Clinical, laboratory, and radiologic findings associated with mortality in COVID-19: A systematic review and meta-analysis

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Abstract

Although there has been a surge in reports on coronavirus disease 2019 (COVID-19), the clinical signs and findings associated with fatal outcomes have rarely been studied. This systematic review and meta-analysis aimed to investigate the clinical, laboratory, and radiologic features associated with mortality in COVID-19. A comprehensive search was performed using PubMed, Embase, Web of Science, and other databases including government sources, for articles and reports published until May 1, 2020. We extracted the number of events (mortality and non-mortality) from case series and case-control and cross-sectional studies. Hazard ratios (HR) of each finding were extracted from studies with time-to-outcome analysis. In total, 23 studies met the inclusion criteria. Of them, 18 studies were case-control, cross-sectional, and case series study. Whereas, only 5 studies included time-to-outcome analysis. Male sex, age over 80 years, dyspnea, cardiovascular disease, chronic kidney disease, increased troponin I level, acute respiratory distress syndrome, acute kidney injury, and need of invasive mechanical ventilation were significantly associated with mortality. The identification of patients at higher risk of mortality has an utmost importance to achieve better treatment outcomes. The findings from our study may aid the prioritization in times of severe shortages of medical resources. Further studies analyzing diverse demographic and geographic populations are needed to generalize the findings from this study.

Introduction

On December 31, 2019, Chinese Health officials informed the World Health Organization (WHO) of 41 cases of unusual pneumonia in Wuhan city, Hubei Province (1). The causal virus was named 'severe acute respiratory syndrome coronavirus 2' (SARS-CoV-2), due to its similarity to the coronavirus responsible for severe acute respiratory syndrome, SARS-CoV. The disease caused by SARS-CoV-2 was later named 'coronavirus disease 2019' (COVID-19). Similar to other *Betacoronaviruses*, such as Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and SARS-CoV, human-to-human transmission of SARS-CoV-2 has been confirmed (2, 3).

COVID-19 is highly contagious and has rapidly spread worldwide (4). On January 30, 2020, WHO declared the novel coronavirus (2019-nCoV) outbreak a public health emergency of international concern. As of May 8, 2020, 3,822,989 cases of COVID-19 have been reported in 213 countries, resulting in 265,084 deaths, leading to the declaration of COVID-19 as a pandemic.

The clinical spectrum of COVID-19 varies from asymptomatic infection to severe illness with respiratory failure, multiple organ failure, and even death (5, 6). There are no approved antiviral drugs or vaccines against COVID-19, so supportive care for symptoms like dyspnea and protecting multi-organ function may be the best practice for preventing fatal outcomes (7). For handling the current explosive number of cases with limited medical resources, it is crucial to identify high-risk groups that require intensive treatment and close monitoring (7). Although many studies reported epidemiologic and clinical characteristics of COVID-19, there has rarely been a comprehensive review of the signs and findings that are more frequently observed in patients with fatal outcomes. Therefore, the purpose of this systematic review and meta-analysis was to investigate the clinical, laboratory, and radiological findings of mortality cases comparing to non-mortality cases.

Results

Study selection and characteristics

The PRISMA flow diagram is presented in Figure 1. Among 2,012 publications screened, 138 full-text articles were assessed for their eligibility. A total of 23 studies were qualitatively analyzed (Table 1 and Supplementary Table S1)(6, 7, 9–29). In total, 227,856 patients with COVID-19 and 18,038 mortality cases were identified. Of them, 18 studies were case-control, cross-sectional, and case series studies. Whereas, only five studies included time-to-outcome analysis. The Newcastle-Ottawa scale for assessing the quality of case-control studies and cohort studies is presented in Supplementary Tables S2 and S3. The summary statistics of the former studies are shown in Figure 2. However, the latter studies could not be meta-analyzed since the findings and their definitions were highly heterogeneous despite the insufficient number of analyzed studies. Therefore, we performed only qualitative synthesis for longitudinal studies reporting HRs (Table 2).

