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Research article

Respiratory supports of COVID-19 patients in intensive care unit: A systematic review

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ABSTRACT

Introduction: We aimed to describe the respiratory supports and determine their association with clinical outcomes of COVID-19 patients in intensive care unit (ICU).

Methods: A systemic literature search was conducted in PubMed, EMBASE, MedRxiv and BioRxiv database from December 2019 to 2 July 2020. Studies reporting the application of respiratory supports in COVID-19 patients admitted to ICU were included.

Results: Forty studies with 15320 COVID-19 patients were included in this systematic review. The proportion of invasive mechanical ventilation (IMV) application in ICU patients with COVID-19 was 73.8%. Further analysis elucidated that the use rate of IMV in Asia, Europe and North America was 47%, 76.2% and 80.2%, respectively. The proportion of patients treated with prone positioning and IMV was 29.4%. 25.5% of COVID-19 patients requiring IMV developed ventilator-associated pneumonia. The mortality of patients treated with IMV was 51.1%, while only 17.5% of critically ill COVID-19 patients treated with non-IMV respiratory support died. Additionally, the utilization rate of IMV in non-survival patients was shown 17.26-folds (95%CI 2.89–103.24, $p = 0.002$) higher than that in survival patients, while the use rate of ECMO was no significant difference.

Conclusions: Our findings highlight respiratory supports of COVID-19 patients admitted to ICU in different continents. IMV is a life-saving strategy for critically ill COVID-19 patients with ARDS, yet the mortality remains very high.

1. Introduction

Coronavirus disease 2019 (COVID-19) is a disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which widely spreads over many countries and results in high mortality. COVID-19 is of clustering onset which mainly affects the respiratory system, and some patients may quickly progress to acute respiratory distress syndrome (ARDS) [1]. The development of ARDS in the context of SARS-CoV-2 infection is a crucial factor for prognosis [2]. Recently, it is reported that the incidence of ARDS among patients with SARS-CoV-2 infection is approximately 15% [3]. Moreover, study suggested that hypoxemia or respiratory exhaustion developed in 50%–85% of patients admitted to intensive care unit (ICU) [4]. Thus, timely and effective respiratory supportive strategies are important for the clinical outcomes of critically ill patients.

Advanced respiratory supports ranging from oxygen supplementation through non-invasive ventilation (NIV) and high flow nasal cannula (HFNC), to invasive mechanical ventilation (IMV) and extracorporeal membrane oxygenation (ECMO) are required for patients in ICU with respiratory dysfunction. Currently, published studies did not report the utilization of different respiratory supports according to COVID-19-related ARDS classification. Due to the enormous burdens and shortage of medical care systems, the application of respiratory supports for COVID-19 patients with respiratory dysfunction in ICU appeared variable among different countries. A systematic review of available published literatures is warranted to gain a better understanding of respiratory

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supports and clinical outcomes for COVID-19 patients in ICU. Therefore, this systematic review was conducted to report the respiratory supports and clinical outcomes of COVID-19 patients in ICU.

2. Material and methods

The systematic review was performed in accordance with the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions. We used Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines as the basis of this systematic review.

2.1. Search strategy

Articles published from December 2019 to 2 July 2020 in Pubmed, EMBASE, MedRxiv and BioRxiv Database were searched. We used the following terms alone or in combination to identify all the articles displaying the respiratory supports of COVID-19 patients in ICU: "coronavirus", "COVID19", "SARS-Cov-2", "2019-ncov", "intensive care" and "ICU".

2.2. Inclusion and exclusion criteria

Inclusion criteria were as follows: (1) subjects: adult patients diagnosed with COVID-19 according to the WHO guidelines for the diagnosis and treatment of novel coronavirus disease; (2) clinical features: adult COVID-19 patients admitted to ICU; (3) outcomes: COVID-19 patients in ICU with application of respiratory supports, exact values of IMV patterns, mortality of IMV and non-IMV respiratory supports as well as comparison data of respiratory supports between survivors and non-survivors.

Exclusion criteria included: (1) Studies with special populations including children, elderly, pregnant women; (2) case reports, meta-analysis, reviews, and comments; (3) studies without available data. The flow diagram of the study selection process was depicted in accordance with the PRISMA guideline.

