Original Article

Clinical characteristics, laboratory abnormalities and CT findings of COVID-19 patients and risk factors of severe disease: a systematic review and meta-analysis

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Background: The coronavirus disease 2019 (COVID-19) is an emerging pandemic of global public health concern. We aimed to summarize the characteristics of COVID-19 patients in the early stage of the pandemic and explore the risk factors of disease progression.

Methods: We conducted a systematic review with meta-analysis, searching three databases for studies published between January 1, 2020, and March 18, 2020. We used random-effects models to calculate the 95% confidence intervals of pooled estimated prevalence and the odds ratio between the severe and non-severe cases.

Results: Ninety studies involving 16,526 COVID-19 patients were included. Hypertension (19.1%) and diabetes (9.5%) were the most common comorbidities. The most prevalent clinical symptoms were fever (78.4%), cough (58.5%), and fatigue (26.4%). Increased serum ferritin (74.2%), high C-reactive protein (73.3%), and high erythrocyte sedimentation rate (ESR) (72.2%) were the most frequently reported laboratory abnormalities. Most patients had bilateral lung involvement (82.2%) and showed peripheral (66.9%) and subpleural (62.1%) distribution, with multifocal involvement (73.1%). And the most common CT features were vascular enlargement (64.3%), ground-glass opacity (GGO) (60.7%), and thickened interlobular septa (55.1%). Respiratory failure was the most common complication (30.7%) and the overall case-fatality rate (CFR) was 4.2%. Moreover, male, history of smoking, and comorbidities might influence the prognosis. Most clinical symptoms such as fever, high fever, cough, sputum production, fatigue, shortness of breath, dyspnoea, and abdominal pain were linked to the severity of disease. Some specific laboratory indicators implied the deterioration of disease, such as leucocytosis, lymphopenia, platelet, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, creatinine, creatine kinase (CK), lactic dehydrogenase (LDH), C-reactive protein, procalcitonin (PCT), and D-dimer. Besides, the risk of bilateral pneumonia, consolidation, pleural effusion, and enlarged mediastinal nodes was higher in severe cases.

Conclusions: Most COVID-19 patients have fever and cough with lymphopenia and increased inflammatory indices, and the main CT feature is GGO involved bilateral lung. Patients with comorbidities and worse clinical symptoms, laboratory characteristics, and CT findings tend to have poor disease progression.

Keywords: Coronavirus disease 2019 (COVID-19); clinical characteristics; laboratory abnormalities; CT findings; risk factors

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Introduction

In late December 2019, the coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome CoV-2 (SARS-CoV-2), has become an emerging pandemic of global public health concern (1). Then, the number of confirmed cases has exploded. As of March 30, 2020, almost 690 thousand confirmed patients have been reported with over 30 thousand deaths worldwide (2).

In 2003 and 2012, severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) caused epidemics respectively. According to the prior studies, the SARS-CoV-2, a betacoronavirus, is both similar and different to the SARS-CoV and MERS-CoV (3). As reported, the mortality of SARS-CoV and MERS-CoV is higher than that of SARS-CoV-2. But the pandemic caused by COVID-19 has exceeded the previous two diseases (4).

It is important to find out the epidemiological, clinical, laboratory and image features of patients with SARS-CoV-2 infection and risk factors of severe illness for better prevention and treatment of this disease. Large quantities of researches have made effort to understand this subject, but most were case series, cross-sectional studies, and case reports which were conducted in a particular hospital or area (5-20). Because of different study designs, small samples, and incomplete information, the characteristics and risk factors of COVID-19 are still unclear.

Some systematic reviews and meta-analyses have been already published, they summarized the clinical, laboratory and chest CT findings of COVID-19 patients (21,22). However, they included a relatively small number of studies which were limited to China. In addition, few meta-analyses studied the risk factors related to poor outcomes owing to the lack of prognostic information in early studies. In this review, we summarized the prevalence of comorbidities, clinical symptoms, laboratory characteristics, chest CT findings, and complications of patients with SARS-CoV-2 infection in the early stage of the pandemic. Moreover, we analyzed the features of severe cases and non-severe cases and identified the risk factors of disease progression to offer clinicians references for clinical application and follow-up studies. We presented the following article in accordance with the PRISMA reporting checklist (available at http://dx.doi.org/10.21037/apm-20-1863).

Methods

Search strategy and selection criteria

Our systematic review was in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (23). We searched three databases, PubMed, Chinese medical journal network, and CNKI (China national knowledge infrastructure) to select relevant studies reporting COVID-19 which were published between Jan 1, 2020, and Mar 18, 2020. We used the following search terms: “COVID-19” or “Novel coronavirus” or “Novel coronavirus 2019” or “2019 nCoV” or “SARS-CoV-2”. In order to ensure the comprehensiveness and accuracy of our study, we also reviewed the references of each included article.

We included studies that reported more than 50 cases of SARS-CoV-2 infection confirmed by real-time reverse transcriptase-polymerase chain reaction (RT-PCR) with demographical, clinical, laboratory, and image characteristics. Study type limit was not set, and we applied no language restrictions. We excluded the studies that only reported the infection in children, the elderly, or asymptomatic patients and the studies that lacked complete information or clear diagnostic criteria, as well as study sample was smaller than 50. Duplicate reports, review articles, commentary articles, and opinion articles were also excluded.

Data extraction and quality assessment

Three independent researchers (JX, TZ, YX) conducted data extraction and evaluated the literature quality. Any disagreement was resolved by another researcher (PZ). We collected the following variables from each included

study: first author, the publishing institution, publication time, area, number of patients with COVID-19, median or mean age, sex ratio, smoking history, comorbidities, clinical symptoms, laboratory characteristics, image features, complications, and clinical outcome. All the outcomes of laboratory testing and chest CT we extracted were at the time of admission. We also extracted information of non-severe and severe patients respectively. When the authors had no diagnostic criteria for severe illness, patients in the intensive care unit (ICU) were classified as severe cases. In the whole meta-analysis of pooled estimated prevalence, we excluded studies that only provided information of severe cases or non-severe cases, but included them in the meta-analysis that was limited to severe cases or non-severe cases, respectively. We used the MINORS to assess bias risk (24).

Statistical analysis of data

For pooled estimated prevalence, State software version 15.0 was used to analyze the data we extracted. We used random-effects models to calculate 95% confidence intervals (95% CI) of pooled estimated prevalence (sex ratio, smoking history, comorbidities, clinical symptoms, laboratory characteristics, image features, and complications of COVID-19 patients). If the included article had a prevalence of 0% or 100%, it would affect the accuracy of overall estimates. As reported, the Freeman-Tukey double arcsine transformation might minimize the effect, so we used this transformation to stabilize the variance before analysis (25). For calculating the odds ratio (OR), random-effects models were used by Review Manager software version 5.3 due to the heterogeneity between the studies. Besides, the I^2 statistic and Cochran's Q test were used to evaluate the degree of heterogeneity. Because most confirmed COVID-19 cases in China occurred in Wuhan and the Chinese government adopted different epidemic prevention measures in Wuhan and other cities, we conducted a subgroup analysis by city groups (Wuhan or other cities) to explore the possible source of heterogeneity and find out whether the prevalence of outcomes differed by different areas. $P<0.05$ was considered to be statistically significant. Besides, we evaluated publication bias by Begg's test.

Results

Study selection and quality assessment

We searched 4,219 papers from the online databases by the above search strategy. A total of 3,712 papers were retained after the deletion of duplicate papers. By reading the titles and abstracts, 3,461 papers were excluded. Then, we assessed the full texts of the remaining 251 articles, of which 124 had a sample size less than 50, 5 did not report clear diagnostic criteria, 3 only focused on infection in children, the elderly, or asymptomatic patients, and 29 did not report complete information or original data. Finally, we included 90 papers in our meta-analysis (*Figure 1*). We divided them into 4 parts, part 1 (5-20), part 2 (26-50), part 3 (51-75), part 4 (76-99). Among the included studies, five studies only provided information of severe cases and two studies only provided information of non-severe cases, which were excluded from the whole meta-analysis but were included in the meta-analysis limited to severe cases and non-severe cases, respectively. In addition, 28 studies provided information on both severe and non-severe patients and we included them in the meta-analysis to identify the risk factors of disease progression.

Table 1 lists the baseline characteristics of the included studies. All of the included studies were published between Jan 30, 2020, and Mar 18, 2020, in a sample size ranging from 50 to 1,590 patients. Among the included 90 studies with a total of 16,526 patients, 88 (97.8%) were from China, of which 37 (41.1%) were from Wuhan. Mean or median age of patients ranged from 37 to 68 years (median 48.8 years; 74 studies). Moreover, the proportion of severe cases ranged from 0.0% to 100.0% (median 23.1%; 65 studies).

Table S1 lists the bias risk assessment of the included studies. Overall, according to the MINORS, all the included studies were rated fair for quality. The scores of these 90 studies ranged from 9 to 14.

Demographical characteristics and comorbidities

The proportion of men in the 77 studies was 53.1% (95% CI, 41.3–55.0%). Moreover, the proportion of patients who had a history of smoking was 10.2% (95% CI, 7.1–13.4%). 32.5% of the patients had comorbidities (95% CI, 29.0–36.1%), and the most common were hypertension (19.1%, 95% CI, 16.4–21.8%), diabetes (9.5%, 95% CI, 8.1–10.8%), and cardiovascular disease (5.4%, 95% CI, 4.2–6.7%) (*Figure 2*).

Clinical symptoms and laboratory characteristics

We analyzed the prevalence of 22 clinical symptoms. In which, the most prevalent were fever (78.4%, 95% CI, 74.5–82.3%), cough (58.5%, 95% CI, 51.4–65.6%), fatigue

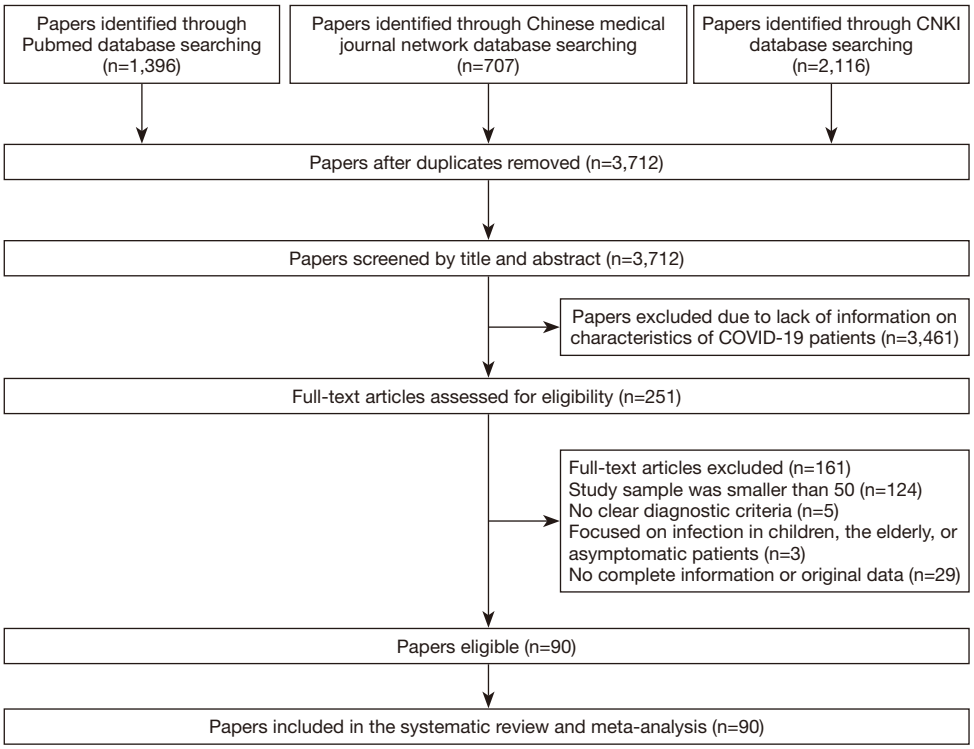

Figure 1 Flow diagram of the study selection process.

