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Chest CT features in COVID–19 patients: A systematic review and meta–analysis

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ABSTRACT

Objective: To derive the pooled estimate of chest computed tomography (CT) findings in coronavirus disease 2019 (COVID-19) patients.

Methods: A comprehensive systematic search was conducted according to the PRISMA checklist from January 2020 to September 2020 in electronic databases including PubMed, Google Scholar, and Scopus based on search terms in title and texts. Original descriptive studies with epidemiological parameters of interest were included into the systematic review and meta-analysis.

Results: Totally 54 articles comprised of 4 879 patients with a mean age of 49.05 years were eligible for this study. The pooled prevalence for abnormal CT images was 86.0%. Pooled prevalence for ground-glass opacity was 68.0%, 71.0% for bilateral abnormalities, 47.0% for mixed ground-glass opacity and consolidation and 29.0% for consolidation. In addition, 64.0% of lesions were peripheral, and 12.0% were central while 28.0% were both central and peripheral. Furthermore, 61.0% of lower lungs were involved, and 7.0% and 5.0% of the cases presented with pleural effusion and pericardial effusion, respectively. Besides, 11% of the cases showed lymphadenopathy, and 37% had air broncho gram sign. The pooled prevalence of other chest CT findings ranged from 8.0% to 65.0%.

Conclusions: Chest CT can be used as predictive tools for the detection of COVID-19 disease along with clinical manifestations and the RT-PCR method.

KEYWORDS: Systematic review; Meta-analysis; CT; Coronavirus; COVID-19

Significance

To date, computed tomography (CT) findings have been recommended as major evidence for clinical diagnosis of COVID-19. Typical CT findings including bilateral ground-glass opacity, pulmonary consolidation, and prominent distribution in the posterior and peripheral parts of the lungs are the main clinical characteristics in patients with COVID-19 which can help clinicians for differential diagnosis of the disease. This study proved that chest CT can be used as predictive tools for the detection of COVID-19 disease along with clinical manifestations and RT-PCR.

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1. Introduction

Coronaviruses are a large family of viruses and can cause different complications from the mild symptoms such as cold to severe symptoms. Before the coronavirus disease 2019 (COVID-19) pandemic, four coronaviruses were discovered, and two of them were responsible for pandemics since the beginning of the 21st century. The first epidemic was severe acute respiratory syndrome (SARS) which was caused by SARS-associated coronavirus (SARS-CoV) in 2003 and known as atypical pneumonia, with a mortality rate of 9.6%. The second was Middle East respiration syndrome (MERS) cause by MERS-associated coronavirus in 2012 and 2015, with a mortality rate of 35.7%, and now COVID-19 or SARS-CoV-2 with a mortality rate of approximately 10.0% emerged with an overwhelming trend[1,2]. The virus is very similar to MERS and SARS in nature and can cause viral pneumonia with different severities. Initial reports showed that up to 50% of people with chronic diseases are at risk of death[2,3]. The main clinical symptoms of COVID-19 including dry cough, shortness of breath, fever, weakness, myalgia, body pain, lost sense of smell and taste, and gastrointestinal symptoms have been identified. Also, with the spread of this pandemic in the world, we have witnessed different symptoms and involvement of other organs in the body such as the cardiovascular system, kidney, and liver[4-8].

Although real-time reverse-transcription polymerase chain reaction (RT-PCR) has been widely used to diagnose COVID-19, the accuracy of this method is controversial due to the false-negative results[9]. Therefore, other laboratories and paraclinical findings are used for screening COVID-19[10]. Among all, lung high resolution computed tomography (HR-CT) can help to identify viral lung infection in the early stages[8]. It is known that CT imaging findings are strongly related to the pathology and clinical improvement of the disease[11]. In the majority of COVID-19 cases, the first CT findings of the lungs are abnormal and maybe worsen in two weeks in untreated cases[12]. Considering the importance of chest CT in the diagnosis of COVID-19, radiologists need to be familiar with the typical CT features of COVID-19 pneumonia as well as the imaging criteria for differential diagnosis[13]. In this study, we aim to systematically present and analyze the meat data of typical chest CT features in patients with COVID-19 pneumonia to differentiate from the other pneumonia.

2. Materials and methods

2.1. Bibliographic search

The search was carried out in databases including PubMed, Google Scholar, and Scopus, from January 2020 to September 2020. Duplicates and studies out of search items were excluded. All original descriptive studies (designated a cross-sectional) in COVID-19 were concerned. The process is shown in Figure 1.

