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Timing of tracheostomy in acute traumatic spinal cord injury: A systematic review and meta-analysis

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BACKGROUND: Patients with acute traumatic cervical or high thoracic level spinal cord injury (SCI) typically require mechanical ventilation (MV) during their acute admission. Placement of a tracheostomy is preferred when prolonged weaning from MV is anticipated. However, the optimal timing of tracheostomy placement in patients with acute traumatic SCI remains uncertain. We systematically reviewed the literature to determine the effects of early versus late tracheostomy or prolonged intubation in patients with acute traumatic SCI on important clinical outcomes.

METHODS: Six databases were searched from their inception to January 2020. Conference abstracts from relevant proceedings and the gray literature were searched to identify additional studies. Data were obtained by two independent reviewers to ensure accuracy and completeness. The quality of observational studies was evaluated using the Newcastle Ottawa Scale.

RESULTS: Seventeen studies (2,804 patients) met selection criteria, 14 of which were published after 2009. Meta-analysis showed that early tracheostomy was not associated with decreased short-term mortality (risk ratio [RR], 0.84; 95% confidence interval [CI], 0.39–1.79; $p = 0.65$; n = 2,072), but was associated with a reduction in MV duration (mean difference [MD], 13.1 days; 95% CI, –6.70 to –21.11; $p = 0.0002$; n = 855), intensive care unit length of stay (MD, –10.20 days; 95% CI, –4.66 to –15.74; $p = 0.0003$; n = 855), and hospital length of stay (MD, –7.39 days; 95% CI, –3.74 to –11.03; $p < 0.0001$; n = 423). Early tracheostomy was also associated with a decreased incidence of ventilator-associated pneumonia and tracheostomy-related complications (RR, 0.86; 95% CI, 0.75–0.98; $p = 0.02$; n = 2,043 and RR, 0.64; 95% CI, 0.48–0.84; $p = 0.001$; n = 812 respectively). The majority of studies ranked as good methodologic quality on the Newcastle Ottawa Scale.

CONCLUSION: Early tracheostomy in patients with acute traumatic SCI may reduce duration of mechanical entilation, length of intensive care unit stay, and length of hospital stay. Current studies highlight the lack of high-level evidence to guide the optimal timing of tracheostomy in acute traumatic SCI. Future research should seek to understand whether early tracheostomy improves patient comfort, decreases duration of sedation, and improves long-term outcomes. (*J Trauma Acute Care Surg.* 2022;92: 223–231. Copyright © 2021 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.)

LEVEL OF EVIDENCE: Systematic Review, level III.

KEY WORDS: Acute spinal cord injury; traumatic spinal cord injury; critical care; tracheostomy timing; mechanical ventilation.

Patients with acute traumatic spinal cord injury (SCI) at the cervical or high thoracic level typically experience severe respiratory complications, resulting in the need for mechanical ventilation (MV).[1–3] In cervical SCI, patients have significantly reduced vital capacity and ventilatory reserve because of interruption of neural pathways to the diaphragm and respiratory muscles of the chest and abdomen, leading to a restrictive ventilatory impairment, while the loss of sympathetic innervation results in increased bronchial tone and mucous secretions.[4,5] Many patients, therefore, require endotracheal intubation and initiation of MV. In thoracic SCI, respiratory insufficiency and MV are more commonly related to direct chest trauma and pulmonary injury.[1,6]

Tracheostomy is typically preferred in situations where prolonged MV is required or weaning from MV is anticipated to be prolonged.[2,7] Tracheostomy may facilitate weaning by reducing airway resistance and may prevent complications from prolonged orotracheal intubation, such as ulceration, granulation tissue formation, subglottic edema, and tracheal and laryngeal stenosis.[8–10] Other posited benefits of tracheostomy include improved patient comfort, swallowing, early phonation, and ease of access for tracheal suctioning to manage respiratory secretions.[2,11,12] It is, however, an invasive procedure with the potential for multiple complications.[13–15] The decision to convert an endotracheal intubation to a tracheostomy, therefore, requires anticipation of the expected duration MV and a careful assessment of the benefits and risks of the procedure.

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For patients with acute traumatic SCI, there is no consensus on the optimal time to perform a tracheostomy.[16] Clinicians may wait in the hope that the patient will be extubated or may delay the placement of a tracheostomy following anterior cervical spine fixation.[17] Guidelines for the respiratory management after SCI were published in 2005; however, these recommendations were not specific to the acute care setting, focused mainly on evidence from noncritically ill SCI patients, and did not provide recommendations on the optimal timing of tracheostomy.[18] Although individual studies have investigated whether early (within 7 d of intubation) or late (after 7 d of intubation) tracheostomy improves outcomes, including mortality, ventilator-associated pneumonia, and length of hospital and intensive care unit (ICU) stay, the results remain inconclusive. In addition, whether more patient-orientated outcomes, such as the ability to speak or maintain oral intake, are improved by early tracheostomy remain unknown. We performed a systematic review to evaluate and synthesize evidence regarding the timing of tracheostomy in patients with acute traumatic SCI.

