography”, “Imaging”, “radiological”. The searches were concluded by April 16, 2020, and three independent reviewers evaluated search results.

2.2 Eligibility criteria

The included articles were subject to the following criteria: (a) Publications were full-text original articles (b) The study took the RT-PCR assay as a reference standard

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and proposed the sensitivity and/or specificity of CT. (c) sufficient data available to the chest CT imaging characteristic of patients with SARS-CoV-2 infection. The exclusion criteria were as follows: (a) insufficient relevant result parameters and research data about chest CT. (b) reviews of the literature, case reports, or series. (c) literature with restrictions on the type of population or age. (c) study with a sample size less than 5. For studies with overlapping data, only data from the study with the most appropriate date or the largest sample size was included.

2.3. Data Extraction and quality evaluation

Two authors（Wu XT，Qin WY）used standardized data tables to extract the following data independently. (1) study characteristics: authors, journal, date (Month/Day), the region of studies, number of patients, study design (prospective or retrospective), and basic characteristics of the reference standard and index test. (2) diagnostic performance of RT-PCR and CT: When possible, we collect data including true negatives, true positives, false negatives, and false positives about CT. Furthermore, information about the sensitivity of the RT-PCR was collected. (3) patient characteristics: gender, mean or median age, epidemiological history, fever, cough, chest CT imaging features (GGO, consolidation, crazy paving pattern, airways abnormalities, air bronchogram, interlobular septal thickening, lymphadenopathy, pleural effusion, lesion location, and distribution).

An author (Zhong YH) extracted data on the quality of study and the risk of bias. We evaluate the quality of this meta-analysis using the tool of Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) [14].

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2.4 Statistical analysis

The sensitivity and/or specificity of CT in suspected COVID-19 patients were obtained from each study. We considered it as positive when pulmonary infiltration could be seen on CT：A patient that RT-PCR confirmed as COVID-19 was considered a true positive (TP) case, whereas one or more RT-PCR assay showed negative was considered a false positive (FP) case. No abnormality in chest CT was considered negative: A patient that RT-PCR confirmed as COVID-19 was considered a false negative (FN) case, whereas one or more PCR assay showed negative was considered a true negative (TN) case. Sensitivity was determined based on formula TP/(TP+FN) and specificity based on formula TN/(TN+FP). Incidences were pooled by the Freeman-Tukey Double arcsine transformation [15]. Pooled data and 95% CI were carried out by a random effect model. The overall diagnostic accuracy was graphically exhibited by the area under the SROC curves [16].

We used the I^2 statistic and Cochran's Q-test to assess heterogeneity between studies. Several covariates were as follows：(1)region of studies (Wuhan or not）;（2）size of the study population (≥100 or < 100); (3) Studies mentioned the time interval between reference standard and CT (yes or not). Publication bias was estimated using the Deeks funnel plot asymmetry test. All data analysis was conducted using the Stata 15.1 and “meta” package in R software version 3.6.3.

3. Results

3.1 Study Selection and characteristics

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The process of study selection is described in Figure 1. The overall computer study search of the 5 databases yielded 1518 potentially relevant records. After removing duplicates and irrelevancies, there was still 63 literature, of which 723 were excluded base on titles or abstracts. At last, we read the full text of the remaining 63 documents carefully and excluded 38 studies. Therefore, a total of 25 papers were selected in this study (Table 1) [7, 9-11, 17-37].

Table1-2 list the characteristics of the included studies. This review of 25 studies included 4,857 patients, published from February 12, 2020, to April 16, 2020, most of them from China and two from Italy and Japan [9, 21]. Except for two studies [9, 18], the designs were all retrospective studies. Taking RT-PCR as the standard, 25 studies reported the diagnostic sensitivity of CT, and 11 studies reported the diagnostic specificity of CT [5, 9, 17-19, 21, 23, 26, 35-37]. Furthermore, there are 10 studies reported the diagnostic sensitivity of the initial PCR assay [7, 10, 11, 18, 22, 29, 32, 34-36], while 5 of them mentioned the rate of missed diagnosis after the second tests [10, 22, 29, 32, 35]. We analyzed a total of 33 variables for the meta-analyses (Table 3).

3.2 Quality assessment and Publication bias

In general, according to QUADAS-2, the 25 studies in this meta-analysis showed moderate methodological quality (Figure 2). Since most of the literature we included were retrospective studies, there was a high risk of bias for patient selection in 8 (32%) studies. The index tests of 14 studies showed low risk, while the rest of the studies did not know the risk of bias due to lack of information. The blind interpretation of index tests and reference standards in 12 studies is unclear. In several studies, the lack of

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description of reference standards was not considered to raise concerns about the applicability of the results.

We evaluated the publication bias of 11 studies, which detailed the diagnostic performance of CT (true positive, false positive, true negative, and false negative). As a result, the funnel plot appeared to be symmetrical, with a P-value of 0.87, indicating a low risk of publication bias (Figure 3).

3.3 Meta-analysis results

3.31 Demographical characteristics and Clinical features

The mean or median age of patients diagnosed with COVID-19 ranged from 41 to 58, and the proportion of males was 57% (95%CI 62-72%). A total of 81% (95%CI 72-89%) of patients had an epidemiological history. The incidence of fever was 79% (95%CI 66-90%), and that of cough was 58% (95%CI 48-68%).