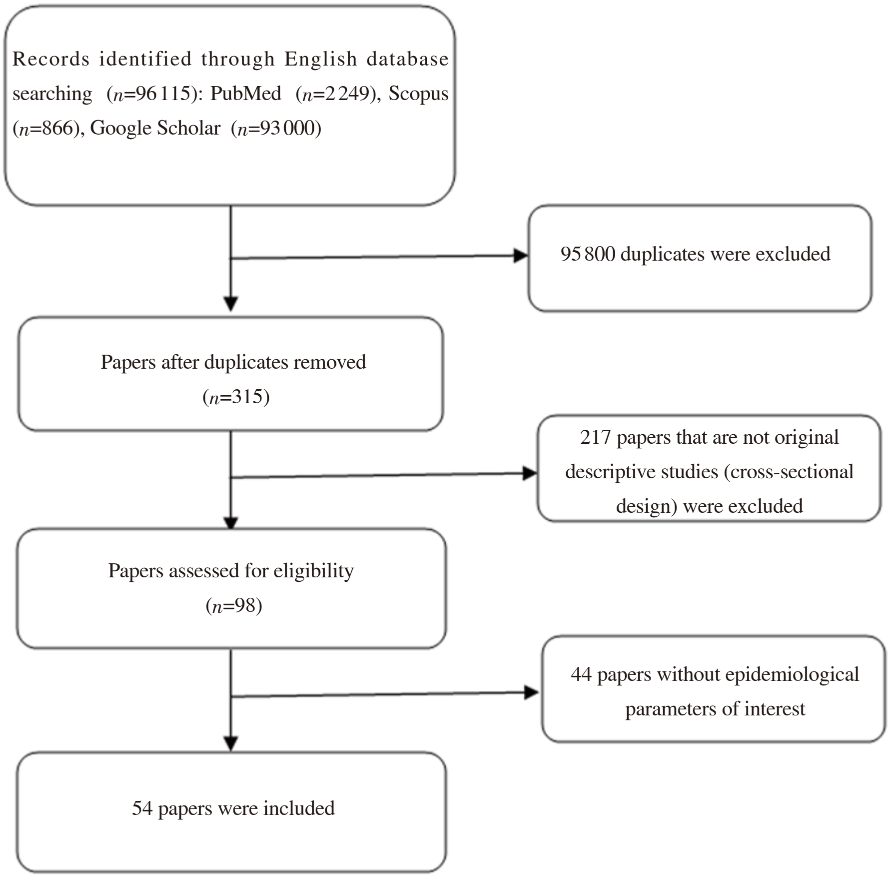

Figure 1. The study flowcahrt.

Table 1. Basic characteristics of the included studies.