METHODS

This systematic review was performed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses and guided by an a priori protocol registered with PROSPERO (ID: CRD42020162488).[19]

Search Strategy

Studies were identified by searching MEDLINE, EMBASE, CINAHL, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) from their inception to January 2020, with no limitations on time or language of publication. An experienced health sciences librarian assisted in development of the strategy (Supplemental Appendix 1, http://links.lww.com/TA/C132). The reference lists of retrieved articles were investigated to identify additional studies. Abstracts were searched from the conference proceedings listed in Supplemental Appendix 1, http://links.lww.com/TA/C132, within the past 10 years, and the gray literature was searched using Google Scholar. A sensitivity analysis was performed using 10 preidentified studies (Supplemental Appendix 2, http://links.lww.com/TA/C132).

Study Selection

Studies were initially screened for eligibility by title, keywords, and abstract using the Covidence software (Melbourne, Australia) by the primary reviewer (S.J.F.).[20] Studies passing the initial screen were subsequently reviewed in full by two reviewers (S.J.F., S.T.) to confirm eligibility for inclusion. Studies included (i) randomized controlled trials (RCTs) that compared either the timing of tracheostomy, or tracheostomy and prolonged intubation, in patients with acute SCI, and (ii) cohort studies that included acute SCI patients receiving early tracheostomy or late tracheostomy/prolonged intubation while admitted in the ICU. There were no exclusion criteria based on the level of SCI used in the studies. Differences between the two reviewers (S.J.F. and S.T.) regarding eligible studies were resolved in consultation with a third reviewer (V.A.M.).

Data Abstraction and Quality Assessment

Data were independently extracted from included studies by two reviewers (S.J.F and S.T.) using a standardized data collection form (Supplemental Appendix 3, http://links.lww.com/TA/C132). The Newcastle-Ottawa Scale (NOS) was used to assess the quality of included studies (Supplemental Appendix 4, http://links.lww.com/TA/C132).[21] All of the studies, with the exception of 1 case series, were cohort studies and thus the NOS was used as it is one of two tools recommended by the Cochrane Handbook to assess the quality of nonrandomized studies of interventions (Supplemental Appendix 5, 6, http://links.lww.com/TA/C132).[22]

Outcomes

The primary outcome was short-term mortality, defined as mortality in the ICU or hospital. Secondary outcomes included long-term mortality (defined as death at hospital discharge, 6 months or 1–2 years following the acute illness), duration of MV, ICU length of stay (LOS), hospital LOS, duration of sedation, incidence of ventilator-associated pneumonia (VAP), rate of tracheostomy procedures performed and tracheostomy-associated complications (airway stenosis, bleeding, stoma site infection, tracheoesophageal fistula, tracheal granuloma, mediastinal abscess, vocal cord dysfunction and dysphonia), ICU-associated complications (deep vein thrombosis [DVT], pulmonary embolus, decubitus ulcers), long-term benefits (quality of life [QOL] measures including Life Satisfaction Index, Beck Depression Inventory), time to swallowing and phonation, as well as time to decannulation (Supplemental Appendix 7, http://links.lww.com/TA/C132). Analyses of the following subgroups were planned: spinal cord damage (level of injury and American Spinal Injury Association [ASIA] grade/complete versus incomplete), patients with concomitant injuries, mechanism of injury, management in a specialized SCI versus nonspecialized SCI center, patients who underwent anterior cervical spine fixation approach versus posterior approach, type of tracheostomy (percutaneous vs. open surgical), patient demographics (age <18 vs. >18 years and <65 vs. >65 years, smokers vs. nonsmokers, females vs. males), timing of early tracheostomy (within 4, 7, or 10 days), year of publication (studies published within the last 5 years vs. older publications), and type of publication (studies published in peer-reviewed journals vs. others). Finally, patient and surgical factors associated with the timing of tracheostomy were explored.

Quantitative Data Synthesis

Meta-analysis was performed using Review Manager 5.4. The qualitative terms of "early" and "late" tracheostomy as defined by the researchers of each study were used in the analysis. Dichotomous data were analyzed using the DerSimonian and Laird random effects model to produce the effect measure as a risk ratio (RR). Continuous data were analyzed using an inverse variance random effects model and reported as the mean difference. A 95% study confidence interval (CI) was used for the analysis of all outcomes. Heterogeneity was assessed using the I^2 statistic, the χ^2 test for homogeneity, and visual inspection of the forest plots. A z test of interaction was performed for all subgroup comparisons, which tests the null hypothesis that the treatment effects in each subgroup are the same.