3.32 Pooled Diagnostic Performance

For these 25 studies, the diagnostic sensitivity and specificity of CT for COVID-19 ranged from 69% to 100% and from 0% to 96%, with pooled estimates of 93% (95% CI, 89-96%) and 44% (95% CI, 27-62%) (Figure 4), respectively. The pooled positive predictive value and negative predictive value of CT for COVID-19 were 0.55 (95% CI, 0.41-0.68) and 0.97 (95% CI, 0.91-1.00), respectively. The Q-test $P<0.01$ and $I^2>50\%$ indicated heterogeneity of sensitivity and specificity between studies. We plotted the SROC curve to display the diagnosis results graphically and the area under the SROC curve was 0.94 (95% CI, 0.91-0.96). The SROC curve did not suggest that there is a threshold effect (Figure 5).

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For the 10 studies with repeated PCR assay, the pooled sensitivity of the initial RT-PCR test in diagnosis of COVID-19 was 76% (95% CI: 59-89%; I^2=96%). Besides, 5 studies conducted three or more PCR tests for patients with detailed records of each positive result. For suspected cases with initially negative RT-PCR test, the missed diagnosis rate of COVID-19 when only took second-round RT-PCR examination was 26% (95% CI: 14-39%; I^2=45%) (Figure 6).

3.33 Imaging features of Chest CT

GGO was a key sign of CT imaging, and its incidence was 58% (95% CI: 49-70%) in patients with SARS-CoV-2 infection. Other common signs included air bronchogram 51% (95% CI: 31-70%), interlobular septal thickening 32% (95% CI: 17-49%), airways abnormalities 31% (95% CI: 7-61%), linear opacities 29% (95% CI: 3-66%), consolidation 20% (95%CI: 7-37%), and crazy-paving pattern 17% (95 CI: 4-36%). We found that nodules, pleural effusion and lymphadenopathy are less frequent findings in this meta-analysis, and their incidences were 5% (95% CI: 1-12%), 4% (95% CI: 2-6%) and 4% (95% CI: 0-10%), respectively.

Pneumonia lesions were inclined to distribute in peripheral 64% (95% CI: 49-78%) and bilateral 69% (95% CI: 58-79%) lung lobes. The incidence of two or more lobes affected and a simultaneous involvement of all five lobes was 61% (95% CI: 48-74%) and 48% (95% CI: 30-66%), respectively. For each lung lobe, the right lower lobe and the left lower lobe had the highest frequency of involvement, with an incidence of 51% (95% CI: 35-67%) and 49% (95% CI: 34-64%), respectively.

3.4 meta-regression analyses

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The results of heterogeneity exploration were presented in Table 4. Among several covariates assessed for the sensitivity of chest CT, only the study region significantly affected the heterogeneity ($p < 0.05$). Moreover, the sample size and time interval between reference standard and CT did not show an effect on CT sensitivity (p = 0.68-0.84). For the diagnostic sensitivity of CT, none of the three variables showed significant effect on heterogeneity (p = 0.07- 0.81). Both regions and sample sizes did not affect the premier sensitivity of RT-PCR (p = 0.09- 0.39).

4. Discussion

In this study, the meta-analysis was used to quantify the diagnostic performance of CT for COVID-19. We found that the comprehensive diagnostic performance of CT for COVID-19 was good. Specifically, the pooled sensitivity and specificity were 93% (95% CI, 89-96%) and 44% (95% CI, 27-62%), respectively, with an AUC of 0.94 (95% CI,0.91-0.96). However, the diagnostic specificity of CT for patients suspected of being infected with SARS-CoV-2 was low. Our results showed that the pooled sensitivity of the initial RT-PCR assay was 76% (95% CI: 59-89%; I^2=96%). It is worth noting that even after taking second-round PCR tests, about 26% (95% CI: 14-39%) of patients who have been infected with coronavirus will still be missed. The positive findings of chest CT images suggest acute alveolitis, which is a similar common manifestation of various viral pneumonia, partial bacterial pneumonia and lung damage caused by immune diseases, but not a specific sign of COVID-19 [38]. COVID-19 is an infectious disease, which still needs to be confirmed by etiological testing. Because imaging

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features of CT might be similar in different diseases, it could not replace the etiological examination in the diagnosis of COVID-19.

Although the specificity of CT was not high, our results in this meta-analysis indicated that CT was indispensable in screening patient with 2019 novel coronavirus when considering the following factors: (1) given the current global outbreak of COVID-19, RT-PCR testing is time-consuming and the kits in some areas are insufficient, which will lead to the gathering of people in emergency departments and the flow of sources of infection. CT examination has the advantages of rapid, objective, and reproducible; (2) there may be false-negative cases in RT-PCR assay, so using the RT-PCR for screening alone may result in a certain number of missed diagnoses. The high sensitivity of CT can compensate for the deficiency of RT-PCR screening; (3) PCR testing requires a complex sample collection process. Some patients have more virus in the nasopharynx and some in the oropharynx, while a few patients can only find the virus in bronchoalveolar lavage fluid, so it is prone to sampling errors; (4) different CT image manifestations can be used to assess the clinical course and severity of the disease[39]. Of course, there are some shortcomings in CT inspection, including poor air permeability in the operating room and cumbersome disinfection. These may lead to potential cross-infection. Therefore, we can consider adopting time-sequence, low-to-high risk order, and strict disinfection to reduce the risk.