2.3. Data extraction and quality assessment

Included studies were checked independently by two investigators, and disagreements were resolved by a third investigator. The following data were extracted: study characteristics, demographic data, research period, numbers of COVID-19 patients using IMV or NIV or HFNC or ECMO, detailed data of IMV application (including duration of IMV, tidal volume, compliance, FiO2, positive end expiratory pressure [PEEP], PaO2/FiO2 ratio, proportion of ventilator associated pneumonia, ratio of prone position in IMV) and clinical outcomes. The data shown as median and interquartile range were transformed into mean and standard deviation (SD) according to the formula below (http://www.math.hkbu.edu.hk/~tongt/papers/median_2mean.html). The relationship of respiratory supports with clinical outcomes of COVID-19 patients in ICU was evaluated between survival and non-survival group.

According to the Newcastle-Ottawa scale (NOS), the quality of studies was assessed through three aspects (selection, comparability and outcomes). Scores range from 0 to 9, and studies with the score $\geq$6 were classified as high-quality studies.

2.4. Statistical analysis

Data were analyzed by the Review Manager meta-analysis software (version 5.4). The pooled odds ratio (ORs) was used to analyze the incidence of respiratory supports between survival and non-survival patients admitted to ICU. I^2 test was used to assess heterogeneity due to probability variance across studies; these results were illustrated using forest plots. Statistically significant heterogeneity among studies was defined as $I^2 > 50\%$; $p < 0.05$ was considered statistically significant. Continuous variables were descripted as the means $\pm$ standard deviations. Categorical variables were expressed as frequencies or percentages.

3. Results

3.1. Study selection

According to the search terms, 2790 articles were identified regarding the COVID-19 patients in ICU. Firstly, duplicate articles (n = 27) were excluded. After screening the titles and abstracts, 2706 articles were ruled out. The remaining 57 articles were full-text reviewed for eligibility. 2 reviews, 1 case report, 2 comments, 1 meta-analysis, 1 study with special population and 10 studies without available data were excluded, 40 articles with 15320 patients were included in the systematic review. Four articles were combined to analyze the relationship of respiratory supports with clinical outcomes of COVID-19 patients in ICU. Figure 1 summarized the flow chart of study selection process.

3.2. Characteristics of included studies

As shown in Table 1, 18 of the included studies were from Asia [5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22], 10 from Europe [23, 24, 25, 26, 27, 28, 29, 30, 31, 32] and 12 from North American [33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44]. 23 studies (57.5%) were conducted in single center and 17 were (42.5%) multicenter. The size of the study population ranged from 11 to 10287 patients, in which the small series were from reports of larger cohorts comprising ICU and non-ICU patients. All the included articles were respective or cohort studies which reported the respiratory supportive strategies of critically ill COVID-19 patients in ICU. The utilization and parameters of IMV were analyzed in 2–27 studies. Only 4 studies reported the criteria for utilization of respiratory supports [16, 24, 30, 32]. Definitions of ARDS were reported by 18 studies, 15 of which used the Berlin definition of ARDS [5, 6, 11, 12, 13, 15, 16, 18, 20, 21, 28, 30, 36, 42, 44] and only 3 studies [7, 17, 19] used the WHO definition. Four studies reported both the respiratory supports and clinical outcomes of critically ill COVID-19 patients [5, 12, 17, 35]. 36 studies (90%) with a score $\geq$6 were considered to be high quality according to the NOS criteria. Only 4 studies of NOS score were 5.

