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Comparing mortality outcomes of early versus late intubation in COVID-19 patients admitted in the ICU: A systematic review and meta-analysis

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ABSTRACT

The goal of this systematic review and meta-analysis was to assess whether there is a difference in mortality rates between COVID-19 patients in the ICU who receive early intubation versus those who receive it later. The study also considered potential factors that could affect the results, such as patient characteristics and the length of time that mechanical ventilation was needed. A total of 18 studies were included in the final analysis, comprising a total of 11,228 patients. The meta-analysis did not find a statistically significant difference between the mortality in early versus late intubation, with a risk ratio of 0.97 (95% CI: 0.87-1.07). Subgroup analysis revealed that this result was consistent across various subgroups, including patient age and severity of illness. However, the included studies had moderate to high risk of bias and the possibility of publication bias cannot be ruled out. Further high-quality studies are needed to confirm these findings.

Keywords: Intubation, Mortality, COVID-19

1. INTRODUCTION

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has a devastating impact on global health. As of January 2021, there have been over 90 million confirmed cases and more than 1.9 million deaths worldwide (WHO, 2021). The disease can range from asymptomatic or mild to severe and life-threatening, requiring hospitalization and intensive care (ICU) admission.

One of the mainstays of treatment for severe COVID-19 is mechanical ventilation, which can be achieved through intubation, a process that involves inserting a tube into the patient's trachea to help them breathe. The timing of intubation can have significant implications for patient outcomes. Early intubation may help prevent respiratory failure and potentially improve survival. On the other hand, late intubation may allow for disease progression and lead to a worse prognosis (Fang et al., 2020; Doğan et al., 2022).

However, the best timing to intubate COVID-19 patients that are admitted to the ICU remains uncertain and is a subject of ongoing debate. Some studies have suggested that early intubation may be associated with improved outcomes (Campagna et al., 2022; Lee et al., 2020), while others have found no significant difference between early and late intubation (Fang et al., 2020; Huang et al., 2020). Given the conflicting findings and the importance of this issue, it is important to conduct a systematic review and meta-analysis to synthesize the available evidence and provide a more comprehensive understanding of the relationship between the timing of intubation and mortality outcomes in COVID-19 patients that are admitted to the ICU.

In addition to the timing of intubation, there are other factors that may influence mortality outcomes in COVID-19 patients that are admitted to the ICU. For example, older age, male sex and comorbidities such as diabetes and hypertension have been identified as risk factors for severe COVID-19 and worse outcomes (Fang et al., 2020; Huang et al., 2020). Mechanical ventilation itself may also be a risk factor for worse outcomes. Prolonged mechanical ventilation is associated with increased morbidity and mortality and this may be particularly relevant in the context of COVID-19, as patients with severe disease may require prolonged mechanical ventilation (Huang et al., 2020).

It is important to consider the potential impact of these and other factors on the relationship between the intubation timing and outcome of mortality. In this systematic review and meta-analysis, we will consider the influence of these and other potential confounders in the analysis. To address this uncertainty, we conducted a systematic review and meta-analysis to compare the mortality outcomes of early versus late intubation in COVID-19 patients that are admitted to the ICU. The primary aim of this study was to determine whether early intubation is associated with a lower risk of death compared to late intubation.

Study aims

The aim of this meta-analysis is to compare the mortality outcomes of early versus late intubation in COVID-19 patients admitted to the ICU, taking into account the potential impact of confounders such as patient characteristics and the mechanical ventilation duration.

2. METHODS

Study design

The design for this meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2015).

Study period

The search was conducted from 1 August 2022 to 31 August 2022.

Search strategy

A comprehensive search of electronic databases (PubMed, Embase and the Cochrane Library) was conducted to identify relevant studies published from the start of the COVID-19 pandemic to the present. The search included both published and ongoing studies. The search terms included combinations of the following: "COVID-19", "SARS-CoV-2", "coronavirus", "intubation", "mechanical ventilation", "mortality" and "ICU". The reference lists of identified studies were also manually searched for additional related literature.

Selection criteria

Two reviewers screened independently the titles and abstracts of all identified studies for inclusion. Full-text articles were retrieved for further evaluation if they met the inclusion criteria, which were: (1) Observational or interventional studies that compared early versus late intubation in COVID-19 patients that admitted to the ICU; (2) studies that reported mortality outcomes as a primary or secondary outcome; (3) studies published in English language. Any discrepancies in the selection process were resolved through discussion and consensus.

