Sensitivity of Chest Computed Tomography Scan in Diagnosis of SARS-CoV-2: A Meta-analysis Study

Original Article

Mohamed Shehata Taha, Peter Milad, Ahmed Nabil Abdelhamid Ahmed, Tarek Abdel Hamid Hamdy

Department of Otorhinolaryngology, Faculty of Medicine, Ain Shams University, Cairo, Egypt.

ABSTRACT

Background: Early diagnosis of Coronavirus disease 2019 (COVID-19) is crucial for disease treatment and control. Compared to Real-time Reverse-transcription polymerase chain reaction (rRT-PCR), chest computed tomography (CT) scan imaging may be a more practical and rapid method to diagnose and assess COVID-19, especially in the pandemic.
Aim: To conduct a meta-analysis study regarding the sensitivity of chest CT scan in detecting Coronavirus Disease 2019 (COVID-19).
Patients and Methods: Using MEDLINE database (https://pubmed.ncbi.nlm.nih.gov/), Google Scholar and Scopus, we conducted a systematic search to identify relevant studies published within the last 6 months (from November 2019 till 20th of April 2020), appropriate articles were accessed in full text to determine eligibility and extract data by two reviewers.
Results: Fifteen retrospective studies were included, and their results were pooled in this meta-analysis. Chest CT scan showed positive finding in 2714 out of 3130 scanned patients. Sensitivity of the chest CT scan for diagnosis of COVID-19 could be extracted from all studies ranging from 0.61-0.99. There was considerable heterogeneity across studies. There was no evidence of publication bias.
Conclusion: Chest CT scan can provide a speedy and effective method to early recognize suspicious COVID-19 cases, contributing to reduction of cross infection due to its great sensitivity. But we should be cautious during interpreting these results since established available information about COVID-19 are rapidly evolving all over the world, in addition, most of the published information are incomplete.

Key Words: CHEST CT, CORONA VIRUS, COVID-19, PNEUMONIA, SARS-COV-2.

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Corresponding Author: Peter Milad, MD, Department of Otorhinolaryngology, Faculty of Medicine, Ain Shams University, Cairo, Egypt, **Tel.:** +201006371645, **E-mail**: dr.peter.milad@gmail.com

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INTRODUCTION

In December 2019, an outbreak of Novel Coronavirus 2019 (COVID-19) pneumonia began in Wuhan (Hubei, China) and rapidly spread.[1] Due to absence of a therapeutic vaccine or specific antiviral medication, prompt detection and isolation became essential against this novel coronavirus. According to the latest guidelines of diagnosis and treatment of pneumonitis caused by COVID-19 (trial sixth version) published by the China government, the standard diagnostic method being used is real-time reverse transcription polymerase chain reaction (rRT-PCR) to detect viral nucleotides from specimens obtained by nasopharyngeal or oropharyngeal swab, tracheal aspirate and bronchoalveolar lavage.[2,3]

However, recent reports have revealed that RT-PCR has a sensitivity as low as 60%-71% for detecting COVID-19 which can possibly be attributed to low viral load present in test specimens or laboratory error.[4-6] These false negatives hinder quarantine efforts, necessitate repeat testing and has the potential to overload the current supply of testing kits and related infrastructure.[6,7]

Chest CT scan as a routine diagnostic imaging tool for pneumonia, is relatively easy to perform and can produce fast diagnosis. Also, it may provide a benefit for diagnosis of COVID-19. Chung *et al*., reported that chest CT scan demonstrates typical radiographic features in nearly all COVID-19 patients, including ground-glass opacities, multifocal patchy consolidation, reverse halo sign and/or interstitial changes.[8] Moreover, chest CT may reveal pulmonary abnormalities consistent with COVID-19 in patients with initial negative RT-PCR results.[7,9]

Aim of the study

This work aims at conducting a meta-analysis study regarding the sensitivity of chest CT scan in detecting Coronavirus Disease 2019 (COVID-19).

