

Risk factors for mortality of coronavirus disease 2019 (COVID-19) patients during the early outbreak of COVID-19: a systematic review and meta-analysis

Yanyan Wu^{1,2#}, Hongyu Li^{1,2#}, Zhongheng Zhang³, Wenhua Liang⁴, Tiansong Zhang⁵, Zhenhua Tong⁶, Xiaozhong Guo^{1,2}, Xingshun Qi^{1,2}

¹Liver Cirrhosis Study Group, Department of Gastroenterology, General Hospital of Northern Theater Command (formerly called General Hospital of Shenyang Military Area), Shenyang, China; ²Postgraduate College, Jinzhou Medical University, Jinzhou, China; ³Department of Emergency Medicine, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, Hangzhou, China; ⁴Department of Thoracic Oncology and Surgery, China State Key Laboratory of Respiratory Disease & National Clinical Research Center for Respiratory Disease, the First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; ⁵Department of Traditional Chinese Medicine, Jing'an District Central Hospital, Shanghai, China; ⁶Section of Medical Service, General Hospital of Northern Command (formerly General Hospital of Shenyang Military Area), Shenyang, China

Contributions: (I) Conception and design: X Qi; (II) Administrative support: X Qi; (III) Provision of study materials or patients: Y Wu, H Li; (IV) Collection and assembly of data: Y Wu, H Li, X Guo, X Qi; (V) Data analysis and interpretation: Y Wu, H Li, Z Zhang, T Zhang, X Qi; (VI) Manuscript writing: All Authors; (VII) Final approval of manuscript: All Authors.

"These authors contributed equally to this work.

Correspondence to: Dr. Xingshun Qi, MD. Department of Gastroenterology, General Hospital of Northern Theater Command (formerly called General Hospital of Shenyang Military Area), No. 83 Wenhua Road, Shenyang 110840, China. Email: xingshunqi@126.com.

Background: Identification of risk factors for poor prognosis of patients with coronavirus disease 2019 (COVID-19) is necessary to enable the risk stratification and modify the patient's management. Thus, we performed a systematic review and meta-analysis to evaluate the in-hospital mortality and risk factors of death in COVID-19 patients.

Methods: All studies were searched via the PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), VIP, and Wanfang databases. The in-hospital mortality of COVID-19 patients was pooled. Odds ratios (ORs) or mean difference (MD) with 95% confidence intervals (CIs) were calculated for evaluation of risk factors.

Results: A total of 80 studies were included with a pooled in-hospital mortality of 14% (95% CI: 12.2–15.9%). Older age (MD =13.32, 95% CI: 10.87–15.77; P<0.00001), male (OR =1.66, 95% CI: 1.37–2.01; P<0.00001), hypertension (OR =2.67, 95% CI: 2.08–3.43; P<0.00001), diabetes (OR =2.14, 95% CI: 1.76–2.6; P<0.00001), chronic respiratory disease (OR =3.55, 95% CI: 2.65–4.76; P<0.00001), chronic heart disease/cardiovascular disease (OR =3.15, 95% CI: 2.43–4.09; P<0.00001), elevated levels of high-sensitive cardiac troponin I (MD =66.65, 95% CI: 16.94–116.36; P=0.009), D-dimer (MD =4.33, 95% CI: 2.97–5.68; P<0.00001), C-reactive protein (MD =48.03, 95% CI: 27.79–68.27; P<0.00001), and a decreased level of albumin at admission (MD =–3.98, 95% CI: -5.75 to -2.22; P<0.0001) are associated with higher risk of death. Patients who developed acute respiratory distress syndrome (OR =62.85, 95% CI: 29.45–134.15; P<0.00001), acute cardiac injury (OR =25.16, 95% CI: 6.56–96.44; P<0.00001), acute kidney injury (OR =22.86, 95% CI: 4.60–113.66; P=0.0001), and septic shock (OR =24.09, 95% CI: 4.26–136.35; P=0.0003) might have a higher in-hospital mortality.

Conclusions: Advanced age, male, comorbidities, increased levels of acute inflammation or organ damage indicators, and complications are associated with the risk of mortality in COVID-19 patients, and should be integrated into the risk stratification system.

Keywords: Coronavirus disease 2019 (COVID-19); severe acute respiratory syndrome coronavirus 2 (SARS-

5070

CoV-2); meta-analysis; mortality; risk factors

Submitted Dec 22, 2020. Accepted for publication Mar 12, 2021. doi: 10.21037/apm-20-2557 View this article at: http://dx.doi.org/10.21037/apm-20-2557

Introduction

According to the World Health Organization, a novel pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2, previously known as 2019-nCoV) is designated as coronavirus disease 2019 (COVID-19) (1). SARS-CoV-2 belongs to the coronavirus family together with SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), but has more rapid transmission than SARS-CoV and MERS-CoV (2-4), which leads to a dramatic increase in the number of confirmed cases during a short period, thereby posing a serious threat for health systems worldwide. Till August 4, 2020, a cumulative total of 18,142,718 confirmed COVID-19 cases and 691,013 deaths have been reported in 216 countries (5).

Fever and cough are main clinical manifestations of COVID-19 patients (6). Most of COVID-19 patients have a favorable outcome, but a minority of them may develop severe pneumonia, dyspnea and hypoxemia, and progress into respiratory or multi-organ failure and even death (7). Based on 55,924 laboratory confirmed cases in China, the overall national mortality rate is 3.8%, but the fatality rate of patients over 80 years old is up to 22% (8). Besides, male, pre-existing comorbidities, elevated inflammatory markers, and complications [i.e., acute respiratory distress syndrome (ARDS), acute cardiac injury, acute kidney injury and sepsis] were associated with an increased risk of death (9-15).

In the early stages of COVID-19 outbreak, because effective vaccines and antiviral drugs for SARS-CoV-2 are lacking, the management of critically ill patients is often challenging. Thus, it is very essential to identify the risk factors associated with poor outcome of COVID-19 patients and perform early interventions for high-risk patients. The present study aimed to systematically review the evidence on the in-hospital mortality of COVID-19 patients and elucidate the risk factors of mortality in COVID-19 patients.

Methods

This meta-analysis was conducted based on Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines and results were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (available at http:// dx.doi.org/10.21037/apm-20-2557).

Registration

This study was registered at PROSPERO (registration number: CRD42020169921).

Search strategy

All relevant studies regarding mortality of COVID-19 patients were retrieved via the PubMed, Embase, Cochrane Library, China National Knowledge Infrastructure (CNKI), VIP, and Wanfang databases. The search terms were ("2019-nCoV" OR "SARS-CoV-2" OR "COVID-19" OR "new coronary pneumonia" OR "corona virus" OR "novel coronavirus" OR "nCoV" OR "severe acute respiratory syndrome coronavirus 2") AND ("death" OR "died" OR "die" OR "mortality" OR "survival" OR "survivor" OR "fatal" OR "outcome" OR "decease" OR "deadly" OR "lethal" OR "fatality"). The last search was performed on May 26, 2020.

Study selection

There was neither publication language nor publication status restriction. All eligible studies should report the mortality and/or risk factors for death in COVID-19 patients. Exclusion criteria were as follows: (I) duplicates; (II) case reports, reviews or meta-analyses, guidelines, consensus, experimental or animal studies, comments, notes, and correspondences; (III) irrelevant papers; (IV) data regarding the mortality and/or risk factors cannot

be extracted; and (V) duplicate study population. As for duplicate studies, we selected only one original study with more comprehensive clinical and laboratory data. Casecontrol studies were excluded from the proportion metaanalyses regarding mortality of COVID-19 patients due to their potential patient selection bias.

Data extraction

The following data were extracted from the included studies: the first author, publication year, region, source of cases, enrollment period, follow-up periods, number of COVID-19 patients, number of COVID-19 patients with severe disease, number of non-survivors and survivors, age, gender, and other potential risk factors for death.

Study quality

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of included studies. It includes study selection (four items), comparability (two items), and exposure/outcome (three items). The highest NOS score was 9, and studies with a NOS score of >6 were considered as high quality.

Statistical analysis

All meta-analyses were performed using STATA version 12.0 (Stata Corp., College Station, Texas, USA) and Review Manager software version 5.4 (Cochrane collaboration, the Nordic Cochrane Centre, Copenhagen, Denmark). The meta-analyses were conducted by using a random-effect model. We pooled the in-hospital mortality in COVID-19 patients, and then calculated the pooled proportion with 95% confidence interval (CI). We collected the risk factors for death in COVID-19 patients, and then calculated the odds ratios (ORs) or mean difference (MD) with 95% CIs. The heterogeneity among studies was evaluated by Cochrane Q test and the I² statistics, and $I^2 > 50\%$ and/ or P<0.1 were considered to have statistically significant heterogeneity. Publication bias was assessed with Egger test. P<0.1 was considered as a statistically significant publication bias. Subgroup analyses, meta-regression analyses, and sensitivity analyses would be performed to explore the sources of heterogeneity among studies. Subgroup analyses were conducted according to the sample size (>100 versus ≤100), source of cases (single-center versus multiplecenter), NOS (>6 versus ≤6), region (Asia versus Europe versus North America), study design (retrospective versus

5071

prospective), longest follow-up duration (>30 days versus \leq 30 days), and proportion of patients with severe disease (>50% versus \leq 50%). Meta-regression analyses were also grouped in terms of the variables mentioned above. Scattered plots were drawn to show the trend in overall inhospital mortality according to the proportion of severe COVID-19 patients included. The correlation between them was evaluated using Spearman correlation analysis in the IBM SPSS 22.0 (IBM Corp, Armonk, NY, USA). Coefficients were calculated. A two-sided P<0.05 indicates a statistical significance.

Results

Study selection

A total of 7,003 studies were identified via the 6 databases, and 6 studies were identified via a manual search. Finally, 80 studies with 25,385 COVID-19 patients were included (*Figure 1*). All included studies are listed in the Appendix.

Study characteristics

Characteristics of the included studies were listed in *Table 1*. Forty-three studies were published as full texts, 32 was published in press (i.e., available online ahead of print), and 5 studies were preprinted. The sample size ranged from 8 to 2,964. Sixty-one studies were performed in Asia, 11 in Europe, and 8 in North America; 72 of them were retrospective and 8 were prospective; 56 and 24 studies were single-center and multi-center studies, respectively.

Study quality

The NOS score ranged between 3 and 8. Twenty-two studies were considered to be of high quality and 3 were of low quality (Table S1).

Mortality

The results of the meta-analyses regarding in-hospital mortality of COVID-19 patients are summarized in *Table 2*.

Overall analyses

Eighty studies reported the in-hospital mortality of COVID-19 patients, and the pooled in-hospital mortality of COVID-19 patients was 14% (95% CI: 12.2–15.9%). The heterogeneity was statistically significant ($I^2 = 97.8\%$;



Figure 1 Flow chart of study selection.

P<0.001). Fifty studies reported the number of severe COVID-19 patients, and the pooled incidence of severe COVID-19 patients was 49.6% (95% CI: 43.6–55.6%). The heterogeneity was statistically significant (I^2 =99.9%; P<0.001).

Subgroup analyses

The pooled in-hospital mortality of COVID-19 patients was 10.1%, 23.7%, and 25.4% in Asia, Europe, and North America, respectively. The pooled in-hospital mortality of COVID-19 patients was 13.7% and 15.2% in studies with a sample size of >100 and \leq 100, respectively. The pooled in-hospital mortality of COVID-19 patients was 14.2% and 13.6% in single-center and multiple-center studies, respectively. The pooled in-hospital mortality of COVID-19 patients was 13.6% and 18% in retrospective and prospective studies, respectively. The pooled in-hospital mortality of COVID-19 patients was 13.6% and 18% in retrospective and prospective studies, respectively. The pooled in-hospital mortality of COVID-19 patients was the same between the studies with NOS >6 and NOS \leq 6 (both 14%). The pooled in-hospital mortality of COVID-19 patients was 15.1% and 17.3% in studies with the longest follow-up duration of >30 days and \leq 30 days, respectively. The

pooled in-hospital mortality of COVID-19 patients was 22.5% and 7.7% in studies with the proportion of patients with severe disease of >50% and \leq 50%, respectively. The heterogeneity was statistically significant in all subgroup analyses.

Meta-regression analyses

The results of meta-regression analyses are shown in Table S2. Meta-regression analyses indicated that region (Asia versus Europe versus North America) (P=0.0001), proportion of patients with severe disease (>50%) versus \leq 50%) (P<0.001), rather than sample size (>100 versus \leq 100) (P=0.456), source of cases (single-center versus multiple-center) (P=0.756), NOS (>6 versus \leq 6) (P=0.956), study design (retrospective versus prospective) (P=0.403), and longest follow-up duration (>30 versus \leq 30 days) (P=0.624), might be related to the heterogeneity.

Sensitivity analyses

The sensitivity analysis showed that none of these included studies could significantly influence the results of the metaanalysis.

Table 1 Characteristics of studies included in the meta-analysis

	<u> </u>		Enrollment period	Longest follow-up	No. of severe	Sample		Non-survivors			3	
First author (year)	Country	Source of cases	Enrollment period	periods	patients (%)	size	N (%)	Age, years ^a	Male (%)	N (%)	Age, years ^a	Male (%)
Aggarwal S [2020]	United States	UnityPoint Clinic	2020.03.01-2020.04.04	NA	NA	16	3 (18.8)	NA	NA	13 (81.3)	NA	NA
Barrasa H [2020]	Spain	University Hospital Araba	2020.03.04-2020.03.31	33 days	48 (100.0)	48	14 (29.2)	NA	NA	34 (70.8)	NA	NA
Benussi A [2020]	Italy	ASST Spedali Civili di Brescia Hospital	2020.02.21-2020.04.05	NA	NA	56	21 (37.5)	NA	NA	35 (62.5)	NA	NA
Bhatraju PK [2020]	United States	Nine hospital in the Seattle	2020.02.24-2020.03.09	28 days	24 (100.0)	24	12 (50.0)	NA	NA	12 (50.0)	NA	NA
Bianchetti A [2020]	Italy	Acute Hospital in Brescia Province, Northern Italy	NA	NA	NA	627	194 (30.9)	NA	NA	433 (69.1)	NA	NA
Borghesi A [2020]	Italy	Radiological Sciences and Public Health, University of Brescia	2020.03.04-2020.03.24	NA	NA	302	65 (21.5)	77 [70.5–81]	50 (76.9)	237 (78.5)	64 [54–73.3]	144 (60.8)
Buckner FS [2020]	United States	Three University of Washington affiliated hospitals	2020.03.02-2020.03.26	67 days	51 (48.6)	105	35 (33.3)	NA	NA	70 (66.7)	NA	NA
Cai Q [2020]	China	Third People's Hospital of Shenzhen	2020.01.11-2020.02.06	55 days	58 (19.5)	298	3 (1.0)	NA	NA	295 (99.0)	NA	NA
Cecconi M [2020]	Italy	Humanitas Research Hospital	2020.02.22-2020.03.22	32 days	27 (11.3)	239	36 (15.1)	NA	NA	203 (84.9)	NA	NA
Chen R [2020]	China	575 hospitals in China	As of January 31, 2020	NA	NA	1590	50 (3.1)	68 [51–86]	39/50 (78.0)	1,540 (96.9)	48[1–94]	865/1,528 (56.6)
Andrea C [2020]	Italy	San Raffaele Hospital	2020.02.27-2020.03.17	42 days	NA	191	42 (22.0)	75.3±12.9	31 (73.8)	149 (78.0)	60.4±13.7	100 (67.1)
Cummings MJ [2020]	United States	Milstein Hospital and Allen Hospital	2020.03.02-2020.04.01	57 days	257 (100.0)	257	101 (39.3)	NA	NA	156 (60.7)	NA	NA
Deng Y [2020]	China	Hankou and Caidian branch of Tongji Hospital, and Hankou branch of Central Hospital of Wuhan	2020.01.01-2020.02.21	NA	104 (10.8)	964	109 (11.3)	69 [62–74]	73 (67.0)	855 (88.7)	NA	NA
Dong XC [2020]	China	Designated hospitals in Tianjin	NA	NA	62 (45.9)	135	3 (2.2)	NA	NA	132 (97.8)	NA	NA
Du RH [2020]	China	Wuhan Pulmonary Hospital	2019.12.25-2020.02.07	90 days	NA	179	21 (11.7)	70.2±7.7	10 (47.6)	158 (88.3)	56.0±13.5	87 (55.1)
Gao L [2020]	China	Hubei General Hospital	NA	15 days	54 (100.0)	54	18 (33.3)	NA	NA	36 (66.7)	NA	NA
Giacomelli A [2020]	Italy	Luigi Sacco Hospital in Milan	2020.02.21-2020.03.19	28 days	88 (37.8)	233	48 (20.6)	NA	39 (81.3)	185 (79.4)	NA	122 (65.9)
Guo T [2020]	China	Seventh Hospital of Wuhan	2020.01.23-2020.02.23	33 days	NA	187	43 (23.0)	NA	NA	144 (77)	NA	NA
Hong KS [2020]	South Korea	Yeungnam University Medical Center	As of March 29, 2020	NA	NA	98	5 (5.1)	NA	NA	93 (94.9)	NA	NA
Hou W [2020]	China	Beijing YouAn Hospital	2020.01.21-2020.03.09	NA	22 (21.8)	101	5 (5.0)	NA	NA	96 (95.0)	NA	NA
Hu H [2020]	China	Renmin Hospital of Wuhan University (Sichuan Medical Team)	2020.02.07-2020.03.07	NA	105 (100.0)	105	19 (18.1)	75.05±12.94	14 (73.7)	86 (81.9)	57.71±15.34	48 (55.8)
Hu L [2020]	China	Tianyou Hospital in Wuhan	2020.01.08-2020.02.20	62 days	172 (53.3)	323	35 (10.8)	NA	NA	288 (89.2)	NA	NA
Huang J [2020]	China	Third People's Hospital of Yichang	2020.01.25-2020.03.24	NA	NA	299	16 (5.4)	69.2±9.7	11 (68.8)	283 (94.6)	52.5±16.6	149 (52.7)
Inciardi RM [2020]	Italy	Civil Hospitals of Brescia	2020.03.04-2020.03.25	14 days	NA	99	26 (26.3)	NA	NA	73 (73.7)	NA	NA
Israelsen SB [2020]	Denmark	Hvidovre Hospital	2020.03.10-2020.04.23	41 days	NA	175	43 (24.6)	NA	NA	132 (75.4)	NA	NA
Itelman E [2020]	Israel	Sheba Medical Center	2020.02.01-2020.04.10	NA	26 (16.0)	162	5 (3.1)	NA	NA	157 (96.9)	NA	NA
Javanian M [2020]	Iran	Ayatollah Rohani, Shahid Beheshti and Yahyanejad hospitals	2020.02.25-2020.03.12	21 days	NA	100	19 (19.0)	69.26±11.10	12 (63.2)	81 (81.0)	57.74±13.58	39 (48.1)
Ji D [2020]	China	Fuyang Second People's Hospital and Fifth Medical Center of Chinese PLA General Hospital	2020.01.20-2020.02.22	58 days	0 (0)	208	2 (1.0)	NA	NA	206 (99.0)	NA	NA
Klang E cohort1 [2020]	United States	Mount Sinai Hospital, Mount Sinai Brooklyn, Mount Sinai Queens, Mount Sinai Morningside and Mount Sinai West	2020.03.01-2020.05.17	NA	NA	572	60 (10.5)	46.5 [42.8–49]	45 (75.0)	512 (89.5)	40 [34–46]	352 (68.8)
Klang E cohort2 [2020]	United States	Mount Sinai Hospital, Mount Sinai Brooklyn, Mount Sinai Queens, Mount Sinai Morningside and Mount Sinai West	2020.03.01-2020.05.17	NA	NA	2,834	1,076 (38.0)	76 [67–84]	615 (57.2)	1,758 (62.0)	68 [60–77]	949 (54.0)
Li J [2020]	China	Central Hospital of Wuhan	2020.01.15-2020.03.15	NA	173 (47.8)	362	77 (21.3)	72 [64.5–82]	50 (64.9)	285 (78.7)	65 [57.5–71]	139 (48.7)
Li R [2020]	China	Hanchuan City People's Hospital	2020.01.20-2020.02.14	40 days	37 (16.4)	225	2 (0.9)	NA	NA	223 (99.1)	NA	NA
Li X [2020]	China	Designated hospitals in Guizhou	2020.01.20-2020.02.12	NA	NA	135	1 (0.7)	NA	NA	134 (99.3)	NA	NA

Table 1 (continued)

5074

Table 1 (continued)