3.3. Application of respiratory supportive strategies

All studies reported the utilization rate of IMV for COVID-19 patients in ICU. 10482 out of 14210 COVID-19 patients in ICU required IMV (73.8%, with individual study percentages ranging from 15.4% to 100%). Of these studies, 18 were from Asia, 10 were from Europe and the remaining were from North America. 659 out of 1401 critically ill COVID-19 patients in Asia (47%, ranged from 15.4% to 100%), 8542 out of 11212 patients in Europe (76.2%, ranged from 68.6% to 100%), and 1281 out of 1597 patients in North America required IMV (80.2%, ranged from 54.4% to 93.2%). 17 studies reported data of NIV use which consisted of 10 studies from Asia, 2 studies from Europe and 5 studies from North America. 420 out of 3101 COVID-19 patients in ICU required NIV therapy (13.5%, ranged from 0 to 61.9%). Of these 3101 patients, 254 out of 1098 patients in Asia (23.1%, ranged from 8.8% to 61.9%), 137 out of 1348 patients in Europe (10.2%, ranged from 0 to 10.5%), and 29 out of 655 patients in North America required NIV (4.4%, ranged from 0 to 19%). 14 studies reported data of HFNC use which consisted of 6 studies from Asia, 2 studies from Europe and 6 studies from North America. 262 out of 1498 critically ill COVID-19 patients required HFNC therapy (17.5%, ranged from 4.7% to 63.5%). Of these 1498 patients, 143 out of 714 patients in Asia (20%, ranged from 10.2% to 63.5%), 19 out of 92 patients in Europe (20.7%, ranged from 6.3% to 36.4%), and 100 out of 692 patients in North America required HFNC (14.5%, ranged from 4.7% to 42.3%). Data of ECMO use were available in 26 studies consisted of 14 studies in Asia, 4 studies in Europe and 8 studies in North America. 155 out of 2496 COVID-19

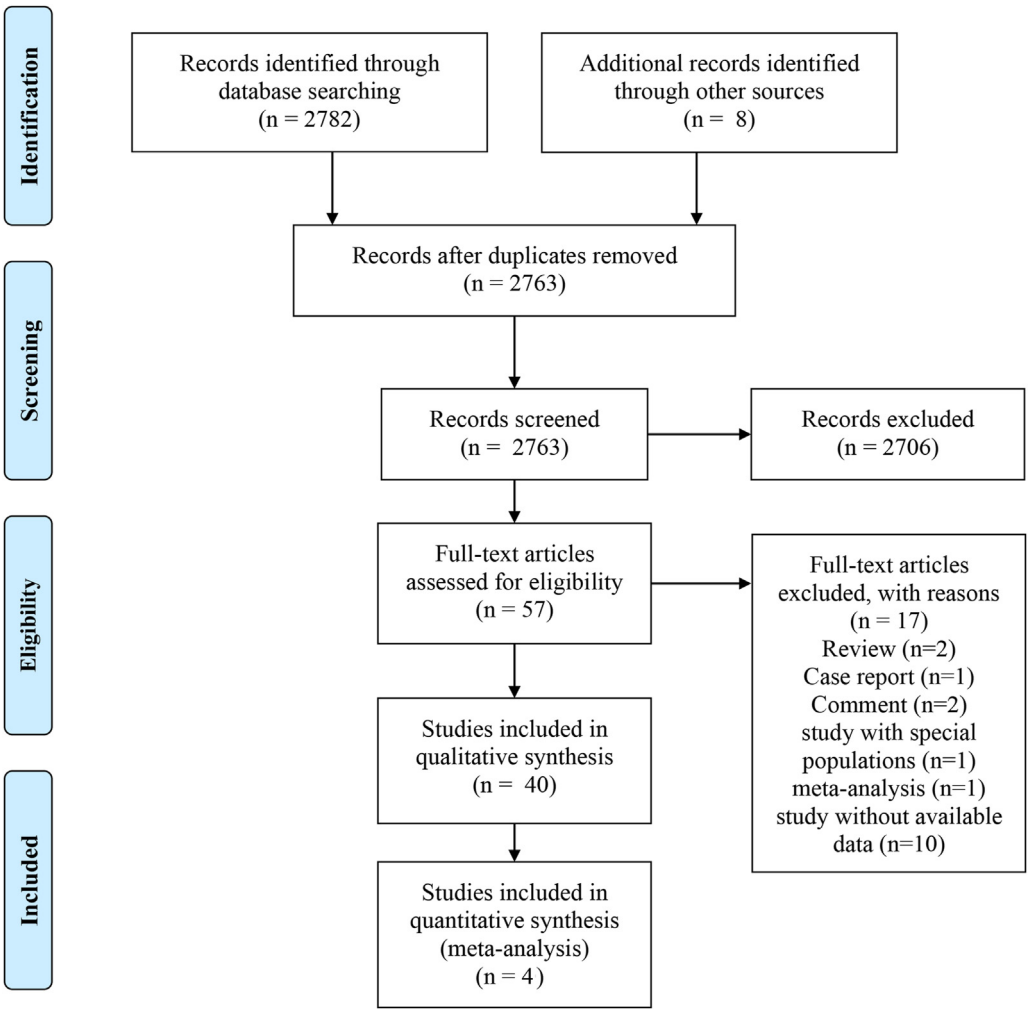

Figure 1. PRISMA flowchart of included and excluded studies.