(26.4%, 95% CI, 21.4–31.4%), sputum production (22.7%, 95% CI, 18.2–27.2%), chest distress (18.7%, 95% CI, 12.5–25.0%), and shortness of breath (18.5%, 95% CI, 12.9–24.2%). The proportions of high fever, myalgia or arthralgia, dyspnoea, chills, and anorexia were also above 10% (*Figure 3*).

Regarding the 32 frequently reported laboratory findings, the most common abnormalities were increased serum ferritin (74.2%, 95% CI, 64.9–83.5%), high C-reactive protein (CRP) (73.3%, 95% CI, 65.2–80.6%), high ESR (72.2%, 95% CI, 62.1–82.3%), decreased eosinophil (59.2%, 95% CI, 40.9–77.4%), increased interleukin 6 (IL-6) (58.2%, 95% CI, 32.7–83.6%), lymphopenia (46.5%, 95% CI, 38.5–54.4%), high lactic dehydrogenase (LDH) (41.6%, 95% CI, 22.5–60.7%), and hyperglycemia (40.1%, 95% CI, 29.5–50.6%) (*Figure 4*).

Chest CT findings

The proportion of patients who had normal CT imaging features was 6.1%. Eighty-two point two percent of the patients had bilateral lung involvement, 66.9% showed peripheral distribution, 73.1% showed multifocal involvement, and 62.1% showed subpleural distribution. Although all lung lobes can be involved, right lower lobe (65.1%) and left lower lobe (70.4%) were more likely to be involved. More than half of the COVID-19 patients had >3 lobes involved (57.9%) (*Figure 5*).

The most common characteristics seen on chest CT were vascular enlargement (64.3%, 95% CI, 50.7–77.8%), ground-glass opacity (GGO) (60.7%, 95% CI, 51.1–70.3%), thickened interlobular septa (55.1%, 95% CI, 38.2–72.1%), interstitial abnormalities (48.3%, 95% CI, 4–92.7%), mixed GGO and consolidation (44.5%, 95% CI, 29–60%), and air bronchogram (39.9%, 95% CI, 21.3–58.5%). Pericardial effusion (4.4%), pleural effusion (4.2%), and enlarged mediastinal nodes (2.9%) were rare (*Figure 5*).

Complications and outcomes

Among the COVID-19 patients, respiratory failure was the most common complication (30.7%, 95% CI, 10.2–51.1%). In addition, 15.5% of the patients had acute respiratory distress syndrome (ARDS), 10.7% had acute cardiac injury, 4.5% had acute kidney injury, 9.6% had secondary infection, and 4.6% had shock. The overall mortality was

Table 1 Baseline characteristics of the included studies

Author	Date (MM/DD)	City	No. of patients	Quality score	Age [median (IQR)/mean ± SD, years]	Age range (years)	Male (%)	Severe/critical (%)	Outcomes		
									Hospitalization (%)	Discharge (%)	Death (%)
Liu W	2/28	Wuhan	78	12	38 (33.0–57.0)	–	39 (50.0)	8 (10.3)	–	–	2 (2.6)
Chen C	3/6	Wuhan	150	10	59±16	–	84 (56.0)	24 (16.0)	–	–	11 (7.3)
Tian S	2/27	Beijing	262	13	47.5 (median)	1–94	127 (48.5)	46 (17.6)	214 (81.7)	45 (17.2)	3 (1.1)
Li K	2/29	Chongqing	83	10	45.5±12.3	–	44 (53.0)	25 (30.1)	–	–	–
Xu YH	2/25	Beijing	50	12	43.9±16.8	3–85	29 (58.0)	13 (26.0)	–	–	–
Yang W	2/26	Wenzhou	149	13	45.11±13.35	–	81 (54.4)	0 (0)	76 (51.0)	73 (49.0)	0 (0)
Guan WJ	2/28	Multi–city	1,099	14	47.0 (35.0–58.0)	–	637/1,096 (58.1)	173 (15.7)	1,029 (93.6)	55 (5.0)	15 (1.4)
Wu J	2/29	Jiangsu	80	13	46.10±15.42	–	39 (48.8)	3 (3.8)	61 (76.3)	21 (26.3)	0 (0)
Mo, P.	3/16	Wuhan	155	13	54 (42.0–66.0)	–	86 (55.5)	92 (59.4)	–	–	22 (14.2)
Zhou F	3/11	Wuhan	191	14	56.0 (46.0–67.0)	18–87	119 (62.3)	119 (62.3)	0 (0)	137 (71.7)	54 (28.3)
Liu K	3/11	Hainan	56	13	–	–	31 (55.4)	9 (16.1)	0 (0)	53 (94.6)	3 (5.4)
Xu T	3/13	Changzhou	51	13	–	–	25 (49.0)	–	–	–	–
Wang Z	3/16	Wuhan	69	13	42.0 (35.0–62.0)	–	32 (46.4)	–	44 (63.8)	18 (26.1)	5 (7.2)
Xu XW	2/19	Zhejiang	62	13	41 (32.0–52.0)	–	35 (56.5)	1 (1.6)	61 (98.4)	1 (1.6)	0 (0)
Ruan Q	3/3	Wuhan	150	9	–	–	102 (68.0)	41 (27.3)	0 (0)	82 (54.7)	68 (45.3)
Chen J	3/11	Shanghai	249	13	51 (36.0–64.0)	–	126 (50.6)	22 (8.8)	32 (12.9)	215 (86.3)	2 (0.8)
Lin D	3/5	Shenzhen	92	10	–	–	–	–	–	–	–
Li Y	3/4	Wuhan	51	10	58±17	26–83	28 (54.9)	–	–	–	–
COVID–19 team Australia	3/11	Australia	71	10	45 (median)	0–94	–	–	47 (66.2)	22 (31.0)	2 (2.8)
Zhou S	3/5	Wuhan	62	10	52.8±12.2	–	39 (62.9)	–	–	–	–
Wang J	2/24	Zhejiang	52	10	44±14	13–73	29 (55.8)	–	–	–	–
Qin C	3/12	Wuhan	452	10	58 (47.0–67.0)	22–95	235 (52.0)	286 (63.3)	–	–	–
Han R	3/17	Wuhan	108	10	45 (mean)	21–90	38 (35.2)	–	–	–	–
Sun WW	3/15	Zhejiang	391	9	–	–	192 (49.1)	–	–	–	–
Dong XC	3/13	Tianjin	135	9	48.62±16.83	8–90	72 (53.3)	62 (45.9)	–	–	3 (2.2)
Xiao F	3/3	Guangdong	73	10	–	–	32 (43.8)	4 (5.5)	–	–	–
Fan BE	3/4	Singapore	67	10	42 (35.0–54.0)	–	37 (55.2)	9 (13.4)	–	–	0 (0)
Shi Y	3/18	Zhejiang	487	12	46 (median)	–	259 (53.2)	49 (10.1)	–	–	–
Xu X	2/28	Guangzhou	90	13	50 (median)	18–86	39 (43.3)	–	–	–	–
He XW	3/15	Wuhan	54	10	68.0 (59.8–74.3)	–	34 (63.0)	54 (100.0)	–	–	–

Table 1 (*continued*)

Table 1 (*continued*)

Author	Date (MM/DD)	City	No. of patients	Quality score	Age [median (IQR)/mean ± SD, years]	Age range (years)	Male (%)	Severe/critical (%)	Outcomes		
									Hospitalization (%)	Discharge (%)	Death (%)
Wu J	3/3	Multi–city	130	9	43±15	25–80	78 (60.0)	–	–	–	–
Han H	3/16	Wuhan	94	10	–	–	48 (51.1)	–	–	–	–
Shi H	2/24	Wuhan	81	13	49.5±11.0	25–81	42 (51.9)	–	16 (19.8)	62 (76.5)	3 (3.7)
Zhao W	3/3	Hunan	101	9	44.44±12.32	17–75	56 (55.4)	14 (13.9)	–	–	–
Wu C	3/13	Wuhan	201	13	51 (43.0–60.0)	21–83	128 (63.7)	53 (26.4)	144 (71.6)	13 (6.5)	44 (21.9)
Wang SH	3/9	Wuhan	333	10	62 (median)	26–88	72 (21.6)	57 (17.1)	–	–	–
Shi JH	3/12	Wuhan	54	13	62.5 (50.5–68.5)	–	31 (57.4)	16 (29.6)	39 (72.2)	11 (20.4)	4 (7.4)
Zhao Y	3/14	Xinyang	106	10	48.9±13.1	19–80	66 (62.3)	15 (14.2)	–	–	–
Ling Y	3/18	Shanghai	292	10	49.9±16.3	–	154 (52.7)	21 (7.2)	–	–	1 (0.3)
Cheng JL	3/2	Henan	1,265	10	–	–	573/1,079 (53.1)	72 (5.7)	632 (50.0)	614 (48.5)	19 (1.5)
Huang L	2/11	Wuhan	103	10	57±24	20–89	60 (58.3)	45 (43.7)	–	–	2 (1.9)
Lu XF	2/12	Wuhan	141	10	49 (median)	9–87	77 (54.6)	139 (98.6)	–	–	–
Liu HF	2/13	Wuhan	106	10	57±15	22–82	64 (60.4)	–	–	–	–
Yu CC	2/19	Guangzhou	91	10	50 (33.0–62.0)	–	39 (42.9)	8 (8.8)	–	–	–
Li XH	2/27	Anhui	60	12	39±11	15–57	40 (66.7)	2 (3.3)	0 (0)	60 (100.0)	0 (0)
Hu R	3/5	Shiyan	105	12	44.38±15.69	0–88	55 (52.4)	–	–	–	–
Lv ZB	3/13	Beijing	64	13	45±15	18–76	32 (50.0)	–	44 (68.8)	20 (31.3)	0 (0)
Li Y	3/12	Wuhan	93	10	65 (50.0–72.0)	–	51 (54.8)	12 (12.9)	–	–	–
Shi YL	2/27	Guangzhou	164	10	–	–	75 (45.7)	14 (8.5)	–	–	–
Li RQ	2/26	Xiaogan	205	10	49.1±13.6	–	106 (51.7)	–	–	–	–
Bai P	3/7	Wuhan	58	13	62.12±12.95	30–92	28 (48.3)	58 (100.0)	30 (51.7)	21 (36.2)	7 (12.1)
Sun DW	3/16	Wuhan	51	10	–	–	–	30 (58.8)	–	–	–
Wan Q	2/28	Chongqing	153	13	46 (median)	10–74	77 (50.3)	21 (13.7)	148 (96.7)	5 (3.3)	0 (0)
Lu YF	2/10	Shanghai	50	9	50.4±16.8	–	28 (56.0)	–	–	–	–
Yu SM	3/9	Beijing	50	10	40.0±18.4	3–79	32 (64.0)	–	–	–	–
Yang K	3/3	Nanjing	57	13	37 (median)	5–97	29 (50.9)	0 (0)	0 (0)	57 (100.0)	0 (0)
Xu S	3/16	Wuhan	62	13	62.9±15.3	–	39 (62.9)	62 (100.0)	29 (46.8)	19 (30.6)	14 (22.6)
Ma PQ	3/10	Anhui	75	10	43.9±15.1	8–82	46 (61.3)	–	–	–	–
Wang Y	3/14	Anhui	80	10	45.33 (median)	4–91	45 (56.3)	–	–	–	–
Chen X	3/13	Chongqing	139	10	46 (36.0–54.0)	15–79	76 (54.7)	31 (22.3)	–	–	–
Fang L	3/12	Huangshi	308	10	–	30–86	152 (49.4)	121 (39.3)	–	–	16 (5.2)