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PATIENTS AND METHODS:

This study was done in the following steps

Searching for relevant studies

Using MEDLINE database (https://pubmed.ncbi.nlm.nih.gov/), Google Scholar and Scopus, we conducted a systematic literature search to identify relevant articles published within the last 6 months (from November 2019 to end of April 2020) using a combination of the following keywords (chest CT, COVID-19, corona virus, pneumonia, SARS-COV-2 and severe acute respiratory syndrome). Appropriate articles were accessed in full text to determine eligibility and extract data by two reviewers.

The electronic search was supplemented by scanning the reference lists from retrieved articles to identify additional studies that may have been missed during the initial search. Included medical articles are only those published in English language and have mentioned sensitivity of chest CT scan for COVID-19 diagnosis along with clear identification of the number of patients with positive and negative CT scan chest finding. Excluded articles are those articles which miss one or more of the above-mentioned inclusion criteria, duplicated studies and studies that provided insufficient data.

Study Identification and Eligibility

Our search identified 2124 potentially relevant studies in MEDLINE. Records after duplicates removed were 1437 articles. Out of them, there were 300 potentially eligible studies. We excluded 180 out of the 300 studies because they missed one or more of the above-mentioned inclusion criteria or were outdated by other more recent ones. Thus, 120 studies remained for possible inclusion and were retrieved in full text version. After reviewing the full article, 105 studies were excluded for the following reasons: some of them were essay studies while others did not mention the sensitivity of CT scan chest or the number of positive and negative CT scan finding. This process left 15 original articles which fulfilled the inclusion criteria, thus were included and used for further analyses (Fig.1).