patients admitted to ICU required ECMO (6.2%, ranged from 0 to 35.6%). Of these 2496 patients, 98 out of 935 patients in Asia (10.5%, ranged from 3.7% to 35.6%), 35 out of 641 patients in Europe (5.5%, ranged from 2.1% to 33.3%), and 22 out of 920 patients in North America required ECMO (2.4%, ranged from 0 to 9.4%).

3.4. Utilization of IMV

As shown in Table 2, the parameters of mechanical ventilation in ICU patients with COVID-19 were variable across studies. In COVID-19 patients admitted to ICU, the mean value of PaO_2/FiO_2 ratio ranged from 91.6 to 181.4mmHg. The volume or pressure-controlled ventilatory mode were applied, with mean value of IMV duration ranged from 4.7 to 17.1 days. The mean value of FiO_2 from day 1 of mechanical ventilation ranged from 50% to 93%, with pulmonary compliance ranged from 33.8 to 44.7 ml/cm H_2O, tidal volume ranged from 6.2 to 7 ml/kg, and PEEP ranged from 9.3 to 16.7cm H_2O.

Information about the prone position was available in 1841 COVID-19 patients requiring IMV and 541 of these have accessed to prone position (29.4%, ranged from 15.9% to 75%). Of these 1841 patients, 94 out of 276 patients in Asia (34.1%, ranged from 22.2% to 69.5%), 312 out of 988 patients in Europe (31.6%, ranged from 27.4% to 75%), and 135 out of 577 patients in North America utilized prone position ventilation (23.4%, ranged from 15.9% to 65%). Four studies with 322 patients reported the rate of ventilator associated pneumonia. Of these studies, 2 were from North America, 1 was from Asia and the remaining one was from Europe. During the use of IMV, 82 of 322 patients (25.5%, ranged from 23.5% to 31%) were suffered from ventilator associated pneumonia. Meanwhile, eleven studies with 7796 COVID-19 patients receiving IMV therapy in ICU were included to assess the mortality rate. Of these, 3984 patients died (51.1%, ranged from 0 to 97%). Furthermore, seven studies with 4966 COVID-19 patients treated with non-IMV respiratory supports were included to determine the mortality rate. Of these, only 871 patients died (17.5%, ranged from 0 to 92.3%).

3.5. Association of respiratory supports with the clinical outcomes

As shown in Figure 2, four studies with 679 patients were included to analyze the association of respiratory supports with the clinical outcomes of COVID patients admitted to ICU. The random-effects model was applied considering the high heterogeneity of IMV proportion between the survival and non-survival group (I^2 = 88%). The following result elucidated that proportion of IMV utilization was 17.26-fold higher in non-survival group than that in survival group [OR = 17.26, 95%CI 2.89–103.24, Z = 3.12, p = 0.002]. In addition, our study showed that there was no significant difference in ECMO application between the survival and non-survival group in three studies with 335 patients [OR = 1.19, 95%CI 0.34–4.16, Z = 0.27, I^2 = 0, p = 0.79].

4. Discussion

To my knowledge, this is the first systemic review which comprehensively elucidates the application of respiratory supportive strategies

Table 1. Characteristics of included studies for review on respiratory supports for COVID-19 patients in ICU.