Ground-glass opacities were the most typical manifestation in this study. Most of the lesions showed peripheral distribution with or without interlobular septal thickening. The mechanism of these changes may be the fluid exudation in the alveolar cavity

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caused by telangiectasia of the alveolar septum and interstitial edema of the interlobular septum [40]. In addition, our study showed that the incidence of air bronchogram is high, and consolidation is relatively rare. However, the main feature of pulmonary manifestations in SARS was large pulmonary consolidation, which was often accompanied by obvious air bronchogram [41]. Liu et al analyzed the CT findings of 73 patients with SARS-CoV-2 infection and found that pulmonary consolidation mainly occurred in severe and critically ill patients [40]. This meta-analysis suggested that about 4% of patients had pleural effusion, which might be a sign of a poor prognosis [42]. COVID-19 also needs to be distinguished from MERS (Middle East respiratory syndrome). Both of them showed multiple ground glass shadow lesions under the bilateral pleura [43].

There was considerable heterogeneity between the literature included in our study. According to the results of meta-regression analysis, in high-prevalence regions, the diagnostic sensitivity of CT for COVID-19 was significantly higher than that in low-prevalence regions. It meant that CT could be used as an effective screening tool for COVID-19 outbreak areas. However, we have not yet been able to explore the factors that affect the specificity of CT and the sensitivity of the initial RT-PCR test. More studies are needed to confirm the involved factors, such as the internal diagnostic thresholds of chest CT imaging, the turn-around time of sample in transportation, and the type of kits.

Our review had several limitations. Only two documents came from non-Chinese regions, and the detailed information of CT in different regions was

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lacking. Information about the diagnostic specificity of CT could not be obtained from most studies. Therefore, we only included 11 articles with 2 × 2 tables to draw the SROC curve. Some studies did not mention the time of CT and RT-PCR examination. When exploring heterogeneity, the literature with the interval between CT and PCR examinations less than two weeks was divided into one group, and the rest constituted another group. It was best to obtain the specific time interval information to fully understand the factors influencing diagnostic sensitivity of CT. In addition, the study did not obtain sufficient CT image data to explain the relationship between imaging manifestations and duration of Infection.

In conclusion, CT was highly sensitive in the diagnosis of COVID-19. There were still several cases of missed diagnosis after multiple RT-PCR examinations. In high-prevalence areas, CT can be recommended as an auxiliary screening method for RT-PCR. In the future, large samples and high-quality prospective studies can make up for the deficiency of the current small sample size and further verify the results.

Acknowledgments

The authors state that this work has not received any funding.

Declaration of Competing Interest

The authors in this study have no conflict of interest.

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Figure and table legends

Figure 1: Flow diagram for study selection.

Figure 2: Quality Assessment of Diagnostic Accuracy Studies (QUADAS)-2 graphs of CT in diagnosing COVID-19.

Figure 3: Deeks' funnel plot of 11 included studies (p = 0.87 in Deeks' asymmetry test).

Figure 4: Forest plots of the diagnostic performance of chest CT. A: A plot of 25 individual studies and pooled sensitivity of chest CT in patients with suspicious COVID-19. B: A plot of 11 individual studies and pooled specificity of chest CT in patients with suspicious COVID-19.

Figure 5: Summary receiver operating curves (SROC) for the diagnostic performance of CT.

Figure 6: Forest plots of the diagnostic performance of chest CT. A: A plot of 10 individual studies and pooled sensitivity of the initial RT-PCR assay in patients with suspicious COVID-19. B: A plot of 5 individual studies and pooled rate of missed diagnosis after the second-round RT-PCR examinations.

Table 1: The characteristics of the literature included in meta-analysis. M/D=

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Month/Day, RT-PCR= reverse transcriptase polymerase chain reaction. Sample collection: #1= bronchoalveolar lavage; #2= endotracheal aspirate; #3= nasopharyngeal swab; #4= oropharyngeal swab; ＃5= sputum samples; ＃6= specimens from blood.

Table 2: Diagnostic performance of chest CT for COVID-19 using the RT-PCR as the reference standard. TP=true positive, TN=true negative, FP=false positive, FN=false negative, PPV= positive predictive value, NPV= negative predictive value.

Table 3: Meta-analysis outcomes (random-effects model). 95% CI = 95% confidence interval.

Table 4: Results of meta-regression analysis. 95% CI = 95% confidence interval.

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Table 1. The characteristics of the literature included in meta-analysis

