Chest CT for Detecting COVID-19: A Systematic Review and Meta-Analysis of Diagnostic Accuracy

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Abstract

OBJECTIVE: The purpose of this article was to perform a systematic review and meta- analysis regarding the diagnostic test accuracy of chest CT for detecting Coronavirus Disease 2019 (COVID-19).

METHODS: PubMed, EMBASE, Web of Science and CNKI were searched up to March 12, 2020. We included studies providing information regarding diagnostic test accuracy of chest CT for COVID-19 detection. The methodologic quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies−2 tool. Sensitivity and specificity were pooled.

RESULTS: Ten studies (n = 2657 patients) were included. The risks of bias in all studies were moderate in general. Pooled sensitivity was 93% (95% CI: 85 - 97%), and only one study reported specificity (25%, 95% CI:22-30%). There was substantial heterogeneity according to the Cochran Q test (p < 0.01) and Higgins $I2$ heterogeneity index (96% for sensitivity). After dividing the studies into two groups based on the study site, we found that the sensitivity of chest CT was great in Wuhan (the most affected city by the epidemic) and the sensitivity values were very close to each other (97%, 96% and 99%, respectively). In the regions other than Wuhan, the sensitivity varied from 69% to 98%.

CONCLUSION: Chest CT offers the great sensitivity for detecting COVID-19, especially in region with severe epidemic situation. However, the specificity is low. In the context of emergency disease control, chest CT provide a fast, convenient and effective method to early recognize suspicious cases and might contribute to confine epidemic.

Abbreviations

COVID-19 = Coronavirus Disease 19⬚

GGO = ground-glass opacity⬚

RT-PCR = reverse-transcription−polymerase-chain-reaction

SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

Introduction

In December 2019, an outbreak of pneumonia associated with a novel coronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was reported in Wuhan, Hubei Province, China.[1] Thereafter WHO named the disease as Coronavirus Disease 2019 (COVID-19). As spreading rapidly across the world, WHO characterizes COVID-19 as a pandemic.

The keys to control COVID 19 are early discovery, early isolation and early treatment. At present, real-time reverse-transcription-polymerase-chain-reaction (RT-PCR) assay remains the standard of reference, but it was reported that some patients with initial negative RT-PCR presented abnormal chest CT images and

the results of RT-PCR might turn positive after multiple tests. [2] Moreover, shortage of laboratory test kits limited the use of RT-PCR with the spread of the epidemic, especially in Wuhan. Therefore, some experts suggested that chest CT could be regarded as diagnosis standard of COVID-19. The guideline of Diagnosis and Treatment of Pneumonitis Caused by 2019-nCoV (trial sixth version) published by the China government recommended chest CT as an effective method to screen suspicious case. [3] The addition of chest CT for diagnosis resulted in tens of thousands of clinically diagnosed cases in China which played an important role in controlling epidemic situation. [4] Therefore, comprehensive and timely evaluation of effectiveness of chest CT for COVID-19 diagnosis remains urgent and mandatory. In the present study, we validated the effectiveness of chest CT for COVID-19 diagnosis through a systematical meta-analysis.

Material And Methods

Search Strategy and Eligibility Criteria

PubMed, Embase, Web of Science and CNKI (until March 12, 2020) were searched for articles that focused on the role of chest CT in diagnosis of COVID-19; there were no language restrictions. The key words were "COVID-19" or "SARS-CoV-2" or "novel coronavirus" or "2019 nCov". We also checked the reference lists of all key articles for any additional eligible articles. Studies were included if they met the following criteria: (1) reported the performance of chest CT in diagnosing COVID-19; (2) participants were diagnosed as COVID-19 based on the results of multiple RT-PCR; (3) studies directly or indirectly provided enough information to extract 2*2 table information of diagnostic test of chest CT for COVID-19; (4) study sample was larger than 30. We excluded duplicate reports, abstracts from meeting proceedings. The selection of eligible articles was performed by 2 investigators independently. Disparities between investigators were resolved by discussion between them.

Data Extraction and Quality Assessment

The following data were extracted from each study: study site, sample size, characteristics of participants, chest CT findings, the results of multiple RT-PCR and 2*2 table information. The methodological quality was evaluated by using the QUADAS-2. QUADAS-2 entries include 4 domains: patient selection, index test, reference standard and flow and timing. Definitions and judgment criteria for each domain are available in *Cochrane Handbook*. Data Extraction and Quality Assessment were conducted by two independent authors. Disparities between investigators were resolved by discussion between them.