Demographic characteristics and clinical symptoms

Males (OR, 1.79; 95% confidence interval [CI], 1.59–2.01) showed higher mortality than females. Among the age groups of COVID–19 patients, age over 80 years (OR, 7.56; 95% CI, 4.26–13.44) and age between 60 and 80 years (OR, 2.37; 95% CI, 1.47–3.83) were strongly associated with mortality (Figure 2). Furthermore, age over 65 years (HR 6.07; 95% CI 1.65–22.35) had a higher risk of mortality (Table 2) (14). However, there was a possible publication bias among the studies that reported age under 20 years and age between 40 and 60 years.

Among the clinical symptoms of COVID–19, tachypnea (OR, 8.88; 95% CI, 5.64–13.97) and dyspnea (OR, 4.83; 95% CI, 2.85–8.16) showed the strongest association with mortality compared to any other symptoms such as fever (OR, 0.99; 95% CI, 0.71–1.38) or cough (OR, 1.48; 95% CI, 0.67–3.23). However, possible publication bias was detected among the studies reporting fever.

Comorbidities

Chronic kidney disease (CKD) (OR, 6.32; 95% CI, 3.62–11.03) and cardiovascular disease (OR, 5.06; 95% CI, 3.54–7.24) showed considerable associations with mortality (Figure 2). Chronic liver disease (OR 1.36; 95% CI 0.68–2.74) also exhibited a positive association. Moreover, the presence of one or more comorbidities (HR 2.13; 95% CI 1.39–3.26) was strongly associated with mortality (Table 2) (20). However, there was a possible publication bias among the studies reporting diabetes.

Laboratory findings and radiologic findings

Increased troponin I level (TnI) (OR, 28.31; 95% CI, 10.55–75.96), increased pro-calcitonin level (OR, 12.70; 95% CI, 6.71–24.03), and leukocytosis (OR 6.57; 95% CI 2.41–17.91) were more strongly associated with higher mortality than other laboratory findings (Figure 2). Among radiologic findings, patients with bilateral lung involvement in computed tomography (CT) findings (OR, 1.80; 95% CI, 0.79–4.10) had a higher risk of mortality.

Complications and clinical courses

Some patients developed complications such as acute respiratory distress syndrome (ARDS) or acute kidney injury (AKI) after hospital admission. ARDS (OR, 57.58; 95% CI, 16.76–197.80) and AKI (OR, 24.42; 95% CI, 8.78–67.93) had a higher risk of mortality (Figure 2). Moreover, acute cardiac injury (HR 3.89; 95% CI 2.51–6.01) was strongly associated with mortality (Table 2) (19). Both the need of invasive mechanical ventilation (OR, 31.30; 95% CI, 9.99–98.06) and the need of non-invasive mechanical ventilation (OR, 14.15; 95% CI, 8.11–24.67) were associated with higher mortality. In addition, the mortality rate was higher among patients treated with extracorporeal membrane oxygenation (ECMO) (OR, 10.28; 95% CI, 2.62–40.38).

Discussion

This study demonstrated that COVID–19 patients with mortality had distinct characteristics in their clinical, laboratory, and radiologic findings compared to patients with non-mortality. Amongst a few recent systematic reviews on COVID–19, Wang et al. reported the relationship between severity of COVID–19 and comorbidities by analyzing ten studies from China (30); Li et al. focused on analyzing COVID–19 patients' clinical characteristics and overall fatality rate by analyzing six studies from China (31). Zheng et al. analyzed risk factors of critical and mortal cases with 12 studies from China (32). However, previous studies on COVID–19 were limited to the literature from China despite the fact that the Western countries have become the new COVID–19 ground zero (32–34). In addition, the reports from government data source and the studies with time-to-event analysis were rarely analyzed.

