INTRODUCTION

In early December 2019, the first case of a novel coronavirus disease 2019 (Covid-19) was reported in Wuhan, Hubei province, China.1 The World Health Organization (WHO) has declared that Covid-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),2 is posing a great threat to public health.

Since the first study reported on the clinical characteristics of Covid-19,3 hundreds of clinical articles have been published on topics ranging from clinical characteristics,1-3 radiological finding4-6 to epidemiological features.7-9 The National Health Commission (NHC) issued the China Guidelines for the Diagnosis and Treatment Plan of Novel Coronavirus (COVID-19).10 With the increasing number of patients diagnosed, China has also carried out more than one hundred clinical trials of Covid-19, including antiviral drugs, antimalarial...
drugs, glucocorticoids, plasma therapy, virus vaccine and other western drugs. However, information regarding the epidemiology and clinical features of severe Covid-19 is relatively scarce at present. In this study, we carried out a comprehensive systemic review of studies that evaluated the clinical features, laboratory and radiological findings comparing severe vs non-severe patients with confirmed Covid-19 pneumonia. The aim of this meta-analysis was to explore the relative risk factor for severe Covid-19, which might be useful for medical clinicians to quickly define whether a patient is susceptible to severe Covid-19 or whether a non-severe person would progress into severe Covid-19.

2 | MATERIALS AND METHODS

The present review was conducted strictly according to “Handbook for systematic Reviews of Interventions Version 5.1.0.”

2.1 | Literature search

First, we searched for related literature with keyword of “2019-nCoV,” “Covid-19” and “SARS-CoV-2” on PubMed and web of science. No restriction was used so that all the possible studies would be systematically checked. Then, Additional articles were retrieved by screening the reference lists of the included studies. The literature search was last updated (10 April 2020) to ensure a comprehensive investigation. This is a meta-analysis that collected data from published papers. Thus, ethics approval was not necessary.

2.2 | The inclusive and exclusive criteria

All search items were evaluated for eligibility by two reviewers (YJ Zhang and SL Han). Consensus was reached by negotiation.

2.2.1 | Inclusive criteria

To be included in the final review, the following criteria should be met:

1. Type of studies: Randomised or non-randomised controlled trials, prospective or retrospective cross-sectional studies;
2. Participants: Confirmed case of Covid-19 was defined as a positive result on high throughput sequencing or real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR);
3. Comparison: Severe (severe/critical) group vs Non-severe (common/mild) group;
4. Outcome: Demography characteristics (eg, sex, age), comorbidities, signs and symptoms, laboratory findings and image data about chest computer tomography (CT).

We defined the degree of severity of Covid-19 (eg, mild, common, severe and critical) according to the China Guidelines for the Diagnosis and Treatment Plan of Novel Coronavirus (2019-nCoV) Infection by the National Health Commission (Trial Version 5).

2.2.2 | Exclusive criteria

Case reports, letters to editor and correspondence that did not report explicit data were excluded. Articles unrelated to the aim of our topic and published repeatedly were also excluded. When two or more articles reported on overlapping patients, only the article with the largest sample size was included.

2.3 | Data abstraction

Firstly, two investigators (YJ Zhang and SL Han) independently extracted data using a prior structured study recording form. We extracted the following study design characteristics: first author name, year of publication, patient source, study design, sample volume, baseline demographic characteristics of patients, comorbidities, signs and symptoms, laboratory findings and outcomes about abnormal chest computer tomography (CT). Then double-check procedure was performed to ensure the accuracy of the data extracted. At last, a manager (XF Sun) inputted the extracted data into a spreadsheet.

2.4 | Statistical analysis

Meta-analysis was performed on the crude data extracted from the text. We calculated the weighted mean difference (WMD) for continuous outcomes and the odds ratio (OR) for the dichotomous
data, along with the 95% confidence intervals (CIs). In the absence of reported standard errors, we calculated the standard error of mean difference according to the methods described in Cochrane Handbook.13

Prior to analysing the data, heterogeneity was assessed by the Cochran Q test along with visual inspection of the forest plot. Then, it was quantified by the $I^2$ test. A fixed-effect model was used when the effects were assumed to be homogenous ($P > .05$ or $I^2 < 50\%$).13 However, given that the clinical settings differed across studies, we assumed the presence of heterogeneity and used random-effects model in all subsequent analyses, for the outcome of which were more conservative as they considered differences both within and among studies in calculating the error terms used in the analysis.13

Funnel plots were employed for detection of publication bias, in which the effect sizes (eg, OR or WMD) are plotted on the horizontal axis and its variance (eg, the standard error of the log effect) on the vertical axis. Bias was revealed if the plots were asymmetrical about the pooled value.

