Risk factors associated with fatal outcomes of novel coronavirus infection pneumonia (COVID-19): A systematic review and meta-analysis

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Systematic Review

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Abstract

Background: The COVID-19 infection has caused 111652 deaths worldwide as of 13 April 2020. Risk factors for fatal outcomes of COVID-19 have varied across studies due to limited samples and have lacked effective qualitative and quantitative measurements. We performed a meta-analysis to evaluate risk factors for fatal outcomes of COVID-19.

Methods: Data on demographic, clinic, laboratory findings and complications were extracted. Quantitative and qualitative synthesis was conducted for weighted-mean-difference (*WMD*) and odds-ratio (*OR*).

Results: A total of 30 studies involving 5741 survivors and 1670 deaths were included. The death cases were significantly older than survivors (*WMD*=15.36, 95% *CI*: 12.90-17.82), male and smoking history showed higher risk to develop fatal outcome (*OR*=3.37, 95% *CI*: 2.27-5.01; *OR*=1.37, 95% *CI*: 1.02-1.83, respectively). The clinical symptoms including dyspnea (*OR*=4.63, 95% *CI*: 2.85-7.54), hemoptysis (*OR*=3.11, 95% *CI*: 1.26-7.56), malaise (*OR*=2.44, 95% *CI*: 1.49-3.97). comorbidities with coronary heart disease (*OR*=4.36, 95% *CI*: 1.91-9.97), COPD (*OR*=3.70, 95% *CI*: 2.03-6.73) and cardiovascular disease (*OR*=3.45, 95% *CI*: 2.54-4.70). Compared to survivors, many laboratory indexes increased in deaths group, including serum ferritin (*WMD*=741.47, 95% *CI*: 566.77-916.16), lactate dehydrogenase (*WMD*=226.86, 95% *CI*: 177.08-276.64) and myoglobin (*WMD*=102.58, 95% *CI*: 65.12-140.04), and the decreased indexes included *PaO₂/FiO₂* (*WMD*=-71.61, 95% *CI*: -134.11 to -9.11), platelets (*WMD*=-41.09, 95% *CI*: -47.33 to -34.85) and *PaO₂* (*WMD*=-26.09, 95% *CI*: -38.9 to -13.29). Main complications contributed to the fatal outcome included sepsis (*OR*=184.61, 95% *CI*: 33.43-1019.42), shock (*OR*=133.76, 95% *CI*: 36.86-485.34) and respiratory failure (*OR*=47.37, 95% *CI*: 20.65-108.66).

Conclusion: The main risk factors associated with fatal outcome of COVID-19 involved male, older age, smoking history, chronic medical conditions including coronary heart disease, COPD and cardiovascular disease, clinical symptoms including dyspnea, hemoptysis and malaise, the increased laboratory indexes including serum ferritin, lactate dehydrogenase and myoglobin, the decreased indexes including *PaO₂/FiO₂*, platelets and *PaO₂*, main complications including sepsis, shock and respiratory failure. These factors could be considered in triaging patients and allocating medical resources when such medical resources are scarce, devising improved protocols for patient diagnosis and management, and developing new drugs and other therapies to treat COVID-19 patients.

Background

Since a novel coronavirus (COVID-19)-induced pneumonia was first reported in December 2019, it has spread rapidly worldwide [1]. On 11 March 2020, the World Health Organization (WHO) defined it as pandemic disease [2], and as of 13 April 2020, a total of 1773084 cases and 111652 deaths (6.30%) have been confirmed in 212 countries/territories/areas worldwide [3]. The outbreak of COVID-19 with high fatality rate has seriously threatened global health. The numbers of cases with COVID-19 increased sharply in a short period of time in many cities have caused instantaneous shortage of medical resources and even paralysis of the medical system [4-6]. It is a major challenge for many countries to identify what measures could be used to avoid severe illness or even death and how medical resources can be more efficiently allocated during a COVID-19 pandemic.

