Longer prehospitalization and preintubation periods in intubated nonsurvivors and ECMO patients with COVID-19: A systematic review and meta-analysis

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Supplement

Table S1. PRISMA checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	# 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	# 4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	# 4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	# 5-7

Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	# 5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	# 5-6
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	# 5-6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	# 5-6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	# 6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	# 6-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	# 6-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	# 7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of	# 6-7

		consistency (e.g., I^2) for each meta-analysis.	
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	# 6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were prespecified.	# 7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	# 7-8, Fig 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table S2 Fig S1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	# 8-10 Fig 2-5 Fig S2-3
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	# 11-13 Fig 2-5

			Fig S2-3
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Table S3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Fig S3
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	# 10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	# 13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	# 14
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	#14-15

Table S2. Study Quality Assessment Tools (Quality Assessment of Systematic Reviews and Meta-Analyses) from the National Heart, Lung, and Blood Institute (NHLBI)

IMV/ECMO	Study	Study design	Criteria									
			1[a]	2[b]	3[c]	4[d]	5[e]	6[f]	7[g]	8[h]	9[i]	Total points
IMV	Abe et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Argenziano et al.	Case series	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Barrasa et al.	Case series	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Beigmohammadi et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Bhatraju et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	Yes	Yes	6
IMV	Cauchois et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	Yes	Yes	7
IMV	Chen et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
IMV	Christie 3rd et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	NA	Yes	6
IMV	Cummings et al.	Case control	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
IMV	Dai et al.	Case control	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	8
IMV	Dastan et al.	Case control	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9

IMV	De Luca et al.	Case series	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
IMV	Dogan et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	NA	Yes	6
IMV	Elder et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Falces-Romero et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Flikweert et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Gavin et al.	Case series	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Grasselli et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Grein et al.	Case control	Yes	Yes	NR	No	Yes	Yes	Yes	Yes	Yes	7
IMV	Halvatsiotis et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Hernandez-Romieu et al.	Case control	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Kato et al.	Case series	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Ketcham et al.	Case series	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Kewan et al.	Case series	Yes	Yes	Yes	No	Yes	Yes	Yes	NA	Yes	7
IMV	Khullar et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Konopka et al.	Case series	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Krishnan et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8

IMV	Kristinsson et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
IMV	Lê et al.	Case series	Yes	Yes	No	NA	No	Yes	Yes	Yes	Yes	6
IMV	LeBrun et al.	Case series	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Lechien et al.	Case series	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Lee et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
IMV	Liu et al.	Case control	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	8
IMV	Lowe et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
IMV	Maritati et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Morassi et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Morillas et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	Yes	Yes	7
IMV	Navarro-Millán et al.	Case series	Yes	Yes	NR	NA	Yes	Yes	Yes	NA	Yes	6
IMV	Novelli et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Pan et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	NA	Yes	6
IMV	Peng et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	NA	Yes	6
IMV	Plotnikow et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Radnis et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5

IMV	Riker et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Rizo-Téllez et al.	Case control	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Sakr et al.	Case series	Yes	Yes	NR	No	No	Yes	Yes	NA	Yes	5
IMV	Schaefer et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Shen et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	Yes	Yes	7
IMV	Singh et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	Yes	Yes	6
IMV	So et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	NA	Yes	6
IMV	Søvik et al.	Case control	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Stony Brook COVID-19 Research Consortium	Case control	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Wali et al.	Case series	Yes	Yes	NR	No	Yes	Yes	Yes	NA	Yes	6
IMV	Wang et al.	Case control	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
IMV	Wang et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
IMV	Weiskopf et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	Yes	Yes	6
IMV	Wilk et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
IMV	Zhang et al.	Case series	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
IMV	Ziehr et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7

ECMO	Akhtar et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
ECMO	Alnababteh et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Beyls et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
ECMO	Charlton et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
ECMO	Dastan et al.	Case control	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	9
ECMO	Falcoz et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
ECMO	Goursaud et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
ECMO	Grein et al.	Case control	Yes	Yes	NR	No	Yes	Yes	Yes	Yes	Yes	7
ECMO	Guihaire et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	Yes	Yes	6
ECMO	Guo et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
ECMO	Heman-Ackah et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	NA	Yes	5
ECMO	Huette et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
ECMO	Jäckel et al.	Case series	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Jacobs et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Kon et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
ECMO	Le Breton et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6

