Review Article

A systematic review of chest imaging findings in COVID-19

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Abstract: Chest computed tomography (CT) is frequently used in diagnosing coronavirus disease 2019 (COVID-19) for detecting abnormal changes in the lungs and monitoring disease progression during the treatment process. Furthermore, CT imaging appearances are correlated with patients presenting with different clinical scenarios, such as early versus advanced stages, asymptomatic versus symptomatic patients, and severe versus nonsevere situations. However, its role as a screening and diagnostic tool in COVID-19 remains to be clarified. This article provides a systematic review and meta-analysis of the current literature on chest CT imaging findings with the aim of highlighting the contribution and judicious use of CT in the diagnosis of COVID-19. A search of PubMed/Medline, Web of Science, ScienceDirect, Google Scholar and Scopus was performed to identify studies reporting chest imaging findings in COVID-19. Chest imaging abnormalities associated with COVID-19 were extracted from the eligible studies and diagnostic value of CT in detecting these abnormal changes was compared between studies consisting of both COVID-19 and non-COVID-19 patients. A random-effects model was used to perform meta-analysis for calculation of pooled mean values and 95% confidence intervals (95% CI) of abnormal imaging findings. Fifty-five studies met the selection criteria and were included in the analysis. Pulmonary lesions more often involved bilateral lungs (78%, 95% CI: 45–100%) and were more likely to have a peripheral (65.35%, 95% CI: 25.93–100%) and peripheral plus central distribution (31.12%, 95% CI: 1.96–74.07%), but less likely to have a central distribution (3.57%, 95% CI: 0.99–9.80%). Ground glass opacities (GGO) (58.05%, 95% CI: 16.67–100%), consolidation (44.18%, 95% CI: 1.61–71.46%) and GGO plus consolidation (52.99%, 95% CI: 19.05–76.79%) were the most common findings reported in 94.5% (52/55) of the studies, followed by air bronchogram (42.50%, 95% CI: 7.78–80.39%), linear opacities (41.29%, 95% CI: 7.44–65.06%), crazy-paving pattern (23.57%, 95% CI: 3.13–91.67%) and interlobular septal thickening (22.91%, 95% CI: 0.90–80.49%). CT has low specificity in differentiating pneumonia-related lung changes due to significant overlap between COVID-19 and non-COVID-19 patients with no significant differences in most of the imaging findings between these two groups (P>0.05). Furthermore, normal CT (13.31%, 95% CI: 0.74–38.36%) was reported in 26 (47.3%) studies. Despite widespread use of CT in the diagnosis of COVID-19 patients based on the current literature, CT findings are not pathognomonic as it lacks specificity in differentiating imaging appearances caused by different types of pneumonia. Further, there is a relatively high percentage of normal CT scans. Use of CT as a first-line diagnostic or screening tool in COVID-19 is not recommended.

Keywords: Coronavirus infections; COVID-19; computed tomography (CT); diagnosis; imaging; sensitivity; specificity

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Introduction

Coronavirus disease 2019 (COVID-19) has rapidly spread across many cities in China and other countries. As of 4 April, 2020, there are over 1,000,000 confirmed cases with more than 50,000 deaths, of which more than 50% of diagnosed cases and deaths have been observed in Unites States, Spain, Italy, and Germany (1). Since the onset of COVID-19 in December 2019, many studies have reported the clinical characteristics and chest imaging appearances of COVID-19, specifically describing a variety of abnormalities in the lungs (2-4).

Although the diagnosis of COVID-19, in terms of a positive or negative test, is primarily based on laboratory tests, chest imaging modalities, including chest X-ray (CXR) and computed tomography (CT), are routine diagnostic approaches used to detect abnormal lung changes. This is due to the fact that coronavirus diseases mainly cause respiratory tract infections as seen in severe acute respiratory syndrome (SARS) and middle east respiratory syndrome (MERS) (5-7), although other organs, including the gastrointestinal tract and cardiovascular system, can also be affected (8-10). However, chest abnormalities associated with COVID-19 are different from those associated with SARS and MERS to some extent, and they are also related to the disease extent and clinical symptoms; thus, the recognition of both common and uncommon imaging findings on chest CT examinations is clinically important. Furthermore, there are some arguments about whether CT should be used as a first-line imaging technique in the diagnosis of COVID-19. In this systematic review and meta-analysis, we analyze the currently available studies documenting radiologic findings and aim to clarify the role of CT imaging in the diagnosis of patients with COVID-19.

Methods

Literature search

We performed a search of PubMed/Medline, Web of Science, ScienceDirect, Google Scholar and Scopus to identify studies reporting about COVID-19 according to the preferred reporting items for systematic reviews and meta-analysis (last search 31 March, 2020) (11,12). Different search terms were used including "novel coronavirus OR SARS-Cov-2 OR COVID-19" and "pneumonia OR infection OR chest CT OR chest imaging". Because we intended to analyze the chest imaging appearances of patients with COVID-19 in this review, only studies meeting the following criteria were included in the analysis: original research studies reported clinical characteristics and imaging features of COVID-19 patients; studies included at least 10 patients; and studies were published in English literature. Isolated case reports or case series with a sample size of <10 were excluded due to low level of evidence. Editorials, commentaries, opinions and other types of publications were also excluded.

Data extraction

Two independent assessors (ZS and NZ) performed the data extraction with agreement reached by consensus. The following information was extracted from each study for the analysis of chest imaging findings: number of patients enrolled; mean/or median age and sex of participants; lung involvement in terms of the bilateral or unilateral lungs; lesion distribution in lungs including peripheral, central or both peripheral and central distribution; typical abnormalities including ground glass opacities (GGO) and consolidation; and less common findings including a crazy-paving pattern, air bronchogram, patchy shadow, linear opacities, bronchial wall thickening or bronchiectasis, vascular enhancement, and pleural effusion and others. The diagnostic value of CXR or chest CT in the diagnostic assessment of COVID-19 was also analyzed if data were available in the studies. Furthermore, the degree of lung involvement in terms of lesion distribution comparing peripheral with central regions, and the number of affected lobes was analyzed when information was available.

Statistical analysis

We conducted a systematic review of studies regarding diagnostic value of CT in COVID-19, comparison of CT imaging appearances in different clinical groups and COVID-19 on pregnant women or pediatric patients. We conducted a meta-analysis using a random-effects model to calculate the pooled values and their corresponding 95% confidence intervals (95% CI) of different imaging features associated with COVID-19 patients. The Likelihood ratio (LR) Chi-squared statistic test was used to assess the homogeneity across studies of the proportions of patients presenting with the specified imaging features. Measures of homogeneity between studies comparing COVID-19 with non-COVID-19 using Cochran's Q statistic were performed. Data were entered into SPSS 25.0 (version 24.0; IBM Corporation, Armonk, NY, USA) for statistical analysis.

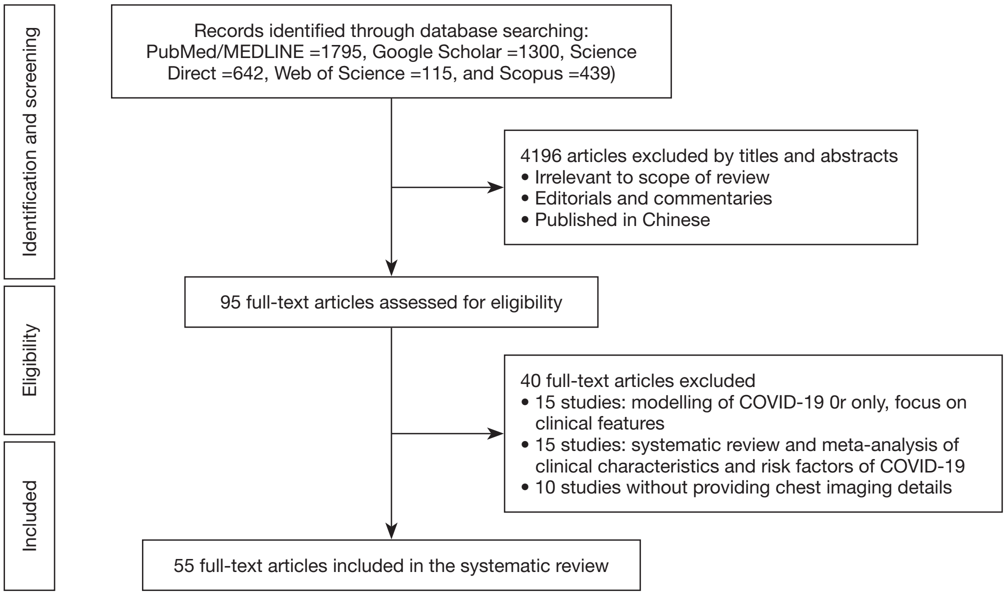

Figure 1 Flow chart showing the selection process of identifying studies that met the inclusion criteria.

Results

A total of 55 studies were determined (13-32) through the search with reported cases (33-52) ranging from 10 to 1,099 (53-67). *Figure 1* is a flow chart outlining the search strategy of selecting these studies. *Table 1* lists basic demographics and main chest imaging findings reported in each study. There is very highly significant heterogeneity between studies with respect to mean patient age. After excluding studies which only provided an age range rather than a standard deviation, 25 studies with admissible data were pooled together for analysis of patient's age with the mean value being 48 years (95% CI: 45.1–50.9). In the following sections, we provided detailed review and analysis of chest imaging findings in COVID-19 patients in these eligible studies.