Demographic characteristics

Age is considered the most deterministic factor that affects the clinical outcome in patients with COVID–19. Our data agreed with the previous finding that fatality rate is closely associated with the patients' age (7). The pediatric population (age 0–20 years) reported only two fatality out of 17,070 cases, while young adulthood (age 20–40 years) maintained a minimal mortality rate. The middle-aged population (age 40–60 years) maintained relatively low, but increased, mortality rate. Throughout late adulthood (age 60–80 year), the mortality rate is increased drastically. Patients' ages and COVID–19 mortality risk have a considerable correlation, especially in the

senior population over 60 years of age. Sex was shown to be either statistically insignificant, or males had significantly higher mortality. This unequal mortality rate between the two sexes may have ensued from the male population having more preexisting chronic diseases or from the older median age, as both were suggested in a Spanish government report (24).

Symptoms

COVID-19 presented with a wide range of symptoms, with certain manifestations leading to a higher mortality rate. Among respiratory symptoms, patients with tachypnea, dyspnea, or hemoptysis had a significantly higher rate of mortality. However, other upper respiratory symptoms, such as cough and sputum, were not associated with higher mortality. Tachycardia, although statistically insignificant, tended to be associated with greater mortality. In contrast, symptoms associated with other organ systems, such as gastrointestinal symptoms and non-specific symptoms including fatigue and fever, showed minimal associations with mortality. Tachycardia may result from high cytokine levels, which activate cardiac pacemaker cells in the state of infection, or from direct myocardial invasion, as multiple studies have suggested (35, 36). Since tachycardia is one of the initial manifestations of acute heart failure, patients presenting tachycardia may need evaluation for acute cardiac injury, a fatal complication of COVID-19.

Comorbidities

The presence of comorbidity was another significant determinant of mortality. Of commonly reported comorbidities, CKD was related to a strongly increased mortality rate. High risk of mortality in CKD patients may result from an alteration in immune response. Several studies have reported that the combined effects of CKD in cellular immune function lead to a reduced number and malfunction of T-lymphocytes, especially T4 cells (37).

Cardiovascular disease (CVD) and hypertension also increased the risk of mortality. The strong positive relationship between COVID-19 severity and the presence of CVD has been suggested (38, 39), and our study demonstrated consistent results. History of CVD and atherosclerotic risk factors put an individual at a higher risk of developing acute coronary syndrome in the setting of acute infection (40). Patients with heart failure are more likely to fall into a decompensated state, which leads to other organ damage, including cardiac injury. However, dyspnea and hypoxemia are also common manifestations shared by COVID-19 and heart failure, and therefore can be challenging to distinguish between in a clinical setting. Detailed history taking and diagnostic testing are warranted in patients with suspected CVD.

Patients with diabetes mellitus (DM) had a significantly increased mortality rate in COVID-19, similar to MERS-CoV but to a lesser extent, and those with metabolic syndrome-related disorders had a higher odds of severe infection, ranging from 7.2 to 15.7 (41). These findings may have ensued from DM being an independent risk factor of higher mortality, and the demographic distribution of the mortality group mostly comprised patients with advanced age, which may also have contributed to the high prevalence of DM (42).

Laboratory and radiologic findings

Multiple blood biomarker concentrations showed significant differences in the mortality group. Increased LDH, a non-specific marker of tissue damage, showed an association with higher mortality rate (43). An increased TnI concentration, which has excellent specificity in myocardial tissue, was associated with higher mortality (44); this finding can be interpreted as being related to the fatal complications of acute cardiac injury. Alanine aminotransferase (ALT) is relatively specific to liver tissue damage, and patients with increased ALT had a moderately higher mortality.

Increased acute phase reactants (APR) such as pro-calcitonin, C-reactive protein (CRP), and D-dimer were positively associated with mortality (45). All high APRs were associated with higher mortality rates, with pro-calcitonin having the strongest association. Previous studies demonstrated a positive correlation between APR concentration and severity of infection outcome (46, 47). Ruan et al. reported that mean CRP concentration was 4-fold higher in the mortality cases than in discharged cases ($p < 0.001$) (48).