All statistical analyses were done with Review Manager 5.3.5 (Cochrane Collaboration, Oxford, UK). Results were regarded as statistically significant if $P < .05$.

3 | RESULT

3.1 | Trial flow

The search strategy yielded 6721 citations (3516 from Pubmed and 3205 from ISI web of science). All the documents were selected strictly according to the criteria described above. Subsequent scrutiny of the titles and abstracts excluded 6677 of these articles on the grounds that they were irrelevant or duplicative for the aim of this meta-analysis. 21 articles were further excluded as irrelevant to our purposes. The full publications were obtained for the remaining 23 articles.

Based on the inclusion criteria, 9 articles were further excluded, leaving 14 studies eligible for this article.14-27 Specially, two articles were excluded either for overlapping patients with included studies,3 or for they defined the degree of severity of Covid-19 with the different criteria.3,28 One article reporting results regarding 55 cases of 2019-nCoV were also excluded, since it did not report the origin of the patients.29 For three articles reporting outcomes in Wuhan Tongji hospital,17,30,31 three articles reporting outcomes in Jiangsu Province27,32,33 and three articles reporting outcomes in Zhejiang province,33-35 only studies with the largest simple volume were included in this article.13,27,33 No additional articles were retrieved from the citation list of included studies. The details of study selection flow were explicitly described in Figure 1.

3.2 | Study characteristics

Finally, 14 retrospective cross-sectional studies on different populations, from which conclusions could be drawn from the origin of patients, were suitable for this meta-analysis14-22: four multi-centre studies19-21,27 and ten single-centre studies.14-18,22-26 All the eligible studies were from China and published in 2020. As a result of the instinctive design of this meta-analysis, no randomised or non-randomised controlled trials were eligible for this meta-analysis. A total of 2566 individuals were identified (771 in the severe group and 1795 in the non-severe group).14-27 Characteristics of eligible studies were shown in Table 1.

![FIGURE 1 Literature search and selection of studies. 14 studies were included according to selection criteria](image)
| Study ID | Location | Hospital | Date (month, day) | Study type | Sample size | Severe group | Non-severe group |
|----------|----------|----------|------------------|------------|-------------|--------------|-----------------|
| Tian et al | Beijing, China | Designated hospitals in Beijing | Jan 20 to Feb 10 | Multi-centre | 262 | Severe: 46 | Common: 216 |
| Li et al | Chongqing, China | Second Affiliated Hospital of Chongqing Medical University | Jan to Feb | Single-centre | 83 | Severe/critical: 25 | Common: 98 |
| Qin et al | Wuhan, Hubei province | Tongji Hospital | Jan 10 to Feb 12 | Single-centre | 452 | Severe: 286 | Non-severe: 166 |
| Qu et al | Huizhou, Guangdong Province | Huizhou municipal central hospital | Jan to Feb | Single-centre | 30 | Severe: 3 | Non-severe: 27 |
| Shi et al | Zhejiang Province | Designated hospitals in Zhejiang Province | Up to Feb 17 | Multi-centre | 487 | Severe: 49 | Mild: 438 |
| Zhao et al | Hunan Province | Designated hospitals in Hunan Province | NR | Multi-centre | 101 | Severe/critical: 14 | Common/Mild: 87 |
| Zhang et al | Wuhan, Hubei Province | No.7 hospital of Wuhan | Jan 16 to Feb 3 | Single-centre | 140 | Severe: 58 | Non-severe: 82 |
| Wu et al | Yancheng and Wuxi, Jiangsu province; Fuyang, Anhui Province | First People’s Hospital of Yancheng; Second People’s Hospital of Fuyang; Second People’s Hospital of Yancheng; Fifth People’s Hospital of Wuxi | Jan 20 to Feb 19 | Multi-centre | 280 | Severe/critical: 83 | Common/Mild: 197 |
| Zhang et al | Wuhan, Hubei Province | Xinzhou District People’s Hospital | Up to Mar 2 | Single-centre | 95 | Severe: 32 | Non-severe: 63 |
| Zheng et al | Wuhan, Hubei Province | Wuhan Union Hospital | Up to Feb 15 | Single-centre | 55 | Severe: 21 | Common: 34 |
| Han et al | Wuhan, Hubei province | Renmin Hospital of Wuhan University | Jan 1 to Feb 18 | Single-centre | 273 | Severe/critical: 75 | Mild: 198 |
| Xie et al | Wuhan, Hubei province | Wuhan Jinyintan hospital | Feb 2 to Feb 23 | Single-centre | 79 | Severe: 28 | Common: 51 |
3.3 | The demography