Statistical Analysis

A bivariate random-effects model was used to analyze and pool diagnostic performance (sensitivity and specificity) measurements across studies. The χ2-based Q test was performed to test heterogeneity among studies. And the $I2$ value was used to evaluate the percentage of inter-study variation in the total

variation When P <0.05 and/or $I2$ >50%, significant heterogeneity was presumed. The meta-analysis was conducted using the "midas" and "metandi" modules in Stata 12.0 software.

Results

Characteristics of Studies and Quality Assessment

The study selection process is presented in Figure 1. Briefly, 573 references were identified after searching databases. 7 references were removed due to duplication. After scanning the titles and abstracts, 544 records were excluded and 22 full-text articles were assessed for eligibility. Finally, 10 studies were included in our meta-analysis involving 2657 patients. [5-14] Of these patients, 2244 patients had positive RT-PCR results. Nine studies only enrolled patients diagnosed as COVID-19. [6-14] Therefore, we could only calculate sensitivity from the information provided in these studies. Three studies were conducted in Wuhan [5, 8 ,12]; Six studies were conducted in other regions and the remaining one collected data throughout China [6, 7, 9-11, 14]. The mean age of patients ranged from 45 to 58. Five studies reported the proportion of severe illness which ranged from 3.8-41% [6, 10-12, 14]. The characteristics of eligible studies were summarized in Table 1.

The risk of bias and applicability concerns for included studies are showed in Figure 2. Over all, none of the studies was considered to be seriously flawed according to the QUADAS-2 assessment. At least 4 of 7items of QUADAS-2 tool were met in all studies. All studies were considered to have a low risk of bias for patient selection and reference standard domain. Only one study reported that the radiologists reading the chest CT images were blinded to the results of RT-PCR which was classified as low risk of bias in index test domain [5]. The remaining studies were considered to have an unclear risk of bias regarding the index test domain [6-14]. We noted that seven studies had an ambiguous risk of bias due to absence of mean interval data between chest CT and the RT-PCR assay [6, 7, 10-14].

Diagnostic Performance of Chest CT for Diagnosing COVID-19

Sensitivity was available in all studies ranging from 0.69-0.99. However, only one study reported the specificity (25%, 95% CI:22-30%) of chest CT for diagnosing COVID-19. We pooled the sensitivity values (93%, 95% CI: 85 - 97%) (Figure 3). The Cochran Q test revealed a significant heterogeneity (Q=213, P<0.01; I^2 =95.78). Given that the severity of illness, experience of radiologists and severity of epidemic might contribute to the heterogeneity, we classified the studies into two categories according to whether the study site was located in Wuhan where the epidemic was the most severe, patients suffered more severe illness and the radiologists might have more experience. Three studies were conducted in Wuhan which reported sensitivity values about 97% (95% CI: 95-98%) [5], and 96% (0.87-100%) [8] and 99% (95% CI: 96-100%) [12], respectively. Due to the small number of enrolled studies, it was inappropriate to pool sensitivity among these three studies, but the sensitivity values were very close to each other. After excluding these three studies, we pooled the sensitivity values of the remaining studies. Nevertheless, the heterogeneity was still so significant that it was inappropriate to pool the sensitivity (Q=58, P<0.01;

I^2=89.6). The sensitivity value of the individual study ranged from 0.69 to 0.98 and was summarized in Figure 3.

Due to the specificity was only reported in one study [5], it was inappropriate to plot hierarchical summary receiver operating characteristics (HSROC) curves.

Discussion

The main results of this meta-analysis are as follows: 1) the sensitivity of chest CT for COVID-19 was great in Wuhan, but varied among other regions; 2) few studies reported the specificity of chest CT which was about 25%.

  Chest CT plays an important role in detection of COVID-19, especially in the initial and peak period of epidemic, in China. Although the RT-PCR assay remains the standard of reference, it has been reported that false negative after the initial test was not rare and shortage of laboratory kit in the early stage of the outbreak restricted the early detection of COVID-19. As our findings, chest CT had great sensitivity for early detecting COVID-19, especially in regions more affected by epidemic such as Wuhan. Therefore, a clinical diagnosis criteria based on typical CT imaging features was temporarily adopted in the Guideline of Diagnosis and Treatment, which was only applicable in Hubei Province, China.[3] This move allowed to early detect a large number of clinical diagnoses of COVID-19 under the background of shortage of RT-PCR assay which contributed to effective control of epidemic situation in China. Nevertheless, as mentioned above, among regions other than Wuhan, the reported sensitivity of chest CT varied and generally lower than that in Wuhan. Several reasons might underlie this phenomena, such as heterogeneity of experience of radiologists, severity of illness and epidemic. However, unfortunately, most studies did not provide relative informations. Wu Jian et al. reported a relative low sensitivity of chest CT (69%) and in their study the proportion of severe patients was only about 3.8% far less than the average level of China which was about 15%.[6, 11] Moreover, Harrison et al. investigated the performance of radiologists in reading chest CT images of COVID-19 which found the experience of radiologists had a great impact on the diagnosis accuracy of chest CT.[15] Overall, chest CT has a great sensitivity for detecting COVID-19, especially in regions with severe epidemic situation, and was helpful to early detect suspicious cases, which was vital to control epidemic.