Study characteristics and lung involvement

CT was used in 52 studies for the diagnosis of COVID-19, whereas in the study by Arentz *et al.* (14), CXR was the only imaging modality used in diagnosing all patients. Both CXR and CT were used in one study (21), with chest CT showing superiority over CXR in detecting all types of lung abnormalities, indicating the limited value of CXR (*Table 1*). Another study by Wong *et al.* analyzed CXR findings in 64 COVID-19 patients with 69% sensitivity with reverse transcription-polymerase chain reaction (RT-PCR sensitivity 91%) as the gold standard (47). Although CXR resembles CT findings (in 28 patients) in these common abnormal lung findings, it is less sensitive than CT in detecting the abnormalities.

A total of 36 studies (65.5%) reported details regarding bilateral or unilateral lung involvement (*Figure 2*); of which 17 studies reported a higher percentage of bilateral lung involvement (78.22%, 95% CI: 45–100%) than unilateral lung involvement (20.23%, 95% CI: 9.90–30%) (*Tables 1* and *2*). These studies consistently reported that the involvement of the bilateral lungs was much higher than that of the unilateral lung in patients with COVID-19, or bilateral involvement was more frequently observed in severe or emergency cases.

Of the remaining 19 studies that did not report the details of lung involvement on chest CT, 8 reported involvement of pulmonary lobes or segments, with more than two lobes observed in all the studies (*Table 1*). Two studies only reported the percentage of lung abnormalities on CXR and chest CT (17,21), while the remaining nine studies did not report lung involvement (25,27,32,39,42,52,63,65,66). Eighteen studies (32.7%) reported the percentages of distribution of abnormalities or lesions in the peripheral or central or both peripheral and central lung regions on chest CT, with peripheral distribution (65.35%, 95% CI: 25.93–100%), peripheral plus central (31.12%, 95% CI: 1.96–74.07%) showing

Table 1 Basic clinical characteristics and chest imaging findings of studies in COVID-19 patients

Author	No. of patients	Male/female	Age (years), mean/range	Chest imaging findings									
				Bilateral/unilateral lung involvement	Normal chest imaging	GGO	Consolidation	GGO + consolidation	Interlobular septal thickening	Crazy-paving pattern	Pleural effusion	Air bronchogram	Other findings
Ai *et al.* (13)	1,014	467/547	51±15; 2–95	Bilateral: 90%	12%	46%	50%	-	1%	-	-	-	Nodular lesions: 3%
Arentz *et al.* (14)	21	11/10	70; 43–92	Bilateral: 52.4%	4.8%	47.6%	19%	-	-	-	28.6%	-	Peribronchial thickening: 23.8%
Bai *et al.* (15)	All patients: 424; COVID-19: 219; Non-COVID-19: 205	119/100; 103/102	44.8±14.5; 64.7±18.6	73%/22%; COVID-19/non-COVID-19: 75%/19%, 70%/25%; peripheral/central: 69%/4%, 80%/1% and 57%/6%*	–	80%/91%/68%	72%/69%/75%	61%/64%/58%	35%/35%/34%	5%/5%/5%	21%/4%/39%	18%/14%/23%	Linear opacity: 54%/51%/58%; fine reticular opacity: 40%/56%/22/%; nodule: 31%/32%/30%; lymphadenopathy: 6%/3%/10%
Bernheim *et al.* (16)	121	61/60	45.3; 18–80	60%/17%; >2 lobes involved: 51%; peripheral/central: 52/0%	22%	34%	2%; either GGO or consolidation: 78%	41%; absence of both GGO and consolidation: 22%	–	5%	–	–	Linear opacities: 7%; rounded morphology of opacities: 54%
Chang *et al.* (17)	13	10/3	34; 34–48	Abnormalities: 61.5%	38.5%	46%	–	–	–	–	–	–	Scattered opacities in left lower lung: 7%
Chen *et al.* (18)	99	67/32	55.5±13.1; 21–82	75%/25%	0	–	–	GGO and multiple mottling: 14%	–	–	–	–	Pneumothorax: 1%
Cheng *et al.* (19)	COVID-19: 11; non-COVID-19 22	8/3; 7/15	50.3±15.5; 43.5±16.0	Peripheral/central: 100%/0%, 31.8%/68.2%; affected lobes: 5 [4–5]/3.5 [2–4]; affected segments: 15 [11–17]/9 [2–11]	0	100%/90.9%	54.5%/77.3%	63.6%/72.7%	–	–	0%/22.7%	72.7%/27.3%	Centrilobular nodules: 27.3%/77.3%; tree-in-bud sign: 9.1%/27.3%; reticular pattern: 81.8%/22.7%; subpleural linear opacity: 18.2%/27.3%; bronchial dilatation: 27.3%/13.6%
Chung *et al.* (20)	21	13/8	51±14.5; 29–77	Bilateral lungs: 76%; >2 lobes involved: 71%; peripheral: 33%	–	57%	Either GGO or consolidation: 86%	29%; absence of both GGO and consolidation: 14%	–	19%	–	–	Round morphology: 33%; linear opacities: 14%
Guan *et al.* (21)	1,099	640/459	47; 35–58	Abnormalities on CXR/CT: 49.1%/86.2%	11.3%	CXR/CT 20.1%/56.4%	–	–	–	–	–	–	CXR/CT: local patchy shadowing: 28.1%/41.9%; bilateral patchy shadowing: 36.5%/51.8%; interstitial abnormalities: 4.4% and 14.7%
Guan *et al.* (22)	53	25/28	42; 1–86	Bilateral: 78.7%	11.3%	100%	63.8%	–	–	89.4%	0	76.6%	Stripe: 57.5%; nodules: 2.1%
Han *et al.* (23)	108	38/70	45; 21–90	Peripheral/central/both: 90%/2%/8%	0	60%	6%	41%	–	40%	0	48%	Vascular thickening: 80%; halo sign: 64%
Huang *et al.* (24)	41	30/11	49; 41–58	Bilateral: 98%	0	–	–	Bilateral GGO+ subsegmental consolidation	–	–	–	–	–
Hu *et al.* (25)	24	8/16	32.5; 5–95	–	29.2%	GGO or patchy shadows: 50%	–	–	–	–	–	–	Stripe shadows: 20.8%
Inui *et al.* (26)	112	59/53	60±17; 31–87	Bilateral: 82%; peripheral/central/both: 56%/7%/37%	39%	37%	–	47%	With GGO: 16/%	–	–	–	Radiation dose: 2.8 mSv
Li *et al.* (27)	53	29/24	58±17; 26–83	–	–	35.3%	5.9%	54.9%; absence of both GGO and consolidation: 3.9%	–	70.6%	2%	68.6%	Vascular enlargement: 82.4%; air trapping: 11.8%; bronchial deformation: 19.6%; nodules: 21.6%
Li *et al.* (28)	83	44/39	45.5±12.3	Bilateral: 95.2%	–	97.6%	63.9%	–	62.7%	36.1%	8.4%	–	Bronchial wall thickening: 22.9%; lymphadenopathy: 8.4%; linear opacities: 65.1%; nodule: 7.2%
Li *et al.* (29)	78	38/40	44.6±17.9	Bilateral: 57.7%; >2 lobes: 51.3%; peripheral: 87.5%	28.2%	80.4%	21.4%	76.8%	44.6%	–	8.9%	73.2%	Fibrotic lesions: 53.6%; peribronchovascular distribution: 32.1%
Liu *et al.* (30)	137	61/76	57; 20–83	Bilateral: 84.7%	–	40.1%	18.2%	–	–	–	–	–	Multiple patch–like shadows: 26.3%

Table 1 (*continued*)

Table 1 (*continued*)