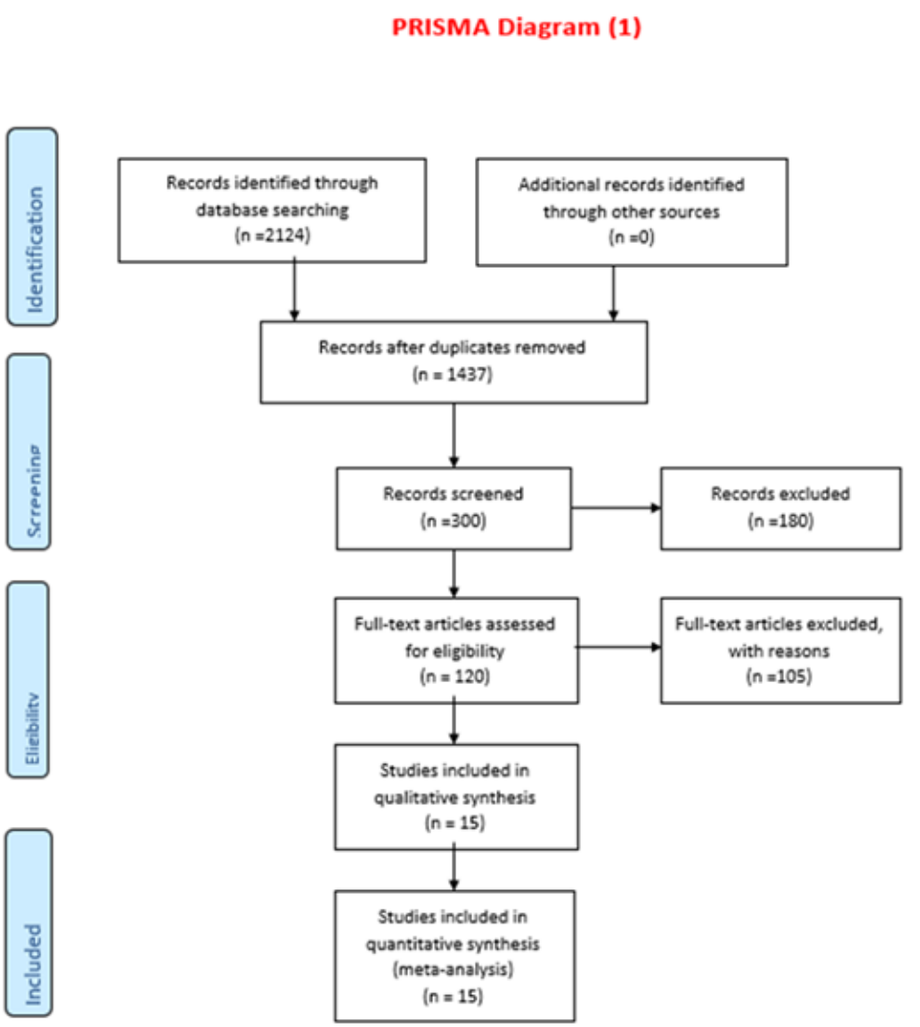

Fig. 1: PRISMA Diagram

Data extraction:

From each relevant article, we extracted the following information: type of the study (meta-analysis, randomized control trials, prospective, retrospective or systematic review), sensitivity of chest CT scan and number of patients with positive and negative CT scan chest finding.

Statistical Analysis:

Statistical analysis was done using the Jamovi version 1.1, 2019 computer software (https://www.jamovi.org) and Open MetaAnalyst software (http://www.cebm.brown.edu/openmeta/). Data were adequate to conduct a meta-analysis for the sensitivity of CT scan chest in detecting COVID-19 disease. Studies included in this meta-analysis were tested for heterogeneity and publication bias.

Testing for heterogeneity

Studies included in this meta-analysis were tested for heterogeneity of the estimates using the following tests:

• Cochran Q Chi square test: a statistically significant test (*p value < 0.1*) indicated heterogeneity among the included articles.

• I square (I2) index which reflects the inconsistency in the effect size measured in the meta-analysis study.

Examination of publication bias

Publication bias was assessed by examination of funnel plots of the estimated effect size versus its standard error. The Rosenthal fail-safe number and both the rank correlation test and Egger regression tests were used to test asymmetry of funnel plots.

Pooling of estimates

Effect sizes were pooled using random-effects maximum likelihood model. Pooled sensitivity is reported with 95% confidence limits.

RESULTS:

Fifteen retrospective studies were included in this study (Table 1). Chest CT scan showed positive finding in 2714 out of 3130 scanned patients. Sensitivity could be extracted from all studies ranging from 0.61-0.99. We pooled the sensitivity values (90% - 95% CI = 85% to 95%). There was considerable heterogeneity across included studies (Cochran Q test *P-value < 0.01*, I-squared = 96%) (Figure 2). Cumulative forest plot for the sensitivity of initial CT scan chest conform 90% sensitivity of its use to diagnose COVID-19 (Figure 3). Effect sizes with any single study removed showed very fine fluctuation up or down the pooled estimate for the whole included studies (Figure 4). There was no evidence of publication bias (Rosenthal fail-safe number = 232, 792, rank correlation test for funnel plot asymmetry *P-value = 0.169*, regression test for funnel plot asymmetry *P-value = 0.148*) (Figure 5).

Table 1: Included articles

Study	Total number of cases	CT scan chest		Study type
		Positive findings	Negative finding	
1. Ai *et al*. 2020[4]	1014	888	126	Retrospective
2. Fang *et al*. 2020[5]	51	50	1	Retrospective
3. Xie *et al*. 2020[7]	167	160	7	Retrospective
4. Chung *et al*. 2020[8]	21	18	3	Retrospective
5. Huang *et al*. 2020[9]	41	41	0	Retrospective
6. Bai *et al*. 2020[10]	350	280	70	Retrospective
7. Bernheim *et al*. 2020[11]	121	94	27	Retrospective
8. Chen *et al*. 2020[12]	99	99	0	Retrospective
9. Chen *et al*. 2020[13]	9	8	1	Retrospective
10. Guan *et al*. 2020[14]	975	840	135	Retrospective
11. Inui *et al*. 2020[15]	112	68	44	Retrospective
12. Ming-Yen *et al*. 2020[16]	21	19	2	Retrospective
13. Shi *et al*. 2020[17]	81	81	0	Retrospective
14.Song *et al*. 2020[18]	51	51	0	Retrospective
15. Zhang *et al*. 2020[19]	17	17	0	Retrospective

