BMJ Open

Timing dilemma: a systematic review and meta-analysis of short-term mortality in patients with COVID-19 undergoing tracheostomy with varied timing, including 7, 10 and 14 days

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To cite: Kim BK, Choi H, Kim CY. Timing dilemma: a systematic review and meta-analysis of short-term mortality in patients with COVID-19 undergoing tracheostomy with varied timing, including 7, 10 and 14 days. *BMJ Open* 2024;**14**:e084405. doi:10.1136/bmjopen-2024-084405

► Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (https://doi.org/10.1136/bmjopen-2024-084405).

Received 17 January 2024
Accepted 18 November 2024

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ABSTRACT

Objective To analyse the effects of tracheostomy timing on COVID-19 outcomes by comparing mortality rates at different time points (7, 10 and 14 days).

Design Systematic review and meta-analysis.

Data sources PubMed, Embase, Cochrane Library, Web of Science and Scopus were searched from 31 August 2023 to 6 September 2023.

Primary and secondary outcomes measures The primary outcome was short-term mortality, defined as intensive care unit (ICU) mortality, hospital mortality and 28-day or 30-day mortality. The secondary outcomes included mechanical ventilation duration, ICU and hospital days.

Results Among 3465 patients from 12 studies, the 10-day subgroup analysis revealed higher mortality for earlier tracheostomy than for later tracheostomy (49.7% vs 32.6%, OR 1.91, 95% CI 1.37–2.65). No significant differences were observed at 7- and 14-day marks. Earlier tracheostomy was associated with shorter mechanical ventilation (mean difference=−7.35 days, 95% CI −11.63 to −0.38) and ICU stays (mean difference=−11.24 days, 95% CI −18.50 to −3.97) compared with later tracheostomy. Regarding hospital stay, the later tracheostomy group exhibited a trend towards longer-term inpatients, with no significant difference.

Conclusions No significant difference in short-term mortality was observed between patients undergoing tracheostomy at 7 and 14 days; however, at 10 days, later tracheostomy resulted in a lower mortality rate. Accordingly, subtle timing differences may impact short-term results in COVID-19 patients. Considering that the later tracheostomy group had longer mechanical ventilation and ICU stays, additional research is required to determine an optimal timing that reduces mortality cost-effectively.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The present study included high-quality studies with stringent inclusion and exclusion criteria to assess clinical outcomes in patients undergoing early and late tracheostomy during the COVID-19 pandemic.
⇒ The meta-analysis included data from an observational study, which poses potential confounding factors.
⇒ Consistency of the results is limited by considerable heterogeneity in the criteria and definitions used among the included studies.
⇒ The study was conducted in the early stages of COVID-19 pandemic; thus, it could not capture most recent advancements in its treatment.
⇒ Our study focused only on short-term mortality.

INTRODUCTION

The coronavirus disease (COVID-19) spread rapidly, leading to a global pandemic within 3 months of its emergence.[1] Although most infected patients experienced mild upper respiratory symptoms, approximately 44.1% of severe cases required admission to the intensive care unit (ICU), and up to 23.6% required mechanical ventilation.[2] Notably, with the development of drugs such as dexamethasone and tocilizumab that improve COVID-19 outcomes,[3 4] an increasing number of patients faced the possibility of requiring prolonged mechanical ventilation.

Tracheostomy is a common procedure performed to replace the endotracheal tube in cases of prolonged mechanical ventilation. While it is a temporary device and not a therapy, it offers several advantages, including easier separation from mechanical ventilation, reducing complications associated with prolonged intubation, preventing laryngeal damage, improving patient comfort and facilitating oral feeding and communication.[5] However, tracheostomy also carries the risk of acute complications, such as haemorrhages and infections, as well as long-term complications such as laryngeal stenosis and fistulas.[6 7] Therefore, determining the appropriate timing for tracheostomy is important to maximise its benefits and minimise its drawbacks.

The ongoing debate on the optimal timing of tracheostomy for improving COVID-19 outcomes further complicates the decision-making process for healthcare providers. Initial reports during the early stages of the COVID-19 pandemic highlighted high mortality rates and concerns about virus transmission to healthcare workers during tracheostomy, leading to recommendations against early tracheostomy (ET) in most published guidelines.[8–10] Previous meta-analyses that examined the impact of ET and late tracheostomy (LT) on mortality did not provide a clear conclusion, primarily due to variations in the definition of ET in different studies and the fact that many studies were conducted during the initial phases of the pandemic from 2020 to 2021.[11 12] In the present study, we addressed this inconsistency by analysing mortality outcomes at different ET intervals (≤7 days, ≤10 days and ≤14 days). By examining these distinct time points, we aim to suggest the value of consistent ET definitions for future studies. This approach addresses the 'timing dilemma' observed in the literature, which may have meaningful implications for optimising COVID-19 patient outcomes and guiding clinical practice with clearer timing considerations.

