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CT Manifestations and Clinical Characteristics of 1115 Patients with Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-analysis

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Rationale and Objectives: We aimed to assess the prevalence of significant computed tomographic (CT) manifestations and describe some notable features based on chest CT images, as well as the main clinical features of patients with coronavirus disease 2019 (COVID-19).

Materials and Methods: A systematic literature search of PubMed, EMBASE, the Cochrane Library, and Web of Science was performed to identify studies assessing CT features, clinical, and laboratory results of COVID-19 patients. A single-arm meta-analysis was conducted to obtain the pooled prevalence and 95% confidence interval (95% CI).

Results: A total of 14 articles (including 1115 patients) based on chest CT images were retrieved. In the lesion patterns on chest CTs, we found that pure ground-glass opacities (GGO) (69%, 95% CI 58–80%), consolidation (47%, 35–60%) and “air bronchogram sign” (46%, 25–66%) were more common than the atypical lesion of “crazy-paving pattern” (15%, 8–22%). With regard to disease extent and involvement, 70% (95% CI 46–95%) of cases showed a location preference for the right lower lobe, 65% (58–73%) of patients presented with ≥ 3 lobes involvement, and meanwhile, 42% (32–53%) of patients had involvement of all five lobes, while 67% (55–78%) of patients showed a predominant peripheral distribution. An understanding of some important CT features might be helpful for medical surveillance and management. In terms of clinical features, muscle soreness (21%, 95% CI 15–26%) and diarrhea (7%, 4–10%) were minor symptoms compared to fever (80%, 74–87%) and cough (53%, 33–72%).

Conclusion: Chest CT manifestations in patients with COVID-19, as well as its main clinical characteristics, might be helpful in disease evolution and management.

Keywords: COVID-19; CT manifestations; Clinical features; Laboratory; Meta-analysis.

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Abbreviations: CI confidence interval, **COVID-19** coronavirus disease 2019, **2019-nCoV** 2019 novel coronavirus, **CT** computed tomographic, **GGO** ground-glass opacities, **MERS-CoV** Middle East respiratory syndrome coronavirus, **NIH** National Institutes of Health, **PHEIC** public health emergency of international concern, **PRISMA** Preferred Reporting Items for Systematic Review and Meta-Analysis, **RT-PCR** real-time fluorescence polymerase chain reaction, **SARS-CoV** severe acute respiratory syndrome coronavirus, **SARS-CoV-2** severe acute respiratory syndrome coronavirus 2, **WHO** World Health Organization

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INTRODUCTION

In the past few months, the global world has witnessed an epidemic of a new respiratory coronavirus that started in Wuhan with an unknown origin, which was named 2019 novel coronavirus (2019-nCoV) by the World Health Organization (WHO). On February 15, the outbreak of this disease was named coronavirus disease (COVID-19) for the first time (1), and on January 30, 2020, WHO declared the outbreak of this highly contagious coronavirus pneumonia a public health emergency of international concern (2).

This novel coronavirus is called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which belongs to

the Coronaviridae family that includes severe acute respiratory syndrome (SARS-CoV) (3,4) and Middle East respiratory syndrome coronavirus (MERS-CoV) (5,6). As of April 13, 2020, 1,773,084 cases have been diagnosed with COVID-19 globally, mainly consisting of 913,349 cases in the European region and 610,742 cases in the United States, resulting in 111,652 deaths to now (7). Governments have taken decisive and comprehensive measures to contain the spread of the disease, including early isolation of suspected patients to cut off the transmission route and frequent disinfection. The medical authorities and workers have made great efforts in developing a curative vaccine for the disease, which is still in clinical trials for further effect validation.

Patients were infected or highly suspicious for SARS-CoV-2 infection present with clinical symptoms of fever and cough, which resemble common influenza and make early detection of this disease a challenge (8). Therefore, it is now the focus of research workers to effectively detect and diagnose COVID-19 as early as possible. Currently, a positive result of real-time fluorescence polymerase chain reaction (RT-PCR) is considered the reference standard for diagnosing COVID-19, which is a time-consuming laboratory test, and a large number of countries may confront a shortage of the detection kits for SARS-CoV-2. It may also yield a false-negative result in the early stages of the disease in some cases (9,10). Chest computed tomographic (CT) may prove to be a valuable diagnostic method in patients with typical clinical characteristics, because some features of the disease may be present on CT images even when the RT-PCR screening test is negative (11).

Notably, pneumonia is the most common clinical manifestation since the respiratory tract is the main target of this coronavirus, and a series of studies have revealed that chest CT might be useful as a capable surveillance method in suspected COVID-19 patients, for both initial evaluation and follow-up (12–14). Several studies have further indicated that imaging features on chest CT have the potential to predict the severity of SARS-CoV-2 infection (8,14–16). These studies investigated some major CT features of the extent of disease involvement and lesion patterns, including ground-glass opacities (GGO), consolidation, and peripheral distribution. However, there is still a limited sample size describing the CT features as well as the clinical characteristics, and consensus has not been reached about the prevalence of CT manifestations. In addition, some other important features have not been investigated in patients with 2019-nCoV infections.

To our knowledge, several previous meta-analyses revealed the mortality rate and incidence of clinical symptoms in patients with 2019-nCoV infection (17,18), while no previous meta-analysis based on chest CT manifestations has been performed. Therefore, we conducted a systematic review and meta-analysis in a large sample based on CT images, aiming to further reveal the prevalence of notable chest CT features in COVID-19 patients, as well as some main clinical characteristics and laboratory test data. We hope

that this report can help radiologists and clinicians with early recognition and management of COVID-19.

MATERIALS AND METHODS

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analysis guidelines (19).

Search Strategy

A systematic literature search of PubMed, EMBASE, the Cochrane Library and Web of Science was performed to identify relevant studies using the following search terms: “coronavirus”, “2019 novel coronavirus”, “Wuhan virus”, “2019-nCoV”, “COVID-19”, “SARS-CoV-2”, “CT”, “computed tomography” and “imaging”. The search was limited from January 1, 2019 to March 15, 2020, since this outbreak started in late December 2019. All eligible literature was retrieved and their reference lists were checked for additional relevant publications.

Inclusion and Exclusion Criteria

Two reviewers (SW and MQL) screened the titles and abstracts of the studies independently to identify potential eligibility; then, the full texts of potentially eligible studies were reviewed for final inclusion. Studies were included according to the following criteria: (1) patients with COVID-19 diagnosed with RT-PCR, (2) RT-PCR is considered as the reference standard, (3) studies conducted both RT-PCR and chest CT with positive CT findings, and (4) the CT features, clinical characteristics and laboratory results of COVID-19 patients can be extracted. Exclusion criteria were as follows: (1) duplications, case reports, reviews, conference abstracts, letters, nonoriginal studies, and irrelevant studies; (2) studies with a small sample size (patients <5); and (3) studies we were unable to extract sufficient data from for the meta-analysis.