ECMO	Li et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
ECMO	Liu et al.	Case control	Yes	Yes	NR	Yes	Yes	Yes	Yes	Yes	Yes	8
ECMO	Liu et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Loforte et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
ECMO	Matsunaga et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
ECMO	Miike et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	Yes	Yes	6
ECMO	Mustafa et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
ECMO	Osho et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
ECMO	Ronit et al.	Case series	Yes	Yes	No	NA	No	Yes	Yes	NA	Yes	5
ECMO	Schmidt et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Shih et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
ECMO	Sultan et al.	Case control	Yes	Yes	Yes	NA	No	Yes	Yes	NA	Yes	6
ECMO	Usman et al.	Case control	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
ECMO	Xu et al.	Case series	Yes	Yes	Yes	NA	No	Yes	Yes	Yes	Yes	7
ECMO	Xuan et al.	Case series	Yes	Yes	No	NA	No	Yes	Yes	NA	Yes	5
ECMO	Yang et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8

ECMO	Zayat et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Zeng et al.	Case series	Yes	Yes	NR	NA	No	Yes	Yes	Yes	Yes	6
ECMO	Zeng et al.	Case series	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Zhang et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	8
ECMO	Zhang et al.	Case series	Yes	Yes	NR	Yes	No	Yes	Yes	Yes	Yes	7
ECMO	Zheng et al.	Case control	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	7

*The total score was calculated based on the study quality assessment tools from the NHLBI.

NA, not applicable; NR, not reported

[a]Criterion 1: Was the study question or objective clearly stated?

[b]Criterion 2: Was the study population clearly and fully described, including a case definition?

[c]Criterion 3: Were the cases consecutive?

[d]Criterion 4: Were the subjects comparable?

[e]Criterion 5: Was the intervention clearly described?

[f]Criterion 6: Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants?

[g]Criterion 7: Was the length of follow-up adequate?

[h]Criterion 8: Were the statistical methods well-described?

[i]Criterion 9: Were the results well-described?