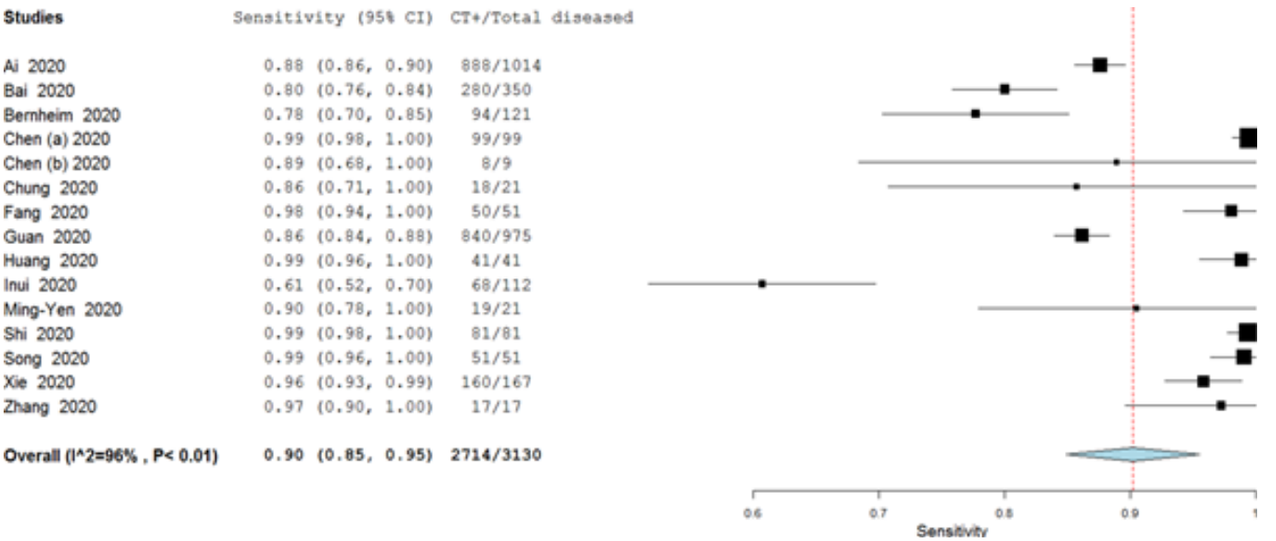

Fig. 2: Forest plot for sensitivity of initial CT scan. There is considerable heterogeneity across studies (Cochran Q test *P-value* < *0.01*, I-squared = 96%). Pooled sensitivity = 90% (95% CI = 85% to 95%).

