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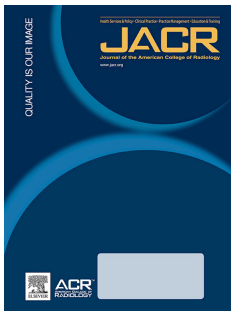

COVID-19 Computed Tomography Findings: A Systematic Review and Meta-Analysis

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COVID-19 Computed Tomography Findings: A Systematic Review and Meta-Analysis

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Author Contributions

Cuiping Bao extracted data, analyzed statistics, analyzed and interpreted data, drafted the manuscript. Xuehuan Liu critically reviewed/edited the manuscript for important intellectual content. Han Zhang participated in the study search strategy. Yiming Li designed the study and contributed to the data interpretation, critically reviewed/edited the manuscript. Jun Liu originated and designed the study, analyzed

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and interpreted data, and critically reviewed/edited the manuscript for important intellectual content.

Disclosure

No potential conflicts of interest relevant to this article were reported.

The authors declare that they had full access to all of the data in this study and the authors take complete responsibility for the integrity of the data and the accuracy of the data analysis

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Title: COVID-19 Computed Tomography Findings: A Systematic Review and Meta-Analysis

Abstract

Purpose To date, there remain considerable knowledge gaps regarding the chest CT imaging features of COVID-19. We performed a systematic review and meta-analysis aimed to quantitatively summarize results from published studies to date to provide a summary of evidence on detection of COVID-19 by chest CT and the expected CT imaging manifestations.

Methods Studies were identified by searching PubMed database for articles published December 2019 – February 2020. Pooled CT positive rate of COVID-19 and pooled incidence of CT imaging findings were estimated using a random-effect model.

Results A total of 13 studies met inclusion criteria. The pooled positive rate of the CT imaging was 89.76% and 90.35% when only including thin-section chest CT. Typical CT signs were ground glass opacities (GGO) (83.31%), GGO with mixed consolidation (58.42%), adjacent pleura thickening (52.46%), interlobular septal thickening (48.46%), and air bronchograms (46.46%). Other CT signs included crazy paving pattern (14.81%), pleural effusion (5.88%), bronchiectasis (5.42%), pericardial effusion (4.55%) and lymphadenopathy (3.38%). The most anatomic distributions were bilateral lung infection (78.2%) and peripheral distribution (76.95%). The incidences were highest in the right lower lobe (87.21%), left lower lobe (81.41%),

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and bilateral lower lobes (65.22%). The right upper lobe (65.22%), right middle lobe (54.95%) and left upper lobe (69.43%) were also commonly involved. The incidence of bilateral upper lobes was 60.87%. A considerable proportion of patients had 3 or more lobes involved (70.81%).

Conclusions The detection of COVID-19 chest CT imaging is very high among symptomatic individuals at high risk, especially using thin-section chest CT. The most common CT features in patients affected by COVID-19 included GGO and consolidation involving the bilateral lungs in a peripheral distribution.

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Key words COVID-19; thin-section chest computed tomography; CT imaging findings; ground glass opacities; meta analysis

Beginning in December 2019, a number of cases with pneumonia of unexplained cause occurred in Wuhan, Hubei province, China. Deep sequencing from lower respiratory tract samples confirmed infection caused by a novel coronavirus which had previously not been found in humans or animals. Subsequently, this novel coronavirus was named corona virus disease 2019 (COVID-19) by the World Health Organization[1]. COVID-19 infections cause clusters of severe respiratory illness and its main clinical manifestations are fever, cough, shortness of breath and myalgia or fatigue[2,3]. Not only patients with symptoms, but also patients in the incubation period, can become the source of infection. Therefore, early diagnosis is very important.

Radiological examinations, as a routine imaging tool for pneumonia diagnosis, is of great importance in the early detection and treatment of patients affected by COVID-19. Radiological examinations are relatively easy to perform and can produce fast diagnosis. Chest radiography is not sensitive for the detection of ground-glass opacity (GGO) and may demonstrate normal findings in early stage of infection. In contrast, thin-section chest CT examination plays a key role in assisting diagnosis. To

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date, there remains considerable knowledge gaps in the chest CT imaging features of COVID-19.

In this systematic review and meta-analysis, we aim to quantitatively summarize results from published studies to date in order to provide a more precise estimate of detection of COVID-19 by chest CT and report on the most common imaging findings on chest CT imaging.

Materials and methods

Retrieval of studies

We searched PubMed for studies reporting CT imaging features of COVID-19 published between 1 December 2019 to 29 February 2020. The search terms included (COVID-19) OR (2019 Novel Coronavirus) OR (2019-nCoV). In addition, we reviewed the reference lists of retrieved articles for additional articles. Two independent investigators screened titles/abstracts according to the inclusion and exclusion criteria. The meta-analysis was performed using PRISMA guidelines.