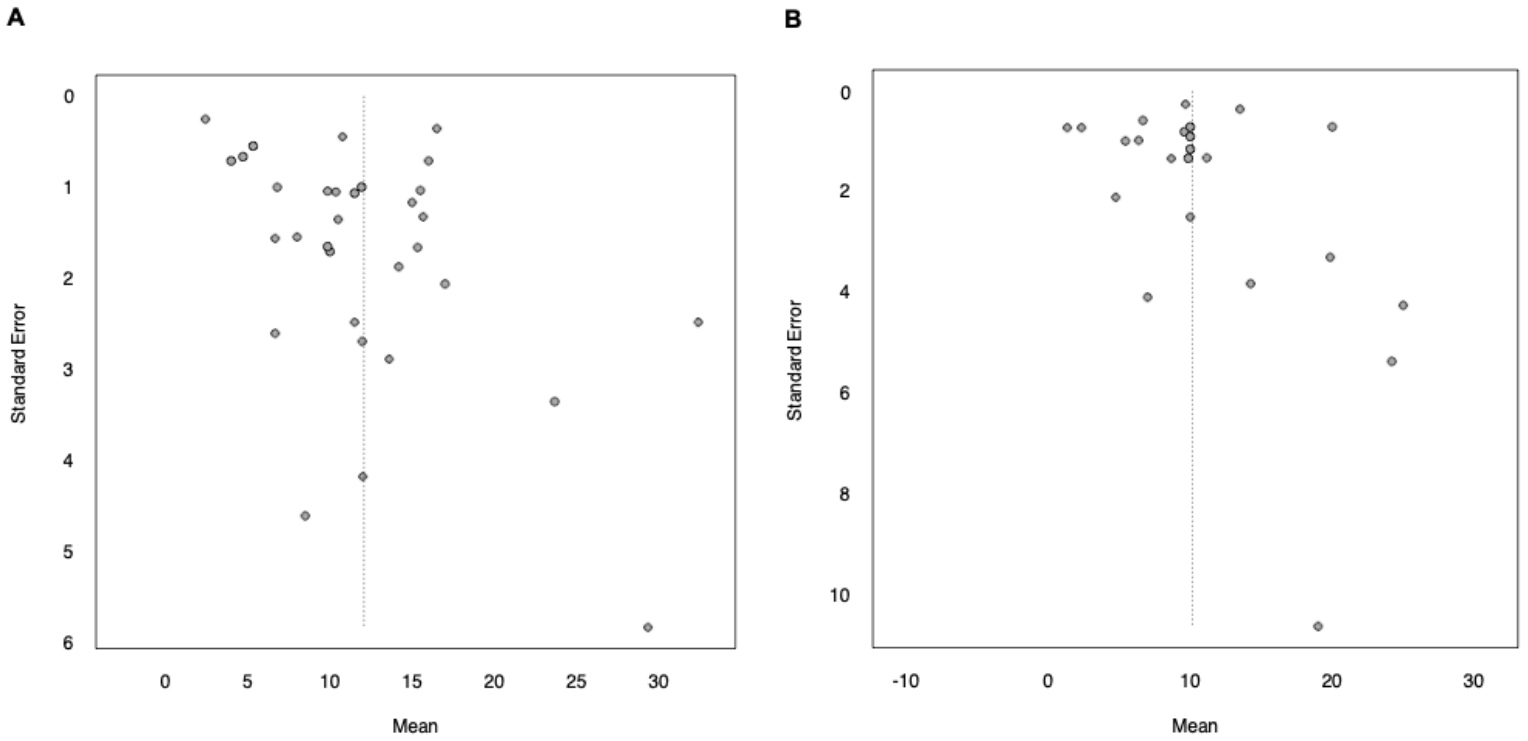

Figure S1. Funnel plot for the intubation period of intubated COVID-19 survivors (A) and the intubation-death period of intubated COVID-19 nonsurvivors (B).