						Reference standard		CT			
Author	**Journal**	**Date M/D**	**Region/Country**	**N**	**Study design**	**Method of RT-PCR**	**CT-Reference interval**	**Reader Number**	**Consensus reading**	**slice thickness**	**reference**
Bernheim et al.	Radiology	02/20	Nanchang et al/China	121	Retrospective	#1#2#3#4	< 2 weeks	2	Consensus	1/8mm	11
Caruso et al.	Radiology	04/03	Rome/ Italy	158	Prospective	#3#4#6	-	2	-	1.25mm	9
Xie et al.	Radiology	02/12	Hunan/China	167	Retrospective	#4	0 days	2	Consensus	-	7
Guan et al.	N Engl J Med	02/28	30 provinces /China	1099	Retrospective	#3#4	-	2	Consensus	-	24
Wu et al.	Clin Infect Dis	02/29	Jiangsu/China	80	Retrospective	#3#4	-	-	-	-	31
Ai et al.	Radiology	02/26	Wuhan/China	1014	Retrospective	#4	< 7days	2	Consensus	10mm	27
Feng et al.	Guangdong Medical Journal	02/28	Wuhan/China	38	Retrospective	#3#4	0 days	-	-	1mm	21
Long et al.	Eur J Radiol	03/25	Yichang/China	87	Retrospective	-	0 days	2	Consensus	2mm	34
Li et al.	AJR Am J Roentgenol	03/04	Wuhan/China	51	Retrospective	#4	-	2	Consensus	1.25mm	19
Fang et al.	Radiology	02/19	Taizhou/China	51	Retrospective	#4#5	< 3days	-	-	5mm	10
Zhang et al.	Chin J Tuberc Respir Dis	03/17	Ningxia/China	34	Retrospective	#3	-	-	-	-	28
Li K et al.	Eur Radiol	03/25	Zhuhai/China	78	Retrospective	#3	-	2	Consensus	1mm	30
Xiong et al.	Chin J Nosocomiology	03/11	Hunan/China	47	Prospective	#3	-	2	Consensus	-	17
Xu et al.	Eur.J.Nucl. Med. Mol. Imaging	02/28	Guangzhou/China	90	Retrospective	-	-	2	Consensus	1mm	23
Deng et al.	Chin J Radiol	03/-	Wuhan/China	587	Retrospective	#4#5	-	2	Consensus	1mm	16
Wang et al.	Clinical Radiology	03/23	Xiaogan/China	114	Retrospective	-	-	-	-	1mm	29
Yang et al.	Chin J infect	03/-	Nanchang /China	274	Retrospective	-	-	2	Independent	-	22
Dai et al.	Int. J. Infect. Dis	04/06	Jiangsu/China	234	Retrospective	#3#4#6	-	2	Independent	5mm	33
Zhu et al.	J. Med. Virol	03/13	Anhui/China	116	Retrospective	#3#4	0 days	2	Independent	-	25
Yang W et al.	J. Infect	02/26	Wenzhou/China	149	Retrospective	#3#4#5	-	2	Consensus	1-1.5mm	26
Shi et al.	Lancet Infect Dis	02/24	Wuhan/China	81	Retrospective	#3#4	-	2	Consensus	-	32
Himoto et al.	Jpn J Radiol	03/30	-/ Japan	21	Retrospective	-	-	2	Independent	1-7mm	20

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Cheng et al.	AJR Am J Roentgenol	03/14	Shanghai/China	38	Retrospective	# 3 # 4	-	3	Consensus	1-1.5mm	18
He et al.	Respir Med	04/16	Shenzhen//China	82	Retrospective	# 1 # 2 # 3 # 4	0 days	2	Independent	1mm	35
Li Y et al	Chin J Emerg Med	04/-	Beijing/China	46	Retrospective	#3	-	-	-	-	36

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Table 2: Diagnostic performance of chest CT for COVID-19 using the RT-PCR as the reference standard.

		Chest CT									Positive result of RT-PCR				
Author	**N**	TP	TN	FP	FN	Sensitivity	Specificity	PPV	NPV	Accuracy	The first time	The Second time	The third or more times	Eventually positive result	reference
Bernheim et al.	121	94	-	-	27	0.78	-	-	-	-	90	-	-	121	11
Caruso et al.	158	60	54	42	2	0.97	0.56	0.59	0.96	0.72	-	-	-	62	9
Xie et al.	167	160	-	-	7	0.96	-	-	-	-	162	-	-	167	7
Guan et al.	1099	840	-	-	135	0.86	-	-	-	-	-	-	-	1099	24
Wu et al.	80	55	-	-	25	0.69	-	-	-	-	41	30	9	80	31
Ai et al.	1014	580	105	308	21	0.97	0.25	0.65	0.83	0.68	-	-	-	601	27
Feng et al.	38	37	-	-	1	0.97	-	-	-	-	9	25	4	38	21
Long et al.	87	35	0	51	1	0.97	0.00	0.41	0.00	0.40	30	3	3	36	34
Li et al.	51	49	-	-	2	0.96	-	-	-	-	-	-	-	51	19
Fang et al.	51	50	-	-	1	0.98	-	-	-	-	36	12	3	51	10
Zhang et al.	34	29	-	-	5	0.85	-	-	-	-	22	6	6	34	28
Li K et al.	78	56	-	-	22	0.72	-	-	-	-	-	-	-	78	30
Xiong et al.	47	19	19	8	1	0.95	0.70	0.70	0.95	0.81	14	-	-	20	17
Xu et al.	90	69	-	-	21	0.77	-	-	-	-	-	-	-	90	23
Deng et al.	587	423	83	71	10	0.98	0.54	0.86	0.89	0.86	-	-	-	433	16
Wang et al.	114	110	-	-	4	0.96	-	-	-	-	-	-	-	114	29
Yang et al.	274	48	151	70	5	0.91	0.68	0.41	0.97	0.73	-	-	-	53	22
Dai et al.	234	219	-	-	15	0.94	-	-	-	-	228	-	-	234	33
Zhu et al.	116	30	28	56	2	0.94	0.33	0.31	0.93	0.50	-	-	-	32	25
Yang W et al.	149	132	-	-	17	0.89	-	-	-	-	-	-	-	149	26
Shi et al.	81	81	-	-	0	1.00	-	-	-	-	-	-	-	81	32
Himoto et al.	21	6	3	12	0	1.00	0.20	0.33	1.00	0.43	-	-	-	6	20
Cheng et al.	38	11	5	22	0	1.00	0.19	0.33	1.00	0.42	-	-	-	11	18
He et al.	82	26	46	2	8	0.76	0.96	0.93	0.85	0.88	27	-	-	34	35
Li Y et al	46	9	21	16	0	1.00	0.57	0.36	1.00	0.65	-	-	-	9	36

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Table 3: Meta-analysis outcomes (random-effects model).