Inclusion and exclusion criteria

Titles and abstracts of the articles were screened using the following inclusion criteria to identify all eligible studies: (1) original articles with full text; (2) the mean/median age of the study population above 18 years; (3) at least one of the outcomes was chest CT imaging features of COVID-19; (4) the number of patients with corresponding imaging features was reported in the study. Studies were excluded

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if: (1) they lacked corresponding outcome parameters or research data; (2) did not have available full texts. When there were multiple publications from the same population, only data from the most recent report or the study with the larger sample size was included.

Data extraction

We extracted the following information from each publication: the first author's full name, study sample size, mean/median age, gender distribution, application of thin-section chest CT, results of chest CT imaging features and the number of patients with each corresponding imaging features. The recorded chest CT imaging features mainly included the following aspects: (1) patterns of the lesion (GGO; consolidation; GGO mixed consolidation; air bronchogram; interlobular septal thickening; crazy paving pattern; bronchiectasis; adjacent pleura thickening; pleural effusion; pericardial effusion; lymphadenopathy); (2) lesion distribution (bilateral lung, peripheral, central); and (3) lobe distribution and the number of lobes involved (Figure 1).

Statistical analysis

In this systematic review and meta-analysis, we pooled data using the single arm analysis. Because some proportions extracted from the original data were too high or too low, we transformed the data using the double arcsine method into a normal distribution. We conducted the meta-analysis using the transformed data. The pooled proportion was calculated using the result of the meta-analysis by the formula

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($P=(\sin(tp/2))^2$). Statistical heterogeneity between studies was evaluated with Cochran's Q test and the I^2 statistic [4]. For the Q statistic, a p value < 0.10 was considered statistically significant for heterogeneity; for I^2, a value >50% was considered to have severe heterogeneity. Publication bias was evaluated by constructing a funnel plot and by Egger's test [5]. For Egger's test, a p value < 0.10 was considered to be statistically significant. All statistical analyses were performed with Stata SE 13 for Windows.

Results

Characteristics of the subjects in selected studies

Detailed search procedures are summarized in Figure 2. All of the full texts of the 41 identified articles was retrieved for detailed evaluation. Of them, 28 articles did not meet the inclusion criteria, including 6 duplicated populations, 15 case reports/case series, 3 without related data, and 4 review articles. The remaining 13 independent studies were used in the current analysis [6-18]. Of these studies, 10 studies reported one or more chest CT imaging signs [6-8,10-12,14-16,18], 11 studies reported at least one kind of lung distribution [6-8,10,11,13-18], 5 studies reported the lobes and total number of lobes involved [7,9,11,15,16].

The 13 studies had 2738 participants with 2386 having abnormal CT imaging features. In the primary meta-analysis, we found that the pooled positive rate of the CT imaging was 89.76% (95%CI: 84.42%, 93.84%) (Figure 3). When we excluded the studies without mention of thin-section chest CT, the result was 90.35% (95%CI: 83.68%, 95.42%).

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Patterns of the lesion

In this meta-analysis, we found that typical CT imaging appearance for COVID-19 patients was GGO. The incidence of GGO was 83.31% (95% CI: 69.43%, 93.35%). When we excluded the studies without mention of thin-section chest CT, the incidence of GGO was 85.49% (95% CI: 64.74%, 97.89%). The incidence of GGO with mixed consolidation was 58.42% (95%CI: 48.46%, 67.58%). The incidences of interlobular septal thickening, adjacent pleura thickening and air bronchogram were also high: 48.46% (95% CI: 11.44%, 86.19%), 52.46% (95% CI:15.53%, 87.54%) and 46.46% (95% CI: 17.76%, 76.95%) respectively. The incidence of crazy paving pattern was 14.81% (95%CI: 6.61%, 25.99%). Other atypical CT imaging findings included bronchiectasis (5.42%, 95% CI:0.02%, 19.31%), pleural effusion (5.88%, 95% CI:3.38%, 8.73%), pericardial effusion (4.55%, 95% CI: 2.09%, 7.90%) and lymphadenopathy (3.38%, 95% CI: 1.00%, 6.86%) respectively (Table 2).

Lesion distribution

We found that most patients with COVID-19 have bilateral lung infection; the incidence was 78.2% (95%CI: 65.69%, 88.19%). When we excluded the studies without mention of thin-section chest CT, bilateral lung infection was seen in 81.80% of patients (95% CI: 73.94%, 88.51%). The lesions were mostly located in the peripheral area (76.95%, 95% CI: 57.43%, 91.50%). Fewer lesions were located in the central (peribronchovascular) area (10.81%, 95% CI: 0.12%, 41.50%) (Table 2).