A series of studies have reported its clinical characteristics [7-8] with about 15% of those infected having severe illness and 5% have critical illness [9], with some patients presenting with organ dysfunction including acute respiratory distress syndrome (*ARDS*), multiple organ dysfunction syndrome (*MODS*) and even death [10]. The progress of some patients with severe COVID-19 illness deteriorates rapidly. Under these conditions, it is important to explore risk factors associated with fatal outcomes of COVID-19. Several clinical features and laboratory findings have been recognized as high risk factors associated with the fatal outcomes of patients with COVID-19 such as older age, elevated troponin T, high-sensitivity c-reactive protein (*hs-CRP*), and D-dimer [11-12]. However, each study published to date has been based on relatively limited samples and has lacked qualitative and quantitative effective measurements, risk factors associated with fatal outcome of COVID-19 also varied across studies. The current understanding of risk factors for death in patients with COVID-19 is still limited.

In this study, we systematically analyzed the data of demographical, clinical features, chronic medical conditions, laboratory findings and complications between survivors and deaths, in order to explore critical risk factors associated with fatal outcome of COVID-19, which could be used to sort patients and allocate scarce medical resources.

Methods

Our meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols (*PRISMA-P*) guidelines [13].

Search strategy and selection criteria

A comprehensive systematic literature search on the studies published from December 31, 2019 to April 2, 2020 was conducted through the databases including PubMed, Web of Science, BioRxiv, MedRxiv and China National Knowledge Infrastructure (CNKI). The search strategy was as follows: (COVID-19 OR 2019-nCoV OR SARS-CoV-2 OR novel coronavirus) (Additional table 1). The studies included with those sufficient data (e.g. categorical variables: events cases/total cases or continuous variables: total cases, mean/median and standard deviation (*SD*) /interquartile range (*IQR*)) described the demographical and clinical characteristics (e.g. symptoms, laboratory findings, complications) of deaths and survivors. The duplicate publications data, case reports, review and population with possible severe selection bias (e.g. research based on diabetic patients or haematological disorders patients or COVID-19 patients with ARDS) were excluded. The data on age was a continuous variable in our study; if the mean and standard deviation were not provided, the data on age was also excluded. If a study included more than one independent dataset of deaths and survivors, each of them was formed a separate dataset in the meta-analysis.

Screening, data extraction and quality assessment

After removing duplicates, two reviewers independently screened searching results based on the eligibility criteria and uncertainties were resolved by consensus. The collected data include basic information of the studies (e.g. first author, journal name), demographic data (e.g. age, gender), clinical features (e.g. fever, cough), laboratory findings (e.g. leucocytes, lymphocyte), and complication (e.g. shock, ARDS). The new castle-Ottawa Scale was suitable for non-randomized studies such as case-control or cohort studies and used to assess the quality of each study [14]. The scale consists of 8 items, including 3 parts: selection, comparability and exposure or outcome. Star awarded was adopted for each quality item assessment with a full score of nine stars. The EndNote (version X9) was used to manage the articles and citations.

Statistical analysis

The variables with unit discordance were converted units to standard measurement. Continuous variables were described by mean and SD. Continuous variables presented by median and IQR in the original lectures were converted to mean and SD by using an online tool (<http://www.comp.hkbu.edu.hk/~xwan/median2mean.html>) developed by Dehui Luo [15]. For selected studies, the meta-analysis was conducted. The weighted mean difference (WMD) and its 95% confidence interval (95% CI) was calculated to estimate statistical differences of the continuous variables in death and survivor group, while the odds ratio (OR) and its 95% CI was calculated to estimate whether the categorical variables increased the risk of death. I^2 was used to evaluate the heterogeneity among each study and the random-effects model was chosen when the $I^2 > 50\%$ showed the high heterogeneity among the data, otherwise fixed effect model was used [16]. The funnel plot and Egger weighted regression was used to appraised potential publication bias [17]. All data clearing and analyses were performed using Microsoft Excel 2016 and R version 3.2.3.

Results

Search results

A total of 9027 records were identified through database search. The titles and abstracts of 4855 published literature were screened after duplicates removed and then 166 articles were selected for detailed assessment. Among them, 28 studies had no clinical feature data, 88 studies did not report the clinical outcome of survivors and deaths, 15 studies had only deaths clinical outcome, 3 studies included population with possible selection bias and 2 studies were duplicated publications data. Finally, 30 studies containing 32 datasets with 5741 survivors and 1670 deaths were included to perform the meta-analysis in our study (Figure 1). All studies were from China. The details were showed in table 1.