Regarding complete blood count findings, leukocytosis and lymphocytosis are the commonly known physiologic responses to viral infection, and lymphopenia was reported in multiple COVID-19 cases (49, 50). Lymphopenia was strongly associated with a higher

chance of death in our findings. Previous studies implied that lymphopenia can have a prognostic value in viral infections (51), and a recent study reported that COVID-19 patients with low blood lymphocyte percentages had poor outcomes (5, 52).

Since chest imaging still constitutes a substantial portion of the diagnostic process, as well as being widely used for severity assessment in conventional viral pneumonia, several studies have focused on the radiologic findings of COVID-19 (1, 53). Our study demonstrated that the findings of consolidation, ground glass opacity (GGO), and bilateral lung involvement were all associated with a higher mortality rate in different degrees. GGO was the most common feature overall, while consolidation had the greatest association with higher mortality. However, the number of studies that have reported radiologic findings is too low for effective quantitative analysis. Further studies are needed to generalize the observation.

Complication and clinical course

Acute cardiac injury was a relatively common complication, with strong positive correlation with mortality. Potential causes of acute cardiac injury include the following: multi-organ failure due to cytokine storm, increased myocardial demand and cardiac decompensation, high pro-inflammatory cytokine level and destabilization of atherosclerotic plaques, a higher chance of acute coronary syndrome during infection, and direct myocardial damage (54–56). Although direct viral invasion lacks definitive evidence to date, MERS-CoV was reported to cause acute viral myocarditis (57). Therefore, further investigation is needed considering SARS-CoV-2's striking affinity to the angiotensin-converting enzyme 2 receptor (58).

AKI was one of the most commonly reported complications, with a greater incidence in the mortality group. In AKI, inflammatory cytokines play a key role in the initiation and extension phase of renal injury, thereby leading to renal hemodynamic disturbances (59). An inflammatory cytokine surge indicates severe COVID-19, as previous studies have reported significantly higher mean pro-inflammatory cytokine levels in the mortality group compared to the controls (7, 48). ARDS, another relatively common complication that arises in systemic infection, was also associated with increased mortality. Patients with sepsis or shock experienced the highest mortalities amongst all those with other complications.

Patients who needed invasive mechanical ventilation and non-invasive mechanical ventilation showed an increased mortality rate. Intensive care unit (ICU) admission indicated a 6-fold greater mortality rate. Patients who needed ECMO or continuous renal replacement therapy also had a drastically increased mortality rate, as both are life-saving, last resorts in major organ failure.

Limitations

The primary limitation of this study is the lack of regional diversity in the studied populations. Although studies from Korea, United States, Italy, and Spain were included in our analysis, many were still from China. Second, some findings were reported by too few studies to be meta-analyzed. Third, some meta-analyzed statistics showed relatively high heterogeneity. However, it had been expected since COVID-19 affects patients of all ages and regions with different availabilities of medical care, and also because of the intrinsic properties of observational studies. Therefore, further studies utilizing restricted data collection processes are necessary as more specific information on individual patients' ages, disease severity, and other information becomes available.

Nevertheless, our study presents a comprehensive review of the clinical, laboratory, and radiologic features associated with mortality of COVID-19, which have rarely been studied. Moreover, a range of data sources, including governmental reports from Western countries, were included in order to obtain widely representative and the most updated results.

Materials And Methods

Search strategy

We performed a comprehensive literature search according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guidelines. MEDLINE, Embase, Web of Science, and other official sources, including the government data, the Centers for Disease Control, and Prevention, and the WHO COVID-19 database, were searched. The search keywords were "COVID-19", "2019-nCoV", "coronavirus", "SARS-CoV-2", "fatal", "mortality", and "clinical manifestations". Our initial literature search included the studies published until March 30, 2020. However, since research on COVID-19 is increasingly being reported, an

additional literature search was performed for the studies published until May 1, 2020, using the same databases and search strategy. Any articles written in English, Korean, and Spanish were included because of the authors' proficiency in these languages.