Table 1 (continued)												
First author (year)	Country	Source of cases	Enrollment period	Longest follow-up	No. of severe	Sample		Non-survivors			Survivors	
	Country		Enforment period	periods	patients (%)	size	N (%)	Age, years ^a	Male (%)	N (%)	Age, years ^a	Male (%)
Ling L [2020]	China	Prince of Wales Hospital's	2020.01.22-2020.02.11	28 days	8 (100.0)	8	1 (12.5)	NA	NA	7 (87.5)	NA	NA
Liu J [2020]	China	Two COVID-19 designated hospitals in Hunan	As of February 16, 2020	NA	0 (0)	24	1 (4.2)	NA	NA	23 (95.8)	NA	NA
Liu K [2020]	China	Hainan General Hospital	2020.01.01-2020.02.15	NA	NA	56	3 (5.4)	NA	NA	53 (94.6)	NA	NA
Liu K [2020]	China	Nine tertiary hospitals in Hubei	2019.12.30-2020.01.24	NA	NA	137	16 (11.7)	NA	NA	121 (88.3)	NA	NA
Long L [2020]	China	First People's Hospital of Jingzhou and Xiangyang Central Hospital	2020.01.16-2020.02.24	45 days	48 (15.9)	301	17 (5.6)	NA	NA	284 (94.4)	NA	NA
Luo X [2020]	China	Eastern Campus of Renmin Hospital of Wuhan University	2020.01.30-2020.02.20	21 days	157 (52.7)	298	84 (28.2)	71 [64–80]	51 (60.7)	214 (71.8)	51 [37–63]	99 (46.3)
Mehta V [2020]	United States	Montefiore Medical Center and Albert Einstein College of Medicine	2020.03.18-2020.04.08	25 days	NA	218	61 (28.0)	76 [10–92]	36 (59.0)	157 (72.0)	66 [10–92]	91 (58.0)
Nikpouraghdam M [2020]	Iran	Baqiyatallah hospital in Tehran	2020.02.19-2020.04.15	NA	NA	2,964	239 (8.1)	NA	NA	2,725 (91.9)	NA	NA
Nowak B [2020]	Poland	Central Clinical Hospital of the Ministry of the Interior and Administration	2020.03.16-2020.04.07	22 days	41 (24.3)	169	46 (27.2)	75.3±11.9	30 (65.2)	123 (72.8)	59.3±20.1	57 (46.3)
Qi X [2020]	China	16 designated hospitals in China	2019.12.31-2020.03.24	84 days	NA	21	5 (23.8)	68 [50–75]	4 (80.0)	16 (76.2)	69 [52–75]	7 (43.8)
Renieris G [2020]	Greece	Eight departments participating in the Hellenic Sepsis Study Group	NA	28 days	NA	74	10 (13.5)	NA	9 (90.0)	64 (86.5)	NA	45 (70.3)
Shekerdemian LS [2020]	United States	NA	2020.03.14-2020.04.03	27 days	33 (68.8)	48	2 (4.2)	NA	NA	46 (95.8)	NA	NA
Sun H [2020]	China	Sino-French New City Branch of Tongji Hospital	2020.01.29-2020.03.05	36 days	NA	244	121 (49.6)	72 [66–78]	82 (67.8)	123 (50.4)	67 [64–72]	51 (41.5)
Tan ND [2020]	China	West Campus of Wuhan Union Hospital (First Affiliated Hospital of Sun Yat-sen University Medical Team)	2020.01.28-2020.04.08	30 days	87 (87.0)	100	11 (11.0)	NA	NA	89 (89.0)	NA	NA
Tang N [2020]	China	Tongji Hospital in Wuhan	2020.01.01-2020.02.13	72 days	449 (100.0)	449	134 (29.8)	68.7±11.4	90 (67.2)	315 (70.2)	63.7±12.2	178 (56.5)
Tian S [2020]	China	Designated hospitals in Beijing	2020.01.20-2020.02.10	21 days	46 (17.6)	262	3 (1.1)	NA	NA	259 (98.9)	NA	NA
Wan S [2020]	China	Chongqing University Three Gorges Hospital	2020.01.23-2020.02.08	16 days	40 (29.6)	135	1 (0.7)	NA	NA	134 (99.3)	NA	NA
Wang D [2020]	China	Zhongnan Hospital of Wuhan University and Xishui People's Hospital	As of February 10, 2020	NA	NA	544	19 (3.5)	73 [64–81]	16 (84.2)	525 (96.5)	NA	NA
Wang K [2020]	China	First People's Hospital of Jiangxia District in Wuhan	2020.01.07-2020.02.11	35 days	NA	296	19 (6.4)	65.6±12.6	11 (57.9)	277 (93.6)	46.0±14.4	129 (46.6)
Wang Z [2020]	China	Main campus of Union Hospital in Wuhan	2020.01.16-2020.01.29	19 days	NA	69	5/67 (7.5)	NA	NA	62/67 (92.5)	NA	NA
Wei JF [2020]	China	Public Health Clinical Centre of Chengdu and West China Hospital, Sichuan University	2020.01.16-2020.03.10	NA	37 (36.6)	101	3 (3.0)	NA	NA	98 (97.0)	NA	NA
Wu J [2020]	China	Tongren Hospital of Wuhan University	2020.01.30-2020.03.10	49 days	NA	101	9 (8.9)	NA	NA	92 (91.1)	NA	NA
Xie J [2020]	China	Wuhan Union Hospital (Beijing Medical Team)	2020.01.28-2020.02.28	45 days	97 (69.3)	140	36 (25.7)	NA	25 (69.4)	104 (74.3)	NA	NA
Xu B [2020]	China	Hubei Provincial Hospital of traditional Chinese and Western medicine	2019.12.26-2020.03.01	NA	107 (57.2)	187	28 (15.0)	73 [68–77.3]	17 (60.7)	159 (85.0)	NA	NA
Yang Q [2020]	China	Wuhan Third Hospital	2020.01.28-2020.02.12	NA	33 (24.3)	136	23 (16.9)	NA	NA	113 (83.1)	NA	NA
Yu Y [2020]	China	16 designated hospitals in Wuhan	2020.02.26-2020.02.27	43 days	226 (100.0)	226	87 (38.5)	NA	NA	139 (61.5)	NA	NA
Zhang H [2020]	China	Huanggang Central Hospital and The Second Affiliated Hospital of Shandong First Medical University	2020.01.22-2020.02.28	41 days	37 (19.1)	194	9 (4.6)	NA	NA	185 (95.4)	NA	NA
Zhang J [2020]	China	Liyuan Hospital	2020.01.16-2020.02.20	NA	19 (100.0)	19	8 (42.1)	77 [66–91]	5 (62.5)	11 (57.9)	68 [38–87]	6 (54.5)
Zhang J [2020]	China	Renmin Hospital of Wuhan University	2020.01.11-2020.02.06	29 days	409 (61.7)	663	25 (3.8)	67.1 [61–78]	15 (60.0)	638 (96.2)	59.1 [43–68]	306 (48.0)
Zhang L [2020]	China	Wuhan Asia General Hospital	2020.01.12-2020.03.15	NA	NA	343	13 (3.8)	NA	NA	330 (96.2)	NA	NA
Zhang Y [2020]	China	West Court of Union Hospital in Wuhan	2020.01.29-2020.02.12	43 days	171 (66.3)	258	15 (5.8)	NA	NA	243 (94.2)	NA	NA

Table 1 (continued)

Wu et al. Risk factors of mortality in COVID-19 patients

Table 1 (continued)

First author (year)			Envolument period	Longest follow-up	No. of severe	Sample		Non-survivors		Survivors			
First autrior (year)	Country	Source of cases	Enroiment period	periods	patients (%)	size	N (%)	Age, years ^a	Male (%)	N (%)	Age, years ^a	Male (%)	
Zhang YT [2020]	China	Designated hospitals in Guangdong	2020.01.15-2020.03.04	69 days	222 (16.4)	1,350	8 (0.6)	NA	NA	1,342 (99.4)	NA	NA	
Zhao XY [2020]	China	Jingzhou Central Hospital	2020.01.16-2020.02.10	25 days	30 (33.0)	91	2 (2.2)	NA	NA	89 (97.8)	NA	NA	
Zhou F [2020]	China	Jinyintan Hospital and Wuhan Pulmonary Hospital	2019.12.29-2020.01.31	33 days	119 (62.3)	191	54 (28.3)	69 [63–76]	38 (70.4)	137 (71.7)	52 [45–58]	81 (59.1)	
Zhou X [2020]	China	Wuhan Fourth Hospital	2020.01.25-2020.02.20	NA	NA	110	9 (8.2)	NA	NA	101 (91.8)	NA	NA	
An W [2020]	China	Hubei No. 3 People's Hospital	2020.01.24-2020.02.19	NA	15 (13.6)	110	11 (10.0)	72.4±7.1	6 (54.5)	99 (90.0)	54.6±15.6	38 (38.4)	
Chang Z [2020]	China	Wuhan Puren Hospital	2020.01-2020.02	NA	57 (38.0)	150	20 (13.3)	NA	NA	130 (86.7)	NA	NA	
Foy BH [2020]	United States	Massachusetts General Hospital, Brigham and Women's Hospital, North Shore Medical Center and Newton-Wellesley Hospital	2020.03.04-2020.04.28	55 days	NA	1,198	155 (12.9)	75±13.2	98 (63.2)	1,043 (87.1)	59.6±17.5	563 (54.0)	
Guo F [2020]	China	First Affiliated Hospital of Bengbu Medical College	2020.01.22-2020.03.08	NA	31 (39.2)	79	5 (6.3)	NA	NA	72 (91.1)	NA	NA	
Li JW [2020]	China	Wuhan Red Cross Hospital in Wuhan	2020.01.21-2020.02.14	24 days	NA	161	65 (40.4)	67 [31–87]	42 (64.6)	96 (59.6)	46 [22–87]	38 (39.6)	
Luo M [2020]	China	Wuhan Tongren Hospital of Wuhan University (Wuhan Third Hospital)	2020.01.17-2020.02.25	NA	152 (11.6)	1,305	69 (5.3)	NA	46 (66.7)	1,236 (94.7)	NA	NA	
Fang XW [2020]	China	Infectious Hospital of Anhui Provincial Hospital	2020.01.22-2020.02.18	27 days	24 (30.4)	79	1 (1.3)	NA	NA	78 (98.7)	NA	NA	
Yang H [2020]	China	Sino-French Eco-City section of Tongji Hospital (Peking University Supporting Medical Team)	2020.01.29-2020.03.10	68 days	19 (20.2)	94	13 (13.8)	77 [67.5–83]	8 (61.5)	81 (86.2)	66 [59.0–72.5]	37 (45.7)	
Yang JK [2020]	China	Wuhan Union Hospital (Beijing Tongren Hospital Medical Team)	2020.01.29-2020.03.20	55 days	46 (66.7)	69	16 (23.2)	64 [57–68]	13 (81.3)	53 (76.8)	60 [51–67]	21 (39.6)	
Zhang CS [2020]	China	Dabieshan Medical Center	2020.01.30-2020.02.14	NA	32 (100.0)	32	6 (18.8)	59.3±11.1	3 (50.0)	26 (81.3)	57.9±12.4	17 (65.4)	
Zhang F [2020]	China	Wuhan No.1 Hospital	2019.12.25-2020.01.15	NA	22 (45.8)	48	17 (35.4)	78.65±8.31	12 (70.6)	31 (64.6)	66.16±13.66	21 (67.7)	
Zhang G [2020]	China	Wuhan Xinzhou District People's Hospital	2020.01.16-2020.02.25	46 days	32 (33.7)	95	6 (6.3)	66 [38.3–76.8]	6 (100.0)	89 (93.7)	49 [39.5–57]	47 (52.8)	
Zhang JG [2020]	China	The First People's Hospital of Jiangxia District (The Affiliated Hospital of Jiangsu University Medical Team)	2020.02.01-2020.03.15	NA	30 (22.2)	135	18 (13.3)	65 [56.8–76.8]	9 (50.0)	117 (86.7)	NA	NA	

^a, age data presented as median (interquartile range), mean (standard deviation) or median (range).

0	N	Dana	Pooled proportion using random-	Hetero	geneity	Publication bias: 95% Cl	
Groups	NO. STUDIES	Range	effects model	l ²	Р	P _{egger: bias}	
Overall mortality	79	0.6–50%	0.140 (95% CI: 0.122-0.159)	97.80%	<0.001	3.896–7.253; <0.001	
Sample size							
>100	54	0.6-40.4%	0.137 (95% Cl: 0.115–0.158)	98.40%	<0.001	5.011–9.934; <0.001	
≤100	25	0.6-40.5%	0.153 (95% Cl: 0.114-0.192)	86.80%	<0.001	3.255–5.424; <0.001	
Region							
Asia	61	0.6–50%	0.101 (95% Cl: 0.086–0.115)	95.60%	<0.001	3.477–5.847; <0.001	
Europe	11	13.5–37.5%	0.237 (95% Cl: 0.197–0.276)	77.80%	<0.001	-4.227 to 4.729; 0.902	
North America	7	4.2-39.3%	0.254 (95% Cl: 0.150-0.359)	98.60%	<0.001	-15.421 to 14.102; 0.917	
Source of cases							
Single-center	55	0.7-42.1%	0.142 (95% Cl: 0.121-0.163)	95.70%	<0.001	3.585–6.639; <0.001	
Multiple-center	24	0.6–50%	0.136 (95% Cl: 0.099–0.173)	98.90%	<0.001	2.029–11.399; 0.007	
Study quality							
NOS >6	21	0.7-35.4%	0.140 (95% CI: 0.106–0.174)	93.70%	<0.001	2.264–6.298; <0.001	
NOS ≤6	58	0.6–50%	0.140 (95% CI: 0.118-0.162)	98.30%	<0.001	3.866–8.353; <0.001	
Study design							
Retrospective	71	0.6–50%	0.136 (95% CI: 0.117-0.156)	97.90%	<0.001	3.594–7.186; <0.001	
Prospective	8	0.7–39.3%	0.180 (95% CI: 0.093-0.267)	97.80%	<0.001	3.937–15.797; 0.007	
Longest follow-u	р						
>30 days	24	0.9–38%	0.151 (95% CI: 0.118–0.184)	96.80%	<0.001	4.754–9.401; <0.001	
≤30 days	21	0.7–50%	0.173 (95% CI: 0.127-0.220)	96.70%	<0.001	4.347–9.276; <0.001	
Proportion of pat	ients with seve	re disease					
>50%	20	3.8–50%	0.225 (95% CI: 0.165–0.284)	96.10%	<0.001	2.808–8.163; <0.001	
≤50%	30	0.7-35.4%	0.077 (95% CI: 0.061–0.094)	94.70%	<0.001	2.934–6.010; <0.001	

Table 2 Mortality of COVID-19 patients: results of meta-analyses

NOS, Newcastle-Ottawa scale.

Risk factors

A total of 31 studies reported the detailed data regarding the association of demographic and clinical characteristics, laboratory data, imaging features, and complications with mortality of COVID-19 patients, of which 25 performed both univariate and multivariate analyses (Table S3).

The detailed results of meta-analyses are presented in *Table 3* and forest plots in the Supplementary Materials.

Demographics

Meta-analyses indicated that male (OR =1.66, 95% CI: 1.37–2.01; P<0.00001) and older age (MD =13.32, 95% CI:

10.87–15.77; P<0.00001) were significant risk factors for death of COVID-19 patients.

Comorbidities

Meta-analyses indicated that hypertension (OR =2.67, 95% CI: 2.08–3.43; P<0.00001), diabetes (OR =2.14, 95% CI: 1.76–2.6; P<0.00001), chronic respiratory disease (OR =3.55, 95% CI: 2.65–4.76; P<0.00001), chronic heart disease/cardiovascular disease (OR =3.15, 95% CI: 2.43–4.09; P<0.00001), cerebrovascular disease (OR =5.92, 95% CI: 4.16–8.42; P<0.00001), chronic kidney disease (OR =3.04, 95% CI: 2.12–4.36; P<0.00001), cancer (OR =3.05,

 Table 3 Comparison of demographic characteristics, comorbidities, clinical symptoms, laboratory data, imaging features, and complications between non-survivors and survivors of COVID-19

	No				Heterogeneity		
Parameter	studies	Pooled MD (95% CI)	Pooled OR (95% CI)	P value	l ²	Cochran's Q P value	
Demographics and clinical characteristics							
Male	31	-	1.66 (1.37, 2.01)	<0.00001	57%	<0.0001	
Older age	30	13.32 (10.87, 15.77)	-	<0.00001	94%	<0.00001	
Time from illness onset to hospital admission, days	11	0.49 (-0.34, 1.33)	-	0.25	56%	0.01	
Comorbidities							
Hypertension	24	-	2.67 (2.08, 3.43)	<0.00001	68%	<0.00001	
Diabetes	24	-	2.14 (1.76, 2.6)	<0.00001	37%	0.04	
Chronic respiratory disease	21	-	3.55 (2.65, 4.76)	<0.00001	25%	0.14	
CHD/cardiovascular disease	24	-	3.15 (2.43, 4.09)	<0.00001	58%	0.0001	
Cerebrovascular disease	10	-	5.92 (4.16, 8.42)	<0.00001	0%	0.63	
Chronic kidney disease	15	-	3.04 (2.12, 4.36)	<0.00001	62%	0.0005	
Smoking	8	-	1.32 (1.07, 1.62)	0.01	5%	0.40	
Cancer	17	-	3.05 (1.92, 4.85)	<0.00001	62%	0.0002	
Clinical symptoms							
Fever	19	-	1.12 (0.82, 1.53)	0.48	25%	0.16	
Cough	17	-	1.02 (0.75, 1.39)	0.90	42%	0.03	
Dyspnea	13	-	5.31 (2.74, 10.28)	<0.00001	81%	<0.00001	
Myalgia	9	-	0.91 (0.64, 1.31)	0.62	0%	0.52	
Fatigue	11	-	1.47 (0.93, 2.34)	0.10	61%	0.004	
Hemoptysis	3	-	1.25 (0.38, 4.14)	0.72	0%	0.37	
Sputum production	11	-	1.88 (1.39, 2.55)	<0.0001	22%	0.24	
Diarrhea	12	-	1.14 (0.83, 1.56)	0.43	0%	0.51	
Laboratory tests							
White blood cell count, ×10 ⁹ /L	18	3.23 (2.63, 3.83)	-	<0.00001	52%	0.005	
Lymphocyte count, ×10 ⁹ /L	15	-0.41 (-0.52, -0.30)	-	<0.00001	82%	<0.00001	
Neutrophil count, ×10 ⁹ /L	10	2.47 (0.06, 4.88)	_	0.04	95%	<0.00001	
Platelet count, ×10 ⁹ /L	11	-44.37 (-53.01, -35.74)	_	<0.00001	0%	0.68	
Hemoglobin, g/L	7	-5.59 (-10.64, -0.54)	_	0.03	69%	0.004	
Albumin, g/L	7	-3.98 (-5.75, -2.22)	-	<0.0001	81%	<0.0001	
ALT, U/L	13	6.72 (1.80, 11.64)	-	0.007	72%	<0.0001	
AST, U/L	13	16.78 (11.78, 21.78)	_	<0.00001	60%	0.003	
TBIL, μmol/L	6	1.59 (0.06, 3.11)	-	0.04	0%	0.52	

Table 3 (continued)

Table 3	(continued)
---------	-------------

	NL				Heterogeneity		
Parameter	NO. studies	Pooled MD (95% Cl)	Pooled OR (95% CI)	P value	l ²	Cochran's Q P value	
LDH, U/L	10	288.29 (225.73, 350.85)	-	<0.00001	59%	0.009	
High-sensitive cardiac troponin I, pg/mL	4	66.65 (16.94, 116.36)	-	0.09	78%	0.04	
Hypersensitive troponin I, >26.2 pg/mL	3	-	26.80 (8.99, 79.94)	<0.00001	3%	0.36	
NT-proBNP, µg/L	3	1.08 (0.79, 1.36)	-	<0.00001	0%	0.82	
CK, U/L	9	96.64 (47.87, 145.41)	-	0.0001	76%	< 0.0001	
CK-MB, U/L	5	6.37 (3.72, 9.03)	-	<0.00001	0%	0.58	
PT, s	8	0.73 (0.20, 1.25)	-	0.006	45%	0.08	
APTT, s	6	1.17 (-3.68, 6.02)	-	0.64	92%	<0.00001	
D-dimer, mg/L	13	4.33 (2.97, 5.68)	-	<0.00001	92%	<0.00001	
CRP, mg/L	11	48.03 (27.79, 68.27)	-	<0.00001	83%	<0.00001	
ESR, mm/h	5	7.87 (2.53, 13.21)	-	0.004	51%	0.09	
IL-6, pg/mL	3	47.98 (-8.34, 104.29)	-	0.09	97%	<0.00001	
Procalcitonin, ng/mL	6	0.23 (0.06, 040)	-	0.007	89%	<0.00001	
Serum ferritin, mg/L	3	0.92 (0.67, 1.17)	-	< 0.00001	48%	0.15	
Fasting blood glucose, mmol/L	4	1.42 (0.68, 2,16)	-	0.0002	0%	0.81	
Serum creatinine, µmol/L	15	26.11 (12.61, 39.61)	-	0.0002	93%	<0.00001	
SpO ₂ , %	6	-8.32 (-11.49, -5.15)	_	<0.00001	80%	<0.00001	
Imaging features							
Bilateral involvement	5	-	3.33 (1.57, 7.05)	0.002	46%	0.11	
Ground-glass opacity	3	-	3.67 (0.85, 15.79)	0.08	63%	0.07	
Complications							
ARDS	8	-	62.85 (29.45, 134.15)	<0.00001	47%	0.06	
Acute cardiac injury	6	-	25.16 (6.56, 96.44)	<0.00001	73%	0.002	
Acute kidney injury	7	-	22.86 (4.60, 113.66)	0.0001	68%	0.005	
Septic shock	7	-	24.09 (4.26, 136.35)	0.0003	76%	0.0003	

OR, odds ratio; WMD, weighted mean difference; COPD, chronic obstructive pulmonary disease; CHD, chronic heart disease; ALT, alanine aminotransferase; AST, aspartate transaminase; LDH, lactate dehydrogenase; NT-proBNP, amino-terminal pro-brain natriuretic peptide; CK, creatine kinase; CK-MB, creatine kinase-MB; PT, prothrombin time; APTT, activated partial thromboplastin time; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SpO₂, peripheral oxygen saturation; ARDS, acute respiratory distress syndrome.

95% CI: 1.92–4.85; P<0.00001), and smoking (OR =1.32, 95% CI: 1.07–1.62; P=0.01) were significant risk factors for death of COVID-19 patients.

Clinical symptoms

Meta-analysis indicated that dyspnea (OR =5.31, 95% CI:

2.74–10.28; P<0.00001) and expectoration (OR =1.88, 95% CI: 1.39–2.55; P<0.0001) at admission were significant risk factor for death of COVID-19 patients, but fever (OR =1.12, 95% CI: 0.82–1.53; P=0.48), cough (OR =1.02, 95% CI: 0.75–1.39; P=0.90), myalgia (OR =0.91, 95% CI: 0.64–1.31; P=0.62), fatigue (OR =1.47, 95% CI: 0.93–2.34;



Figure 2 Scattered plots of association of mortality with the proportion of severe COVID-19 patients. (A) Scattered plots showing an increased trend of overall mortality with the proportion of severe COVID-19 patients included. (B) In studies with the proportion of severe patients >50%, an increased trend of mortality with the proportion of severe COVID-19 patients included. (C) In studies with the proportion of severe patients >50%, an increased trend of mortality with the proportion of severe COVID-19 patients included. (C) In studies with the proportion of severe patients >50%, an increased trend of mortality with the proportion of severe COVID-19 patients included.

P=0.10), hemoptysis (OR =1.25, 95% CI: 0.38-4.14; P=0.72), and diarrhea (OR =1.14, 95% CI: 0.83-1.56; P=0.43) at admission were not significantly associated with mortality.