METHODS

This article followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines for reporting, and detailed information regarding the reporting process is available in online supplemental table 1. Informed consent was not required for this study because it involved a systematic analysis using previously published data.

Search strategy and study selection

A systematic review was conducted by two independent investigators (BKK and EJK) from 31 August 2023 to 6 September 2023, up to the final search date. We systematically searched the following databases: PubMed, Embase, Cochrane Library, Web of Science and Scopus, using Boolean operators such as AND, OR or NOT to refine and broaden search results.

The included studies included articles written in English and studies involving human subjects, with no restriction on region, race or sample size. Detailed search strategies are provided in online supplemental table 2. Abstracts, case reports, reviews, editorials, commentaries and practice guidelines were excluded from the analysis. Additionally, we reviewed all cited references as an additional search tool to identify relevant literature that met our criteria.

Two investigators (BKK and CYK) independently assessed the eligibility of titles and abstracts. Full-text articles were examined to evaluate the suitability of our analysis. In cases of discord, suitability was discussed and resolved through consensus.

Inclusion and exclusion criteria

Studies were included in the analysis if they met the following inclusion criteria: focused on patients confirmed with COVID-19; provided short-term mortality data for patients who underwent ET or LT, with a clear definition of the exact 'early' timing within the study and reported on patients requiring mechanical ventilation due to respiratory failure who underwent a percutaneous or open surgical tracheostomy.

Studies that met the following exclusion criteria were excluded from this analysis: irrelevant publication types, study results that did not align with the scope of our analysis and the timing of the tracheostomy was unclear or did not align with our criteria.

Data collection and quality assessment

Data collection was conducted by two independent reviewers (BKK and CYK) using a predetermined data extraction form. The following data were collected: author, publication year, study design, definition of mortality, study country, study period, tracheostomy method, definition of ET, number of participants, age, sex, short-term mortality, duration of mechanical ventilation, length of stay in the ICU and days in the hospital.

The primary outcome of this study was short-term mortality, defined as ICU mortality, hospital mortality and 28-day or 30-day mortality. If no clear definition of mortality was provided in the study, it was considered short-term mortality. The study initially analysed outcomes for ET and LT as defined in each paper, regardless of their specific definitions. Subsequently, 'earlier' and 'later' were further classified into ≤7 days versus >7 days, ≤10 days versus >10 days and ≤14 days versus >14 days for further comparisons. The secondary outcomes of this study were mechanical ventilation duration, length of stay in the ICU and hospital days, whenever relevant data were available.

The quality assessment of the studies was conducted using the Newcastle–Ottawa Scale (NOS),[13] and the results are presented in online supplemental table 3. Briefly, the NOS is used to evaluate the quality of observational or cohort studies, with scores assigned for selection (0–4 points), comparability (0–2 points) and outcome (0–3 points). A higher total score is considered indicative of higher methodological quality: low quality (scores 0–3), moderate quality (scores 4–6) and high quality (scores 7–9).

Statistical analysis

For dichotomous outcomes, two different groups were expressed as ORs with 95% CIs using the Mantel–Haenszel statistical method. Continuous outcomes are represented as weighted mean differences with a 95% CI using the inverse variance statistical method. Continuous variables are reported as medians and SD from IQRs (Wan *et al*).[14] Individual study weights were calculated based on the variance of their estimates, assigning less weight to smaller studies with larger variances and more weight to larger studies with smaller variances.

Kim BK, *et al. BMJ Open* 2024;**14**:e084405. doi:10.1136/bmjopen-2024-084405

Heterogeneity was assessed using the I^2 statistic, following the Cochrane Handbook (Cochrane Handbook for Systematic Reviews of Interventions V.6.5, published 2024, accessed 27 October 2024, available at https://training.cochrane.org/handbook/current) guidelines, with a random-effects model applied in cases of substantial heterogeneity ($I^2 \geq 50\%$) and a fixed-effects model used when heterogeneity was not substantial ($I^2 < 50\%$). Sensitivity analyses were conducted by removing one study at a time, starting with the study with the highest I^2, to assess its impact on heterogeneity. Publication bias was evaluated using funnel plots, considering a p value <0.05 as statistically significant. All statistical analyses were conducted using Review Manager 5.2 (RevMan 5.2; The Cochrane Collaboration, Oxford, UK) and R V.4.3.1 (R Foundation for Statistical Computing, Vienna, Austria).