Table 1 (*continued*)

Table 1 (*continued*)

Author	Date (MM/DD)	City	No. of patients	Quality score	Age [median (IQR)/mean ± SD, years]	Age range (years)	Male (%)	Severe/critical (%)	Outcomes		
									Hospitalization (%)	Discharge (%)	Death (%)
Fang XW	2/25	Anhui	79	13	45.1±16.6	5–91	45 (57.0)	24 (30.4)	44 (55.7)	34 (43.0)	1 (1.3)
Zhong Q	3/16	Zhejiang	67	10	–	15–90	–	29 (43.3)	–	–	–
Ran J	3/6	Chongqing	209	10	46.52±15.71	14–71	123 (58.9)	37 (17.7)	–	–	–
Yuan J	3/6	Chongqing	223	13	46.5±16.1	–	105 (47.1)	31 (13.9)	111 (49.8)	112 (50.2)	0 (0)
Xiao KH	2/27	Chongqing	143	13	45.13±1.04	–	73 (51.0)	36 (25.2)	25 (17.5)	117 (81.8)	1 (0.7)
Wang AH	3/18	Chongqing	90	10	48.19±17.85	3–89	58 (64.4)	13 (14.4)	22 (24.4)	68 (75.6)	0 (0)
Wang XJ	3/17	Gansu	91	10	45 (median)	1–94	32 (35.2)	15 (16.5)	24 (26.4)	65 (71.4)	2 (2.2)
Li JS	3/12	Henan	524	10	45 (33.0–55.0)	–	304 (58.0)	175 (33.4)	–	–	–
Han J	3/16	Wuhan	120	10	53±14	15–89	63 (52.5)	41 (34.2)	71 (59.2)	40 (33.3)	9 (7.5)
Dai ZH	3/6	Hunan	918	10	44. 73±16. 00	0–88	478 (52.1)	77 (8.4)	–	–	–
Chen W	3/17	Jingmen	91	10	41.59±15.53	2–85	43 (47.3)	21 (23.1)	0 (0)	86 (94.5)	5 (5.5)
Cheng KB	3/12	Wuhan	463	13	51 (43.0–60.0)	15–90	244 (52.7)	181 (39.1)	0 (0)	463 (100.0)	0 (0)
Zhou SY	3/13	Shandong	537	10	–	–	299 (55.7)	28 (5.2)	371 (69.1)	164 (30.5)	2 (0.4)
Sui HY	2/24	Tianjin	88	10	48.52±15.67	9–91	49 (55.7)	32 (36.4)	–	–	–
Zhou YP	3/4	Xianning	107	10	–	–	–	–	–	–	–
Ding Y	3/17	Wuhan	56	10	54.6±15.5	24–86	30 (53.6)	5 (8.9)	45 (80.4)	11 (19.6)	0 (0)
Xiong J	3/3	Wuhan	89	13	53.0±16.9	–	41 (46.1)	31 (34.8)	0 (0)	82 (92.1)	7 (7.9)
Hou KK	3/17	Chengdu	56	13	48±13.5	19–84	29 (51.8)	18 (32.1)	0 (0)	53 (94.6)	3 (5.4)
Chen ZY	3/17	Wuhan	64	10	54.55±14.04	28–84	31 (48.4)	–	–	–	–
Chang ZY	3/5	Wuhan	150	10	55.27±6.33	27–81	80 (53.3)	57 (38.0.)	–	–	20 (13.3)
Qian ZC	3/17	Wuhan	50	13	57.6 (mean)	30–84	25 (50.0)	50 (100.0)	0 (0)	43 (86.0)	7 (14.0)
Lu ZL	3/10	Wuhan	101	10	–	–	34 (33.7)	34 (33.7)	–	–	12 (11.9)
Chen NS	1/30	Wuhan	99	14	55.5±13.1	21–82	67 (67.7)	23 (23.2)	57 (57.6)	31 (31.3)	11 (11.1)
Liang W	2/14	Multi–city	1,590	13	–	–	910 (57.2)	131 (8.2)	–	–	–
Yang XB	2/21	Wuhan	52	14	59.7±13.3	–	35 (67.3)	52 (100.0)	12 (23.1)	8 (15.4)	32 (61.5)
Wang DW	2/7	Wuhan	138	14	56 (42.0–68.0)	–	75 (54.3)	36 (26.1)	85 (61.6)	47 (34.1)	6 (4.3)
Liu K	2/7	Wuhan	137	13	55±16	20–83	61 (44.5)	–	77 (56.2)	44 (32.1)	16 (11.7)
Pan YY	2/13	Wuhan	63	10	44.9±15.2	–	33 (52.4)	–	–	–	–
Zhang JJ	2/19	Wuhan	140	13	57 (median)	25–87	71 (50.7)	58 (41.4)	–	–	–

–, not available, not reported. MM/DD, Month, Day.

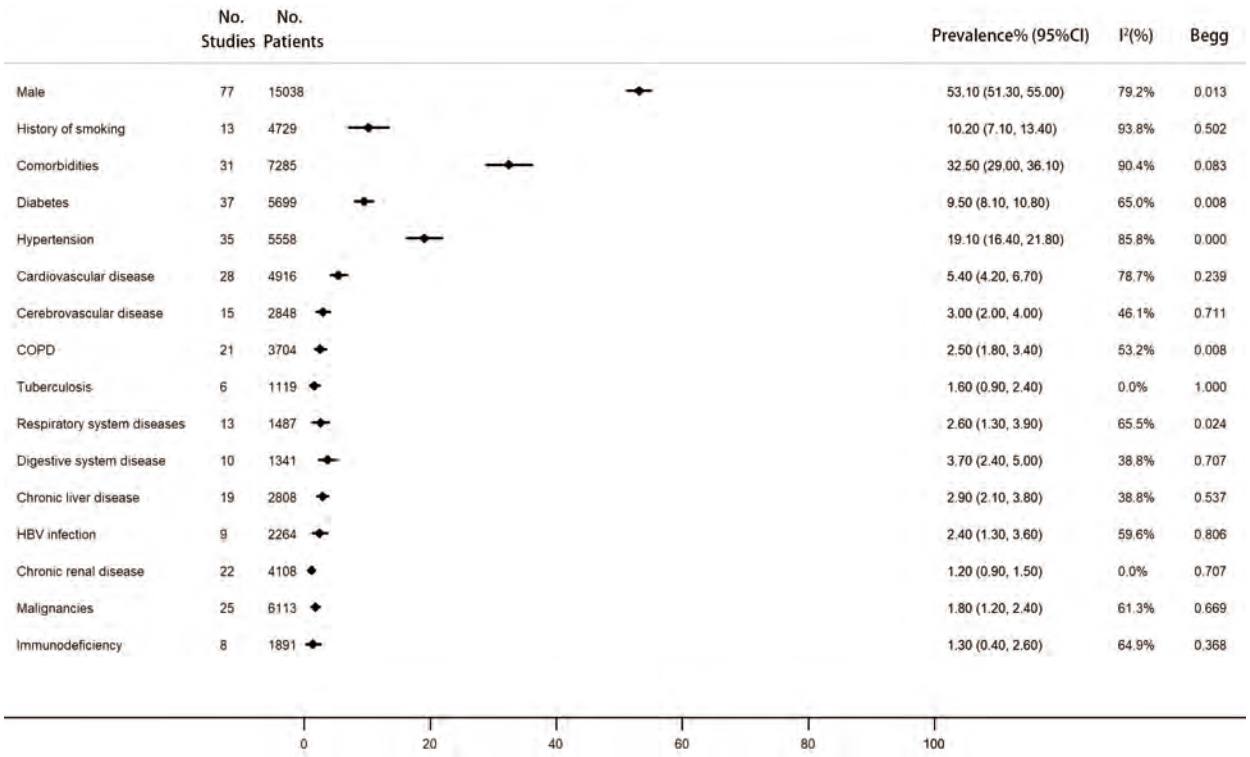

Figure 2 Meta-analysis of the sex ratio, smoking history, comorbidities of COVID-19 patients. COPD, chronic obstructive pulmonary disease; HBV, hepatitis B virus.

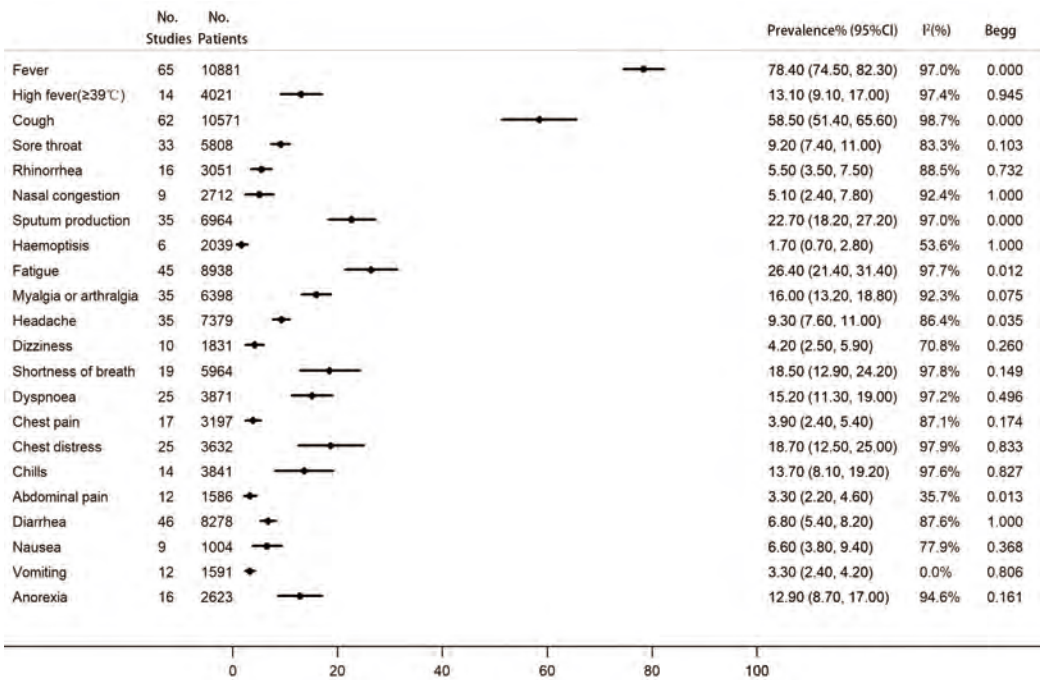

Figure 3 Meta-analysis of the prevalence of clinical symptoms in COVID-19 patients.

