Supplementary Appendix

The Timing Dilemma: A Systematic Review and Meta-analysis of Short-Term Mortality in Patients With COVID-19 Undergoing Tracheostomy With Varied Definitions of Early, Including 7, 10, and 14 Days

Beong Ki Kim, MD; Hangseok Choi, PhD; and Chi Young Kim, MD, PhD

Table of Contents

Page

Supplementary Table 1. PRISMA 2020 checklist……..2

Supplementary Table 2. Detailed search strategy of individual databases ……..5

Supplementary Table 3. Results of quality assessment by the Newcastle–Ottawa Scale ……..8

Supplementary Table 4. Clinical characteristics of studies included in a systematic review……9

Supplementary Table 5. Categorisation of the study and baseline characteristics ……11

Supplementary Figure 1. Funnel plot for overall short-term mortality……12

Supplementary Table 1. PRISMA 2020 checklist

Section and topic	Item #	Checklist item	Location where the item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	N/A
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 6
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Pages 7-8
Information sources	6	Specify all databases, registers, websites, organisations, reference lists, and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 7, Figure 1
Search strategy	7	Present the full search strategies for all databases, registers, and websites, including any filters and limits used.	Supp Table 2
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 7
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 7
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 7
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Pages 7-8
Study risk of bias assessment	11	Specify the methods used to assess the risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 9
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 9
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 9
	13c	Describe any methods used to tabulate or visually display the results of individual studies and syntheses.	Table 1
	13d	Describe any methods used to synthesise results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 9

Section and topic	Item #	Checklist item	Location where the item is reported
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page9, Table 2
	13f	Describe any sensitivity analyses conducted to assess the robustness of the synthesised results.	Figure 2
Reporting bias assessment	14	Describe any methods used to assess the risk of bias due to missing results in a synthesis (arising from reporting biases).	Supp figure 1
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Figure 2
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Pages 9-10, Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Pages 9-10, Figure 1
Study characteristics	17	Cite each included study and present its characteristics.	Table 1
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supp. Table 3
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table 1, Figure 2
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 10
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Figure 2
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 10
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesised results.	Page 10
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	Page 10
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Pages 10-11
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Pages 11-12
	23b	Discuss any limitations of the evidence included in the review.	Page 14
	23c	Discuss any limitations of the review processes used.	Page 14
	23d	Discuss the implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and	24a	Provide registration information for the review, including the register name and registration number, or state that the review was not registered.	

Section and topic	Item #	Checklist item	Location where the item is reported
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 7
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 7
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 15
Competing interests	26	Declare any competing interests of review authors.	Page 15
Availability of data, code, and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	N/A

From: Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71
For more information, visit: http://www.prisma-statement.org/