Author	No. of patients	Male/female	Age (years), mean/range	Chest imaging findings									
				Bilateral/unilateral lung involvement	Normal chest imaging	GGO	Consolidation	GGO + consolidation	Interlobular septal thickening	Crazy-paving pattern	Pleural effusion	Air bronchogram	Other findings
Liu *et al.* (31)	78	39/39	38; 33–57	57.7%/29.5%	–	16.7%	–	–	–	–	–	–	Multifocal opacity 56.4%
Liu *et al.* (32)	15	Pregnant women	32±5; 23–40	Total CT score for stage 1/stage 2/ stage 3/stage 4: 4/7±3/11±3/15±3	0	–	–	GGO and crazy paving pattern	–	–	–	–	$CTDI_{vol}$: 4.1±0.9 mGy
Liu *et al.* (33)	55	5/50	30; 22–42	67.3%/27.3%; peripheral/central: 98.2%/1.8%	5.5%	78.2%	45.5%	60%	–	–	23.6%	–	–
Mo *et al.* (34)	155	86/69	54; 42–66	Bilateral: 92.3%	–	–	–	–	–	–	10.3%	–	–
Ng *et al.* (35)	21	13/8	56; 37–65	Peripheral/lower/upper zone: 86%/38%/38%	9.5%	86%	62%	19%	–	–	–	–	Solid nodules: 4.7%
Pan *et al.* (36)	63	33/30	44.9±15.2	No. of affected lobes: 3.3 ±1.8	–	22.2%	19%	Patchy/punctate GGO: 85.7%	–	–	–	–	Fibrous stripes: 17.5%; irregular solid nodules: 12.7%
Pan *et al.* (37)	21	6/15	40±9; 25–63	Peripheral: 54–70%*; No. of affected lobes: 22±2/3±2/4±2/3±2*	17%	65–82%*	42–91%*	–	–	0–53%*	–	–	Mean $CTDI_{vol}$: 8.4 ±2.0 mGy
Qian *et al.* (38)	91	37/54	50; 5–96	67%/27.5%	5.5%	–	–	Patchy ground glass shadows	–	–	–	–	–
Qiu *et al.* (39)	36	23/13	8.3; 1–16	–	–	53%	–	–	–	–	–	–	–
Shi *et al.* (40)	81	42/39	49.5±11; 25–81	Bilateral: 79%; peripheral/diffuse distribution: 54%/44%	–	65%	–	–	35%	10%	5%	47%	Pleural thickening: 32%; bronchiectasis: 11%; lymphadenopathy: 6%
Song *et al.* (41)	51	25/26	49±16	86%/14%; peripheral/central/both: 86%/10/2%	–	77%	55%	59%	75%	–	8%	80%	Reticulation: 22%; pericardial effusion: 6%; lymphadenopathy: 6%
Su *et al.* (42)	14 adults and 9 children	8/6; 3/6	42.9 (30–72); 11m–9 years	–	28.6%/55.6%	35.7%	50%	11.1%*	–	–	–	–	Nodules: 42.9%; bronchitis: 22.2%*; bronchopneumonia: 11.1%*
Wang *et al.* (43)	138	75/63	56; 42–68	Bilateral: 100%	–	GGO and patch shadows 100%	–	–	–	–	–	–	–
Wang *et al.* (44)	18	10/8	39; 29–55	Bilateral: 73.3%	16.7%	100%	46.6%	–	–	–	–	–	–
Wang *et al.* (45)	90	33/57	45±14	83.3%/16.7%	0	62%/45%/61%*	23%/24%*	–	–		7%	–	–
Wang *et al.* (46)	114	58/56	53; 23–78	85.5%/14.5%; peripheral/both: 43.6%/56.4%	2.6%	27.3%	27.3%	45.4%	–	–	0.9%	–	–
Wong *et al.* (47)	64	26/38	56±19; 16–96	63%/38%; peripheral: 51%	31%	41%	59%	–	–	–	3%	–	Sensitivity for RT–PCR and CXR: 91%/69%
Wu *et al.* (48)	80	39/41	46.1±15.42	45%/23.8%	31.3%	–	–	Bilateral or unilateral GGO	–	–	–	–	–
Wu *et al.* (49)	80	42/38	44±11; 15–79	Average lung segments involved: 12 [6]	–	91%	63%	–	59%	29%	6%	–	"Spider web sign": 25%; subpleural line: 21%; lymphadenopathy: 4%; bronchial wall thickening: 11%
Xia *et al.* (50)	20	13/7	2 y and 1.5 m; 1 d to 14 y	50%/30%	20%	60%	Consolidation with halo sign: 50%	–	–	–	–	–	Subpleural lesions: 100%; tiny nodules: 15%
Xu *et al.* (51)	90	39/51	50; 18–86	Bilateral: 59%; bilateral upper and lower lobes involved: 44%/52% Peripheral: 51%	–	72%	13%	–	37%	12%	4%	8%	Linear opacities: 61%; adjacent pleural thickening: 56%; lymphadenopathy: 1%

Table 1 (*continued*)

Table 1 (*continued*)

Author	No. of patients	Male/female	Age (years), mean/range	Chest imaging findings									
				Bilateral/unilateral lung involvement	Normal chest imaging	GGO	Consolidation	GGO + consolidation	Interlobular septal thickening	Crazy-paving pattern	Pleural effusion	Air bronchogram	Other findings
Xu *et al.* (52)*	50	29/21	43.9±16.8; 3–85	–	18%	–	–	–	80.5%	–	9.7%	53.6%	Enlarged mediastinal nodes: 3.6%
Xu *et al.* (53)	62	36/27*	41; 32–52	Bilateral: 84%	1.6%	–	–	Bilateral GGO or multiple lobular or subsegmental consolidation	–	–	–	–	–
Yang *et al.* (54)	149	81/68	45.11±13.35	Peripheral/central/both: 35.9%/2.2%/8.1%; lobes/segments involved: 3±4/6±10.5	11.4%	12.1%	7.2%	26.8%	–	–	6.7%	56.3%	Reticular pattern: 53%; subpleural linear opacity: 20.8%; bronchial dilatation 17.4%; lymphadenopathy: 4.6%; centrilobular nodules: 2%
Yuan *et al.* (55)	27	12/15	60; 47–69	86%/15%; peripheral/both: 26%/74%	0	67%	19%	30%	–	–	4%	30%	Nodules: 7%
Zeng *et al.* (56)	33 neonates	16/14; 3/0*	–	0/100%	100%/0%	–	–	–	–	–	–	–	–
Zhang *et al.* (57)	140	71/69	57; 25–87	89.6%/9.6%	0.7%	–	–	Multiple GGO or consolidation	–	–	–	–	–
Zhang *et al.* (58)	60	43/17	64.4±11	Bilateral: 100%	0	97%	68%	–	–	92%	25%	93%	Clear margin: 20%; blur margin: 98%; linear opacities: 22%; pericardial effusion: 3%
Zhang *et al.* (59)	645	295/278; 33/39*	46.7±13.8; 34.9±14.2	Bilateral: 67%; >2 lobes involved: 35.7%	11.2%	–	–	Either GOO or consolidation or both: 88.8%	–	–	–	–	–
Zhao *et al.* (60)	101	56/45	44.4±12.3; 17–75	82.2%/9.9%; peripheral/central: 87.1/1%	7.9%	86.1%	43.6%	64.4%	–	–	–	–	Vascular enlargement: 71.3%; centrilobular nodules: 22.8%; bronchial wall thickening: 28.7%; lymphadenopathy: 1%
Zhao *et al.* (61)	34 COVID-19: 19 Non-COVID-19: 15	11/8; 6/9	48, 25–76; 35, 27–46	78.9%/21.1%; 26.7%/73.3%	–	–	–	GGO and multiple mottling: 89.5%/6.7%	–	–	–	–	–
Zheng *et al.* (62)	25	14/11	3; 2–9	45.8%/20.8%	33.3%	–	–	–	–	–	–	–	–
Zhou *et al.* (63)	62	39/23	52.8±12.2; 30–77	Peripheral/both: 77.4%/22.6%	–	40.3%	33.9%	GGO + reticular pattern: 62.9%	–	–	9.7%	72.6%	Vacuolar sign: 54.8%; fibrotic streaks: 56.5%; bronchiectasis: 32.2%; pleural thickening: 48.4%; pleural retraction sign: 56.5%
Zhou *et al.* (64)	191	119/72	56; 18–87	Bilateral: 75%	–	71%	59%	–	–	–	–	–	–
Zhou *et al.* (65)	62	34/38	20–91	Peripheral/central/both: 33.9%/3.2%/62.9%	–	61.3%	1.6%	35.5%	–	25.8%	3.2%	22.6%	Rounded opacities: 25.8%; halo sign: 11.3%; pulmonary fibrosis: 1.6%; lymphadenopathy: 1.6%
Zhu *et al.* (66)	10	10	30.7±3.12; 25–34	Abnormalities in 7 neonates: infections (n=4), NRDS (n=2) and pneumothorax (n=1)	0	–	Pregnant women all had GGO + consolidation	Neonates: GGO, patchy shadows and blurred markings in lungs	–	–	–	–	–
Zhu *et al.* (67)	32	15/17	46; 35–52	Bilateral: 91%	–	47%	13%	–	–	3%	6%	–	Lymph node enlargement: 3%; spider web sign: 13%

Bai *et al.* (15): * refers to comparison of findings including imaging features between all patients, COVID-19 and non-COVID-19 patients; Pan *et al.* (37): * depends on the stages of disease onset (details see *Table 2*); Su *et al.* (42): * refers to findings in pediatric cases; Wang *et al.* (45): * refers the percentage of GGO at different stages of disease onset (days 0–5 to days 12–17 and days ≥24) and consolidation at days 0–5 and 6–11; Xu *et al.* (52): * details of GGO and consolidation are shown in *Table 2*; Xu *et al.* (53): * there is an error in male/female ratio from the original study; Zeng *et al.* (56): * refers to 30 neonates born to mothers with COVID-19 with 30 negative and 3 positive cases; Zhang *et al.* (59): * refers to normal imaging findings. CT, computed tomography; CXR, chest X-ray; GGO, ground glass opacity; NRDS, neonatal respiratory distress syndrome; RT-PCR, reverse transcription-polymerase chain reaction; TB, tuberculosis.

significant dominance compared with central distribution (3.57%, 95% CI: 0.99–9.80%). Wu *et al.* reported only the average involvement of lung segments (49), while three studies analyzed the risk of pregnant women and neonates born to mothers with COVID-19 (32,56,66), and another four studies reported COVID-19 in adults and children (39,42,50,62) which were described in detail later.