Laboratory tests

Meta-analysis indicated that increased levels of white blood cells (WBC) (MD =3.23, 95% CI: 2.63-3.83; P<0.00001), alanine aminotransferase (ALT) (MD =6.72, 95% CI: 1.80-11.64; P=0.007), aspartate aminotransferase (AST) (MD =16.78, 95% CI: 11.78-21.78; P<0.00001), total bilirubin (TBIL) (MD =1.59, 95% CI: 0.06-3.11; P=0.04), lactate dehydrogenase (LDH) (MD =288.29, 95% CI: 225.73-350.85; P<0.00001), high-sensitive cardiac troponin I (hs-cTnI) (MD =66.65, 95% CI: 16.94–116.36; P=0.009), D-dimer (MD =4.33, 95% CI: 2.97-5.68; P<0.00001), C-reactive protein (MD =48.03, 95% CI: 27.79-68.27; P<0.00001), and serum creatinine (MD =26.11, 95% CI: 12.61-39.61; P=0.0002) at admission were significant risk factors for death of COVID-19 patients; and decreased levels of albumin (MD =-3.98, 95% CI: -5.75 to -2.22; P<0.0001), lymphocytes (MD =-0.41, 95% CI: -0.52 to -0.30; P<0.00001), hemoglobin (MD =-5.59, 95% CI: -10.64 to -0.54; P=0.03), platelet (MD =-44.37, 95% CI: -53.01 to -37.74; P<0.00001), and peripheral oxygen saturation (SpO₂) (MD =-8.32, 95% CI: -11.49 to -5.15; P<0.00001) at admission were significant risk factors for death of COVID-19 patients. Additionally, hs-cTnI >26.2 pg/mL as a categorical variable (OR =26.80, 95%

CI: 8.99–79.94; P<0.00001) at admission was significantly associated with an increased risk of COVID-19 mortality.

Imaging features

Meta-analysis indicated that bilateral involvement was a significant risk factor for death of COVID-19 patients (OR =3.33, 95% CI: 1.57–7.05; P=0.002), but ground-glass opacity was not significantly associated with mortality (OR =3.67, 95% CI: 0.85–15.79; P=0.08).

Complications

Meta-analysis indicated that ARDS (OR =62.85, 95% CI: 29.45–134.15; P<0.00001), acute cardiac injury (OR =25.16, 95% CI: 6.56–96.44; P<0.00001), acute kidney injury (OR =22.86, 95% CI: 4.60–113.66; P=0.0001), and septic shock (OR =24.09, 95% CI: 4.26–136.35; P=0.0003) were significant risk factors for death of COVID-19 patients.

Scattered plots demonstrated an increased trend of overall mortality with the proportion of severe COVID-19 patients included (P<0.001, r=0.631) (*Figure 2A*). In studies with the proportion of severe patients >50%, the trend remained statistically significant (P=0.008; r=0.577) (*Figure 2B*). In studies with the proportion of severe patients \leq 50%, the trend remained not statistically significant (P=0.059, r=0.349) (*Figure 2C*).

Discussion

The present meta-analysis suggested that the pooled in-

hospital mortality of COVID-19 patients was 14%. By comparison, previous meta-analyses reported that the mortality of COVID-19 patients was relatively lower [i.e., 3.2% in the Hu' meta-analysis (16) or 7.7% in our previous meta-analysis (6)]. This discrepancy can be explained by the difference in the severity of COVID-19 patients included among them. Indeed, the proportion of severe COVID-19 patients was higher in the present meta-analysis than the previous meta-analysis [49.6% versus 18% (16)], which might overestimate the overall mortality.

Severe disease status was an independent risk factor for death in COVID-19 patients (17,18). Our subgroup analyses also found that the in-hospital mortality of COVID-19 patients in studies with the proportion of patients with severe disease of >50% was higher than those $\leq 50\%$ (22.5% versus 7.7%). Severe patients had more prominent laboratory abnormalities [i.e., leukopenia, lymphopenia, elevated levels of C-reactive protein and interleukin 6 (IL-6)] as compared to non-severe patients. Increased levels of C-reactive protein and inflammatory cytokines, such as IL-6, may induce "cytokines storm", thereby aggravating systemic inflammatory response syndrome in patients with severe disease, which may be a driving factor of acute lung injury and ARDS and even death (19-21). The mortality in COVID-19 patients with ARDS was up to 39% (22). We also confirmed that ARDS was associated with a 62.85-fold increase in the risk of death in COVID-19 patients.

The mortality of COVID-19 patients greatly varies among regions. It seems to be the lowest in China (3.1%)and the highest in the United Kingdom (20.8%) and New York State (20.99%) (23). Our subgroup analysis also demonstrated that the in-hospital mortality of COVID-19 patients in Europe and North America were higher than Asia (23.7% and 25.4% versus 10.1%). This might be explained by the aging of patients in Europe and North America. It has been reported that 37.6% of COVID-19 patients are beyond 70 years old in Italy, but only 11.9% in China (24). As shown by our meta-analysis and others (23), age is a significant risk factor of death in COVID-19 patients. In other words, a higher proportion of elderly patients is often in parallel with an increased mortality. This phenomenon could be attributed to the relationship of aging with immune response impairment and chronic inflammation (25) and a high prevalence of comorbidities, such as hypertension, diabetes, and cardiovascular disease, in elderly patients. Obesity is common in Western countries with an increasing prevalence of obesity, and associated with poor prognosis of COVID-19 patients

(26,27). Angiotensin-converting enzyme 2 (ACE2) is the receptor of SARS-CoV-2 infection target cells, and ACE2 expression level in adipocytes is higher than that in lung tissue. Obese people have more adipose tissue and therefore higher ACE2 levels. Among the obese population, the renin-angiotensin-aldosterone system is overactive, increasing the production of angiotensin II (26). Elevated angiotensin II levels in COVID-19 patients are related to the severity of lung injury (28), which will increase the risk of death. Additionally, it has been confirmed that obesity increases the risk of cardiovascular disease and its mortality (29). Besides, the difference in public prevention and control strategies of COVID-19 among countries is another major explanation for this variation (30).

Pre-existing comorbidities correlated with an increased risk of mortality in COVID-19 patients, probably because patients with hypertension and diabetes have higher circulating ACE2 levels (31,32). A wider distribution of ACE2 in cardiac epithelial cells as well as respiratory, kidney, and liver is associated with organ failure in patients with SARS (33-35). Therefore, it is postulated that patients with cardiovascular disease are more prone to use angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs), thereby elevating the ACE2 expression and then increasing the risk of SARS-CoV-2 infection and disease progression (36).

Acute cardiac injury was also associated with poor outcomes in COVID-19 patients. Similarly, previous studies suggested that COVID-19 patients with abnormal troponin I, which is a marker of acute myocardial injury, had worse prognosis (37,38). Underlying mechanisms for explaining this phenomenon are as follows. First, the release of proinflammatory cytokines, endothelial dysfunction, and increased oxidative stress can lead to a hypercoagulable state, which is prone to coronary arterial thrombosis and triggers acute coronary syndrome (25). Second, SARS-CoV-2 binds to ACE2 receptor, which is widely expressed in cardiomyocytes, thereby attacking cardiac epithelial cells and inducing cardiac injury (39-41).

Lung pathology of critically ill patients showed occlusion and micro-thrombosis in pulmonary vessels (42). Additionally, severe COVID-19 patients, especially those with sepsis, are often at a hypercoagulable state (20,43). Our study confirmed that D-dimer level, a convenient biomarker of thrombotic events (44), was associated with the mortality of COVID-19 patients.

Of note, non-survival group had a significantly higher

proportion of male than survival group. This may be attributed to the difference in the levels and types of sex hormones between males and females. Estrogen can modulate the responses of adaptive and innate immunity, which can reduce the susceptibility of females to viral infections (45). On the contrary, males are more susceptible to SARS-CoV-2 infection (46).

Major limitations of the present work should be that all studies included in this meta-analysis were observational with different patient characteristics and follow-up periods, a majority of studies were retrospective, and some of them were of low quality, which might produce the potential selection bias and recall bias. Additionally, the heterogeneity in most of meta-analyses was significant. Although we performed subgroup, meta-regression, and sensitivity analyses, the source of heterogeneity was not clearly identified.

In conclusion, based on the systematic review and meta-analysis, the in-hospital mortality of COVID-19 patients was up to 14%. Older age, male, comorbidities (i.e., hypertension, diabetes, cardiovascular diseases, and respiratory diseases), clinical presentations with dyspnea and expectoration, and laboratory abnormalities (i.e., WBC, AST, ALT, serum creatinine, C-reactive protein, LDH, hscTnI, and D-dimer), should be important predictors for mortality of COVID-19 patients. Moreover, patients who develop ARDS, acute cardiac injury, acute kidney injury, and septic shock are at higher risk of death.

Acknowledgments

Funding: None.

Footnote

Reporting Checklist: The authors have completed the MOOSE and PRISMA reporting checklists. Available at http://dx.doi.org/10.21037/apm-20-2557

Peer Review File: Available at http://dx.doi.org/10.21037/ apm-20-2557

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi. org/10.21037/apm-20-2557). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Open Access Statement: This is an Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License (CC BY-NC-ND 4.0), which permits the non-commercial replication and distribution of the article with the strict proviso that no changes or edits are made and the original work is properly cited (including links to both the formal publication through the relevant DOI and the license). See: https://creativecommons.org/licenses/by-nc-nd/4.0/.

References

- WHO. Situation Report 22 2020. Available online: https://www.who.int/docs/default-source/ coronaviruse/situation-reports/20200211-sitrep-22-ncov. pdf?sfvrsn=fb6d49b1_2. Accessed on August 4, 2020.
- Li Q, Guan X, Wu P, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. N Engl J Med 2020;382:1199-207.
- Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020;579:270-3.
- Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420-2.
- WHO. Coronavirus disease 2019 (COVID-19) Situation Report. Available online: https://www.who.int/ emergencies/diseases/novel-coronavirus-2019. Accessed on August 4, 2020.
- Wu YY, Li HY, Xu XB, et al. Clinical features and outcome of treatment for novel coronavirus pneumonia: a metaanalysis. Zhonghua Gan Zang Bing Za Zhi 2020;28:240-6.
- Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-13.
- WHO. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). WHO. 2020. Available online: https://www.who.int/docs/default-source/ coronaviruse/who-china-joint-mission-on-covid-19--final-report-1100hr-28feb2020-11mar-update.pdf?sfvrsn= 1a13fda0_2&download=true. Accessed on August 4, 2020.
- Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-

Wu et al. Risk factors of mortality in COVID-19 patients

Infected Pneumonia in Wuhan, China. JAMA 2020;323:1061-9.

- Guan WJ, Ni ZY, Hu Y, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med 2020;382:1708-20.
- Wang X, Fang X, Cai Z, et al. Comorbid Chronic Diseases and Acute Organ Injuries Are Strongly Correlated with Disease Severity and Mortality among COVID-19 Patients: A Systemic Review and Meta-Analysis. Research (Wash D C) 2020;2020:2402961.
- 12. Martins-Filho PR, Tavares CSS, Santos VS. Factors associated with mortality in patients with COVID-19. A quantitative evidence synthesis of clinical and laboratory data. Eur J Intern Med 2020;76:97-9.
- Parohan M, Yaghoubi S, Seraji A, et al. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. Aging Male 2020;23:1416-24.
- 14. Tian W, Jiang W, Yao J, et al. Predictors of mortality in hospitalized COVID-19 patients: A systematic review and meta-analysis. J Med Virol 2020;92:1875-83.
- 15. Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. Pol Arch Intern Med 2020;130:304-9.
- Hu Y, Sun J, Dai Z, et al. Prevalence and severity of corona virus disease 2019 (COVID-19): A systematic review and meta-analysis. J Clin Virol 2020;127:104371.
- 17. Sun DW, Zhang D, Tian RH, et al. The underlying changes and predicting role of peripheral blood inflammatory cells in severe COVID-19 patients: A sentinel? Clin Chim Acta 2020;508:122-9.
- Luo M, Jiang B, Xu HJ, et al. Analysis of influencing factors of death in patients with COVID-19. Chinese Traditional and Herbal Drugs 2020;51:1450-4.
- Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet 2020;395:1033-4.
- Lin L, Lu L, Cao W, et al. Hypothesis for potential pathogenesis of SARS-CoV-2 infection-a review of immune changes in patients with viral pneumonia. Emerg Microbes Infect 2020;9:727-32.
- Ulhaq ZS, Soraya GV. Interleukin-6 as a potential biomarker of COVID-19 progression. Med Mal Infect 2020;50:382-3.
- 22. Hasan SS, Capstick T, Ahmed R, et al. Mortality in COVID-19 patients with acute respiratory distress syndrome and corticosteroids use: a systematic review and

meta-analysis. Expert Rev Respir Med 2020;14:1149-63.

- 23. Bonanad C, Garcia-Blas S, Tarazona-Santabalbina F, et al. The Effect of Age on Mortality in Patients With COVID-19: A Meta-Analysis With 611,583 Subjects. J Am Med Dir Assoc 2020;21:915-8.
- Onder G, Rezza G, Brusaferro S. Case-Fatality Rate and Characteristics of Patients Dying in Relation to COVID-19 in Italy. JAMA 2020;323:1775-6.
- 25. Libby P. Inflammation in atherosclerosis. Nature 2002;420:868-74.
- 26. Sanchis-Gomar F, Lavie CJ, Mehra MR, et al. Obesity and Outcomes in COVID-19: When an Epidemic and Pandemic Collide. Mayo Clin Proc 2020;95:1445-53.
- 27. Sharma A, Garg A, Rout A, et al. Association of Obesity With More Critical Illness in COVID-19. Mayo Clin Proc 2020;95:2040-2.
- Liu Y, Yang Y, Zhang C, et al. Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury. Sci China Life Sci 2020;63:364-74.
- 29. Pranata R, Huang I, Lim MA, et al. Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19-systematic review, metaanalysis, and meta-regression. J Stroke Cerebrovasc Dis 2020;29:104949.
- Hradsky O, Komarek A. Demographic and public health characteristics explain large part of variability in COVID-19 mortality across countries. Eur J Public Health 2021;31:12-6.
- Patel SK, Velkoska E, Freeman M, et al. From gene to protein-experimental and clinical studies of ACE2 in blood pressure control and arterial hypertension. Front Physiol 2014;5:227.
- 32. Soro-Paavonen A, Gordin D, Forsblom C, et al. Circulating ACE2 activity is increased in patients with type 1 diabetes and vascular complications. J Hypertens 2012;30:375-83.
- 33. Yang JK, Feng Y, Yuan MY, et al. Plasma glucose levels and diabetes are independent predictors for mortality and morbidity in patients with SARS. Diabet Med 2006;23:623-8.
- 34. Li R, Qiao S, Zhang G. Analysis of angiotensin-converting enzyme 2 (ACE2) from different species sheds some light on cross-species receptor usage of a novel coronavirus 2019-nCoV. J Infect 2020;80:469-96.
- 35. Yang JK, Lin SS, Ji XJ, et al. Binding of SARS coronavirus to its receptor damages islets and causes acute diabetes. Acta Diabetol 2010;47:193-9.
- 36. Fang L, Karakiulakis G, Roth M. Are patients with

5082

hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020;8:e21.

- Lippi G, Lavie CJ, Sanchis-Gomar F. Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Prog Cardiovasc Dis 2020;63:390-1.
- Vrsalovic M, Vrsalovic Presecki A. Cardiac troponins predict mortality in patients with COVID-19: A meta-analysis of adjusted risk estimates. J Infect 2020;81:e99-100.
- Chen Y, Guo Y, Pan Y, et al. Structure analysis of the receptor binding of 2019-nCoV. Biochem Biophys Res Commun 2020;525:135-40.
- 40. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 2020;395:565-74.
- 41. Turner AJ, Hiscox JA, Hooper NM. ACE2: from vasopeptidase to SARS virus receptor. Trends Pharmacol

Cite this article as: Wu Y, Li H, Zhang Z, Liang W, Zhang T, Tong Z, Guo X, Qi X. Risk factors for mortality of coronavirus disease 2019 (COVID-19) patients during the early outbreak of COVID-19: a systematic review and meta-analysis. Ann Palliat Med 2021;10(5):5069-5083. doi: 10.21037/apm-20-2557

Sci 2004;25:291-4.

- Luo W, Yu H, Gou J, et al. Clinical Pathology of Critical Patient with Novel Coronavirus Pneumonia (COVID-19). Preprints 2020. Available online: https://wwwpreprintsorg/ manuscript/2020020407/v4. Accessed 13 Aug 2020.
- 43. Levi M, van der Poll T. Coagulation and sepsis. Thromb Res 2017;149:38-44.
- Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and Thrombotic or Thromboembolic Disease: Implications for Prevention, Antithrombotic Therapy, and Follow-Up: JACC State-of-the-Art Review. J Am Coll Cardiol 2020;75:2950-73.
- Jaillon S, Berthenet K, Garlanda C. Sexual Dimorphism in Innate Immunity. Clin Rev Allergy Immunol 2019;56:308-21.
- 46. Vahidy FS, Pan AP, Ahnstedt H, et al. Sex differences in susceptibility, severity, and outcomes of coronavirus disease 2019: Cross-sectional analysis from a diverse US metropolitan area. PLoS One 2021;16:e0245556.

Appendix: References of all included studies

1.	Aggarwal S, Garcia-Telles N, Aggarwal G, et al. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): Early report from the United States. JMIR Public Health Surveill 2020;7:91-6.
2.	Barrasa H, Rello J, Tejada S, et al. SARS-CoV-2 in Spanish Intensive Care Units: Early experience with 15-day survival in Vitoria. Anaesth Crit Care Pain Med 2020;39:553-61.
3.	Benussi A, Pilotto A. Clinical characteristics and outcomes of inpatients with neurologic disease and COVID-19 in Brescia, Lombardy, Italy. Neurology 2020;95:e910-20.
4.	Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically III Patients in the Seattle Region - Case Series. N Engl J Med 2020;382:2012-22.
5.	Bianchetti A, Rozzini R, Guerini F, et al. Clinical Presentation of COVID19 in Dementia Patients. J Nutr Health Aging 2020:24:560-2.
6.	Borghesi A, Zigliani A, Golemi S, et al. Chest X-ray severity index as a predictor of in-hospital mortality in coronavirus disease 2019: A
	study of 302 patients from Italy. Int J Clin Pract Suppl 2020;96:291-3.
7.	Buckner FS, McCulloch DJ, Atluri V, et al. Clinical Features and Outcomes of 105 Hospitalized Patients With COVID-19 in Seattle, Washington. Clin Infect Dis 2020;71:2167-73.
8.	Cai Q, Huang D, Ou P, et al. COVID-19 in a designated infectious diseases hospital outside Hubei Province, China. Allergy 2020;75:1742-52.
9.	Cecconi M, Piovani D, Brunetta E, et al. Early Predictors of Clinical Deterioration in a Cohort of 239 Patients Hospitalized for Covid-19 Infection in Lombardy, Italy. J Clin Med 2020;9:1548.
10.	Chen R, Liang W, Jiang M, et al. Risk Factors of Fatal Outcome in Hospitalized Subjects With Coronavirus Disease 2019 From a Nationwide Analysis in China. Chest 2020;158:97-105.
11.	Andrea C, Francesco M, Antonio N, et al. RAAs inhibitors and outcome in patients with SARS-CoV-2 pneumonia. A case series study. Hypertension 2020;76:e10-2.
12.	Cummings MJ, Baldwin MR, Abrams D, <i>et al.</i> Epidemiology, clinical course, and outcomes of critically ill adults with COVID-19 in New York City: a prospective cohort study. Lancet 2020;395:1763-70.
13.	Deng Y, Liu W, Liu K, <i>et al.</i> Clinical characteristics of fatal and recovered cases of coronavirus disease 2019 in Wuhan, China: a retrospective study. Chin Med J (Engl) 2020;133:1261-7.
14.	Dong XC, Li JM, Bai JY, et al. Epidemiological characteristics of confirmed COVID-19 cases in Tianjin. Zhonghua Liu Xing Bing Xue Za Zhi 2020;41:638-41.
15.	Du RH, Liang LR, Yang CQ, <i>et al.</i> Predictors of mortality for patients with COVID-19 pneumonia caused by SARSCoV- 2: A prospective cohort study. Eur Respir J 2020;55:2000524.
16.	Gao L, Jiang D, Wen XS, et al. Prognostic value of NT-proBNP in patients with severe COVID-19. Respir Res 2020;21:83.
17.	Giacomelli A, Ridolfo AL, Milazzo L, et al. 30-day mortality in patients hospitalized with COVID-19 during the first wave of the Italian epidemic: A prospective cohort study. Pharmacol Res 2020;158:104931.
18.	Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients with Coronavirus Disease 2019 (COVID-19). JAMA Cardiol 2020;5:1-8.
19.	Hong KS, Lee KH, Chung JH, <i>et al.</i> Clinical features and outcomes of 98 patients hospitalized with sars-cov-2 infection in daegu, south korea: A brief descriptive study. Yonsei Med J 2020;61:431-7.
20.	Hou W, Zhang W, Jin R, et al. Risk factors for disease progression in hospitalized patients with COVID-19: a retrospective cohort study. Infect Dis (Lond) 2020;52:498-505.
21.	Hu H, Yao N, Qiu Y. Comparing Rapid Scoring Systems in Mortality Prediction of Critically III Patients With Novel Coronavirus Disease. Acad Emerg Med 2020;27:461-8.
22.	Hu L, Chen S, Fu Y, et al. Risk Factors Associated With Clinical Outcomes in 323 Coronavirus Disease 2019 (COVID-19) Hospitalized Patients in Wuhan, China. Clin Infect Dis 2020;71:2089-98.
23.	Huang J, Cheng A, Kumar R, et al. Hypoalbuminemia predicts the outcome of COVID-19 independent of age and co-morbidity. J Med Virol 2020;92:2152-8.
24.	Inciardi RM, Adamo M, Lupi L, <i>et al.</i> Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. Eur Heart J 2020;41:1821-9.
25.	Israelsen SB, Kristiansen KT, Hindsberger B, et al. Characteristics of patients with COVID-19 pneumonia at Hvidovre Hospital, March- April 2020. Dan Med J 2020;67:A05200313.
26.	Itelman E, Wasserstrum Y, Segev A, et al. Clinical Characterization of 162 COVID-19 patients in Israel: Preliminary Report from a Large Tertiary Center. Isr Med Assoc J 2020;22:271-4.
27.	Javanian M, Bayani M, Shokri M, <i>et al.</i> Clinical and laboratory findings from patients with COVID-19 pneumonia in Babol North of Iran: a retrospective cohort study. Rom J Intern Med 2020;58:161-7.
28.	Ji D, Zhang D, Xu J, et al. Prediction for Progression Risk in Patients With COVID-19 Pneumonia: The CALL Score. Clin Infect Dis 2020;71:1393-9.
29.	Klang E, Kassim G, Soffer S, et al. Severe Obesity as an Independent Risk Factor for COVID-19 Mortality in Hospitalized Patients Younger than 50. Obesity (Silver Spring) 2020;28:1595-9.
30.	Li J, Wang X, Chen J, <i>et al.</i> Association of Renin-Angiotensin System Inhibitors With Severity or Risk of Death in Patients With Hypertension Hospitalized for Coronavirus Disease 2019 (COVID-19) Infection in Wuhan, China. JAMA Cardiol 2020;5:825-30.
31.	Li R, Tian J, Yang F, et al. Clinical characteristics of 225 patients with COVID-19 in a tertiary Hospital near Wuhan, China. J Clin Virol 2020:127:104363.