Supplementary Table 2. Detailed search strategy of individual databases

Databases	**No.**	**Search Query**	**Search Results**
PubMed	#1	Tracheostomy[mh] OR tracheostom*[tw] OR tracheotom*[tw]	30,084
	#2	early[tw] AND (late[tw] OR delayed[tw])	254,764
	#3	Time Factors[mh] OR early[tw] OR late[tw] OR delayed[tw] OR timing[tw]	3,685,033
	#4	Comparative Study[pt] OR compar*[tw] OR versus[tw] OR group*[tw]	10,392,629
	#5	timing[ti] OR early tracheostom*[ti] OR late tracheostom*[ti] OR delayed tracheostom*[ti]	27,929
	#6	#2 OR (#3 AND #4) OR #5	1,659,421
	#7	#1 AND #6	2,513
	#8	COVID-19[mh] OR SARS-CoV-2[mh] OR COVID-19[tw] OR COVID19[tw] OR severe acute respiratory syndrome coronavirus 2[tw] OR SARS-CoV-2[tw] OR coronavirus disease 2019[tw] OR novel coronavirus[tw] OR 2019-nCoV[tw] OR 2019nCoV[tw] OR coronavirus 2019[tw] OR SARS-CoV2[tw] OR SARS coronavirus 2[tw] OR corona virus disease 2019[tw] OR COVID-2019[tw] OR novel corona virus[tw] OR COVID2019[tw] OR novel 2019 coronavirus[tw] OR nCoV 2019[tw] OR SARS-CoV-19[tw] OR nCoV2019[tw] OR corona virus 2019[tw] OR HCoV-19[tw] OR NCOVID-19[tw] OR 2019 new coronavirus[tw] OR human coronavirus 2019[tw]	377,901
	#9	#7 AND #8	124
	#10	(Animals[mh] NOT Humans[mh]) OR Models, Animal[mh:noexp] OR Disease Models, Animal[mh] OR Animal Experimentation[mh]	5,358,021
	#11	Case Reports[pt] OR case report*[tw] OR case stud*[tw] OR case series[tw] OR case[ti] OR cases[ti]	3,064,578
	#12	English[la]	31,336,147
	#13	#9 NOT #10 NOT #11 AND #12	110
Embase	#1	tracheostomy/exp OR (tracheo$tom*):ti,ab,kw	49,101
	#2	early:ti,ab,kw AND (late OR delayed):ti,ab,kw	338,210
	#3	('time factor'/de OR (early OR late OR delayed OR timing):ti,ab,kw)	3,496,033
	#4	('comparative study'/de OR (compar* OR versus OR group*):ti,ab,kw)	13,044,874
	#5	timing:ti OR ((early OR late OR delayed) NEXT/1 tracheo*tom*):ti	35,008
	#6	#2 OR (#3 AND #4) OR #5	1,685,889
	#7	#1 AND #6	3,873
	#8	('coronavirus disease 2019'/exp OR (COVID-19 OR COVID19 OR 'severe acute respiratory syndrome coronavirus 2' OR SARS-CoV-2 OR 'coronavirus disease 2019' OR 'novel coronavirus' OR 2019-nCoV OR 2019nCoV OR 'coronavirus 2019' OR SARS-CoV2 OR 'SARS coronavirus 2' OR 'corona virus disease 2019' OR COVID-2019 OR 'novel corona virus' OR COVID2019 OR 'novel 2019 coronavirus' OR 'nCoV 2019' OR SARS-CoV-19 OR nCoV2019 OR 'corona virus 2019' OR HCoV-19 OR NCOVID-19 OR '2019 new	445,528