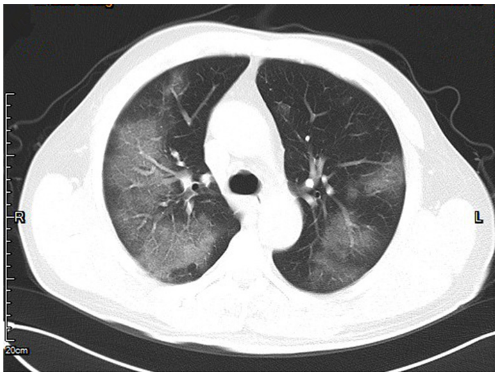

Figure 2 Bilateral lung involvement in a 50-year-old male diagnosed with COVID-19. An axial CT image shows multiple patchy areas of pure ground glass opacities.

Normal chest CT images

Of the 55 studies, 26 (47.3%) reported normal chest CT findings in patients with COVID-19 (*Table 1*). The percentage of normal chest CT findings ranged from the lowest 0.7% to the highest 56%, depending on the severity of the disease with high normal rates reported in asymptomatic patients or with mild symptoms. The pooled value was 13.31% (95% CI: 0.74–38.36%). Furthermore, ≥20% of normal chest CT findings were noted in 10 out of 26 studies (38.5%).

Most common chest CT imaging findings

GGO and consolidation represented the most common abnormalities and were reported in 94.5% (52/55) of the studies (*Table 1*). The imaging appearances of these two abnormal findings were presented as either pure GGO (58.05%, 95% CI: 16.67–100%) (*Figures 2,3*) or GGO mixed with consolidation (52.99%, 95% CI: 19.05–76.79%)

Table 2 Summary of single arm meta analyses of chest imaging findings

Feature	Minimum %	Overall %	Maximum %	LR Chi χ^2	df	P
Bilateral lung involvement	45.00	78.22	100.00	476.16	35	***
Unilateral lung involvement	9.90	20.23	30.00	45.00	16	***
Normal imaging	0.74	13.31	38.46	205.28	25	***
Peripheral distribution	25.93	65.35	100.00	228.00	17	***
Central distribution	0.99	3.57	9.80	10.59	6	0.102
Peripheral & central distribution	1.96	31.12	74.07	159.09	8	***
Ground glass opacity	16.67	58.05	100.00	715.55	36	***
Consolidation	1.61	44.18	71.46	669.81	27	***
GGO & consolidation	19.05	52.99	76.79	78.93	14	***
Interlobular septal thickening	0.90	22.91	80.49	676.21	8	***
Crazy paving pattern	3.13	23.57	91.67	458.30	12	***
Pleural effusion	0.91	11.09	28.57	110.01	20	***
Air bronchogram	7.78	42.50	80.39	381.18	14	***
Lymphadenopathy	0.99	4.86	8.43	15.28	9	0.084
Nodules	2.01	11.69	42.86	262.15	12	***
Linear opacity	7.44	41.29	65.06	180.61	7	***

***, P<0.001. df, degrees of freedom = number of contributing studies less 1. LR, Likelihood ratio.

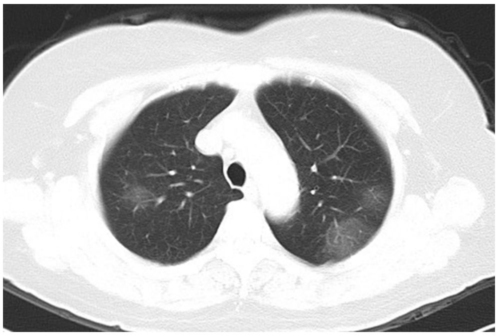

Figure 3 Ground glass opacity (GGO) in a 68-year-old female with confirmed COVID-19. Axial CT images shows multiple round morphology of GGOs in the bilateral upper lobes. Lesions are located in peripheral lung fields.

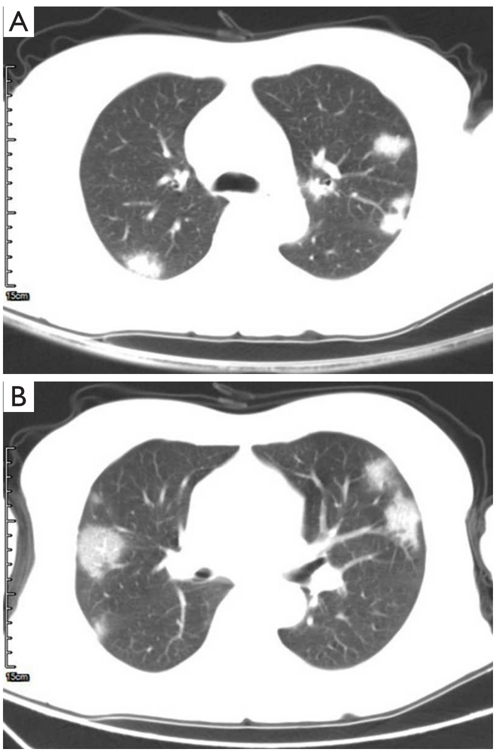

Figure 4 Consolidation in a 48-year-old man with COVID-19 pneumonia. (A,B) CT images show bilateral multiple lobular and subsegmental areas of consolidation with a clear margin.

or consolidation (44.18%, 95% CI: 1.61–71.46%) only (*Figure 4*). The percentage of GGO or consolidation or both of them was reported in 80% of the studies (44/55) whereas in the remaining 11 studies, only bilateral GGO with or without consolidation was reported in 5 studies

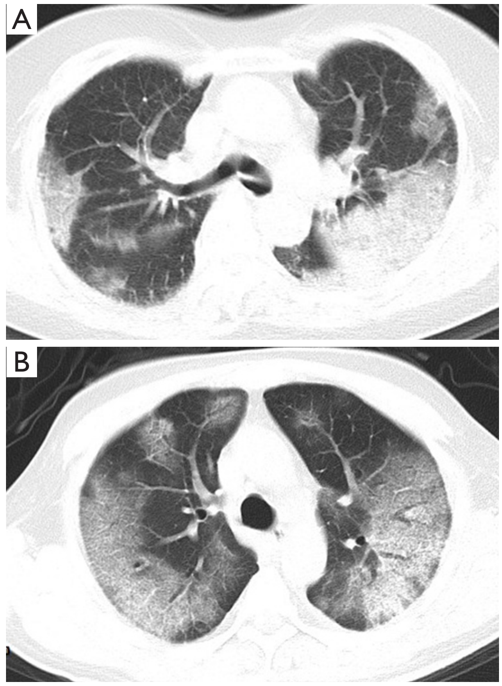

Figure 5 Crazy-paving pattern in two patients with COVID-19. (A) A 72-year-old woman with lesions more severe on the left lung compared with the right lung. (B) A 51-year-old man showing increased opacities of consolidation in both the lungs with presence of air bronchogram.

without providing details regarding the percentage of these lesions in study participants (24,48,53,57,59), and GGO with patchy shadows or crazy-paving pattern in 3 studies (32,38,66). The remaining 3 studies did not provide any information about these abnormal changes (34,56,62).

Other common and less common chest CT imaging findings

In addition to GGO and consolidation, other abnormal changes in the lungs were reported in 50% of the studies (28/55) (*Table 1*). These included common findings such as a crazy-paving pattern (*Figure 5*), air bronchogram (*Figure 6*), linear opacities (*Figure 7*), local or bilateral patchy shadowing (*Figure 8*), and interlobular septal thickening (*Figure 9*). Less common appearances were shown in 61.8% of the studies (34/55) including fibrous stripes (*Figure 10*), vascular enhancement (*Figure 11*), bronchiectasis (*Figure 12*), pleural effusion (*Figure 13*), nodules (*Figure 14*), bronchial wall thickening, spider web sign, and lymphadenopathy and others (*Table 1*).

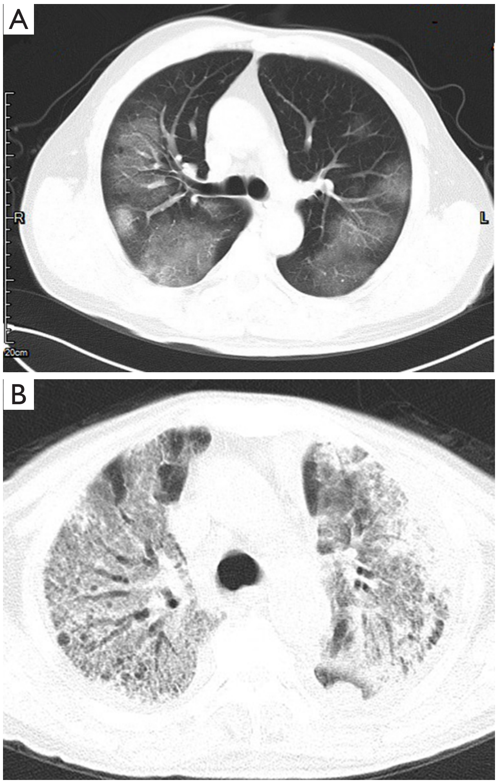

Figure 6 Air bronchogram in two patients with COVID-19 pneumonia. (A) In a 76-year-old man, air bronchogram is seen in multiple GGO lesions. (B) In a 73-year-old male, air bronchogram is clearly seen in extensive consolidation areas in both the lungs. GGO, ground glass opacity.