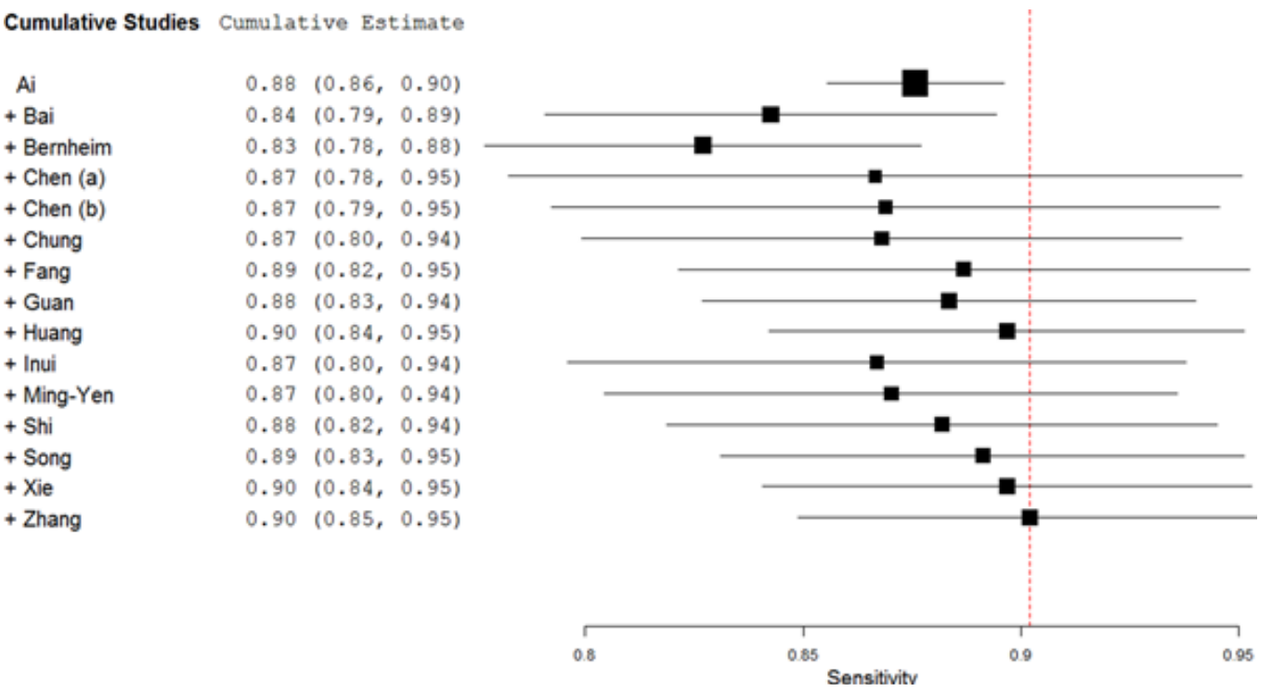

Fig. 3: Cumulative forest plot for sensitivity of initial CT scan.