Author	Year of publication	Country/ region	Province /City	Total patients, *n*	Age, years	Male, *n* (%)	Female, *n* (%)	Abnormal CT, *n*	Normal CT , *n*
Zhao *et al*.[14]	2020	China	Hunan	101	44.44	56 (55.4%)	45 (44.6%)	93	8
Pan *et al*.[15]	2020	China	Wuhan	63	44.90	33 (52.4%)	30 (47.6%)	ND	ND
Zhang *et al*.[16]	2020	China	Beijing	9	35.20	5 (55.6%)	4 (44.4%)	7	2
Zhou *et al*.[17]	2020	China	Chongqing	62	44.30	34 (54.8%)	28 (45.2%)	60	2
Bai *et al*.[18]	2020	China	Hunan	219	45.00	119 (54.3%)	100 (45.7%)	205	14
Guan *et al*.[11]	2020	China	Beijing	53	41.50	25 (47.2%)	28 (52.8%)	47	6
Zhou *et al*.[19]	2020	China	Wuhan	62	52.80	39 (62.9%)	23 (37.1%)	ND	ND
Xu *et al*.[20]	2020	China	Foshan	21	43.10	10 (47.6%)	11 (52.4%)	ND	ND
Xu *et al*.[21]	2020	China	Beijing	50	-	29 (58.0%)	21 (42.0%)	41	9
Yoon *et al*.[22]	2020	Korea	-	9	54.00	4 (44.4%)	5 (55.6%)	5	4
Xia *et al*.[23]	2020	China	Wuhan	20	-	13 (65.0%)	7 (35.0%)	16	4
Bernhiem *et al*.[24]	2020	China	Wuhan	121	45.00	61 (50.4%)	60 (49.6%)	101	20
Colombi *et al*.[25]	2020	Italy	Piacenza	236	68.00	177 (75.0%)	59 (25.0%)	ND	ND
Wang *et al*.[26]	2020	China	-	90	45.00	33 (36.7%)	57 (63.3%)	ND	ND
Parry *et al*.[27]	2020	India	Wuhan	147	40.90	104 (70.7 %)	43 (29.3 %)	51	96
Long *et al*.[28]	2020	China	-	36	44.80	20 (55.6%)	16 (44.4%)	35	1
Liu *et al*.[29]	2020	China	Hubei	55	-	-	-	52	3
Meng *et al*.[30]	2020	China	Wuhan	58	42.60	26 (44.8%)	32 (55.2%)	ND	ND
Grassi *et al*.[31]	2020	Italy	-	134	-	91 (67.9%)	43 (32.1%)	ND	ND
Chung *et al*.[32]	2020	China	Guangdong	21	51.00	13 (61.9%)	8 (38.1%)	18	3
Caruso *et al*.[33]	2020	Italy	Rome	158	57.00	83 (52.5%)	75 (47.5%)	58	100
Xiong *et al*.[34]	2020	China	-	42	49.50	25 (59.5%)	17 (40.5%)	ND	ND
Ng *et al*.[35]	2020	China	Shenzhen	21	56.00	13 (61.9%)	8 (38.1%)	19	2
Song *et al*.[36]	2020	China	Shanghai	51	49.00	25 (49.0%)	26 (51.0%)	ND	ND
Huang *et al*.[37]	2020	China	Wuhan	41	49.00	30 (73.2%)	11 (26.8%)	41	0
Chen *et al*.[2]	2020	China	Wuhan	99	55.50	67 (67.7%)	32 (32.3%)	-	-
Inui *et al*.[38]	2020	Japan	-	104	62.00	54 (51.9%)	50 (48.1%)	63	41
Wu *et al*.[39]	2020	China	-	80	44.00	42 (52.5%)	38 (47.5%)	76	4
Zhang *et al*.[40]	2020	China	-	5	39.60	1 (20.0%)	4 (80.0%)	4	1
Chen *et al*.[41]	2020	China	Zhejiang	3	52.30	2 (66.7%)	1 (33.3%)	ND	ND
Zhang *et al*.[42]	2020	China	Wuhan	60	64.40	43 (71.7%)	17 (28.3%)	ND	ND
Chen *et al*.[43]	2020	China	Zhejiang	98	43.00	46 (46.9%)	52 (53.1%)	91	7
Shi *et al*.[44]	2020	China	Wuhan	81	49.50	42 (51.9%)	39 (48.1%)	ND	ND
Xu *et al*.[45]	2020	China	Guangdong	90	50.00	39 (43.3%)	51 (56.7%)	ND	ND
Xie *et al*.[46]	2020	China	Hunan	5	48.40	4 (80.0%)	1 (20.0%)	ND	ND
Li *et al*.[47]	2020	China	-	83	45.50	44 (53.0%)	39 (47.0%)	ND	ND
Li *et al*.[48]	2020	China	-	78	44.60	38 (48.7%)	40 (51.3%)	56	22
Pan *et al*.[49]	2020	China	-	21	40.00	6 (28.6%)	15 (71.4%)	17	4
Zhang *et al*.[50]	2020	China	-	140	57.00	71 (50.7)	69 (49.3)	134	6
Xiang *et al*.[51]	2020	China	-	53	53.00	31 (58.5%)	22 (41.5%)	50	3
Zhou *et al*.[21]	2020	China	-	62	-	39 (62.9%)	23 (37.1%)	ND	ND
Luo *et al*.[52]	2020	China	-	73	41.00	37 (50.7)	36 (49.3)	ND	ND
Liu *et al*.[53]	2020	China	Guangdong	122	48.00	61 (50.0%)	61 (50.0%)	ND	ND
Tung-Chen *et al*.[54]	2020	Spain	-	51	61.40	28 (54.9%)	23 (45.1%)	ND	ND
Cui *et al*.[55]	2020	China	Guangdong	95	42.00	53 (55.8%)	42 (44.2%)	90	5
Wang *et al*.[56]	2020	China	-	114	53.00	58 (50.9%)	56 (49.1%)	110	4
Yang *et al*.[57]	2020	China	Zhejiang	149	45.11	81 (54.4%)	68 (45.6%)	ND	ND
Ai *et al*.[58]	2020	China	-	888	51.00	420 (47.3%)	468 (52.7%)	762	126
Dai *et al*.[59]	2020	China	Guangzhou	4	52.20	4 (100%)	0	ND	ND
Wang *et al*.[3]	2020	China	Wuhan	138	56.00	75 (54.3)	63 (45.7)	ND	ND
Li *et al*.[60]	2020	China	-	51	58.00	28 (54.9)	23 (45.1)	ND	ND
Han *et al*.[61]	2020	China	-	108	45.00	38 (35.2%)	70 (64.8%)	ND	ND
Zhao *et al*.[62]	2020	China	Hubei	19	48.00	11 (57.9%)	8 (42.1%)	ND	ND
Mohamed *et al*.[63]	2020	Somalia	-	27	43.00	19 (70.4%)	8 (29.6%)	25	2

2.2. Search strategy

The search was performed by using terms as follows “Corona virus”, “COVID-19”, “nCOV”, ”SARS-Co-V-2”, “Respiratory”, “Pneumonia”, “CT scan”, “Computerize”, “Tomography”, “Chest imaging”, “GGO”, “Ground glass opacity”, “Epidemiology,” “Consolidation”, “Crazy paving pattern” and “Prevalence” alone or in combination.

2.3. Data collection

A diverse search was conducted in all databases and then the collected papers were screened carefully to eliminate duplicates. Finally, papers with epidemiological parameters of interest were selected, and 54 articles meet the inclusion criteria. Those reported CT findings in COVID-19 patients were included in the study (Table 1). Data were extracted from articles including author (s), the year of publication, demographic information (age and gender), nationality, and also geographical region of study, number of examined patients, number of patients with lung involvements, number of patients with ground glass opacity (GGO), consolidation, crazy pave pattern and other findings in patients CT scan were extracted.

2.4. Data analysis

Statistical analyses were performed using Stata, version 11.0 (Stata Corp, College Station, TX, USA) and Stat Direct statistical software.1. The quality of the meta-analysis was evaluated with the STROBE checklist. A checklist including 22 items was considered for well reporting of observational studies. These items are related to the article’s title, abstract, introduction, methods, results, and discussion sections. A score under 7.75 is considered as poor quality, between 7.76-15.5 low, between 15.6-23.5 moderate, and more than 23.6 high quality[64]. The mean score of the STROBE checklist for 54 articles was 18.03, which is considered moderate quality. Point estimates and 95% confidence intervals (*CI*) of the prevalence were calculated. The prevalence and standard error (SE) of each study were estimated concerning binomial distribution and studies combined according to sample size and variance. An overall prevalence and group-specific prevalence were calculated according to the age groups, gender, and ethnicity. The Egger statistical test was applied to check the existence of publication bias. A forest plot was employed to visualize the heterogeneity among studies. The heterogeneity was expected in advance, and statistical methods, I^2 and Cochrane Q statistics (with significance of $P<0.05$) were used to quantify the variations. For the meta-analysis, we assumed that the included studies are random samples from a population under study and a random-effects model was employed. Proportions of individual studies and overall prevalence were presented by forest plots.