00	·
32.	Li X, Wang X, Liu J, et al. Epidemiological characteristics of confirmed COVID-19 in Guizhou province, China. Disaster Med Public Health Prep 2020. [Epub ahead of print]. doi: 10.1017/dmp.2020.134.
33.	Ling L, So C, Shum HP, et al. Critically ill patients with COVID-19 in Hong Kong: a multicentre retrospective observational cohort study. Crit Care Resusc 2020;22:119-25.
34.	Liu J, Chen T, Yang H, et al. Clinical and radiological changes of hospitalised patients with COVID-19 pneumonia from disease onset to acute exacerbation: a multicentre paired cohort study. Eur Radiol 2020;30:5702-8.
35.	Liu K, Chen Y, Lin R, et al. Clinical features of COVID-19 in elderly patients: A comparison with young and middle-aged patients. J Infect 2020;80:e14-8.
36.	Liu K, Fang YY, Deng Y, et al. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. Chin Med J (Engl) 2020;133:1025-31.
37.	Long L, Zeng X, Zhang X, et al. Short-term outcomes of COVID-19 and risk factors for progression. Eur Respir J 2020;55:2000990.
38.	Luo X, Zhou W, Yan X, et al. Prognostic Value of C-Reactive Protein in Patients With Coronavirus 2019. Clin Infect Dis 2020;71:2174-9.
30	Mahta V Goal S. Kabarriti B. et al. Case Estality Bate of Cancer Batients with COVID-19 in a New York Hospital System. Cancer Discov
40.	Nikpouraghdam M, Jalali Farahani A, Alishiri G, et al. Epidemiological characteristics of coronavirus disease 2019 (COVID-19) patients in IRAN: A single center study. J Clin Virol 2020;127:104378.
41.	Nowak B, Szymański P, Pańkowski I, et al. Clinical characteristics and short-term outcomes of patients with coronavirus disease 2019: a retrospective single-center experience of a designated hospital in Poland. Pol Arch Intern Med 2020;130:407-11.
42.	Qi X, Liu Y, Wang J, et al. Clinical course and risk factors for mortality of COVID-19 patients with pre-existing cirrhosis: a multicentre cohort study. Gut 2021;70:433-6.
43.	Renieris G, Katrini K, Damoulari C, et al. Serum Hydrogen Sulfide and Outcome Association in Pneumonia by the SARS-CoV-2 Coronavirus. Shock 2020;54:633-7.
44.	Shekerdemian LS, Mahmood NR, Wolfe KK, <i>et al.</i> Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. JAMA Pediatr 2020;174:868-73.
45.	Sun H, Ning R, Tao Y, et al. Risk Factors for Mortality in 244 Older Adults With COVID-19 in Wuhan, China: A Retrospective Study. J Am Geriatr Soc 2020;68:E19-23.
46.	Tan ND, Qiu Y, Xing XB, <i>et al.</i> Associations Between Angiotensin-Converting Enzyme Inhibitors and Angiotensin II Receptor Blocker Use, Gastrointestinal Symptoms, and Mortality Among Patients With COVID-19. Gastroenterology 2020;159:1170-1172.e1.
47.	Tang N, Bai H, Chen X, et al. Anticoagulant treatment is associated with decreased mortality in severe coronavirus disease 2019 patients with coagulopathy. J Thromb Haemost 2020;18:1094-9.
48.	Tian S, Hu N, Lou J, et al. Characteristics of COVID-19 infection in Beijing. J Infect 2020;80:401-6.
49.	Wan S, Xiang Y, Fang W, et al. Clinical features and treatment of COVID-19 patients in northeast Chongqing. J Med Virol 2020;92:797- 806.
50.	Wang D, Yin Y, Hu C, <i>et al.</i> Clinical course and outcome of 107 patients infected with the novel coronavirus, SARS-CoV-2, discharged from two hospitals in Wuhan, China. Crit Care 2020;24:188.
51.	Wang K, Zuo P, Liu Y, et al. Clinical and Laboratory Predictors of In-hospital Mortality in Patients With Coronavirus Disease-2019: A Cohort Study in Wuhan, China. Clin Infect Dis 2020;71:2079-88.
52.	Wang Z, Yang B, Li Q, <i>et al.</i> Clinical Features of 69 Cases With Coronavirus Disease 2019 in Wuhan, China. Clin Infect Dis 2020;71:769-77.
53.	Wei JF, Huang FY, Xiong TY, et al. Acute myocardial injury is common in patients with COVID-19 and impairs their prognosis. Heart 2020;106:1154-9.
54.	Wu J, Li J, Zhu G, et al. Clinical Features of Maintenance Hemodialysis Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. Clin J Am Soc Nephrol 2020;15:1139-45.
55.	Xie J, Covassin N, Fan Z, <i>et al.</i> Association Between Hypoxemia and Mortality in Patients With COVID-19. Mayo Clin Proc 2020;95:1138-47.
56.	Xu B, Fan CY, Wang AL, et al. Suppressed T cell-mediated immunity in patients with COVID-19: A clinical retrospective study in Wuhan, China. J Infect 2020;81:e51-60.
57.	Yang Q, Xie L, Zhang W, et al. Analysis of the clinical characteristics, drug treatments and prognoses of 136 patients with coronavirus disease 2019. J Clin Pharm Ther 2020;45:609-16.
58.	Yu Y, Xu D, Fu S, et al. Patients with COVID-19 in 19 ICUs in Wuhan, China: a cross-sectional study. Crit Care 2020;24:219.
59.	Zhang H, Shang W, Liu Q, et al. Clinical characteristics of 194 cases of COVID-19 in Huanggang and Taian, China. Infection 2020;48:687-94.
60.	Zhang J, Liu P, Wang M, et al. The clinical data from 19 critically ill patients with coronavirus disease 2019: a single-centered, retrospective, observational study. Z Gesundh Wiss 2020. [Epub ahead of print]. doi:10.1007/s10389-020-01291-2.
61.	Zhang J, Wang X, Jia X, <i>et al.</i> Risk factors for disease severity, unimprovement, and mortality in COVID-19 patients in Wuhan, China. Clin Microbiol Infect 2020;26:767-72.
62.	Zhang L, Yan X, Fan Q, <i>et al.</i> D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost 2020;18:1324-9.
63.	Zhang Y, Cui Y, Shen M, <i>et al.</i> Association of diabetes mellitus with disease severity and prognosis in COVID-19: A retrospective cohort study. Diabetes Res Clin Pract 2020;165:108227.
64.	Zhang YT, Deng AP, Hu T, <i>et al.</i> Clinical outcomes of COVID-19 cases and influencing factors in Guangdong province. Zhonghua Liu Xing Bing Xue Za Zhi 2020;41:1999-2004.
65.	Zhao XY, Xu XX, Yin HS, <i>et al.</i> Clinical characteristics of patients with 2019 coronavirus disease in a non-Wuhan area of Hubei Province, China: a retrospective study. BMC Infect Dis 2020;20:311.

66. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective

cohort study. Lancet 2020;395:1054-62.

67. Zhou X, Zhu J, Xu T. Clinical characteristics of coronavirus disease 2019 (COVID-19) patients with hypertension on renin-angiotensin system inhibitors. Clin Exp Hypertens 2020;42:656-60.

68. An W, Xia F, Chen M, et al. Clinical features of 11 deaths cases with COVID-19. The Journal of Practical Medicine 2020;36:1125-30.

- 69. Chang Z, Yang W, Wang Q, et al. Clinical significance of serum hs-CRP, IL-6, and PCT in diagnosis and prognosis of patients with COVID-19. Drugs & Clinic 2020;35:417-20.
- 70. Foy BH, Carlson JCT, Reinertsen E, et al. Elevated RDW is Associated with Increased Mortality Risk in COVID-19. medRxiv preprint 2020. doi: https://doiorg/101101/2020050520091702.
- 71. Guo F, Zhu L, Xu H, et al. Analysis on correlation between image features multislice spiral computed tomography and prognosis in patients with novel coronavirus pneumonia. Journal of Jilin University (Medicine Edition) 2020;46:554-61.
- 72. Li JW, Long X, Luo HL, et al. Clinical characteristics of deceased patients infected with SARS-Cov-2 in Wuhan, China. bioRxiv preprinted 2020. https://ssrncom/abstract=3546043.
- 73. Luo M, Jiang B, Xu HJ, et al. Analysis of influencing factors of death in patients with COVID-19. Chinese Traditional and Herbal Drugs 2020;51:1450-4.
- 74. Fang XW, Mei Q, Yang TJ, et al. Clinical characteristics and treatment strategies of 79 patients with COVID-19. Chinese Pharmacological Bulletin 2020;36:453-9.
- 75. Yang H, Yang LC, Zhang RT, et al. Risks factors for death among COVID-19 patients combined with hypertension, coronary heart disease or diabetes. Journal of Peking University (Health Sciences) 2020;52:420-4.
- 76. Yang JK, Jin JM, Liu S, et al. Blood glucose is a representative of the clustered indicators of multi-organ injury for predicting mortality of COVID-19 in Wuhan, China. medRxiv preprint 2020. doi: https://doiorg/101101/2020040820058040.
- 77. Zhang CS, Hu J, Zhan ZB, et al. Correlation between serum cystatin C and prognosis of patients with COVID-19. The Journal of Practical Medicine. 2020;36:1418-20.
- 78. Zhang F, Yang DY, Li J, et al. Myocardial injury is associated with in-hospital mortality of confirmed or suspected COVID-19 in Wuhan, China: A single center retrospective cohort study. medRxiv preprint 2020. https://doiorg/101101/2020032120040121.
- 79. Zhang G, Zhang J, Wang B, et al. Analysis of clinical characteristics and laboratory findings of 95 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a retrospective analysis. Respir Res 2020;21:74.
- 80. Zhang JG, Ding DY, Cao C, et al. Myocardial characteristics as the prognosis for COVID-19 patients. medRxiv preprint 2020. https://doi org/101101/2020050620068882.

 $Table \; S1 \; {\rm Quality} \; {\rm of} \; {\rm included} \; {\rm studies} \\$

References	Quality Score	Se	election	(☆☆☆	☆)	Compara	bility(☆☆)	Out	come (☆☆☆)
Aggarwal S (2020)	7	${\sim}$	☆	☆	/	$\overset{\wedge}{\sim}$	\$	☆	/	\$
Barrasa H (2020)	6	☆	-	☆	☆	/	/	☆	☆	\$
Benussi A (2020)	5	$\overset{\wedge}{\sim}$	☆	\$	/	/	\$	☆	/	/
$\frac{1}{2} = \frac{1}{2} + \frac{1}{2} + \frac{1}{2} = \frac{1}{2} + \frac{1}$	5	_^_	1	_/_			1	-A-	, _/_	-^-
Bhatraju F (2020)	5	X	/	X	/	/	/	X	×	24
Bianchetti A (2020)	4	**	\$	\$	/	/	/	☆	/	/
Borghesi A (2020)	5	☆	☆	\$	/	/	/	☆	/	/
Buckner F (2020)	6	\$	☆	☆	/	/	/	☆	☆	\$
Cai Q (2020)	6	☆	☆	☆	/	/	/	☆	☆	☆
Cecconi M (2020)	5	$\overset{\sim}{\sim}$	/	☆	/	/	/	☆	☆	☆
Chen B (2020)	6	5~	545	5~	/	/	/	5~	547	54
And $rac C (2020)$	6	-^-	_A_	_A_	,	,	,	_A_	_A_	-^-
Andrea C (2020)	0	X	X	X	/	/	/	X	X	X
Cummings M (2020)	6	\$	/	\$	$\overrightarrow{\mathbf{x}}$	/	/	☆	\$	☆
Deng Y (2020)	4	$\overset{\wedge}{\sim}$	☆	☆	/	/	/	☆	/	/
Dong X (2020)	5	\$	\overleftrightarrow	☆	/	/	/	☆	/	☆
Du R (2020)	7	\$	☆	☆	$\overset{\sim}{\sim}$	/	/	☆	☆	\$
Gao L (2020)	7	☆	☆	☆	/	/	$\overset{\sim}{\sim}$	☆	☆	${\nabla}$
Giacomelli A (2020)	7	5~2	5.7	5^2	5.7	/	/	5.7	5.2	547
$C_{\rm Ho} T (2020)$		_A_	-^-	_A_		,	,	_A_		1
	4	24	24	N	,	/	,	24	,	,
Hong K (2020)	1	**	\$	\$	/	/	\$	☆	\$	**
Hou W (2020)	5	☆	☆	\$	/	/	${\leftrightarrow}$	☆	/	/
Hu H (2020)	4	${\bigtriangledown}$	$\stackrel{\frown}{\simeq}$	☆	/	/	/	☆	/	/
Hu L (2020)	7	\$	\overleftrightarrow	☆	/	☆	/	☆	☆	\$
Huang J (2020)	4	☆		☆	/	/	/	☆	/	/
Inciardi R (2020)	7	\$	☆	☆	/	$\overset{\wedge}{\swarrow}$	/	☆	☆	$\overset{\sim}{\sim}$
Israelsen S (2020)	R	~~	~~	51-5	/	~	۲ <u>۲</u>	≺^>	512	51-2
$\frac{1}{2} \log \left(\sum_{i=1}^{n} \sum_{j=1}^{n} \sum_{i=1}^{n} \sum_{$	ۍ ۸	~	~	~	,	~	N	~	~ /	~
	4	¥	¥	¥	/	/	/	¥	/	/
Javanian M (2020)	6	\$	\$	☆	/	1	/	☆	☆	${\bigtriangledown}$
Ji D (2020)	6	\$	☆	☆	/	/	/	☆	\$	\$
Klang E cohort1 (2020)	4	\$	☆	☆	/	/	/	☆	/	/
Klang E cohort2 (2020)	4	\$	☆	\$	/	/	/	☆	/	/
Li J (2020)	5	$\overset{\sim}{\sim}$	☆	☆	/	\$	/	☆	/	/
Li B (2020)	5	5~2	/	5^2	/	/	/	5.7	5.7	54
Li X (2020)	2	-^-	,	~	,	,	,	~	,	~
	5	24	,	24	,	/	,	24	,	/
Ling L (2020)	5	¥	/	72	/	/	/	**	**	Ŵ
Liu J (2020)	5	\$	/	\$	/	/	/	☆	\$	☆
Liu K (2020)	6	$\stackrel{\sim}{\sim}$	\$	☆	/	\$	\$	☆	/	/
Liu K (2020)	3	$\stackrel{\wedge}{\sim}$	/	☆	/	/	/	☆	/	/
Long L (2020)	7	$\overset{\wedge}{\sim}$	☆	☆	$\overset{\wedge}{\sim}$	/	/	${\simeq}$	☆	\mathcal{L}
Luo X (2020)	6	☆	☆	☆	/	/	/	☆	☆	\$
Mehta V (2020)	6	\$	☆	\$	/	/	/	☆	☆	\$
Nikpouraghdam M (2020)	3	\$	/	☆	/	/	/	☆	/	/
Nowak B (2020)	6	\$	☆	\$	/	/	/	☆	\$	\$
Oi X (2020)	8	5/2	542	545	/	~~	51/2	542	515	51/2
Reprincip $G(2020)$	7	~~	~~	~~	,	1	~~~	~~	~~	~~~
	r F	~	~	~	,	/	~	~	~	~
Shekerdemian L (2020)	5	×		ж	/	/	/	×	ж	×
Sun H (2020)	7	¥	¥	72	W	/	/	**	**	¥
Tan N (2020)	8	\$	\$	\$	/	☆	\$	☆	\$	☆
Tang N (2020)	7	☆	☆	\$	/	/	${\leftrightarrow}$	☆	☆	☆
Tian S (2020)	6	☆	☆	☆	/	/	/	☆	☆	\$
Wan S (2020)	7	\$	☆	\$		/	/	☆	☆	$\overset{\sim}{\sim}$
Wang D (2020)	6	Δ	☆	☆	/	/	/	☆	☆	\$
Wang K (2020)	6	*	\$	5	/	/	/	\$	5	5
Wang 7 (2020)	6	~~	~~	-A-	,	,	,	~~~	-A-	~^~
Wally 2 (2020)	6	~	~	~	^	/	,	~	~	~
Wei J (2020)	5	ж	ж	ж	X	/	/	×	/	/
Wu J (2020)	6	\$	\$	\$	/	/	/	☆	\$	☆
Xie J (2020)	6	☆	☆	☆	/	/	/	☆	☆	
Xu B (2020)	4	$\stackrel{\wedge}{\sim}$	☆	☆	/	/	/	☆	/	/
Yang Q (2020)	4	\$	☆	☆	/	/	/	$\stackrel{\wedge}{\simeq}$	/	/
Yu Y (2020)	6	\$	/	☆		/	/	☆	☆	\$
Zhang H (2020)	5	$\overset{\wedge}{\sim}$	/	☆	/	/	/	☆	$\overset{\sim}{\sim}$	\mathcal{L}
Zhang J (2020)	4	☆	☆	☆	/	/	/	☆	/	/
Zhang .I (2020)	6	5~	545	5/2	/	/	/	5~	547	54
Zhang L (2020)	4	~~	~	~	,	,	,	~	1	1
Zhang V (0000)		~	~	~	,	~ ~~	,	~	_^_	, _^_
	7	ж ,	24	×	/	×	/	24	×	×
Zhang Y (2020)	6	¥	¥	\$	/	/	/	**	**	Ŵ
Zhao X (2020)	6	☆	☆	☆	/	/	/	\$	\$	\$
Zhou F (2020)	6	\$	☆	☆	/	/	/	☆	☆	
Zhou X (2020)	4	$\stackrel{\wedge}{\sim}$	$\stackrel{\wedge}{\sim}$	☆	/	/	/	$\stackrel{\wedge}{\simeq}$	/	/
An W (2020)	5	*	\$	$\overset{\wedge}{\swarrow}$	/	/	\mathcal{L}	☆	/	/
Chang Z (2020)	7	☆	☆	/	\$	$\overset{\sim}{\sim}$	/	☆		\$
Foy B (2020)	6	☆	☆	☆	/	/	/	☆	☆	$\overset{\sim}{\sim}$
Guo F (2020)	7	5.7	<u>~</u> ~	5.7	/	- 	- 	5.47	1	5.7
	r G	~~	~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	~~	,	~	~ /	~~	, ~^~	~~
	0	x ,	x ,	× ^	/	/	/	X . ^	¥ . ^	× ^
Luo IVI (2020)	(¥7	¥	<u>ت</u> ک	/	¥	/	¥	¥	22
⊢ang X (2020)	6	\$	\$	\$	/	1	/	☆	☆	\$
Yang H (2020)	7	$\overset{\sim}{\sim}$	☆	\$	/	☆	/	☆		
Yang J (2020)	6	\$	☆	☆	/	/	/	☆	☆	\$
Zhang C (2020)	7	$\overset{\sim}{\sim}$	☆		/	\$	/	☆		${\leftrightarrow}$
Zhang F (2020)	7	\$	☆	☆	/	/	/	$\stackrel{\wedge}{\simeq}$	☆	\$
Zhang G (2020)	7	*	\$	$\overset{\wedge}{\swarrow}$	/	\$	/	☆	☆	\$
Zhang J (2020)	6	☆	\$	☆	/	☆		☆	/	/

/ indicates no star.

Table S2 Results of meta-regression analyses

Covariates	P value
Sample size (≥100 versus <100)	0.456
Region (Asia versus Europe versus North America)	0.0001
Source of cases (single-center versus multiple-center)	0.756
NOS (>6 versus ≤6)	0.956
Study design (retrospective versus prospective)	0.403
Longest follow-up (>30 versus ≤30 days)	0.624
Proportion of patients with severe disease (>50% versus ≤50%)	<0.001

NOS, Newcastle-Ottawa Scale.

© Annals of Palliative Medicine. All rights reserved.