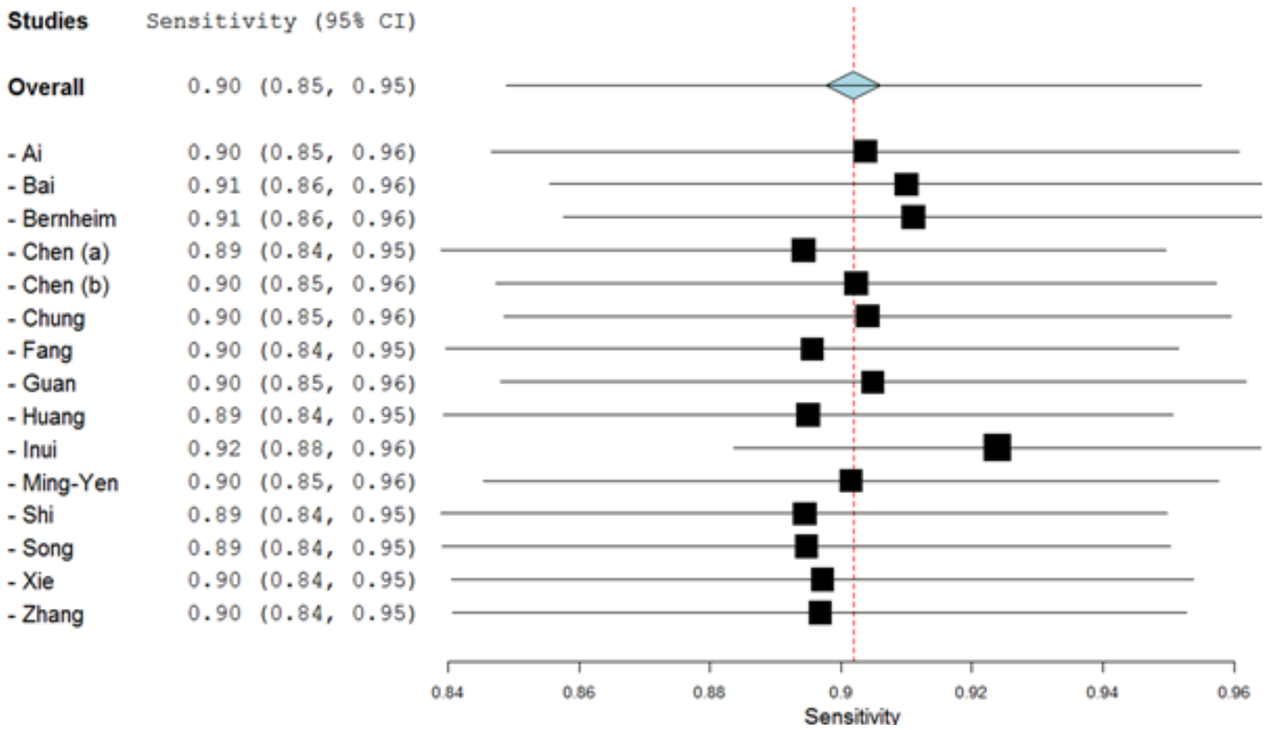

Fig. 4: Leave-one-study forest plot for sensitivity of initial CT scan. Effect sizes with any single study removed show very fine fluctuation up or down the pooled estimate with all studies included.