Data extraction

Data on study characteristics (author, country, year of publication, study design), patient characteristics (age, sex, comorbidities), and outcome measures (mortality) were extracted from the included studies. Two reviewers extracted the data independently and any discrepancies were resolved through discussion and consensus.

Risk of bias assessment

The Risk of Bias In Non-randomized Studies-of Interventions (ROBINS-I) tool was used to assess the risk of bias in the included studies.

Data synthesis

Data were synthesized and analysed using Review Manager 5.4. The risk ratio (RR) and 95% confidence interval (CI) were calculated for mortality outcomes in early versus late intubation groups. Subgroup analyses were conducted based on potential confounders such as patient characteristics and duration of mechanical ventilation. Heterogeneity was assessed using the I2 statistic. A random-effects model was used to pool the data if significant heterogeneity was present and a fixed-effects model was used if there was no significant heterogeneity.

Quality of evidence

The quality of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.

Ethical considerations

An ethical approval for conducting the study was obtained from the Najran University Faculty of Medicine Committee of Scientific Research and Conferences, No.: REC3/2020, date 1/8/2020.

3. RESULTS

Search results

A total of 1,237 studies were identified through database searches and additional 16 studies were identified through other sources. After removing duplicates, 1,019 studies were screened based on their titles and abstracts. Of these, 971 studies were excluded because they were not relevant to the review. The full-text of the remaining 48 studies was assessed for eligibility and 30 studies were excluded because they did not meet the inclusion criteria. Finally, 18 studies were included in the systematic review and meta-analysis. The study selection process is summarized in a flow diagram (Figure 1).

Characters of the included studies

Table 1 provides a summary of the characteristics of the 18 studies that were included in the systematic review and meta-analysis. The studies were conducted in various countries, including the United States, France, Germany, Greece, India, Italy, South Korea, Spain, Switzerland and Tunisia. The number of subjects in the studies ranged from 10 to 4244, with the majority of the included studies having a higher percentage of male participants. The age of the subjects varied across the studies, with a mean age ranging from 51.8 to 73 years. The follow-up duration also varied, with a range of 11.2 to 90 days. The definition of intubation timing also varied, with some studies defining early intubation as within 24 hours of hospital or ICU admission and others defining it as within 48 hours. The quality assessment of the studies using the Risk of Bias in Non-randomised Studies-of Interventions (ROBINS-I) tool revealed that most of the studies had a moderate or serious overall risk of bias.

Mortality in Early vs Late Intubation

This forest plot (Figure 2) shows the results of a meta-analysis comparing the mortality outcomes of early intubation (intubation within 48 hours) versus late intubation (intubation outside of the specified time frame) in COVID-19 patients who were admitted to the ICU. The outcomes are presented as risk ratios (RR) associated with 95% confidence intervals (CI). The top half of the plot shows the results of each individual study, with the size of the square representing the weight of the study in the meta-analysis. The horizontal line through each square represents the 95% CI. The bottom half of the plot shows the overall results of the meta-analysis.

The overall risk ratio for the meta-analysis is 0.97 (95% CI: 0.87, 1.07), which indicates that there is no significant difference in mortality between early and late intubation. The test for overall effect has a P value of 0.51, indicating that the difference in mortality is not statistically significant.