Patient and public involvement

This study follows a meta-analysis design, and there was no direct participation from patients or the public. The research was conducted using previously published data, and therefore, there is no additional information to provide in this section.

RESULTS

Study selection and clinical characteristics

We performed a search using five databases (PubMed, Embase, Cochrane Library, Web of Science and Scopus) and retrieved a total of 651 studies. After excluding 348 duplicate studies, we reviewed the titles and abstracts of the remaining 303 studies. During this review, BKK and CYK discussed and excluded five studies through consensus. Consequently, considering the suitability of the research, we selected 21 studies as final candidates and thoroughly examined the full texts of these studies. In the subsequent review, we excluded 13 studies that did not meet the inclusion criteria, leaving us with eight studies for the final analysis. Furthermore, by checking the references of other studies, we identified four studies relevant to our research, which were added, resulting in a total of 12 studies included in the final analysis. No further disagreements requiring additional consensus occurred. The study selection flow chart can be found in figure 1.

A total of 3465 patients from 12 studies conducted between 2020 and 2023 were included in the final analysis.[15–26] Most of these studies were rated as of high quality, scoring 7 or higher on the NOS scale (refer to online supplemental table 3). All studies were conducted between 2020 and 2021, and most published their results in 2022 (5 of 12, 41.7%). Most of the studies were retrospective in nature (9 of 12, 75.0%), with an equal representation of single-centre and multicentre studies. Tracheostomy was performed using open surgical and percutaneous methods in most studies (5 of 12, 41.7%), and in half of the studies, ET was defined as within 10

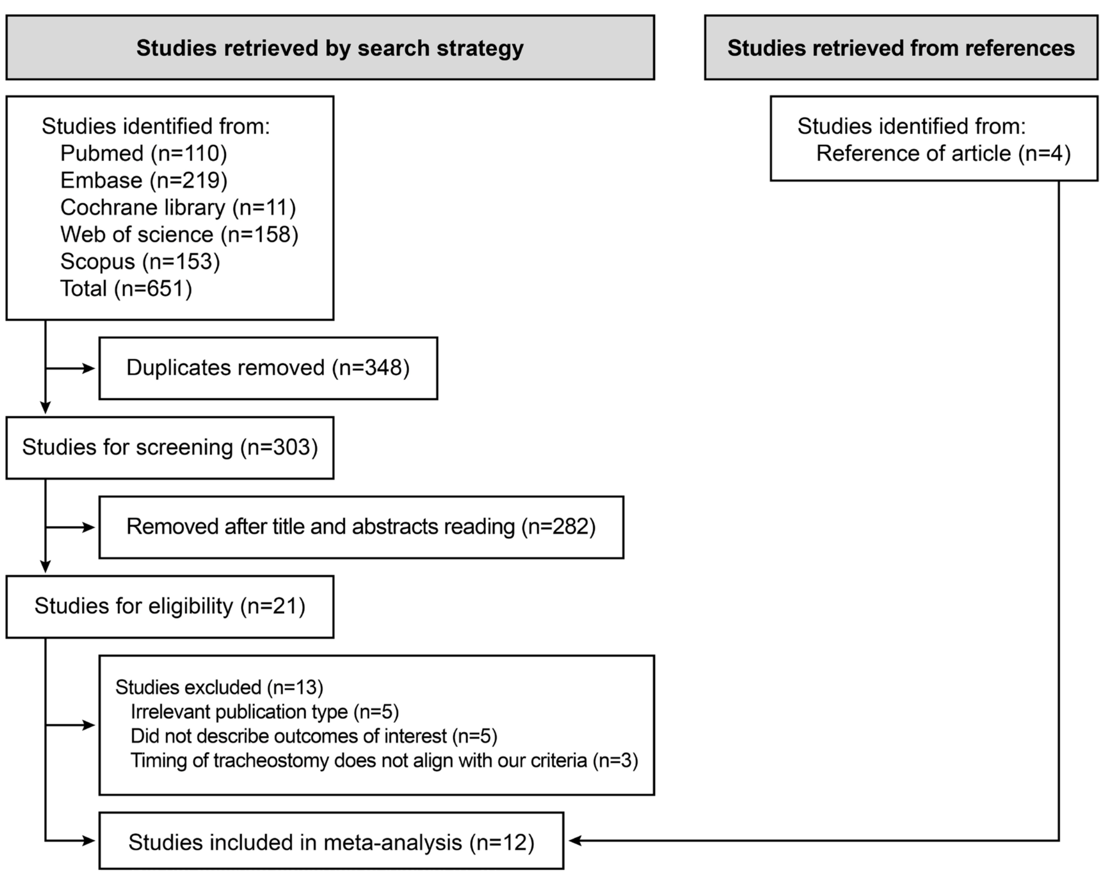


Figure 1 Flow diagram for study inclusion in the meta-analysis.