Twelve studies reported 409 males out of 747 patients in the severe group (54.8%) and 843 males in 1724 out of the Non-severe group (48.9%). The pooled OR was 1.30 (95% CI: 1.07 to 1.57), demonstrating that males were associated with significantly increased risk of severe Covid-19 (P = .007). Consistently, of 14 studies reporting the age of patients, it was revealed that older individuals were more susceptible to severe Covid-19 (WMD: 11.12, 95% CI: 6.70 to 15.55, P < .00001). The outcomes were explicitly expressed in Table 2.

3.4 | Comorbidity

In 7 eligible trials, hypertension was noted in 166 of 497 patients in the severe group (33.4%) and 151 of 973 patients in the non-severe group (15.5%). With pooled OR of 2.30 (95% CI: 1.35 to 3.92), it was demonstrated that patients with hypertension were associated with significantly increased risk of severe Covid-19 (P = .002). Consistently, with pooled OR of 2.62 for diabetes (95% CI: 1.27 to 5.44, P = .009), 4.02 for heart disease (95% CI: 2.08 to 7.77, P < .00001) and 4.20 for chronic obstructive pulmonary disease (95% CI: 1.61 to 10.95, P = .003), it was revealed that patients with diabetes, heart disease and chronic obstructive pulmonary disease were more susceptible to severe Covid-19. Conversely, with pooled OR of 1.81 for cerebrovascular disease (95% CI: 0.56 to 5.84, P = .32), 1.28 for chronic liver disease (95% CI: 0.60 to 2.71, P = .53), 2.12 for chronic kidney disease (95% CI: 0.80 to 5.61, P = .13) and 2.69 for tuberculosis (95% CI: 0.66 to 10.97, P = .17), it was demonstrated that patients with cerebrovascular disease, chronic liver disease, chronic kidney disease and tuberculosis were not associated with increased risk of severe Covid-19. What’s more, smoking did not statistically increase the risk of severe Covid-19 (OR: 1.07, 95% CI: 0.40 to 2.85, P = .90).

Overall, 4 trials reported any comorbidity with 226 of 398 patients in the severe group (56.8%) and 137 of 430 in the non-severe group (31.9%). With pooled OR of 3.61 (95% CI: 1.62 to 8.01), it was revealed that individuals with comorbidities were more susceptible to severe Covid-19 (P = .002). The outcomes were explicitly expressed in Table 2.

3.5 | Signs and symptoms

Among 9 studies reporting the clinical characteristics of fever in Covid-19, the incidence was 93.1% (552 in 593) in the severe group and 83.1% (795 in 957) in the non-severe group. With pooled OR of 1.93 (95% CI: 0.94 to 3.96), it was demonstrated that severe Covid-19 patients were associated with slightly increased risk of fever. But meta-analysis did not reveal any statistical difference (P = .07). Consistently, with pooled OR of 1.79 for expectoration (95% CI: 0.79 to 4.05, P = .17), 1.43 for headache (95% CI: 0.91 to 2.26, P = .12), 1.75 for fatigue (95% CI: 0.89 to 3.44, P = .11) and 2.22 for myalgia (95% CI: 0.65 to 7.52, P = .20), it was demonstrated that patients with expectoration, headache, fatigue and myalgia were unrelated to severity of Covid-19.