Table 1. Studies and characteristics of COVID-19 patients included in this meta-anlysis

Study ID	Journal name	Published year	Study period	Region	Survivor cases (median age, years)	Death cases (median age, years)	Female/male	Study Quality [19]
Xiaobo Yang ^[18]	The Lancet	2020	2019/12/24-2020/01/26	Wuhan, China	20 (51.9)	32 (64.6)	17/35	7
Zhibing Lu ^[11]	The Lancet	2020	2019/01/01-2019/02/15	Wuhan, China	92 (53.0)	31 (72.0)	62/61	7
Fei Zhou ^[12]	The Lancet	2020	2019/12/29-2020/01/31	Wuhan, China	137 (52.0)	54 (69.0)	72/119	7
Dawei Wang ^[19]	Research Square	2020	2020/02/10	Wuhan, China	88 (46.1)	19 (72.7)	50/57	7
Qirong Ruan ^[20]	Intensive Care Med	2020	NA	Wuhan, China	82 (50.0)	68 (67.0)	48/102	6
Yan Deng ^[21]	National Medical Journal of China	2020	2020/01/01-2020/2/21	Wuhan, China	116 (40.0)	109 (69.0)	101/124	6
Min Chen ^[22]	Herald of Medicine	2020	2020/01/24-2020/02/08	Wuhan, China	23(49.0)	6(70.0)	NA	6
Xiaoxiong Liu ^[23]	The Lancet Respiratory Medicine	2020	2020/01/01-2020/01/31	Wuhan, China	74(48.2)	12(66.7)	51/35	6
Jin Shang ^[24]	The Lancet	2020	2019/12/27-2020/02/17	Hubei, China	226(46.0)	51(67.0)	157/120	7
Meng Luo ^[25]	Chinese Traditional and Herbal Drugs	2020	2020/01/17-2020/02/25	Wuhan, China	406(NA)	69(NA)	244/231	7
Zhongyong Chang ^[26]	Drugs & Clinic	2020	2020/01-2020/02	Wuhan, China	130(NA)	20(NA)	NA	6
Ning Tang ^[27]	Journal of Thrombosis and Haemostasis	2020	2020/01/01-2020/02/03	Wuhan, China	162(52.4)	21(64.0)	85/98	6
Tao Bai ^[28]	The Lancet Respiratory Medicine	2020	2019/12/26-2020/1/31	Wuhan, China	91(50.0)	36(67.0)	47/80	7
Mingli Yuan ^[29]	PLOS ONE	2020	2020/01/01-2020/01/25	Wuhan, China	17(55.0)	10(68.0)	14/13	6
Chengyun Liu ^[30]	The Lancet Respiratory Medicine	2020	2020/01/07-2020/02/11	Wuhan, China	283(46.4)	22(65.6)	163/142	7
Gu-qin Zhang ^[31]	The Lancet Infectious Diseases	2020	2020/01/02-2020/02/10	Wuhan, China	23(62.0)	9(76.0)	10/22	7
Bo Hu ^[32]	Research Square	2020	2020/01/08-2020/02/09	Wuhan, China	20(56.0)	16(66.5)	12/24	7
Yingjie Wu ^[33]	MedRxiv	2020	2019/12-2020/02/02	Wuhan, China	280(NA)	17(NA)	150/147	6
Shuai Zhang ^[34]	The Lancet Infectious Diseases Manuscript Draft	2020	2020/01/12-2020/02/03	Wuhan, China	268(56.0)	47(66.0)	140/175	7
Wen Cao ^[35]	The Lancet(Manuscript Draft)	2020	2020/01-2020/02	Wuhan, China	27(56.0)	34(65.0)	25/36	7
Sheng Zhang ^[36]	The Lancet Infectious	2020	2019/12/29-2020/02/17	Wuhan, China	176(49.9)	86(66.5)	122/140	7