		coronavirus' OR 'human coronavirus 2019'):ti,ab,kw)	
	#9	#7 AND #8	256
	#10	(animal/exp NOT human/exp) OR 'animal model'/exp OR 'animal experiment'/exp OR [animal cell]/lim OR [animal experiment]/lim OR [animal model]/lim OR [animal tissue]/lim	7,161,734
	#11	('case report'/de OR 'case study'/exp OR (case NEXT/1 (report* OR stud* OR series)):ti,ab,kw OR (case OR cases):ti)	3,832,070
	#12	[english]/lim	37,311,026
	#13	#9 NOT #10 NOT #11 AND #12	219
	#1	[mh Tracheostomy] OR (tracheo?tom*):ti,ab,kw	1,690
Cochrane Library	#2	early:ti,ab,kw AND (late OR delayed):ti,ab,kw	17,482
	#3	[mh "Time Factors"] OR (early OR late OR delayed OR timing):ti,ab,kw	261,116
	#4	[mh "Comparative Study"] OR (compar* OR versus OR group*):ti,ab,kw	1,386,488
	#5	timing:ti OR ((early OR late OR delayed) NEXT tracheo*tom*):ti	2,966
	#6	#2 OR (#3 AND #4) OR #5	207,488
	#7	#1 AND #6	346
	#8	[mh "COVID-19"] OR [mh "SARS-CoV-2"] OR ("COVID-19" OR COVID19 OR "severe acute respiratory syndrome coronavirus 2" OR "SARS-CoV-2" OR "coronavirus disease 2019" OR "novel coronavirus" OR "2019-nCoV" OR 2019nCoV OR "coronavirus 2019" OR SARS-CoV2 OR "SARS coronavirus 2" OR "corona virus disease 2019" OR "COVID-2019" OR "novel corona virus" OR COVID2019 OR "novel 2019 coronavirus" OR "nCoV 2019" OR "SARS-CoV-19" OR nCoV2019 OR "corona virus 2019" OR "HCoV-19" OR "NCOVID-19" OR "2019 new coronavirus" OR "human coronavirus 2019"):ti,ab,kw	17,477
	#9	#7 AND #8	11
	#1	TS=(tracheostom* OR tracheotom*)	19,583
Web of Science	#2	TS=(early) AND TS=(late OR delayed)	585,096
	#3	TS=(early OR late OR delayed OR timing)	13,456,156
	#4	TS=(compar* OR versus OR group*)	15,939,532
	#5	TI=(timing) OR TI=((early OR late OR delayed) NEAR/0 tracheo*tom*)	1,173,166
	#6	#2 OR (#3 AND #4) OR #5	5,836,600
	#7	#1 AND #6	3,420
	#8	TS=(COVID-19 OR COVID19 OR "severe acute respiratory syndrome coronavirus 2" OR SARS-CoV-2 OR "coronavirus disease 2019" OR "novel coronavirus" OR 2019-nCoV OR 2019nCoV OR "coronavirus 2019" OR SARS-CoV2 OR "SARS coronavirus 2" OR "corona virus disease 2019" OR COVID-2019 OR "novel corona virus" OR COVID2019 OR "novel 2019 coronavirus" OR "nCoV 2019" OR SARS-CoV-19 OR nCoV2019 OR "corona virus 2019" OR HCoV-19 OR NCOVID-19 OR "2019 new coronavirus" OR "human coronavirus 2019")	470,591
	#9	#7 AND #8	174

	#10	TS=(case NEAR/0 (report* OR stud* OR series)) OR TI=(case OR cases)	2,038,667
	#11	#9 NOT #10	161
	#12	Language restriction	158
	#1	TITLE-ABS-KEY(tracheo?tom*)	34,924
Scopus	#2	TITLE-ABS-KEY(early) AND TITLE-ABS-KEY(late OR delayed)	528,582
	#3	TITLE-ABS-KEY(early OR late OR delayed OR timing)	5,682,642
	#4	TITLE-ABS-KEY(compar* OR versus OR group*)	22,905,832
	#5	TITLE(timing) OR TITLE((early OR late OR delayed) PRE/0 tracheo*tom*)	67,099
	#6	#2 OR (#3 AND #4) OR #5	2,366,929
	#7	#1 AND #6	2,594
	#8	TITLE-ABS-KEY(COVID-19 OR COVID19 OR "severe acute respiratory syndrome coronavirus 2" OR SARS-CoV-2 OR "coronavirus disease 2019" OR "novel coronavirus" OR 2019-nCoV OR 2019nCoV OR "coronavirus 2019" OR SARS-CoV2 OR "SARS coronavirus 2" OR "corona virus disease 2019" OR COVID-2019 OR "novel corona virus" OR COVID2019 OR "novel 2019 coronavirus" OR "nCoV 2019" OR SARS-CoV-19 OR nCoV2019 OR "corona virus 2019" OR HCoV-19 OR NCOVID-19 OR "2019 new coronavirus" OR "human coronavirus 2019")	560,787
	#9	#7 AND #8	175
	#10	TITLE-ABS-KEY(case PRE/0 (report* OR stud* OR series)) OR TITLE(case OR cases)	4,825,604
	#11	#9 AND NOT #10	157
	#12	Language restriction	153

Supplementary Table 3. Results of quality assessment by the Newcastle–Ottawa Scale