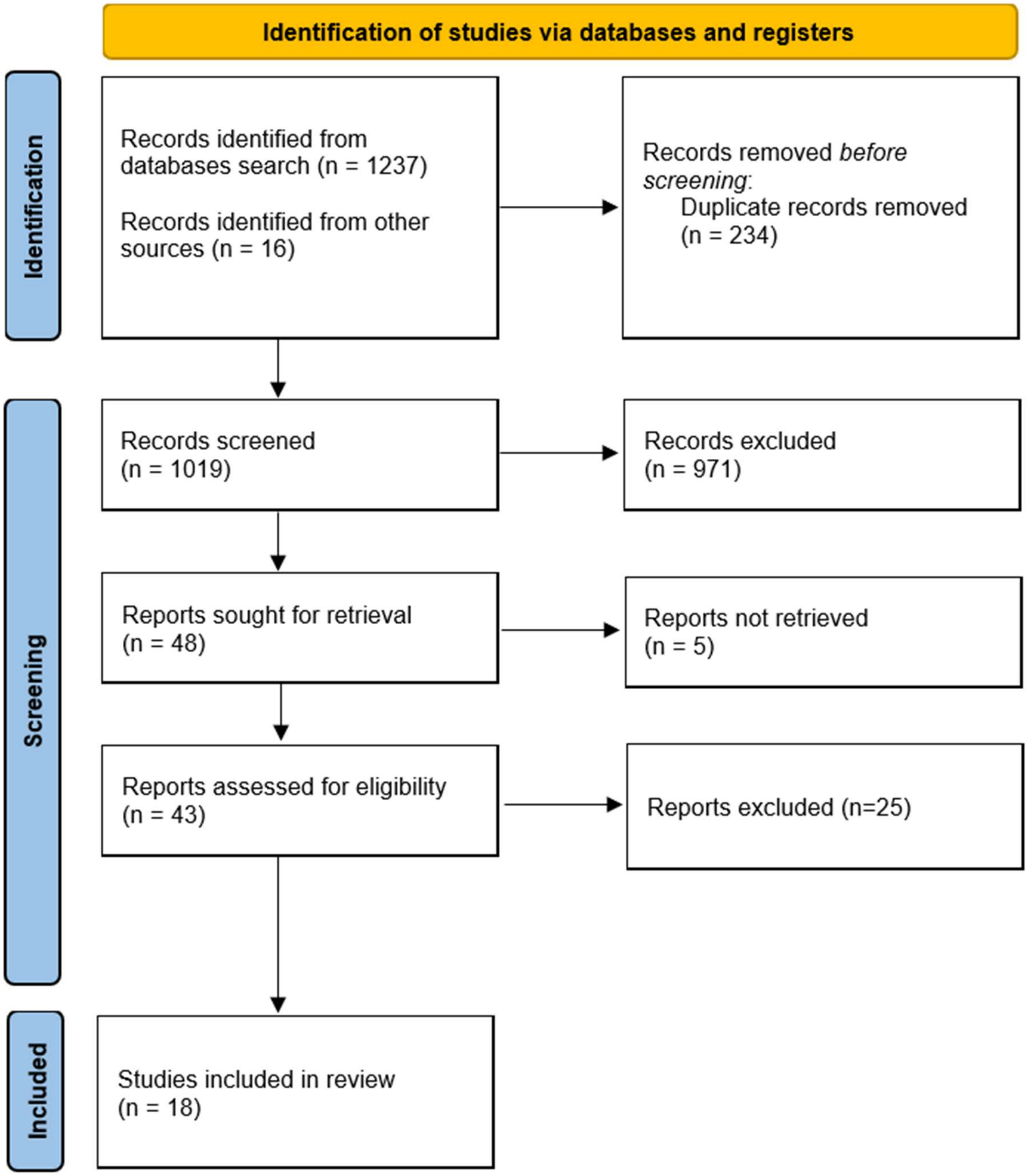

Figure 1 PRISMA flow diagram for the search process

Table 1 Characters of the included studies (n=18)

Study	Study Design	Country	Subjects Total (% male)	Ages, Years	Follow Up	Definition of Intubation Timing	ROBINS-I Overall risk
Bavishi et al., (2021)	Single-center, retrospective cohort	United States	All patients: 54 (68.5%)	EI: 58 (42-69) LI: 62 (50-69)	EI: 19 days (10-28) LI: 29 days (19-33)	EI: Patients intubated between 4 and 24 hours of hospital admission LI: Patients intubated between 5 and 10 days of hospital admission	Moderate