  In contrast to the great sensitivity of chest CT, the specificity was relative low with reporting about 25%. The typical chest CT findings of COVID-19 included ground-glass opacities (GGOs), consolidations and interlobular thickening, which were usually multifocal and involved bilateral lungs.[16] In mild patients or early period of COVID-19, chest CT could be negative or pure GGO lesions. The CT imaging features might overlap between COVID-19 and other viral pneumonia, which could reduce the specificity of chest COVID-19. Nevertheless, considering the rapidly spreading epidemic of COVID-19, it was priority to identify any suspicious case in order to isolate the patients and avoid cross infection. Therefore, In the context of emergency disease control, sensitivity was more important than specificity. On the other hand, as mentioned above, although RT-PCR was still regarded as standard reference, false negative results

were not rare. Actually, in the study reporting specificity of chest CT, the results of RT-PCR turned from negative to positive in 15 patients and of these patients, 14 patients had positive findings in the initial chest CT.[5]

In addition to detection, chest CT also play an important role in management of COVID-19. As other pneumonias, the severity of COVID-19 is also positively related to chest CT findings. Intensive care unit (ICU) patients on admission often presented with bilateral multiple lobular and subsegmental consolidation, while non-ICU patients presented with bilateral GGOs and subsegmental consolidation. [17] Moreover, chest CT is helpful to surveil disease progression of COVID-19. Pan et al. investigated 21 confirmed patients and summarized four stages of COVID-19: early, progressive, peak, and absorption. [18] Growth of GGOs and expansion of consolidation are indicator of disease progression, and otherwise might indicate the improvement. [19-22]

In conclusion, on the basis of limited and heterogeneous data, chest CT offers the great sensitivity for detecting COVID-19, especially in region with severe epidemic situation. The specificity is low. In the context of emergency disease control, chest CT provide a fast, convenient and effective method to early recognize suspicious cases, and contribute to reduction of cross infection.

Declarations

Acknowledgments: None.

Conflict of Interest: No conflicts of interest have been declared.

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Table 1

Table 1. Characteristics of eligible studies

Author	Sample size	Site	Gender (male%)	Age	Severity (severe %)	Median Interval between CT and RT-PCR (days)	Chest CT finding [b]
Ai Tao et al. [5]	1014	Wuhan	46%	Mean age: 51	NA	1	GGO (46%); consolidation(50%); thickened interlobular septa (1%); nodular lesions (3%).
Guan WJ et al. [6]	1099 [a]	Throughout China	58.1%	Median age: 47	15.7	NA	GGO (56%); local patchy shadowing (42%); bilateral patchy shadowing (52%); interstitial abnormalities (15%).
Xu XW et al. [7]	62	No Wuhan	56%	Median age: 47	NA	NA	Most patients showed bilateral or multiple lobular or subsegmental areas of consolidation or bilateral GGO.
Li Y et al. [8]	51	Wuhan	55%	Mean age :58	NA	3	GGO (90%); consolidation (41%); vascular enlargement (82%); thickened interlobular septa (71%).
Fang YC et al. [9]	51	No Wuhan	57%	Median age: 45	NA	3	Most patients had GGO.
Yang WJ et al. [10]	149	No Wuhan	54%	Mean age: 45	8.7%	NA	GGO and consolidation were the most common presentation.
Wu Jian et al. [11]	80	No Wuhan	51%	Mean age: 46	3.8%	NA	GGO was the most common presentation.
Zhang JJ et al. [12]	140 [a]	Wuhan	49%	Median age: 57	41%	NA	Most patients had bilateral multiple GGO and consolidation.
Xu X et al. [13]	90	No Wuhan	43%	Mean age: 50	NA	NA	GGO (72%); consolidation (13%); interlobular thickening (37%).
Xu YH et al. [14]	50	No Wuhan	58%	Median age: 45	26%	NA	GGO (60%); consolidation (30%); thickened intralocular septa (60%); thickened interlobular septa (66%).