	Diseases(Manuscript Draft)							
Juyi Li ^[37]	The Lancet Infectious Diseases(Manuscript Draft)	2020	2020/01/01-2020/02/20	Wuhan, China	17(55.0)	42(70.0)	NA	7
Tao Chen ^[38]	BMJ	2020	2020/01/13-2020/02/28	Wuhan, China	161(51.0)	113(68.0)	103/171	7
Bin Zhu ^[39]	MedRxiv	2020	2020/01/29-2020/02/23	Wuhan, China	91(57.9)	16(68.1)	53/54	6
Jianfeng Xie-1 ^[40]	MedRxiv	2020	2020/01-2020/02	Wuhan, China	144(56.0)	155(69.0)	155/144	6
Jianfeng Xie-2 ^[40]	MedRxiv	2020	2020/01-2020/02	Wuhan, China	76(47.0)	69(67.0)	50/95	6
Meng Jiang-1 ^[41]	The Lancet (Manuscript Draft)	2020	2019/12/28-2020/03/10	Wuhan, China	1516(60.0)	201((70.0)	843/874	7
Meng Jiang-2 ^[41]	The Lancet (Manuscript Draft)	2020	2019/12/28-2020/03/10	Wuhan, China	161(62.1)	27(66.7)	90/98	7
Lin Fu ^[42]	The Lancet Respiratory Medicine	2020	2020/01/01-2020/01/30	Wuhan, China	166(NA)	34(NA)	101/99	7
Ning Tang ^[43]	Journal of Thrombosis and Haemostasis	2020	2020/01/01-2020/02/13	Wuhan, China	315(63.7)	134(68.7)	181/268	7
Xiaomin Luo ^[44]	EBioMedicine	2020	2020/01/30-2020/02/25	Wuhan, China	303(49.0)	100(71.0)	210/193	6
Nan Zhang ^[45]	Research Square	2020	2020/01/09-2020/02/19	Wuhan and Huaihua, China	50(62.6)	10(70.6)	17/43	6

Demographical and clinical features

Compared to COVID-19 survivors, the deaths were significantly older than survivors (MD=15.36, 95% CI: 12.90-17.82), and male showed higher risk to develop fatal outcome than female (OR=3.37, 95% CI: 2.27-5.02) (Figure 2A). The clinical symptoms including dyspnea (OR=4.63, 95% CI: 2.85-7.54), hemoptysis (OR=3.28, 95% CI: 1.36-7.91), malaise (OR=2.44, 95% CI: 1.49-3.97), sputum production (OR=1.51, 95% CI: 1.13-2.03) and fever (OR=1.33, 95% CI: 1.09-1.63) were more likely to predict the death outcome (Figure 2B). The time from onset of symptom to death was faster than the time from onset of symptom to discharge (WMD=-5.78, 95% CI: from -10.36 to -1.20) and death cases showed shorter hospital stay (WMD=-3.66, 95% CI: from -6.06 to -1.26) (Additional figure 1). The patients with chronic medical conditions were association with fatal outcome (OR=2.87, 95% CI: 2.51-3.29). Among them, coronary heart disease (OR=4.36, 95% CI: 1.91-9.97) showed highly dangerous and followed by any of chronic medical conditions (OR=4.3, 95% CI: 2.68-7.00), COPD (OR=3.70, 95% CI: 2.03-6.73), cardiovascular disease (OR=3.45, 95% CI: 2.54-4.70), cerebrovascular disease (OR=3.41, 95% CI: 2.33-4.98), lung disease (OR=3.36, 95% CI: 2.44-4.65), malignancy (OR=2.81, 95% CI: 1.60-4.92), hypertension (OR=2.81, 95% CI: 2.15-3.67), heart disease (OR=2.54, 95% CI: 1.64-3.93), chronic kidney disease (OR=2.17, 95% CI: 1.14-4.10), diabetes (OR=2.12, 95% CI: 1.77-2.54), smoking history (OR=1.37, 95% CI: 1.02-1.83) (Figure 4A, Additional figure 2).