Variable	**Pooled Proportion**	**95% CI**	**p**	**I^2 (%)**	**t^2**
Diagnostic performance of CT					
Sensitivity of CT	0.93	0.89-0.96	P<0.01	89	0.0164
Specificity of CT	0.44	0.27-0.62	P<0.01	97	0.0808
PPV	0.55	0.41-0.68	P<0.01	96	0.0450
NPV	0.97	0.91-1.00	P<0.01	65	0.0099
Diagnostic performance of RT-PCR					
Sensitivity of initial RT-PCR assay	0.76	0.59-0.89	P<0.01	96	0.0762
Missed diagnosis rate after the second-round RT-PCR assay	0.26	0.14-0.39	P=0.12	45	0.0106
Imaging features of chest CT					
GGO	0.58	0.45-0.70	P<0.01	94	0.0401
Air bronchogram	0.51	0.31-0.70	P<0.01	96	0.0720
Interlobular septal thickening	0.32	0.17-0.49	P<0.01	95	0.0418
Airways abnormalities	0.31	0.07-0.61	P<0.01	98	0.1724
Linear opacities	0.29	0.03-0.66	P<0.01	97	0.1077
Consolidation	0.20	0.07-0.37	P<0.01	94	0.0660
Crazy-paving pattern	0.17	0.04-0.36	P<0.01	95	0.0714
Nodules	0.05	0.01-0.12	P<0.01	88	0.0274
Pleural effusion	0.04	0.02-0.06	P<0.01	63	0.0054
Lymphadenopathy	0.04	0.00-0.10	P<0.01	92	0.0375
Bilateral lung distribution	0.69	0.58-0.79	P<0.01	94	0.0291
Peripheral distribution	0.64	0.49-0.78	P<0.01	94	0.0467
1 lobe involved	0.09	0.06-0.12	P=0.24	25	0.0009
2 lobes involved	0.06	0.03-0.09	P=0.26	25	0.0012
3 lobes involved	0.08	0.05-0.12	P=0.28	21	0.0010
4 lobes involved	0.11	0.08-0.15	P=0.42	0	0.0000
5 lobes involved	0.48	0.30-0.66	P<0.01	92	0.0432
More than 2 lobes involved	0.61	0.48-0.74	P<0.01	90	0.0212
Right upper lobe	0.38	0.29-0.49	P<0.01	82	0.0110
Right middle lobe	0.35	0.28-0.43	P<0.01	70	0.0055
Right lower lobe	0.51	0.35-0.67	P<0.01	93	0.0305
Left upper lobe	0.41	0.30-0.54	P<0.01	88	0.0169
Left lower lobe	0.49	0.34-0.64	P<0.01	92	0.0283
Clinical characteristics					
Gender(male)	0.57	0.52-0.62	P<0.01	74	0.0067
Epidemiological history	0.81	0.72-0.89	P<0.01	91	0.0318
Fever	0.79	0.66-0.90	P<0.01	97	0.0696
Cough	0.58	0.48-0.68	P<0.01	93	0.0295

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Table 4: Results of meta-regression analysis.

Variable	No. of studies	Pooled Sensitivity of CT (95% CI)	P value	No. of studies	Pooled Specificity of CT (95% Cl)	P value	No. of studies	Pooled Sensitivity of initial RT-PCR (95% CI)	P value
Hubei/China			0.03			0.07			0.39
Yes	8	0.96 (0.92; 0.99)		3	0.22 (0.02; 0.54)		2	0.54 (0.04; 0.99)	
No	17	0.90 (0.84; 0.95)		8	0.54 (0.37; 0.71)		8	0.81 (0.65; 0.92)	
Sample size			0.84			0.81			0.09
≥100	12	0.92 (0.87; 0.95)		5	0.47 (0.29; 0.66)		4	0.87 (0.68; 0.99)	
<100	13	0.94 (0.87; 0.99)		6	0.41 (0.06; 0.82)		6	0.66 (0.47; 0.82)	
CT-Reference interval			0.68			0.43	-	-	-
Mentioned (≤2 weeks)	8	0.93 (0.87; 0.98)		4	0.35 (0.06; 0.73)		-	-	-
Not mentioned	17	0.92 (0.88; 0.96)		7	0.51 (0.39; 0.63)		-	-	-