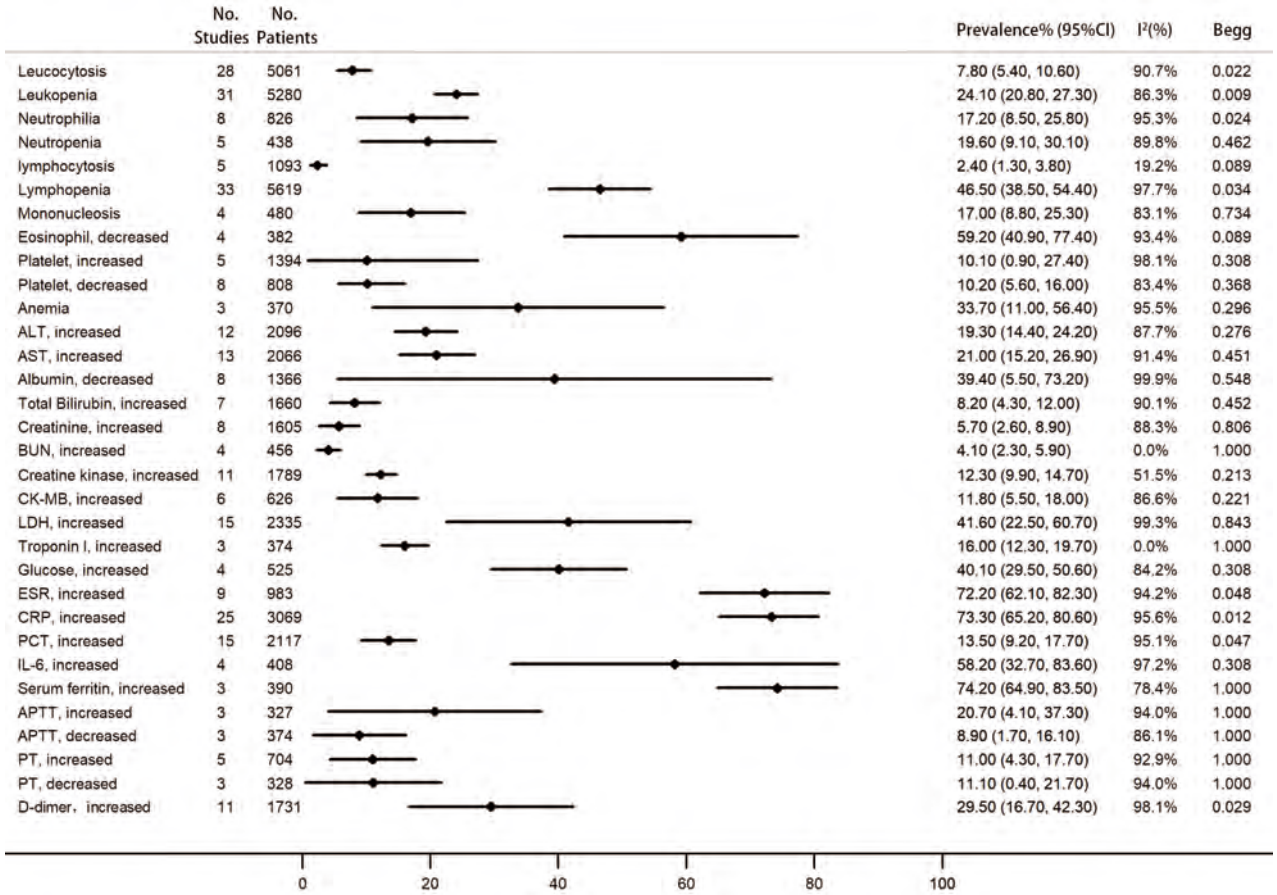

Figure 4 Meta-analysis of the proportion of laboratory abnormalities in COVID-19 patients. ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CK-MB, creatine kinase-MB; LDH, lactic dehydrogenase; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; PCT, procalcitonin; IL-6, interleukin 6; APTT, activated partial thromboplastin time; PT, prothrombin time.

4.2% (95% CI, 2.6–6.3%) (*Figure 6*).

Subgroup analysis

According to the subgroup analysis, the prevalence of comorbidities, clinical symptoms, laboratory abnormalities, and complications most was higher in Wuhan than in other cities. However, the proportions of patients who had a history of smoking and abnormal chest CT characteristics (such as GGO, consolidation, and pleural effusion) were higher in other cities. Besides, we also found a significantly higher CFR in Wuhan than in other cities (10.4%, 95% CI, 6.3–15.5%; versus 1.3%, 95% CI, 0.7–1.9%) (*Table 2*).

Comparison between severe and non-severe cases and risk factors of severe illness

Among the included 90 studies, 30 and 35 studies reported information of non-severe and severe cases, respectively. The proportion of male was significantly higher in severe patients compared with non-severe patients (60.9%, 95% CI, 57.3–64.4%; versus 49.5%, 95% CI, 46.6–52.4%). We compared the differences in the comorbidities, clinical symptoms, laboratory abnormalities, image findings, and complications between the two groups. Most of the proportions were higher among severe cases, except for chronic liver disease and headache. In addition, the

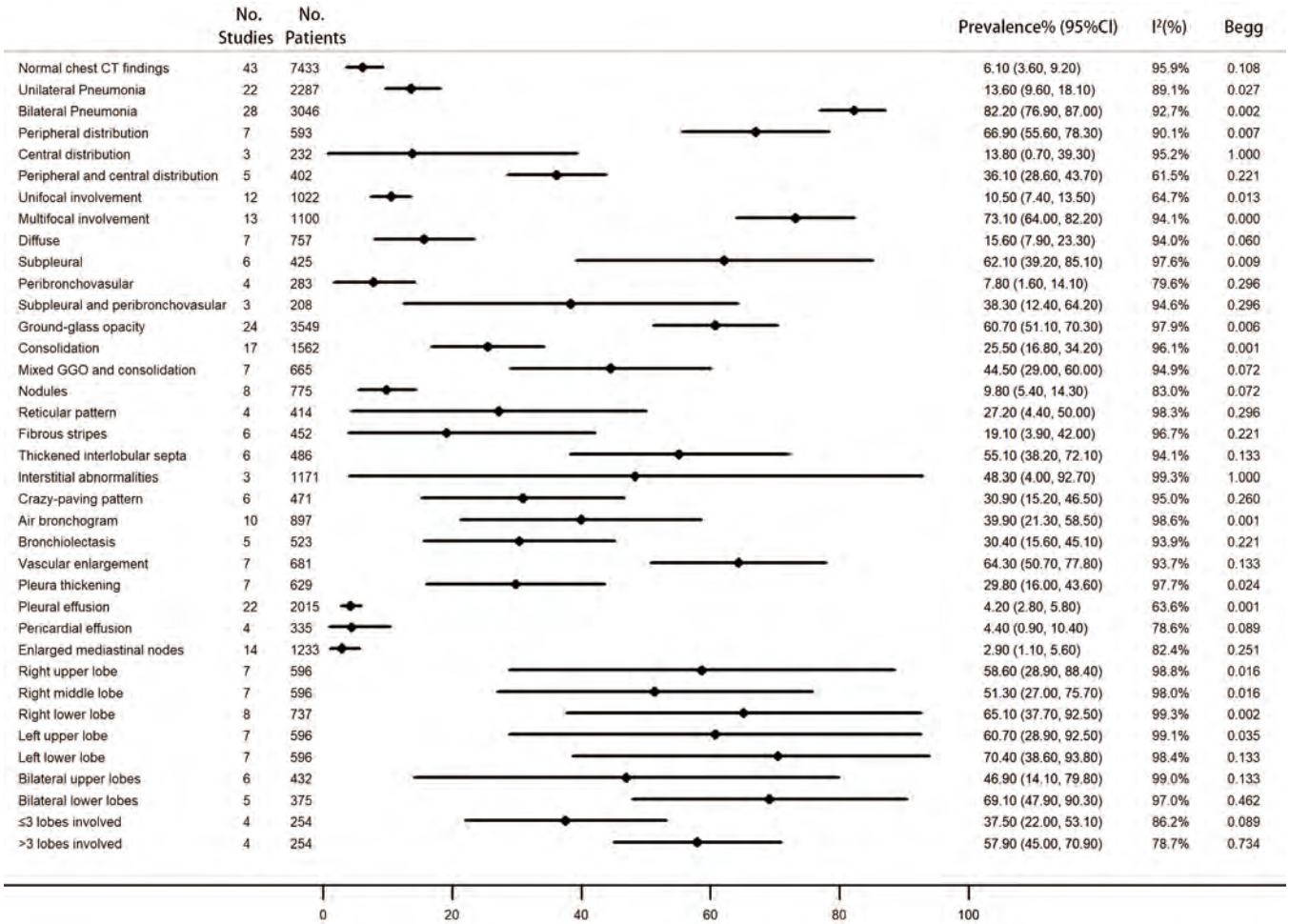

Figure 5 Meta-analysis of the prevalence of chest CT findings of COVID-19 patients. GGO, ground-glass opacity.

mortality rate in severe patients was significantly higher than that in non-severe patients (12.6%, 95% CI, 6.6–20.3%; versus 0.2%, 95% CI, 0.1–0.4%) (*Table 3*).

The results obtained by calculating the OR were similar to those obtained by direct comparison of prevalence. Male (OR 1.43, P<0.0001), history of smoking (OR 1.55, P=0.005), and comorbidities (OR 2.87, P<0.00001) such as hypertension, diabetes, cardiovascular disease, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), malignancies, and chronic renal disease might influence the prognosis of the patients with SARS-CoV-2 infection (Figure S1, *Table 4*). Most clinical symptoms such as fever, high fever, cough, sputum production, fatigue, shortness of breath, dyspnea, and abdominal pain were linked to the severity of the disease, while there was no statistical difference between the two groups in sore throat, myalgia or arthralgia, headache, chest distress, and diarrhea (Figure S2, *Table 4*). Many laboratory indicators implied the deterioration of disease, such as leucocytosis, lymphopenia, platelet, alanine aminotransferase (ALT), aspartate aminotransferase (AST), albumin, creatinine, creatine kinase (CK), LDH, CRP, procalcitonin (PCT), and D-dimer. However, the prevalence of leukopenia was not significantly higher in severe cases than in non-severe cases (OR 1.32, P=0.35) (Figure S3, *Table 4*). For chest CT findings, the risk of bilateral pneumonia, consolidation, pleural effusion, and enlarged mediastinal nodes was higher in severe patients than in non-severe patients. But the analysis did not present that the difference in GGO between severe and non-severe patients was statistically significant (OR 1.03, P=0.92) (Figure S4, *Table 4*).

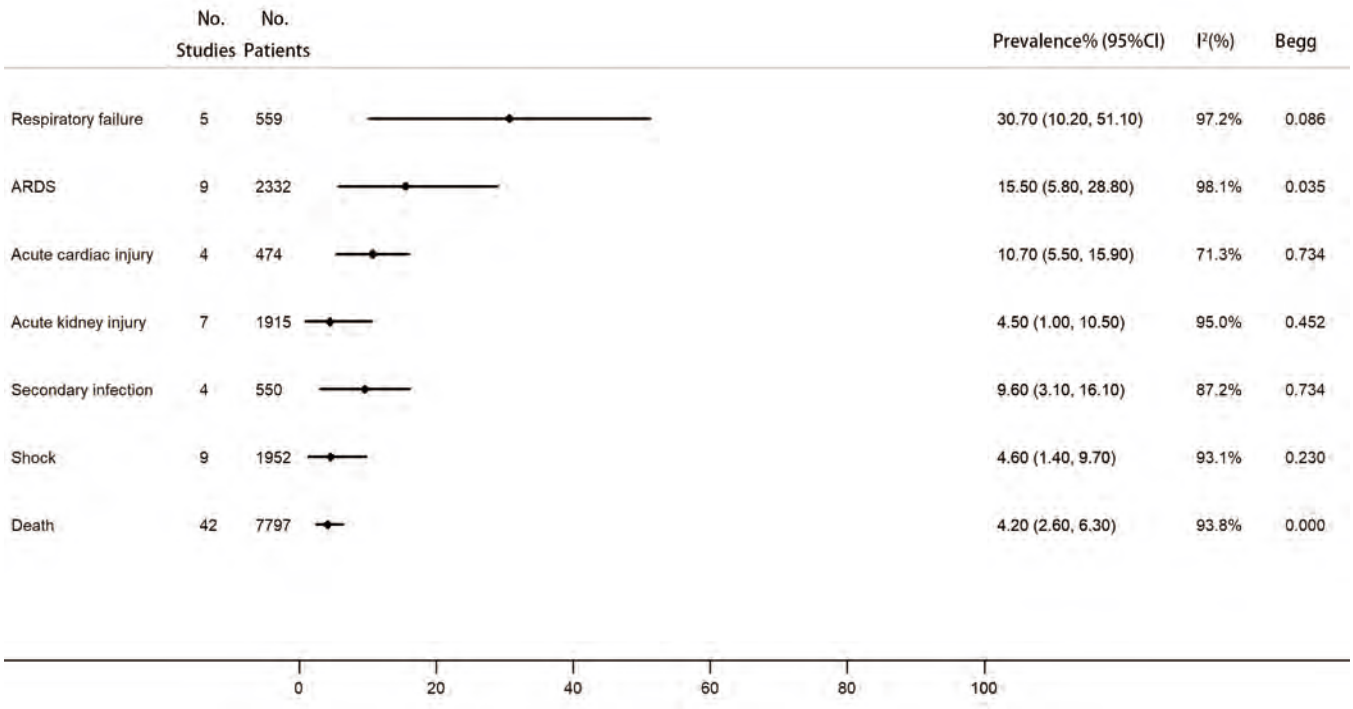

Figure 6 Meta-analysis of the prevalence of complications and clinical outcomes of COVID-19 patients. ARDS, acute respiratory distress syndrome.