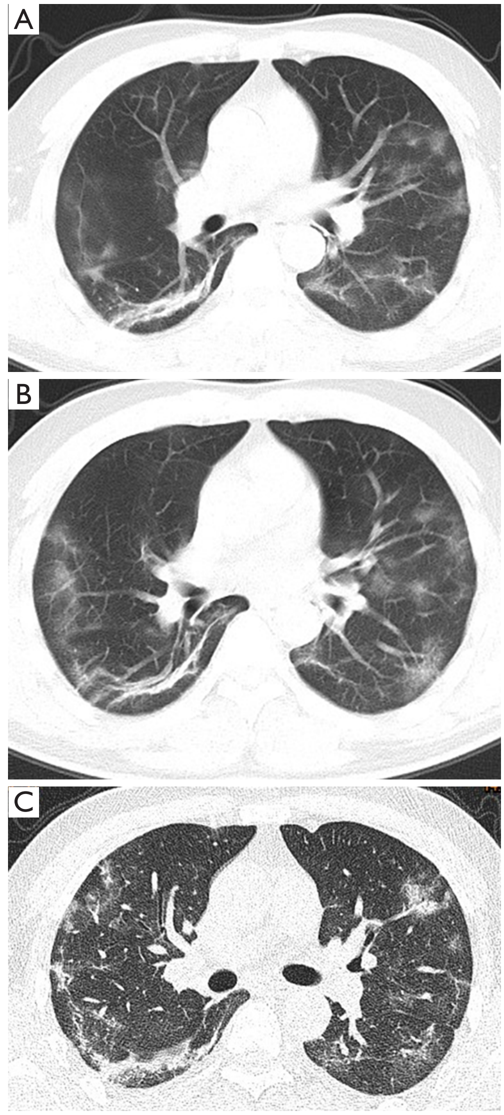

Figure 7 Linear opacities in a 48-year-old male with COVID-19. (A,B) CT images show multiple linear shadows seen in the bilateral lungs. (C) HRCT reveals linear opacities more clearly than standard CT. The opacities are predominantly distributed peripherally. HRCT, high resolution computed tomography.

Table 2 is a summary of the meta-analysis of these imaging findings. As shown in the table, there was highly significant heterogeneity across studies with regard to the reported percentages of these findings (P<0.001), except for central distribution of pulmonary lesions and lymphadenopathy which did not show significant difference (P=0.084–0.102).

Diagnostic value of chest CT in COVID-19

The performance of chest CT in the diagnostic assessment of COVID-19 patients was reported in 9 studies documenting different aspects related to chest CT performance (13,15,19,27-29,45,61,67). The study conducted by Ai and colleagues is the first study thus far to determine the diagnostic value of chest CT in patients with COVID-19 (13). The authors analyzed 1,014 patients with suspected COVID-19, and all these patients underwent chest CT scans and nucleic acid test (RT-PCR). Of the 1,014 patients, 601 (59%) had positive RT-PCR results, and positive chest CT findings were observed in 97% of the 601 patients. With RT-PCR as the diagnostic reference for COVID-19, their results showed that the sensitivity, specificity, positive predictive value, and negative predictive value of CT were 97%, 25%, 65% and 83%, respectively. The high false positive rate of CT in detecting abnormal

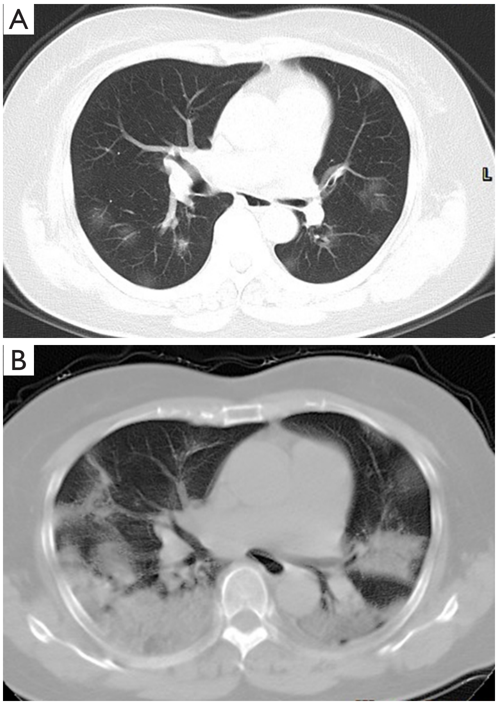

Figure 8 Local and bilateral patchy shadowing in a 63-year-old female with COVID-19. (A) CT image at the initial examination shows small patchy shadows in the peripheral regions of both the lungs. (B) CT taken 5 days later shows apparent progression of disease with increased density areas in both the lungs.

lung changes could be due to significant overlap with pneumonia caused by other factors such as viral pneumonia. The authors also conducted a further analysis of 258 patients who underwent multiple RT-PCR tests, and 15 of these patients showed conversion from initial negative to later positive test results. Initial chest CT images were positive in 67% of these patients, and 93% of the patients presented with typical CT imaging appearances consistent with COVID-19 diagnosis. Based on the results of a comparative analysis of the diagnostic value of CT, similar diagnostic performance was found with no significant differences between different age groups (<60 *vs.* ≥60 years) and between male and female patients (13). CT changes were also comparable with RT-PCR conversion according to the study conducted by Wang *et al.* (44).

The study conducted by Bai *et al.* reported the performance of radiologists in interpreting chest CT images for differentiation of COVID-19 from viral pneumonia (15). In this retrospective study, the authors assessed the accuracy of three Chinese radiologists in reading the chest CT

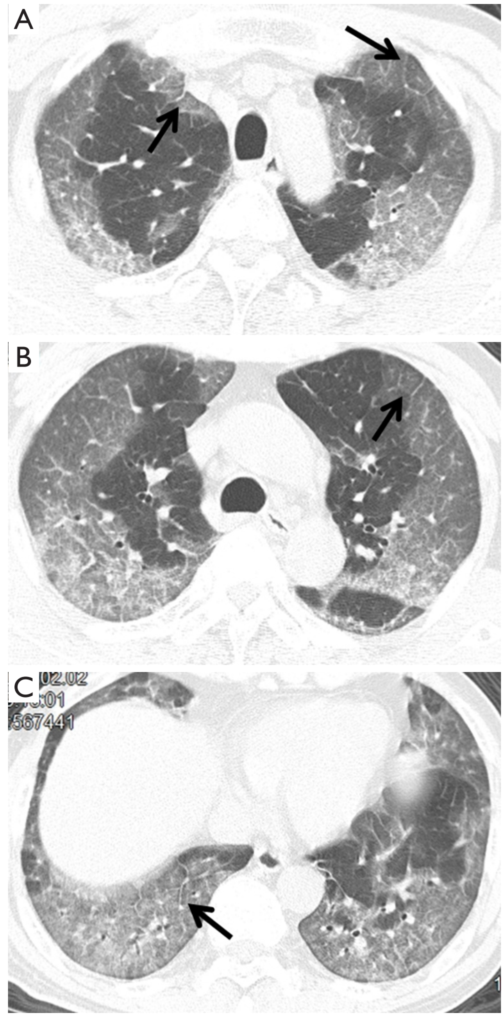

Figure 9 Interlobular septal thickening in a 63-year-old man with COVID-19 pneumonia. (A,B,C) Multiple consolidation areas with interlobular septal thickening (arrows) are seen on both the lungs. The disease has a prominent peripheral distribution.

images of 219 patients with COVID-19 and 205 patients without COVID-19. Four American radiologists reviewed 58 age-matched cases by using the similar approach as the Chinese radiologists did. The sensitivity of these seven radiologists was 80%, 67%, 97%, 93%, 83%, 73%, and 70%, respectively, and the specificity was 100%, 93%, 7%, 100%, 93%, 93%, and 100%, respectively. This study concluded that the radiologists from these two countries demonstrated high specificity but moderate sensitivity in differentiating CT images of COVID-19 from those of viral pneumonia (15). However, results of this study need to be interpreted with caution due to selection bias of participant

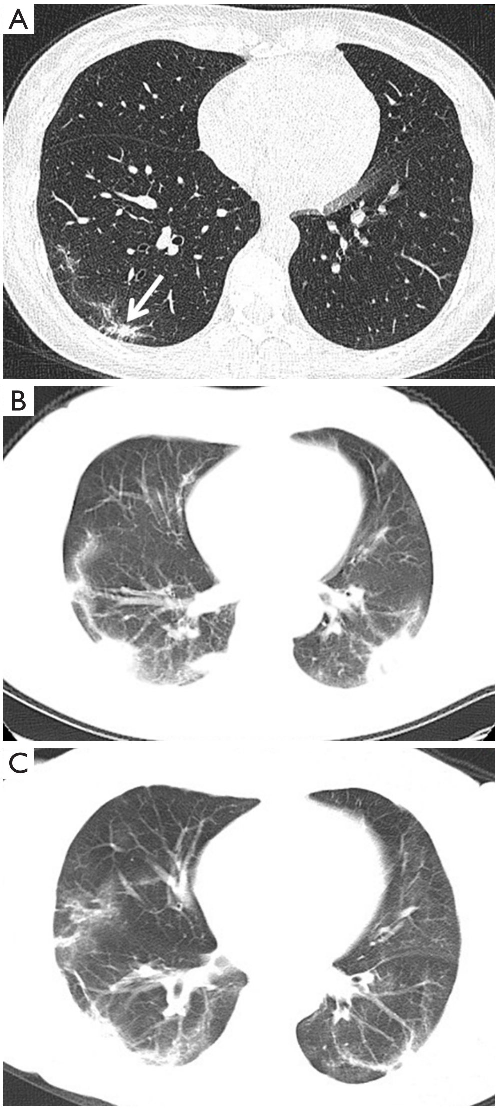

Figure 10 Fibrous stripes in two patients with COVID-19. (A) In a 48-year-old woman, fibrous streak lesion (arrow) is noted in the right lower lung. (B,C) In a 56-year-old woman, multiple fibrous stripes are seen in the peripheral regions of both the lower lungs.