GGO: Ground-glass opacity; NA: not available.

a: not all patients received chest CT.

b: only described chest CT findings among patients with abnormal CT images.
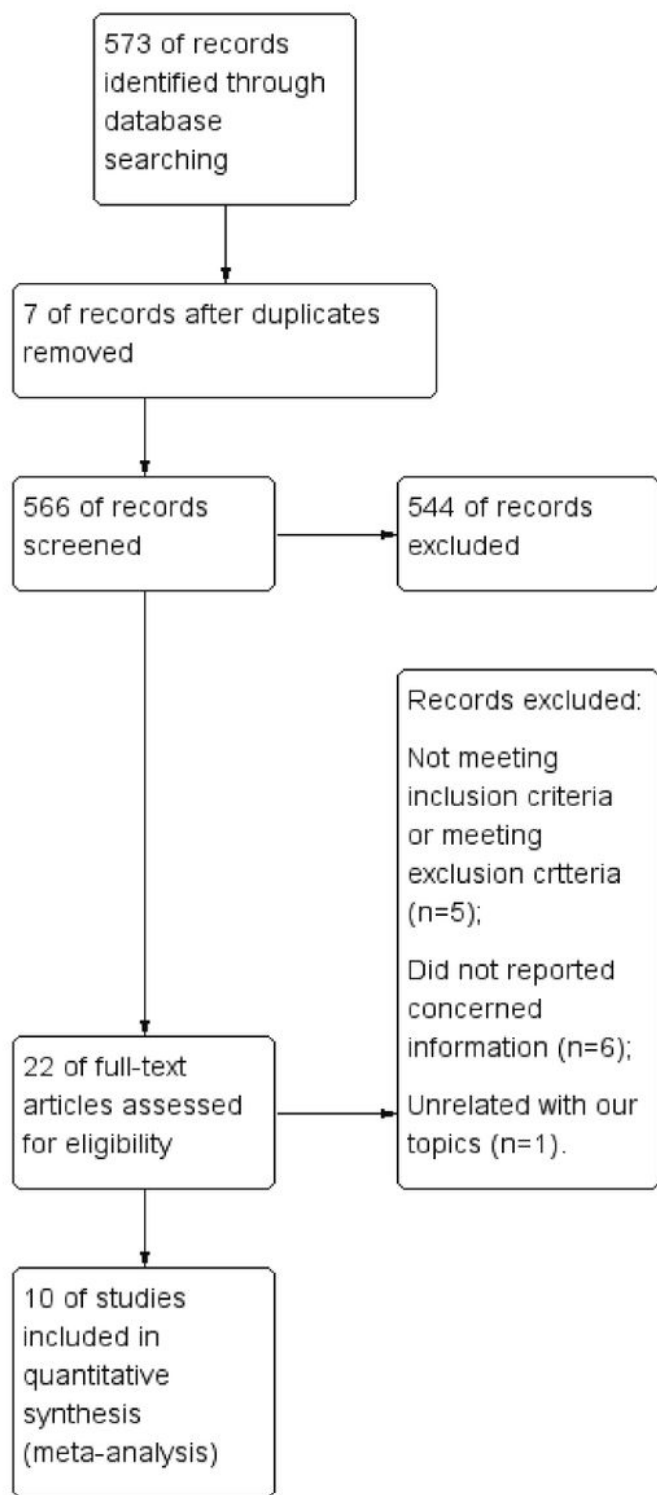
Figures