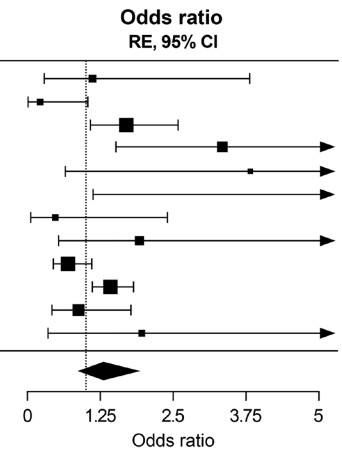
days. Detailed information can be found in online supplemental tables 4 and 5.

Overall mortality and subgroup analysis between early and late tracheostomy

A total of 1426 patients (41.1%) underwent ET, whereas 2039 patients (58.8%) underwent LT, according to the timing defined in each individual study, with a total of 3456 patients analysed. The overall mortality rate was 27.4% (n=951/3,465), and there were no significant differences in short-term mortality between the ET and LT groups (29.1% vs 26.3%, OR 1.30, 95% CI 0.89–1.90, I^2=60.65%, p=0.003) (figure 2). Furthermore, when observing the funnel plot, the symmetry of overall

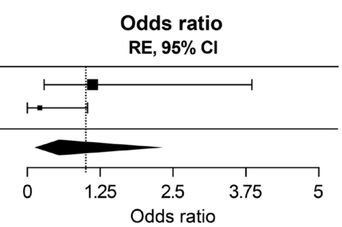
Study Overall		Early tracheostomy Event	Total	Percent	Late tracheostomy Event	Total	Percent	Weight	Odds ratio RE, 95% CI
Hansson et al	2022	6	56	10.7%	6	61	9.8%	6.35%	1.10 [0.33, 3.63]
Livneh et al	2021	8	19	42.1%	14	19	73.7%	5.31%	0.26 [0.07, 1.02]
Vuu et al	2023	67	150	44.7%	81	245	33.1%	14.25%	1.63 [1.08, 2.48]
Flinspach et al	2022	43	61	70.5%	24	56	42.9%	10.14%	3.19 [1.48, 6.83]
Evrard et al	2021	3	10	30.0%	4	38	10.5%	3.84%	3.64 [0.66, 20.01]
Volo et al	2021	6	9	66.7%	3	14	21.4%	3.27%	7.33 [1.11, 48.26]
Avilés-Jurado et al	2021	4	32	12.5%	4	18	22.2%	4.53%	0.50 [0.11, 2.30]
Chandran et al	2022	23	32	71.9%	11	19	57.9%	6.36%	1.86 [0.56, 6.13]
Shreckengost et al	2022	42	132	36.4%	164	417	43.4%	14.28%	0.72 [0.48, 1.09]
Navaratnam et al	2022	194	851	22.8%	162	926	17.5%	16.19%	1.39 [1.10, 1.76]
Bui et al	2023	16	50	32.0%	59	169	34.9%	11.16%	0.88 [0.45, 1.72]
Takhar et al	2020	3	24	12.5%	4	57	7.0%	4.31%	1.89 [0.39, 9.19]
Total		**415**	**1426**	**29.1%**	**536**	**2039**	**26.3%**	**100%**	**1.30 [0.89, 1.90]**

I^2 (total heterogeneity / total variability) = 60.65%
H^2 (total variability / sampling variability) = 2.54
Test for heterogeneity: Q (df=11) = 27.954, *p*=0.003



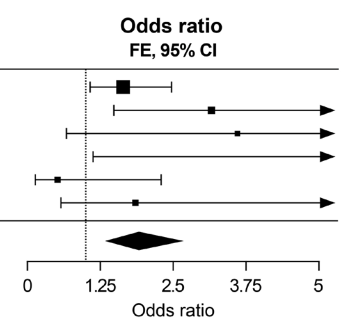
Subgroup 7 days		Early tracheostomy Event	Total	Percent	Late tracheostomy Event	Total	Percent	Weight	Odds ratio RE, 95% CI
Hansson et al	2022	6	56	10.7%	6	61	9.8%	52.78%	1.10 [0.33, 3.63]
Livneh et al	2021	8	19	42.1%	14	19	73.7%	47.22%	0.26 [0.07, 1.02]
Total		**14**	**75**	**18.7%**	**20**	**80**	**25.0%**	**100%**	**0.56 [0.14, 2.28]**

I^2 (total heterogeneity / total variability) = 58.78%
H^2 (total variability / sampling variability) = 2.43
Test for heterogeneity: Q (df=1) = 2.426, *p*=0.119