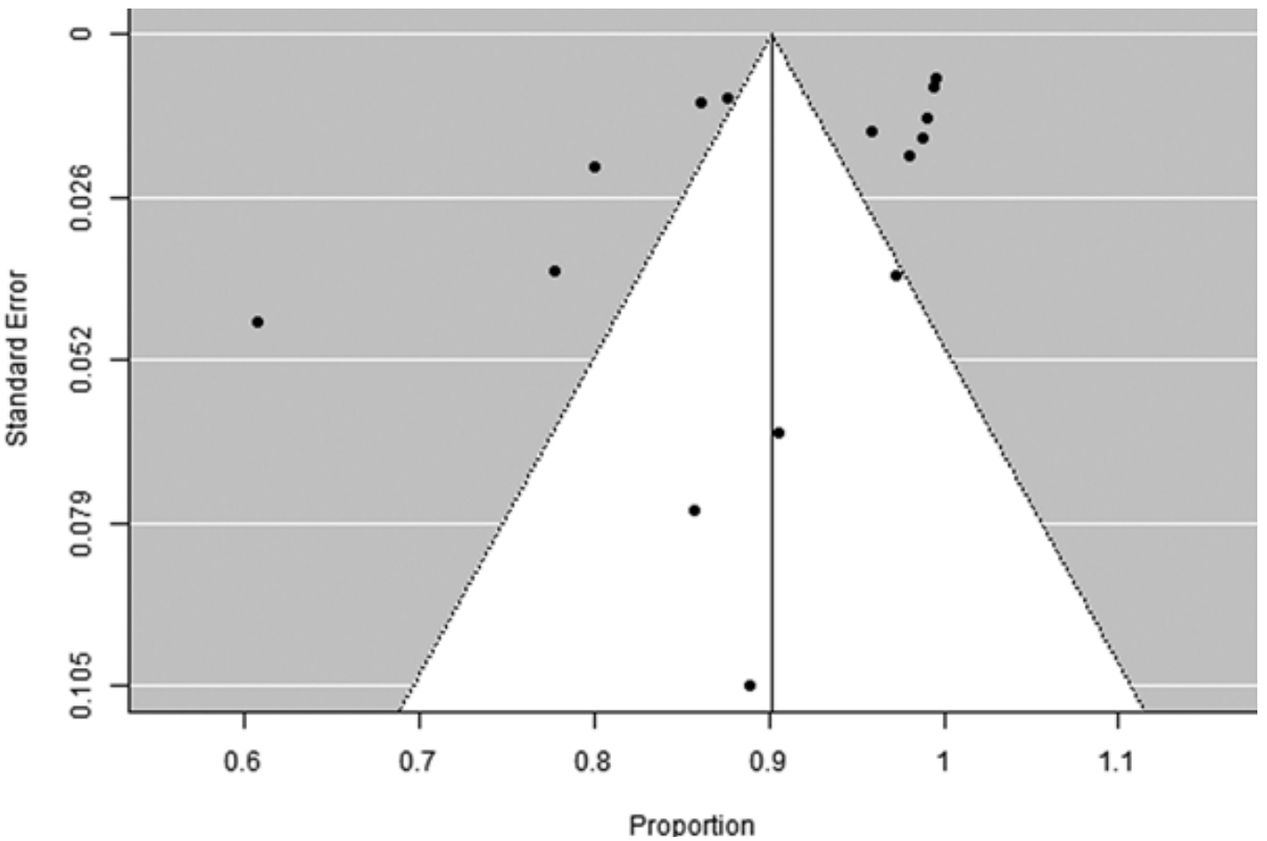

Fig. 5: Funnel plot for sensitivity of initial CT scan. There is no evidence of publication bias (Rosenthal fail-safe number = 232,792, rank correlation test for funnel plot asymmetry *P-value = 0.169*, regression test for funnel plot asymmetry *P-value = 0.148*).

DISCUSSION

On 26th of April 2020 at 10:16 AM, there were 2, 933, 384 confirmed patients with COVID-19, of whom 839269 recovered with 203, 612 deaths all over the world. So quick and early diagnosis of (COVID-19) is crucial for disease treatment and control. Compared to RT-PCR, chest CT scan imaging is a rapid way to diagnose COVID-19 particularly in the pandemic. Just as clinicians are evaluating more suspected patients, radiologists are similarly interpreting more chest CT scans in suspected cases. Chest CT scan is a vital component in the diagnostic algorithm for patients with suspected COVID-19 infection. Therefore, due to the limited number of rRT-PCR kits in some centers and the possibility of false negative results, the National Health Commission of the People's Republic of China has encouraged diagnosis based on clinical and chest CT scan findings alone.[4]

Review of the retrieved data from the included 15 articles revealed that, rRT-PCR assay plays a vital role in determining hospitalization and isolation for patients. In contrast, it is less sensitive than chest CT scan (70% versus 98% respectively).[4] In addition, several external factors may affect rRT-PCR testing results including specimens' source (upper or lower respiratory tract), sampling operations, sample timing (different period of the disease development).[3] As such, the results of rRT-PCR tests must be cautiously interpreted.

Chest CT scan is a non-invasive, imaging modality with high accuracy and speed. Recently in the literature, nearly all patients with COVID-19 had characteristic chest CT scan features (different degrees of ground glass opacities with/without crazy-paving sign, reverse halo sign, multifocal organizing pneumonia, linear opacities and architectural distortion in a peripheral distribution).[8,11,20,21] Ai T *et al*. in their study mentioned that about 60% (34/57) cases had typical CT features consistent with COVID-19 prior to (or parallel) the initial positive RT-PCR results and almost all patients (56/57) had initial positive chest CT scans before or within 6 days of the initial positive rRT-PCR results. This indicates that chest CT scan imaging can be very helpful in rapid detection of suspected cases as authors said.[4]

Pan *et al*. studied 21 confirmed COVID-19 patients and summarized four radiologic stages of the disease in CT chest: early, progressive, peak, and absorption.[21] Appearance of ground glass opacities and consolidation expansion are markers of disease progression.[17,18,23]

The standard established diagnostic method for COVID-19 now is rRT-PCR to detect viral nucleotides from specimens obtained by oropharyngeal swab, nasopharyngeal swab, bronchoalveolar lavage, or tracheal aspirate.[3] However, many reports have shown that rRT-PCR has a sensitivity as low as 60%-71% for detecting COVID-19 which may be attributed to low viral load present in test specimens or laboratory error. In contrast, chest CT scan has demonstrated about 56% - 98% sensitivity in detecting COVID-19 at initial presentation.[4,5,7,20] Recently, Xie reported 5 of 167 patients (3%) who had negative rRT-PCR for COVID-19 at initial presentation despite chest CT scan findings typical of viral pneumonia.[7]