3. Results

Among all databases searched from January 2020 to September 2020, a total of 54 articles comprise of 4 879 patients with mean age of 49.05, were eligible. Based on the selected studies, the pooled effect size (prevalence) for abnormal CT images was 86.0% (95% *CI*: 79.0%-92.0%; I^2=95.0%, $P<0.001$). Based on 54 included studies, the pooled effect size for normal CT under a random-effects model was estimated 15.0% (95% *CI*: 9.0%-22.0%; I^2=94.0%, $P<0.001$) (Table 2). Among all characteristics, GGO under a random-effects model was estimated 68.0% (95% *CI*: 59.0%-75.0%) (Figure 2). Other characteristics such as consolidation was estimated 29.0% (95% *CI*: 22.0%-37.0%) and mixed GGO and consolidation was achieved 47.0% (95% *CI*: 40.0%-54.0%) (Figure 3) (Table 2). As results in Table 2, the most predominant finding in lung HR-CT was GGO with prevalence of 68.0% (95% *CI*: 59.0%-75.0%) which was mostly bilateral 71.0% (95% *CI*: 61.0-79.0%) while mixed GGO+consolidation in 47.0% (95% *CI*: 40.0%-54.0%) of the studied cases.

An important finding in patients infected with COVID-19 was crazy paving pattern that was observed 31.0% (95% *CI*: 20.0%-43.0%). In most of the cases 64.0% (95% *CI*: 55.0%-73.0%) the lesions were peripheral and only in 12.0% (95% *CI*: 6.0%-19.0%) were centrally distributed while in 28.0% (95% *CI*: 18%-40.0%) both central and peripheral distribution was seen. The most pulmonary lesions were mainly distributed in lower lungs 61.0% (95% *CI*: 26.0%-91.0%). CT halo sign was achieved in 17.0% (95% *CI*: 2.0%-41.0%) and pleural effusion in 7.0% (95% *CI*: 4.0%-10.0%) while pricardial effusion was seen in 5.0% (95% *CI*: 1.0%-12.0%) of cases. Besides, 11% (95% *CI*: 5.0%-19.0%) of cases showed lymphadenopathy, 37% (95% *CI*: 26.0%-48.0%) had air bronchogram sign (Table 2). Subgroup analysis of articles that were clarified the exposure, 60.0% (95% *CI*: 45.0%-74.0%) had direct exposure with COVID-19 infected cases. Among studied cases, 76.0% (95% *CI*: 68.0%-83.0%) had fever and 52.0% (95% *CI*: 45.0%-60.0%) had cough. Myalgia/fatigue, dyspnea and muscle pain were observed in 29.0% (95% *CI*: 22.0%-36.0%), 16.0% (95% *CI*: 11.0%-22.0%) and 18.0% (95% *CI*: 11.0%-25.0%)of studied cases. Diarrhea was observed in only 7.0% (95% *CI*: 5.0%-9.0%) of cases (Table 3). Funnel plot of standard error (SE) by effect size (ES) for mixed GGO consolidation and GGO is shown in Figure 4.

Visual inspection of the funnel plot for mixed GGO+consolidation and GGO revealed symmetry and Egger’s test for mixed GGO+consolidation (P=0.597) and GGO (P=0.728) confirmed that there was no potential publication bias.

4. Discussion

We comprehensively searched the databases and collected all available data about radiographic characteristics of confirmed

Table 2. Summary of CT findings in studied COVID-19 cases.