Table 2 Subgroup analysis comparing studies from Wuhan and those from other cities

Variables	Wuhan				Other cities			
	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)
Male	29	3,721	53 (48.1–57.9)	89.3	45	8,501	52.7 (51.2–54.2)	37.9
History of smoking	5	1,016	4.3 (1.9–6.7)	68.6	6	1,038	17.1 (10.6–23.5)	86.9
Comorbidities	9	1,409	40.5 (30.9–50.1)	92.9	20	3,187	29.7 (26.1–33.3)	78.5
Diabetes	18	2,482	12.5 (10.7–14.3)	45.3	18	2,118	6.4 (5.4–7.5)	0.0
Hypertension	18	2,482	23 (18.5–27.6)	87.1	16	1,977	14.9 (11.9–17.8)	70.9
Cardiovascular disease	15	2,253	7.4 (5.8–9)	52.8	12	1,564	3.2 (1.8–4.6)	63.6
Cerebrovascular disease	10	1,414	3.9 (2.6–5.2)	34.7	4	335	2.2 (0.6–3.7)	0.0
COPD	11	1,653	3 (2.3–3.9)	0.0	9	952	2.1 (0.8–4)	65.5
Chronic liver disease	10	1,529	2.9 (1.7–4)	46.1	9	1,279	3.1 (2–4.3)	20.3
Chronic renal disease	12	1,910	1.7 (1.1–2.3)	0.0	9	1,099	1.4 (0.7–2.1)	0.0
Malignancies	14	2,044	3 (1.8–4.3)	70.9	9	1,380	1.2 (0.5–2)	31.1
Fever	23	2,818	85.1 (81.8–88.5)	89.6	41	6,982	75.8 (71.3–80.3)	95.7
High fever (≥39 ℃)	5	642	30.3 (7.7–52.9)	98.4	8	2,298	4.1 (2.2–6)	80.1
Cough	21	2,557	63.4 (50.1–76.7)	98.7	40	6,915	55.7 (46.9–64.5)	98.7

Table 2 (*continued*)

Table 2 (*continued*)

Variables	Wuhan				Other cities			
	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)
Sputum production	15	2,089	25.8 (17.9–33.6)	95.5	19	3,776	19.3 (14.5–24.1)	95.9
Fatigue	16	2,000	33.2 (22.5–43.9)	97.1	28	5,839	22.1 (16.8–27.3)	97.1
Myalgia or arthralgia	12	1,626	20.5 (14.9–26)	88.6	22	3,673	13.4 (10.3–16.5)	91.0
Headache	12	1,594	8.6 (6.6–10.6)	48.8	22	4,686	9.1 (7–11.3)	87.5
Shortness of breath	5	959	34.1 (22.8–45.3)	91.9	12	2,512	11.5 (7.2–15.7)	93.6
Dyspnoea	11	1,270	27.4 (13.4–41.4)	98.2	14	2,601	6.5 (3.7–9.3)	93.7
Chest distress	9	880	27.1 (14.7–39.6)	95.6	16	2,752	14.2 (7–21.4)	98.2
Abdominal pain	8	1,189	4.3 (3.2–5.5)	0.0	4	397	1.7 (0.6–3.3)	13.4
Diarrhea	16	2,088	7.6 (4.5–10.8)	90.3	29	5,091	6.5 (4.9–8.1)	86.2
Leucocytosis	11	1,253	13 (7.7–19.5)	90.0	16	2,785	4.9 (3.3–6.7)	73.3
Leukopenia	9	923	26.1 (18.1–34.1)	88.6	21	3,379	22.6 (19.4–25.8)	78.9
Lymphopenia	11	1,227	54.7 (43.5–66)	94.6	21	3,513	40.3 (33.3–47.3)	94.7
Platelet, decreased	3	371	5.2 (0.5–14.3)	88.7	5	437	14.1 (9.6–19.4)	54.1
ALT, increased	4	555	27.8 (22.3–33.4)	51.1	7	800	14.1 (8.8–19.4)	80.5
AST, increased	4	447	36.1 (25.9–46.2)	80.0	8	862	13.8 (8.9–18.7)	79.2
Albumin, decreased	3	630	81.3 (19.6–95.4)	99.6	5	736	16.7 (6.7–30.1)	94.6
Creatinine, increased	3	483	4 (2.3–5.8)	0.0	4	370	9.9 (0.6–19.2)	92.9
Creatine kinase, increased	3	327	11.1 (7–15.2)	29.5	7	805	12.7 (8.9–16.5)	62.9
LDH, increased	4	542	70.9 (47.4–94.3)	98.2	10	1,118	29.8 (23.8–35.7)	79.7
ESR, increased	5	442	75.6 (61.8–89.3)	92.6	4	541	68.1 (51.2–85)	94.7
CRP, increased	10	964	87.1 (80–92.8)	88.7	14	1,312	62.5 (51.4–73.1)	94.2
PCT, increased	5	581	17.8 (6.6–29)	94.4	9	903	12.4 (7–17.8)	95.3
D–dimer, increased	5	605	43.5 (25.2–61.9)	95.7	5	566	11.8 (4.6–19)	89.9
Normal chest CT findings	14	1,402	0.9 (0.2–1.9)	65.3	26	3,336	10 (7–13.5)	89.2
Bilateral pneumonia	15	1,736	86.7 (80.5–91.8)	92.0	12	1,180	75 (65–83.8)	92.9
Ground–glass opacity	10	961	48.3 (30.4–66.1)	97.7	12	1,483	72 (60.9–83.1)	97.0
Consolidation	8	756	22.5 (9.8–35.2)	95.7	9	806	28.3 (15.1–41.6)	96.6
Pleural effusion	9	819	4.1 (2–6.8)	67.1	12	1,066	4.4 (2.5–6.7)	65.7
Enlarged mediastinal nodes	5	482	5.4 (0.9–13.6)	90.0	9	751	1.8 (0.6–3.7)	62.1
ARDS	5	779	30 (20.7–40.2)	89.1	3	454	3.3 (0.1–10.3)	88.2
Shock	5	568	9 (3.8–16)	84.6	3	285	1.1 (0–5)	73.8
Death	18	2,122	10.4 (6.3–15.5)	91.9	23	4,576	1.3 (0.7–1.9)	64.1

COPD, chronic obstructive pulmonary disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactic dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin; ARDS, acute respiratory distress syndrome.

Table 3 Comparison between severe COVID-19 patients and non-severe COVID-19 patients

Variables	Severe patients				Non-severe patients			
	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)
Male	27	1,624	60.9 (57.3–64.4)	46.9	24	4,187	49.5 (46.6–52.4)	68.3
History of smoking	8	860	9.2 (4.2–14.3)	88.5	7	2,181	7.9 (4.2–11.7)	90.7
Comorbidities	16	1,289	51.7 (45.8–57.7)	75.9	12	2,660	26 (17.9–34)	96.5
Diabetes	20	1,301	16.1 (14.1–18.1)	0.0	16	2,893	7.3 (5.7–9.2)	62.7
Hypertension	19	1,249	33.9 (28–39.8)	79.4	16	2,893	15.1 (12–18.3)	81.1
Cardiovascular disease	17	1,199	9.7 (7.3–12.4)	49.2	14	2,703	2.7 (1.7–3.9)	62.7
Cerebrovascular disease	11	973	4.8 (2.9–6.7)	38.8	8	1,709	1.8 (1.1–2.7)	20.5
COPD	12	977	5.2 (3.4–7.4)	41.0	10	1,959	1.4 (0.7–2.2)	29.7
Chronic liver disease	11	795	3.3 (1.9–5)	23.3	10	1,545	4.1 (3–5.5)	28.4
Chronic renal disease	11	992	2.6 (1.6–3.6)	0.0	9	2,176	1.6 (0.8–2.6)	50.9
Malignancies	12	1,022	4.5 (2.9–6.5)	39.8	8	2,065	1.8 (0.6–2.9)	68.1
Fever	25	1,629	85 (76.9–91.5)	94.0	22	4,085	74.4 (65.7–83.2)	98.1
High fever (≥39 ℃)	7	667	17.4 (7–27.7)	96.5	6	1,986	7.5 (3.4–11.6)	95.8
Cough	24	1,456	70.8 (64.7–76.9)	86.6	20	3,644	59.9 (54.5–65.3)	90.5
Sore throat	16	1,088	11.5 (7.2–15.7)	87.5	14	2,173	6.9 (4.3–9.6)	81.2
Sputum production	17	1,144	30.6 (21.2–40.1)	92.7	15	3,120	21.1 (14.6–27.6)	95.2
Fatigue	18	1,212	38.5 (29.8–47.3)	90.6	18	3,447	31 (23.3–38.6)	96.4
Myalgia or arthralgia	17	1,160	15.5 (11.5–19.5)	70.5	16	3,155	13.7 (10.5–17)	85.8
Headache	15	1,082	8.9 (6–11.7)	58.5	16	3,370	9.1 (7.1–11.2)	71.6
Shortness of breath	8	690	32.3 (20.1–44.6)	90.5	6	1,631	13.5 (5.3–21.7)	97.5
Dyspnoea	13	585	36.1 (23.8–48.5)	91.9	11	1,204	5.7 (0.7–15.1)	96.7
Chest distress	5	126	11.5 (2.8–20.1)	63.6	6	419	7.2 (2.3–14.7)	83.7
Abdominal pain	7	481	6.4 (4.3–8.9)	4.2	7	609	2.2 (0.8–4.3)	50.7
Diarrhea	15	1,162	8.3 (4.2–13.6)	87.3	14	3,080	7 (4.8–9.2)	83.4
Leucocytosis	13	805	12.9 (8.5–18)	72.9	12	2,673	3.3 (2.1–5)	70.6
Leukopenia	11	702	23.6 (13.1–36)	91.7	10	2,572	19.9 (15.3–24.5)	86.1
Lymphopenia	14	763	69.7 (58.2–81.3)	94.2	13	2,679	50 (36.1–64)	98.4
Platelet, decreased	4	396	21.1 (2.6–50.7)	97.0	3	1,053	20.1 (2.4–37.8)	97.9
ALT, increased	5	328	33.9 (18.5–49.4)	90.1	2	798	18.2 (14.3–22.2)	45.4
AST, increased	5	335	43.6 (35.1–52.2)	57.9	2	807	14.5 (6.8–22.1)	88.0
Albumin, decreased	3	270	55.7 (29.2–82.2)	94.0	2	474	22.1 (18.4–25.9)	0.0
Creatinine, increased	3	369	4.8 (2.6–7)	0.0	2	896	1.1 (0.4–1.8)	0.0
Creatine kinase, increased	4	358	16.9 (8–25.8)	76.0	4	1,040	7.6 (2.8–12.3)	86.9