Table S3 Risk of factors in COVID-19 patients

First author (year)	Risk factors of death in the univariate analysis	Risk factors of death in the multivariate analysis
Benussi A (2020)	Older age, hypertension, qSOFA score, thrombocytopenia, elevated C-reactive protein, and lactate dehydrogenase	qSOFA score, thrombocytopenia, elevated lactate deh
Borghesi A (2020)	Older age, male, Brixia score, hypertension, cardiovascular disease, diabetes, oncologic history within the past 5 years, immunosuppressive conditions	Older age, Brixia score, immunosuppressive condition
Chen R (2020)	Age ≥75, Male, CHD, CVD, COPD, diabetes, hypertension, malignancy, chronic renal diseases, abnormal chest X-ray, Dyspnea, PCT >0.5 ng/mL, LDH ≥250 U/L, AST >40 U/L, ALT >40 U/L, TBIL ≥17.1, creatinine kinase ≥200, creatinine ≥133, D-dimer ≥0.5	Age ≥75, CHD, CVD, dyspnea, PCT >0.5 ng/mL, AST :
Andrea C (2020)	Older age, hypertension, heart failure, diabetes, COPD, cancer, CKD, ACEI/ARBs and B-blocker	Older age, heart failure and CKD
Cummings M (2020)	Older age, hypertension, chronic cardiac disease, chronic pulmonary disease, diabetes, higher concentrations of IL-6 and D-dimer	Older age, chronic cardiac disease, chronic pulmonary
Du R (2020)	Age \geq 65 years, hypertension, cardiovascular or cerebrovascular diseases, dyspnea, fatigue, sputum production, headache, WBC >10×10 ⁹ /L, neutrophil counts >6.3×10 ⁹ /L, CD3 ⁺ CD8 ⁺ T cells \leq 75 cell/mL, cardiac troponin I \geq 0.05 ng/mL, myoglobin>100 ng/mL, creatinine \geq 133 µmol/L, D-dimer \geq 0.5 mg/L, PaO ₂ \geq 80 or <60 mmHg	Age ≥65 years, cardiovascular or cerebrovascular dise
Gao L (2020)	Older age, male, hypertension, leukocytosis, lymphopenia, elevated NT-proBNP, Myoglobin, creatine kinase-MB, hs-Tnl, urea, creatinine, CRP and procalcitonin	Elevated NT-proBNP and procalcitonin, leukocytosis, l
Giacomelli A (2020)	Older age, comorbidity, obesity, treated with at least one anti-hypertensive, severe disease, critical disease, anemia, lymphopenia, elevated D-dimer, CRP, creatinine, and creatine kinase	Older age, obesity, critical disease, elevated CRP, crea
Huang J (2020)	Older age, any comorbidity, lymphopenia, hypoalbuminemia	Any comorbidity, lymphopenia, hypoalbuminemia
Klang E cohort 1 (2020)	BMI ≥40 kg/m²	Age, BMI \geq 40 kg/m ² , congestive heart failure, chronic l
Klang E cohort 2 (2020)	Coronary artery disease, congestive heart failure, hypertension, diabetes mellitus, hyperlipidemia, chronic kidney disease	Older age, male sex, BMI ≥40 kg/m ² , coronary artery d mechanical ventilation
Mehta V (2020)	Age >65 years, ICU admission, hypertension, chronic lung disease, CAD, CHF, reduced baseline hemoglobin and nadir hemoglobin, leukocytosis, lymphopenia, elevated D-dimer, lactate and LDH	Age >65 years, higher composite comorbidity score, IC
Renieris G (2020)	Age ≥64 years, Charlson's comorbidity index ≥3, APACHE II score ≥10, pneumonia severity index ≥11, SOFA ≥4, serum H ₂ S on day 1 ≥150.44 µM, severe respiratory failure	Serum H2S on day 1 \geq 150.44 µM, severe respiratory fa
Sun H (2020)	Older age, Male, SpO ₂ , increased heart rate and respiratory rate, consciousness disorders, hypertension, previous respiratory diseases, leukocytosis, lymphopenia, elevated NT-proBNP, PCT, hs-Tnl, D-dimer, AST, ALT, creatinine, eGFR, and hs-CRP	Older age, leukocytosis, lymphopenia
Tang N (2020)	Older age, male, higher PT, lower platelet count, higher D-dimer, more sepsis-induced coagulopathy	Older age, higher PT, lower platelet count, higher D-dir
Wang D (2020)	Older age, male, hypertension, diabetes, cardiovascular disease, leukocytosis, thrombocytopenia, elevated neutrophil counts, CK-MB, lactate dehydrogenase, ALT, AST, and creatinine	Older age, male
Wang K (2020)	Older age, hypertension, CHD, elevated neutrophil, hs-CRP, D-dimer, AST, and GFR, decreased SpO ₂ , lymphopenia	Older age, decreased $\mbox{SpO}_{\mbox{\tiny 2}},$ elevated neutrophil, hs-Cf
Xie J (2020)	Age ≥60 years, male, hypertension, dyspnea, SpO₂≤90%, leukocytosis, thrombocytopenia, elevated CRP, D-dimer, and neutrophil count	Dyspnea, SpO ₂ \leq 90%, leukocytosis, elevated neutroph
Xu B (2020)	Lower T lymphocyte subsets levels (lower T lymphocyte subsets lymphocyte <500/µL, CD3 ⁺ T-cell <200/µL, CD4 ⁺ T cell <100/µL, CD8 ⁺ T cell <100/µL, NK-cell <50/µL, and B-cell <50/µL counts)	Lower T lymphocyte subsets levels (lower T lymphocyte
Zhou F (2020)	Older age, coronary heart disease, diabetes, hypertension, respiratory rate >24/min, lymphopenia, leukocytosis, and elevated ALT, lactate dehydrogenase, hs-Tnl, creatine kinase, D-dimer, serum ferritin, IL-6, prothrombin time, creatinine, and procalcitonin, SOFA score, qSOFA score	Age, SOFA score, D-dimer >1
Foy B (2020)	Older age, elevated RDW, lymphopenia, D-dimer	Elevated RDW (>14.5%)
Luo M (2020)	Male, age ≥70 years, use traditional Chinese medicine, clinical classification (severe/critical), hypertension, coronary heart disease, diabetes, tumors, uremia, nucleic acid test (+)	Use traditional Chinese medicine, clinical classification tumors, uremia
Yang H (2020)	Older age, SpO ₂ , lymphocyte, myocardial injury, IL-2R >710 U/mL, IL-6 >35 ng/L, IL-10 >9.1 ng/L	Older age, SpO ₂ , IL-10 >9.1 ng/L
Yang J (2020)	Male, fasting blood glucose ≥7 mmol/L, Elevated lactate dehydrogenase, creatinine, and hydroxybutyrate dehydrogenase	Fasting blood glucose ≥7 mmol/L.
Zhang F (2020)	Decreased SpO ₂ , elevated creatinine, D-dimer, and hs-TnI	Decreased $\ensuremath{SpO_2}\xspace,$ elevated D-dimer and hs-TnI

qSOFA, quick Sequential Organ Failure Assessment; CHD, coronary heart disease; CVD, cerebrovascular disease; COPD, chronic obstructive pulmonary disease; CAD, coronary artery disease; CHF, chronic heart failure; ICU, intensive care unit; ACEI, angiotensin converting enzyme inhibitors; ARBs, angiotensin receptor blockers; CKD, chronic kidney disease; RDW, red blood cell distribution width; IL-6, interleukin-6; NT-proBNP, N-terminal pro-brain natriuretic peptide; CK-MB, creatine kinase-MB; HsTnl, high-sensitivity troponin-l; WBC, white blood cell; CRP, C-reactive protein; PCT, procalcitonin; LDH, lactate dehydrogenase; BUN, blood urea nitrogen; AST, aspartate aminotransferase; TBIL, total bilirubin; Brixia score, chest X-ray scoring system; APACHE, acute physiology and chronic health evaluation; SOFA, sequential organ failure; SpO₂, peripheral capillary oxygen saturation.

nydrogenase Is >40 U/L

y disease, higher concentrations of IL-6 and D-dimer eases, CD3⁺CD8⁺ T cells ≤75 cell/µL, cardiac troponin I ≥0.05 ng/mL

lymphopenia

atine kinase

kidney disease, intubation and mechanical ventilation

disease, diabetes mellitus, chronic kidney disease, intubation and

CU admission, elevated D-dimer, lactate and LDH

ailure

mer

RP, and GFR

hil count, and CRP

rte subsets lymphocyte <500/µL, CD3 $^{\circ}$ T cell <200/µL, CD4 $^{\circ}$ T cell <cell <50/µL counts)

(severe/critical), hypertension, coronary heart disease, diabetes,

1. Demographics and clinical characteristics

1.1 Old age

	Non-survivors		ors	S	urvivor	5		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV. Random, 95% CI
An W (2020)	72.4	7.1	11	54.6	15.6	99	3.3%	17.80 [12.60, 23.00]	
Borghesi A (2020)	76.17	7.96	65	63.77	14.4	237	3.8%	12.40 [9.73, 15.07]	
Chen R (2020)	68.75	7.8	50	47,75	13.89	1540	3.8%	21.00 [18.73, 23.27]	-
Conversano A (2020)	75.3	12.9	42	60.4	13.7	149	3.5%	14.90 [10.42, 19.38]	
Deng Y (2020)	68.33	9.02	109	43.33	18.02	855	3.8%	25.00 [22.92, 27.08]	
Du R (2020)	70.2	7.7	21	56	13.5	158	3.6%	14.20 [10.29, 18.11]	
Foy B (2020)	75	13.2	155	59.6	17.5	1043	3.8%	15.40 [13.07, 17.73]	
Hu H (2020)	75.05	12.94	19	57.71	15.34	86	3.0%	17.34 [10.68, 24.00]	
Huang J (2020)	69.2	9.7	16	52.5	16.6	238	3.3%	16.70 [11.50, 21.90]	
Javanian M (2020)	69.26	11.1	19	57.74	13.58	81	3.2%	11.52 [5.72, 17.32]	
Klang E cohort1(2020)	46.14	4.71	60	40	8.92	512	3.9%	6.14 [4.72, 7.56]	-
Klang E cohort2 (2020)	75.67	12.62	1076	68.33	12.61	1758	3.9%	7.34 [6.38, 8.30]	-
Li J (2020)	63	11.95	65	50.25	13.08	96	3.6%	12.75 [8.84, 16.66]	
Li J1 (2020)	72.83	13.22	77	64.5	10.06	285	3.7%	8.33 [5.15, 11,51]	
Luo X (2020)	71.67	12.07	84	50.33	19.41	213	3.6%	21.34 [17.67, 25.01]	
Mehta V (2020)	63.5	17.68	61	58.5	15.45	157	3.4%	5.00 [-0.05, 10.05]	
Nowak B (2020)	75.3	11.9	46	59.3	20.1	123	3.4%	16.00 [11.06, 20.94]	
QI X (2020)	64.33	25.14	5	65.33	18.69	16	0.8%	-1.00 [-24.86, 22.86]	
Sun H (2020)	72	9	121	62.67	6	123	3.8%	9.33 [7.41, 11.25]	-
Tang N (2020)	68.7	11.4	134	63.7	12.2	315	3.8%	5.00 [2.65, 7.35]	-
Wang D (2020)	72.67	13.62	19	46.1	17.94	525	3.1%	26.57 [20.26, 32.88]	
Wang K (2020)	65.6	12.6	19	46	14.4	277	3.2%	19.60 [13.69, 25.51]	
Yang H (2020)	75.83	12.87	13	65.83	10.19	81	2.9%	10.00 [2.66, 17.34]	
Yang J (2020)	64	8.94	16	59.33	12.19	53	3.3%	4.67 [-0.80, 10.14]	
Zhang C (2020)	59.33	11.11	6	57.88	12.43	26	2.4%	1.45 [-8.64, 11.54]	
Zhang F (2020)	78.65	8.31	17	66.16	13.66	31	3.1%	12.49 [6.27, 18.71]	
Zhang G (2020)	61.78	15.02	6	48.63	3.51	89	2.0%	13.15 [1.11, 25.19]	
Zhang J (2020)	69.43	13.36	25	55.7	18.57	638	3.3%	13.73 [8.30, 19.16]	
Zhang J1 (2020)	66.2	16.09	18	56.83	20.55	12	1.7%	9.37 [-4.43, 23.17]	
Zhang J2 (2020)	77.75	8.72	8	65.25	15.38	11	2.2%	12.50 [1.59, 23.41]	
Zhou F (2020)	69.33	9.9	54	51,67	9.74	137	3.7%	17.66 [14.56, 20.76]	
Total (95% CI)			2437			9964	100.0%	13.32 [10.87, 15.77]	•
Heterogeneity: Tau ² = 39	0.78; Chi	= 515.	02, df =	30 (P	< 0.000	01); I ² =	94%		-20 -10 0 10 20

Heterogeneity: Tau² = 39.78; Chi² = 515.02, df = 30 (P < 0.00001); i² = 94% Test for overall effect: Z = 10.66 (P < 0.00001)



1.2 Male

	Non-surv	vivors	Surviv	ors		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random. 95% C	M-H. Random, 95% Cl
An W (2020)	6	11	38	99	1.8%	1.93 [0.55, 6.75]	
Borghesi A (2020)	50	65	144	237	4.1%	2.15 [1.14, 4.05]	
Chen R (2020)	39	50	865	1528	3.8%	2.72 [1.38, 5.35]	
Conversano A (2020)	100	149	31	42	3.4%	0.72 [0.34, 1.56]	
Deng Y (2020)	73	109	51	116	4.6%	2.58 [1.50, 4.44]	
Du R (2020)	10	21	87	158	2.8%	0.74 [0.30, 1.85]	
Foy B (2020)	563	1043	98	155	5.9%	0.68 [0.48, 0.97]	-
Hu H (2020)	14	19	48	86	2.1%	2.22 [0.73, 6.70]	
Huang J (2020)	11	16	149	283	2.2%	1.98 [0.67, 5.84]	
Javanian M (2020)	12	19	39	81	2.4%	1.85 [0.66, 5.17]	
Klang E cohort1(2020)	45	60	352	512	4.2%	1.36 [0.74, 2.52]	
Klang E cohort2 (2020)	615	1076	949	1758	7.0%	1.14 [0.98, 1.33]	*
Li J (2020)	42	65	38	96	4.0%	2.79 [1.45, 5.35]	
Li J1 (2020)	50	77	139	285	4.8%	1.95 [1.15, 3.28]	
Luo X (2020)	51	84	99	214	4.8%	1.80 [1.07, 3.00]	
Mehta V (2020)	36	61	91	157	4.3%	1.04 [0.57, 1.90]	-
Nowak B (2020)	30	46	57	123	3.7%	2.17 [1.08, 4.38]	
Qi X (2020)	4	5	7	16	0.6%	5.14 [0.46, 56.90]	
Sun H (2020)	82	121	51	123	4.7%	2.97 [1.76, 5.01]	
Tang N (2020)	90	134	178	315	5.4%	1.57 [1.03, 2.41]	-
Wang D (2020)	16	19	41	88	1.7%	6.11 [1.66, 22.49]	
Wang K (2020)	11	19	129	277	2.7%	1.58 [0.62, 4.04]	
Xu B (2020)	17	28	86	159	3.1%	1.31 [0.58, 2.98]	
Yang H (2020)	8	13	37	81	1.9%	1.90 [0.57, 6.32]	
Yang J (2020)	13	16	21	53	1.6%	6.60 [1.68, 26.01]	
Zhang C (2020)	3	6	17	26	1.0%	0.53 [0.09, 3.18]	
Zhang F (2020)	12	17	21	31	1.7%	1.14 [0.32, 4.14]	
Zhang G (2020)	6	6	47	89	0.4%	11.63 [0.64, 212.68]	
Zhang J (2020)	15	25	306	638	3.2%	1.63 [0.72, 3.68]	+
Zhang J1 (2020)	9	18	6	12	1.4%	1.00 [0.23, 4.31]	
Zhang J2 (2020)	5	8	6	11	0.9%	1.39 [0.22, 8.92]	· · · · · · · · · · · · · · · · · · ·
Zhou F (2020)	38	54	81	137	3.8%	1.64 [0.84, 3.23]	
Total (95% CI)		3460		7986	100.0%	1.66 [1.37, 2.01]	•
Total events	2076		4309				
Heterogeneity: Tau ² = 0. Test for overall effect: Z	13; Chi ² = 7 = 5.15 (P <	2.54, df 0.00001	= 31 (P <)	0.0001); l ² = 57%		0.005 0.1 1 10 20 Favours [experimental] Favours [control]

1.3 Time from illness onset to bospital admission, days

	Non	-survi	vor	SI	rvivo	r		Mean Difference		Mean	Differend	ce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI		IV, Ran	dom. 95	% CI	
Conversano A (2020)	6.4	3.9	42	6.5	3.8	149	12.8%	-0.10 [-1.43, 1.23]			-		
Deng Y (2020)	9.5	4.13	109	7.33	3.75	116	14.7%	2.17 [1.14, 3.20]			1.00		-
Hu H (2020)	8.37	5.78	19	10.24	7.51	86	5.4%	-1.87 [-4.92, 1.18]		-	-		
Huang J (2020)	5.08	4.27	16	3.33	2.24	283	8.6%	1.75 [-0.36, 3.86]			+		_
Luo X (2020)	10	5.28	84	8.33	3.73	214	13.4%	1.67 [0.44, 2.90]			_	*	
Qi X (2020)	8.67	17.1	5	9	8.94	16	0.3%	-0.33 [-15.95, 15.29]			-		_
Sun H (2020)	11	6	121	11	6	123	11.7%	0.00 [-1.51, 1.51]		-	-		
Nang D (2020)	5.67	2.4	19	6.6	5.13	88	11.6%	-0.93 [-2.45, 0.59]		-	-		
rang J (2020)	10.93	5.45	16	12.33	3.05	53	6.1%	-1.40 [-4.19, 1.39]	_		-		
Zhang F (2020)	7,17	6.87	17	6.33	4.66	31	4.1%	0.84 [-2.81, 4.49]			-		_
Zhou F (2020)	11.33	5.33	54	10.67	3.75	137	11.4%	0.66 [-0.89, 2.21]		-	-	_	
Total (95% CI)			502			1296	100.0%	0.49 [-0.34, 1.33]			-		
Heterogeneity: Tau ² =	0.96; Chi	2 = 22.	62, df =	= 10 (P	= 0.01); 2 = 5	6%		1	1	1	1	1
fest for overall effect: 2	Z = 1.16	(P = 0.	25)						-4 Favours [e	-2 xperimenta	J Favor	urs [coni	trol]



1.41 Hypertension

Experimental		Contr	ol		Odds Ratio	Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% Cl	M-H. Random, 95% Cl
An W (2020)	2	11	19	99	1.8%	0.94 [0.19, 4.69]	
Borghesi A (2020)	42	65	112	237	5.4%	2.04 [1.15, 3.60]	
Chen R (2020)	28	50	241	1540	5.4%	6.86 [3.86, 12.19]	
Conversano A (2020)	34	42	62	149	4.1%	5.96 [2.58, 13.76]	
Deng Y (2020)	40	109	18	116	5.1%	3.16 [1.67, 5.96]	
Du R (2020)	13	21	45	158	3.6%	4.08 [1.58, 10.51]	· · · · · · · · · · · · · · · · · · ·
Foy B (2020)	62	155	229	1043	6.5%	2.37 [1.66, 3.37]	
Hu H (2020)	6	19	22	86	3.1%	1.34 [0.46, 3.96]	
Huang J (2020)	11	16	63	283	3.1%	7.68 [2.57, 22.93]	
Javanian M (2020)	12	19	20	81	3.2%	5.23 [1.81, 15.09]	
Klang E cohort1(2020)	24	60	151	512	5.5%	1.59 [0.92, 2.76]	
Klang E cohort2 (2020)	864	1076	1260	1758	7.2%	1.61 [1.34, 1.93]	· ·
Luo X (2020)	49	84	37	214	5.5%	6.70 [3.83, 11.73]	
Mehta V (2020)	47	61	100	157	4.8%	1.91 [0.97, 3.78]	
Nowak B (2020)	27	46	53	123	4.8%	1.88 [0.94, 3.73]	
Qi X (2020)	2	5	5	16	1.2%	1.47 [0.18, 11.72]	
Sun H (2020)	76	121	62	123	5.7%	1.66 [1.00, 2.77]	
Wang D (2020)	10	19	16	88	3.2%	5.00 [1.75, 14.30]	
Wang K (2020)	9	19	33	277	3.5%	6.65 [2.52, 17.57]	
Xu B (2020)	10	28	40	159	4.0%	1.65 [0.71, 3.87]	
Yang H (2020)	7	13	47	81	2.8%	0.84 [0.26, 2.74]	
Zhang C (2020)	2	6	3	26	1.2%	3.83 [0.48, 30.70]	
Zhang F (2020)	12	17	20	31	2.6%	1.32 [0.37, 4.73]	
Zhang J2 (2020)	5	8	6	11	1.5%	1.39 [0.22, 8.92]	
Zhou F (2020)	26	54	32	137	4.9%	3.05 [1.57, 5.92]	
Total (95% CI)		2124		7505	100.0%	2.67 [2.08, 3.43]	•
Total events	1420		2696				
Heterogeneity: Tau ² = 0.2 Test for overall effect: Z =	22; Chi ² = 7 = 7.66 (P <	4.90, df 0.00001	= 24 (P <	0.000	01); l ² = 68	%	0.01 0.1 1 10 Favours [experimental] Favours [control]

1.42 Diabetes

	Non-survivor		Surviv	or		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% Cl	M-H. Random, 95% Cl
An W (2020)	0	11	3	99	0.4%	1.20 [0.06, 24.70]	
Borghesi A (2020)	13	65	25	237	4.8%	2.12 [1.02, 4.42]	
Chen R (2020)	13	50	117	1540	5.5%	4.27 [2.21, 8.26]	
Conversano A (2020)	11	42	17	149	3.9%	2.76 [1.17, 6.47]	
Deng Y (2020)	17	109	9	116	3.9%	2.20 [0.93, 5.16]	
Du R (2020)	6	21	27	158	2.9%	1.94 [0.69, 5.45]	
Foy B (2020)	36	155	167	1043	9.1%	1.59 [1.06, 2.39]	
Hu H (2020)	0	19	4	86	0.4%	0.47 [0.02, 9.10]	
Huang J (2020)	4	16	31	283	2.3%	2.71 [0.82, 8.92]	
Javanian M (2020)	10	19	27	81	3.0%	2.22 [0.81, 6.11]	
Klang E cohort1(2020)	24	60	129	512	6.8%	1.98 [1.14, 3.44]	
Klang E cohort2 (2020)	607	1076	839	1758	13.8%	1.42 [1.22, 1.65]	•
Li J1 (2020)	38	77	89	285	7.4%	2.15 [1.29, 3.58]	
Luo X (2020)	18	84	27	214	5.5%	1.89 [0.98, 3.65]	
Mehta V (2020)	27	61	53	157	6.2%	1.56 [0.85, 2.85]	+
Nowak B (2020)	16	46	16	123	4.2%	3.57 [1.60, 7.96]	
Qi X (2020)	2	5	2	16	0.7%	4.67 [0.46, 47.63]	
Sun H (2020)	27	121	24	123	6.0%	1.18 [0.64, 2.20]	
Wang D (2020)	5	19	6	88	1.9%	4.88 [1.31, 18.18]	
Wang K (2020)	6	19	24	277	2.8%	4.87 [1.70, 13.96]	
Yang H (2020)	2	13	3	81	1.0%	4.73 [0.71, 31.52]	
Zhang C (2020)	3	6	1	26	0.6%	25.00 [1.93, 323.55]	· · · · · · · · · · · · · · · · · · ·
Zhang F (2020)	5	17	5	31	1.7%	2.17 [0.53, 8.93]	
Zhang J2 (2020)	3	8	1	11	0.6%	6.00 [0.49, 73.45]	
Zhou F (2020)	17	54	19	137	4.7%	2.85 [1.35, 6.05]	
Total (95% Cl)		2173		7631	100.0%	2.14 [1.76, 2.60]	•
Total events	910		1665			and the state	
Heterogeneity: Tau ² = 0.1	07; Chi ² = 3	7.88, df	= 24 (P =	= 0.04);	12 = 37%		
Test for overall effect: Z	= 7.64 (P <	0.00001)				Favours [experimental] Favours [control]