Figure

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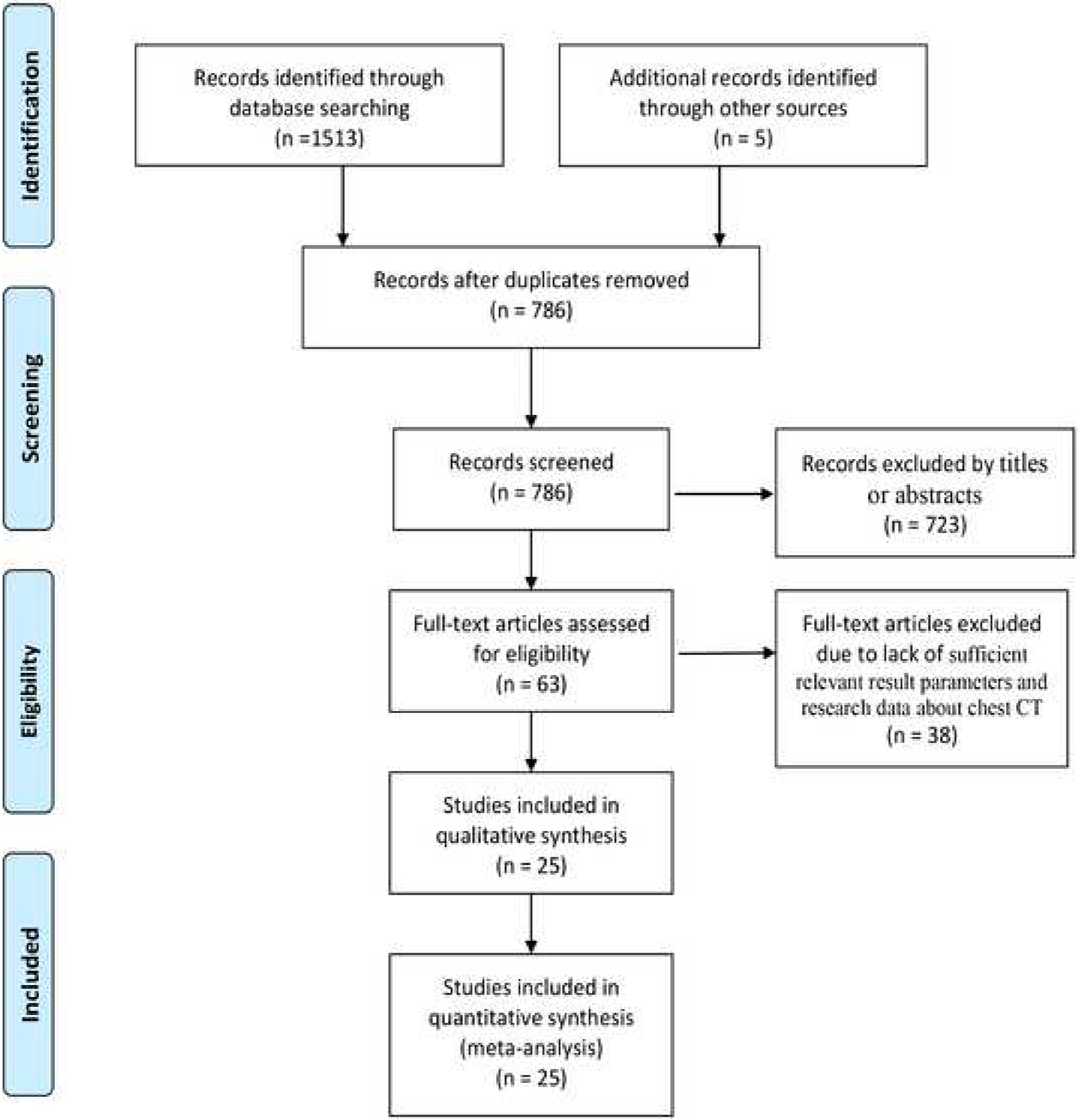

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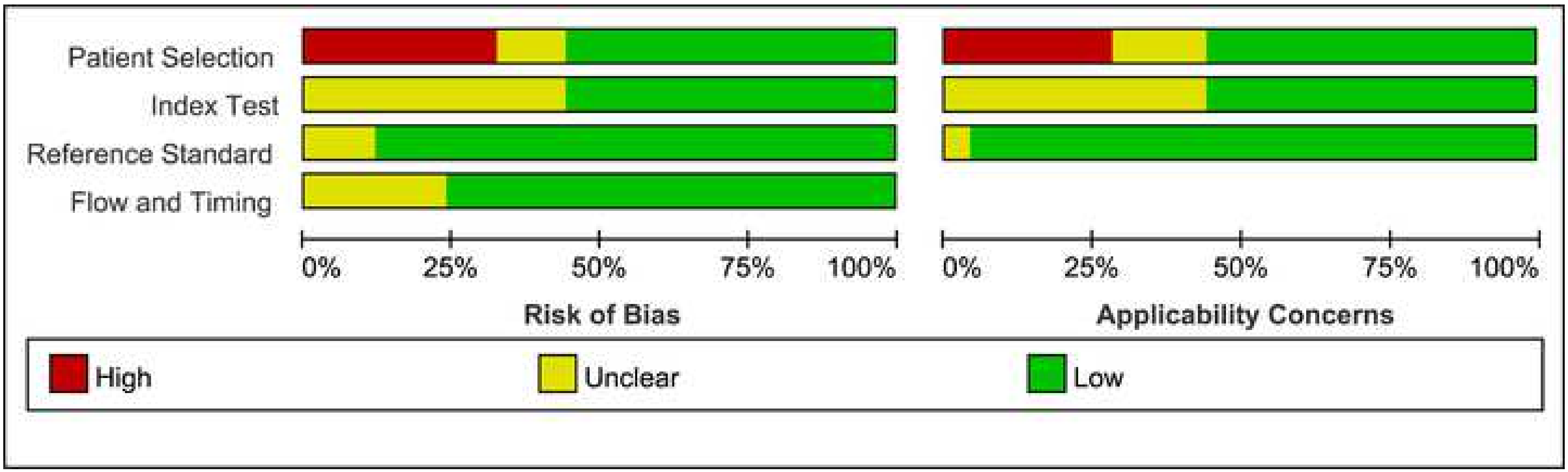