Lobe distribution and number of lobes involved

COVID-19 infection can involve all lobes. In this pooled meta-analysis, we found that the right lower lobe and left lower lobe were the most commonly involved;

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87.21% (95% CI: 80.23%, 92.84%) and 81.41% (95% CI: 76.1%, 86.53%), respectively. The incidence of bilateral lower lobes was 65.22% (95% CI: 55.95%, 73.94%). The right upper lobe and left upper lobe were also commonly involved; 65.22% (95%CI: 54.95%, 75.24%) and 69.43% (95%CI:58.91%, 79.02%), respectively. The incidence of bilateral upper lobes was 60.87% (95% CI: 51.46, 69.43%). More than half patients had right middle lobe infection (54.95%, 95% CI: 47.96%, 61.36%). There were 39.54% (95%CI: 33.76%, 45.96%) of patients with all lobes affected and 20.51% (95%CI: 13.76%, 28.22%) patients with 4 lobes affected. A significant proportion of patients had 3 or more lobes involved (70.81%, 95% CI: 61.75%, 79.10%) (Table 2).

Publication bias

P values for Egger's regression asymmetry test are shown in Table 3. There was a low probability of publication bias in the following subgroups: GGO mixed consolidation, air bronchogram, crazy paving pattern, pleural effusion, pericardial effusion, lymphadenopathy, peripheral, lobe of lesion distribution and number of lobes involved. However, there was publication bias in the subgroup of abnormal GGO, consolidation, and bilateral lung involvement. Because there were only two studies in the subgroup of bronchiectasis, adjacent pleura thickening, central, bilateral upper lobes and bilateral lower lobes, the publication bias could not be evaluated.

Discussion

Our systematic review and meta-analysis suggests that the proportion of COVID-19 detected by chest CT imaging is very high. The most typical CT imaging

finding is GGO. Other common CT features in patients affected by COVID-19 included consolidation, interlobular septal thickening, adjacent pleura thickening, and air bronchograms. More than half of the patients manifested as GGO, consolidation and adjacent pleura thickening. Imaging findings mostly involved the bilateral lungs and were located in the peripheral area of the lungs. The infection can involve all the lobes, and mostly the bilateral lower lobes.

Some patients who had negative reverse transcription polymerase chain reaction (RT-PCR) for COVID-19 at initial presentation may still show chest CT abnormalities [19]. Fang et al reported that the sensitivity of first RT-PCR is 71%, which may be lower than that of chest CT [20]. In our meta-analysis of 2738 cases, the pooled positive rate of CT imaging was 89.76% among patients suspected to have COVID-19. Thus, chest CT plays an important role in the early diagnosis of COVID-19.

In this analysis, we found that the typical CT features of COVID-19 are GGO and lung consolidation. Some of the GGO were further developed into reticular interlobular septa thickening and “crazy paving pattern”, indicating that the infection leads to diffuse alveolar edema and interstitial inflammatory [21,22]. Several patients appeared to have pleural effusion, which may represent a poor prognostic indicator [23]. Generally, viral pneumonias have similar etiological mechanisms and typical imaging findings of COVID-19. Thus, these findings also appear in other viral pneumonia such as the common cold, influenza, and other coronaviruses diseases including SARS and MERS [24-28].

Since COVID-19, SARS and MERS all belong to family of coronaviruses, the

CT imaging signs are more similar. Still, there appear to be unique imaging characteristics for COVID-19. Unilateral involvement is more common in the early stage of SARS and MERS [29,30]. In contrast, COVID-19 infection appears to be more commonly bilateral. In this meta-analysis, most patients had bilateral lung involvement, especially the bilateral lower lobes. Overall, 70% of patients had 3 or more lobes involved.

Our meta-analysis has several strengths. First, the number of cases included was relatively large for 3 months of early publications, providing aggregate evidence for evaluating diagnosis of COVID-19 by chest CT. Second, the included studies were conducted in different hospitals and settings, making the results more generalizable. Third, in this analysis, we extract varieties of different imaging features, including both specific imaging features and distribution patterns in the lungs.

Our meta-analysis also has several limitations. First a majority of the studies included did not distinguish between clinically mild, moderate, and severe patients. Furthermore, some patients may have co-morbidities and chronic diseases such as diabetes and hypertension that we cannot account for. These factors may be affect imaging appearances. Second, due to different CT scanners and interpreting radiologists, the reported imaging features may be variable across sites.

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Figure 1 Baseline CT images (a-d) of a 50 year-old man admitted for symptoms of fever for 1 day: there were multiple patchy ground-glass opacities in the left upper lobe and right lower lobe (a and b); air bronchogram and crazy paving pattern can be visible(c); the lesions located in the peripheral area of the lung(d).