Table 3 (*continued*)

Table 3 (*continued*)

Variables	Severe patients				Non-severe patients			
	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)	No. reports	No. patients	Prevalence% (95% CI)	I^2 (%)
LDH, increased	6	439	62.5 (53–71.9)	71.9	5	1,185	27.7 (14.7–40.7)	96.0
CRP, increased	9	599	82 (75–89.1)	82.4	7	1,287	59.4 (47.7–71.2)	94.0
PCT, increased	9	458	39.7 (21.8–57.6)	96.2	6	906	11.2 (2.8–24.1)	95.3
D–dimer, increased	3	205	66.2 (53.9–78.5)	70.6	2	494	36.9 (22.1–51.7)	77.8
Bilateral Pneumonia	9	479	97.9 (94.5–99.7)	72.5	7	847	87.1 (78.5–93.7)	90.6
Ground–glass opacity	8	472	72.1 (52.1–88.4)	94.3	10	1,662	66 (53.3–78.6)	96.9
Consolidation	7	315	48.8 (28.1–69.5)	93.4	8	850	12.3 (3.1–26.4)	96.2
Pleural effusion	6	162	13 (6.0–20.0)	45.6	7	493	1.6 (0.1–4.7)	76.3
Enlarged mediastinal nodes	4	97	9.9 (1.8–23.3)	68.7	5	348	0.5 (0–1.5)	0.0
ARDS	3	261	47.6 (9.3–85.9)	97.3	2	1,028	2.6 (0.1–7.9)	83.1
Acute cardiac injury	3	119	20.7 (13.4–27.9)	0.0	2	160	2.4 (0.6–5.4)	0.0
Acute kidney injury	4	292	10.3 (1.3–19.3)	82.9	3	1,086	1.1 (0–3.9)	73.4
Shock	3	240	13.6 (1.9–25.3)	79.0	3	1,086	0.3 (0–0.9)	17.3
Death	19	946	12.6 (6.6–20.3)	90.1	16	2,735	0.2 (0.1–0.4)	0.00

COPD, chronic obstructive pulmonary disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactic dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin; ARDS, acute respiratory distress syndrome.

Heterogeneity and publication bias

We meta-analyzed 114 features of COVID-19 patients. Among them, 36 (31.6%) presented publication bias (*Figures 2-6*, P<0.05 by Begg's test). In the meta-analysis of prevalence, most of the analyses had high heterogeneity (*Figures 2-6*). And in the meta-analysis of risk factors for severity, most had low or moderate heterogeneity (Figures S1-S4).

Discussion

Based on the information from 90 studies with 16,526 laboratory-confirmed COVID-19 patients, our systematic review and meta-analysis provided a comprehensive description of the characteristics of COVID-19 patients, including comorbidities, clinical symptoms, laboratory characteristics, chest CT features, and complications and identified the risk factors of severe disease.

In our article, the overall CFR of confirmed patients was 4.2%, which is close to the estimate (4.8%) reported by the World Health Organization as of March 30, 2020 (33,106 deaths among 693,224 confirmed cases) (2). The Chinese Center for Disease Control and Prevention (China CDC) reported that the overall CFR was 4.1% among 81,518 confirmed patients in mainland China as of March 30, 2020, and the CFR in Wuhan was 5.1% (2,548 deaths among 50,006 confirmed cases) (100). Our subgroup analysis also found a CFR of 10.4% in Wuhan comparing to 1.3% in other cities. This may indicate that earlier outbreak caused more deaths and effective disease control and prevention measures can significantly decline the CFR of communicable diseases.

The population is generally susceptible to COVID-19 at all ages, the median age we analyzed was 48.8 years. We found that the proportion of male patients was 53.1% and it was significantly higher in severe cases than in non-severe cases. A previous meta-analysis found a similar finding that male was a risk factor for severe illness in COVID-19 patients (101). But another study did not find significant differences in CFR and the proportion of severe patients between male and female (22). Some studies explained that there are differences between the immune system of men

Table 4 Meta-analysis of risk factors for severity

Variables	No. of studies	No. of patients	OR [95% CI]	P value
Male	22	5,363	1.43 [1.21, 1.69]	<0.0001
History of smoking	7	2,989	1.55 [1.14, 2.10]	0.005
Comorbidities				
Comorbidities	12	3,727	2.87 [2.13, 3.86]	<0.00001
Hypertension	15	3,854	2.50 [1.80, 3.47]	<0.00001
Diabetes	15	3,854	2.46 [1.77, 3.40]	<0.00001
Cardiovascular disease	13	3,612	3.28 [2.27, 4.75]	<0.00001
Cerebrovascular disease	8	2,453	2.78 [1.49, 5.19]	0.001
COPD	10	2,820	3.60 [2.08, 6.23]	<0.00001
Malignancies	8	2,861	1.80 [1.08, 3.00]	0.02
Chronic liver disease	10	2,278	0.82 [0.48, 1.42]	0.49
Chronic renal disease	9	3,048	1.94 [1.09, 3.42]	0.02
Clinical symptoms				
Fever	20	5,266	1.78 [1.31, 2.42]	0.0002
High fever (≥39 ℃)	6	2,603	2.25 [1.42, 3.58]	0.0006
Cough	19	4,760	1.63 [1.28, 2.09]	0.0001
Sore Throat	13	2,983	1.22 [0.82, 1.82]	0.32
Sputum production	15	4,144	1.40 [1.08, 1.81]	0.01
Fatigue	16	4,375	1.57 [1.21, 2.04]	0.0008
Myalgia or arthralgia	14	3,975	1.32 [0.96, 1.80]	0.09
Headache	14	4,228	1.25 [0.96, 1.61]	0.09
Shortness of breath	6	2,209	3.81 [2.39, 6.07]	<0.00001
Dyspnoea	11	1,683	11.68 [4.13, 33.07]	<0.00001
Chest distress	5	437	2.36 [0.85, 6.54]	0.1
Abdominal pain	7	1,090	2.60 [1.05, 6.39]	0.04
Diarrhea	12	3,896	1.34 [0.95, 1.88]	0.09
Laboratory abnormalities				
Leucocytosis	10	3,144	2.97 [2.15, 4.10]	<0.00001
Leukopenia	9	3,058	1.32 [0.74, 2.35]	0.35
Lymphopenia	11	3,153	2.78 [1.85, 4.19]	<0.00001
Platelet, decreased	3	1,399	2.35 [1.43, 3.88]	0.0008
ALT, increased	2	964	2.14 [1.03, 4.45]	0.04
AST, increased	2	980	3.53 [2.02, 6.17]	<0.00001
Albumin, decreased	2	686	2.84 [1.34, 6.02]	0.006
Creatinine, increased	2	1,215	3.63 [1.63, 8.05]	0.002

Table 4 (*continued*)

Table 4 (*continued*)

Variables	No. of studies	No. of patients	OR [95% CI]	P value
Creatine kinase, increased	4	1,398	2.51 [1.45, 4.37]	0.001
LDH, increased	5	1,566	3.70 [2.03, 6.73]	<0.0001
CRP, increased	6	1,668	3.40 [2.23, 5.17]	<0.00001
PCT, increased	6	1,194	5.39 [3.51, 8.28]	<0.00001
D-dimer, increased	2	641	2.45 [1.27, 4.71]	0.007
CT findings				
Bilateral Pneumonia	7	1,224	3.16 [1.37, 7.29]	0.007
Ground-glass opacity	8	1,962	1.03 [0.56, 1.88]	0.92
Consolidation	7	1,057	6.70 [3.03, 14.78]	<0.00001
Pleural effusion	6	547	7.15 [2.96, 17.27]	<0.0001
Enlarged mediastinal nodes	4	337	9.37 [1.77, 49.51]	0.008

COPD, chronic obstructive pulmonary disease; ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactic dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin.

and women which may cause a high risk of viral infection for men (102,103). Patients with underlying diseases have lower immunity and are more likely to be severely ill. In our study, hypertension (19.1%), diabetes (9.5%), and cardiovascular disease (5.4%) were the most common comorbidities, and the proportion was higher among severe patients. The finding was consistent with another study that found the most prevalent comorbidities were hypertension (21.1%) and diabetes (9.7%), followed by cardiovascular diseases (8.4%) and hypertension, cardiovascular disease, and respiratory system disease were independent risk factors of severe disease in patients with SARS-CoV-2 infection (104).

Guan *et al.* and Chen *et al.* reported that fever and cough were the most common clinical manifestations, and nausea or vomiting and diarrhea were uncommon (11,98). Our study also reached a similar conclusion that the most prevalent symptoms were fever (78.4%) and cough (58.5%), however, the proportion was a little lower than the previous studies (fever, 87–88%; cough 67.8–82%). And gastrointestinal symptoms were rare. Comparing to non-severe patients, most symptoms were more common in severe patients, particularly shortness of breath and dyspnoea. It suggested that severe patients might have worse lung function. The most common laboratory abnormalities showed in our article were increased serum ferritin (74.2%,), high CRP (73.3%), high ESR (72.2%), decreased eosinophil (59.2%), increased interleukin 6 (58.2%), lymphopenia (46.5%), high LDH (41.6%), and hyperglycemia (40.1%). Compared with non-severe patients, the laboratory abnormalities occurred more frequently in severe patients. And we also proposed a link between some specific laboratory indicators (leucocytosis, lymphopenia, platelet, ALT, AST, albumin, creatinine, CK, LDH, CRP, PCT, and D-dimer) and disease severity of COVID-19 patients. This finding suggested that the pathophysiological hallmark of COVID-19 tend to be the sustained inflammatory response and cytokine storm which is similar to those previously found in patients infected with the SARS-CoV and MERS-CoV, and severe inflammation would lead to immune deficiency, hepatic damage, myocardial damage, kidney damage, and coagulation activation (94). A review demonstrated that the evaluation of lymphocyte count, biomarkers (serum PCT and ferritin), and inflammatory indices, such as LDH, CRP, and IL-6 might contribute to identify patients with poor prognosis (105). This conclusion was consistent with our comparison between severe and non-severe patients. Regarding serum ferritin, two studies presented that higher serum ferritin was related to disease progression (14,106), but no study supported the general elevation of serum ferritin in patients with SARS-CoV-2 infection. We just included 3 studies in the meta-analysis of the prevalence of increased serum ferritin, so the result needed more studies to confirm.

Although the imaging manifestations of viral pneumonia are generally considered to be non-specific (107), with the in-depth studies of the imaging features of COVID-19, some relatively special CT characteristics were found (42,59,108,109). And there are obvious differences between patients of different clinical types and stages (59,109). According to previous studies, typical CT findings of COVID-19 patients were bilateral lung involvement with diffuse distribution and lesions mostly were located peripherally (42,108). The main patterns were groundglass opacity, air bronchograms, and interstitial abnormalities. And pulmonary cavitation, discrete pulmonary nodules, lymphadenopathy, and pleural effusions were absent (42,108). In our study, the finding was similar. Most cases had bilateral lung involvement and presented peripheral and subpleural distribution, with multifocal involvement. More than half of patients had >3 lobes involved and the right lower lobe and the left lower lobe were more likely to be involved. The most common CT features were vascular enlargement, ground-glass opacity, thickened interlobular septa, interstitial abnormalities, mixed GGO and consolidation, and air bronchogram. Pericardial effusion, pleural effusion, and enlarged mediastinal nodes were rare. In addition, our analysis showed that patients presented with bilateral pneumonia, consolidation, pleural effusion, and enlarged mediastinal nodes faced a higher risk of developing a serious illness. In the whole, Chest CT acts a crucial part in the diagnosis and treatment for patients with SARS-CoV-2 infection.