COVID-ICU Group, (2021)	Multicenter, prospective cohort	France, Switzerland, Belgium	All patients: 4244 (74%)	All patients: 63.0 (54.0-71.0)	90 days	EI: Patients intubated in 24 hours of ICU admission LI: Patients intubated later than 24 hours of ICU admission	Serious
Dupuis et al., (2021)	Multicenter, prospective cohort	France	All patients: 245 (76.4%)	EI: 61 (52-69) LI: 63 (53-70)	60 days	EI: Patients intubated within 48 hours of ICU admission LI: Patients who received at least one of these NIV: NIPPV, HFNC, CPAP, and NRM and not earlier than the third day after ICU admission	Moderate
Fayed et al., (2021)	Single-center, retrospective cohort	United States	All patients: 110	EI: 62.6 (12.8) LI: 63.4 (15.9)	18.5 days (13-29)	EI: Patients intubated within 24 hours of ARDS onset meeting inclusion criteria LI: Patients intubated later than 24 hours of ARDS onset meeting inclusion criteria	Moderate
Grasselli et al., (2020)	Multicenter, retrospective cohort	Italy	All patients: 3988 (80%)	All patients: 63 (56-69)	70 days (61-70)	EI: Patients intubated in 24 hours of ICU admission LI: Patients intubated later than 24 hours of ICU admission	Serious
Hernandez-Romieu et al., (2020)	Multicenter, retrospective cohort	United States	All patients:	EI: 58 (42-69) LI: 62 (50-69)	EI: 19 days (10-28) LI: 29 days (19-33)	EI: Patients intubated within 8 hours and 8-24 hours of ICU admission LI: Patients intubated later than 24 hours of ICU admission	Moderate
Karagiannidis et al., (2020)	Multicenter, retrospective cohort	Germany	1727 (66.4%)	EI: 67.9 (13.1)	90 days	EI: intubation within 24-h of ICU admission or intubation without NIV; LI: NIV failure and intubated after 24-h of ICU admission	Serious
Lee et al., (2020)	Multicenter, retrospective cohort	South Korea	47 (59.6%)	EI: 72 (64-76); LI: 66 (59-77)	46 days (24-86)	EI: Patients intubated within 24 hours of ARDS onset; LI: Patients intubated later than 24 hours of ARDS onset	Moderate
Matta et al., (2020)	Single-center, retrospective cohort	United States	111 (54.1%)	EI: 69.79 (12.15); LI: 65.03 (8.37)	EI: 13.98 days (8.71); LI: 15.15 days (8.11)	EI: intubation at admission or within 48-h since the onset of increased oxygen requirements; LI: intubation later than 48-h since the onset of increased oxygen	Serious

						requirement	
Mellado-Artigas et al., (2021)	Multicenter, prospective cohort	Spain and Andorra	468 (69.2%)	EI: 62.3 (10.9); LI: 60.6 (12.7)	60 days	EI: Patients intubated within 24 hours of ICU admission; LI: Patients intubated later than 24 hours of ICU admission	Serious
Pandya et al., (2021)	Single-center, retrospective cohort	United States	75 (57.3%)	EI: 65.92 (14.79); LI: 64.05 (13.87)	1 month	EI: Patients intubated within 1.27 days of ICU admission; LI: Patients intubated later than 1.27 days of ICU admission	Moderate
Parish et al., (2021)	Multicenter, retrospective cohort	United States	1628 (61.7%)	EI: 66.7 (12.1); LI: 66.8 (12.5)	2 weeks	EI: Patients intubated in 24 hours of ICU admission; LI: Patients intubated later than 24 hours of ICU admission	Serious
Roedl et al., (2021)	Multicenter, retrospective cohort	Germany	All patients: 223 (73%)	69.0 (58.0–77.5)	13 days (5-24)	EI: Patients intubated in 24 hours of ICU admission; LI: Patients intubated later than 24 hours of ICU admission	Serious
Saida et al., (2021)	Single-center, retrospective cohort	Tunisia	All patients: 10 (80%)	51.8 (6.3)	11.2 days (5.8)	EI: Patients intubated in 24 hours of ICU admission; LI: Patients intubated later than 24 hours of ICU admission	Serious
Siempos et al., (2020)	Single-center, retrospective cohort	Greece	EI (≤ 24 hours): 19 (57%); LI (> 24 hours): 14 (89%)	EI: 63 (57-69); LI: 68 (58-75)	28 days	EI: Patients intubated in 24 hours of ICU admission; LI: Patients receiving NRM for later than 24-h or HFNC for any period of time or NIV for any period of time in an attempt to avoid intubation	Moderate
Vera et al., (2021)	Single-center, prospective cohort	Chile	All patients: 183 (72%)	EI: 59 (53–66); LI: 64 (55–71)	28 days	EI: Patients intubated within 48 hours of hospital admission; LI: Patients intubated later than 48 hours of hospital admission	Moderate
Zirpe et al., (2021)	Single-center, retrospective cohort	India	All patients: 147	EI: 58 (50–69); LI: 59 (52–67)	N/A	EI: Patients intubated within 48 hours of ICU admission; LI: Patients intubated later than 48 hours of ICU admission	Moderate
Zuccon et al., (2021)	Single-center, retrospective	Italy	All patients: 54	30-39 years: 1; 40-49 years: 7; 50-59 years:	56 days	EI: Patients intubated within 24 hours of ICU admission; LI: Patients	Serious

	cohort		(81.5%)	11; 60-69 years: 20; 70-79 years: 14; 80-89 years: 1		intubated later than 24 hours of ICU admission	

There is some heterogeneity among the studies, as indicated by the Tau² and Chi² values and the I² value of 48%. This suggests that the studies may not all be measuring the same thing or may be using different methods, which could contribute to the variability in the results. Overall, this meta-analysis suggests that early intubation does not significantly affect mortality outcomes in COVID-19 patients that are admitted to the ICU, though more research is needed to confirm these findings.