In 5 trials reporting data on dyspnoea, 82 of 192 patients in the severe group (42.7%) and 52 of 477 in the non-severe group (10.9%) were found to have dyspnoea. With pooled OR of 7.83 (95% CI: 1.75 to 34.99), it was demonstrated that patients with dyspnoea were more likely to progress into severe Covid-19 too (P = .007). The outcomes were explicitly expressed in Table 2.

3.6 | Laboratory findings

Of 7 studies reporting data on blood tests, lymphocyte count was revealed in all 7 studies. With pooled WMD of -0.42 (95% CI: -0.64 to -0.20), it was revealed that severe Covid-19 case was more likely to have decreased lymphocyte count when compared with non-severe case (P = .0002). However, no significant difference was found in leucocytes, neutrophils and monocyte count.

3.7 | Imaging features

Among 5 studies reporting data on chest CT, the incidence of bilateral pneumonia was 95.8% (162 in 219) in the severe group and 73.4% (378 in 515) in the non-severe group. With pooled OR of 1.48 (95% CI: 0.50 to 4.35), it was demonstrated that severe Covid-19 patient was associated with slightly increased risk of bilateral pneumonia. But meta-analysis did not reveal any statistical difference (P = .48). Consistently, with pooled OR of 0.98 for unilateral pneumonia (95% CI: 0.40 to 2.42, P = .97), 3.71 for ground-glass opacities (95% CI: 0.45 to 30.23, P = .22), 3.32 for consolidation (95% CI: 1.00 to 11.03, P = .05) and 8.23 for bronchial wall thickening (95% CI: 0.59 to 115.05, P = .12), it was demonstrated that unilateral pneumonia and ground-glass opacities consolidation and bronchial wall thickening were unrelated to the severity of Covid-19.

However, in 2 trials reporting data on reticulation in CT, 12 of 39 patients in the severe group (30.8%) and 40 of 145 in the non-severe group (27.9%) were found to have reticulation in chest CT. With pooled OR of 2.86 (95% CI: 1.01 to 8.14, P < .05), it was demonstrated that patients with reticulation in CT were more likely to progress into severe Covid-19.