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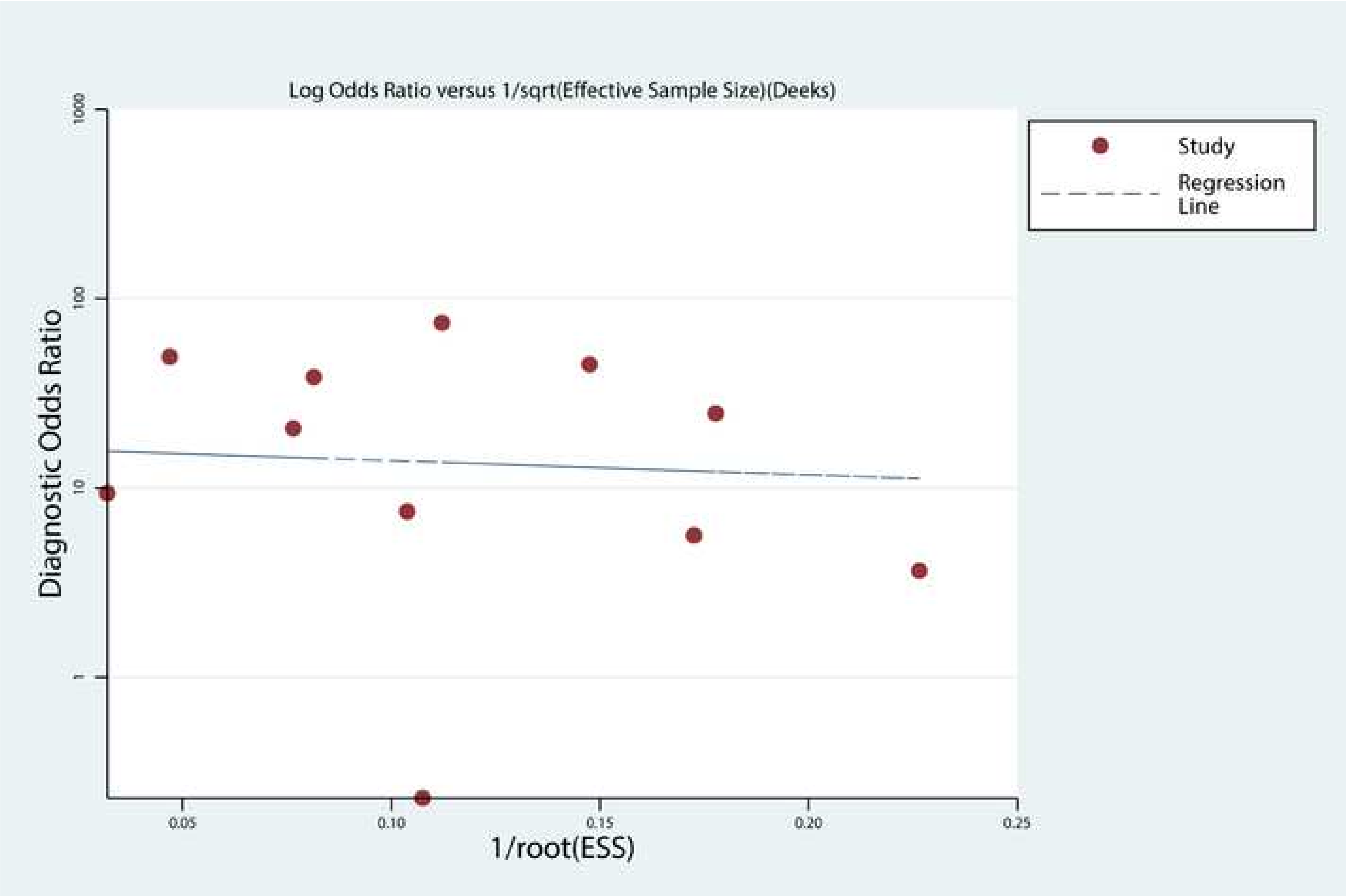

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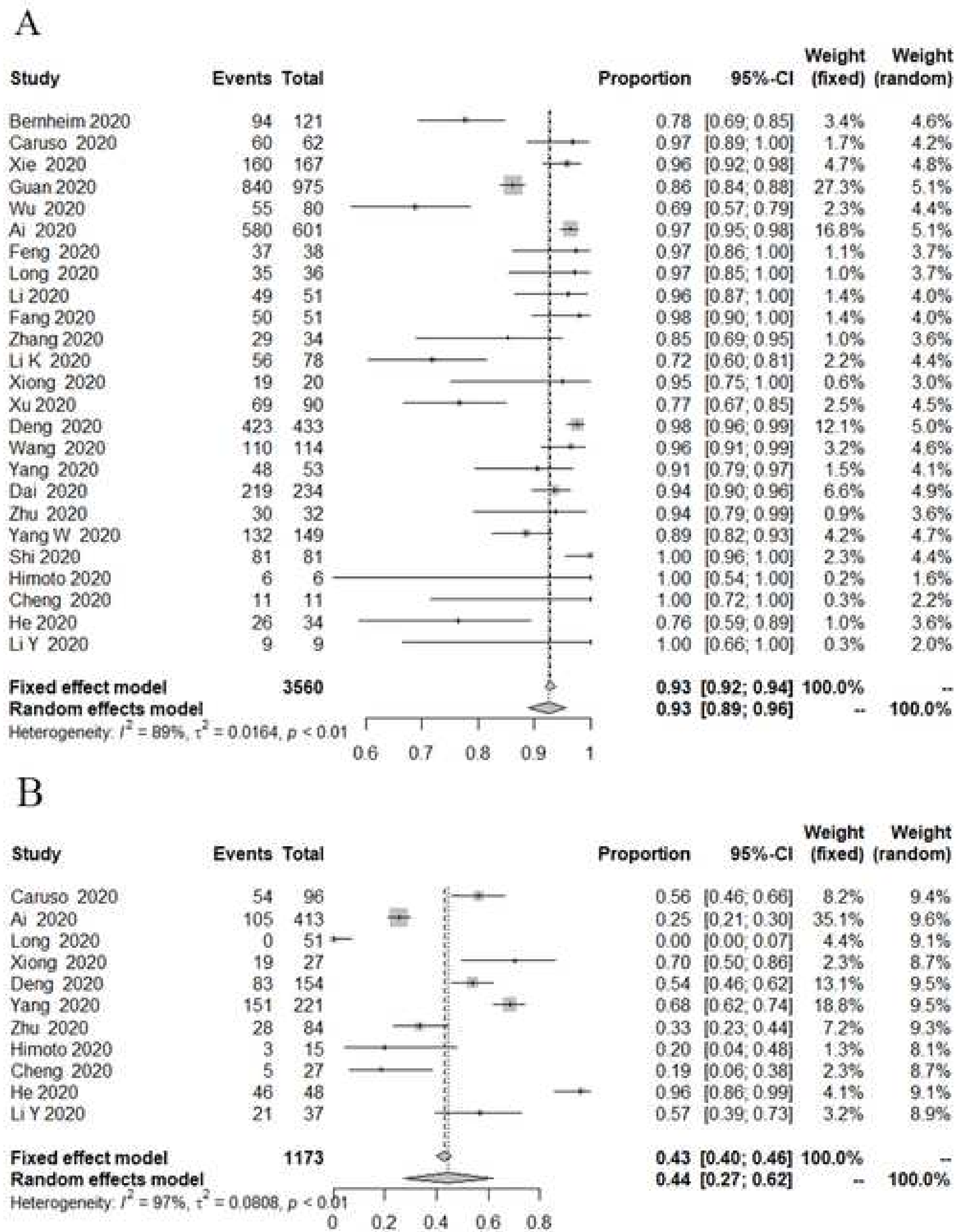