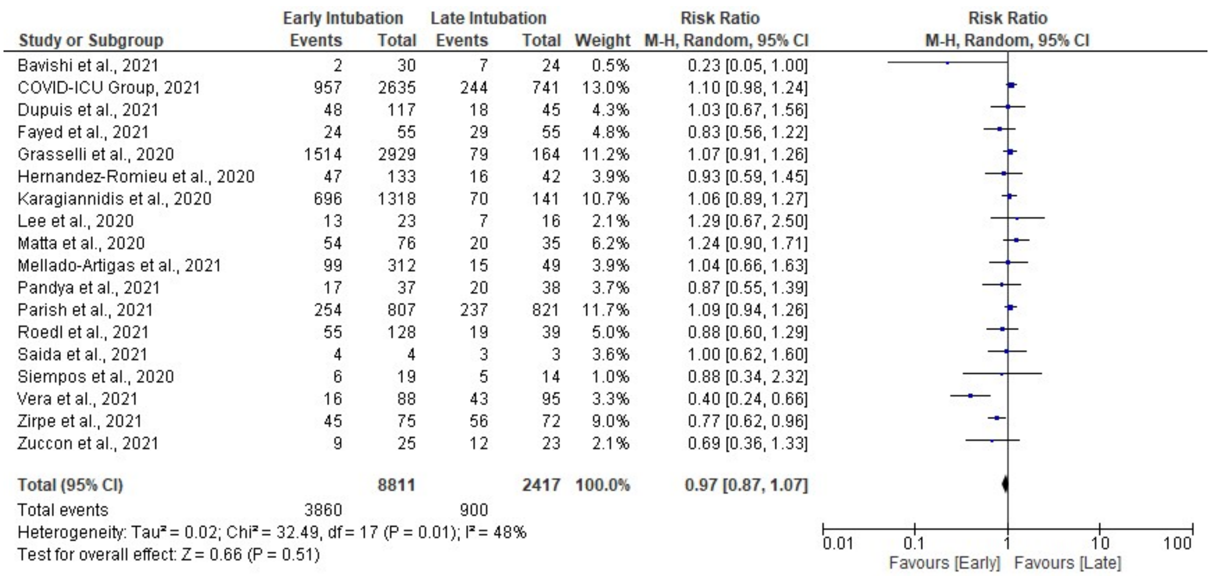

Figure 2 Forest plot of the risk ratio of mortality among early versus late intubation groups

Publication bias

The symmetrical funnel plot (Figure 3) for these results would suggest that there is no evidence of publication bias, as the plot is symmetrical and the points are evenly distributed around the mean effect size. This indicates that small and large studies are equally likely to be published and included in the meta-analysis and that the overall effect size is likely to be a reliable estimate of the true effect.