Figure 1

Flow diagram showing study selection process for meta-analysis
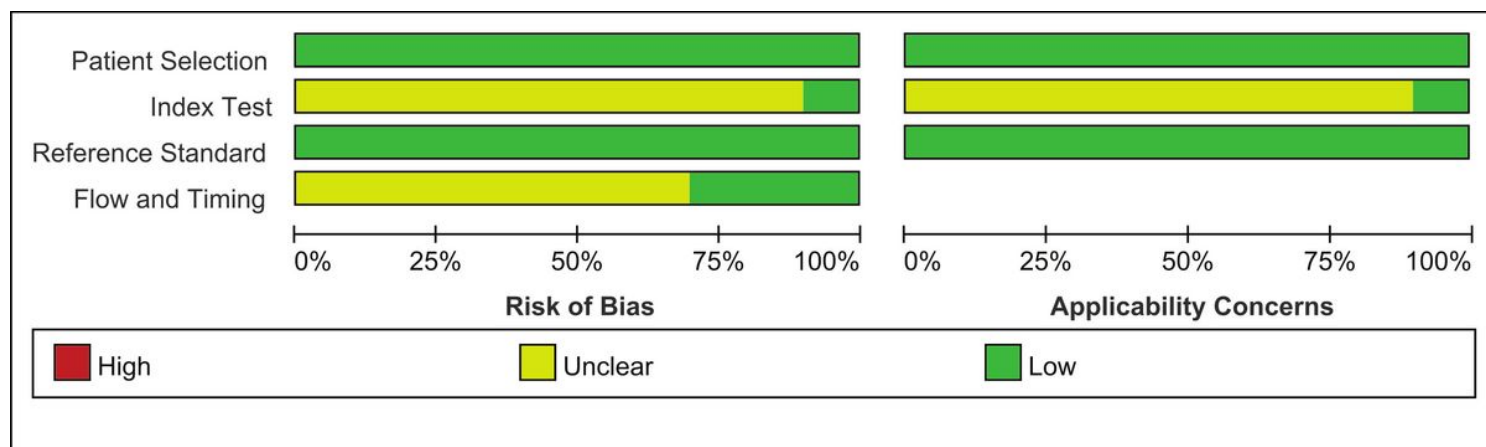
Figure 2

Grouped bar charts of risk of bias (left) and concerns for applicability (right) of 10 included studies using Quality Assessment of Diagnostic Accuracy Studies−2 (QUADAS-2) tool.
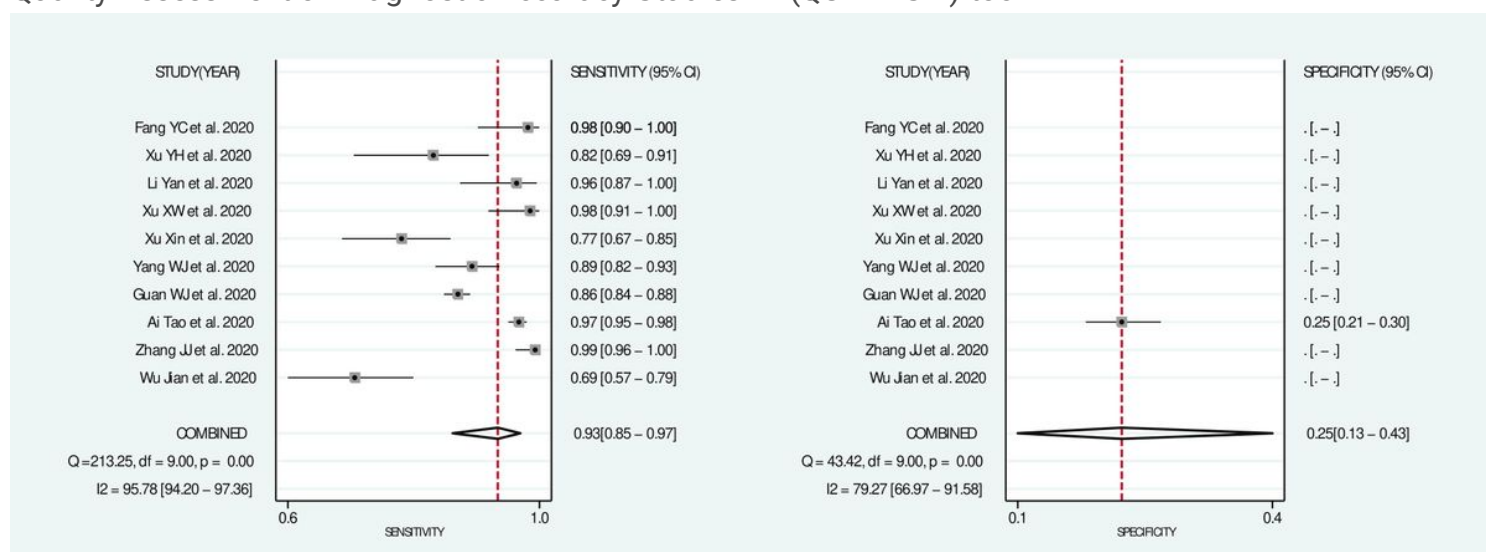

Figure 3

Coupled forest plots of pooled sensitivity and specificity. Numbers are pooled estimates (dots within squares) with 95% CIs (horizontal lines). Corresponding heterogeneity statistics are provided at bottom.