1.43 Chronic respiratory disease

	Non-sur	Non-survivor		TOV		Odds Ratio		Odds	s Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	1	M-H, Ran	dom, 95% Cl	
Borghesi A (2020)	13	65	31	237	9.3%	1.66 [0.81, 3.40]			-	
Chen R (2020)	6	50	18	1540	6.3%	11.53 [4.37, 30.46]				1. T
Conversano A (2020)	6	42	4	149	4.0%	6.04 [1.62, 22.54]				
Deng Y (2020)	22	109	3	116	4.4%	9.52 [2.76, 32.86]				
Foy B (2020)	16	155	42	1043	11.1%	2.74 [1.50, 5.01]				
Hu H (2020)	5	19	7	86	4.2%	4.03 [1.12, 14.51]				
Huang J (2020)	3	16	5	283	3.1%	12.83 [2.76, 59.59]				_
Javanian M (2020)	5	19	7	81	4.2%	3.78 [1.05, 13.61]				
LI J (2020)	7	65	3	96	3.7%	3.74 [0.93, 15.05]				
Li J1 (2020)	6	77	12	285	6.0%	1.92 [0.70, 5.30]		-	-	
Luo X (2020)	13	84	10	214	7.4%	3.74 [1.57, 8.89]				
Mehta V (2020)	28	61	34	157	10.6%	3.07 [1.63, 5.77]				
Nowak B (2020)	9	46	13	123	6.8%	2.06 [0.81, 5.21]				
Sun H (2020)	20	121	4	123	5.3%	5.89 [1.95, 17.80]				
Wang D (2020)	1	19	2	88	1.3%	2.39 [0.21, 27.78]				
Wang K (2020)	1	19	1	277	1.0%	15.33 [0.92, 255.33]				-+
Xu B (2020)	0	28	3	159	0.9%	0.78 [0.04, 15.60]				
Zhang C (2020)	1	6	2	26	1.2%	2.40 [0.18, 31.88]		7		
Zhang J (2020)	5	25	46	638	5.9%	3.22 [1.15, 8.97]				
Zhang J2 (2020)	0	8	3	11	0.9%	0.14 [0.01, 3.21]	+		_	
Zhou F (2020)	4	54	2	137	2.5%	5.40 [0.96, 30.40]				
Total (95% CI)		1088		5869	100.0%	3.55 [2.65, 4.76]			+	
Total events	171		252			and the second second				
Heterogeneity: Tau ² = ().11; Chi? =	26.79,	df = 20 (F	= 0.14); 12 = 25%	6	-	1	1	
Test for overall effect: 2	2 = 8.47 (P	< 0.000	01)		4. A. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1.		0.01 Fa	vours [experimental]	Favours [control]	100

1.44 CHD/cardiovascular disease

	Non-survivor		Surviv	vor		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H. Random, 95% CI
An W (2020)	1	11	4	99	1.1%	2.38 [0.24, 23.36]	
Borghesi A (2020)	42	65	84	237	6.4%	3.33 [1.87, 5.90]	
Chen R (2020)	8	50	51	1540	4.9%	5.56 [2.48, 12.45]	
Conversano A (2020)	9	42	19	149	4.5%	1.87 [0.77, 4.50]	
Deng Y (2020)	13	109	4	116	3.3%	3.79 [1.20, 12.01]	
Foy B (2020)	28	155	83	1043	7.2%	2.55 [1.60, 4.07]	
Hu H (2020)	1	19	5	86	1.2%	0.90 [0.10, 8.18]	
Huang J (2020)	4	16	14	283	3.0%	6.40 [1.83, 22.41]	
Javanian M (2020)	8	19	12	81	3.5%	4.18 [1.40, 12.54]	
Klang E cohort1(2020)	6	60	26	512	4.3%	2.08 [0.82, 5.27]	
Klang E cohort2 (2020)	354	1076	358	1758	9.0%	1.92 [1.61, 2.28]	-
Lī J (2020)	39	65	20	96	5.6%	5.70 [2.83, 11.47]	
Li J1 (2020)	21	77	41	285	6.2%	2.23 [1.22, 4.07]	
Luo X (2020)	13	84	13	214	4.9%	2.83 [1.25, 6.40]	
Mehta V (2020)	34	61	42	157	6.1%	3.45 [1.86, 6.39]	
Nowak B (2020)	19	46	33	123	5.5%	1.92 [0.94, 3.90]	
Qi X (2020)	2	5	2	16	1.1%	4.67 [0.46, 47.63]	
Sun H (2020)	20	121	15	123	5.4%	1.43 [0.69, 2.94]	
Wang D (2020)	7	19	6	88	3.0%	7.97 [2.29, 27.75]	
Wang K (2020)	5	19	5	277	2.7%	19.43 [5.03, 75.02]	
Yang H (2020)	0	13	6	81	0.7%	0.43 [0.02, 8.09]	
Zhang F (2020)	4	17	9	31	2.6%	0.75 [0.19, 2.94]	
Zhang J (2020)	16	25	148	638	4.8%	5.89 [2.55, 13.59]	
Zhang J2 (2020)	3	8	0	11	0.6%	14.64 [0.64, 335.65]	· · · · ·
Zhou F (2020)	13	54	2	137	2.2%	21.40 [4.64, 98.76]	
Total (95% CI)		2236		8181	100.0%	3.15 [2.43, 4.09]	•
Total events	670		1002				
Heterogeneity: Tau ² = 0.1	19; Chi2 = 5	7.70, df	= 24 (P =	= 0.000	1); 12 = 58%	6	
Test for overall effect: Z	= 8.63 (P <	0.00001	1)				Favours [experimental] Favours [control]

1.45 Cerebrovascular disease

	Non-sur	vivor	Surviv	/or		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H, Random, 95% Cl
Chen R (2020)	6	50	24	1540	14.0%	8.61 [3.35, 22.13]	
Hu H (2020)	3	19	1	86	2.3%	15.94 [1.56, 163.04]	
Huang J (2020)	2	16	11	283	4.9%	3.53 [0.71, 17.49]	
Javanian M (2020)	2	19	1	81	2.1%	9.41 [0.81, 109.82]	
Li J1 (2020)	37	77	31	285	36.7%	7.58 [4.23, 13.57]	
Luo X (2020)	17	84	15	214	22.3%	3.37 [1.59, 7.11]	
Wang D (2020)	3	19	3	88	4.4%	5.31 [0.98, 28.71]	
Wang K (2020)	3	19	4	277	5.0%	12.80 [2.64, 62.10]	
Zhang F (2020)	6	17	5	31	6.5%	2.84 [0.71, 11.28]	
Zhang J2 (2020)	2	8	1	11	1.8%	3.33 [0.25, 45.11]	
Total (95% CI)		328		2896	100.0%	5.92 [4.16, 8.42]	•
Total events	81		96			a respective service	
Heterogeneity: Tau ² =	0.00; Chi2	= 7.03. 0	f = 9 (P =	= 0.63)	$1^2 = 0\%$		
Test for overall effect:	Z = 9.88 (P	< 0.000	001)				Eavours [experimental] Favours [control]

1.46 Chronic kidney disease

	Non-sur	vivor	Survivor			Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random. 95% C	M-H. Random, 95% Cl			
Chen R (2020)	5	50	16	1540	6.6%	10.58 [3.71, 30.15]				
Conversano A (2020)	22	42	28	149	9.3%	4.75 [2.29, 9.88]				
Toy B (2020)	36	155	94	1043	12.4%	3.05 [1.99, 4.69]				
lavanian M (2020)	5	19	7	81	5.2%	3.78 [1.05, 13.61]				
lang E cohort1(2020)	17	60	53	512	10.3%	3.42 [1.82, 6.42]				
lang E cohort2 (2020)	299	1076	298	1758	14.5%	1.89 [1.57, 2.26]				
J1 (2020)	20	77	15	285	9.3%	6.32 [3.05, 13.08]				
uo X (2020)	2	84	3	214	3.1%	1.72 [0.28, 10.45]				
lehta V (2020)	21	61	33	157	10.1%	1.97 [1.03, 3.79]				
lowak B (2020)	8	46	27	123	8.0%	0.75 [0.31, 1.79]				
Qi X (2020)	0	5	2	16	1.2%	0.53 [0.02, 12.82]				
Vang D (2020)	1	19	2	88	1.9%	2.39 [0.21, 27.78]				
Vang K (2020)	1	19	4	277	2.2%	3.79 [0.40, 35.71]				
(u B (2020)	2	28	4	159	3.3%	2.98 [0.52, 17.11]				
chang F (2020)	5	17	0	31	1.3%	27.72 [1.42, 539.38]				
2hou F (2020)	2	54	0	137	1.3%	13.10 [0.62, 277.33]				
otal (95% CI)		1812		6570	100.0%	3.04 [2.12, 4.36]	•			
otal events	446		586							
leterogeneity: Tau ² = 0.1	22; Chi ² = 3	9.59, df	= 15 (P =	0.000	5); 1 ² = 629	6				
lest for overall effect: Z	= 6.05 (P <	0.00001)		1.0.2		Favours [experimental] Favours [control]			

1.47 Smoking

	Non-sun	vivors	Surviv	ors		Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C		M-H. Rand	om. 95% Cl	
Chen R (2020)	5	50	106	1540	4.7%	1.50 [0.58, 3.87]		-	-	
Huang J (2020)	6	16	42	283	3.7%	3.44 [1.19, 9.98]				
Klang E cohort1(2020)	13	60	63	512	9.1%	1.97 [1.01, 3.85]				
Klang E cohort2 (2020)	288	1076	429	1758	70.6%	1.13 [0.95, 1.35]				
Li J (2020)	4	65	3	96	1.8%	2.03 [0.44, 9.40]		-		
Luo X (2020)	8	84	13	214	4.9%	1.63 [0.65, 4.08]				
Wang K (2020)	1	19	11	277	1.0%	1.34 [0.16, 10.99]				
Zhang C (2020)	3	6	14	26	1.4%	0.86 [0.15, 5.06]				
Zhou F (2020)	5	54	6	137	2.8%	2.23 [0.65, 7.63]		-		
Total (95% CI)		1430		4843	100.0%	1.32 [1.07, 1.62]			•	
Total events	333		687						1	
Heterogeneity: Tau ² = 0.0	01; Chi ² = 8	40, df =	8 (P=0.	40); 12 =	= 5%		-	1	1	
Test for overall effect: Z =	= 2.59 (P =	0.010)					0.01 Favor	urs [experimental]	Favours [control]	100

1.48 Cancer

	Non-sur	vivor	Surviv	/or	Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% Cl	M-H, Random, 95% Cl
Borghesi A (2020)	20	65	36	237	10.7%	2.48 [1.31, 4.68]	
Chen R (2020)	3	50	15	1540	6.6%	6.49 [1.82, 23.18]	
Conversano A (2020)	11	42	16	149	9,1%	2.95 [1.25, 6.98]	
Deng Y (2020)	6	109	2	116	5.1%	3.32 [0.66, 16.82]	
Du R (2020)	1	21	.3	158	3.1%	2.58 [0.26, 26.04]	
Hu H (2020)	1	19	5	86	3.3%	0.90 [0.10, 8.18]	
Huang J (2020)	4	16	5	283	5.8%	18.53 [4.41, 77.92]	
Javanian M (2020)	3	19	1	81	3.1%	15.00 [1.47, 153.55]	
Klang E cohort1(2020)	9	60	30	512	9.6%	2.84 [1.28, 6.30]	
Klang E cohort2 (2020)	201	1076	290	1758	13.1%	1.16 [0.95, 1.42]	*
Li J (2020)	2	65	0	96	2.0%	7.60 [0.36, 160.90]	
Li J1 (2020)	5	77	6	285	7.0%	3.23 [0.96, 10.88]	
Nowak B (2020)	15	46	20	123	9.7%	2.49 [1.14, 5.44]	
Qi X (2020)	1	5	2	16	2.5%	1.75 [0.12, 24.65]	
Wang K (2020)	1	19	0	277	1.8%	45.00 [1.77, 1143.31]	
Zhang C (2020)	1	6	1	26	2.1%	5.00 [0.27, 93.96]	
Zhang J (2020)	1	25	13	638	3.6%	2.00 [0.25, 15.95]	
Zhou F (2020)	0	54	2	137	2.0%	0.50 [0.02, 10.53]	
Total (95% CI)		1774		6518	100.0%	3.05 [1.92, 4.85]	+
Total events	285		447				
Heterogeneity: Tau ² = 0.4	42; Chi ² = 4	5.22, df	= 17 (P =	0.000	2); 1 ² = 62 ⁴	%	
Test for overall effect: Z =	= 4.73 (P <	0.00001)				Favours [experimental] Favours [control]

1.5 Clinical symptoms

1.51 Fever

	Non-sur	vivor	r Survivor			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% Cl
An W (2020)	5	11	55	99	5.0%	0.67 [0.19, 2.33]	
Chen R (2020)	42	48	1309	1488	8.4%	0.96 [0.40, 2.28]	
Deng Y (2020)	95	109	94	116	10.4%	1.59 [0.77, 3.29]	+
Du R (2020)	21	21	156	158	1.0%	0.69 [0.03, 14.79]	
Huang J (2020)	14	16	244	283	3.6%	1.12 [0.24, 5.11]	· · · · · · · · · · · · · · · · · · ·
Javanian M (2020)	15	19	62	81	5.2%	1.15 [0.34, 3.88]	
Li J (2020)	59	65	60	96	7.6%	5.90 [2.31, 15.04]	
Nowak B (2020)	16	46	58	123	10.8%	0.60 [0.30, 1.21]	
Qi X (2020)	5	5	11	16	1.0%	5.26 [0.24, 113,13]	
Sun H (2020)	107	121	104	123	10.2%	1.40 [0.67, 2.93]	
Wang D (2020)	19	19	85	88	1.1%	1.60 [0.08, 32.19]	
Wang K (2020)	10	19	203	277	7.6%	0.41 [0.16, 1.04]	
Xu B (2020)	23	28	130	159	6.5%	1.03 [0.36, 2.93]	
Yang J (2020)	15	16	47	53	1.9%	1.91 [0.21, 17.20]	
Zhang F (2020)	12	17	22	31	4.7%	0.98 [0.27, 3.60]	
Zhang G (2020)	6	6	81	89	1.1%	1.36 [0.07, 26.22]	
Zhang J (2020)	19	25	508	638	7.6%	0.81 [0.32, 2.07]	
Zhang J2 (2020)	6	8	7	11	2.2%	1.71 [0.23, 12.89]	
Zhou F (2020)	51	54	129	137	4.3%	1.05 [0.27, 4.13]	
Total (95% CI)		653		4066	100.0%	1.12 [0.82, 1.53]	+
Total events	540		3365				
Heterogeneity: Tau ² =	0.11; Chi2	= 23.95	df = 18 (P = 0.1	6); I ² = 25	%	
Test for overall effect:	Z = 0.70 (P	^o = 0.48)					0.05 0.2 1 5 20 Favours [experimental] Favours [control]

1.52 Cough

	Non-sur	vivor	Surviv	VOF		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H. Random, 95% Cl
An W (2020)	11	11	59	99	1.1%	15.66 [0.90, 273.21]	
Chen R (2020)	37	48	1015	1450	8.9%	1.44 [0.73, 2.85]	
Deng Y (2020)	47	109	38	116	10.6%	1.56 [0.90, 2.68]	
Du R (2020)	14	21	132	158	5.9%	0.39 [0.14, 1.07]	
Huang J (2020)	14	16	208	283	3.3%	2.52 [0.56, 11.37]	
Javanian M (2020)	16	19	66	81	3.9%	1.21 [0.31, 4.70]	
Li J (2020)	42	65	66	96	9.1%	0.83 [0.43, 1.62]	
Nowak B (2020)	7	46	49	123	6.9%	0.27 [0.11, 0.65]	
Qi X (2020)	4	5	11	16	1.5%	1.82 [0.16, 20.71]	
Sun H (2020)	88	121	91	123	10.3%	0.94 [0.53, 1.65]	
Wang D (2020)	11	19	56	88	5.9%	0.79 [0.29, 2.16]	
Wang K (2020)	15	19	182	277	5.1%	1.96 [0.63, 6.06]	
Xu B (2020)	23	28	122	159	5.7%	1.40 [0.50, 3.93]	
Yang J (2020)	13	16	32	53	3.8%	2.84 [0.72, 11.20]	
Zhang J (2020)	16	25	394	638	7.4%	1.10 [0.48, 2.53]	
Zhang J2 (2020)	3	8	5	11	2.3%	0.72 [0.11, 4.62]	· · · · · · · · · · · · · · · · · · ·
Zhou F (2020)	39	54	112	137	8.3%	0.58 [0.28, 1.21]	
Total (95% CI)		630		3908	100.0%	1.02 [0.75, 1.39]	• • • • • • • • • • • • • • • • • • •
Total events	400		2638				
Heterogeneity: Tau ² =	0.16; Chi2	= 27.65	df = 16 (P = 0.0	3); I ² = 42	%	
Test for overall effect:	Z = 0.13 (F	P = 0.90)				Favours [experimental] Favours [control]

1.53 Dyspnea

	Non-sur	vivor	Surviv	VOF		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H. Random, 95% Cl
An W (2020)	7	11	4	99	6.5%	41.56 [8.52, 202.65]	
Chen R (2020)	37	50	294	1540	9.5%	12.06 [6.33, 22.98]	
Deng Y (2020)	77	109	22	116	9.6%	10.28 [5.53, 19.13]	
Du R (2020)	18	21	71	158	7.6%	7.35 [2.08, 25.97]	
Huang J (2020)	10	16	32	283	8.2%	13.07 [4.45, 38.38]	
Javanian M (2020)	16	19	66	81	7.3%	1.21 [0.31, 4.70]	
LI J (2020)	65	65	29	96	3.6%	299.75 [17.94, 5007.68]	
Nowak B (2020)	23	46	38	123	9.4%	2.24 [1.12, 4.47]	
Qi X (2020)	3	5	9	16	5.2%	1.17 [0.15, 9.01]	
Wang D (2020)	15	19	20	88	7.8%	12.75 [3.80, 42.77]	
Yang J (2020)	8	16	22	53	8.1%	1.41 [0.46, 4.33]	
Zhang J (2020)	10	17	35	56	8.1%	0.86 [0.28, 2.59]	
Zhang J2 (2020)	11	25	150	638	9.1%	2.56 [1.14, 5.75]	
Total (95% CI)		419		3347	100.0%	5.31 [2.74, 10.28]	•
Total events	300		792				
Heterogeneity: Tau ² =	1.08; Chi2	= 62.11,	df = 12 (P < 0.0	0001); I2:	= 81%	
Test for overall effect:	Z = 4.95 (F	^o < 0.000	001)				Favours [experimental] Favours [control]

1.54 Myalgia

	Non-sur	vivor	Surviv	/or		Odds Ratio		Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C		M-H. Rand	lom, 95% Cl	
An W (2020)	0	11	6	99	1.5%	0.63 [0.03, 11.84]	+			-
Chen R (2020)	8	43	226	1295	20.9%	1.08 [0.49, 2.36]				
Du R (2020)	7	21	27	158	12.8%	2,43 [0.89, 6.58]				
Javanian M (2020)	9	19	41	81	12.8%	0.88 [0.32, 2.39]				
Li J (2020)	8	65	18	96	15.8%	0.61 [0.25, 1.50]			-	
Wang D (2020)	5	19	28	88	10.3%	0.77 [0.25, 2.33]				
Xu B (2020)	3	28	31	159	8.0%	0.50 [0.14, 1.75]				
Zhang J (2020)	0	25	63	638	1.6%	0.18 [0.01, 2.95]	+	+		
Zhou F (2020)	8	54	21	137	16.4%	0.96 [0.40, 2.32]				
Total (95% CI)		285		2751	100.0%	0.91 [0.64, 1.31]		-		
Total events	48		461							
Heterogeneity: Tau ² =	0.00; Chi? :	= 7.16,	df = 8 (P =	= 0.52)	I# = 0%		+	1	1	+
Test for overall effect:	Z = 0.49 (P	= 0.62	1				0.05 Fav	ours [experimental]	Favours [control]	20

1.55 Fatigue

	Non-sur	vivor	Surviv	vor		Odds Ratio	Odd	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H. Ran	lom, 95% Cl	
An W (2020)	3	11	57	99	6.6%	0.28 [0.07, 1.10]		+	
Chen R (2020)	19	43	565	1322	12.7%	1.06 [0.58, 1.96]		-	
Du R (2020)	13	21	58	158	9.7%	2.80 [1.10, 7.16]			
Javanian M (2020)	15	19	62	81	7.6%	1.15 [0.34, 3.88]			
Li J (2020)	56	65	45	96	10.8%	7.05 [3.14, 15.85]			
Nowak B (2020)	16	46	41	123	11.7%	1.07 [0.52, 2.18]		-	
Wang D (2020)	14	19	55	88	8.4%	1.68 [0.55, 5.09]	-		
Yang J (2020)	8	16	18	53	8.2%	1.94 [0.63, 6.04]	-		
Zhang J (2020)	9	25	199	638	10.6%	1.24 [0.54, 2.86]	-		
Zhang J2 (2020)	0	8	2	11	1.9%	0.22 [0.01, 5.34]	•		
Zhou F (2020)	15	54	29	137	11.6%	1.43 [0.70, 2.95]			
Total (95% CI)		327		2806	100.0%	1.47 [0.93, 2.34]		•	
Total events	168		1131						
Heterogeneity: Tau ² =	0.34; Chi2	= 25.61	df = 10 (P=0.0	$(04); 1^2 = 6$	1%	0.01 0.1	10 11	-
Test for overall effect:	Z = 1.64 (F	P = 0.10)				Favours (experimental)	Favours (control)	00

1.56 Expectoration

	Non-sur	vivor	Surviv	/or		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% CI	M-H. Random, 95% Cl
An W (2020)	4	11	14	99	4.6%	3.47 [0.90, 13.41]	
Chen R (2020)	23	46	490	1378	16.6%	1.81 [1.01, 3.26]	
Deng Y (2020)	35	109	14	116	13.6%	3.45 [1.73, 6.86]	
Du R (2020)	12	21	43	158	8.6%	3.57 [1.40, 9.06]	
Huang J (2020)	10	16	125	283	7.2%	2.11 [0.75, 5.95]	
Javanian M (2020)	7	19	38	81	7.3%	0.66 [0.24, 1.85]	
Li J (2020)	28	65	26	96	14.2%	2.04 [1.05, 3.97]	
Qi X (2020)	2	5	5	16	2.1%	1.47 [0.18, 11.72]	
Yang J (2020)	2	16	10	53	3.2%	0.61 [0.12, 3.15]	
Zhang J (2020)	9	25	157	638	10.2%	1.72 [0.75, 3.98]	
Zhou F (2020)	14	54	30	137	12.5%	1.25 [0.60, 2.59]	
Total (95% CI)		387		3055	100.0%	1.88 [1.39, 2.55]	•
Total events	146		952			1	
Heterogeneity: Tau ^z =	0.06; Chi2	= 12,76	df = 10 (P=0.2	4); 12 = 22	%	
Test for overall effect:	Z = 4.06 (F	o < 0.00	D1)				Eavours [experimental] Eavours [control]