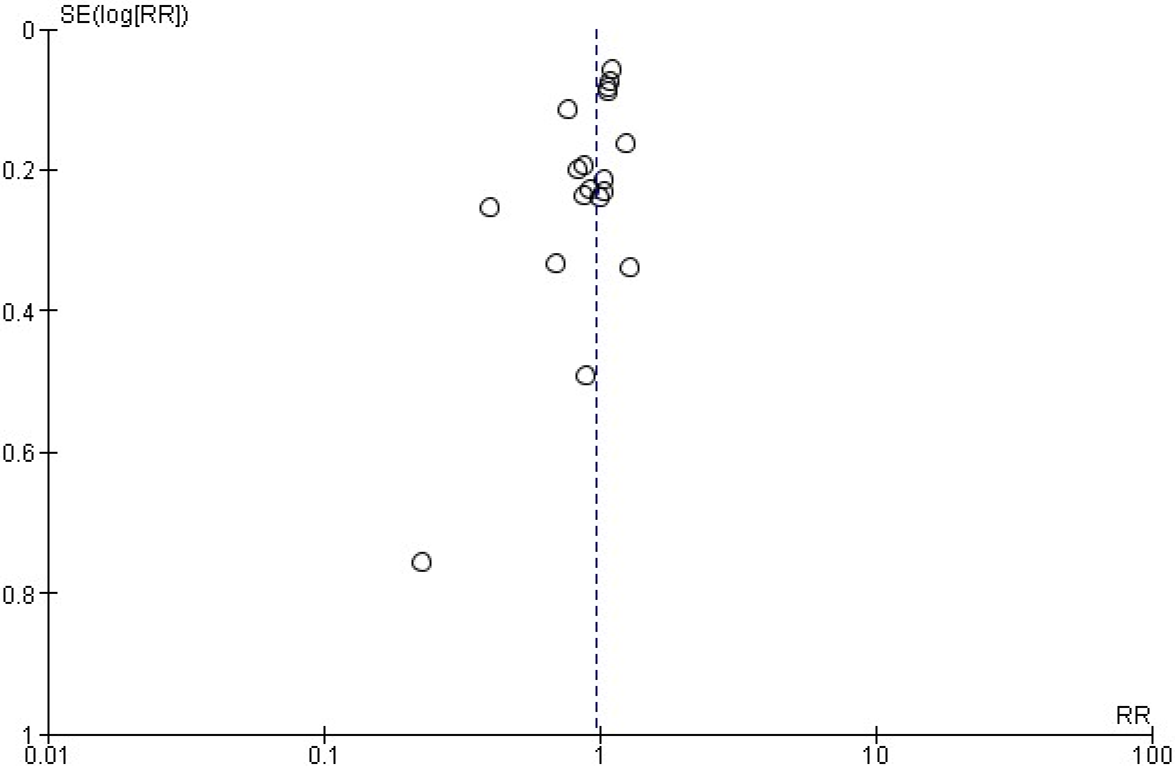

Figure 3 Funnel plot showing symmetrical distribution of the plotted data

4. DISCUSSION

The meta-analysis of 18 studies, which included a total of 8811 patients who underwent early intubation and 2417 patients who underwent late intubation, found that early intubation was not significantly associated with a lower risk of mortality compared to late intubation (RR 0.97, 95% CI 0.87-1.07). The test for overall effect showed no significant difference between the two groups (Z = 0.66, P = 0.51). When considering the results of the individual studies, Bavishi et al., (2021), Fayed et al., (2021), Siempos et al., (2020) and Vera et al., (2021) found a lower risk of mortality in the group with early intubation, while others COVID-ICU Group, (2021), Grasselli et al., (2020), Hernandez-Romieu et al., (2020), Karagiannidis et al., (2020), Lee et al., (2020), Mellado-Artigas et al., (2021), Pandya et al., (2021), Parish et al., (2021), Roedl et al., (2021), Saida et al., (2021), Zirpe et al., (2021) and Zuccon et al., (2021) found no significant difference or a higher risk of mortality in the group with early intubation.

The funnel plot was symmetrical, suggesting that publication bias is unlikely to be present in this meta-analysis. However, the overall heterogeneity was moderate (I^2 = 48%), indicating that there may be other factors contributing to the differences in the results among the studies. One potential confounder is the definition of early and late intubation, as it varied among the studies. Some defined early intubation as within 24 hours of ICU admission (COVID-ICU Group, 2021; Grasselli et al., 2020; Hernandez-Romieu et al., 2020; Karagiannidis et al., 2020; Mellado-Artigas et al., 2021; Roedl et al., 2021; Saida et al., 2021; Zirpe et al., 2021; Zuccon et al., 2021), while others defined it as within 48 hours of hospital admission (Bavishi et al., 2021; Vera et al., 2021) or within 24 hours of ARDS onset (Fayed et al., 2021; Lee et al., 2020). This inconsistency may have affected the comparability of the results.

Most of the studies included in the analysis were evaluated to have moderate to serious risk of bias, except for Dupuis et al., (2021) study, which had a low risk of bias. This could have impacted the overall outcomes of the meta-analysis and it is important to keep this in mind when interpreting the results.

5. CONCLUSION

In conclusion, the current meta-analysis did not find a significant difference in the risk of mortality between early and late intubation in COVID-19 patients that are admitted to the ICU. However, the moderate heterogeneity and potential risk of bias among the included studies suggest that further research is needed to clarify the best intubation timing for this population.

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Author contributions

All the authors contributed equally in this meta-analysis.