Study selection

Three main reviewers (H.R, J.P, and Y.L) independently evaluated the titles and abstracts of retrieved studies. Any disagreements between the reviewers regarding the suitability of the studies were discussed with two other reviewers (S.K and M.Y) and resolved by consensus. All observational studies on COVID-19 that investigated both patients (with mortality and without mortality) were included, whereas the followings were excluded: 1) non-research articles, 2) studies that reported cases which did not fulfill the diagnostic criteria of WHO interim guidance, 3) studies that only investigated either mortality or non-mortality cases (non-comparability), and 4) studies with insufficient sample size ($n < 10$).

Data extraction and quality assessment

Data regarding publication details, population demographics, clinical manifestations, comorbidities, laboratory findings, radiologic findings, complications, and clinical courses were extracted from each study. The number of events and total observations in both the mortality cases and the non-mortality cases for any outcomes associated with clinical, laboratory, and radiologic features were extracted from case-control, cross-sectional, and case series studies. For cohort studies and any other studies with time-to-outcome analysis, hazard ratios (HR) for each finding were directly extracted. The Newcastle-Ottawa scale for assessing the quality of case-control studies and cohort studies was used for the assessment of the analyzed studies. Finally, the articles with adequate quality (score ≥ 5) were included in the quantitative meta-analysis (8).

Data synthesis and outcomes

For case-control, cross-sectional, and case-series studies, we calculated the odds ratio (OR) as a statistic to summarize the characteristic findings of the mortality cases compared to the non-mortality cases. Whereas the HRs obtained from each study were to be meta-analyzed with time-to-outcome analysis. A random-effects model was used to conduct the meta-analysis because a significant heterogeneity between the included studies was expected. The I^2 statistic was used to estimate and quantify heterogeneity between the studies. Egger's linear regression test was performed to evaluate publication bias. The analysis was performed using R version 3.5.0 (R foundation for statistical computing). A P value < 0.05 was considered statistically significant.

Declarations

Code and data availability

The final datasheet for extraction, the program code used for the quantitative synthesis, and the forest plots for individual analyses can be accessed at our public repository: <http://dx.doi.org/10.17632/h55cyhs82c.1>

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None

Author Contributions

Rhim and S.L designed and conceptualized the study. Ahn supervised the project. Rhim, Park, Y.L, Kwon, Yu, H.L and S.L performed the calculations and data analyses. Rhim, park, Y.L drafted the manuscript. All authors revised the manuscript. S.L and Ahn validated the results. All authors finally reviewed the manuscript.

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Additional Information

The authors declare no competing interests.