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Figure 2 Flow chart on the articles selection process

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Figure 3 Forest plot of the studies for abnormal CT among presumed COVID-19 infection

Figure 4 Forest plot of the studies for CT findings (GGO, consolidation, GGO with mixed consolidation)

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Table 1 Characteristics of 13 Reviewed Studies

Author	Sample size	Mean/median age	Gender	Thin-section chest CT	CT abnormal	CT imaging manifestations
Zhang Mingqiang et al.	9	35	Male:5 Female:4	Yes	7	GGO; consolidation; bilateral lung Pleural effusion
Fengxiang Song et al.	51	49	Male:25 Female:26	Yes	51	GGO; consolidation; bilateral lung; peripheral; central; pleural effusion; pericardial effusion; lymphadenopathy
Yueying Pan et al.	63	44.9	Male:33 Female:30	Yes	63	GGO; consolidation
Jiong Wu et al.	80	44	Male:42 Female:38	Yes	76	GGO; consolidation; interlobular septal thickening; crazy paving pattern; pleural effusion; pericardial effusion; lymphadenopathy; peripheral; central;
Adam Bernheim et al.	121	45.3	Male:61 Female:60	Yes (22 with conventional CT)	94	GGO; consolidation; crazy paving pattern; pleural effusion; bronchiectasis; lymphadenopathy; peripheral; central;
Tao Ai et al.	1014	51	Male:467 Female:547	Yes	888	bilateral lung; GGO; consolidation; interlobular septal thickening
Heshui Shi et al.	81	49.5	Male:42 Female:39	Yes	81	bilateral lung; GGO; consolidation; interlobular septal thickening; adjacent pleura thickening; air bronchogram; pleural effusion; bronchiectasis; lymphadenopathy; peripheral;
WANG Jincheng et al.	52	44	Male:29 Female:23	Yes	50	GGO; consolidation; interlobular septal thickening
Yu-Huan Xu et al.	50	43.9	Male:29 Female:21	Yes	41	GGO; consolidation; interlobular septal thickening; air bronchogram; pleural effusion; peripheral; central;
Jin-jin Zhang	140 (135 with chest CT scan)	57	Male:69 Female:71	Without mention	134	Bilateral Lung

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W. Guan et al.	1099 (975 with chest CT scan)	47	Male: 637 Female: 459	Without mention	840	bilateral lung; GGO; interlobular septal thickening;
Jian Wu *et al.*	80	46.1	Male: 39 Female: 41	Without mention	55	bilateral lung
Xi Xu *et al.*	90	50	Male: 39 Female: 51	Yes	69	bilateral lung; GGO; consolidation; crazy paving pattern; interlobular septal thickening; air bronchogram; adjacent pleura thickening; pleural effusion; pericardial effusion; lymphadenopathy; peripheral

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Table 2 CT Imaging Findings in the Meta-Analysis

CT manifestations	Pooled transformed results (95 % CI)	Pooled proportion (95 % CI)*
Patterns of the lesion		
GGO	2.3 (1.97, 2.62)	83.31 (69.43, 93.35)
Consolidation	1.45 (1.22, 1.68)	43.97 (32.82, 55.45)
GGO mixed consolidation	1.74 (1.54, 1.93)	58.42 (48.46, 67.58)
Air bronchogram	1.5 (0.87, 2.14)	46.46 (17.76, 76.95)
Interlobular septal thickening	1.54 (0.69, 2.38)	48.46 (11.44, 86.19)
Crazy paving pattern	0.79 (0.52, 1.07)	14.81 (6.61, 25.99)
Bronchiectasis	0.47 (0.03, 0.91)	5.42 (0.02, 19.31)
Adjacent pleura thickening	1.62 (0.81, 2.42)	52.46 (15.53, 87.54)
Pleural effusion	0.49 (0.37, 0.6)	5.88 (3.38, 8.73)
Pericardial effusion	0.43 (0.29, 0.57)	4.55 (2.09, 7.90)
Lymphadenopathy	0.37 (0.2, 0.53)	3.38 (1.00, 6.86)
Lesion distribution		
Bilateral Lung	2.17 (1.89, 2.44)	78.2 (65.69, 88.19)
Peripheral	2.14 (1.72, 2.55)	76.95 (57.43, 91.50)
central	0.67 (-0.07, 1.4)	10.81 (0.12, 41.50)
Lobe of lesion distribution		
Right upper lobe	1.88 (1.67, 2.1)	65.22 (54.95, 75.24)
Right middle lobe	1.67 (1.53, 1.8)	54.95 (47.96, 61.36)
Right lower lobe	2.41 (2.22, 2.6)	87.21 (80.23, 92.84)
Left upper lobe	1.97 (1.75, 2.19)	69.43 (58.91, 79.02)
Left lower lobe	2.25 (2.12, 2.39)	81.41 (76.1, 86.53)
Bilateral upper lobes	1.79 (1.6, 1.97)	60.87 (51.46, 69.43)
Bilateral lower lobes	1.88 (1.69, 2.07)	65.22 (55.95, 73.94)
Number of Lobes involved		
1	0.81 (0.52, 1.09)	15.53 (6.61, 26.88)
2	0.75 (0.62, 0.87)	13.42 (9.31, 17.76)
3	0.67 (0.55, 0.8)	10.81 (7.37, 15.16)
4	0.94 (0.76, 1.12)	20.51 (13.76, 28.22)
5	1.36 (1.24, 1.49)	39.54 (33.76, 45.96)
lobes Involved ≥3	2 (1.808, 2.192)	70.81 (61.75, 79.10)