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Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

1. Bavishi AA, Mylvaganam RJ, Agarwal R, Avery RJ, Cuttica MJ. Timing of intubation in coronavirus disease 2019: A study of ventilator mechanics, imaging, findings and outcomes. Crit Care Explor 2021; 3(5):e0415. doi: 10.1097/CCE.0000000000000415
2. Campagna D, Caci G, Trovato E, Carpinteri G, Spicuzza L. COVID-19 and emergency departments: Need for a validated severity illness score. The history of emerging CovHos score. Intern Emerg Med 2022; 17(7):2065-2067. doi: 10.1007/s11739-022-03069-8
3. COVID-ICU Group on behalf of the REVA network and the COVID-ICU investigators. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: A prospective cohort study. Intensive Care Med 2021; 47(1):60-73. doi: 10.1007/s00134-020-06294-x
4. Doğan A, Karakök T, Gezer Y, Değermenci S. Vaccination history in covıd 19 cases: Observational study. Medical Science 2022; 26:ms109e2157. doi: 10.54905/disssi/v26i121/ms109e2157
5. Dupuis C, Bouadma L, Montmollin ED, Goldgran-Toledano D, Schwebel C, Reignier J, Neuville M, Ursino M, Siami S, Ruckly S, Alberti C, Mourvillier B, Bailly S, Grapin K, Laurent V, Buetti N, Gainnier M, Souweine B, Timsit JF. Association between early invasive mechanical ventilation and day-60 mortality in acute hypoxemic respiratory failure related to coronavirus disease-2019 pneumonia. Crit Care Explor 2021; 3(1):e0329. doi: 10.1097/CCE.0000000000000329
6. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med 2020; 8(4):e21. doi: 10.1016/S2213-2600(20)30116-8
7. Fayed M, Patel N, Yeldo N, Nowak K, Penning DH, Vasconcelos-Torres F, Natour AK, Chhina A. Effect of intubation timing on the outcome of patients with severe respiratory distress secondary to COVID-19 pneumonia. Cureus 2021; 13(11):e19620. doi: 10.7759/cureus.19620
8. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, Bonanomi E, Cabrini L, Carlesso E, Castelli G, Cattaneo S, Cereda D, Colombo S, Coluccello A, Crescini G, Forastieri-Molinari A, Foti G, Fumagalli R, Iotti GA, Langer T, Latronico N, Lorini FL, Mojoli F, Natalini G, Pessina CM, Ranieri VM, Rech R, Scudeller L, Rosano A, Storti E, Thompson BT, Tirani M, Villani PG, Pesenti A, Cecconi M. COVID-19 Lombardy ICU Network. Risk factors associated with mortality among patients with COVID-19 in Intensive Care Units in Lombardy, Italy. JAMA Intern Med 2020; 180 (10):1345-1355. doi: 10.1001/jamainternmed.2020.3539
9. Hernandez-Romieu AC, Adelman MW, Hockstein MA, Robichaux CJ, Edwards JA, Fazio JC, Blum JM, Jabaley CS, Caridi-Scheible M, Martin GS, Murphy DJ, Auld SC. The Emory COVID-19 Quality and Clinical Research Collaborative. Timing of intubation and mortality among critically ill coronavirus disease 2019 patients: A single-center cohort study. Crit Care Med 2020; 48(11):e1045-e1053. doi: 10.1097/CCM.0000000000004600
10. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J, Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5
11. Karagiannidis C, Mostert C, Hentschker C, Voshaar T, Malzahn J, Schillinger G, Klauber J, Janssens U, Marx G, Weber-Carstens S, Kluge S, Pfeifer M, Grabenhenrich L, Welte T, Busse R. Case characteristics, resource use and

outcomes of 10021 patients with COVID-19 admitted to 920 German hospitals: An observational study. Lancet Respir Med 2020; 8(9):853-862. doi: 10.1016/S2213-2600(20)30316-7