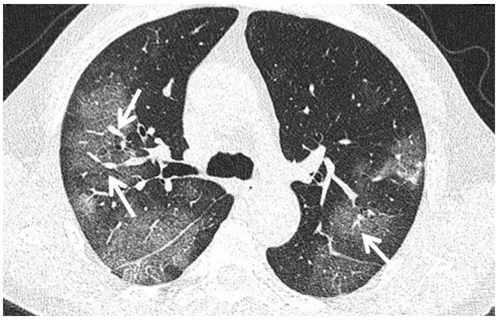

Figure 11 A 52-year-old man with COVID-19. High-resolution CT image shows ground glass opacities with vascular enhancement (arrows).

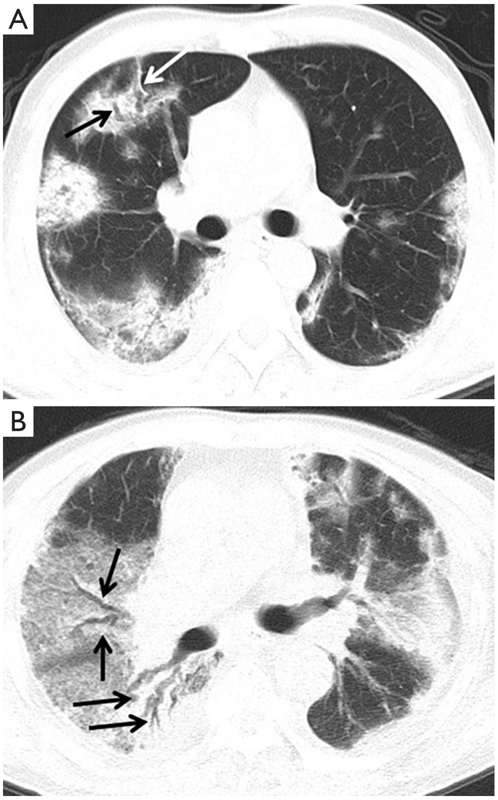

Figure 12 Bronchiectasis in two patients with COVID-19 pneumonia. (A) In a 50-year-old man, multiple patchy shadows are observed in the bilateral peripheral lung fields with dilated bronchia (arrows). (B) In a 73-year-old man, multiple consolidation areas are seen in both the lungs and dilated bronchi within the density areas of the right lung (arrows).

screening strategy and the stage of pneumonia associated with the diagnostic value of CT.

The study conducted by Li *et al.* further confirmed the high performance of CT in the diagnosis of COVID-19 (27). By reviewing the CT images of 51 patients with COVID-19

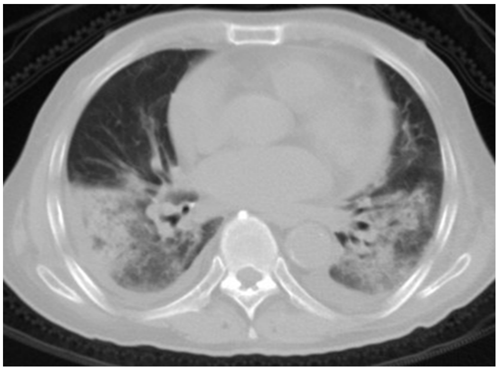

Figure 13 Pleural effusion in a 78-year-old male with COVID-19 pneumonia. Consolidation is seen in the bilateral lower lung fields with air bronchogram. Pleural effusion is present on both sides.

and 2 patients with viral pneumonia, they reported a misdiagnosis rate of 3.9% for CT for COVID-19. Similar to the limitation inherent in the study by Bai *et al.*, selection bias of the number of patients with different types of pneumonia raises concerns about concluding CT with high diagnostic value. Although their findings support the use of CT as a standard technique for the diagnosis of COVID-19, CT lacks specificity in distinguishing abnormal lung changes caused by different types of viruses (27). Similar findings were shown in Li's study with 28% of COVID-19 patients having normal chest CT (29). Authors used CT visual quantitative method to assess lung involvement which is defined as total severity score. They concluded that chest CT alone is not suitable as a screening tool due to its association with misdiagnosis in some patients, while their approach of visual quantitative analysis has 82.6% sensitivity and 100% specificity, thus, serving as an accurate technique to assess clinical severity of COVID-19. With use of similar CT cutoff score, Li *et al.* (28) reported the CT sensitivity and specificity of 80% and 82.8% for detecting abnormal changes.

The study by Wang *et al.* reported temporal changes of CT findings in 90 patients over different stages of disease progression (45). Their results showed the pattern of CT findings was related to the disease extent and progression, reaching peaked during days of 6–11, followed by persistence of high levels. This study provides insight into the change of CT imaging patterns in COVID-19 patients.

Three studies conducted by Cheng *et al.*, Zhao *et al.* and Zhu *et al.* along with Bai *et al.* reported chest CT imaging differences between COVID-19 and non-COVID-19 patients (15,19,61,67). The study by Bai *et al.* compared

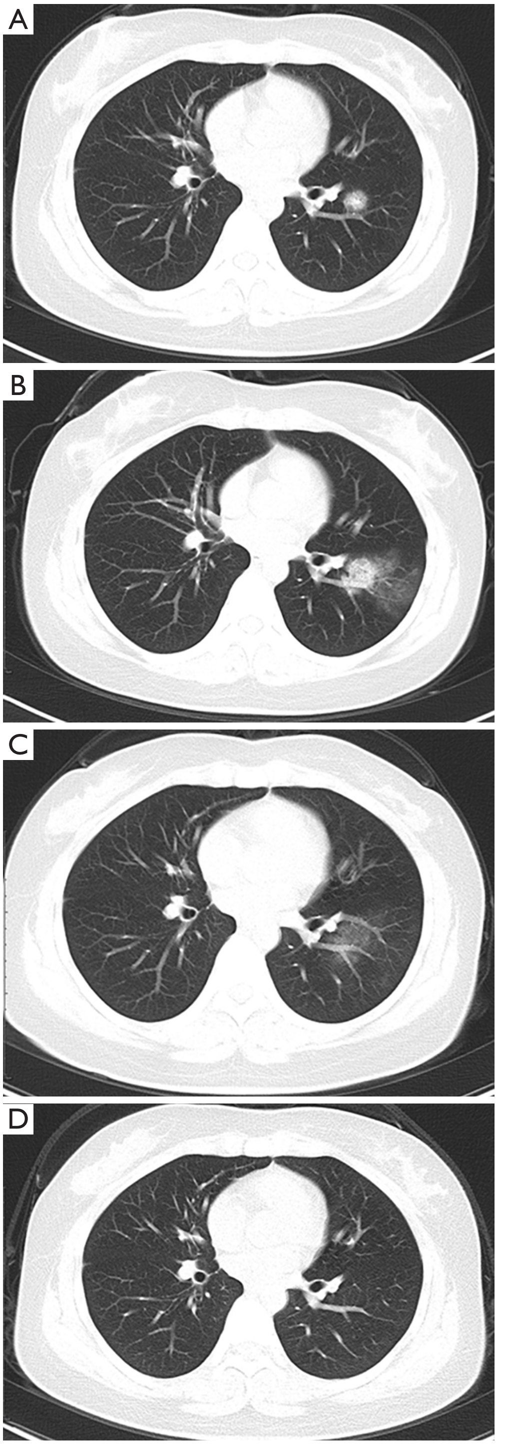

Figure 14 Pulmonary nodule in a 23-year-old female with confirmed COVID-19. (A) Initial CT image on January 26, 2020 shows a nodule in the left lower lung. (B,C) The lesion progressed with a patchy shadow on CT images taken on January 30 and February 5, 2020. (D) CT scan on March 2, 2020 shows resolution of the nodule.