Study	Centers	Country	First admission	Last admission	Patients in ICU	IMV (%)	NIV (%)	HFNC (%)	ECMO(%)
Shi M [10]	Multiple	China	01 Jan 2020	01 Mar 2020	161	43.5	31.7	NR	3.73
Grasselli G [29]	Multiple	Italy	20 Feb 2020	18 Mar 2020	1591	88	11	NR	1
Mitra AR [40]	Single	Canada	21 Feb 2020	14 Apr 2020	117	63.2	12.8	36.8	2.6
Rubin S [31]	Single	France	3 Mar 2020	14 Apr 2020	71	77	NR	NR	NR
Arentz M [33]	Single	USA	20 Feb 2020	5 Mar 2020	21	71	19	NR	NR
Argenziano MG [34]	Single	USA	1 Mar 2020	5 Apr 2020	236	93.2	3	8.1	2.1
Suleyman G [43]	Multiple	USA	9 Mar 2020	27 Mar 2020	141	80.8	NR	NR	NR
Lenka J [39]	Single	USA	14 Mar 2020	12 Apr 2020	32	71.9	NR	15.6	9.4
Zheng Y [20]	Single	China	22 Jan 2020	5 Mar 2020	34	44.1	NR	52.9	32.4
Wang DW [11]	Single	China	1 Jan 2020	28 Jan 2020	36	47.2	41.7	NR	11.1
Alshukry A [5]	Single	Kuwait	24 Feb 2020	24 May 2020	82	75.6	NR	NR	NR
Wang Y [12]	Single	China	25 Jan 2020	25 Feb 2020	344	29.1	9.9	10.2	NR
Yang XB [17]	Single	China	Dec 2019	26 Jan 2020	52	42	56	63.5	11.5
Hong KS [6]	Single	Korea	NR	NR	13	84.6	NR	53.8	30.8
Huang CL [7]	Single	China	16 Dec 2019	2 Jan 2020	13	15	NR	NR	15
Shah SJ [42]	Single	USA	3 Feb 2020	31 Mar 2020	11	55	NR	NR	0
Xu YH [13]	Multiple	China	14 Jan 2020	20 Feb 2020	45	44.4	13.3	28.9	20
Richardson S [41]	Multiple	USA	1 Mar 2020	4 Apr 2020	371	86.3	NR	NR	NR
Zhou F [21]	Multiple	China	29 Dec 2019	31 Jan 2020	50	64	NR	NR	6
Bhatraju PK [36]	Multiple	USA	24 Feb 2020	23 Mar 2020	24	75	0	42	0
Barrasa H [24]	Multiple	Spain	4 Mar 2020	31 Mar 2020	48	93.8	0	6.3	2.1
Zhou YQ [22]	Single	China	28 Jan 2020	2 Mar 2020	21	38.1	61.9	NR	4.8
ICNARC [25]	Multiple	UK	1 Mar 2020	2 Jul 2020	10287	74.3	NR	NR	NR
Simonnet S [32]	Single	France	27 Feb 2020	5 Apr 2020	124	68.5	NR	NR	NR
Liu J [8]	Single	China	22 Jan 2020	20 Mar 2020	23	61	NR	NR	26
Khan SH [38]	Multiple	USA	1 Mar 2020	27 Apr 2020	144	72.9	NR	NR	NR
Yang LH [14]	Single	China	30 Jan 2020	20 Feb 2020	29	48.3	NR	NR	NR
Shahriarirad R [9]	Multiple	Iran	20 Feb 2020	20 Mar 2020	11	18.2	54.5	NR	NR
Cummings MJ [37]	Multiple	USA	2 Mar 2020	1 Apr 2020	257	79	1.2	4.7	1.9
Yang X [16]	Multiple	China	8 Jan 2020	31 Mar 2020	59	100	NR	NR	35.6
Lemyze M [30]	Single	Franch	NR	NR	44	100	NR	36.4	NR
Rica R [27]	Multiple	Spain	15 Mar 2020	31 Mar 2020	21	100	NR	NR	NR
Vanderburg S [44]	NR	USA	8 Apr 2020	NR	26	77	NR	42	7.7
Yu Y [18]	Multiple	China	NR	27 Feb 2020	226	37.6	8.8	16.4	6.2
Ceruti S [26]	Single	Switzerland	16 Mar 2020	12 Apr 2020	41	83	NR	NR	NR
Yang S [15]	Single	China	13 Feb 2020	14 Mar 2020	66	54.5	16.7	NR	6.1
Arnold F [23]	Single	Germany	26 Feb 2020	21 May 2020	71	73.2	NR	NR	29.6
Dreher M [28]	Single	Germany	Feb	Mar	24	100	NR	NR	33
Zhang P [19]	Multiple	China	28 Jan 2020	21 Feb 2020	136	66	51	NR	5
Auld SC [35]	Multiple	USA	6 Mar 2020	17 Apr 2020	217	76	NR	NR	1.8

NR, not reported. IMV, invasive mechanical ventilation; NIV, non-invasive ventilation; HFNC, high flow nasal canula; ECMO, extracorporeal membrane oxygenation.

in critically ill COVID-19 patients across the globe and potential relationship with the clinical outcomes of COVID-19 patients in ICU.