Characteristics	Model	Prevalence (%, 95% *CI*)	Heterogeneity	
			I^2 (%)	*P*
Abnormal CT	Random	86.0% (79.0%-92.0%)	95.00	<0.001
Normal CT	Random	15.0% (9.0-22.0%)	94.00	<0.001
GGO	Random	68.0% (59.0-75.0%)	97.00	<0.001
Mixed GGO and consolidation	Random	47.0% (40.0-54.0%)	91.00	<0.001
Unilateral involvement	Random	21.0% (14.0%-28.0%)	88.00	<0.001
Bilateral involvement	Random	71.0% (61.0-79.0%)	96.00	<0.001
Crazy paving pattern	Random	31.0% (20.0%-43.0%)	96.00	<0.001
Consolidation	Random	29.0% (22.0%-37.0%)	95.00	<0.001
Patchy consolidation	Random	58.0% (23.0%-89.0%)	96.00	<0.001
Micro vascular dilation sign	Random	37.0% (22.0%-53.0%)	95.00	<0.001
Cobble stone/reticular pattern	Random	19.0% (7.0%-35.0%)	98.00	<0.001
Nodule/thorn pear signs	Random	9.0% (5.0%-15.0%)	92.00	<0.001
Linear opacity	Random	27.0% (12.0%-45.0%)	97.00	<0.001
Rounded opacities	Random	27.0% (16.0%-39.0%)	93.00	<0.001
Bronchiectasis	Random	26.0% (14.0%-41.0%)	96.00	<0.001
Air bronchogram	Random	37.0% (26.0%-48.0%)	96.00	<0.001
Fibrosis	Random	24.0% (11.0%-41.0%)	97.00	<0.001
Sub pleural line	Random	26.0% (15.0%-39.0%)	93.00	<0.001
Thickening of pleura	Random	25.0% (9.0%-45.0%)	96.00	<0.001
Thickened interlobular septa	Random	40.0% (27.0%-54.0%)	96.00	<0.001
Central distribution	Random	12.0% (6.0%-19.0%)	93.28	<0.001
Peripheral distribution	Random	64.0% (55.0%-73.0%)	96.00	<0.001
Both central and peripheral distribution	Random	28.0% (18%-40.0%)	96.00	<0.001
Right upper lobe	Random	41.0% (30.0%-52.0%)	94.00	<0.001
Right middle lobe	Random	37.0% (28.0% -46.0%)	89.00	<0.001
Right lower lobe	Random	57.0% (43.0%-70.0%)	96.00	<0.001
Left upper lobe	Random	46.0% (34.0%-58.0%)	95.00	<0.001
Left lower lobe	Random	55.0% (39.0%-71.0%)	97.00	<0.001
Multifocal	Random	59.0% (36.0%-79.0%)	97.00	<0.001
Single lesion	Random	20.0% (11.0%-32.0%)	88.00	<0.001
Multiple lesions	Random	65.0% (50.0%-77.0%)	93.00	<0.001
One lobe affected	Random	19.0% (9.0%-32.0%)	96.00	<0.001
Two lobe affected	Random	8.0% (5.0%-12.0%)	77.00	<0.001
Tree lobe affected	Random	9.0% (6.0%-12.0%)	66.00	<0.001
Four lobe affected	Random	16.0% (5.0%-31.0%)	98.00	<0.001
Five lobe affected	Random	34.0% (23.0%-45.0%)	94.00	<0.001
Halo sign	Random	17.0% (2.0%- 41.0%)	98.00	<0.001
Reverse halo sign	Random	8.0% (2.0%-17.0%)	85.00	<0.001
Lower lung predominant	Random	61.0% (26.0%-91.0%)	96.60	<0.001
Pericardial effusion	Random	5.0% (1.0%-12.0%)	81.00	<0.001
Pleural effusion	Random	7.0% (4.0%-10.0%)	82.00	<0.001
Lymphadenopathy	Random	11.0% (5.0%-19.0%)	95.00	<0.001
Irregular solid nodules	Random	18.0% (0.0%-57.0%)	94.66	<0.001

GGO: Ground glass opacity.

cases of COVID-19 pneumonia from January 2020 to Sepember 2020. After removing duplicates, a total of 54 articles that were conducted on 4 879 cases met eligibility criteria for meta-analysis. Our meta-analysis revealed that only 15.0% of studied patients had normal CT findings, and 86.0% of cases revealed abnormalities in their lung CT. In most cases (71.0%), bilateral lung involvement was presented. The known imaging features in our studied COVID-19 patients were bilateral, multilobular GGO with a peripheral (64.0%) or posterior distribution, mainly in the lower lobes (61.0%). Other findings such as traction bronchiectasis, septal thickening, pleural thickening, and subpleural involvement were less common findings. Other uncommon findings were including CT halo sign (17.0%), pericardial effusion (5.0%), pleural effusion (7.0%), lymphadenopathy (11.0%), nodular lesions (9.0%) and bronchiectasis (26.0%). The key findings at the first step are the exhibition of CT features with or without pneumonia and lesions location. In COVID-19 patients' lesions commonly involve the lower lobes of both lungs and mostly showed subpleural distribution. A considerable point was that 68% of patients showed GGO in their lung CT. Crazy paving pattern was observed in 31.0% (95% *CI*: 20.0%-43.0%) of patients and air bronchogram in 37.0 (95% *CI*: 26.0%-48.0%). There is a report of 97% sensitivity