Fang *et al*. concluded that the sensitivity of chest CT scan was 98% while that of rRT-PCR was 71% and this is in accordance with our results that support the use of chest CT scan for screening patients for COVD-19 in whom clinical and epidemiologic features are compatible with COVID-19 infection particularly when rRT- PCR testing is negative.[5] Heshui Shi and his colleagues reported that chest CT scan abnormal findings can be present even in asymptomatic patients as patients with asymptomatic infection were discovered on the basis of abnormal lung findings on CT scans, suggesting that chest CT scans should be done in asymptomatic high-risk individuals with a history of exposure to patients with COVID-19 pneumonia to facilitate early identification of the disease.[17] In addition to detection, chest CT scan plays a vital role in management of COVID-19 patients since the severity of COVID-19 disease is also directly related to chest CT findings. Also, chest CT is helpful to surveil disease progression of COVID-19.[9]

In this current meta-analysis study, we aimed to investigate the sensitivity of CT scan chest in diagnosing COVID-19 infection. Fifteen articles were eligible for this study. Analysis of the articles showed positive finding in 2714 out of 3130 scanned patients. CT scan chest sensitivity for COVID-19 diagnosis could be extracted from all studies ranging from 0.61-0.99. There was considerable heterogeneity across the included studies. There was no evidence of publication bias. Pooling of the data together showed that chest CT scan had a great sensitivity (90%) for early detection of COVID-19 (figures 2-5). A meta-analysis study done by Xu B. *et al*. (a preprint article published online in Research Square and has not been peer-reviewed) support the results of our study.[22] This showed that chest CT scan offers a great sensitivity for detecting COVID-19 especially in severe epidemic situation and provides a fast, convenient and effective method to early recognize suspicious cases which was vital to control epidemic.

On the other hand, Chung *et al*. reported that chest CT scan may be negative for viral pneumonia of COVID-19 at initial presentation (3/21 patients).[8] Also, Bernheim *et al*. concluded that Chest CT scan has limited sensitivity and negative predictive value early after onset of the symptoms, thereby unlikely a reliable standalone tool to rule out COVID-19 infection.[11] Moreover, Wu Jian *et al*. reported a relative low sensitivity of chest CT scan (69%).[24] Another study showed that 7 out of 19 asymptomatic cases (37%) had positive rRT-PCR results for SARS-CoV-2 in the absence of chest CT scan changes.[25] Hence, the role of CT scan chest is doubtable for screening asymptomatic patients.

On their comment, The Royal College of Radiologists mentioned that there is no current role for chest CT scan in the diagnostic assessment of patients with suspected coronavirus infection in the UK. However, in their update in 27th of March 2020 they said that the use of chest CT scan to assess cases with suspected COVID-19 infection may have a role in stratifying risk in patients presenting acutely. This is appropriate if other forms of COVID-19 testing can't be rapidly accessed, noting that a negative scan would not exclude COVID-19 infection.[26] In the same way, The American College of Radiology stated that chest CT should not be used as a first-line test to diagnose Covid-19.[27]

Limitations of the current study

1- Two included articles in this meta-analysis (Inui *et al*. 2020 and Ming-Yen *et al*. 2020) weren't published on PubMed and published online (retrieved from Google Scholar).[15,16]

2- We are dealing with a newly discovered disease with limited data available, hence all published articles should be cautiously interpreted in addition to bad need for more comparative studies between the diagnostic tools for COVID-19. Priority should be given for rapid, safe and sensitive diagnostic test.

CONCLUSION

Chest CT scan can provide a speedy and effective method to early recognize suspicious COVID-19 cases, contributing to reduction of cross infection due to its great sensitivity. But we should be cautious during interpreting these results since established available information about COVID-19 are rapidly evolving all over the world, in addition, most of the published information are incomplete, hence using chest CT scan for early diagnosis of COVID-19 requires more evidence particularly in high-risk groups, taking into account hazards of radiation exposure and patient transfer from ICU to radiology department with potential disease spread.

CONFLICT OF INTEREST

There are no conflicts of interest.

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