With regard to the complications, the most common were respiratory failure (30.7%) and ARDS (15.5%), but also, a small percentage of patients had acute cardiac injury, acute kidney injury, secondary infection, and shock. Compared with non-severe cases, severe cases significantly had worse disease progression, particularly ARDS (2.6% versus 47.6%) (*Table 3*). Thus, early identification and timely treatment of severe patients would better improve the prognosis.

Although some systematic reviews and meta-analyses which studied the features of patients with COVID-19 have been published (21,22), our study updated the comprehensive information of clinical characteristics of patients with COVID-19 worldwide and analyzed the risk factors of severe illness. High quality and large sample size of the included studies were the strengths of our study. We also conducted a subgroup analysis based on the area. Nevertheless, our review had a few limitations. First, most of the included studies were single-center retrospective studies which were difficult to control the influence of confounding factors. Second, we found significant heterogeneity and publication bias between studies. Third, most included studies were from China, data from other countries are required. Lastly, some detailed information, such as clinical outcomes and prognosis, was incomplete. Based on updated data all around the world, in-depth studies need to be conducted.

Conclusions

In summary, most patients with COVID-19 have fever and cough with lymphopenia and increased inflammatory indices, and the main CT feature is GGO involved bilateral lung. Patients with comorbidities and worse clinical symptoms, laboratory characteristics, and CT findings tend to have poor disease progression and outcome. COVID-19 is an emerging pandemic of global public health concern. So, the prevention and control of the disease spread are imminent. In addition, more researches are required to elucidate the pathogenesis and the risk factors for severe cases and death.

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Table S1 Bias risk assessment

Study	①	②	③	④	⑤	⑥	⑦	⑧	Score
Liu W	2	2	2	2	2	1	1	0	12
Chen C	2	2	2	2	2	0	0	0	10
Tian S	2	2	2	2	2	1	2	0	13
Li K	2	2	2	2	2	0	0	0	10
Xu YH	2	1	2	2	2	1	2	0	12
Yang W	2	2	2	2	2	1	2	0	13
Guan WJ	2	2	2	2	2	2	2	0	14
Wu J	2	2	2	2	2	1	2	0	13
Mo P	2	2	2	2	2	1	2	0	13
Zhou F	2	2	2	2	2	2	2	0	14
Liu K	2	2	2	2	2	1	2	0	13
Xu T	2	2	2	2	2	1	2	0	13
Wang Z	2	2	2	2	2	1	2	0	13
Xu XW	2	2	2	2	2	1	2	0	13
Ruan Q	2	1	2	2	2	0	0	0	9
Chen J	2	2	2	2	2	1	2	0	13
Lin D	2	2	2	2	2	0	0	0	10
Li Y	2	2	2	2	2	0	0	0	10
COVID–19 team Australia	2	2	2	2	2	0	0	0	10
Zhou S	2	2	2	2	2	0	0	0	10
Wang J	2	2	2	2	2	0	0	0	10
Qin C	2	2	2	2	2	0	0	0	10
Han R	2	2	2	2	2	0	0	0	10
Sun WW	2	1	2	2	2	0	0	0	9
Dong XC	2	1	2	2	2	0	0	0	9
Xiao F	2	2	2	2	2	0	0	0	10
Fan BE	2	2	2	2	2	0	0	0	10
Shi Y	2	1	2	2	2	1	2	0	12
Xu X	2	2	2	2	2	1	2	0	13
He XW	2	2	2	2	2	0	0	0	10
Wu J	2	1	2	2	2	0	0	0	9
Han H	2	2	2	2	2	0	0	0	10
Shi H	2	2	2	2	2	1	2	0	13
Zhao W	2	1	2	2	2	0	0	0	9
Wu C	2	2	2	2	2	1	2	0	13
Wang SH	2	2	2	2	2	0	0	0	10
Shi JH	2	2	2	2	2	1	2	0	13
Zhao Y	2	2	2	2	2	0	0	0	10
Ling Y	2	2	2	2	2	0	0	0	10
Cheng JL	2	2	2	2	2	0	0	0	10
Huang L	2	2	2	2	2	0	0	0	10
Lu XF	2	2	2	2	2	0	0	0	10
Liu HF	2	2	2	2	2	0	0	0	10
Yu CC	2	2	2	2	2	0	0	0	10
Li XH	2	2	2	2	2	1	1	0	12
Hu R	2	2	2	2	2	1	1	0	12
Lu ZB	2	2	2	2	2	1	2	0	13
Li Y	2	2	2	2	2	0	0	0	10
Shi YL	2	2	2	2	2	0	0	0	10
Li RQ	2	2	2	2	2	0	0	0	10
Bai P	2	2	2	2	2	1	2	0	13
Sun DW	2	2	2	2	2	0	0	0	10
Wan Q	2	2	2	2	2	1	2	0	13
Lu YF	2	1	2	2	2	0	0	0	9
Yu SM	2	2	2	2	2	0	0	0	10
Yang K	2	2	2	2	2	1	2	0	13
Xu S	2	2	2	2	2	1	2	0	13
Ma PQ	2	2	2	2	2	0	0	0	10
Zhao CC	2	2	2	2	2	0	0	0	10
Chen X	2	2	2	2	2	0	0	0	10
Fang L	2	2	2	2	2	0	0	0	10
Fang XW	2	2	2	2	2	1	2	0	13
Zhong Q	2	2	2	2	2	0	0	0	10
Ran J	2	2	2	2	2	0	0	0	10
Yuan J	2	2	2	2	2	1	2	0	13
Xiao KH	2	2	2	2	2	1	2	0	13
Wang AH	2	2	2	2	2	0	0	0	10
Wang XJ	2	2	2	2	2	0	0	0	10
Li JS	2	2	2	2	2	0	0	0	10
Han J	2	2	2	2	2	0	0	0	10
Dai ZH	2	2	2	2	2	0	0	0	10
Chen W	2	2	2	2	2	0	0	0	10
Cheng KB	2	2	2	2	2	1	2	0	13
COVID–19 team Shandong	2	2	2	2	2	0	0	0	10
Sui HY	2	2	2	2	2	0	0	0	10
Zhou YP	2	2	2	2	2	0	0	0	10
Ding Y	2	2	2	2	2	0	0	0	10
Xiong J	2	2	2	2	2	1	2	0	13
Hou KK	2	2	2	2	2	1	2	0	13
Chen ZY	2	2	2	2	2	0	0	0	10
Chang ZY	2	2	2	2	2	0	0	0	10
Qian ZC	2	2	2	2	2	1	2	0	13
Lu ZL	2	2	2	2	2	0	0	0	10
Chen NS	2	2	2	2	2	2	2	0	14
Liang W	2	2	2	2	2	1	2	0	13
Yang XB	2	2	2	2	2	2	2	0	14
Wang DW	2	2	2	2	2	2	2	0	14
Liu K	2	2	2	2	2	1	2	0	13
Pan YY	2	2	2	2	2	0	0	0	10
Zhang JJ	2	2	2	2	2	1	2	0	13

① A clearly stated aim; ② Inclusion of consecutive patients; ③ Prospective collection of data; ④ Endpoints appropriate to the aim of the study; ⑤ Unbiased assessment of the study endpoint; ⑥ Follow–up period appropriate to the aim of the study; ⑦ Loss to follow-up less than 5%; ⑧ Prospective calculation of the study size. The items are scored 0 (not reported), 1 (reported but inadequate), or 2 (reported and adequate). The global ideal score being 16 for non–comparative studies.

http://dx.doi.org/10.21037/apm-20-1863

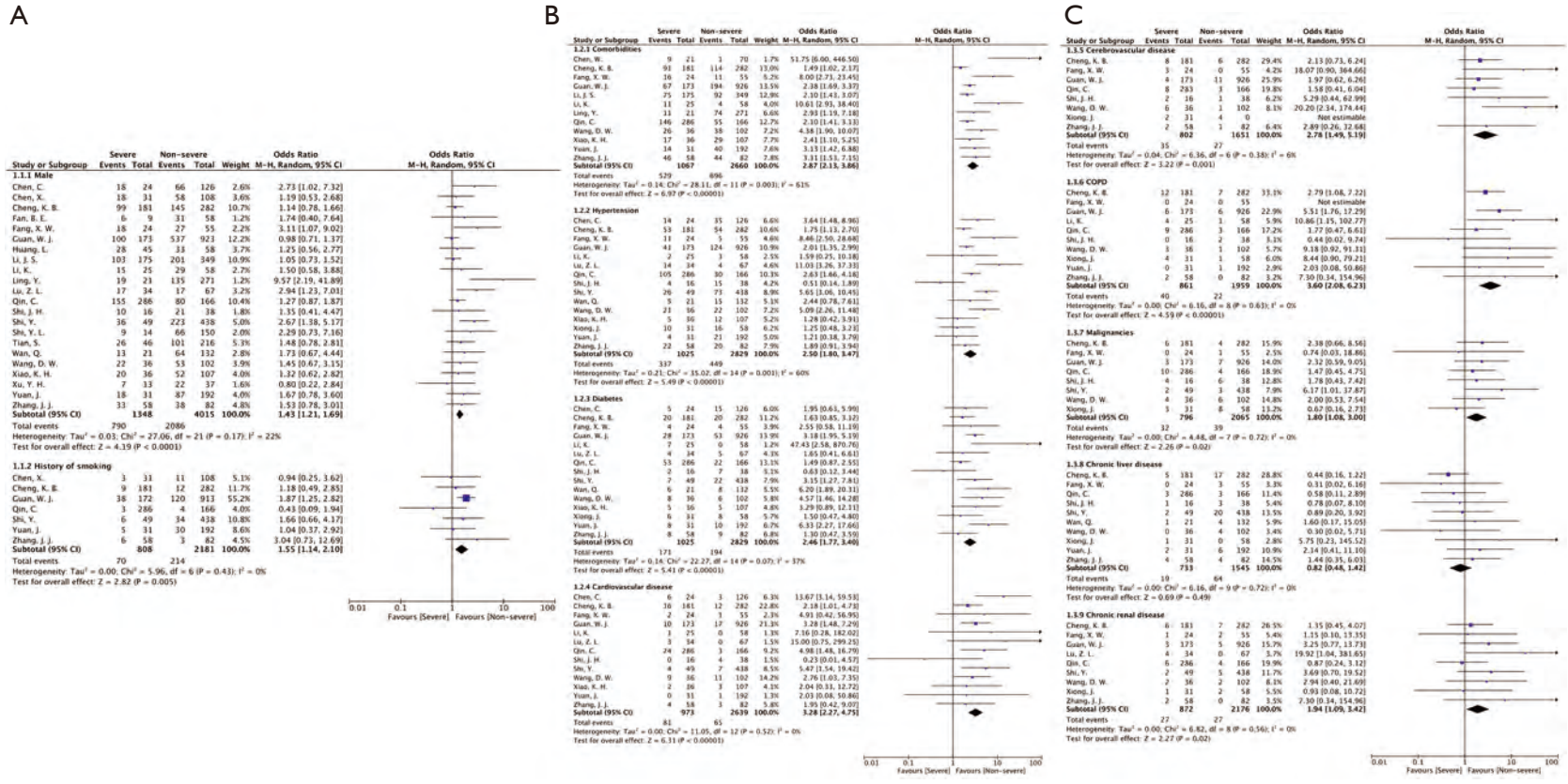

Figure S1 Meta-analysis of male, history of smoking, and comorbidities according to COVID-19 severity. COPD, chronic obstructive pulmonary disease.