Data Extraction and Quality Assessment

The following information was extracted from each included study: first author and publication year; publishing journal; time interval from symptom onset to positive RT-PCR; study region; study design; consecutive enrollment; sample size; mean age; male/female ratio; CT manifestations including pulmonary lobes involved ≥ 3 ; all five lobes involved; right lower lobe involvement; peripheral distribution; consolidation (with or without GGO); pure GGO; “air bronchogram sign”; “crazy-paving pattern”; main clinical characteristics including fever (temperature $\geq 37.3^{\circ}\text{C}$), cough, muscle soreness, and diarrhea; and major laboratory examinations including leukocytopenia, lymphocytopenia and increased C-reactive protein. Among these features, ground-glass opacification was defined as hazy increased lung attenuation with preservation of bronchial and vascular margins, and consolidation was defined as

opacification with obscuration of the margins of vessels and airway walls (14,20,21). The “air bronchogram sign” was formed by bronchus containing air in consolidation (22), and the “crazy-paving pattern” was characterized by the reticular interlobular septa thickening within the patchy GGO (23,24).

Two independent reviewers (SW and MQL) conducted the literature search, study selection, data extraction, and quality assessment, with a third reviewer (CWY) adjudicating on disagreements. The quality assessment was evaluated with the National Institutes of Health Quality Assessment Tool for Case Series Studies (25), and the general quality rating was classified as poor, fair, or good with this tool.

Statistical Analysis and Data Synthesis

Stata V.15.1 (StataCorp LP, College Station, Texas) was used to conduct this single-arm meta-analysis. The incidence of CT features, clinical symptoms, and laboratory results of COVID-19 patients are the outcomes of this meta-analysis.

The incidence and the corresponding 95% confidence intervals (95% CI) were calculated using the collected data, and a forest plot was constructed. Heterogeneity among the included studies was assessed using the Cochran's Q-test (P) and inconsistency index (I^2). A $p < 0.1$ or $I^2 > 50\%$ indicate significant heterogeneity and a random-effects model was used if $I^2 > 50\%$, with $p < 0.05$ indicating statistical significance. A sensitivity analysis was performed to investigate potential sources of heterogeneity by excluding each of the studies in turn, and then reevaluating the remaining combined performance to verify the robustness of the result. Publication bias was not assessed since there does not seem to be a radical necessity in this single-arm meta-analysis (26).

RESULTS

Study Selection

A total of 192 records were retrieved (PubMed, 111 articles; EMBASE, 57 articles; Cochrane Library databases, 1 article; Web of Science, 23 articles). Figure 1 presents the flow diagram of the study selection process. After removing duplications, 124 studies were obtained, and after screening titles and abstracts, studies that were case reports, reviews, meta-analysis, letters, conference abstracts, and irrelevant studies were excluded, leaving 36 potential studies to be downloaded for full-text review. Then, six irrelevant studies without CT manifestations and 16 studies we were unable to collect sufficient data from were excluded. Finally, 14 studies including 1115 patients were selected for this systematic review and meta-analysis.

Study Characteristics and Quality Assessment

The basic characteristics and demographic data of the included studies are summarized in Table 1. A total of 15 variables were extracted and analyzed in our study. All included studies were from China and were retrospective studies.

Among them, five studies were from Wuhan (13,22,27–29), six studies were performed on a single CT modality (16,23,28,30–32), and most of the patients had a recent exposure history to Wuhan or exposure to infected patients. Quality assessment of the included studies was generally considered fair according to the criteria (Table 2).

CT Manifestations

CT Manifestations of Lesion Patterns in COVID-19 Patients

Table 3 shows the CT manifestations of COVID-19. The lesion patterns summarized in our meta-analysis include pure GGO without consolidation, consolidation with or without GGO, “air bronchogram sign” and “crazy-paving pattern”. Figure 2 demonstrates the forest plots for each lesion pattern. A total of 13 studies with 1073 patients were evaluated for the prevalence of pure GGO on chest CT images. The results indicate that the incidence of pure GGO without consolidation is 69% (95% confidence interval [CI] 58–80%, $I^2=96.7\%$). A total of 14 studies with 1115 patients infected were included for the prevalence of consolidation and we found that the incidence of consolidation with or without GGO was 47% (95% CI 35–60%, $I^2=95.6\%$). The incidence of “air bronchogram sign” was 46% (95% CI 25–66%, $I^2=97.6\%$) by assessing eight studies with 565 cases, and the incidence of “crazy-paving pattern” was 15% (95% CI 8–22%, $I^2=89.1\%$) by summarizing seven studies with 695 infected cases, which is less common compared to the other lesion features.

CT Manifestations of Extent and Involvement in COVID-19 Patients

We evaluated the major features of extent and involvement of COVID-19, including right lower lobe involved, three or more lobes involved (lobes ≥ 3), all five lobes involved, and a peripheral distribution (Table 3). Figure 3 demonstrates the forest plots for features of extent and involvement. The results suggest that almost 70% (95% CI 46–95%, $I^2=98.6\%$) of patients had right lower lobe involvement by summarizing eight studies with 547 cases. A close second was 65% (95% CI 58–73%, $I^2=63\%$) of patients had three or more pulmonary lobes involved (lobes ≥ 3) across seven studies with 438 cases, and meanwhile, nearly 42% (95% CI 32–53%, $I^2=84.4\%$) of patients were infected with all five lobes involved with eight studies and 489 cases. With regard to lesions distribution, 67% (95% CI 55–78%, $I^2=93.6\%$) of infected patients had predominant peripheral distribution across nine studies with 817 cases.

For most of the chest CT features, the sensitivity analyses and the reevaluated results indicated none of the studies had a notable impact on the substantial heterogeneity, excepting features of five lobes involvement and three or more pulmonary lobes involvement. The sensitivity analysis indicated that a substantial reduction of heterogeneity in the feature of five lobes involvement could be generated after excluding the study of Li Y et al. (13), with a re-estimated prevalence of