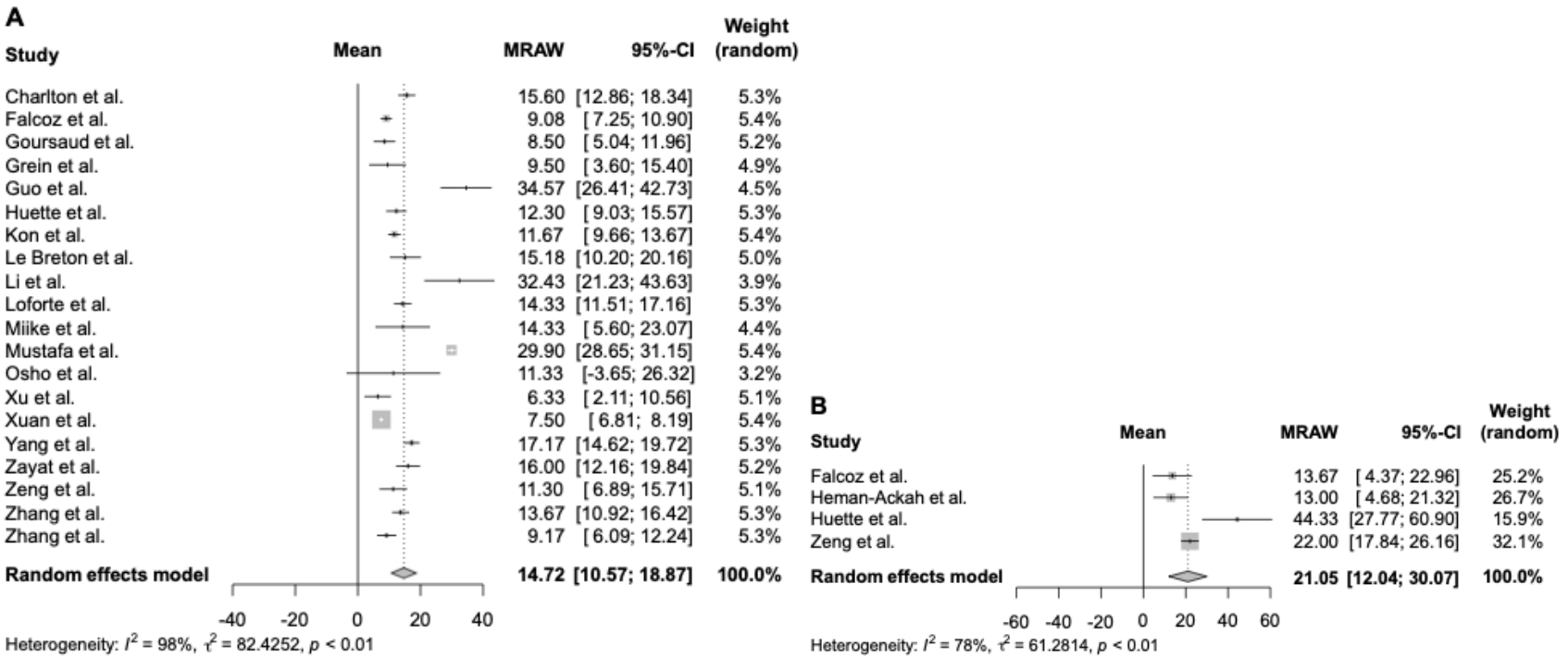

Figure S2. A meta-analysis of the ECMO period (A) and the ECMO-death period (B) was calculated using the random effects model. MRAW: the raw data of mean. 95% CI: 95% confidence interval.

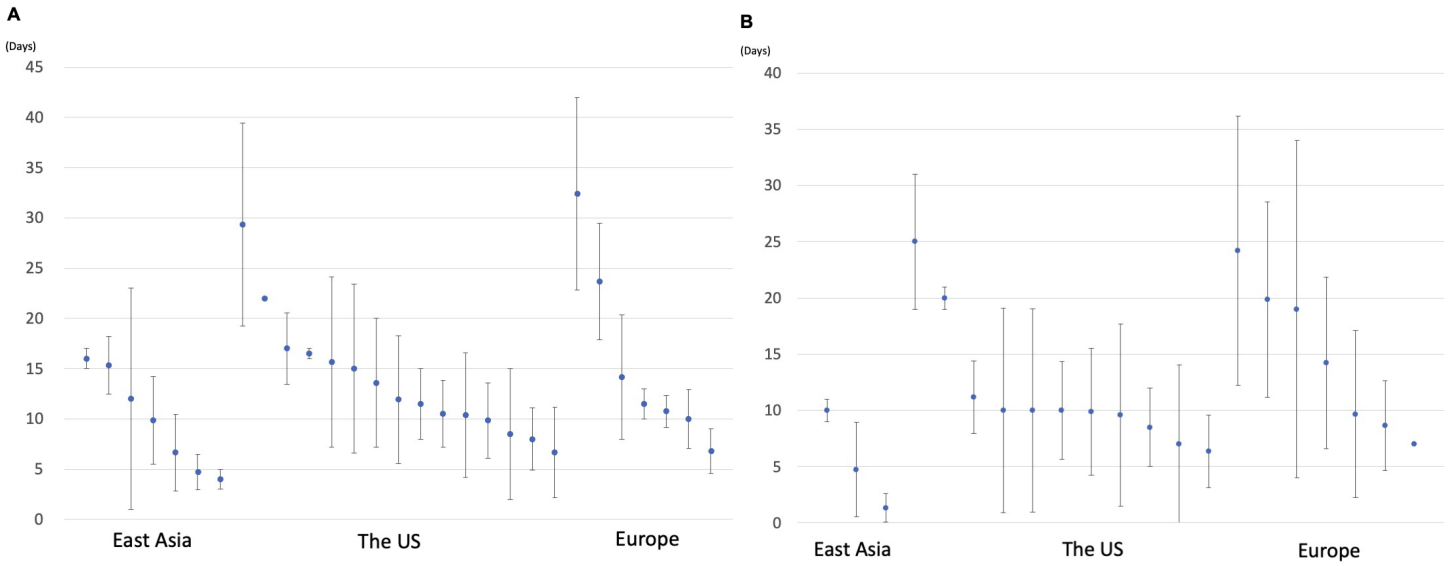

Figure S3. Sensitivity analysis based on regional differences. The mean days and standard deviation (SD) of the intubation period in intubated survivors (**A**) and the intubation-death period in intubated nonsurvivors (**B**) of each study were plotted.

Reference(1–94)

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