In 2 trials reporting data on intrathoracic lymph node enlargement, 8 of 39 patients in the severe group (20.5%) and 0 of 145 in the non-severe group (0%) were found to have intrathoracic lymph node enlargement. With pooled OR of 31.90 (95% CI: 3.65
| Outcome | No. of study | Sample size | Sample size | OR or WMD (95% CI) | Heterogeneity | Difference |
|---------|-------------|-------------|-------------|---------------------|---------------|------------|
| **Demography characteristic** | | | | | | |
| Age | 14 | 771 | 1795 | 11.12 [6.70, 15.55] | P < .0001; I^2 = 92% | P < .00001 |
| Sex (male, year) | 12 | 409 in 747 (54.8%) | 843 in 1724 (48.9%) | 1.30 [1.07, 1.57] | P = .62; I^2 = 0% | P = .007 |
| **Comorbidity** | | | | | | |
| Hypertension | 7 | 166 in 497 (33.4%) | 151 in 973 (15.5%) | 2.30 [1.35, 3.92] | P = .03; I^2 = 57% | P = .002 |
| Diabetes | 7 | 88 in 497 (17.7%) | 65 in 973 (6.7%) | 2.62 [1.27, 5.44] | P = .02; I^2 = 61% | P = .009 |
| Heart disease | 7 | 46 in 497 (9.3%) | 29 in 973 (3.0%) | 4.02 [2.08, 7.77] | P = .29; I^2 = 18% | P < .0001 |
| Cerebrovascular disease | 2 | 10 in 344 (2.9%) | 4 in 248 (1.6%) | 1.81 [0.56, 5.84] | P = .66; I^2 = 0% | P = .32 |
| COPD | 5 | 20 in 492 (4.1%) | 4 in 598 (0.7%) | 4.20 [1.61, 10.95] | P = .42; I^2 = 0% | P = .003 |
| Chronic live disease | 4 | 13 in 476 (2.7%) | 30 in 883 (3.4%) | 1.28 [0.60, 2.71] | P = .45; I^2 = 0% | P = .53 |
| Chronic kidney disease | 4 | 12 in 476 (2.5%) | 10 in 883 (1.1%) | 2.12 [0.80, 5.61] | P = .34; I^2 = 11% | P = .13 |
| Tuberculosis | 2 | 9 in 344 (2.6%) | 2 in 248 (0.8%) | 2.69 [0.66, 10.97] | P = .47; I^2 = 0% | P = .17 |
| Smoke | 4 | 16 in 433 (3.7%) | 49 in 781 (6.3%) | 1.07 [0.40, 2.85] | P = .12; I^2 = 48% | P = .90 |
| Any | 4 | 226 in 398 (56.8%) | 137 in 430 (31.9%) | 3.61 [1.62, 8.01] | P = .003; I^2 = 78% | P = .002 |
| **Signs and symptoms** | | | | | | |
| Fever | 9 | 552 in 593 (93.1%) | 795 in 957 (83.1%) | 1.93 [0.94, 3.96] | P = .007; I^2 = 62% | P = .07 |
| Expectoration | 4 | 144 in 379 (38.0%) | 94 in 370 (25.4%) | 1.79 [0.79, 4.05] | P = .02; I^2 = 69% | P = .17 |
| Headache | 4 | 56 in 397 (14.1%) | 56 in 525 (10.7%) | 1.43 [0.91, 2.26] | P = .74; I^2 = 0% | P = .12 |
| Fatigue | 4 | 210 in 396 (53.0%) | 189 in 522 (36.2%) | 1.75 [0.89, 3.44] | P = .02; I^2 = 69% | P = .11 |
| Myalgia | 3 | 114 in 394 (28.9%) | 70 in 421 (16.6%) | 2.22 [0.65, 7.52] | P < .0001; I^2 = 90% | P = .20 |
| Dyspnoea | 5 | 82 in 192 (42.7%) | 52 in 477 (10.9%) | 7.83 [1.75, 34.99] | P < .0001; I^2 = 86% | P = .007 |
| **Laboratory test (×10^9 per L)** | | | | | | |
| Leucocytes count | 6 | 518 | 649 | 0.65 [-1.02, 2.32] | P < .0001; I^2 = 94% | P = .44 |
| Neutrophils count | 6 | 483 | 601 | 0.33 [-0.66, 1.33] | P < .0001; I^2 = 94% | P = .51 |
| Lymphocyte count | 7 | 539 | 683 | -0.42 [-0.64, -0.20] | P < .0001; I^2 = 92% | P = .0002 |
| Monocyte count | 3 | 384 | 391 | 0.01 [-0.06, 0.09] | P = .05; I^2 = 66% | P = .70 |

(Continues)
to 278.98, \( P = .002 \) it was demonstrated that patients with intrathoracic lymph node enlargement were more likely to progress into severe Covid-19.

In 2 trials reporting data on pleural effusions,\(^{15,21}\) 12 of 39 patients in the severe group (30.8%) and 9 of 145 in the non-severe group (6.2%) were found to have pleural effusions. With pooled OR of 10.84 (95% CI: 1.07 to 109.80, \( P = .04 \)) it was demonstrated that patients with pleural effusions were more likely to progress into severe Covid-19. The outcomes were explicitly expressed in Table 2.

### Table 2 (Continued)

| Outcome | No. of study | Sample size | OR or WMD (95% CI) | Heterogeneity | Difference |
|---------|--------------|-------------|-------------------|---------------|------------|
| Image feature in chest CT | | | | | |
| Bilateral pneumonia | 5 | 162 in 219 (95.8%) 378 in 515 (73.4%) | 1.48 [0.50, 4.35] | \( P = .09; I^2 = 53\% \) | \( P = .48 \) |
| Unilateral pneumonia | 3 | 47 in 154 (30.5%) 99 in 362 (27.3%) | 0.98 [0.40, 2.42] | \( P = .18; I^2 = 42\% \) | \( P = .97 \) |
| Ground-glass opacities | 2 | 39 in 39 (100%) 129 in 145 (89.0%) | 3.71 [0.45, 30.23] | \( P = .66; I^2 = 0\% \) | \( P = .22 \) |
| Consolidation | 2 | 30 in 39 (76.9%) 67 in 145 (46.2%) | 3.32 [1.00, 11.03] | \( P = .17; I^2 = 48\% \) | \( P = .05 \) |
| Reticulation | 2 | 12 in 39 (30.8%) 40 in 145 (27.9%) | 2.86 [1.01, 8.14] | \( P = .34; I^2 = 0\% \) | \( P < .05 \) |
| Bronchial wall thickening | 2 | 22 in 39 (56.4%) 25 in 145 (16.0%) | 8.23 [0.59, 115.05] | \( P = .004; I^2 = 88\% \) | \( P = .12 \) |
| Intrathoracic lymph node enlargement | 2 | 8 in 39 (20.5%) 0 in 145 (0%) | 31.90 [3.65, 278.98] | \( P = .67; I^2 = 0\% \) | \( P = .002 \) |
| Pleural effusions | 2 | 12 in 39 (30.8%) 9 in 145 (6.2%) | 10.84 [1.07, 109.80] | \( P = .13; I^2 = 57\% \) | \( P = .04 \) |