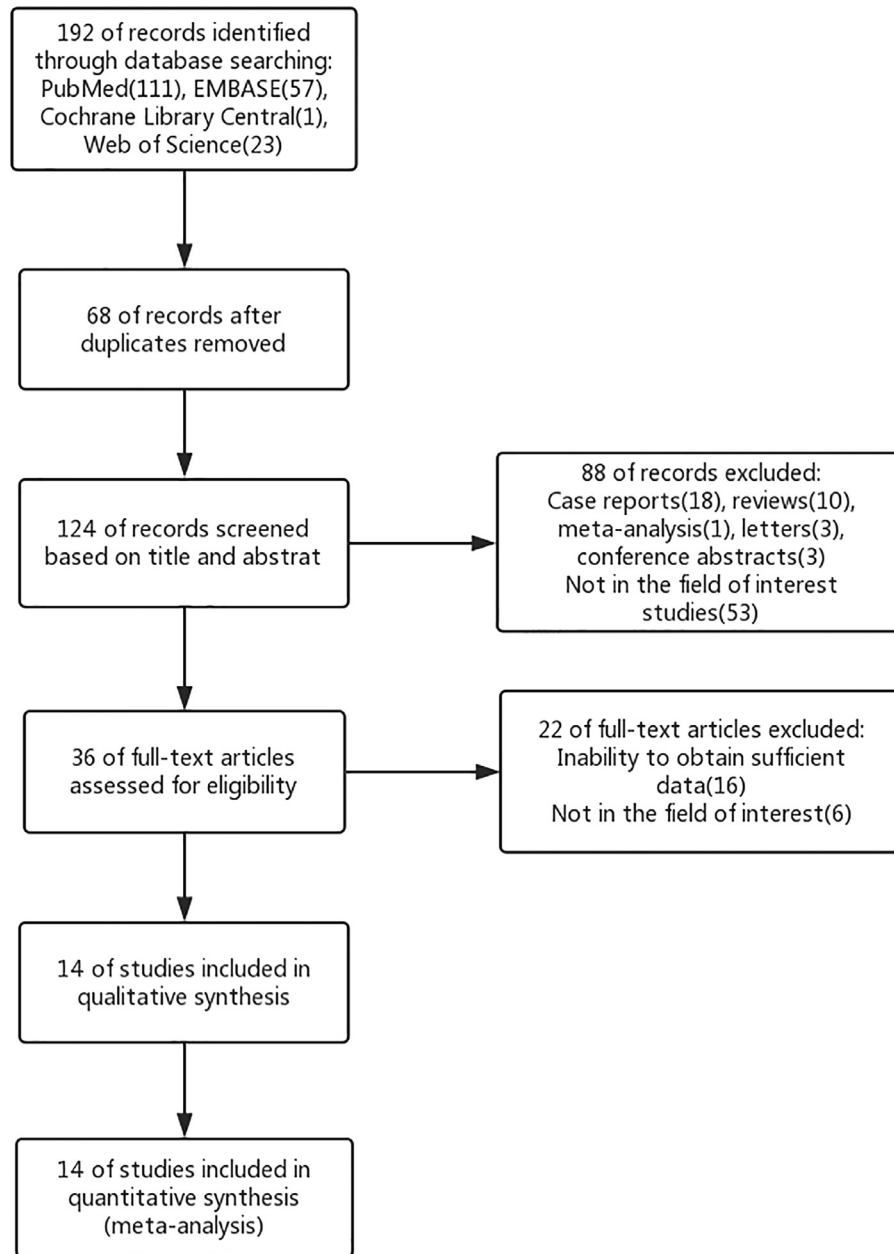


Figure 1. Flow diagram of the study selection process.

37% (95% CI 31–42%, $I^2=33.7\%$)(Fig. 4); likewise, a decrease of heterogeneity could be observed in the feature of three or more pulmonary lobes involvement after excluding the study of Bernheim A et al. (33), with a re-estimated incidence of 68% (95% CI 62–74%, $I^2=26.7\%$)(Fig. 5).

Main Clinical Characteristics and Laboratory Results

Table 4 summarizes the results of the main clinical symptoms and laboratory results of the included studies. The incidence of fever was 80% (95% CI 74–87%), which served as the most prevalent clinical manifestation, followed by cough (53%, 95% CI 33–72%), and minor symptoms were muscle soreness (21%, 95% CI 15–26%) and diarrhea (7%, 95% CI 4–10%).

Additionally, major laboratory items of COVID-19 were analyzed and the results indicated that the incidence of leukocytopenia was 42% (95% CI 4–79%), lymphocytopenia was 51% (95% CI 32–69%), and increased C-reactive protein was 56% (95% CI 45–66%).

DISCUSSION

The new outbreak of COVID-19 has caused countless infections and deaths in the last few months. Medical workers are doing more research concerning public health, and a number of case series have been published to define the CT and clinical features of COVID-19 pneumonia. In particular, a comprehensive understanding of significant imaging and clinical

TABLE 1. Characteristics of the Included Studies of COVID-19

Study, year	Journal	Region	Time Interval*	Study Design	Consecutive Enrolment	Sample Size(N')	Mean Age (Y'')	Male/ Female(N')	CT Technique
Zhou S.C. et al 2020	American Journal of Roentgenology	Wuhan, China	-**	Retrospective	-	62	52.8	39/23	16-MDCT LightSpeed scanner (GE Healthcare); UCT 760 scanner (United Imaging)
Li Y et al 2020	American Journal of Roentgenology	Wuhan, China	-	Retrospective	-	51	58	28/23	UCT 780, United Imaging; Somatom Force, Siemens Healthcare
Xu X et al 2020	European Journal of Nuclear Medicine and Molecular Imaging	Guangzhou, China	-	Retrospective	-	90	50	39/51	CT680 scanner (GE Medical Systems, Milwaukee, WI)
Chung M et al 2020	Radiology	Zhuhai, Nanchang, Qingdao, China	-	Retrospective	Yes	21	51	13/8	UCT 760 scanner(United Imaging, Shanghai, China); Emotion 16 scanner (Siemens Healthineers, Erlangen, Germany); BrightSpeed scanner (GE Medical Systems, Milwaukee, Wis); Aquilion ONE scanner (Toshiba Medical Systems, Tokyo, Japan)
Bernheim A et al 2020	Radiology	Nanchang, Zhuhai, Guilin, Chengdu, China	4.5	Retrospective	Yes	121	45	61/60	Siemens Emotion 16 scanner(Siemens Healthineers; Erlangen,Germany); UCT 760 scanner (United Imaging; Shanghai, China); Revolution scanner (GE Medical Systems; Milwaukee, WI); Philips Brilliance Big Bore scanner(Philips; Amsterdam, Netherlands)
Wu J et al 2020	Investigative Radiology	Chongqing, China	7	Retrospective	-	80	44	42/38	16-row multidetector CT scanner (Siemens Somatom Sensation; Siemens, Erlangen, Germany)
Xu Y. H. et al 2020	Journal of Infection	Beijing, China	-	Retrospective	-	50	43.9	29/21	High-resolution LightSpeed VCT CT64 scanner(GE MEDICAL SYSTEMS, China Branch, Beijing, China)
Xiong Y. et al 2020	Investigative Radiology	Wuhan, China	4.5	Retrospective	-	42	49.5	25/17	LightSpeed Plus (GE, Medical System, Milwaukee, USA); Aquilion ONE(Toshiba Medical System, Tokyo, Japan), and UCT 780 (United Imaging, Shanghai, China)
Song F. et al 2020	Radiology	Shanghai, China	4	Retrospective	-	51	49	25/26	64-section scanner (SCENARIO 64 CT, Hitachi Medical, Japan)
Pan Y. Y. et al 2020	European Radiology	Wuhan, China	-	Retrospective	-	63	44.9	33/30	CT HD750 Discovery, GE
Zhao W. et al 2020	American Journal of Roentgenology	Hunan, China	-	Retrospective	Yes	101	44.44	56/45	Anatom 16HD(Anke Medical Solutions); HiSpeed-Dual (GE Healthcare); 64-MDCT LightSpeed VCT (GE Healthcare); Somatom Emotion (Siemens Healthcare)
Li K.H. et al 2020	Radiology	Chongqing, China	7	Retrospective	-	83	45.5	44/39	16-row multidetector scanner (Siemens Sensation 16, Erlangen, Germany)
Harrison X. B. et al 2020	Radiology	Hunan, China	4.9	Retrospective	-	219	44.8	119/100	Siemens Somatom Definition; SIEMENS Emotion 16; GE BrightSpeed; GE LightSpeed Ultra; Philips Access CT; Hitachi ECLOS; SIEMENS SOMATOM go.Now
Shi H.S. et al 2020	The Lancet Infectious diseases	Wuhan, China	-	Retrospective	-	81	49.5	42/39	Somatom Perspective; Somatom Spirit; Somatom Definition AS+(Siemens Healthineers, Forchheim, Germany)

* mean day from symptom onset to positive RT-PCR.