Vital signs and laboratory findings

Compared to survivors, many indexes increased in deaths group, including heart rate (WMD =5.36, 95% CI: 3-7.72), respiratory rate (WMD=3.04, 95% CI: 1.95-4.13), systolic pressure (WMD=7.62, 95% CI: 2.56-12.68), leucocytes (WMD=3.47, 95% CI: 3.14-3.81), neutrophils (WMD=3.64, 95% CI: 2.87-4.42), neutrophil-to-lymphocyte ratio (WMD=9.84, 95% CI: 7.19-12.5), prothrombin time (WMD=1.05, 95% CI: 0.64-1.45), D-dimer (WMD=4.68, 95% CI: 2.94-6.42), interleukin- 6 (*IL-6*) (WMD=17.78, 95% CI: 10.57-25), hs-CRP (WMD=59.55, 95% CI: 42.13-76.96), procalcitonin (WMD=0.22, 95% CI: 0.12-0.32), serum ferritin (WMD=741.47, 95% CI: 566.77-916.16), high-sensitive cardiac

troponin I (WMD=35.25, 95% CI: 19.67-50.82), lactate dehydrogenase (WMD=226.86, 95% CI: 177.08-276.64), creatine kinase (WMD=55.82, 95% CI: 21.02-90.61), myoglobin (WMD=102.58, 95% CI: 65.12-140.04), aspartate aminotransferase (*ALT*) (WMD=6.89, 95% CI: 0.56-13.21), alanine aminotransferase (*AST*) (WMD=14.44, 95% CI: 10.94-17.94), serum creatinine (WMD=16.62, 95% CI: 11.69-21.54), γ -glutamyl transpeptidase (WMD=11.37, 95% CI: 3.3-19.43), total bilirubin (WMD=4.3, 95% CI: 3.18-5.42), direct bilirubin (WMD=2.61, 95% CI: 1.43-3.79) and blood urea nitrogen (WMD=3.43, 95% CI: 2.48-4.39). The decrease indexes included diastolic pressure (WMD=-6.11, 95% CI: -11.97 to -0.25), PaO₂/FiO₂ (WMD=-71.61, 95% CI: -134.11 to -9.11), PaO₂ (WMD=-26.09, 95% CI: -38.9 to -13.29), SpO₂ (WMD=-8.83, 95% CI: -12.03 to -5.62), lymphocyte (WMD=-0.31, 95% CI: -0.43 to -0.19), platelets (WMD=-41.09, 95% CI: -47.33 to -34.85), and albumin (WMD=-4.76, 95% CI: -5.14 to -4.38) (Figure 3, Additional table 2).

Complications

Nine complications were identified contributed to the fatal outcome, including sepsis (OR=184.61, 95% CI: 33.43-1019.42), shock (OR=133.76, 95% CI: 36.86-485.34), respiratory failure (OR=47.37, 95% CI: 20.65-108.66), ARDS (OR=45.24, 95% CI: 17.49-117.02), acute cardiac injury (OR=30.15, 95% CI: 12.39-73.35), secondary infection (OR=26.4, 95% CI: 14.96-46.59), acute kidney injury (OR=20.61, 95% CI: 12.86-33.02), coagulopathy (OR=19.72, 95% CI: 11.42-34.07) and acute liver injury (OR=9.67, 95% CI: 1.5-62.58) (Figure 4B, Additional figure 3).

Discussion

In this study, the data come exclusively from early studies from China, and this is the first time they have been systematically pooled and analyzed and published in English. It was a large-scale study for risk factors associated with fatal outcome of COVID-19, with a total of 7411 subjects from 30 studies. Samples sizes in these studies ranged from 27 to 1717. Among these studies, 6 researches included over 300 patients and 4 researches below 50, and the majority were between 100 and 300. The overlapping samples had been reported in two of Luo's studies and finally the study with bigger sample size was selected [44]. The pre-print of Lin's study was excluded when the published version was available [42]. All studies included were from China. No study about risk factors to fatal outcome has been reported outside China as of April 2, 2020.