Studies	Cases	Total	Percentage	95% *CI*
Chen *et al*., Apr. 2020	3	3	1.00	0.50-1.00
Dai *et al*., Mar. 2020	4	4	1.00	0.61-1.00
Zhang *et al*., Apr. 2020	3	5	0.60	0.14-0.98
Xie *et al*., Feb. 2020	5	5	1.00	0.68-1.00
Zhang *et al*., Feb. 2020	7	9	0.78	0.44-0.99
Yoon *et al*., Feb. 2020	2	9	0.22	0.01-0.56
Zhao *et al*., Mar. 2020	17	19	0.89	0.71-1.00
Xia *et al*., Feb. 2020	12	20	0.60	0.37-0.81
Xu *et al.*, Mar. 2020	17	21	0.81	0.61-0.95
Chung *et al*., Feb. 2020	12	21	0.57	0.35-0.78
Ming-Ten *et al*., Feb. 2020	18	21	0.86	0.67-0.98
Pan *et al*., Feb. 2020	18	21	0.86	0.67-0.98
Mohamed *et al*., Sep. 2020	20	27	0.74	0.56-0.89
Long *et al*., Mar. 2020	11	36	0.31	0.16-0.47
Xu *et al*., Feb. 2020	30	50	0.60	0.46-0.73
Song *et al*., Apr. 2020	39	51	0.76	0.64-0.87
Tung-Chen *et al*., Jul. 2020	37	51	0.73	0.59-0.84
Li *et al*., Feb. 2020	46	51	0.90	0.80-0.97
Guan *et al*., Mar. 2020	47	53	0.89	0.79-0.96
Xiang *et al*., Aug. 2020	28	53	0.53	0.39-0.66
Liu *et al*., Mar. 2020	43	55	0.78	0.66-0.88
Meng *et al*., Apr. 2020	55	58	0.95	0.87-0.99
Zhang *et al*.,May 2020	58	60	0.97	0.90-1.00
Zhou *et al*., August 2020	38	62	0.61	0.49-0.73
Zhou *et al*., Mar. 2020	25	62	0.40	0.28-0.53
Zhou *et al*., Feb. 2020	25	62	0.40	0.28-0.53
Pan *et al*., Feb. 2020	54	63	0.86	0.76-0.93
Luo *et al*., May 2020	66	73	0.90	0.82-0.96
Li *et al*., Feb. 2020	45	78	0.58	0.47-0.68
Wu *et al*., Feb. 2020	73	80	0.91	0.84-0.97
Shi *et al*., Feb. 2020	67	81	0.83	0.74-0.90
Li *et al*., Jun. 2020	81	83	0.98	0.93-1.00
Wang *et al*., Mar. 2020	49	90	0.54	0.44-0.65
Xu *et al*., Feb. 2020	65	90	0.72	0.62-0.81
Cui *et al*., Feb./Apr. 2020	41	95	0.43	0.33-0.53
Chen *et al*., Mar. 2020	32	98	0.33	0.24-0.42
Chen *et al*., Jan. 2020	14	99	0.14	0.08-0.22
Zhao *et al*., Mar. 2020	87	101	0.86	0.79-0.92
Inui *et al*., Apr. 2020	22	104	0.21	0.14-0.30
Han *et al*., Aug. 2020	65	108	0.60	0.51-0.69
Wang *et al*., Mar. 2020	30	114	0.26	0.19-0.35
Bernheim *et al*., Feb. 2020	41	121	0.34	0.26-0.43
Liu *et al*., May 2020	40	122	0.33	0.25-0.41
Roberto *et al*., Apr. 2020	122	134	0.91	0.86-0.95
Wang *et al*., Apr. 2020	138	138	1.00	0.99-1.00
Parry *et al*., Jun. 2020	51	147	0.35	0.27-0.43
Yang *et al*., Feb. 2020	96	149	0.64	0.57-0.72
Caruso *et al*., Aug. 2020	58	158	0.37	0.29-0.44
Bai *et al*., Mar. 2020	200	219	0.91	0.87-0.95
Colombi *et al*., Apr. 2020	82	236	0.35	0.29-0.41
Ai *et al*., Feb. 2020	409	888	0.46	0.43-0.49
Random-effects model			0.68	0.59-0.75

Heterogeneity: I^2=97%, τ^2=0.0823, χ^2=1473.41 (*P*<0.01)

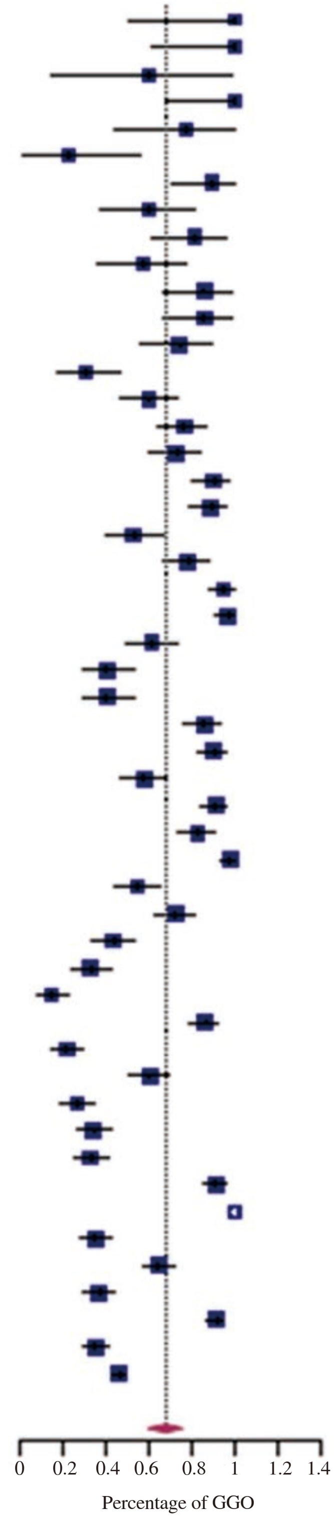

Figure 2. Estimation of ground glass opacity under a random-effects model. GGO: Ground glass opacity.