** -: not available or not reported; 'N: number of patients; ''Y: years old.

TABLE 2. Quality Assessment of the Included Studies According to the National Institutes of Health(NIH) Quality Assessment Tool for Case Series Studies

Study, year	Criteria*									Quality Rating
	1	2	3	4	5	6	7	8	9	
Zhou S.C. et al 2020	Yes	Yes	NR**	CD'	NA''	Yes	Yes	Yes	Yes	Fair
Li Y et al 2020	Yes	Yes	NR	Yes	NA	Yes	CD	CD	Yes	Fair
Xu X et al 2020	Yes	Yes	NR	NA	NA	Yes	CD	Yes	Yes	Fair
Chung M et al 2020	Yes	Yes	Yes	CD	NA	Yes	CD	CD	Yes	Fair
Bernheim A et al 2020	Yes	Yes	Yes	CD	NA	Yes	CD	NA	Yes	Fair
Wu J et al 2020	Yes	Yes	NR	NA	NA	Yes	NA	Yes	Yes	Fair
Xu Y. H. et al 2020	Yes	Yes	NR	CD	NA	Yes	NA	Yes	Yes	Fair
Xiong Y et al 2020	Yes	Yes	NR	CD	NA	Yes	CD	Yes	Yes	Fair
Song F et al 2020	Yes	Yes	NR	CD	NA	Yes	CD	Yes	Yes	Fair
Pan Y. Y. et al 2020	Yes	Yes	NR	NA	NA	Yes	NA	CD	Yes	Fair
Zhao W et al 2020	Yes	Yes	Yes	CD	NA	Yes	NA	Yes	Yes	Fair
Li K.H. et al 2020	Yes	Yes	NR	CD	NA	Yes	CD	Yes	Yes	Fair
Harrison X. B. et al 2020	Yes	Yes	NR	Yes	NA	Yes	CD	Yes	Yes	Fair
Shi H.S. et al 2020	Yes	Yes	NR	CD	NA	Yes	NA	Yes	Yes	Fair

* : The questions of the NIH quality assessment tool for case series studies(1: Was the study question or objective clearly stated?; 2: Was the study population clearly and fully described, including a case definition?; 3: Were the cases consecutive?; 4: Were the subjects comparable?; 5: Was the intervention clearly described?; 6: Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?; 7: Was the length of follow-up adequate?; 8: Were the statistical methods well-described?; 9: Were the results well-described?).

** NR: not reported; 'CD: cannot determine; ''NA: not applicable.

features can be beneficial for effective management and treatment. In this systematic review and meta-analysis, we summarized the prevalence of some notable CT features, as well as the main clinical characteristics and laboratory results, aiming to generate a comprehensive understanding for radiologists and clinical teams.

In this meta-analysis, we described the CT manifestations as the extent of disease involvement and lesion patterns. The presentation of imaging lesions resembles features of other viral pneumonia such as SARS and MERS, which may be related to a similar pathogenesis caused by viruses in the same viral family (14,24). We found that GGO without consolidation presented as the most common lesion, affecting 86.1% of infected patients. When patients presented with GGO without consolidation on chest CT images, this meant that they were in the early period of virus infection or that the lung lesions had begun to be absorbed (34). If the patient's immune system was not strong enough to fight off the virus or effective treatment was not conducted, there was a tendency for lesions to progress to consolidation in some cases.

We also found that 47% of patients with COVID-19 presented with consolidation, which has the potential to increase the risk of pulmonary fibrosis and lower the patients' life quality (34). In addition, consolidative lesions were more commonly seen in severely ill cases and they might be correlated with disease severity (35). "Air bronchogram sign" can be seen in 46% of patients, which was defined as another form of consolidation (22), while the "crazy-paving pattern" that only 15% of patients presented with was considered a less common lesion pattern.

In this study, the extent of disease involvement included right lower lobe involvement, pulmonary lobes involving three or more lobes, and all five lobes involved. Several included studies revealed that the lesions were more likely to be located in the right lower lobe, and our results suggested that 70% of cases occurred in the right lower lobe. This newly described feature has not been evaluated with a large sample size before. One study revealed that the preferred location for this lobe may be correlated with the anatomic characteristics of the right lobar bronchus, the straight and steep bronchus of the right lower lobe, as well as the small angle between the right lower lobe and the long axis of the trachea, which might lead to the preference for invasion of this lobe (22).

In addition, CT features of 2019-nCoV infection presented a predominantly peripheral distribution, with an incidence of 67% in 817 cases, which is relatively consistent with coronavirus reports on SARS, MERS (36), and other positive respiratory pathogens causing viral pneumonia (37).

In terms of the extent of infection involvement, a previous study indicated that if one or two lobes are involved, clinical symptoms of shortness of breath, dyspnea, and the impact on lung function are not significant (34), and the lesions can be absorbed if effective treatment is applied. Xu Y. H. et al. indicated that severe and critically severe COVID-19 cases most commonly had 4–5 lobes involved (31), Bernheim A et al. also suggested that the extent of infection on CT images may have some connection with the progression and severity (33).

We evaluated the prevalence of three or more pulmonary lobes involvement since no previous meta-analysis summarized this feature, and we found that 65% of patients in 438 cases

TABLE 3. CT Manifestations of Included Studies of COVID-19

Study, year	Sample size(N')	Lesion Pattern(N', %)				Extent and Involvement(N', %)			
		Pure GGO*	Consolidation (with or without GGO)	Air bronchogram sign	Crazy-paving pattern	Right lower lobe involved	3 or more lobes involved (lobes \geq 3)	All five lobes involved	Peripheral distribution
Zhou S.C. et al 2020	62	25(40.3)	21(33.9)	45(72.6)	-**	-	-	-	48(77.4)
Li Y et al 2020	51	18(35.3)	31(60.8)	35(68.7)	-	3(5.9)	-	38(74.5)	-
Xu X et al 2020	90	65(72.2)	12(13.3)	7(7.8)	11(12.2)	59(65.6)	53(58.9)	32(35.6)	46(51.1)
Chung M et al 2020	21	12(57.1)	6(28.6)	-	4(19)	16(76.2)	15(71.4)	8(38.1)	-
Bernheim A et al 2020	121	41(33.9)	52(43.0)	-	6(4.9)	79(65.3)	62(51.2)	33(27.3)	63(52.1)
Wu J et al 2020	80	73(91.3)	50(62.5)	-	23(28.8)	69(86.3)	-	-	-
Xu Y. H. et al 2020	50	30(60)	40(80)	22(44)	-	39(78)	34(68)	170.34	39(78)
Xiong Y et al 2020	42	-	23(54.8)	140(33.3)	-	-	32(76.2)	20(47.6)	12(28.6)
Song F et al 2020	51	39(76.5)	28(54.9)	41(80.4)	-	46(90.2)	38(74.5)	20(39.2)	44(86.3)
Pan Y. Y. et al 2020	63	54(85.7)	12(19)	-	-	-	39(61.9)	28(44.4)	-
Zhao W et al 2020	101	87(86.1)	65(64.3)	-	-	-	-	-	88(87.1)
Li K.H. et al 2020	83	81(97.6)	53(63.9)	-	30(36.1)	78(94)	-	-	-
Harrison X. B. et al 2020	219	200(91.3)	150(68.5)	30(13.7)	11(5)	-	-	-	176(80.4)
Shi H.S. et al 2020	81	53(65.4)	14(17.3)	38(46.9)	80(98.8)	-	-	-	44(54.3)

* GGO: ground-glass opacities.