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Tables

Table 1. Characteristics of the included studies on coronavirus disease 2019

Country	Study design	Study population (n)	Age $\pm$ SD (years) / Female (n)	Study population (n) / Age $\pm$ SD in mortality group	Study population (n) / Age $\pm$ SD in non-mortality group
China	Retrospective cohort study	191	56 (46–67) ^a / 72	54 / 69 (63–76) ^a	137 / 52 (45–58) ^a
Italy	Retrospective case series study	1581	63 (56–70) ^a / 287	405 / NA	1176 / NA
China	Cohort study	102	54 (37–67) ^a / 49	17 / 72 (63–81) ^a	85 / 53 (47–66) ^a
China	Retrospective study	27	60 (47–69) ^a / 15	10 / 68 (63–73) ^a	17 / 55 (35–60) ^a
China	Prospective cohort study	179	57.6 $\pm$ 13.7 / 82	21 / 70.2 $\pm$ 7.7	158 / 56.0 $\pm$ 13.5
Spain	Government report	203715	61 (46–78) ^a / 113045	15873 / 83 (75–88)	187842 / 59 (45–75)
China	Retrospective case series study	274	62 (44–70) ^a / 103	113 / 68 (62–77) ^a	161 / 51 (37–66) ^a
China	Case series study	55	74.0 (65–91) ^a / 40	19 / 77	36 / 72
China	Retrospective observational study	52	59.7 $\pm$ 13.3 / 17	32 / 64.6 $\pm$ 11.2	20 / 51.9 $\pm$ 12.9
China	Retrospective study	225	NA / 101	109 / 69 (62–74) ^a	116 / 40 (33–57) ^a
Korea	Government report	10774	NA / 6418	248 / NA	10526 / NA
China	Retrospective study	150	NA / 48	68 / 67 (15–81) ^a	82 / 50 (44–81) ^a
China	Retrospective cohort study	201	51 (43–60) ^a / 73	44 / 68.5 (49.3–75) ^a	157 / NA
China	Retrospective cohort study, multicenter	337	NA / NA	16 / NA	321 / NA
China	Retrospective cohort study	1590	48.9 $\pm$ 16.3 / 674	50 / NA	1540 / NA

Country	Study design	Study population (n)	Age $\pm$ SD (years) / Female (n)	Study population (n) / Age $\pm$ SD in mortality group	Study population (n) / Age $\pm$ SD in non-mortality group
China	Retrospective cohort study	416	64 (21–95) ^a / 211	57 / NA	359 / NA
China	Retrospective cohort study	701	63 (50–71) ^a / 334	113 / NA	588 / NA
China	Retrospective cohort study	269	65 (54–72) ^a / 134	87 / NA	181 / NA
China	Retrospective study	105	60.8 $\pm$ 16.3 / 51	19 / 75.1 $\pm$ 12.9	86 / 57.7 $\pm$ 15.3
China	Retrospective case series study	362	66 (59–73) ^a / 173	77 / 72 (64.5–82) ^a	285 / 65 (57.5–71) ^a
US	Case series study	5700	63 (52–75) ^a / 2263	553 / NA	5147 / NA
China	Retrospective observational study	187	62 (48.5–71) ^a / 84	28 / 73 (68–77.2) ^a	159 / NA
China	Retrospective cohort study	663	55.6 (44–69) ^a / 342	25 / 67.1 (61–78) ^a	638 / 59.1 (43–68) ^a

^aExpressed as median age (interquartile range)

Table 2. Qualitative synthesis of studies with time-to-outcome analysis

Study	Study design	Study population (n) / Mean age $\pm$ SD (years) / Female patients (n)	Study population (n) / Mean age in mortality group (years)	Study population (n) / Mean age in non-mortality group (years)	Outcome
Feng et al. (14)	Retrospective cohort study, multicenter	337 / NA / NA	16 / NA	321 / NA	<p>HR for risk factors associated with mortality in patients with COVID-19</p> <ul style="list-style-type: none"> - Age over 75: 6.07 (1.65–22.35)^b - Leukopenia: 0.66 (0.22–1.96) - Increased D-dimer: 3.26 (0.99–10.72) - Creatine Kinase: 1.01 (1.01–1.02)^b - LDH: 1.002 (1–1.004)^b - Hypertension: 1.45 (0.42–5.83) - Cardiovascular disease: 0.59 (0.1–3.63) - DM: 1.60 (0.34–8.16)
Liang et al. (20)	Retrospective cohort study	1590 / 48.9 $\pm$ 16.3 / 674	50 / NA	1540 / NA	<p>HR for risk factors associated with mortality in patients with COVID-19</p> <ul style="list-style-type: none"> - Age: 1.04 (1.02–1.05)^b - One or more comorbidities: 2.13 (1.39–3.26)^b
Shi et al. (23)	Retrospective cohort study	416 / 64 (21–95) ^a / 211	57 / NA	359 / NA	<p>HR for risk factors associated with mortality in patients with COVID-19 from symptom onset</p> <ul style="list-style-type: none"> - Age: 1.02 (0.99–1.05) - Cardiovascular disease: 1.51 (0.7–3.3) - Cerebrovascular disease: 1.12 (0.46–2.7) - DM: 0.79 (0.41–1.52) - COPD: 0.37 (0.04–3.5) - CKD: 1.1 (0.49–2.44) - Malignancy: 1.75 (0.43–7.16) - ARDS: 7.89 (3.73–16.66)^b - Increased Cr: 0.59 (0.29–1.23) - Increased BNP: 1.16 (0.54–2.47)