Subgroup 10 days		Early tracheostomy Event	Total	Percent	Late tracheostomy Event	Total	Percent	Weight	Odds ratio FE, 95% CI
Vuu et al	2023	67	150	44.7%	81	245	33.1%	62.27%	1.63 [1.08, 2.48]
Flinspach et al	2022	43	61	70.5%	24	56	42.9%	18.64%	3.19 [1.48, 6.83]
Evrard et al	2021	3	10	30.0%	4	38	10.5%	3.74%	3.64 [0.66, 20.01]
Volo et al	2021	6	9	66.7%	3	14	21.4%	3.06%	7.33 [1.11, 48.26]
Avilés-Jurado et al	2021	4	32	12.5%	4	18	22.2%	4.66%	0.50 (0.11, 2.30]
Chandran et al	2022	23	32	71.9%	11	19	57.9%	7.63%	1.86 [0.56, 6.13]
Total		**146**	**294**	**49.7%**	**127**	**390**	**32.6%**	**100%**	**1.91 [1.37, 2.65]**

I^2 (total heterogeneity / total variability) = 35.31%
H^2 (total variability / sampling variability) = 1.55
Test for heterogeneity: Q (df=1) = 7.729, *p*=0.172



Subgroup 14 days		Early tracheostomy Event	Total	Percent	Late tracheostomy Event	Total	Percent	Weight	Odds ratio RE, 95% CI
Shreckengost et al	2022	42	132	36.4%	164	417	43.4%	31.97%	0.72 [0.48, 1.09]
Navaratnam et al	2022	194	851	22.8%	162	926	17.5%	40.94%	1.39 [1.10, 1.76]
Bui et al	2023	16	50	32.0%	59	169	34.9%	21.05%	0.88 [0.45, 1.72]
Takhar et al	2020	3	24	12.5%	4	57	7.0%	6.03%	1.89 [0.39, 9.19]
Total		**255**	**1057**	**24.1%**	**389**	**1569**	**24.8%**	**100%**	**1.04 [0.69, 1.58]**

I^2 (total heterogeneity / total variability) = 64.47%
H^2 (total variability / sampling variability) = 2.81
Test for heterogeneity: Q (df=3) = 8.444, *p*=0.038

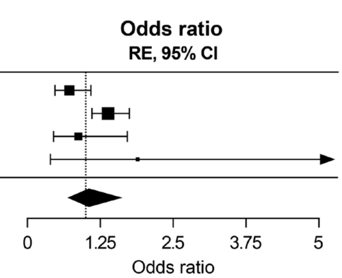


Figure 2 Forest plot of overall mortality and subgroup analysis between early and late tracheostomy in COVID-19 patients. The forest plot illustrates ORs calculated using the Mantel–Haenszel method, with heterogeneity assessed through the I^2 statistic (cut-off at 50%) and the application of a random- or fixed-effects model. In the overall analysis, the terms 'early' and 'late' tracheostomy are used based on the definitions provided in each individual study. For the subgroup analysis, 'early' and 'late' tracheostomy are categorised according to the cut-off points (≤7 days, ≤10 days and ≤14 days) defined in the present study. FE, fixed effect; RE, random effect.

Kim BK, *et al. BMJ Open* 2024;**14**:e084405. doi:10.1136/bmjopen-2024-084405

short-term mortality suggested a low probability of publication bias (online supplemental figure 1).

In the subgroup analysis, according to the 10-day criterion, mortality rates were 49.7% (n=146/294) for ET and 32.6% (n=127/390) for LT, showing a statistically significant difference (OR 1.91, 95% CI 1.37–2.65, I^2=35.31%, p=0.172). However, according to the 7-day and 14-day criteria, there was no difference in mortality rate (ET 18.7% (n=14/75) vs LT 25.0% (n=20/80); ET 24.1% (n=255/1,057) vs LT 24.8% (n=389/1,569), respectively) and in OR and 95% CI between the two groups (OR 0.56, 95% CI 0.14 to 2.28, I^2=58.78%, p=0.119; OR 1.04, 95% CI 0.69–1.58, I^2=64.47%, p=0.038, respectively) (figure 2).

Secondary outcome comparison between early and late tracheostomy

A total of eight studies provided data on the duration of mechanical ventilation. In the ET group, comprising 463 individuals, mechanical ventilation was applied for an average of 17.3 days (SD±1.5 days), whereas in the LT group, consisting of 1019 individuals, mechanical ventilation was applied for an average of 24.4 days (SD±2.9 days). The difference in mechanical ventilation duration between the two groups was −7.35 days (95% CI −11.63 to −3.08), indicating a significantly longer duration in the LT group (I^2=91.71%, p<0.001).