Respiratory supportive strategies are recommended by the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) as the first-line therapy for COVID-19-related respiratory distress and hypoxia [45]. Methods of respiratory supportive strategies vary and should be determined by severity of illness. In general, most of the included studies in this systemic review were from Asia, Europe and North America. The following results of systemic review demonstrated that the proportion of COVID-19 patients requiring IMV was highest in North America, and the application rate of IMV in Asia was lower than that in Europe and North America. In contrast, the utilization ratio of NIV and HFNC was more in Asia than those in Europe and North American. Thus, our study suggested that the usages of NIV and HFNC may reduce the risk of endotracheal intubation, and decrease the need of IMV and incidence of ventilator-associated pneumonia. Jessica SW *et al* elucidated that NIV had been used successfully in COVID-19 patients in China, as well as SARS epidemic in 2003 [46]. NIV may be used in selected patients in early stage with milder acute hypoxemic respiratory failure [47]. HFNC emerged as an alternative to NIV to prevent intubation and reduce mortality in patients with acute hypoxemic respiratory failure [4]. In this systemic review, variation in respiratory supportive strategies among different continents may be closely related to ethnicity, disease severity and access to medical resources.

COVID-19 ARDS is diagnosed when someone with a confirmed COVID-19 infection meets the Berlin 2012 ARDS diagnostic criteria, which include (i) acute hypoxemic respiratory failure; (ii) presentation within 1 week of worsening respiratory symptoms; (iii) bilateral airspace disease on chest x-ray, computed tomography (CT) or ultrasound that is not fully explained by effusions, lobar or lung collapse, or nodules; and (iv) cardiac failure is not the primary cause of acute hypoxemic respiratory failure [48]. Additionally, COVID-19 related ARDS is an etiological subphenotype of ARDS with the following characteristics: frequent diffuse alveolar damage, possibly a higher than expected compliance of the respiratory system, low PaO2/FiO2 values, frequent nonfocal morphology, and some suggestions of profound

Table 2. IMV settings, complication and mortality for COVID-19 patients in ICU.

Study	IMV days (day)	Tidal volumn (ml/kg)	Compliance (ml/cmH_2O)	FiO2 (%)	PaO2/FiO2 (mmHg)	PEEP (cmH_2O)	Prone position (%)	Ventilator associated pneumonia (%)	Mortality (%)
Grasselli G	NR	NR	NR	66.5	164.9	14	27.4	NR	NR
Mitra AR	14.6	NR	36.8	50	181.4	12	28.4	NR	NR
Arentz M	NR	NR	NR	NR	NR	NR	53.3	NR	NR
Argenziano MG	NR	NR	NR	NR	NR	NR	21.8	24.6	NR
Lenka J	NR	NR	44.7	NR	NR	16.7	30.4	NR	17.4
Yang XB	NR	NR	NR	NR	NR	NR	27.3	NR	NR
Shah SJ	NR	NR	NR	NR	NR	NR	16.7	NR	NR
Xu YH	NR	7	NR	67.1	NR	NR	25	NR	NR
Bhatraju PK	NR	NR	NR	NR	NR	NR	27.8	NR	NR
Barrasa H	NR	NR	NR	NR	NR	NR	48.9	NR	NR
Cummings MJ	13	NR	NR	93	137.8	15	15.9	NR	NR
Yang X	4.7	NR	NR	NR	NR	9.3	69.5	NR	NR
Lemyze M	17.1	6.2	33.8	66	121	16.7	75	NR	NR
Vanderburg S	12.8	NR	NR	NR	NR	NR	65	30	NR
Yu Y	NR	NR	NR	NR	NR	NR	25.9	NR	65.3
Dreher M	10	NR	NR	NR	NR	NR	70.8	NR	NR
Zhang P	NR	NR	NR	NR	NR	NR	22.2	NR	NR
Zhou F	NR	NR	NR	NR	NR	NR	NR	31	96.9
Ceruti S	6.5	NR	NR	77.7	91.6	NR	NR	23.5	NR
Liu J	NR	NR	NR	NR	NR	12.9	NR	NR	NR
Khan SH	5.8	NR	NR	NR	107.4	NR	NR	NR	NR
Auld SC	8.7	NR	36.1	NR	NR	NR	NR	NR	NR
Wang Y	5.1	NR	NR	NR	NR	NR	NR	NR	NR
Suleyman G	NR	NR	NR	NR	NR	NR	NR	NR	45.6
Zheng Y	NR	NR	NR	NR	NR	NR	NR	NR	0
Richardson S	NR	NR	NR	NR	NR	NR	NR	NR	88.1
ICNARC	NR	NR	NR	NR	NR	NR	NR	NR	48.6