** -: not available or not reported; 'N': number of patients.

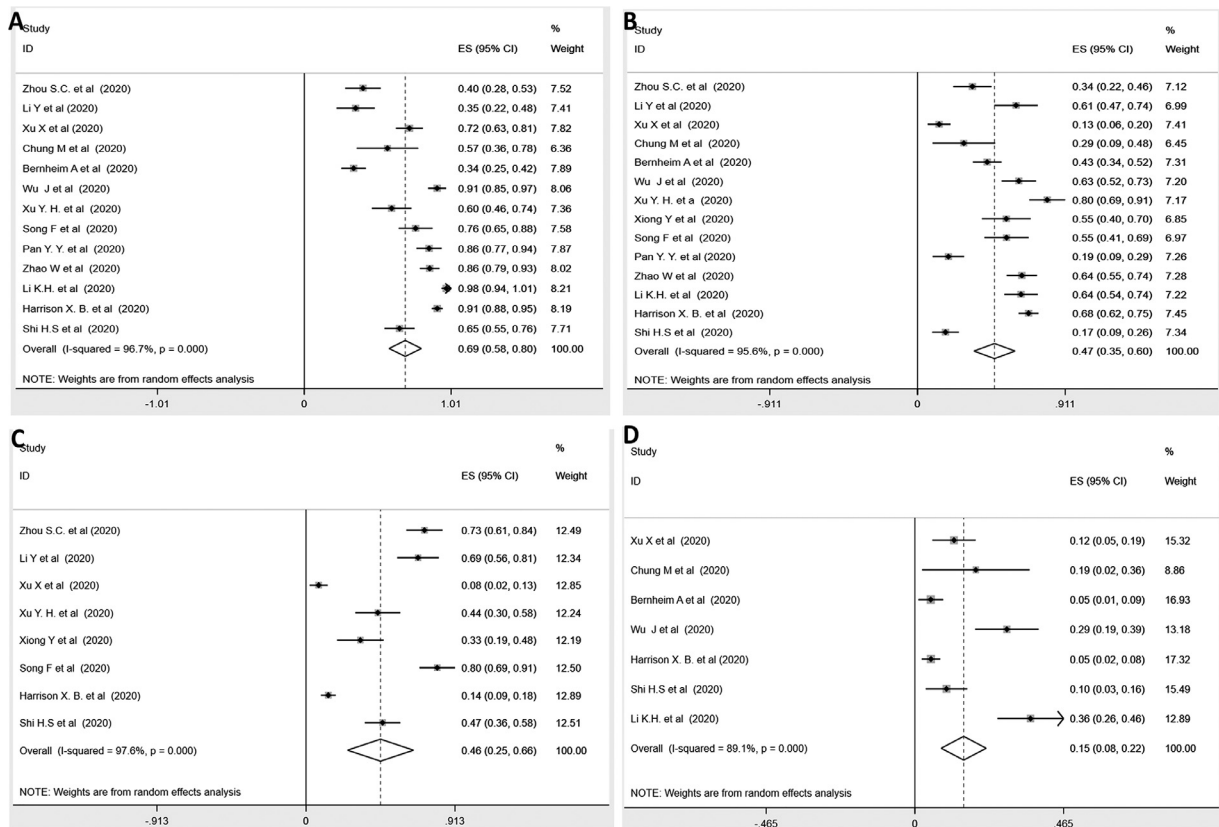


Figure 2. Forest plots of the incidence of lesion patterns on chest CT images in COVID-19 cases. A, B, C, and D represent the prevalence of pure GGO, consolidation (with or without GGO), “air bronchogram sign”, and “crazy-paving pattern”, respectively.

presented with three or more lobes involved, which is also consistent with the previous results of predominantly bilateral involvement (14,29,30,38). In these cases, continuous surveillance might be valuable to monitor the disease progression.

Meanwhile, we also summarized the incidence of all five lobes involvement, which occurred in 42% of infected patients. In some cases, lung function might become impaired with all five lobes involved, and if medical treatment is not given or the immune system is not strong enough to defeat the virus, the lungs may progress into the end stage, which is associated with a poor prognosis (34).

The prevalent clinical characteristics included in our meta-analysis suggest that fever and cough are the most common symptoms, which has also been reported in previous analyses (17,39,40). These results indicate that the incidence of fever (80%) in COVID-19 is lower than that for SARS and MERS (41), while the incidence of cough (53%) in COVID-19 is similar to that of MERS and SARS (around 50%) (41,42). The results also indicated that the incidences of diarrhea (7%) and gastrointestinal symptoms were lower than for SARS and MERS (20–25%) (43,44). The presentation of diarrhea may be related to the pathogenesis of SARS-CoV-2, because this virus binds to human receptor angiotensin-converting enzyme 2 (45), which shows high expression in the gastrointestinal tract (22,46).

More than 20% of patients presented with muscle soreness in addition to the common symptoms of fever and cough.

Patients with gastrointestinal symptoms and muscle soreness, associated with other risk factors, should receive medical attention for early disease recognition.

With regard to laboratory results, we summarized the frequency of three typical laboratory examinations. Similar to the SARS outbreak, we confirmed that lymphopenia and leukopenia (47) may be associated with the cytokine storm induced by the invasion of the virus particles that then evokes a series of immune responses, which may lead to some changes in peripheral white blood cells and immune cells such as lymphocytes (48,49). The increased C-reactive protein level can also be explained by this immune response of the human body.

This is the first systematic review and meta-analysis that has highlighted the importance of chest CT manifestations, as well as some clinical symptoms and laboratory examinations. Meanwhile, we identified some newly described CT features, such as a predominant location in the right lower lobe, three or more lobes involved, and the less common symptom of diarrhea, which has not been investigated and might be ignored in the initial examination for COVID-19. These findings might be suggestive for the medical team.