RESULTS

Literature Search

The database search yielded 3,098 citations. One study was found by gray literature search, three were retrieved from the reference lists of the included studies, and one abstract was included following a search of conference proceedings. In total, 17 studies with 2,804 patients met our inclusion criteria and were included in this systematic review (Fig. 1).

Study Characteristics and Methodological Quality

The characteristics of included studies are summarized in Table 1. Studies differed in their definitions of early and late tracheostomy (Supplemental Appendix 8, http://links.lww.com/TA/C132), although the majority used a range of 7 days or less (from either injury, intubation, or surgery) for early tracheostomy.[23–38] In one study, early and late tracheostomy were defined as 7 days or less and longer than 7 days, respectively, but the time point from which tracheostomy was measured was not specified.[33] Two studies used a range of 10 days or less and longer than 10 days.[26,31] Two studies did not report the specific timing of tracheostomy.[34,38] Patient characteristics from the included studies are reported in Supplemental Appendix 9, http://links.lww.com/TA/C132. In one study of 344 SCI patients, 72 patients also had concomitant traumatic brain injury.[33] One study investigated pediatric patients and was thus excluded.[30]

Quantitative Data Synthesis

Primary Outcome

A summary of the study results is included in Supplemental Appendix 10, http://links.lww.com/TA/C132. Early tracheostomy was not found to be associated with short-term mortality (RR, 0.84; 95% CI, 0.39–1.79; $p = 0.65$; 10 studies; n = 2,072; 125 events; $I^2 = 52\%$; Fig. 2, Table 2). Flanagan et al.[27] also measured 90-day mortality with a mortality rate of 6.3% in the early tracheostomy group and 3.5% in the late tracheostomy group. In addition to hospital mortality, Jeon et al.[31] also reported ICU mortality (2.6% and 4.7% for the early and late tracheostomy groups, respectively).

Subgroup and Sensitivity Analyses

There was no difference in mortality between early and late tracheostomy when a subgroup analysis of study publication year (within the last 5 years vs. older) was performed ($p = 0.58$; 10 studies; n = 2,072; 125 events; $I^2 = 0\%$; Supplemental Appendix 11, http://links.lww.com/TA/C132). There was also no difference in mortality between early and late tracheostomy when sensitivity analyses excluding either studies using less than 10 days for early tracheostomy or high risk of bias studies (unable to rate, NOS < 5/9, case series) were performed (RR, 0.96; 95% CI, 0.38–2.46; $p = 0.94$; eight studies; n = 1,893; 125 events; $I^2 = 61\%$; Supplemental Appendix 12, http://links.lww.com/TA/C132 and RR, 0.92; 95% CI, 0.41–2.09; $p = 0.85$; 9 studies; n = 2,018; 125 events; $I^2 = 56\%$; Supplemental Appendix 12, http://links.lww.com/TA/C132, respectively). Further planned subgroup and sensitivity analyses could not be completed because of insufficient data.

Secondary Outcomes

Secondary outcomes are reported in Table 2. Early tracheostomy was found to be associated with reduced mean duration of MV by 13.91 days (95% CI, –6.70 to –21.11; $p = 0.0002$; 10 studies; n = 855; $I^2 = 96\%$; Fig. 3), reduced mean ICU LOS by 10.20 days (95% CI, –4.66 to –15.74; $p = 0.0003$; 10 studies; n = 855; $I^2 = 90\%$; Fig. 4), as well as reduced mean hospital

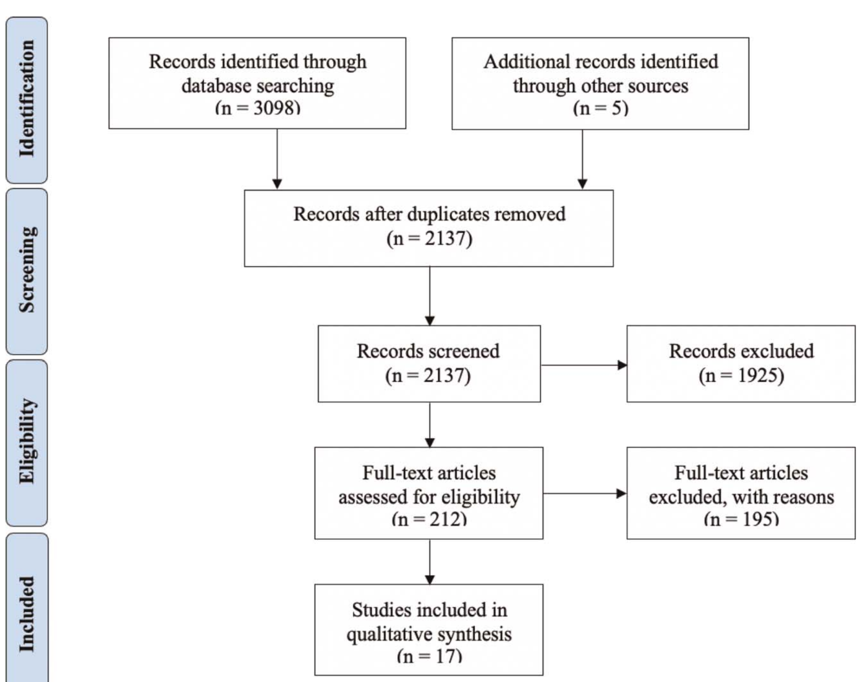

Figure 1. PRISMA flow diagram.[19] PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