Abbreviations: COPD, chronic obstructive pulmonary disease; OR, odds ratio; WMD, weighted mean difference; 95% CIs, 95% confidence intervals.

3.8 | Publication bias

Publication bias statistics were determined by a funnel plot. The plot demonstrated asymmetry of the pooled effects where publication bias may exist (Figure 2).

4 | DISCUSSION

Up to now, this is the first meta-analysis to explore the clinical, laboratory and imaging factors associated with severe vs non-severe Covid-19. Through a systematic and comprehensive review of the current evidence published, 14 studies with a total of 2566 individuals (771 in the severe group and 1795 in non-severe group) were eligible for this meta-analysis,\(^{14-27}\) which retrieved the largest sample size compared with studies on the same topic.\(^{14-27}\) Overlapping patients were checked by examining the first author of the article and the origin of patients, since we recognised that different articles might report the same patients.

Currently, the National Health Commission (NHC) issued the China Guidelines for the Diagnosis and Treatment Plan of Novel Coronavirus (COVID-19), which defined the degree of severity of Covid-19 (ie, mild, common, severe and critical). As we all know, the treatment algorithm of Covid-19 depended on illness severity. The severity of the disease in most infected people is mild to moderate, and they can manage their symptoms at home without the need for hospitalisation. Most severe and critical patients required oxygen therapy and a minority of the patients needed invasive ventilation or even extracorporeal membrane oxygenation. Moreover, there were some patients who developed worsening respiratory failure and acute respiratory distress syndrome (ARDS) rapidly that required intubation.\(^{36}\) According to epidemiological investigation, severe illness occurred in 15.7% of the Covid-19 patients after admission to a hospital. As the clinical spectrum of Covid-19 ranges widely from mild illness to ARDS with a high risk of mortality, there is an urgent need for research to identify early markers of disease severity, which is of great value to clinicians for rapid and accurate diagnosis of Covid-19 severity.

Through the statistical analysis, it was demonstrated that patients in the severe Covid-19 group were older and had a greater number of comorbid conditions (eg, hypertension, diabetes and heart disease) than the non-severe group. Study found that about one-fifth of patients with COVID-19 developed heart disease, which increased the mortality rate.\(^{37}\) Severe and sudden inflammation of the heart muscle can cause arrhythmias and impair the heart’s ability to efficiently pump blood. Therefore, we believe that patients with a history of heart disease and with high blood pressure are at a higher risk of severe Covid-19 and death than the normal individuals. Compromised respiratory status on admission (eg, COPD) was
also associated with severe illness. These suggest that age and comorbidity may be risk factors for poor outcomes. Meanwhile, severe 2019-nCoV infection is more likely to affect males. These data were consistent with the recent report.\(^3\)\(^8\) What's more, our outcome did not support that smoking was associated with the severity of Covid-19 illness. Consistently, Lippi et al conducted a meta-analysis of current evidence and concluded that active smoking does not appear to be significantly associated with an enhanced risk of Covid-19 progression to severe disease, which further confirmed our results.\(^3\)\(^9\)