What’s more, we summarized the prevalence of lesion patterns and extent of involvement of 2019-nCoV infection in this study. Some imaging findings may be associated with disease progressions, such as three or more pulmonary lobes involved, all five lobes involvement and consolidation, and

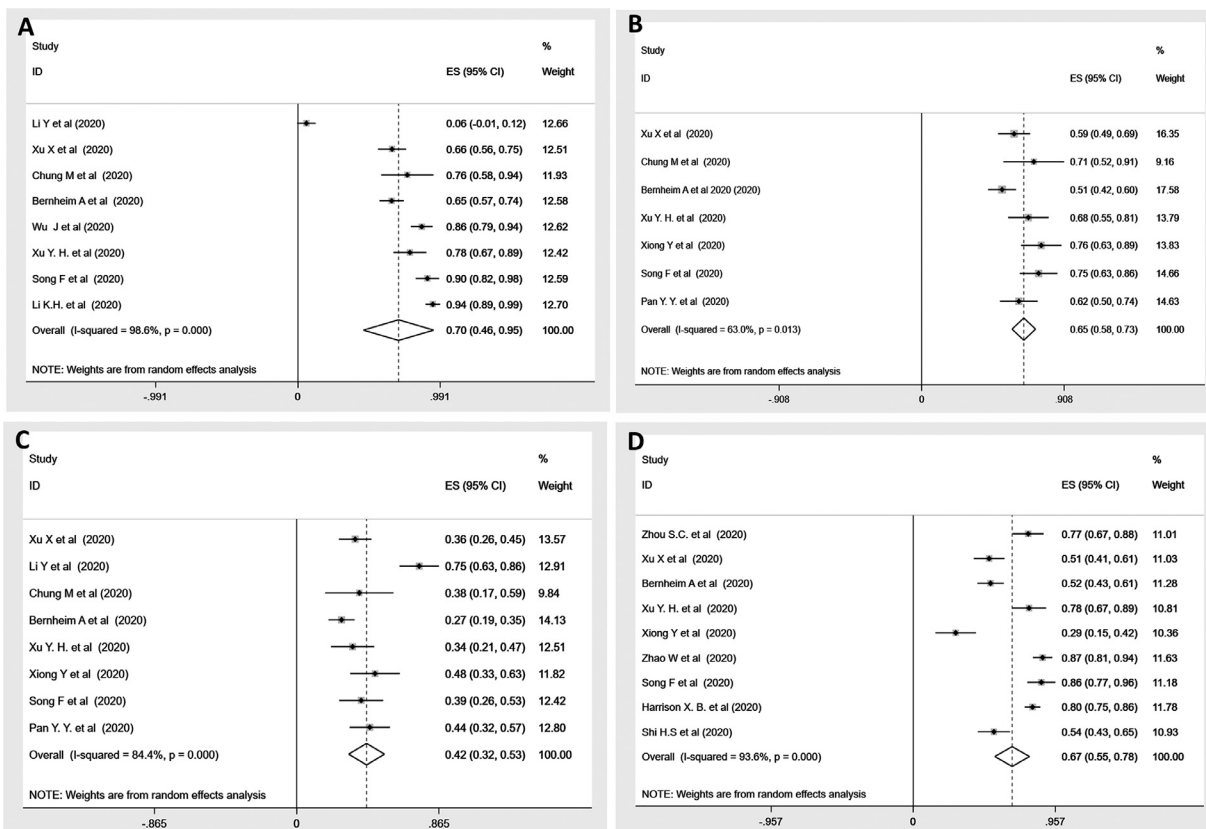


Figure 3. Forest plots of the incidence of extent and involvement in COVID-19 patients. A, B, C, and D represent the right lower lobe involvement, three or more lobes involvement (lobes ≥ 3), all five lobes involvement, and peripheral distribution, respectively.

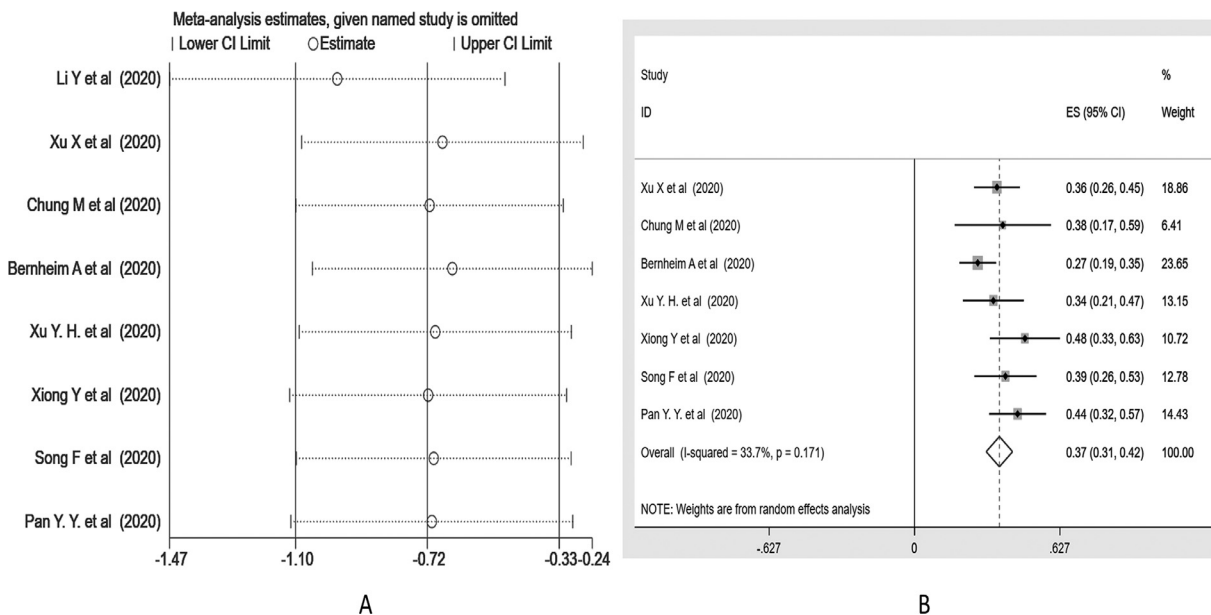


Figure 4. (a). The sensitivity analysis for the feature of five lobes involvement. The sensitivity analysis investigates the influence of each individual study on the overall meta-analysis summary estimate, presenting a forest plot of the results of an influence analysis in which the meta-analysis is re-estimated after omitting each study in turn. The full, “combined” results are shown as the solid vertical lines and the influence of each study is defined as a point estimate. An individual study is suspected of excessive influence if the point estimate of its “omitted” analysis lies outside the confidence interval of the “combined” analysis or it is far away from the solid vertical lines. Some attention should be paid to potential reasons for its excessive influence. (b). Forest plot of the re-estimated prevalence of the incidence for this feature in COVID-19 patients.