Data on the length of stay in the ICU were available in five studies. In the ET group of 231 individuals, the average stay in the ICU was 18.5 days (SD±2.0 days), whereas the LT group, which included 587 individuals, had an average stay in the ICU of 29.9 days (SD±3.9 days). The difference in the length of stay in the ICU between the two groups was −11.24 days (95% CI −18.50 to −3.97), and the LT group showed a significantly longer stay in the ICU (I^2=89.86%, p<0.001).

Hospital days were reported in four studies. In the ET group of 316 individuals, the average hospital stay was 33.6 days (SD±4.4 days), whereas the LT group, consisting of 757 individuals, had an average hospital stay of 43.2 days (SD±5.5 days). The difference in in-hospital stay between the two groups was −9.72 days (95% CI −24.89 to 5.44), indicating a trend of longer hospitalisation in the LT group, which was not statistically significant (I^2=93.11%, p<0.001) (figure 3).

DISCUSSION

This meta-analysis, which involved 3465 patients with COVID-19 from 12 studies, compared short-term mortality between ET and LT. In general, no significant differences were found in short-term mortality between ET and LT. However, in the subgroup analysis, on the 10-day criterion, ET showed significantly higher short-term mortality compared with LT, whereas there were no statistically significant differences on the 7-day and 14-day criteria. These results suggest that the timing of the tracheostomy may influence short-term mortality in patients with COVID-19, providing potential insight for future clinical decisions. Furthermore, the ET group had shorter durations of mechanical ventilation and stays in the ICU compared with the LT, with a trend towards shorter hospital stays in the ET group.

Mechanical ventilation plays a crucial role in the treatment of respiratory failure by reducing respiratory muscle workload and improving oxygenation.[27] However, as the duration of mechanical ventilation increases, it can lead to complications such as laryngeal damage, sinusitis and pneumonia due to prolonged intubation.[28 29] Tracheostomy serves as an alternative to prolonged intubation, offering advantages such as increased patient comfort and reduced resistance of the airways, making oral care easier.[30] Additionally, in clinical practice, the greatest advantage is that tracheostomy facilitates weaning even in patients who do not meet all extubation criteria. However, tracheostomy is associated with short- and long-term complications such as bleeding, stoma infection, stenosis, tracheomalacia and fistula, leading to the ongoing debate on the appropriate timing for this procedure, and a definitive consensus has not yet been reached.[6 7]

Patients with COVID-19 typically present with mild upper respiratory symptoms,[1] but within 8 days, approximately 42% of patients progress to acute respiratory distress syndrome, which requires mechanical ventilation.[31 32] Consequently, in the era of COVID-19, the importance of tracheostomy has become more pronounced. Early guidelines emphasised delayed tracheostomy due to the high risk of transmission to healthcare providers through aerosols generated during the procedure.[8–10] However, with an improved understanding of COVID-19 and the development of treatments that improve patient survival, recent studies suggest that early percutaneous tracheotomy in COVID-19 patients carries a low transmission risk to healthcare personnel,[33] leading to renewed discussion about the appropriate timing for tracheostomy.

Interestingly, a multicentre study conducted in Switzerland found that more than one-third of tracheostomies are performed during the second week of endotracheal intubation. However, the timing of the tracheostomy varies considerably, ranging from within the first week to the third week or even longer.[34] Furthermore, even previous guidelines related to tracheostomy have different definitions for 'early' tracheostomy,[35–37] and there is no clear consensus.[38] It is not yet clear whether discrepancies influenced outcomes, as previous studies have reported that tracheostomy can reduce the incidence of pneumonia, shorten the duration of mechanical ventilation, decrease the sedation time, lower mortality and lead to a shorter ICU stay.[39 40] However, some studies have shown contrasting results, contributing to the lack of a definitive conclusion.[41 42]

Chong and Tan conducted a comparative analysis of clinical outcomes between ET and LT in patients with COVID-19 from January 2020 to December 2021.[11] They included a total of 12 studies involving 2222 patients. Among these patients, 34.5% underwent ET, and there was no significant difference in the mortality rate between