Studies	Cases	Total	Percentage	95% *CI*
Xie *et al.*, Feb. 2020	2	5	0.40	0.02-0.86
Xu *et al.*, Mar. 2020	9	21	0.43	0.22-0.65
Chung *et al.*, Feb. 2020	6	21	0.29	0.11-0.50
Ming-Yen *et al.*, Feb. 2020	4	21	0.19	0.05-0.39
Mohamed *et al.*, Sep. 2020	3	27	0.11	0.02-0.26
Long *et al.*, Mar. 2020	19	36	0.53	0.36-0.69
Xu *et al.*, Feb. 2020	25	50	0.50	0.36-0.64
Song *et al.*, Apr. 2020	30	51	0.59	0.45-0.72
Li *et al.*, Feb. 2020	31	51	0.61	0.47-0.74
Guan *et al.*, Mar. 2020	33	53	0.62	0.49-0.75
Xiang *et al.*, Aug. 2020	24	53	0.45	0.32-0.59
Liu *et al.* Aug., 2020	43	55	0.78	0.66-0.88
Zhou *et al.*, Aug. 2020	22	62	0.35	0.24-0.48
Zhou *et al.*, Mar. 2020	39	62	0.63	0.50-0.75
Luo *et al.*, May 2020	66	73	0.90	0.82-0.96
Li *et al.*, Feb. 2020	43	78	0.55	0.44-0.66
Wang *et al.*, Mar. 2020	30	90	0.33	0.24-0.43
Cui *et al.*, Feb./Apr. 2020	29	95	0.31	0.22-0.40
Zhao *et al.*, Mar. 2020	65	101	0.64	0.55-0.73
Inui *et al.*, Apr. 2020	30	104	0.29	0.21-0.38
Han *et al.*, Aug. 2020	44	108	0.41	0.32-0.50
Wang *et al.*, Mar. 2020	50	114	0.44	0.35-0.53
Bernhiem *et al*., Feb. 2020	50	121	0.41	0.33-0.50
Liu *et al*., May 2020	57	122	0.47	0.38-0.56
Parry *et al*. Jun. 2020	21	147	0.14	0.09-0.20
Yang *et al*., Feb. 2020	71	149	0.48	0.40-0.56
Bai *et al*., Mar. 2020	141	219	0.64	0.58-0.71
Colombi *et al*., Apr. 2020	119	236	0.50	0.44-0.57
Random-effects model			0.47	0.40-0.54

Heterogeneity: I^2=91%, τ^2=0.0307, χ^2=299.77 (P<0.01)

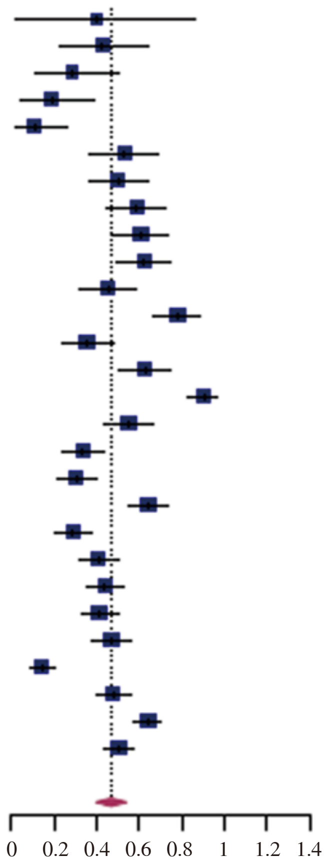

Figure 3. Estimation of ground glass opacity and consolidation under a random-effects model. GGO: Ground glass opacity.

Table 3. Clinical characteristics of the included COVID- 19 cases.

Clinical characteristics	Model	Prevalence (%, 95% *CI*)	Heterogeneity	
			I^2 (%)	*P*
Direct exposure	Random	60.0% (45.0%-74.0%)	98.0	0.000
Indirect exposure	Random	43.0% (22.0%-46.0%)	97.0	<0.001
Fever	Random	76.0% (68.0%-83.0%)	96.0	<0.001
Cough	Random	52.0% (45.0%-60.0%)	95.0	<0.001
Myalgia/Fatigue	Random	29.0% (22.0%-36.0%)	91.0	<0.001
Sore throat	Random	11.0% (8.0%-14.0%)	80.0	<0.001
Rhinorrhea	Random	9.0% (5.0%-15.0%)	79.0	<0.001
Dyspnea	Random	16.0% (11.0%-22.0%)	94.0	<0.001
Muscle pain	Random	18.0% (11.0%-25.0%)	88.0	<0.001
Headache	Random	8.0% (7.0%-10.0%)	22.0	0.180
Diarrhea	Random	7.0% (5.0%-9.0%)	63.0	<0.001
Nausea/vomiting	Random	5.0% (2.0%-8.0%)	75.0	<0.001
No symptom	Random	6.0% (3.0%-10.0%)	45.0	0.090