∗ The results are expressed as a percentage

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Table 3 Results of the Egger test

CT manifestations	P	**Lobe of lesion distribution**	P
Abnormal CT	**<** 0.001	Right upper lobe	0.264
GGO	0.001	Right middle lobe	0.142
Consolidation	0.007	Right lower lobe	0.074
GGO mixed consolidation	0.116	Left upper lobe	0.056
Air bronchogram	0.974	Left lower lobe	0.064
Interlobular septal thickening	0.025	Bilateral upper lobes	NA
Crazy paving pattern	0.456	Bilateral lower lobes	NA
Bronchiectasis	NA	**Number of Lobes involved**	
Adjacent pleura thickening	NA	1	0.379
Pleural effusion	0.675	2	0.189
Pericardial effusion	0.942	3	0.219
Lymphadenopathy	0.716	4	0.563
Lesion distribution		5	0.067
Bilateral lung	**<** 0.001	**lobes Involved ≥3**	0.131
Peripheral	0.890		
central			

NA: The publication bias could not be tested

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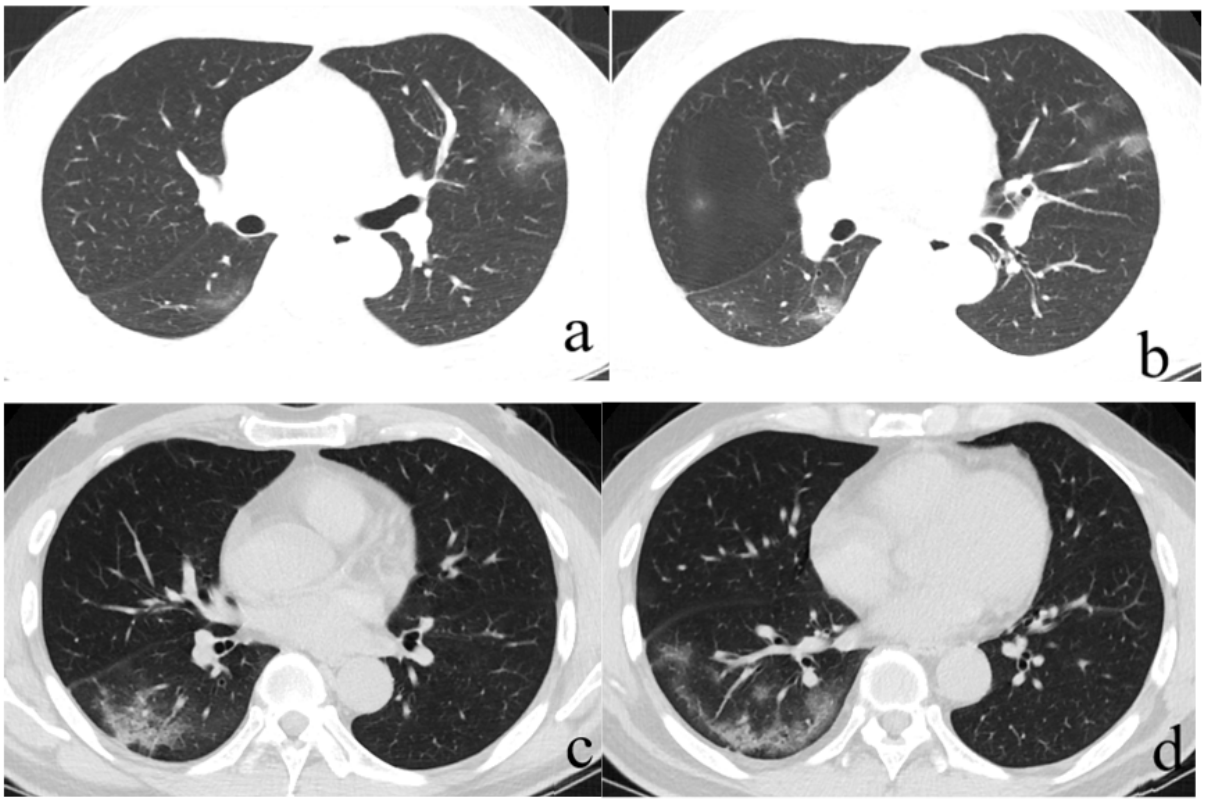
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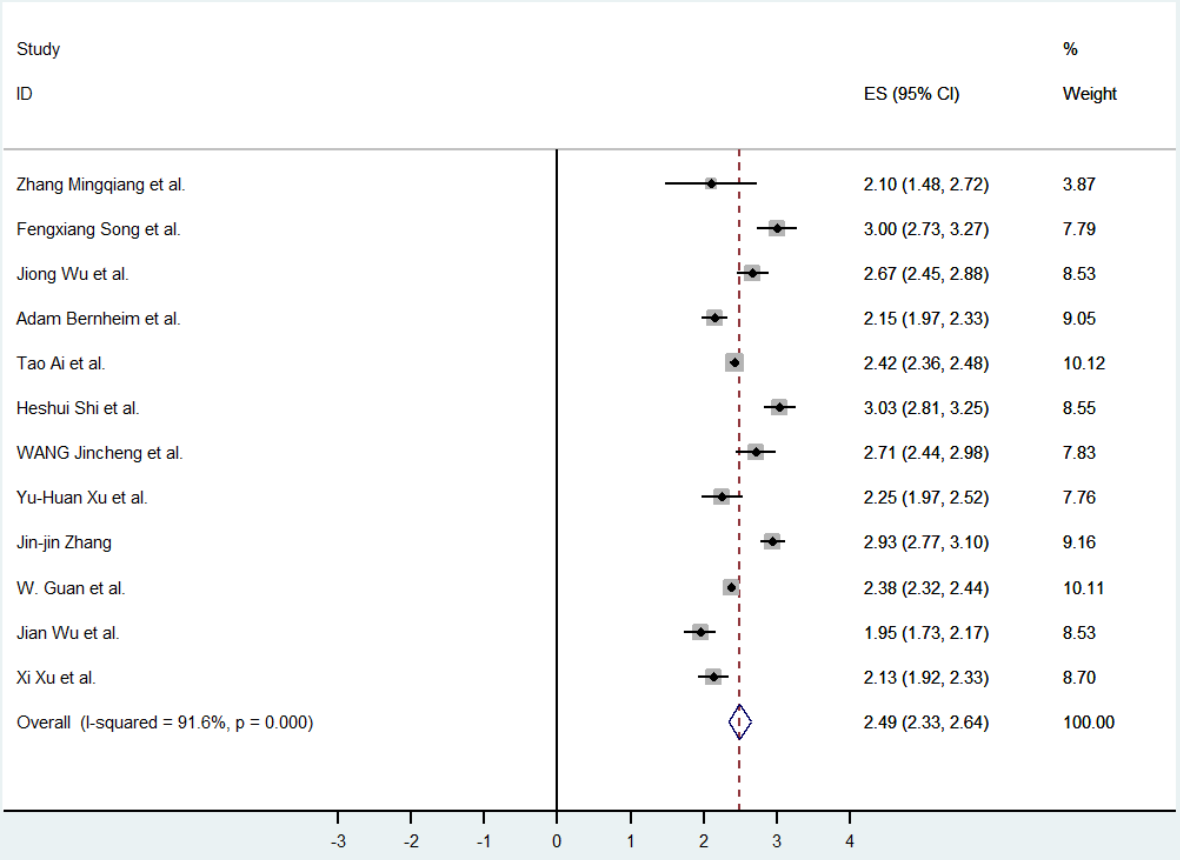
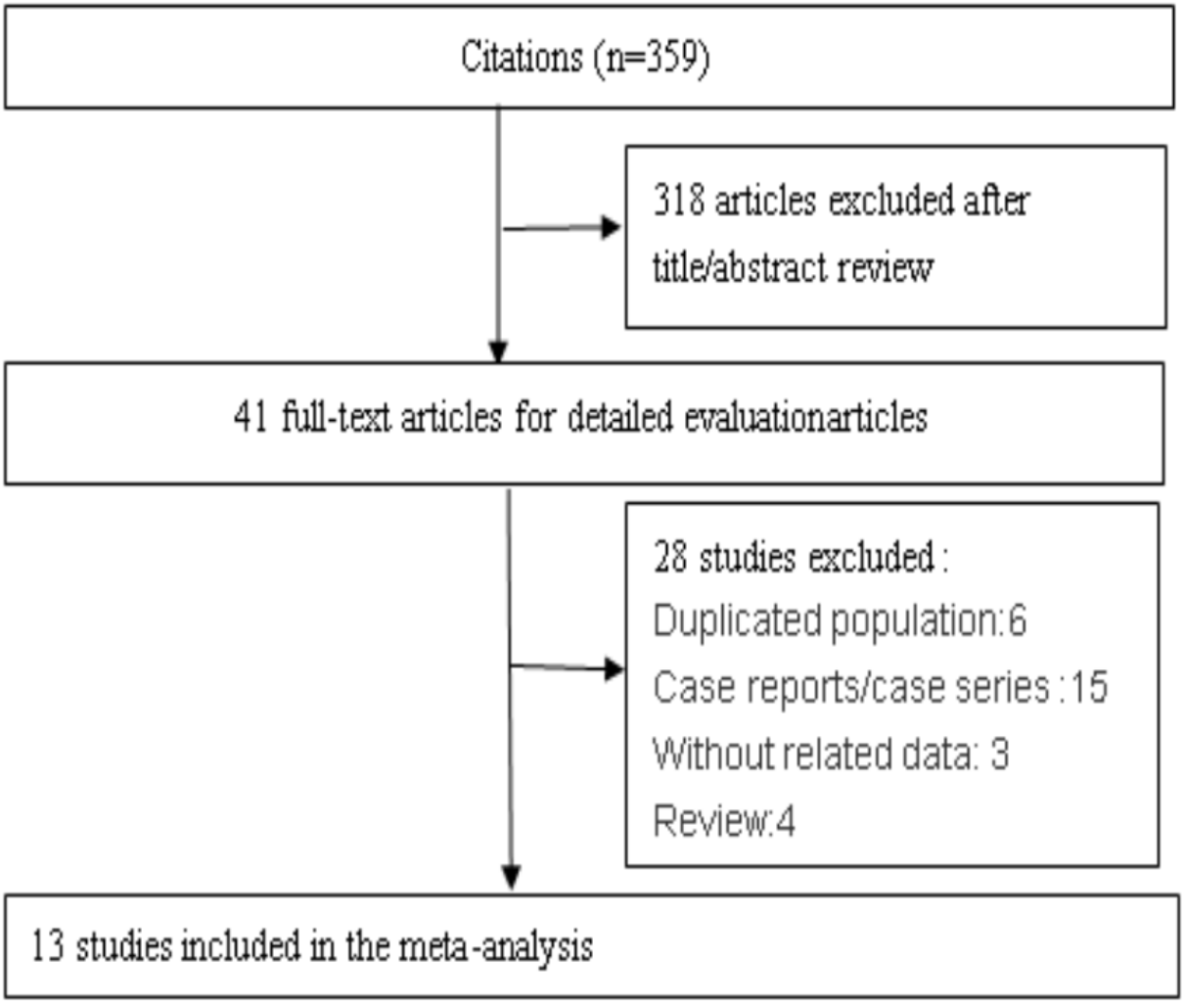
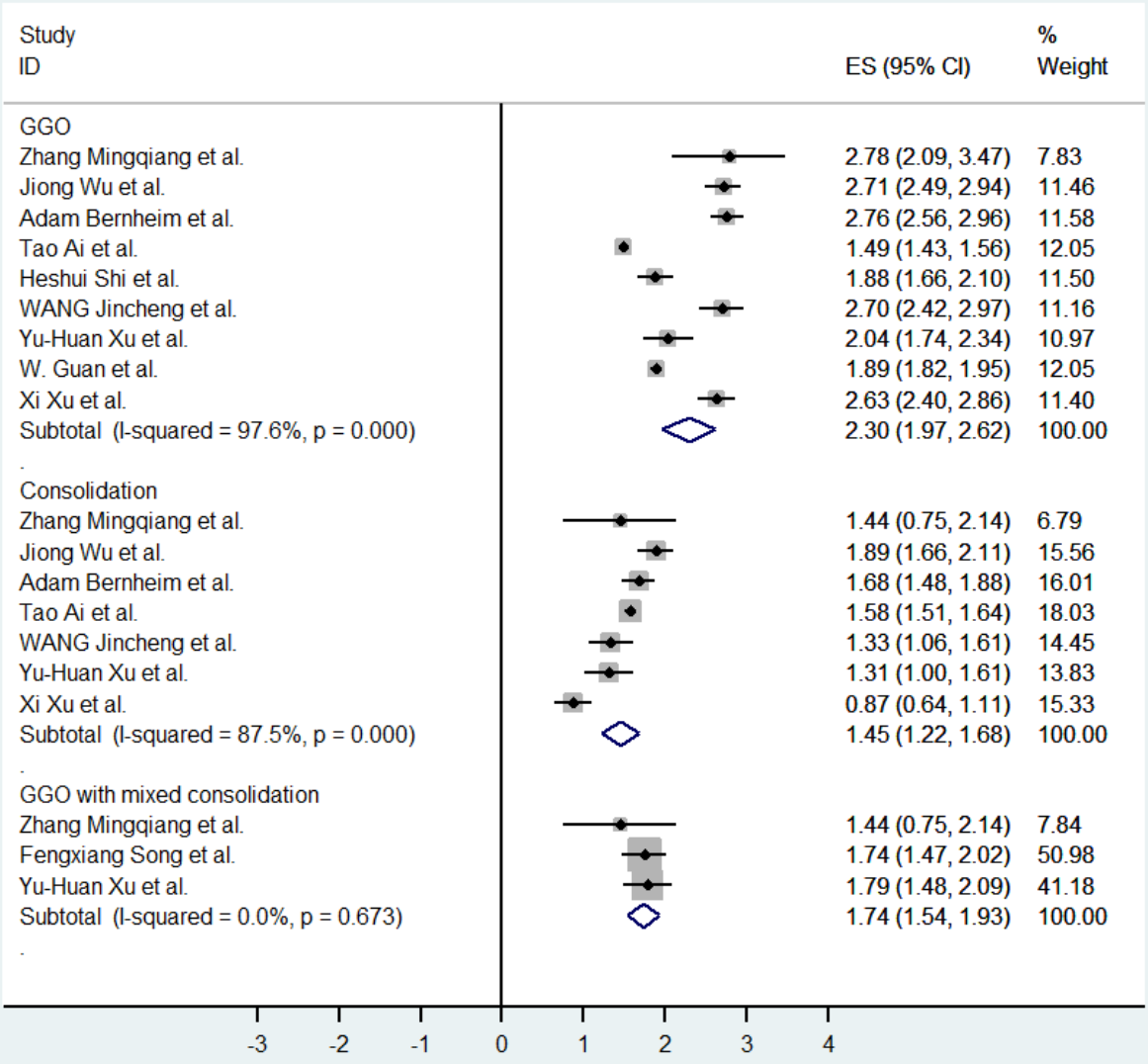