	Non-sur	vivor	Surviv	/or		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H, Random, 95% Cl
An W (2020)	2	11	15	99	3.8%	1.24 [0.24, 6.34]	
Deng Y (2020)	19	109	14	116	17.9%	1.54 [0.73, 3.24]	
Huang J (2020)	1	16	6	283	2.1%	3.08 [0.35, 27.22]	
Javanian M (2020)	2	19	12	81	4.0%	0.68 [0.14, 3.31]	
Li J (2020)	9	65	16	96	12.8%	0.80 [0.33, 1.95]	
Nowak B (2020)	1	46	7	123	2.2%	0.37 [0.04, 3.08]	
Qi X (2020)	1	5	1	16	1.1%	3,75 [0,19, 74.06]	· · · · · · · · · · · · · · · · · · ·
Sun H (2020)	36	121	36	123	33.0%	1.02 [0.59, 1.77]	
Wang D (2020)	4	19	3	88	3.9%	7.56 [1.53, 37.21]	
Xu B (2020)	6	28	37	159	10.5%	0.90 [0.34, 2.38]	
Yang J (2020)	3	16	9	53	4.8%	1.13 [0.27, 4.79]	
Zhou F (2020)	2	54	7	137	3.9%	0.71 [0.14, 3.55]	
Total (95% CI)		509		1374	100.0%	1.14 [0.83, 1.56]	+
Total events	86		163			702-1230-24	
Heterogeneity: Tau ² =	0.00; Chi ²	= 10.28	df = 11 (P = 0.5	1); I ² = 0%	6	
Test for overall effect:	Z = 0.79 (P	= 0.43					Favours [experimental] Favours [control]

2. Laboratory tests

2.1 White blood cell count, $\times 10^9/L$

	Nor	-surviv	or	S	urvivor			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% Cl	IV. Random, 95% CI
An W (2020)	11.23	2.29	11	6.17	5.12	99	6.4%	5.06 [3.37, 6.75]	
Conversano A (2020)	10	5.4	42	7.7	4.6	149	6.0%	2.30 [0.51, 4.09]	
Deng Y (2020)	7.76	4.73	109	4.67	1.7	116	9.7%	3.09 [2.15, 4.03]	
Du R (2020)	8.93	6.6	21	5.4	2.62	158	3.3%	3.53 [0.68, 6.38]	
Foy B (2020)	9.2	5.7	155	7.5	8.5	1043	9.3%	1.70 [0.66, 2.74]	
Huang J (2020)	7	5.2	16	4.8	2.1	283	3.8%	2.20 [-0.36, 4.76]	
Javanian M (2020)	9.07	10.33	19	8	10.64	81	1.2%	1.07 [-4.12, 6.26]	
Li J (2020)	10,36	4	65	5,85	2.03	96	9.2%	4.51 [3.46, 5.56]	
Luo X (2020)	8.85	5.61	84	5.23	1.87	214	8.3%	3.62 [2.39, 4.85]	
Qi X (2020)	5.17	7.23	5	4.18	1.67	16	0.8%	0.99 [-5.40, 7.38]	
Sun H (2020)	9.92	5.41	121	5.5	1.7	123	9.4%	4.42 [3.41, 5.43]	
Wang D (2020)	7.2	4.57	19	4.53	1.81	88	5.0%	2.67 [0.58, 4.76]	
Wang K (2020)	8.13	5.77	19	4.83	2.34	277	3.7%	3.30 [0.69, 5.91]	
Yang H (2020)	10.4	6.98	13	5.97	2.49	81	2.1%	4.43 [0.60, 8.26]	
(ang J (2020)	7.97	2.6	16	6.03	2.29	53	7.5%	1.94 [0.52, 3.36]	
chang F (2020)	7.99	3.4	17	5.76	2.53	31	5.8%	2.23 [0.38, 4.08]	
Zhang J1 (2020)	10,73	5.71	18	9,73	7.55	12	1.3%	1.00 [-4.02, 6.02]	
Zhou F (2020)	10.2	5.3	54	5.7	2.5	137	7.2%	4.50 [3.03, 5.97]	
Total (95% CI)			804			3057	100.0%	3.23 [2.63, 3.83]	•
Heterogeneity: Tau ² =	0.73; Chi	^z = 35.6	1, df =	17 (P =	0.005);	$ ^2 = 52$	%		
Test for overall effect:	Z = 10.56	i (P < 0.	.00001)	1					-10 -5 0 5 Favours [experimental] Favours [control]

2.2 Lymphocyte count, $\times 10^{9}/L$

	Non	-survi	vor	SI	irvivo	r		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV, Random, 95% Cl
An W (2020)	0.27	0.25	11	0.87	0.45	99	8.3%	-0.60 [-0.77, -0.43]	
Deng Y (2020)	0.61	0,29	109	1	0.41	116	9.7%	-0.39 [-0.48, -0.30]	-
Du R (2020)	0.67	0.24	21	0.83	0.37	158	9.3%	-0.16 [-0.28, -0.04]	-
Huang J (2020)	0.6	0.3	16	1.2	0.5	283	8.6%	-0.60 [-0.76, -0.44]	
Javanian M (2020)	1.78	1.84	19	2.25	2,92	81	1.0%	-0.47 [-1.51, 0.57]	
Luo X (2020)	0.85	0.35	84	1.12	0.5	214	9.6%	-0.27 [-0.37, -0.17]	*
Qi X (2020)	0.55	0.91	5	0.95	0.48	16	1.5%	-0.40 [-1.23, 0.43]	
Sun H (2020)	0.53	0.28	121	1	0.48	123	9.6%	-0.47 [-0.57, -0.37]	-
Wang D (2020)	0.8	0.48	19	0.97	0.45	88	7.0%	-0.17 [-0.41, 0.07]	
Wang K (2020)	0.73	0.4	19	1.03	0.52	277	7.9%	-0.30 [-0.49, -0.11]	
Yang H (2020)	0.5	0.33	13	1.1	0.6	81	7.3%	-0.60 [-0.82, -0.38]	
Yang J (2020)	0.7	0.57	16	1.07	0.61	53	5.5%	-0.37 [-0.69, -0.05]	
Zhang F (2020)	0.91	0.63	17	1.02	0.52	31	5.0%	-0.11 [-0.46, 0.24]	
Zhang J1 (2020)	8	6.84	18	7.77	5.87	12	0.1%	0.23 [-4.35, 4.81]	+ +
Zhou F (2020)	0.6	0.2	54	1,3	0.5	137	9.6%	-0.70 [-0.80, -0.60]	-
Total (95% CI)			542			1769	100.0%	-0.41 [-0.52, -0.30]	•
Heterogeneity: Tau ² =	0.03; Ch	ni² = 79	9.95, df	= 14 (P	< 0.0	0001); 1	2 = 82%		
Test for overall effect:	Z = 7.28	(P < 0	0.00001)					Favours [experimental] Favours [control]

2.3 Neutrophil count, ×10⁹/L

	Non	-survi	vor	S	urvivor			Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV, Random, 95% CI	
An W (2020)	10.7	1.95	11	4.4	2.11	99	11.4%	6.30 [5.07, 7.53]		
Du R (2020)	7.4	6.76	21	4.2	2.62	158	10.0%	3.20 [0.28, 6.12]		
Huang J (2020)	5.6	3.4	16	3.2	2	283	11.1%	2.40 [0.72, 4.08]		
Luo X (2020)	7.35	4.87	84	3.43	1.52	214	11.5%	3.92 [2.86, 4.98]	+	
Qi X (2020)	4.33	5.94	5	2.78	2.1	16	7.5%	1.55 [-3.76, 6.86]		
Wang D (2020)	5.7	4.25	19	2.9	1.43	88	10.9%	2.80 [0.87, 4.73]		
Wang K (2020)	3.13	1.79	19	6.53	5.45	277	11.5%	-3.40 [-4.43, -2.37]	-	
Yang H (2020)	9.53	6.98	13	4.13	2.42	81	9.0%	5.40 [1.57, 9.23]		_
Yang J (2020)	7	2.28	16	4.3	2.21	53	11.4%	2.70 [1.43, 3.97]		
Zhang J1 (2020)	85.33	9.09	18	87.2	10,15	12	5.8%	-1.87 [-8.98, 5.24]		
Total (95% Cl)			222			1281	100.0%	2.47 [0.06, 4.88]	•	
Heterogeneity: Tau ² =	12.88; 0	chi² = 1	172.21,	df = 9 (P < 0.0	0001); 1	² = 95%			+
Test for overall effect:	Z = 2.01	(P=(0.04)						Favours [experimental] Favours [control	n l

2.4 Platelet count, ×10⁹/L

	Nor	n-survivo	or i	S	urvivor			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI	IV. Random, 95% Cl
Foy B (2020)	193.2	108	155	236	108	1043	22.5%	-42.80 [-61.02, -24.58]	
Javanian M (2020)	240.33	265.12	19	236.5	261.16	81	0.4%	3.83 [-128.25, 135.91]	
Li J (2020)	190.75	90.72	65	229	85.95	96	9.5%	-38.25 [-66.21, -10.29]	
Luo X (2020)	159,33	76.94	84	202,67	75.38	214	20.0%	-43.34 [-62.65, -24.03]	
Qi X (2020)	71.33	49.28	5	136.67	95.91	16	1.8%	-65.34 [-129.17, -1.51]	
Tang N (2020)	178	92	134	231	99	315	20.6%	-53.00 [-72.03, -33.97]	
Wang D (2020)	127.67	76.09	19	174.67	51.25	88	5.8%	-47.00 [-82.8511.15]	
Yang J (2020)	192.33	71.53	16	234	73.92	53	4.6%	-41.67 [-81.97, -1.37]	
Zhang F (2020)	140	100.24	17	182.33	57.51	31	2.8%	-42.33 [-94.10, 9.44]	
Zhang J1 (2020)	188.77	95.97	18	169.27	58.45	12	2.4%	19.50 [-35.81, 74.81]	
Zhou F (2020)	167.2	92.9	54	219.7	77.2	137	9.5%	-52.50 [-80.45, -24.55]	
Total (95% CI)			586			2086	100.0%	-44.37 [-53.01, -35.74]	•
Heterogeneity: Tau ² =	0.00; Chi	P = 7.43.	df = 10	(P = 0.6)	(8); I ² = 0	%			
Test for overall effect:	Z = 10.07	7 (P < 0.0	00001)	1					-100 -50 0 50 100

2.5 Hemoglobin, g/L

-

	Non	-surviv	or	S	irvivor			Mean Difference		Mean D	lifference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl		IV, Rand	om. 95% Cl
Foy B (2020)	114	25	155	124	22	1043	21.2%	-10.00 [-14.16, -5.84]		-	and the second sec
Javanian M (2020)	120.83	40.85	19	114.33	74.72	81	3.6%	6.50 [-18.04, 31.04]	-		
Li J (2020)	117.75	26.25	65	129.25	19,93	96	16.0%	-11.50 [-19.02, -3.98]	-	-	
Luo X (2020)	125.5	20	84	128	17.2	214	20.1%	-2.50 [-7.36, 2.36]		-	-
Yang J (2020)	134.67	23.57	16	125.33	16	53	10.0%	9.34 [-2.99, 21.67]		-	
Zhang F (2020)	111.35	23.96	17	129.26	16,4	31	9.6%	-17.91 [-30.68, -5.14]			
Zhou F (2020)	126.3	17.5	54	129.3	15	137	19.5%	-3.00 [-8.30, 2.30]		-	
Total (95% CI)			410			1655	100.0%	-5.59 [-10.64, -0.54]		-	
Heterogeneity: Tau ² =	26.80; C	hi ² = 19	11, df	= 6 (P = 0	0.004);	12 = 69%	6		1	10	1 10 00
Test for overall effect:	Z = 2.17	(P = 0.0)	3)		i i i i				-20 Favours le	-10 xperimental]	Favours [control]

2.6 Albumin, g/L

	Nor	n-surviv	or	S	urvivo	n		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV, Random, 95% CI
Du R (2020)	33.33	3.5	21	33.9	5.61	158	16.8%	-0.57 [-2.30, 1.16]	-
Huang J (2020)	30.5	4	16	37.6	6.2	283	15.6%	-7.10 [-9.19, -5.01]	
Qi X (2020)	29.1	13.78	5	34.6	9.02	16	1.7%	-5.50 [-18.36, 7.36]	
Wang K (2020)	34.4	4.5	19	40.4	4.1	277	15.7%	-6.00 [-8.08, -3.92]	
Yang J (2020)	27.33	3.25	16	30.67	6.1	53	15.0%	-3.34 [-5.63, -1.05]	
Zhang J2 (2020)	32.8	1.92	8	35.28	1.73	11	17.0%	-2.48 [-4.16, -0.80]	
Zhou F (2020)	29	3.7	54	33.5	4.3	137	18.3%	-4.50 [-5.72, -3.28]	-
Total (95% CI)			139			935	100.0%	-3.98 [-5.75, -2.22]	+
Heterogeneity: Tau ² =	4.07; Ch	ni² = 31.	05. df =	= 6 (P <	0.000	1): 12 =	81%		
Test for overall effect:	Z = 4.42	(P < 0.	0001)						Favours [experimental] Favours [control]

2.7 ALT, U/L

	Non-survivor		S	Irvivor			Mean Difference	Mean Difference	
Study or Subgroup	Mean SD Total		Mean SD To		Total	Weight	IV. Random, 95% CI	IV. Random, 95% Cl	



2.8 AST, U/L

	Nor	1-surviv	TOT	S	urvivor	· · · · ·		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% Cl
An W (2020)	73.07	32.57	11	32.83	12.49	99	4.8%	40.24 [20.84, 59.64]	
Deng Y (2020)	36	15.03	109	23.8	10.58	116	16.2%	12.20 [8.78, 15.62]	-
Du R (2020)	42.83	27.43	21	29.5	17.21	158	8.7%	13.33 [1.30, 25.36]	
Huang J (2020)	35.4	16.8	16	25.5	18.2	283	11.6%	9.90 [1.40, 18.40]	
Li J (2020)	82.25	50.22	65	48.2	27.05	96	7.8%	34.05 [20.70, 47.40]	
Qi X (2020)	59.67	73.41	5	36	20.32	16	0.6%	23.67 [-41.44, 88.78]	
Sun H (2020)	46.33	25.51	121	29	14.25	123	14.7%	17.33 [12.13, 22.53]	-
Wang D (2020)	65	41.65	19	31	13.57	88	5.0%	34.00 [15.06, 52.94]	
Wang K (2020)	45.93	20.67	19	25.27	9.54	277	10.8%	20.66 [11.30, 30.02]	
Yang J (2020)	49.33	43.89	16	33	20.58	53	3.9%	16.33 [-5.88, 38.54]	
Zhang F (2020)	39.67	38.8	17	34.33	20.98	31	4.7%	5.34 [-14.53, 25.21]	
Zhang J1 (2020)	40.9	27.59	18	56.3	50.32	12	2.2%	-15.40 [-46.59, 15.79]	
Zhang J2 (2020)	54.05	9.76	8	45.73	16.04	11	9.0%	8.32 [-3.32, 19.96]	
Total (95% CI)			445			1363	100.0%	16.78 [11.78, 21.78]	•
Heterogeneity: Tau ² =	37.19; 0	$chi^2 = 30$	0.26, df	= 12 (F	= 0.00	3); 12 =	60%		
Test for overall effect:	Z = 6.58	8 (P < 0.	00001)	1					Favours [experimental] Favours [control]

2.9 TBIL, µmol/L

	Nor	1-surviv	or	S	urvivor			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% C	IV. Random, 95% Cl
Du R (2020)	11.4	6.36	21	9.17	4.34	158	29.6%	2.23 [-0.57, 5.03]	
Huang J (2020)	11	4.6	16	11	6.7	283	40.9%	0.00 [-2.39, 2.39]	
Li J (2020)	28.44	53.37	65	28.95	55.39	96	0.8%	-0.51 [-17.57, 16.55]	• • •
Qi X (2020)	24.47	18.1	5	13.83	9.02	16	0.9%	10.64 [-5.83, 27.11]	
Wang D (2020)	13.8	9.05	19	10.27	3.39	88	13.6%	3.53 [-0.60, 7.66]	
Wang K (2020)	11.03	8.89	19	8.5	4.69	277	14.3%	2.53 [-1.51, 6.57]	
Total (95% CI)			145			918	100.0%	1.59 [0.06, 3.11]	•
Heterogeneity: Tau ² =	0.00; C	ni ² = 4.1	8, df =	5 (P = 0).52); P	= 0%			
Test for overall effect:	Z = 2.04	(P = 0.	04)						Favours [experimental] Favours [control]

2.10 LDH, U/L

	Non-survivor		S	urvivor			Mean Difference	Mean D	ifference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV. Rande	om. 95% Cl
An W (2020)	591	181.52	11	211.67	88.02	99	12.8%	379.33 [270.67, 487.99]		
Huang J (2020)	531.1	487.3	16	229.1	122.5	283	5.1%	302.00 [62.80, 541.20]		
Li J (2020)	829.23	479.39	65	320.48	182.58	96	11.6%	508.75 [386.62, 630.88]		
Qi X (2020)	386.67	397.22	5	289	89.41	16	2.8%	97.67 [-253.25, 448.59]		
Wang D (2020)	432.67	271.48	19	242.33	119.09	88	11.4%	190.34 [65.76, 314.92]		
Wang K (2020)	493.1	219.23	19	214.83	59.99	277	13.7%	278.27 [179.44, 377.10]		
Yang J (2020)	542.67	107.29	16	277	142.5	53	17.0%	265.67 [200.59, 330.75]		
Zhang F (2020)	501.33	659.64	17	308.33	152.33	31	3.3%	193.00 [-125.12, 511.12]		
Zhang J1 (2020)	582.6	434.81	18	431.83	211.08	12	5.3%	150.77 [-82.92, 384.46]		
Zhou F (2020)	517.7	233.1	54	263.5	74.2	137	17.1%	254.20 [190.80, 317.60]		-
Total (95% CI)			240			1092	100.0%	288.29 [225.73, 350.85]		•
Heterogeneity: Tau ² =	4905.11;	Chi ² = 2	1.97, d	f=9(P=	(0.009);	12 = 599	6	The second second s		
Test for overall effect:	Z = 9.03	(P < 0.00	001)						-500 -250 Favours [experimental]	Favours [control]

2.11 High-sensitive cardiac troponin I, pg/mL

Non-survivo		n-survivor		S	urvivo	r		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% C	I IV. Random, 95% CI
Sun H (2020)	97.27	170.39	121	7.43	6.83	123	38.7%	89.84 [59.46, 120.22]	
Yang H (2020)	1,429.67	3,324.71	13	7.1	8,6	81	0.1%	1422.57 [-384.73, 3229.87]	• • • •
Zhang F (2020)	97.33	190.78	17	7.33	9.33	31	18.0%	90.00 [-0.75, 180.75]	
Zhou F (2020)	37	59	54	3.2	3.3	137	43.2%	33.80 [18.05, 49.55]	
Total (95% CI)			205			372	100.0%	66.65 [16.94, 116.36]	-
Heterogeneity: Tau ² =	1423.65; 0	chi ² = 13.42	2, df = 3	B (P = 0.	.004); 1	2 = 789	6		
Test for overall effect:	Z = 2,63 (F	e = 0.009)							Favours [experimental] Favours [control]

2.12 Hypersensitive troponin I, >26.2 pg/mL

Non-surv		vivor	Surviv	vor		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H. Random, 95% Cl
Wang D (2020)	5	19	1	88	23.7%	31.07 [3.37, 286.08]	
Zhang F (2020)	10	17	3	31	48.5%	13.33 [2.88, 61.77]	
Zhou F (2020)	23	50	1	95	27.8%	80.07 [10.34, 620.36]	
Total (95% CI)		86		214	100.0%	26.80 [8.99, 79.94]	•
Total events	38		5				
Heterogeneity: Tau ² =	0.03; Chi2	= 2.06, 0	df = 2 (P :	= 0.36);	1² = 3%		
Test for overall effect:	Z = 5.90 (P	o < 0,000	001)				Favours [experimental] Favours [control]

2.13 NT-proBNP, µg/L

Non-survivo		VOF	S	ovivru	r		Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV. Random, 95% Cl		
An W (2020)	1.36	2.48	11	0.06	0.08	99	3.8%	1.30 [-0.17, 2.77]		-	
Sun H (2020)	1.25	1.67	121	0.2	0.21	123	91.5%	1.05 [0.75, 1.35]			
Yang H (2020)	1.64	2.44	13	0.21	0.26	81	4.7%	1.43 [0.10, 2.76]		_	
Total (95% CI)			145			303	100.0%	1.08 [0.79, 1.36]	•		
Heterogeneity: Tau ² =	0.00 CH	$i^2 = 0$	39 df =	2 (P =	0.82):	$1^2 = 0\%$			- 1 1 1 1	-	

2.14 Creatine kinase

	Nor	-survivo	vivor Survivor		Survivor Mean Difference			Mean Difference		Mean	Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV. Ran	dom. 95% Cl	
An W (2020)	196.57	152.54	11	91.67	66,96	99	11.0%	104.90 [13.80, 196.00]				_
Li J (2020)	769.53	605.11	65	281.38	201.6	96	6.5%	488.15 [335.62, 640.68]				
QI X (2020)	175	372.08	5	90.67	65.84	16	2.0%	84.33 [-243.40, 412.06]			-	
Wang D (2020)	154.67	118.54	19	86.67	51.25	88	14.6%	68.00 [13.63, 122.37]				
Wang K (2020)	126.33	101.72	19	61	41.73	277	15.4%	65.33 [19.33, 111.33]				
Yang J (2020)	153.33	170.69	16	71.33	57.91	53	11.5%	82.00 [-3.08, 167.08]			-	-
Zhang F (2020)	149.5	196.44	17	100.33	76.16	31	10.4%	49.17 [-47.98, 146.32]				
Zhang J1 (2020)	156.43	150.59	18	70.77	78.66	12	11.8%	85.66 [3.07, 168.25]				-
Zhou F (2020)	69.83	100.16	54	27.53	29.67	137	16.9%	42.30 [15.13, 69.47]				
Total (95% CI)			224			809	100.0%	96.64 [47.87, 145.41]			-	
Heterogeneity: Tau ² =	3478.52	Chi ² = 3	3.49. d	f=8(P <	0.0001	$1: 1^2 = 7$	6%		1	1	1 1	
Test for overall effect:	Z = 3.88	(P = 0.00	001)						-200 Favou	-100 s [experimenta	0 100	200

2.15 CK-MB, U/L

	Nor	-surviv	/or	S	Irvivo	r .		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV, Random, 95% Cl
Wang D (2020)	25	24.83	19	12.67	5.28	88	5.6%	12.33 [1.11, 23.55]	
Wang K (2020)	20.77	9.13	19	14	4.25	277	41.1%	6.77 [2.63, 10.91]	
Yang J (2020)	17	11.38	16	11.67	6.1	53	20.8%	5.33 [-0.48, 11.14]	
Zhang F (2020)	12.7	11.32	17	9	3.11	31	23.3%	3.70 [-1.79, 9.19]	
Zhang J1 (2020)	23.17	18.18	18	13	4.53	12	9.1%	10.17 [1.39, 18.95]	
Total (95% CI)			89			461	100.0%	6.37 [3.72, 9.03]	•
Heterogeneity: Tau ² =	0.00; Ch	ni² = 2.8	7, df =	4 (P = 0).58); F	2 = 0%			
Test for overall effect:	Z = 4.71	(P < 0.	00001)	0					Favours [experimental] Favours [control]

2.16 PT, s

	Non	-survi	TON	S	urvivo	r		Mean Difference		Mean D	ifference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% C	1	IV, Rande	om, 95% Cl	
An W (2020)	12.5	3.9	11	10.77	0.75	99	4.4%	1.73 [-0.58, 4.04]				
Du R (2020)	14.17	3.18	21	13.77	2.09	158	9.8%	0.40 [-1.00, 1.80]			-	
Li J (2020)	15.03	2.73	65	13.41	5.47	96	11.1%	1.62 [0.34, 2.90]				
Qi X (2020)	14.4	5.83	5	12.87	2.28	16	1.0%	1.53 [-3.70, 6.76]				
Tang N (2020)	16.5	8.4	134	14.6	2.1	315	9.4%	1.90 [0.46, 3.34]				-
Wang D (2020)	12.67	1.28	19	12.8	1.13	88	22.5%	-0.13 [-0.75, 0.49]			-	
Wang K (2020)	13.7	1.9	19	13.3	1.9	277	17.0%	0.40 [-0.48, 1.28]				
Zhou F (2020)	12.3	1.9	54	11.5	0.7	137	24.9%	0.80 [0.28, 1.32]				
Total (95% CI)			328			1186	100.0%	0.73 [0.20, 1.25]			+	
Heterogeneity: Tau ² =	0.21; C	hi² = 12	2.74, df	=7 (P	= 0.08); = 4	5%		+	1		-+
Test for overall effect:	Z = 2.73	3 (P = 0	0.006)						-4	-2 Favours [experimental]	Favours [control]	4

© Annals of Palliative Medicine. All rights reserved.