NR, not reported; IMV, invasive mechanical ventilation; ICU, intensive care unit; PEEP, positive end expiratory pressure.

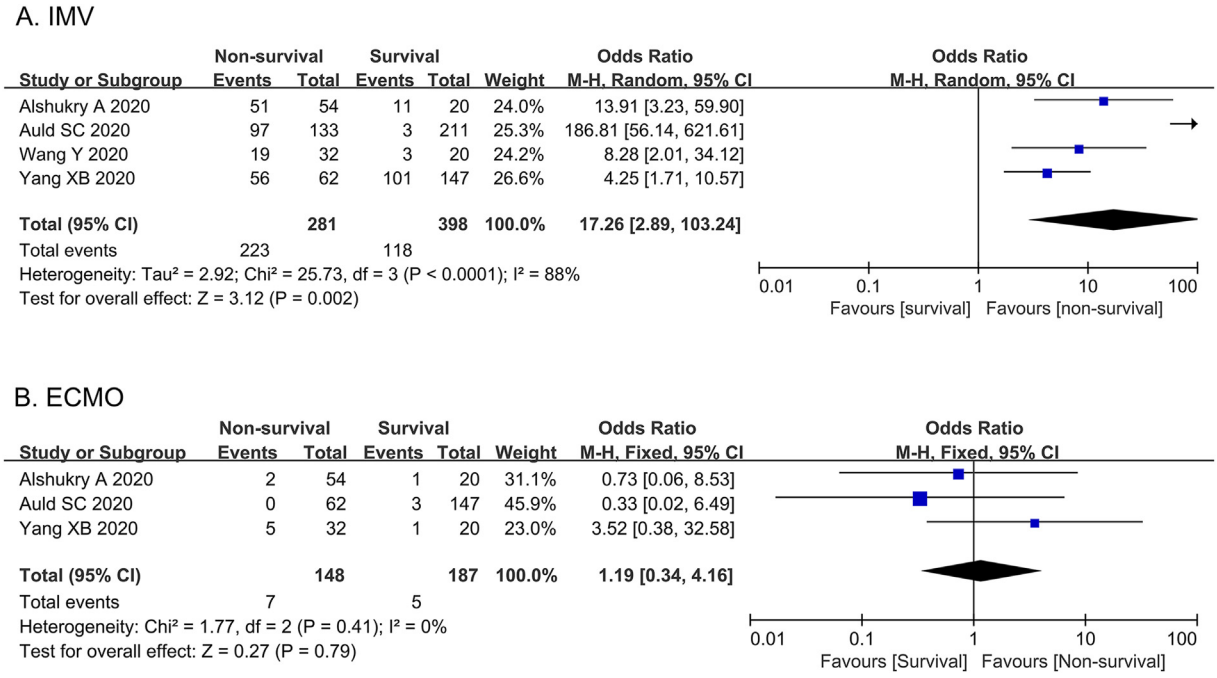

Figure 2. Forest plots represent the comparisons of IMV and ECMO proportion between survival and non-survival cases. A, IMV; B, ECMO. IMV = invasive mechanical ventilation, ECMO = extracorporeal membrane oxygenation.