Common symptoms of Covid-19 at onset of illness were fever, dry cough, expectoration, myalgia, fatigue, and dyspnoea.\(^1\) However, some patients presented initially with atypical symptoms, such as diarrhoea and nausea.\(^4\)\(^0\)\(^4\)\(^1\) By statistically combining the data on common signs and symptoms, the incidence of fever, expectoration, headache, fatigue, myalgia and dyspnoea were more common in the severe group than in the non-severe group. However, only the incidence of dyspnoea was statistically different across groups. Individuals with severe Covid-19 might present with bilateral (95.8%) or unilateral (30.5%) lung pathological changes, ground-glass opacities (100%), consolidation (76.9%) and bronchial wall thickening (56.4%) in chest CT. However, no statistical difference was revealed when compared with the non-severe group. Although reticulation (30.8%), intrathoracic lymph node enlargement (20.5%) and pleural effusions (30.8%) were relatively rare, the meta-analysis revealed that patients with these manifestations in chest CT were more likely to be associated with severe Covid-19. The outcome was further

**FIGURE 2** Funnel plot for publication bias of age, sex, comorbidity, signs and symptoms, laboratory findings and image features in chest CT across severe group vs. non-severe group
confirmed in a study carried by Yuan et al, which investigated the association of radiologic findings with mortality of patients infected with Covid-19. However, only two studies were available for statistical analysis for the outcome of reticulation, intrathoracic lymph node enlargement and pleural effusions. The sample size of patients was small. And older individuals with comorbidities were more susceptible to severe Covid-19. Possible underlying diseases, such as lung cancer, could also give rise to lymph node enlargement and pleural effusion. Thus, we should understand the outcomes carefully. And the results need to be verified by large simple scale trials.

The results should be viewed with recognition of inherent limitations in this study. Firstly, although a broad review scope provides us with a larger sample size and finally adequate statistical power to detect a risk factor, articles reporting data comparing clinical characteristics between severe Covid-19 and non-severe Covid-19 were excluded for overlapping patients. One article that did not report the origin of patients was also excluded from this meta-analysis, which resulted in relative smaller sample size. However, their results further confirmed our conclusion.

Secondly, all eligible studies came from China, since the first Covid-19 was identified in Wuhan, China. Data from other countries are not acceptable right now. Thus, the outcomes of our study could not be considered conclusive on this topic. An update of this article is necessary when needed.

Thirdly, more and more articles on Covid-19 are being published every day. There might be lots of articles evaluating the clinical differences between severe and non-severe Covid-19 that are not published. And the funnel plot of this meta-analysis revealed that publication bias might exist. Thus, it is necessary for clinicians to interpret our outcomes carefully.

In conclusion, older males presenting with dyspnoea, whose blood routine tests revealed lymphopenia should gain more caution for which might be severe Covid-19. Patients with comorbidities, such as hypertension, diabetes and heart disease were more susceptible to severe Covid-19. Compromised respiratory status on admission (eg, COPD) was also associated with severe illness. Specially, although reticulation, intrathoracic lymph node enlargement and pleural effusions were relatively rare, meta-analysis revealed that patients with such presentations in chest CT were more likely to be associated with severe Covid-19.

Although lots of risk factors were filtrated in this article, exploration of predicted value of these factors in severe Covid-19 patients was impossible with aggregated data extracted from published studies. Further diagnostic articles evaluating how to differentiate severe from non-severe Covid-19 manifested in chest CT and studies assessing the relationship between clinical characteristics and severity of Covid-19 with the aid of logistic regression analysis are needed.

DISCLOSURES
The intent of this statement is to display our idea on severe Covid-19. There are no financial and personal relationships with other people or organisations that could inappropriately influence (bias) our work.

AUTHOR CONTRIBUTIONS
Conceptualisation, YJ Zhang and SL Han; methodology, YJ Zhang and SL Han; software, YJ Zhang and SL Han; validation, XF Sun and B Xie.; formal analysis, YJ Zhang and SL Han; investigation, YJ Zhang and SL Han; resources, YJ Zhang and SL Han; data curation, YJ Zhang and SL Han; writing—original draft preparation, YJ Zhang and SL Han; writing—review and editing, YJ Zhang and SL Han; visualisation, YJ Zhang and SL Han; supervision, WJ Feng; project administration, YJ Zhang and SL Han. All authors have read and agreed to the published version of the manuscript.

DATA AVAILABILITY STATEMENT
The data that support the finding of this study are available on request from the corresponding author upon reasonable request.

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