2.17 APTT, s

Contract in the	Nor	-surviv	or	SI	Irvivo	r .		Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI		IV. Rande	om. 95% CI		
An W (2020)	21.6	6.11	11	29.73	5.04	99	18.1%	-8.13 [-11.87, -4.39]					
Du R (2020)	36.7	8.51	21	35.1	6.14	158	18.1%	1.60 [-2.16, 5.36]		-	-		
Li J (2020)	37.73	10.44	65	27.53	10.7	96	18.6%	10.20 [6.88, 13.52]			-	-	
Qi X (2020)	36.47	16.59	5	27.6	8.53	16	6.8%	8.87 [-6.26, 24.00]			-		
Wang D (2020)	32.4	7.61	19	31.57	3.01	88	18.4%	0.83 [-2.65, 4.31]		-	-		
Wang K (2020)	29.3	3	19	30,8	4.1	277	20.0%	-1.50 [-2.93, -0.07]			1		
Total (95% CI)			140			734	100.0%	1.17 [-3.68, 6.02]		-	-		
Heterogeneity: Tau ² =	30.11; 0	$Chi^2 = 60$	0.68, df	= 5 (P	< 0.00	001); P	= 92%		1	10	+ +		+
Test for overall effect:	Z = 0.47	(P=0.	64)						-ZO	-10	Envoure los	Ileater	20

2.18 D-dimer, mg/L

	Nor	1-surviv	/or	SI	urvivo	r		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV. Random, 95% CI
An W (2020)	4.07	5.85	11	0.37	0.3	99	6.9%	3.70 [0.24, 7.16]	-
Du R (2020)	4	8.03	21	0.67	0.67	158	6.9%	3.33 [-0.11, 6.77]	
Foy B (2020)	1.58	1.12	155	1.01	8.38	1043	12.3%	0.57 [0.03, 1.11]	•
Huang J (2020)	6	16.1	16	1.3	3.9	283	2.4%	4.70 [-3.20, 12.60]	
Li J (2020)	44.18	36.25	65	12.3	9.72	96	1.9%	31.88 [22.86, 40.90]	\rightarrow
Luo X (2020)	7.56	12.21	84	0.63	0.6	214	8.5%	6.93 [4.32, 9.54]	
Sun H (2020)	8.88	14.64	121	0.96	0.87	123	8.5%	7.92 [5.31, 10.53]	
Tang N (2020)	9.04	14.67	134	2.14	2.52	315	8.8%	6.90 [4.40, 9.40]	
Wang D (2020)	0.88	1.43	19	0.21	0,17	88	12.2%	0.67 [0.03, 1.31]	
Wang K (2020)	0.77	0,8	19	0.2	0.15	277	12.4%	0.57 [0.21, 0.93]	
Zhang F (2020)	6.57	13.67	17	0.61	0.49	31	3.2%	5.96 [-0.54, 12.46]	
Zhang J2 (2020)	3.73	2.72	8	0.59	0.17	11	10.1%	3.14 [1.25, 5.03]	
Zhou F (2020)	9.3	15	54	0.6	0.5	137	6.0%	8.70 [4.70, 12.70]	
Total (95% CI)			724			2875	100.0%	4.33 [2.97, 5.68]	•
Heterogeneity: Tau ² =	3.82: CI	nP = 148	8.27, df	= 12 (F	< 0.0	0001):	² = 92%		
Test for overall effect:	Z = 6.26	6 (P < 0.	00001)						-20 -10 0 10 20 Favours [experimental] Favours [control]

2.19 CRP, mg/L

Non-survivor		Nr.	S	urvivor			Mean Difference	Mean Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% C	IV. Random. 95% Cl
An W (2020)	60.87	37.75	11	36.3	48.6	99	10.5%	24.57 [0.29, 48.85]	
Conversano A (2020)	134	84.9	42	93.7	71.9	149	10.0%	40.30 [12.15, 68.45]	
Deng Y (2020)	104.84	101.64	109	8.69	15.58	116	11.1%	96.15 [76.86, 115.44]	
Du R (2020)	76.6	53.74	21	48.77	53,64	158	10.5%	27.83 [3.37, 52.29]	
Huang J (2020)	53.5	47.7	16	24.7	33.2	283	10.6%	28.80 [5.11, 52.49]	
Javanian M (2020)	115.67	185.02	19	74.35	129.9	81	3.7%	41.32 [-46.55, 129.19]	
Li J (2020)	113.8	58.91	65	81.78	62,37	96	11.1%	32.02 [13.03, 51.01]	
Luo X (2020)	113.37	89.54	84	17.52	24.56	214	11.1%	95.85 [76.42, 115.28]	
Qi X (2020)	60.1	103.07	5	21.61	44.4	16	3.4%	38.49 [-54.44, 131.42]	
Yang J (2020)	80	63.4	16	31.33	43.44	53	9.3%	48.67 [15.48, 81.86]	
Zhang F (2020)	79.27	64.27	17	42.23	56.59	31	8.8%	37.04 [0.57, 73.51]	
Total (95% CI)			405			1296	100.0%	48.03 [27.79, 68.27]	-
Heterogeneity: Tau ² = 1	863.87: C	$hi^2 = 57.6$	8. df =	10 (P <	0.0000	1); 12 =	83%		
Test for overall effect: 2	Z = 4.65 (P < 0.000	01)						-100 -50 0 50 100 Favours (experimental) Favours (control)

2.20 ESR, mm/b

	Nor	n-surviv	or	Survivor				Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
An W (2020)	50	33.93	11	35.97	29.87	99	5.7%	14.03 [-6.87, 34.93]			
Huang J (2020)	45.3	25.7	16	35.1	25.9	283	12.2%	10.20 [-2.75, 23.15]			
Li J (2020)	50.75	17.29	65	37.75	15.1	96	30.9%	13.00 [7.82, 18.18]			
Sun H (2020)	39	30.01	121	38.33	29.26	123	23.6%	0.67 [-6.77, 8.11]			
Wang K (2020)	36.9	13.1	19	30.9	14.5	277	27.6%	6.00 [-0.13, 12.13]			
Total (95% CI)			232			878	100.0%	7.87 [2.53, 13.21]	+		
Heterogeneity: Tau ² =	17.06; 0	Chi ² = 8.	12, df =	= 4 (P =	0.09); 1	= 51%					
Test for overall effect:	Z = 2.89	(P=0.	004)	1					Favours [experimental] Favours [control]		

2.21 IL-6, pg/mL

Non-survivor			or	S	urvivor		Mean Difference			Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl.		IV. Ran	dom. 95% Cl		
Sun H (2020)	91.1	95.81	121	19.17	28.66	123	35.9%	71.93 [54.12, 89.74]					
Yang H (2020)	94.97	105.48	13	18.8	26.72	81	26.8%	76.17 [18.54, 133.80]					
Zhou F (2020)	11	5.3	54	6.4	2.2	137	37.3%	4.60 [3.14, 6.06]			•		
Total (95% CI)			188			341	100.0%	47.98 [-8.34, 104.29]			-		
Heterogeneity: Tau ² Test for overall effect	= 2215.13	3; Chi2 = 0.0	60.40, (df = 2 (F	e < 0.00	001); P	= 97%		-200	-100	0 100	200	
reacted oreital ende		1. 6.4	is j						Favou	urs lexperimenta	1 Favours [control]		

2.22 Procalcitonin, ng/mL

	Non	-survi	vor	S	ovivru	r		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random, 95% Cl
An W (2020)	0.11	0.1	11	0.05	0.03	99	21.4%	0.06 [0.00, 0.12]	*
Du R (2020)	0.23	0.32	21	0.1	0.15	158	19.1%	0.13 [-0.01, 0.27]	
Huang J (2020)	0.3	0.3	16	0.2	0.6	283	18.2%	0.10 [-0.06, 0.26]	
Luo X (2020)	0.45	0.66	84	0.05	0.03	214	19.0%	0.40 [0.26, 0.54]	
Qi X (2020)	0.45	1.15	5	0.04	0.07	16	2.5%	0.41 [-0.60, 1.42]	
Sun H (2020)	0.5	0.65	121	0.06	0.05	123	19.9%	0.44 [0.32, 0.56]	-
Zhou F (2020)	0.2	0.3	54	0.1	0	137		Not estimable	
Total (95% CI)			312			1030	100.0%	0.23 [0.06, 0.40]	•
Heterogeneity: Tau ² =	0.03; C	hi² = 45	5.24, df	= 5 (P	< 0.00	001); 12	= 89%		
Test for overall effect:	Z = 2.68	8 (P = (0.007)						Favours [experimental] Favours [control]

2.23 Serum ferritin, mg/L

Non-survivor Survivor Mean Difference Mean Difference



2.24 Fasting blood glucose, mmol/L

	Non-survivor		vor	Su	Irvivo	r		Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random, 95% Cl		
An W (2020)	8.67	3.99	11	6.8	1.81	99	9.6%	1.87 [-0.51, 4.25]			
Li J (2020)	9.26	3.21	65	8.13	2.74	96	59.8%	1.13 [0.18, 2.08]	-		
Qi X (2020)	9.23	8.55	5	6.2	2.15	16	0.9%	3.03 [-4.54, 10.60]			
Yang J (2020)	7.97	2.68	16	6.17	1.22	53	29.7%	1.80 [0.45, 3.15]			
Total (95% CI)			97			264	100.0%	1.42 [0.68, 2.16]	•		
Heterogeneity: Tau ² =	0,00; Ci	hi ² = 0.	97, df =	= 3 (P =	0.81);	12 = 0%					
Test for overall effect:	Z = 3.77	(P=0	0.0002)						Favours [experimental] Favours [control]		

2.25 Serum creatinine, µmol/L

	No	n-survive	or		Survivor			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% CI	IV. Random, 95% CI
An W (2020)	54.17	5,51	11	61.33	18.06	99	9.3%	-7.16 [-11.98, -2.34]	-
Deng Y (2020)	98.17	46.2	109	66.12	18.13	116	9.0%	32.05 [22.77, 41.33]	-
Du R (2020)	90	38.96	21	66.67	18.7	158	8.2%	23.33 [6.41, 40.25]	
Huang J (2020)	70.2	14.8	16	66.12	18.13	283	9.1%	4.08 [-3.47, 11.63]	+
Javanian M (2020)	186.67	248.3	19	230	354.75	81	0.9%	-43.33 [-179.10, 92.44]	
Li J (2020)	385.6	281.58	65	74.3	20.37	96	2.7%	311.30 [242.73, 379.87]	
Qi X (2020)	73.33	35.4	5	65.07	33.08	16	5.8%	8.26 [-26.75, 43.27]	
Sun H (2020)	94.67	31.51	121	67.33	21	123	9.2%	27.34 [20.61, 34.07]	-
Wang D (2020)	96	47.26	19	69.67	18.84	88	7.6%	26.33 [4.72, 47,94]	
Wang K (2020)	84.33	39.09	19	62.67	17.66	277	8.1%	21.66 [3.96, 39.36]	
Yang H (2020)	90.67	32.39	13	74.33	26.42	81	8.0%	16.34 [-2.18, 34.86]	
Yang J (2020)	86.33	26.82	16	62.33	16	53	8.5%	24.00 [10.17, 37.83]	
Zhang C (2020)	174.53	133.53	6	72.61	24.35	26	1.4%	101.92 [-5.33, 209.17]	
Zhang F (2020)	118.67	87.31	17	77.67	20.21	31	4.9%	41.00 [-1.11, 83.11]	
Zhang J1 (2020)	67.93	32.1	18	68	29.35	12	7.5%	-0.07 [-22.33, 22.19]	
Total (95% CI)			475			1540	100.0%	26.11 [12.61, 39.61]	•
Heterogeneity: Tau ² =	505.46; (Chi ² = 18	9.09, d	f = 14 (F	< 0.000	01); I2	= 93%		
Test for overall effect:	Z = 3.79	(P = 0.00	002)						-100 -50 0 50 100

2.26 SpO_{2,} %

Non-survive		or	S	urvivo	r		Mean Difference	Mean	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% C	CI IV. Ran	dom. 95% Cl		
Deng Y (2020)	84.33	10.52	109	96.67	2.52	116	21.3%	-12.34 [-14.37, -10.31]				
Hu H (2020)	86.53	12.46	19	96.17	3.1	86	13.4%	-9.64 [-15.28, -4.00]				
Sun H (2020)	88.67	12	121	96.67	2.25	123	21.0%	-8.00 [-10.17, -5.83]				
Wang K (2020)	89.27	11.45	19	97.33	2.24	277	14.4%	-8.06 [-13.22, -2.90]	i			
Yang H (2020)	87.33	13.29	13	96	3.02	81	10.5%	-8.67 [-15.92, -1.42]				
Zhang F (2020)	91.12	5.36	17	94.45	4.35	31	19.4%	-3.33 [-6.30, -0.36]	-	-		
Total (95% CI)			298			714	100.0%	-8.32 [-11.49, -5.15]	-	11.00.00		
Heterogeneity: Tau ² =	11.19; 0	chi² = 28	5.38, df	= 5 (P	= 0.00	01); l ² =	80%		+ +	1 1	+	
Test for overall effect:	Z = 5.15	(P < 0.	00001)	1.1					-20 -10 Favours [experimenta	Favours [control]	20	

3. Imaging features

3.1 Bilateral involvement

	Non-survivor	vivor	Surviv	vor		Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H. Ran	dom, 95% Cl	_	
An W (2020)	10	11	74	99	10.0%	3.38 [0.41, 27.73]				
Conversano A (2020)	16	42	35	149	33.0%	2.00 [0.97, 4.15]				
Li J (2020)	62	65	59	96	20.9%	12.96 [3.79, 44.31]			_	
Nowak B (2020)	14	46	17	123	30.7%	2.73 [1.21, 6.13]				
Wang D (2020)	19	19	86	88	5.3%	1.13 [0.05, 24.42]				
Total (95% CI)		183		555	100.0%	3.33 [1.57, 7.05]		+		
Total events	121		271							
Heterogeneity: Tau ² = (0.30; Chi ² =	7.45, d	f=4 (P=	0.11);	² = 46%		t d	1 1		
Test for overall effect: 2	2 = 3.15 (P	= 0.002)	0.000			6.01 0.1 Favours [experimental]	Favours [control]	100	

3.2 Ground-glass opacity

	Non-sur	vivor	Surviv	vor		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C	M-H, Random, 95% Cl
Li J (2020)	65	65	72	96	18.0%	44.27 [2.64, 742.56]	
Nowak B (2020)	3	46	4	123	34.2%	2.08 [0.45, 9.65]	
Zhou F (2020)	44	54	92	137	47.7%	2.15 [0.99, 4.67]	
Total (95% CI)		165		356	100.0%	3.67 [0.85, 15.79]	
Total events	112		168				
Heterogeneity: Tau ² =	1.01; Chi2	= 5.38, 1	df = 2 (P :	= 0.07)	² = 63%		
Test for overall effect:	Z = 1.74 (F	9 = 0.08)				Favours [experimental] Favours [control]

4. Complications

4.1 ARDS

	Non-sur	vivor	Surviv	or		Odds Ratio	Odds Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	M-H. Random, 95% Cl	_
An W (2020)	11	11	7	99	5.5%	283.67 [15.18, 5299.52]		-
Deng Y (2020)	98	109	10	116	21.2%	94.44 [38.42, 232.12]		
Javanian M (2020)	3	19	1	81	7.9%	15.00 [1.47, 153.55]		
Li J (2020)	27	65	1	96	9.5%	67.50 [8.86, 514.50]		-
Nowak B (2020)	30	46	11	123	21.7%	19.09 [8.02, 45.43]		
Qi X (2020)	5	5	1	16	4.4%	113.67 [4.01, 3224.21]		\rightarrow
Wang D (2020)	17	19	11	88	12.9%	59.50 [12.07, 293.40]		
Zhou F (2020)	50	54	9	137	16.9%	177.78 [52.36, 603.56]	i –	-
Total (95% CI)		328		756	100.0%	62.85 [29.45, 134.15]	•	
Total events	241		51					
Heterogeneity: Tau ² =	0.50; Chi?	= 13.31,	df = 7 (P	= 0.06); 1 = 479	6		
Test for overall effect:	Z = 10.70 (P < 0.00	0001)				Eavours [experimental] Favours [control]	000

4.2 Acute cardiac injury

	Non-survivor		Surviv	/or		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	CI M-H. Random, 95% CI
Deng Y (2020)	65	109	1	116	15.6%	169.89 [22.87, 1261.98]	
Javanian M (2020)	6	19	8	81	20.0%	4.21 [1.25, 14.15]	
Li J (2020)	3	65	0	96	11.0%	10.81 [0.55, 212.83]	
Wang D (2020)	8	19	4	88	19.2%	15.27 [3.94, 59.20]	
Yang H (2020)	10	13	13	81	18.8%	17.44 [4.21, 72.14]	
Zhou F (2020)	32	54	1	137	15.4%	197.82 [25.70, 1522.37]	á –
Total (95% CI)		279		599	100.0%	25.16 [6.56, 96.44]	•
Total events	124		27				
Heterogeneity: Tau ² =	1.97; Chi2	= 18.86	df = 5 (P	= 0.00	2); l ² = 73	3%	
Test for overall effect:	Z = 4.70 (F	o < 0.000	001)				Eavours lexperimental Favours [control]

4.3 Acute kidney injury

Non-	Non-sur	vivor	Survivor			Odds Ratio		Odds Ratio		
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C		M-H. Rand	iom. 95% Cl	
An W (2020)	0	11	1	99	11.8%	2.86 [0.11, 74.25]				
Deng Y (2020)	20	109	0	116	13.5%	53,37 [3,18, 894,38]				
Li J (2020)	2	65	0	96	12.6%	7.60 [0.36, 160.90]		-		
Nowak B (2020)	10	46	7	123	21.0%	4.60 [1.63, 12.97]			_	
Qi X (2020)	1	5	0	16	11.4%	11.00 [0.38, 318.61]				-
Wang D (2020)	14	19	0	88	13.0%	466.64 [24.48, 8896.20]				
Zhou F (2020)	27	54	1	137	16.8%	136.00 [17.72, 1044.04]				
Total (95% CI)		309		675	100.0%	22.86 [4.60, 113.66]			-	
Total events	74		9							
Heterogeneity: Tau ² =	2.91; Chi2	= 18.58	df = 6 (P	= 0.00	5); l ² = 68	3%	-		+ +	1000
Test for overall effect:	Z = 3.82 (F	P = 0.00	01)				Favours [experimental]	Favours [control]	1000

4.4 Septic sbock

	Non-survivor		Survivor		Odds Ratio		Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Random, 95% C	1	M-H. Ran	dom, 95% Cl	
An W (2020)	2	11	7	99	16.9%	2.92 [0.53, 16.21]				
Deng Y (2020)	13	109	0	116	13.1%	32.60 [1.91, 555.42]				
Li J (2020)	1	65	0	96	11.9%	4.49 [0.18, 111.90]				
Nowak B (2020)	11	46	6	123	18.8%	6.13 [2.11, 17.76]				
Qi X (2020)	2	5	1	16	13.6%	10.00 [0.67, 149.04]				-
Wang D (2020)	19	19	3	88	12.6%	952.71 [47.26, 19207.32]			-	*
Zhou F (2020)	38	54	0	137	13.1%	641.67 [37.64, 10939.84]				
Total (95% Cl)		309		675	100.0%	24.09 [4.26, 136.35]			-	
Total events	86		17							
Heterogeneity: Tau ² =	3.87; Chi ²	= 25.08	df = 6 (P	= 0.00	03); l ² = 7	6%			1 10	1000
Test for overall effect: Z = 3.60 (P = 0.0003)							Eavour	U.1 s [experimental]	Favours [control]	1000

© Annals of Palliative Medicine. All rights reserved.

http://dx.doi.org/10.21037/apm-20-2557