systemic inflammation [49]. When COVID-19 patients admitted to ICU, our systemic review elucidated that PaO_2/FiO_2 ratio ranged from 91.6 to 181.4mmHg. Mechanical ventilation through endotracheal intubation may be necessary for COVID-19 patients with ARDS or multisystem organ dysfunction. Current recommendations suggest early intubation of COVID-19 patients mainly for two reasons: (1) severe hypoxemia with PaO2/FiO2 often <200mmHg, fulfilling Berlin criteria of moderate-to-severe ARDS; and (2) to protect staff from viral transmission [50]. Recently, there are no guidelines to ventilatory settings of IMV for patients with COVID-19. Furthermore, there have been reports of different possible phenotypes in COVID-19 related ARDS, in which the IMV strategies do not follow the traditional ARDS IMV protocols [51]. Our results of IMV parameters including FiO_2 from day 1 of mechanical ventilation ranged from 50% to 93%, with pulmonary compliance ranged from 33.8 to 44.7 ml/cm H_2O, tidal volume ranged from 6.2 to 7 ml/kg, and PEEP ranged from 9.3 to 16.7cm H_2O could provide recommendation for clinicians.

It is reported that oxygenation in ARDS could be improved by the prone positioning ventilation, possibly through improvements in ventilation-perfusion matching, the uniformity of ventilation, and gravity-related atelectasis [52]. Recent report mentioned that COVID-19 patients with severe ARDS could benefit from the early application of prone position [53]. Our results showed that the proportion of prone position in IMV was about 29.4%, which was higher in Asia and Europe compared to that in North America. We speculated that the high rate of IMV and prone positioning ventilation are associated with severity of COVID-19 in Europe [54]. Although lung-protective ventilation is mandatory for COVID-19 patients with severe ARDS, mortality during IMV in this systematic review was approximately 51.1%. In contrast, the mortality of critically ill COVID-19 patients treated with non-IMV (NIV and HFNC) respiratory supports was 17.5%. In addition, we also investigated that the relationship of respiratory supportive strategies with the clinical outcomes of COVID-19 patients in ICU. This meta-analysis suggested that the application of ECMO as an alternative to respiratory care, did not significantly improve the mortality in critically ill COVID-19 patients. Through the comparison of IMV utilization between survival and non-survival COVID-19 patients in ICU, the use rate of IMV in non-survival patients was shown 17.26-folds higher than in corresponding survival patients. Thus, we suggest that the effectiveness of IMV in critically ill COVID-19 patients is unclear and maybe more modest than the benefits seen for patients with classic ARDS or other kinds of type 1 respiratory failure. The reason for this is unclear, and may be associated with the multi-factorial influences of clinical outcomes in COVID-19 patients, including severity of COVID-19, patient factors and variation of therapeutic decisions. Besides, mechanical ventilation is a double-edged sword, which is not only a life-saving strategy in COVID-19 patients with severe ARDS, but also may result in lung injury. Consequently, further investigation is needed to find a reasonable and individualized lung-protective ventilator strategy for COVID-19 patients to improve the clinical outcomes.

Our study also has several limitations. Firstly, although we studied the relationship of IMV usage between survival and non-survival COVID-19 patients, we did not analyze the affecting factors involved in clinical outcomes. Secondly, the heterogeneity of this meta-analysis is statistically significant which may be related to the small size of the sample and insufficient length of follow-up in some studies. Finally, we had not compared different respiratory supportive strategies in COVID-19 patients of ICU due to the lack of literatures.

5. Conclusion

Respiratory supportive strategies vary greatly among different continents. The application of NIV or HFNC could possibly reduce the risk of endotracheal intubation, and decrease the need of IMV and incidence of ventilator-associated pneumonia. IMV is a life-saving strategy for COVID-19 patients with ARDS in ICU, yet the mortality remains very high.

Declarations

Author contribution statement

Jie Gong: Conceived and designed the experiments; Wrote the paper.
Lichen Ouyang: Analyzed and interpreted the data; Wrote the paper.
Muqing Yu and Yan Zhu: Contributed reagents, materials, analysis tools or data.

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Data included in article/supplementary material/referenced in article.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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