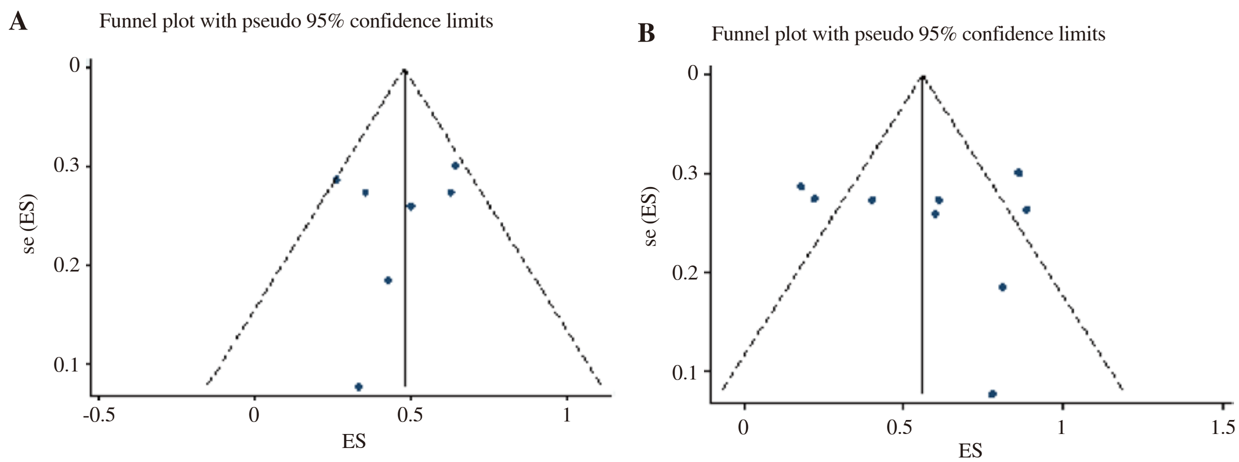

Figure 4. Funnel plot of standard error by effect size. A: Funnel plot for mixed ground glass opacity and consolidation; B: Funnel plot for ground glass opacity; ES: Effect size; se: Standard error.

on chest CT findings in COVID-19 patients while the interval time between initial negative and positive RT-PCR is about 5 d. The increasing of the lesions and involved lobes along with the gradual appearance of consolidative opacities may be presented as previously described by Jin *et al.* who summarized CT findings of COVID-19 in five stages including (1) ultra-early; (2) Early; (3) Rapid progression; (4) Consolidation and dissipation stages[65]. In the ultra-early stage (1-2 weeks after exposure) the patients are symptomless and single or multiple GGO along with patchy consolidative opacities and air bronchograms may be presented in CT. In their study, 54% of their patients were in early-stage and CT findings were single or multiple GGOs or GGO combined with interlobular septal thickening. They declared in the rapid progression stage occurred in 3-7 d after symptoms, CT findings were large, light consolidative opacities and air bronchograms. In stage 4 or 2 weeks after symptoms, the findings were including the reduction of size and density of consolidative opacities, patchy consolidative opacities dispreading in form of strip-like opacities, thickening of the bronchial wall, and interlobular septal thickening[15]. Guan *et al.* in a study carried out on 53 confirmed cases of infection with COVID-19, declared that 88.7% of the patients had the findings of infection with COVID-19. Among all 47 cases, in 78.7% both lungs were involved, and all showed GGO (59.6% round and 40.4% patchy). Also, crazy paving pattern was observed in 89.4% and bronchogram in 76.6%. Air bronchograms were observed within GGO (61.7%) and consolidation (70.3%). Enlarged mediastinal lymph nodes or pleural effusion was not seen in many cases. They followed up 33 patients for 3-6 d. In 75.8% of cases, the lesions were increased and resorbed in 24.2% of patients[11]. Even in some referred cases for reasons other than COVID-19, abnormal CT findings may be found[12]. This shows the importance of CT findings in the early detection and management of pneumonia caused by the COVID-19 virus in cases of being symptomatic at least for three days[13]. But there is an exception in 56% of cases who have normal CT the first two days before symptom onset.

Although we tried to overcome publication bias and also, did subgroup analysis to find the source of heterogeneity, there is some concern about methodology quality in chest CT findings of COVID-19 pneumonia. Another limitation is that we did not include some important databases like Clinical Key, Embase, Cochrane Library in our study. Besides, included studies in a period of 2020 Jan to 2020 Sep and the included data is not the newest.

5. Conclusion

Based on the available data, several chest CT finding seems to be decisive for COVID-19 but, normal chest CT findings do not exclude COVID-19 even in asymptomatic patients. In the present epidemic condition chest CT surely plays a critical role in the early detection of COVID-19 pneumonia. Some typical CT features like peripheral GGO with multifocal distribution and progressive nature of lesions are suggestive for COVID-19 pneumonia. During this time, the number and the size of opacities keep increasing to reach the most severe stage in 10 d after the first symptoms. Chest CT may be used to predict the prognosis of diseases, but the results may be poor in the early detection of complications in patients who require further mechanical ventilation or in patients with consolidative forms. Centrilobular nodules, mucoid impactions, and unilateral segmental or lobar consolidations may be presented in bacterial pneumonia or super infections. Also, RT-PCR should be confirmed finally, but the positive results may be postponed, and sometimes must repeat the test if the CT features are suspected to be COVID-19. To sum up, the collaboration between clinical and laboratory findings with chest CT imaging is needed for the early diagnosis of COVID-19.

Conflict of interest statement

The authors report no conflict of interest.

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Authors' contributions

M.T. was the study designer and critically appraised the manuscript; A.S. was involved in writing, critical apprising, and submitting the manuscript; P.N. was involved in statistical analysis; S.P. gathered the data; S.M. and H.M. were involved in critical apprising.

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