Table 3 Summary of two-arm meta analyses of chest imaging findings between COVID-19 and Non-COVID-19 patients

Feature	No. of studies	Cochran's Q statistic for homogeneity	Significance	Pooled odds ratio	Lower 95% confidence limit	Upper 95% confidence limit
Air bronchogram	2	8.8982	**	1.7278	0.1380	21.6247
Bilateral lung involvement	3	16.7833	***	5.2572	0.8808	31.3799
Central involvement	2	2.3047	ns	0.1067	0.0106	1.0705
Consolidation	3	2.1513	ns	0.7589	0.4792	1.2018
Crazy paving pattern	2	1.6045	ns	1.5246	0.2592	8.9672
Ground glass opacity	4	5.7531	ns	7.0664	3.0037	16.6242
Lymphadenopathy	3	1.2547	ns	0.3185	0.1453	0.6982
Ground glass opacity + consolidation	2	0.7161	ns	1.2531	0.8573	1.8321
Pleural effusion	3	13.6684	**	0.2911	0.0223	3.8004
Peripheral involvement	2	3.2278	ns	8.0191	0.6149	104.5740
Unilateral lung involvement	2	13.3551	***	0.5207	0.0230	11.7804

Degrees of freedom for Q statistic = number of studies less 1; ns, not significant, i.e., P>0.05. **, highly significant, i.e. P < 0.01; ***, very highly significant, i.e., P<0.001.

the two groups of patients with inclusion of more than 200 cases in each group, representing so far the largest sample size in this aspect (15), while the other 3 studies compared two groups of patients with relatively small sample size of less than 100 patients in each group. *Table 3* summarises meta analyses of imaging findings between COVID-19 and non-COVID-19. There is no significance difference in most of the imaging findings, except for bilateral lung involvement and air bronchogram with higher proportions in the COVID-19 group, unilateral lung involvement and pleural effusion which were higher in the non-COVID-19 patients.

Comparison of chest CT findings between clinical groups with COVID-19

Of the 55 studies, nearly half of the studies (43.6%, 24/55) compared chest CT findings in different clinical groups with results demonstrating significant differences in some of the CT appearances in urgent/severe/critically ill patient groups compared with mild/moderate or non-urgent/non-severe patient groups. Of these 24 studies, only 11 provided the details of chest CT imaging appearances in different groups and determined significant differences in particular findings between these groups. *Table 4* lists the results of these 11 studies regarding some specific findings showing significant differences. Due to heterogeneity across these studies, only a systematic review was performed to analyze imaging findings related to different groups.

Of these 11 studies, four compared chest CT findings of patients in different stages (according to the onset of symptoms) (16,37,63,65), three compared patients based on disease severity (28,52,60), another three studies focused on clinical outcomes between patients who died/non-survivor and those who recovered/survivor (55,58,64). The remaining study by Inui *et al.* compared asymptomatic with symptomatic patients from the cruise ship "Diamond Princess", with significantly higher percentage of normal chest CT scans seen in the asymptomatic patients than in the symptomatic group (P=0.012) (26). The frequency of abnormal findings, including linear or fibrous opacities, lymphadenopathy, pleural effusion, and bronchial wall thickening or distortion, was found to be significantly higher in severe/critical groups or patients in advanced situations than in early/intermediate or moderate groups (16,28,55,60,63). Common findings including GGO and consolidation did not show significant differences between different clinical groups in most of the studies, except in the study of Zhou *et al.* (63) who reported a significantly higher prevalence of GGO in the early phase than in the advanced phase of the disease. By contrast, in the same study conducted by Zhou *et al.*, GGO plus reticular pattern was found to be significantly higher in the advanced phase than in the early phase. Five studies compared the crazy-

Table 4 Comparison of chest CT findings among studies comparing different clinical groups in COVID-19 patients

Author	Different clinical groups	Lung involvement			Comparison of CT findings between different groups					
		Bilateral (%)	Severity score	Peripheral distribution (%)	GGO (%)	Consolidation (%)	Crazy-paving pattern (%)	Linear, round or fibrous opacities/ lymphadenopathy (%)	Pleural effusion (%)	Bronchial wall thickening (%)
Bernheim *et al.* (16)	Early (2–2 days)	28	1	22	44	17	0	0	0	11
	Intermediate (3–days)	76	4	64	88	55	3	9	0	12
	Late (6–12 days)	88	6	72	88	60	20	20	0	24
Inui *et al.* (26)	All patients	82	3±3 [1–17]	56	37	–	–	–	–	–
	Asymptomatic	80	4±2 [1–11]	57	41	–	–	–	–	–
	Symptomatic	88	7±4 [1–17]	54	29	–	–	–	–	–
Li *et al.* (28)	All patients	95.2	5 [4–8]	–	97.6	63.9	36.1	65.1	8.4	22.9
	Severe/critical	100	11 [8–15.5]	–	100	88	56	92	28	64
	Ordinary	93.1	5 [2.5–5]	–	96.6	53.4	27.6	53.4	0	5.2
Pan *et al.* (37)	Stage 1 (1–4 days)	42	2±2 [0–6]	54	75	42	25	–	–	–
	Stage 2 (5–8 days)	77	6±4 [1–12]	59	82	47	53	–	–	–
	Stage 3 (9–13 days)	86	7±4 [1–14]	62	71	91	19	–	–	–
	Stage 4 (≥14 days)	80	6±4 [1–14]	70	65	75	0	–	–	–
Xu *et al.* (52)	Moderate	53.6/42.9#	–	96.4/42.9*	75	21.4	–	–	7.1	–
	Severe/critical	92.3/100#	–	92.3/78.6*	69.2	69.2	–	–	15.4	–
Yuan *et al.* (55)	All patients	86	12 [8–29]	26	67	19	–	7	4	–
	Survival group	76	12 [7–13]	35	71	6	–	12	6	–
	Mortality group	100	30 [11–43]	10	60	40	–	0	0	–
Zhang *et al.* (58)	All patients	100	2.2±0.9	100	97	68	92	22	25	–
	Death patients	100	2.0±0.7	100	96	70	90	26	24	–
	Recovery patients	100	3.3±0.5	100	100	60	100	0	6	–
Zhao *et al.* (60)	All patients	82.2	–	87.1	86.1	43.6	–	1.0*	13.9	28.7
	Non-emergency	79.3	–	85.1	83.9	41.4	–	0*	10.3	25.3
	Emergency	100	–	100	100	57.1	–	7.1*	35.7	42.8
Zhou *et al.* (63)	Early phase (≤7 days)	–	–	–	47.5/50*	37.5	–	42.5*	2.5	10
	Advanced phase (8–14 days)	–	–	–	27.3/86.4#	27.3	–	81.8*	22.7	31.8
Zhou *et al.* (64)	All	75	–	–	71	59	–	–	–	–
	Survivor	72	–	–	67	53	–	–	–	–
	Non-survivor	83	–	–	81	74	–	–	–	–
Zhou *et al.* (65)	Early stage	–	4.8±2.8	35.3	64.7	2.9	23.5	29.4/0*	2.9	0
	Progressive stage	–	7.8±4.6	32.1	57.1	0	28.6	21.4/3.6*	3.6	0

Xu *et al.* (52): * indicates peripheral/peripheral involving central distribution, # indicates involvement of bilateral upper/lower lobes; Zhao *et al.* (60): * indicates comparison of lymph node enlargement; Zhou *et al.* (63): * indicates fibrous streaks between these two groups, # refers to the GGO and reticular pattern between these two groups; Zhou *et al.* (65): * refers to comparison of rounded opacities and lymphadenopathy between the two groups. GGO, ground glass opacities.

paving pattern between different groups (16,28,37,58,65), but reported inconsistent findings (*Table 4*).

Chest imaging findings in pregnant women or pediatric patients with COVID-19

Seven studies reported findings in pregnant women with COVID-19 or in pediatric patients or neonates (32,39,42,50,56,62,66). Liu and colleagues reviewed CT scans of 15 pregnant women with confirmed COVID-19 pneumonia (32). In the early stage of disease onset, CT showed GGO, while CT findings evolved into consolidation and crazy-paving pattern as disease progressed. None of the neonates delivered during this study were infected with COVID-19. Su *et al.* analyzed clinical and imaging findings of 9 children and 14 families who tested positive of COVID-19. Although both adults and children presented similar findings of abnormal lung changes, 55.6% of children had normal chest CT scans which is higher than 28.6% of normal chest imaging in the adult patients (42).

The studies by Zeng *et al.* and Zhu *et al.* presented findings from a different perspective as authors performed an analysis of 33 and 10 neonates born to mothers diagnosed with COVID-19, respectively (56,66). In these retrospective studies, the authors analyzed the outcomes of neonates born to mothers with confirmed COVID-19. The chest CT findings of these pregnant women showed typical pneumonia changes such as GGO and consolidation. Zhu *et al.* reported that in 7 out of 10 neonates, CXR showed abnormal appearances consisting of lung infections, respiratory syndrome, and pneumothorax. The test results of COVID-19 were negative in all the neonates (66). This is consistent with the findings of another study reporting similar clinical features in 9 pregnant women with confirmed COVID-19 (68). In contrast, the study by Zeng *et al.* showed that 3 out of 33 neonates tested positive and this indicated that vertical transmission of virus from mothers to fetuses cannot be ruled out, hence close monitoring of neonates is necessary to detect the potential risk of COVID-19 (56).