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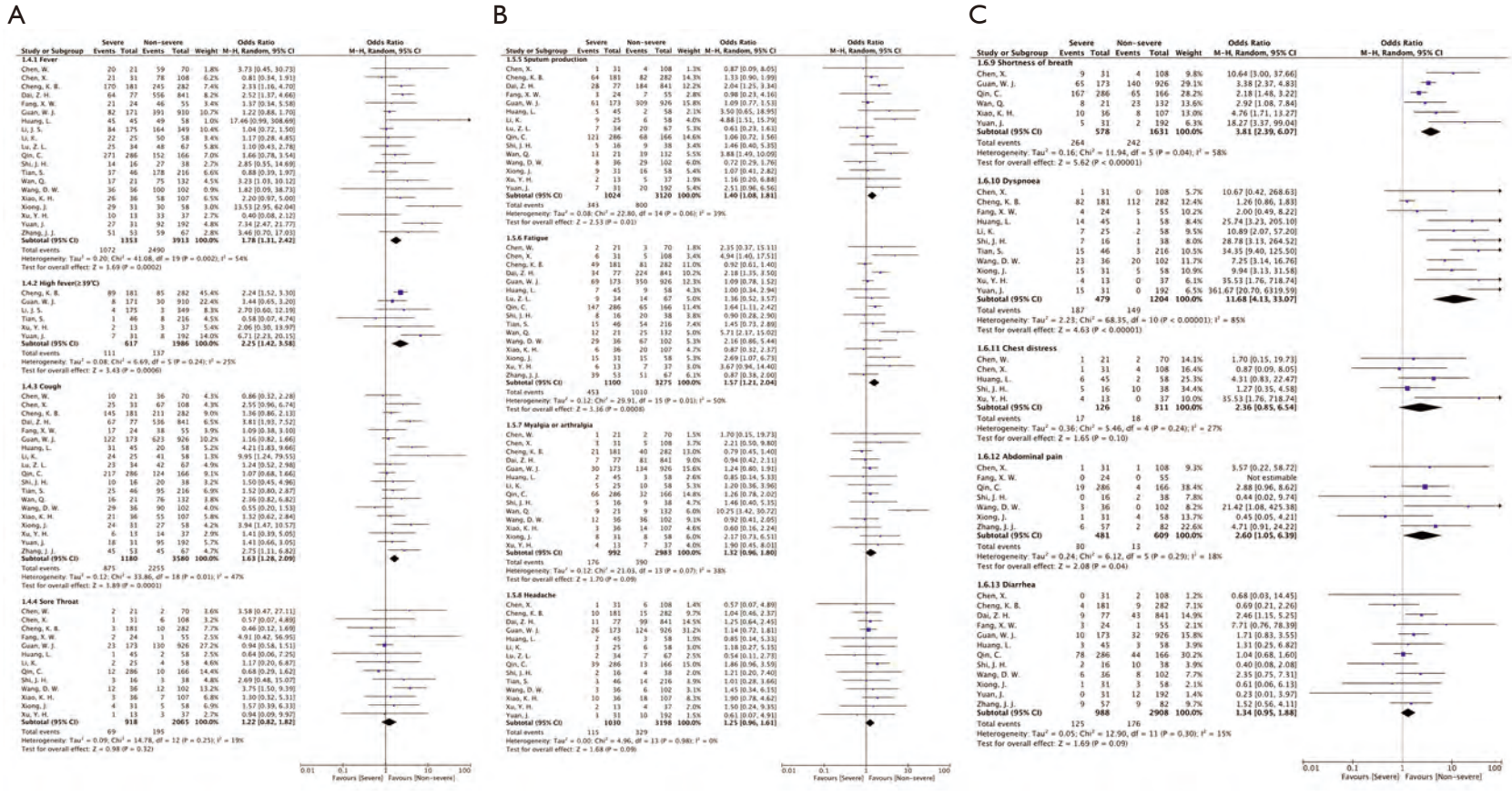

Figure S2 Meta-analysis of clinical symptoms according to COVID-19 severity.

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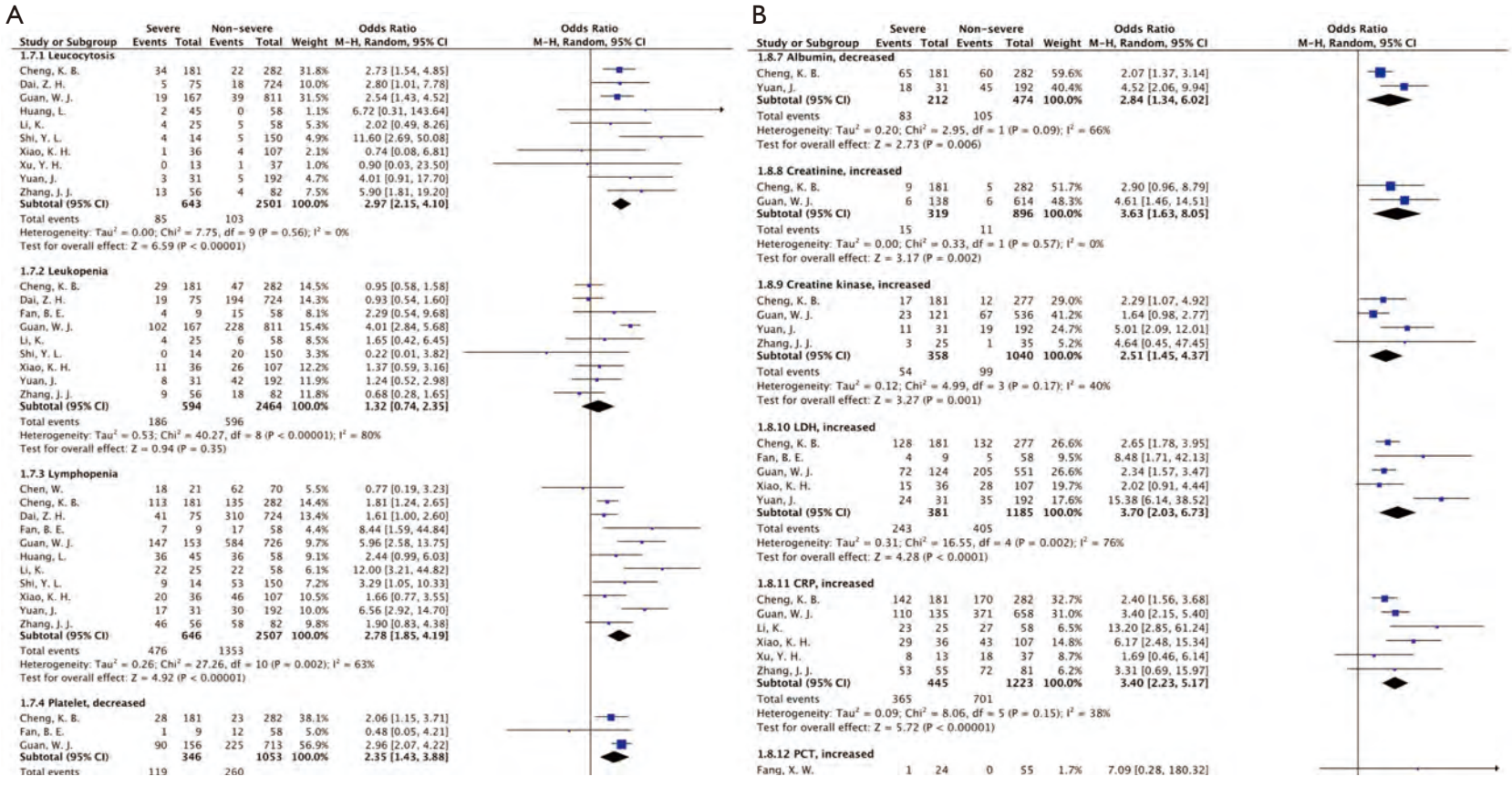

Figure S3 Meta-analysis of laboratory abnormalities according to COVID-19 severity. ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDH, lactic dehydrogenase; CRP, C-reactive protein; PCT, procalcitonin.

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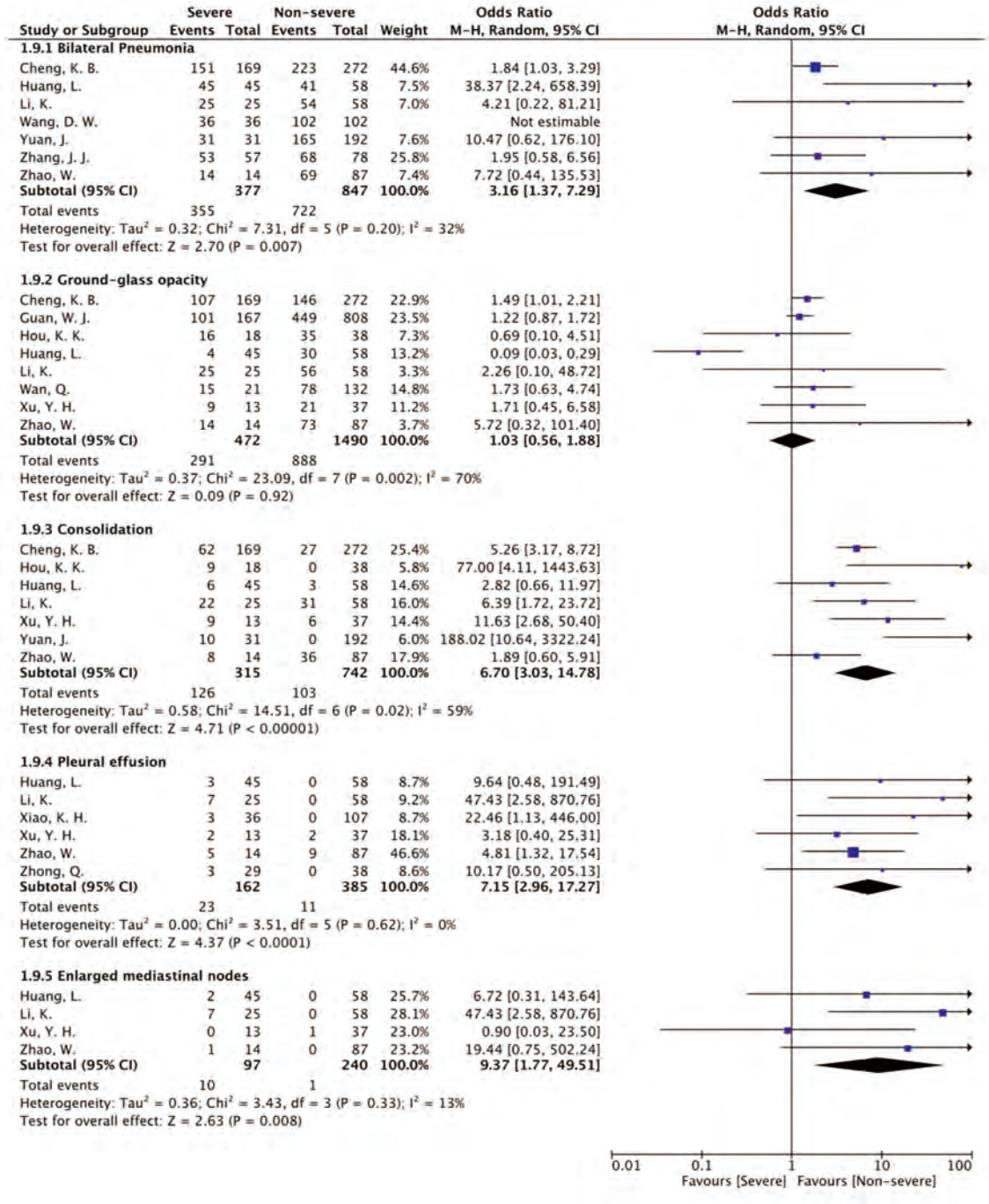

Figure S4 Meta-analysis of CT findings according to COVID-19 severity.

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