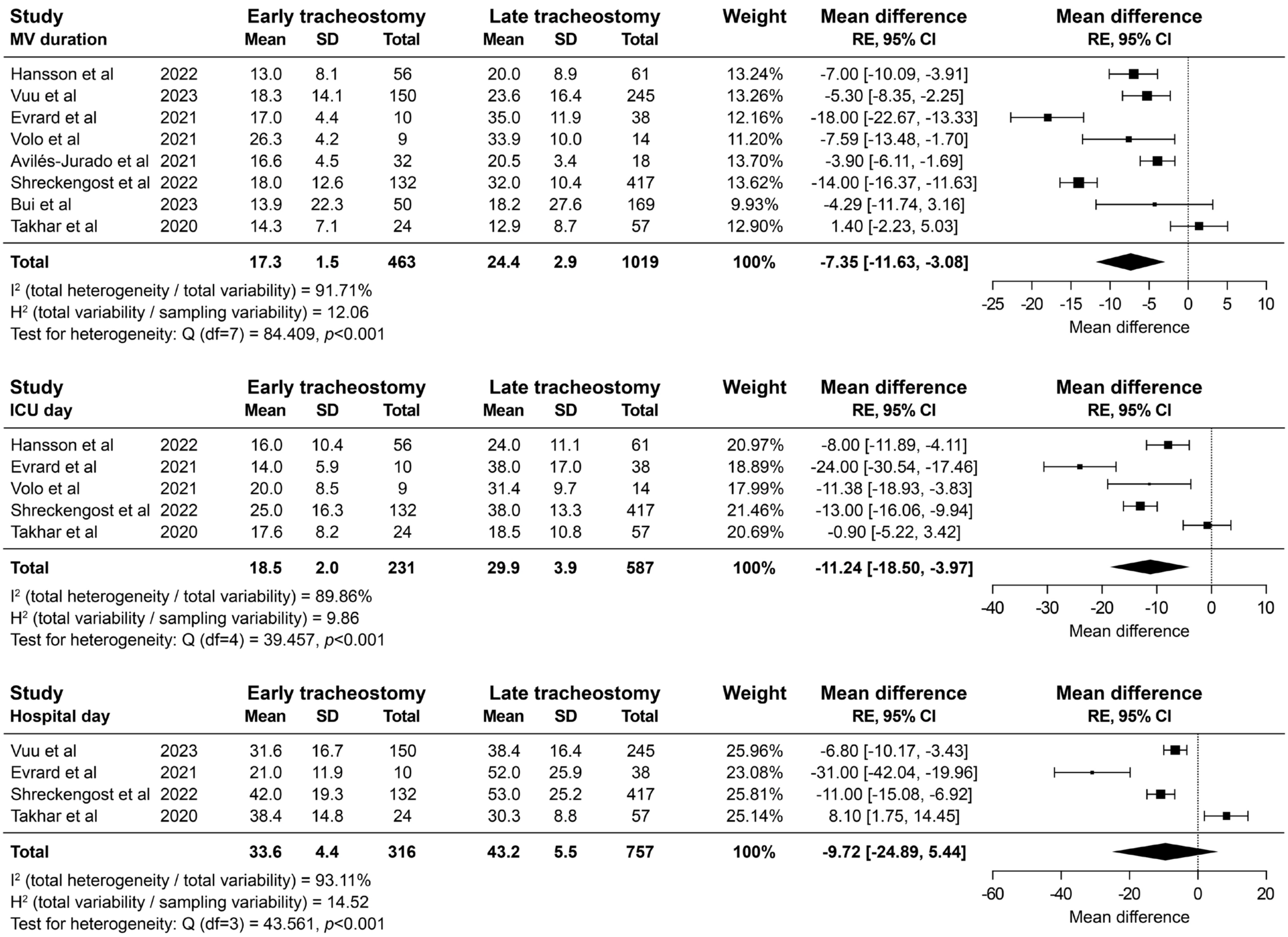


Figure 3 Forest plot comparing mean differences in duration of mechanical ventilation, length of ICU stays and hospital days between early and late tracheostomy in COVID-19 patients. Weighted mean differences were used for continuous outcomes, with a 95% CI. Heterogeneity was assessed using the I^2 statistic, applying a random-effects model for significant heterogeneity (I^2 ≥50%). ICU, intensive care unit; MV, mechanical ventilation; RE, random effect.

the two groups (32.9% vs 33.1%; OR 1.00; p=0.98). Similarly, Ji *et al* reviewed the effects of ET on 2371 patients with COVID-19 in 14 studies from 1 December 2019 to 24 August 2021.[12] Among these patients, 39.6% underwent ET, and there was no significant difference in the mortality rate between the two groups (32.1% vs 29.3%, OR 1.09, p=0.59). Both studies, as in our study, did not identify a significant difference in mortality between the general ET and LT groups. Interestingly, Chong and Tan's study, as in our study, conducted subgroup analyses with a cut-off of 10 and 14 days. However, neither group demonstrated a mortality advantage. A plausible reason for this could be inferred from the selection of studies included in their analysis, whereby mortality at 3 months was included without distinction,[43] and studies that defined the ET group as up to 7–10 days were also incorporated.[44] Such subtle differences could explain the observed variations compared with those in our study.