Author	**Selection**				**Comparability**	**Outcome**			**Total score**
	A	B	C	D		a	b	c	
Hansson et al.	+	+	+	+	+	+	+	+	8
Livneh et al.	+	+	+	+	++	+	+	-	8
Vuu et al.	+	+	+	+	++	+	+	+	9
Flinspach et al.	+	+	+	+	+	+	+	+	8
Evrard et al.	+	+	+	+	++	+	-	+	8
Volo et al.	+	+	+	+	++	+	-	-	7
Avilés-Jurado et al.	+	+	+	+	++	+	-	-	7
Chandran et al.	+	+	+	+	++	+	+	-	8
Shreckengost et al.	-	-	+	+	+	+	+	+	6
Navaratnam et al.	+	+	+	+	+	+	+	-	7
Bui et al.	+	+	+	+	++	+	-	-	7
Takhar et al.	+	+	+	+	+	+	-	-	6

Selection

A. Representatives of the exposed cohort

B. Selection of the non-exposed cohort

C. Ascertainment of exposure

D. Demonstration that the outcome of interest was not present at the start of the study

Comparability

Comparability of cohorts based on the design or analysis

Outcome

a. Assessment of outcomes

b. Was follow-up long enough for outcomes to occur

c. Adequacy of follow-up of cohorts

Supplementary Table 4. Clinical characteristics of studies included in a systematic review

1st author	Publication year	Design	Outcome	Country	Study periods	Approach	Definition of early	No. of patients	Age	Male
Hansson et al.	2022	Retrospective, multicenter	30-day mortality	Sweden	Mar 14, 2020–Mar 13, 2021	Both	≤7 days	117	66 (18–87)	90 (76.9%)
Livneh et al.	2021	Retrospective, single–center	Unspecified mortality	Israel	Mar 2020–Jan 2021	Open	≤7 days	38	64 (56–72)	33 (86.8%)
Vuu et al.	2023	Retrospective, multicenter	In-patients mortality	USA	Jan 1, 2020–Sep 20, 2020	N/A	≤10 days	395	61.9 ± 12.7	222 (56.2%)
Flinspach et al.	2022	Retrospective, single–center	In-hospital mortality	Germany	Mar 2020–Jun 2021	Percutaneous	≤10 days	117	60.1 ± 13.7	97 (82.9%)
Evrard et al.	2021	Retrospective, multicenter	Unspecified mortality	France	Jan 27, 2020–Mar 18, 2020	Both	≤10 days	48	56 (47–65)	36 (75.0%)
Volo et al.	2021	Retrospective, multicenter	In-hospital mortality	Italy	Feb 22, 2020–Apr 26, 2020	Both	≤10 days	23	69 (42–84)	21 (91.3%)
Avilés-Jurado et al.	2021	Prospective, single–center	Unspecified mortality	Spain	Mar 16, 2020–Apr 10, 2020	Open	≤10 days	50	63.8 ± 9.7	33 (66.0%)
Chandran et al.	2022	Prospective, single–center	30-day mortality	India	Apr 1, 2020–Jan 31, 2021	Open	≤10 days	51	52 (23–83)	32 (62.7%)