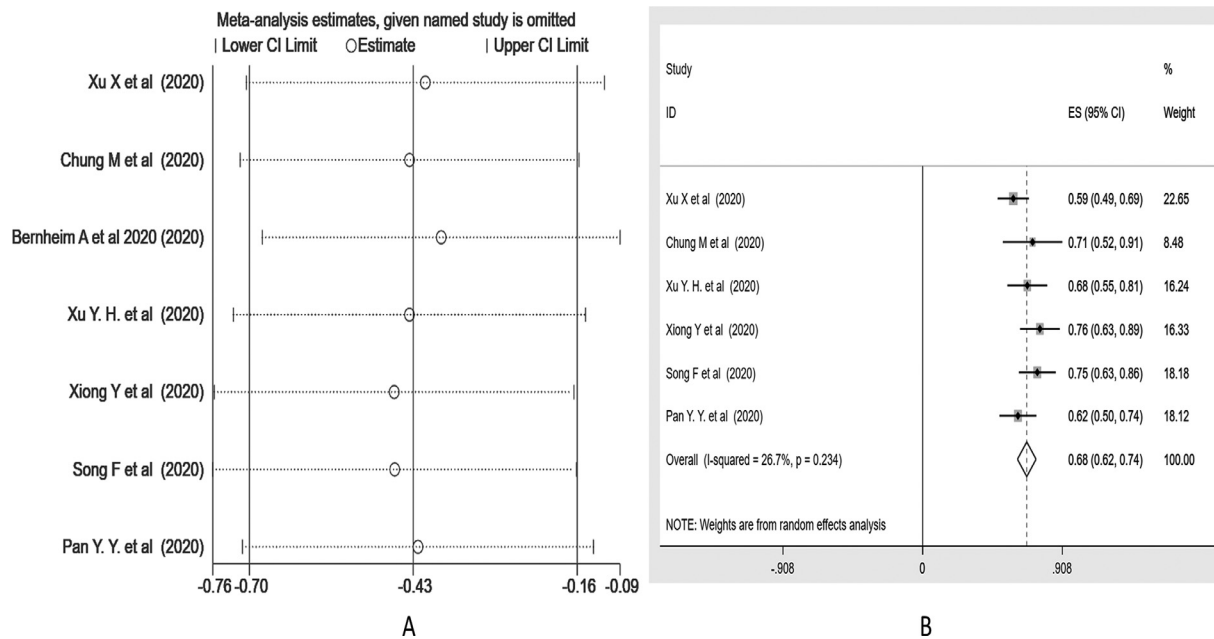


Figure 5. (a). The sensitivity analysis of the feature of three or more lobes involvement (lobes ≥ 3), (b). Forest plot of re-estimated prevalence of the incidence for this feature in COVID-19 patients.

we consider that an understanding of these important features might be helpful for medical surveillance and management, to prevent pulmonary fibrosis and minimize the impact on lung function. We also hope that these findings can assist radiologists and clinicians in assessing infection severity and disease progression.

Several limitations of our study should be noted. First, although we searched the databases rigorously according to the inclusion and exclusion criteria, all of the included studies were retrospective studies and were from China. We will continue to update our results to obtain more convincing evidence if new studies emerge. Second, significant heterogeneity can be

TABLE 4. Main Clinical Characteristics and Laboratory Results of the Included Studies of COVID-19

Study, year	Sample Size(N ¹)	N ¹ (%)						
		Fever	Cough	Muscle Soreness	Diarrhea	Leukocytopenia*	Lymphocytopenia [†]	Increased C-reactive Protein [#]
Zhou S.C. et al 2020	62	54(87.1)	28(45.2)	20(32.2)	9(14.5)	6(9.7)	24(38.7)	27(43.5)
Li Y et al 2020	51	46(90.2)	1(2)	-**	-	-	-	-
Xu X et al 2020	90	70(77.8)	57(63.3)	25(27.8)	5(5)	87(96.7)	-	38(42.2)
Chung M et al 2020	21	14(66.7)	9(43)	3(14.3)	-	-	-	-
Bernheim A et al 2020	121	74(61.2)	78(64.5)	-	-	-	-	-
Wu J et al 2020	80	61(76.3)	38(47.5)	13(16.3)	7(8)	7(8.8)	340.425	37(46.3)
Xu Y. H. et al 2020	50	48(96.0)	27(54)	8(16)	1(2)	49(98)	140.28	26(52)
Xiong Y et al 2020	42	36(85.7)	27(64.3)	-	10(23.8)	10(23.8)	18(42.9)	27(64.3)
Song F et al 2020	51	49(96.1)	24(47.1)	-	5(9)	-	33(64.7)	41(80.4)
Pan Y. Y. et al 2020	63	-	-	-	-	-	-	-
Zhao W et al 2020	101	79(78.2)	63(62.3)	-	3(2.9)	-	-	-
Li K.H. et al 2020	83	72(86.8)	65(78.3)	15(18.1)	7(8.4)	10(12.0)	44(53)	50(60.2)
Harrison X. B. et al 2020	219	142(64.8)	-	-	-	-	183(83.6)	-
Shi H.S. et al 2020	81	59(72.8)	48(59.3)	-	3(3.7)	-	-	-

¹N: number of patients.

** -: not available or not reported.

* Leukocytopenia: leucocytes count $< 4 \times 10^9/L$, [†]Lymphocytopenia: lymphocyte count $< 1 \times 10^9/L$.

[#] Increased C-reactive protein: C-reactive protein $\geq 10mg/L$.

found for the included features; nevertheless, the sensitivity analyses and the re-estimated values suggested the substantial heterogeneity of some features cannot be explained by each study. Therefore, the present results should be interpreted cautiously. Finally, since the funnel plot analyses used to evaluate publication bias have been mainly developed for randomized controlled trials, and the studies included in this report were case series studies, the assessment of publication bias may not be suitable for use with this single-arm meta-analysis. Accordingly, we did not evaluate the possibility of publication bias in this review.

In conclusion, this systematic review and meta-analysis based on chest CT images with a large sample size revealed the prevalence of chest CT manifestations in patients with COVID-19, as well as important clinical characteristics and laboratory data. A comprehensive understanding of significant imaging and clinical manifestations could be beneficial for effective management and treatment.

DISCLOSURES

The authors declare that they have no competing interests.