Our results showed that males were at higher risk to fatality of COVID-19 infection, and the same phenomenon was also observed in SARS-Cov [46]. The decreased susceptibility of female to viral infections could be interpreted as the protection of robust adaptive and innate immunity from sex hormones and the X chromosome [47]. Like many other infectious diseases, the elderly patients were more likely to develop fatal outcome due to lower immunity, poor self-health status and chronic medical conditions [48]. In this study, the mean age was found to be significantly higher among deaths than that of survivors, with a weighted mean difference of 15.36 years (12.90-17.82). This result was supported by the summary report of 44672 confirmed cases in China, in which, the case-fatality rate was 2.3% in all infected individuals, but 14.8% in individuals aged more than 80 years, and 8.0% in individuals aged 70-79 years [9]. In Italy, US and Korea, the COVID-19 deaths were also mainly observed among older, male, and patients who have multiple comorbidities [49-51], but it has not been reported whether differences between survivals and deaths were significant from these countries. 22% of current smokers and 46% of ex-smokers develop severe complications [52], with our study showing that patients infected with COVID-19 with smoking history were 1.37 times (95% CI: 1.02-1.83) more likely to have fatal outcome. In this study, dyspnea was shown to be a large risk contributing to fatal outcomes with pooled OR of 4.63 (2.85-7.54). Dyspnea was reported significantly higher in death group than survivors [29, 34], but the effect values for dyspnea have not been reported. Though fever was inconsistent in some studies [19-21], it also served as risk factor in our study. Hemoptysis, malaise and sputum production were infrequently reported in the COVID-19 fatal patients [18, 20, 22], but proved to be factors when integrated in the larger-scale sample size from each research, especially for hemoptysis with an OR of 3.11 (1.26-7.56). Our results indicate that patients with chronic medical conditions were identified as high risk factors for poor prognosis, including patients with coronary heart disease, cardiovascular disease, hypertension and lung disease [41-42,44]. Furthermore, our analysis also indicates that malignancy, diabetes, COPD, cerebrovascular disease, chronic kidney disease and heart disease were also risk factors, though they varied across the previous studies [18-21, 34-38].

The above factors could be used to discriminate the vulnerable populations who are prone to develop fatal outcomes of COVID-19 and provide targets suggestions in a public health response. The specific susceptibility for COVID-19 was found in Italy with overall fatality rate up to 7.2% due to population aging [53]. It is urgent for Italy to guarantee enough intensive care support and access when facing the increasing number of infected and severe cases. Knowledge on prevalence of chronic medical conditions in the population might help to focus the public health efforts such as risk communication, health inquiry, self-protection and screening of asymptomatic individuals in the target high risk population. It was also could be collected by physician's interrogation at the first visit of patients. Consideration of the numbers of cases with COVID-19 might increase sharply in a short period of time and medical resources might be instantaneous scarce.

These factors could be considered at the first visit to sort patients and allocate medical resources. In the early stage of COVID-19 pandemic, the incidence and mortality of COVID-19 in Wuhan was dozen times higher than that in other regions which was leading to an extreme shortage of medical resources including diagnostic agents, hospital beds in designated hospitals and medical staff. Similarly, higher fatality and lower cure rates were found in cities where medical resources were scarce [54]. Assessing these factors might provide early clinical management decision suggestions, improve allocative efficiency and relieved pressure on medical resources as well as guide the subsequent treatments and distribution of medical resources in which patients should be given high-level treatments or paid close attention.

Besides, in our study, some blood counts, coagulation profiles, inflammatory biomarkers, cardiac injury biomarkers, kidney and liver injury biomarkers were found to be associated with the fatal outcome of COVID-19. It has been reported that COVID-19 could directly attack ACE2-expressing cells which could be found in the lung, heart and kidney; therefore, the virus could invade and damage these organs [10]. The aggravation of the disease was related to the secondary systemic, inflammatory response and cytokine storm with critically ill patients developing to ARDS, septic shock, multiple organ failure and eventually death [55]. Notably, there were significantly difference of severe complications between deaths and survivors such as sepsis, shock and ARDS. The target organ injure were most commonly in the death cases with presented the abnormalities of the relevant biomarkers. In the Liu study, all 25 death cases were died of respiratory failure [56]. Several biomarkers of cardiac injury including the increased high-sensitive cardiac troponin I, myoglobin, creatine kinase, lactate dehydrogenase, AST and AST/ALT ratio, increased risk of death in patients with COVID-19 [42]. The COVID-19 patients presented kidney disease with significantly higher risk for in-hospital death and showed elevated of the creatinine and blood urea nitrogen [57]. Secondary infection usually occurred after ARDS, acute cardiac injury and acute kidney injury and showed highly risk which contributed to the death [12].