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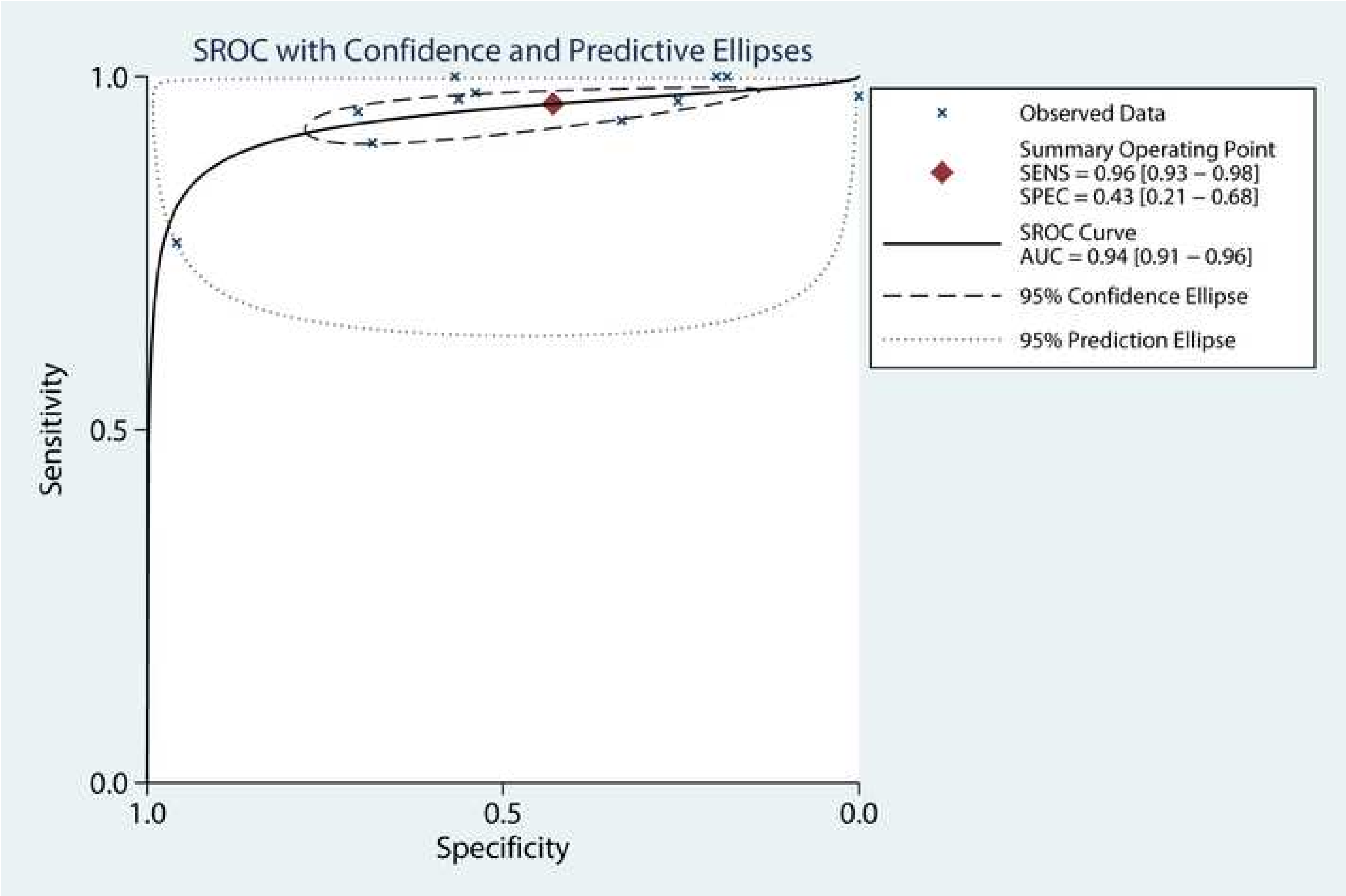

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