Study
ID
ES (95% CI)
%
Weight
Zhang Mingqiang et al.
2.10 (1.48, 2.72)
3.87
Fengxiang Song et al.
3.00 (2.73, 3.27)
7.79
Jiong Wu et al.
2.67 (2.45, 2.88)
8.53
Adam Bernheim et al.
2.15 (1.97, 2.33)
9.05
Tao Ai et al.
2.42 (2.36, 2.48)
10.12
Heshui Shi et al.
3.03 (2.81, 3.25)
8.55
WANG Jincheng et al.
2.71 (2.44, 2.98)
7.83
Yu-Huan Xu et al.
2.25 (1.97, 2.52)
7.76
Jin-jin Zhang
2.93 (2.77, 3.10)
9.16
W. Guan et al.
2.38 (2.32, 2.44)
10.11
Jian Wu et al.
1.95 (1.73, 2.17)
8.53
Xi Xu et al.
2.13 (1.92, 2.33)
8.70
Overall (I-squared = 91.6%, p = 0.000)
2.49 (2.33, 2.64)
100.00
-3
-2
-1
0
1
2
3
4


Citations (n=359)
318 articles excluded after title/abstract review
41 full-text articles for detailed evaluationarticles
28 studies excluded :
Duplicated population:6
Case reports/case series :15
Without related data: 3
Review:4
13 studies included in the meta-analysis


Study ID
ES (95% CI)
% Weight
GGO
Zhang Mingqiang et al. 2.78 (2.09, 3.47) 7.83
Jiong Wu et al. 2.71 (2.49, 2.94) 11.46
Adam Bernheim et al. 2.76 (2.56, 2.96) 11.58
Tao Ai et al. 1.49 (1.43, 1.56) 12.05
Heshui Shi et al. 1.88 (1.66, 2.10) 11.50
WANG Jincheng et al. 2.70 (2.42, 2.97) 11.16
Yu-Huan Xu et al. 2.04 (1.74, 2.34) 10.97
W. Guan et al. 1.89 (1.82, 1.95) 12.05
Xi Xu et al. 2.63 (2.40, 2.86) 11.40
Subtotal (I-squared = 97.6%, p = 0.000) 2.30 (1.97, 2.62) 100.00
Consolidation
Zhang Mingqiang et al. 1.44 (0.75, 2.14) 6.79
Jiong Wu et al. 1.89 (1.66, 2.11) 15.56
Adam Bernheim et al. 1.68 (1.48, 1.88) 16.01
Tao Ai et al. 1.58 (1.51, 1.64) 18.03
WANG Jincheng et al. 1.33 (1.06, 1.61) 14.45
Yu-Huan Xu et al. 1.31 (1.00, 1.61) 13.83
Xi Xu et al. 0.87 (0.64, 1.11) 15.33
Subtotal (I-squared = 87.5%, p = 0.000) 1.45 (1.22, 1.68) 100.00
GGO with mixed consolidation
Zhang Mingqiang et al. 1.44 (0.75, 2.14) 7.84
Fengxiang Song et al. 1.74 (1.47, 2.02) 50.98
Yu-Huan Xu et al. 1.79 (1.48, 2.09) 41.18
Subtotal (I-squared = 0.0%, p = 0.673) 1.74 (1.54, 1.93) 100.00
-3
-2
-1
0
1
2
3
4

Due to the proportion of COVID-19 detected by chest CT imaging is very high, especially thin chest CT plays a huge role in assisting diagnosis and follow-up treatment in clinical application.

Journal Pre-proof

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Take Home Points:

- Our systematic review and meta-analysis of the early literature suggests that the proportion of suspected COVID-19 detected by chest CT imaging is high.
- Chest CT, especially thin-section chest CT can play a central role in early diagnosis of COVID-19.
- The most common CT features in patients affected by COVID-19 included GGO, consolidation, interlobular septal thickening, adjacent pleura thickening, and air bronchograms.
- The infection most commonly involves the bilateral lungs, especially bilateral lower lobes.
- Similar imagine features are seen in other infections, and the final diagnosis of COVID-19 should still be based on RT-PCR.

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