As the disease progresses, many factors in the course of the disease may develop into risk factors for death. It was reported that improved and optimized diagnosis and treatment strategies were critical for saving severe and critical patients [58]. Research on the risk factors leading to the death of COVID-19 can also help reasonably predict and distinguish the high-risk patients who were prone to develop the poor prognosis as early as their initial contact with health services. However, the studies included in this meta-analysis were all from China. It is unclear whether these factors associated with fatal outcome varies among epidemics of different country. More studies from different countries are needed in the future.

Conclusion

This was a large-scale study for risk factors associated with fatal outcome of COVID-19, with a total of 7411 subjects from 30 studies, all from China. The main risk factors associated with fatal outcome of COVID-19 involved male, older age, smoking history, chronic medical conditions including coronary heart disease, COPD and cardiovascular disease, clinical symptoms including dyspnea, hemoptysis and malaise, the increased laboratory indexes including serum ferritin, lactate dehydrogenase and myoglobin, the decreased indexes including PaO₂/FiO₂, platelets and PaO₂, main complications including sepsis, shock and respiratory failure. These risk factors could be considered to sort patients and allocate medical resources when medical resources are scarce. The data come exclusively from early studies from China, and this is the first time they have been systematically pooled and analyzed and published in English, and it can be a major contribution to further analysis of similar data coming from Europe and North America during the current second wave of COVID-19.

Abbreviations

COVID-19, coronavirus infection pneumonia 2019

WMD, weighted-mean-difference

OR, odds-ratio

ARDS, acute respiratory distress syndrome

MODS, multiple organ dysfunction syndrome

hs-CRP, high-sensitivity c-reactive protein

PRISMA-P, Preferred Reporting Items for Systematic Reviews and Meta-Analyses Protocols

CNKI, China National Knowledge Infrastructure

SD, standard deviation

IQR, interquartile range

IL-6, interleukin-6

ALT, aspartate aminotransferase

AST, alanine aminotransferase

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors have no conflicts of interest relevant to this article to disclose.

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Authors' Contributions

SY, LL, CZ and Robert Hecht designed the study. CC, DY, ZY, GT, XL, CH, XF, CD and LL collected data. CC, DY, and ZY analyzed data. JW, CW and WW checked the data and results.

CC, DY and ZY interpreted data and wrote the report. SY, LL, ZH and Robert Hecht revised the report from preliminary draft to submission. SY supervised the study. All authors have read

and approved the manuscript

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Figures

Figure 1

Flow diagram of the study selection process for this meta-analysis

Figure 2

The forest plots of meta-analysis on demographical and clinical features. (A) The forest plots of meta-analysis on age between deaths and survivors of COVID-19 patients; (B) The forest plots of meta-analysis on male, fever, sputum production, hemoptysis, dyspnea and malaise between deaths and survivors of COVID-19 patients.

Figure 3

The estimated weighted mean difference on laboratory findings.(A) The estimated weighted mean difference on vital signs and blood counts between deaths and survivors of COVID-19 patients. (B) The estimated weighted mean difference of coagulation profiles and inflammatory biomarkers between deaths and survivors of COVID-19 patients. (C) The estimated weighted mean difference on cardiac injury biomarkers between deaths and survivors of COVID-19 patients. (D) The estimated weighted mean difference on kidney and liver injury biomarkers between deaths and survivors of COVID-19 patients.

Figure 4

The pooled odd ratio on chronic medical conditions and complications. (A) The pool odd ratios of chronic medical conditions between deaths and survivors of COVID-19 patients; (B) The pool odd ratios of complications between deaths and survivors of COVID-19 patients.

Supplementary Files

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