Chong and Tan reported a shorter duration of mechanical ventilation in the ET group (20.5 days vs 28.9 days, p<0.001) and also a shorter stay in the ICU in the ET group (23.2 days vs 30.5 days, p<0.001).[11] Similarly, Ji *et al* also consistently found a shorter duration of mechanical ventilation of 9.08 days (95% CI (−10.91 to −7.26), p<0.001) and a shorter stay in the ICU of 9.41 days (95% CI (−12.36 to −6.46), p<0.001) in the ET group.[12] This consistent pattern in all studies, including our own, suggests a significant association between the time of the tracheostomy and the duration of mechanical ventilation and ICU stay.

In the present study, there was no significant difference in mortality at other time points; however, when tracheostomy was performed around the 10-day mark, the group that received tracheostomy within 10 days showed higher mortality. The results suggest that subtle differences in the timing of tracheostomy may influence short-term mortality in COVID-19 patients, and the potential mechanisms are as follows. First, patients in the within-10-day group may have been in a more critical condition or deteriorated to the point where tracheostomy was needed urgently. Second, in COVID-19 patients, excessive inflammatory responses such as cytokine storms may occur,[45] and tracheostomy could exacerbate this inflammatory response, adversely affecting patient outcomes.

Third, tracheostomy performed within 10 days may carry risks of various complications, including stomal infection, bleeding and fistula formation,[5] which could have contributed to increased mortality. Lastly, tracheostomy is an invasive procedure that may impose psychological stress on the patient,[46] potentially leading to worsening of their condition. Further research is required to explore these mechanisms in greater depth, verify the proposed pathways, and develop more tailored strategies for determining the optimal timing of tracheostomy in COVID-19 and other critical care settings.

The strengths of our meta-analysis lie in the use of high-quality studies with stringent inclusion and exclusion criteria to assess clinical outcomes in patients undergoing ET and LT during the COVID-19 pandemic. Furthermore, we applied various criteria to systematically classify ET, improving the clarity of its impact on clinical outcomes. However, our study also has a few limitations. First, all the studies included in the meta-analysis were based on data from an observational study, which poses potential confounding factors. Ideally, it would be preferable to evaluate randomised controlled trials, but practical constraints make this challenging under the conditions of the COVID-19 pandemic. As a result, secondary outcomes would ideally be evaluated excluding mortality, but this was limited in our study. Future research should address these factors to provide more precise evaluations. Second, there is considerable heterogeneity in the criteria and definitions used among the included studies, which could limit the consistency of the results. To address this, we conducted the analysis based on a clear definition of mortality and introduced new subgroup definitions for ET and LT in an effort to mitigate this limitation. However, individual participant data meta-analysis, which is the recommended standard for evaluating subgroup effects, was not used in this study due to limited access to individual data. Therefore, caution is required when interpreting the results. Third, although our goal was to include the most recent studies, most of the research was conducted during the early stages of the COVID-19 pandemic, failing to capture important advances in patient treatment. There is uncertainty about how the results might change with future outbreaks or variants. Fourth, by excluding studies in languages other than English, there is a limitation in generalising our meta-analysis results to low- and middle-income countries. Fifth, achieving perfect control over factors such as drugs used and tracheostomy methods (surgical or percutaneous) in the included studies was challenging. Finally, we focused primarily on short-term mortality, and the insufficient information regarding long-term results warrants caution when interpreting the results.

In conclusion, tracheostomy performed at 10 days had a possible association with differences in short-term mortality; however, no significant differences were observed in short-term mortality between ET and LT, as defined in individual studies, or at the 7-day and 14-day benchmarks. The findings suggest that subtle timing differences may affect short-term outcomes in COVID-19 patients, underscoring the importance of determining the optimal timing and establishing a consistent definition for early timing. Taking into account the overall longer duration of mechanical ventilation and stay in the ICU in the LT group, efforts to identify the optimal time to effectively reduce the cost of mortality remain crucial and necessary. This emphasises the need for additional research that can contribute to the development of future treatment strategies and clinical decision-making.

Acknowledgements We would like to express our sincere gratitude to Eun-Ji Kang for her invaluable assistance in developing the search strategy and conducting the systematic analysis for the meta-analysis, and we would like to thank Editage (www.editage.co.kr) for English language editing.

Contributors BKK and CYK: conception and design of the study; selection of studies and data extraction. HC: acquisition and analysis of data. BKK and HC: writing and revision of the manuscript. All authors: read and approved the final version of the article. CYK acted as the guarantor for this study.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, conduct, reporting or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants but an Ethics Committee(s) or Institutional Board(s) exempted this study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information. Data generated or analysed during this study are included in this published article.

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