Study	Study design	Study population (n) / Mean age $\pm$ SD (years) / Female patients (n)	Study population (n) / Mean age in mortality group (years)	Study population (n) / Mean age in non-mortality group (years)	Outcome
Cheng et al. (11)	Retrospective cohort study	701 / 63 (50–71) ^a / 334	113 / NA	588 / NA	<p>HR for risk factors associated with mortality in patients with COVID-19</p> <ul style="list-style-type: none"> - Age over 65: 2.43 (1.66–3.56)^b - Male: 2.15 (1.45–3.21)^b - Severe disease: 6.1 (3.86–9.64)^b - One or more comorbidities: 1.06 (0.73–1.54) - Leukocytosis: 1.06 (0.73–1.54) - Lymphopenia: 1.02 (0.70–1.48) - Proteinuria 1+: 4.12 (1.97–8.62)^b - PU 2+-3+: 10.92 (5.00–23.86)^b - Hematuria 1+: 4.64 (2.24–9.62)^b - HU 2+-3+: 12.2 (6.32–23.53)^b - Increased BUN: 7.15 (4.92–10.39)^b - Increased Cr: 2.99 (2.00–4.47)^b - Peak Cr over 133 μmol/L: 5.88 (3.90–8.87)^b - AKI stage 1: 3.51 (1.53–8.02)^b - AKI stage 2: 6.24 (2.73–14.27)^b - AKI stage 3: 9.81 (5.46–17.65)^b

Study	Study design	Study population (n) / Mean age $\pm$ SD (years) / Female patients (n)	Study population (n) / Mean age in mortality group (years)	Study population (n) / Mean age in non-mortality group (years)	Outcome
Li et al. (19)	Retrospective cohort study	269 / 65 (54–72) ^a / 134	87 / NA	181 / NA	HR for risk factors associated with mortality in severe patients with COVID-19 - Age over 65: 1.69 (1.02–2.59) ^b - Male: 1.96 (1.24–3.11) ^b - Lymphopenia: 3.85 (2.50–5.93) ^b - Increased LDH: 3.94 (2.48–6.28) ^b - Acute cardiac injury: 3.89 (2.51–6.01) ^b

^aMedian age (interquartile range).

^bP-value < 0.05 in the original source.

Abbreviations: SD, standard deviation; HR, hazard ratio (95% confidence interval); PU, proteinuria; HU, hematuria; BUN, blood urea nitrogen; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; LDH, lactate dehydrogenase; Cr, creatinine; BNP, brain natriuretic peptide; ARDS, acute respiratory distress syndrome; AKI, acute kidney injury

Figures

Figure 1

Preferred Reporting Items for Systematic Reviews and Meta-Analyses diagram of study selection. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of literature search and study selection for systematic review of mortality in coronavirus disease 2019 patients.

Figure 2

Risk factors associated with mortality in coronavirus disease 2019 Forest plots depict the odds ratio of the demographic, clinical, laboratory, and radiologic findings in mortality patients compared to non-mortality patients. Abbreviations: OR, odds ratio; 95% CI, 95% confidence interval; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BNP, brain natriuretic peptide; CRP, c-reactive protein; LDH, lactate dehydrogenase; TnI, troponin I; ICU, intensive care unit

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