REFERENCES

- WHO website. Coronavirus disease (COVID-19) technical guidance: early investigations. Available at: <http://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/early-investigations>. Accessed February 15, 2020.
- WHO website. Statement on the second meeting of the International Health Regulations (2005) Emergency Committee regarding the outbreak of novel coronavirus (2019-nCoV). Available at: <http://www.who.int/news-room>. Accessed February 25, 2020.
- KSIAZEK T. A novel coronavirus associated with severe acute respiratory syndrome. *N Engl J Med* 2003; 348:1953–1966.
- Drosten C, Günther S, Preiser W, et al. Identification of a Novel Coronavirus in Patients with Severe Acute Respiratory Syndrome. *N Engl J Med* 2003; 348:1967–1976.
- Zaki AM, van Boheemen S, Bestebroer TM, Osterhaus ADME, Fouchier RAM. Isolation of a Novel Coronavirus from a Man with Pneumonia in Saudi Arabia. *N Engl J Med* 2012; 367:1814–1820.
- De Groot R, Baker S, Baric R, et al. Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Announcement of the Coronavirus Study Group. *J Virol* 2013; 87:7790–7792.
- WHO website. Novel Coronavirus(2019-nCoV): Situation Report—84 - ERRATUM. Available at: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200413-sitrep-84-covid-19.pdf?sfvrsn=44f511ab_2. Accessed April 13, 2020.
- Huang CL, Wang YM, Li XW, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; 395:497–506.
- Xie X, Zhong Z. Chest CT for Typical 2019-nCoV Pneumonia: Relationship to Negative RT-PCR Testing. *Radiology* 2020 Feb 12. [Epub ahead of print].
- Corman VM, Landt O, Kaiser M, et al. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. *Euro Surveill* 2020 Jan 25. [Epub ahead of print].
- Diao K, Han P, Pang T, et al. HRCT imaging features in representative imported cases of 2019 novel coronavirus pneumonia. *Precis Clin Med* 2020; 3:9–13.
- National Health Commission of the people's Republic of China website. Notice on issuing a new coronavirus infected pneumonia diagnosis and treatment plan (trial version 5). Available at: <http://www.nhc.gov.cn/kj/s3577/202002/a5d6f7b8c48c451c87dba14889b30147.shtml>. Accessed February 21, 2020.
- Li Y, Xia L. Coronavirus Disease 2019 (COVID-19): Role of Chest CT in Diagnosis and Management. *AJR Am J Roentgenol* 2020 Mar 4. [Epub ahead of print].
- Chung M, Bernheim A, Mei X, et al. CT imaging features of 2019 Novel Coronavirus (2019-nCoV). *Radiology* 2020; 295:202–207.
- Fang Y, Zhang H, Xu Y, et al. CT manifestations of two cases of 2019 Novel Coronavirus (2019-nCoV) pneumonia. *Radiology* 2020; 295:208–209.
- Song F, Shi N, Shan F, et al. Emerging coronavirus 2019-nCoV pneumonia. *Radiology* 2020; 295:210–217.
- Sun P, Qie S, Liu Z, et al. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: A single arm meta-analysis. *J Med Virol* 2020 Feb 28. [Epub ahead of print].
- Li LQ, Huang T. 2019 novel coronavirus patients' clinical characteristics, discharge rate and fatality rate of meta-analysis. *J Med Virol*. 2020 Mar 12. [Epub ahead of print].
- Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol* 2009; 339:b2700.
- Lei J, Li J, Li X, et al. CT imaging of the 2019 Novel Coronavirus (2019-nCoV) pneumonia. *Radiology* 2020; 295:18.
- Hansell DM, Bankier AA, MacMahon H, et al. Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008; 246:697–722.
- Zhou S, Wang Y, Zhu T, et al. CT features of Coronavirus Disease 2019 (COVID-19) pneumonia in 62 patients in Wuhan, China. *AJR Am J Roentgenol* 2020 Mar 5. [Epub ahead of print].
- Wu J, Wu X, Zeng W, et al. Chest CT findings in patients with Corona Virus Disease 2019 and its relationship with clinical features. *Invest Radiol* 2020 Feb 21. [Epub ahead of print].
- Wong KT, Antonio GE, Hui DSC, et al. Thin-section CT of Severe Acute Respiratory Syndrome: Evaluation of 73 patients exposed to or with the disease. *Radiology* 2003; 228:395–400.
- National Heart L, and Blood Institute website. Study quality assessment tools. Available at: <http://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>. Accessed February 16, 2020.
- Wang N. How to Conduct a Meta-Analysis of Proportions in R: A Comprehensive Tutorial. 2018. DOI: 10.13140/RG.2.2.27199.00161.
- Xiong Y, Sun D, Liu Y, et al. Clinical and high-resolution CT features of the COVID-19 infection: Comparison of the initial and follow-up changes. *Invest Radiol* 2020 Mar 3. [Epub ahead of print].
- Pan Y, Guan H, Zhou S, et al. Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. *Eur Radiol* 2020 Feb 13. [Epub ahead of print].
- Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* 2020; 20:425–434.
- Xu X, Yu C, Qu J, et al. Imaging and clinical features of patients with 2019 novel coronavirus SARS-CoV-2. *Eur J Nucl Med Mol Imaging* 2020; 47:1275–1280.
- Xu YH, Dong JH, An WM, et al. Clinical and computed tomographic imaging features of novel coronavirus pneumonia caused by SARS-CoV-2. *J Infect* 2020; 80:394–400.
- Li K, Wu J, Wu F, et al. The Clinical and chest CT features associated with severe and critical COVID-19 pneumonia. *Invest Radiol* 2020 Feb 29. [Epub ahead of print].
- Bernheim A, Mei X, Huang M, et al. Chest CT findings in Coronavirus Disease-19 (COVID-19): Relationship to duration of infection. *Radiology* 2020 Feb 20. [Epub ahead of print].
- Pan Y, Guan H. IMAGING changes in patients with 2019-nCoV. *Eur Radiol* 2020 Feb 6. [Epub ahead of print].
- Salehi S, Abedi A, Balakrishnan S, et al. Coronavirus Disease 2019 (COVID-19): A systematic review of imaging findings in 919 patients. *AJR Am J Roentgenol* 2020 Mar 14. [Epub ahead of print].
- Ooi GC, Khong PL, Müller NL, et al. Severe acute respiratory syndrome: temporal lung changes at thin-section CT in 30 patients. *Radiology* 2004; 230:836–844.
- Bai HX, Hsieh B, Xiong Z, et al. Performance of radiologists in differentiating COVID-19 from viral pneumonia on chest CT. *Radiology* 2020 Mar 10. [Epub ahead of print].
- Zhao W, Zhong Z, Xie X, et al. Relation between chest CT findings and clinical conditions of Coronavirus Disease (COVID-19) pneumonia: A multicenter study. *AJR Am J Roentgenol* 2020 Mar 3. [Epub ahead of print].
- Rodriguez-Morales AJ, Cardona-Ospina JA, Gutierrez-Ocampo E, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis* 2020 Mar 13. [Epub ahead of print].

40. Yang J, Zheng Y, Gou X, et al. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. *Int J Infect Dis* 2020 Mar 12. [Epub ahead of print].
41. Yin Y, Wunderink RG. MERS, SARS and other coronaviruses as causes of pneumonia. *Respirology* 2008; 23:130–137.
42. de Groot RJ, Baker SC, Baric RS, et al. Middle East respiratory syndrome coronavirus (MERS-CoV): announcement of the Coronavirus Study Group. *J Virol* 2013; 87:7790–7792.
43. Wang C, Horby PW, Hayden FG, et al. A novel coronavirus outbreak of global health concern. *Lancet* 2020; 395:470–473.
44. Srikantiah P, Charles MD, Reagan S, et al. SARS clinical features, United States, 2003. *Emerg Infect Dis* 2005; 11:135–138.
45. Wan Y, Shang J, Graham R, et al. Receptor recognition by the novel Coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS Coronavirus. *J Virol* 2020: 94.
46. Harmer D, Gilbert M, Borman R, et al. Quantitative mRNA expression profiling of ACE 2, a novel homologue of angiotensin converting enzyme. *FEBS Lett* 2002; 532:107–110.
47. Lee N, Hui D, Wu A, et al. A major outbreak of severe acute respiratory syndrome in Hong Kong. *N Engl J Med* 2003; 348:1986–1994.
48. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature* 2020; 579:270–273.
49. Rodríguez-Morales AJ, MacGregor K, Kanagarajah S, Patel D, Schlagenhaut P. Going global - Travel and the 2019 novel coronavirus. *Travel Med Infect Dis* 2020; 33:101578.