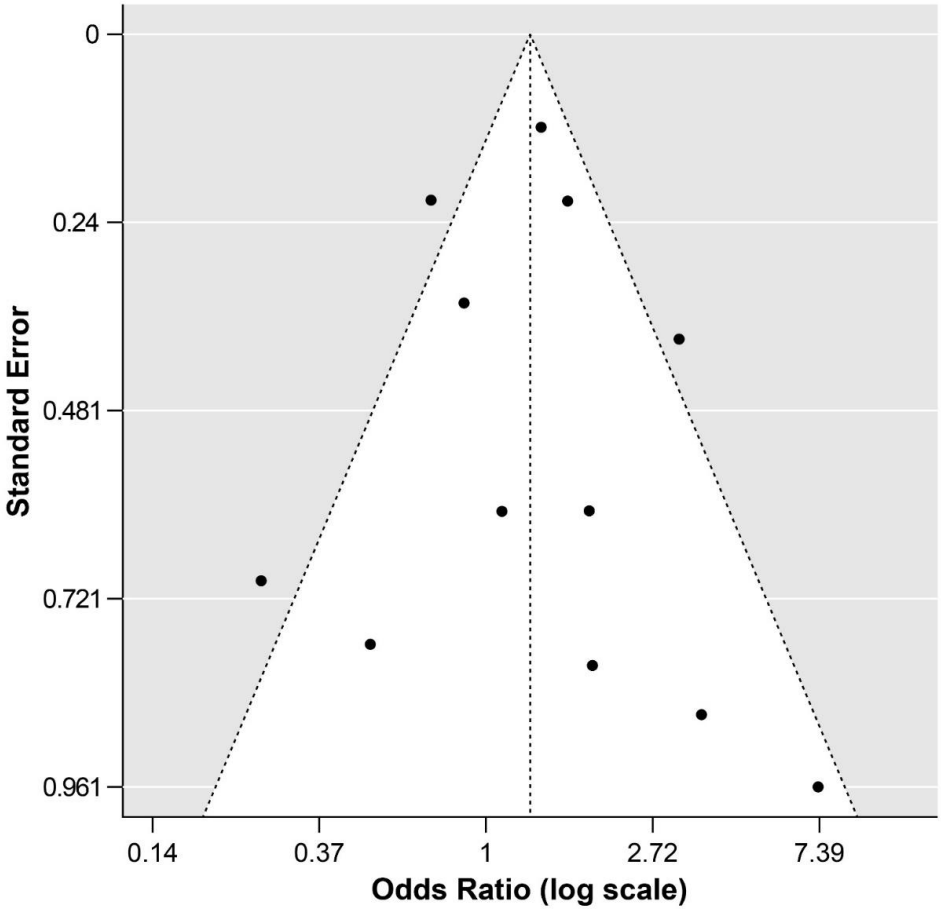
Shreckengost et al.	2022	Retrospective, multicenter	30-day mortality	Global	Mar 1, 2020–Mar 31, 2021	Both	≤14 days	549	N/A		345 (63.8%)
Navaratnam et al.	2022	Retrospective, multicenter	In-hospital mortality	UK	Mar 1, 2020–Oct 31, 2020	N/A	≤14 days	1777	N/A		1528 (70.7%)
Bui et al.	2023	Retrospective, single–center	All-cause mortality	USA	Mar 2020–May 2022	Open	≤14 days	219	N/A		139 (63.5%)
Takhar et al	2021	Prospective, single–center	Unspecified mortality	UK	Mar 21, 2020–May 20, 2020	Both	≤14 days	82	52.9 12.2	±	55 (67.9%)

Categorical data are represented using numbers (percentages), whereas continuous variables are expressed as mean (standard deviation) or median (interquartile range), as reported in each study. Abbreviation: N/A, not applicable; USA, United States of America; UK, United Kingdom

Supplementary Table 5. Categorisation of the study and baseline characteristics

Study and baseline characteristics	**Subcategorisation**	**N (%)**
Publication year	2021	5 (41.7%)
	2022	5 (41.7%)
	2023	2 (16.7%)
Study design	Retrospective	9 (75.0%)
	Prospective	3 (25.0%)
	Single-centre	6 (50.0%)
	Multicentre	6 (50.0%)
Outcome	In-hospital mortality	3 (25.0%)
	30-day mortality	3 (25.0%)
	Unspecified mortality	4 (33.3%)
	All-cause mortality	1 (8.3%)
	In-patient mortality	1 (8.3%)
Continent of Surveyed Country	Europe	6 (50.0%)
	Asia	2 (16.7%)
	North America	1 (8.3%)
	Global	1 (8.3%)
Tracheostomy approach	Both	5 (41.7%)
	Open	4 (33.3%)
	Percutaneous	1 (8.3%)
	N/A	2 (16.7%)
Definition of “early”	≤7 days	2 (16.7%)
	≤10 days	6 (50.0%)
	≤14 days	4 (33.3%)

This data represents a restructured analysis of baseline characteristics of studies included in the current meta-analysis, as provided in Table 1 of the main text, categorised by various parameters. Abbreviation: N/A, not applicable



Supplementary Figure 1. Funnel plot for overall short-term mortality.