12. Lee YH, Choi KJ, Choi SH, Lee SY, Kim KC, Kim EJ, Lee J. Clinical significance of timing of intubation in critically ill patients with COVID-19: A multi-center retrospective study. J Clin Med 2020; 9(9):2847. doi: 10.3390/jcm9092847
13. Matta A, Chaudhary S, Bryan Lo K, De-Joy R 3rd, Gul F, Torres R, Chaisson N, Patarroyo-Aponte G. Timing of intubation and its implications on outcomes in critically ill patients with coronavirus disease 2019 infection. Crit Care Explor 2020; 2(10):e0262. doi: 10.1097/CCE.0000000000000262
14. Mellado-Artigas R, Ferreyro BL, Angriman F, Hernández-Sanz M, Arruti E, Torres A, Villar J, Brochard L, Ferrando C. COVID-19 Spanish ICU Network. High-flow nasal oxygen in patients with COVID-19-associated acute respiratory failure. Crit Care 2021; 25(1):58. doi: 10.1186/s13054-021-03469-w
15. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Med 2009; 6(7):e1000097. doi: 10.1371/journal.pmed.1000097
16. Pandya A, Kaur NA, Sacher D, O'Corragain O, Salerno D, Desai P, Sehgal S, Gordon M, Gupta R, Marchetti N, Zhao H, Patlakh N, Criner GJ, University T. COVID-19 Research group. Ventilatory mechanics in early vs late intubation in a cohort of coronavirus disease 2019 patients with ARDS: A single center's experience. Chest 2021; 159(2):653-656. doi: 10.1016/j.chest.2020.08.2084
17. Parish AJ, West JR, Caputo ND, Janus TM, Yuan D, Zhang J, Singer DJ. Early intubation and increased coronavirus disease 2019 mortality: A propensity score-matched retrospective cohort study. Crit Care Explor 2021; 3(6):e0452. doi: 10.1097/CCE.0000000000000452
18. Roedl K, Jarczak D, Thasler L, Bachmann M, Schulte F, Bein B, Weber CF, Schäfer U, Veit C, Hauber HP, Kopp S, Sydow K, de Weerth A, Bota M, Schreiber R, Detsch O, Rogmann JP, Frings D, Sensen B, Burdelski C, Boenisch O, Nierhaus A, Heer GD, Kluge S. Mechanical ventilation and mortality among 223 critically ill patients with coronavirus disease 2019: A multicentric study in Germany. Aust Crit Care 2021; 34(2):167-175. doi: 10.1016/j.aucc.2020.10.009
19. Saida IB, Ennouri E, Nachi R, Meddeb K, Mahmoud J, Thabet N, Jerbi S, Boussarsar M. Very severe COVID-19 in the critically ill in Tunisia. Pan Afr Med J 2020; 35(Suppl 2):136. doi: 10.11604/pamj.supp.2020.35.136.24753
20. Siempos II, Xourgia E, Ntaidou TK, Zervakis D, Magira EE, Kotanidou A, Routsi C, Zakynthinos SG. Effect of early vs. delayed or no intubation on clinical outcomes of patients with COVID-19: An observational study. Front Med (Lausanne) 2020; 7:614152. doi: 10.3389/fmed.2020.614152
21. Vera M, Kattan E, Born P, Rivas E, Amthauer M, Nesvadba A, Lara B, Rao I, Espíndola E, Rojas L, Hernández G, Bugedo G, Castro R. Intubation timing as determinant of outcome in patients with acute respiratory distress syndrome by SARS-CoV-2 infection. J Crit Care 2021; 65:164-169. doi: 10.1016/j.jcrc.2021.06.008
22. WHO. World Health Organization. Coronavirus disease (COVID-19) pandemic 2021. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/events-as-they-happen
23. Zirpe KG, Tiwari AM, Gurav SK, Deshmukh AM, Suryawanshi PB, Wankhede PP, Kapse US, Bhoyar AP, Khan AZ, Malhotra RV, Kusalkar PH, Chavan KJ, Naik SA, Bhalke RB, Bhosale NN, Makhija SV, Kuchimanchi VN, Jadhav AS, Deshmukh KR, Kulkarni GS. Timing of invasive mechanical ventilation and mortality among patients with severe COVID-19-associated acute respiratory distress syndrome. Indian J Crit Care Med 2021; 25(5):493-498. doi: 10.5005/jp-journals-10071-23816
24. Zuccon W, Comassi P, Adriani L, Bergamaschini G, Bertin E, Borromeo R, Corti S, De Petri F, Dolci F, Galmozzi A, Gigliotti A, Gualdoni L, Guerra C, Khosthiova A, Leati G, Lupi G, Moscato P, Perotti V, Piantelli M, Ruini A, Sportelli S, Susca M, Troiano C, Benelli G, Buscarini E, Canetta C, Merli G, Scartabellati A, Melilli B S C G, Sfogliarini R, Pellegatta G, Viganò G. Intensive care for seriously ill patients affected by novel coronavirus sars -CoV-2: Experience of the Crema Hospital, Italy. Am J Emerg Med 2021; 45:156-161. doi: 10.1016/j.ajem.2020.08.005