The three other studies focused on analysis of pediatric patients with COVID-19 (39,50,62). Qiu *et al.* in their retrospective study investigated clinical features in 36 children with COVID-19 (39). All patients in their cohort presented with mild or moderate symptoms, whereas nearly half of them showed no abnormalities on chest imaging examinations. Similar findings were also reported by Zheng *et al.* who analyzed 25 confirmed pediatric children (62). Nearly one-third of chest CT scans (33.3%) were normal, while abnormal findings of pneumonia-related appearances were similar to those observed in adult patients. Xie *et al.* analyzed the chest CT imaging features of 20 pediatric patients with confirmed COVID-19, of which 13 had a history of close contact with family members who had received a diagnosis of COVID-19 and 7 had co-existing congenital or acquired diseases (50). Common abnormalities, such as GGO and consolidation, were also observed in more than half of the patients, accompanied by fibrotic lesions, air bronchogram, and interlobular septal thickening in the advanced stage. Subpleural lesions with local infiltration were observed in all patients. The “white lung” change was observed in the critical stage showing progression of lesions to diffuse involvement of the lungs. These chest CT findings are considerably similar to those reported in adult patients; thus, the diagnosis of COVID-19 still relies on a combination of clinical and imaging findings.

Findings of these studies indicate that adults tend to be more contracted with COVID-19 than children. When children are infected, the symptoms are mild compared to moderate or severe symptoms that are commonly seen in adults, and this is likely due to the presence of comorbidities in elderly patients such as diabetes, hypertension or cardiovascular disease which are associated with poor prognosis or high mortality.

Discussion

To the best of our knowledge, this is the first comprehensive review and analysis of the current literature on the chest imaging features of patients with COVID-19. The review summarizes the following key findings from the literature. First, chest CT findings, including GGO, consolidation, air bronchogram, crazy-paving pattern, linear opacities and bronchial wall thickening or distortion, are nonspecific because they can also be seen in pneumonia caused by other pathogens such as viral pneumonia. Furthermore, there was a relatively high proportion of normal chest CT scans, especially in early stage or asymptomatic patients (69-71). This highlights the importance of combining CT with clinical examination for the diagnosis of COVID-19. In addition, there exists inconsistency between clinical symptoms and imaging appearances, especially in early stage of COVID-19 (72,73). Second, despite potential role of CT in differentiating nonsevere from severe or critically ill patients and its clinical value in determining the disease extent and progression, this can be achieved with use of

CXR, thus further highlighting the limited value of CT in COVID-19. Third, the analysis of the current literature is based on most of the studies (95%) conducted in China, with nearly all of them advocating the use of chest CT in the diagnosis of COVID-19. More evidence is needed from studies reporting patients with COVID-19 in other countries. Countries such as United States, Italy, Spain, Germany and France have more than 100,000 confirmed cases in each country (1); thus, more research findings from these countries are expected to be reported soon, although CT is not commonly used in these countries according to some early reports (14).

Currently, there are four review articles available on the chest imaging and clinical findings of COVID-19 (74-77). Ye *et al.* in their pictorial review presented a spectrum of chest CT findings associated with COVID-19 including a brief review of 14 studies which reported CT findings (74). Rodriguez-Morales *et al.* conducted a systematic review and meta-analysis of clinical, laboratory and imaging features of COVID-19 (75). Authors included 19 studies for the meta-analysis, while another 39 case reports for the descriptive analysis. Although imaging findings were included in their analysis, only information about bilateral and unilateral lung involvement, and GGO was analyzed, while other detailed findings were not included because their analysis focused more on clinical and laboratory characteristics. Salehi and colleagues analyzed chest imaging findings in 30 studies, of which 19 were case series and 11 were case reports (76). They analysis included GGO, consolidation, lung and lobar involvement, and CT findings in relation to different age groups and stage of the disease, but was limited to the analysis of cases studies. A recent study by Borges do Nascimento *et al.* analyzed chest imaging findings in 51 studies, but authors did not perform meta-analysis of these imaging features in their review as they briefly summarized these imaging findings while focusing more on clinical characteristics (77). Our review represents a more in-depth analysis of 55 original studies with exclusion of isolated case reports. Further, we analyzed typical, atypical CT findings and diagnostic value of CT in COVID-19 patients. In addition, comparisons of COVID-19 with non-COVID-19 studies with regard to imaging differences indicate another unique aspect of this meta-analysis. Analysis of chest abnormalities in pregnant women, children and neonates also adds extra information to these previous reviews. Thus, this systematic review and meta-analysis offers insight into clarifying the role of using chest CT in the diagnosis of COVID-19 patients.

Although increasing studies on this trending topic are available in the literature, the sample size is still small in most of these studies that were reviewed. Majority of the current reports is dominated by case studies documenting individual institution's experience of diagnosing and treatment COVID-19 patients. Only two studies in this review included more than 1,000 cases, whereas 72.2% of the studies included <100 patients (*Table 1*). Furthermore, most of them reported only general imaging findings of chest CT without conducting further analysis or comparison of these findings in different categorized groups. Case reports were excluded from the analysis because they only present some initial experience of chest imaging findings in COVID-19 without providing details of frequency on abnormal lung changes. Publications in Chinese language were also excluded to avoid duplicate publication of similar research findings in English literature. Another limitation is the lack of information on mortality associated with COVID-19 because only six studies thus far have reported mortality, which ranged from 1.4% to 52.4% (14,21,30,45,58,65). Additional studies with short- to long-term follow-up of patients with COVID-19 are required so that our understanding of disease progression, including radiological abnormalities, can be improved.

As the number of COVID-19 cases continue to increase every day with no effective treatment or vaccine available so far, radiologists will encounter an increasing number of cases, with both typical and atypical manifestations of lung infection. Therefore, it is important for them to be familiar with imaging findings of COVID-19 pneumonia and assist their communication with other healthcare providers for management of COVID-19 patients. Recommendations and advice guidelines for the diagnosis and treatment of patients with COVID-19, including pregnant women and pediatric patients, are already available (78-80). The advice guidelines for COVID-19-associated pneumonia include suggestions and recommendations for clinical diagnosis and typical and atypical chest CT/CXR image manifestations based on stages, from ultra-early to progression and dissipation stages (78). This article provides guidance for frontline clinicians, including radiologists, for early diagnosis and identification of abnormal changes associated with COVID-19 and characterization of the disease extent based on CT imaging appearances. Recommendations of the diagnostic strategy for treating pediatric patients with respiratory infection and women with COVID-19 during pregnancy and puerperium are also available (79,80). According to these recommendations, chest imaging, particularly a chest CT scan, is considered an essential technique for the diagnosis and evaluation of abnormalities in the lungs. However, this contradicts with the recent statements about the appropriate use of chest imaging in COVID-19 (81-83).

The American College of Radiology statement states that CT should not be used as the first-line technique to diagnose COVID-19 due to its limited specificity in differentiating lung abnormalities (81). The Radiological Society of North America (RSNA) has also published a statement developed by imaging experts across the United States to provide guidance to radiologists reporting CT findings attributable to suspected COVID-19 pneumonia. Four categories were proposed for reporting CT findings which are potentially related to COVID-19, and routine use of CT as a screening tool is not recommended (82). The Fleischner Society has just released a consensus statement on the role of chest imaging in the management and diagnosis of COVID-19 (83). According to these recommendations, chest imaging is not indicated as a screening tool in asymptomatic or mild clinical feature patients, while chest CT is indicated for moderate to severe features of COVID-19, regardless of the laboratory test results. Although most radiology societies are not recommending the routine use of CT for screening COVID-19, the number of CT scans performed for suspected cases has significantly increased. More evidence is urgently needed to clarify the role of CT in the diagnosis of patients with COVID-19, especially findings from countries outside China are needed to determine its clinical value because most of the studies that support the use of CT as a routine and frontline technique are reported by researchers from China, thus the role of CT could be overestimated (84,85). According to a recent study, only chest radiographs were used in the diagnosis of 21 critically ill COVID-19 patients in Washington State with high accuracy in detecting all abnormal lung changes (14). More research findings from other countries are expected to provide a different view on the judicious use of CT in CIVID-19.

An alternative modality to CXR or chest CT in diagnosing lung changes of COVID-19 is the use of ultrasound which has been reported in some case studies (86-90). These case reports indicate the potential value of lung ultrasound as a secondary screening modality when RT-PCR is not available or as an alternative to CT in pregnant and pediatric patients. A recent study from Italy compared bedside lung ultrasound with CT in 12 patients with COVID-19 and showed excellent correlation between these two modalities in detecting lung abnormalities (88). Further studies are required to confirm the usefulness of lung ultrasound in the diagnosis and management of COVID-19.

In conclusion, this systematic review and meta-analysis provides a detailed analysis of the current literature on chest imaging findings in COVID-19 patients. Despite widespread use of CT in these studies, its clinical value needs to be determined due to lacking specificity in differentiating imaging appearances caused by different types of pneumonia. Diagnosis of COVID-19 is still to be confirmed by clinical and laboratory examinations. CXR still plays a role in the identification and detection of abnormal lung changes, while chest CT could serve as a complementary role in evaluating potential complications, disease severity and progression rather than a routine diagnostic approach. Appropriate guidelines should be followed with regard to the judicious use of CT in the diagnosis of COVID-19.

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Footnote

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