TABLE 1. Summary of Characteristics of Included Studies

Study	Country	Centers	Study Population/ Type of ICU	N (SCI)	Timing of Early Tracheostomy	Timing of Late Tracheostomy or Prolonged Intubation	Time of Primary Mortality Endpoint
Babu et al. (2013)[23]	United States	SC (Duke University Medical Center)	Anterior cervical spine fixation and trach in same hospitalization (SCI (18), DDD (2))	20	≤6 d (n = 9)	LT, Days 7–12 (n = 9)	Hospital and median follow-up of 12.5 mo
Bellamy et al. (1973)[24]	United States	SC (Los Angeles County Hospital)	Cervical spine fractures resulting in quadriplegia	54 (30 patients with complete and 24 patients with incomplete quadriplegia)	Within 3 d of injury (n = 28)	After 3 d of injury (n = 4)	Within first year of injury * Within 14 d of injury was also included but does not allow for timing of tracheostomy to be analyzed (only looked at effect of administration of corticosteroids)
Beom et al. (2018)[25]	South Korea	SC (Chonnam National University Hospital)	Surgery for traumatic cervical SCI with motor weakness	49 (22 w/ trach) (27 in nontrach group, intubation removed within 4 days of surgery)	≤7 d (n = 10)	LT >7 d (n = 12)	NR
Choi et al. (2013)[26]	South Korea	SC (Neurosurgery department at Busan Paik Hospital)	Traumatic cervical SCI	21	Day 1–10 (n = 10)	LT >10 d (n = 11)	NR
Flanagan et al. (2018)[27]	United States	SC (single one trauma center)	Traumatic cervical SCI	70	≤7 d (n = 37)	LT >7 d (n = 33)	In-hospital mortality and 90-d mortality
Galeiras et al. (2018)[28]	Spain	SC (specialized hospital w SCI unit)	Adults with SCI above level D1	56	Before cervical surgery or <4 days after surgery (n = 31)	LT >4 d (n = 25)	Mortality during admission
Ganuza et al. (2011)[6]	Spain	SC (National Hospital of Paraplegics de Toledo)	Traumatic SCI at cervical or thoracic level	297 (required MV) 215 (underwent trach)	<7 d after orotracheal intubation (n = 101)	LT ≥7 days (n = 114)	Mortality at postcervical stabilization surgery
Guirgis et al. (2016)[29]	Oman	SC (ICU of Khoula Hospital)	Adult patients with cervical SCI	69	≤7 d (n = 51)	LT >7 d (n = 18)	ICU mortality
Holscher et al. (2014)[30]	United States	MC (two academic Level I trauma centers	Traumatic injury, <18 y	91	≤7 d (n = 43)	LT >7 d (n = 48)	In-hospital mortality
Jeon et al. (2014)[31]	South Korea	SC (Seoul National University Hospital)	Mechanically ventilated neurosurgical patients admitted to surgical ICU, underwent tracheostomy, and had MV >7 d	166 (125 included in data analysis)	<10 d from MV (n = 39)	≥10 d from MV (n = 86)	ICU and in-hospital mortality
Khan et al. (2020)[32]	United States	MC (American College of Surgeons Trauma Quality Improvement Program (ACS-TQIP) database	Adult trauma patients w/ blunt mechanism of injury, diagnosed with cervical SCI, and who underwent tracheostomy	1139	≤7 d after injury (n = 280)	>7 d after injury (n = 859)	In-hospital mortality
Kornblith et al. (2013)[33]	United States	MC (14 major trauma centers)	SCI requiring MV (72 patients also had TBI)	344	<7 d (48%) (n = 57)	>7 d (52%) (n = 61)	Death due to respiratory complications and overall mortality (unclear at what time)

Leelapattana et al. (2012)[34]	Canada	SC (London Health Science Center)	Adults (>16) with acute cervical SCI	66	There was a moderate positive correlation between the time from injury to tracheostomy and the number of ventilation days after injury. Average time to trach was 12.0 (±10.1)		>7 d after admission
Lozano et al. (2018)[35]	United States	SC (regional SCI center)	Trauma patients with cervical spine trauma + treated with ACF/PCF	98	≤4 days (after ACF) (n = 39)	LT >4 d (after ACF) (n = 59)	In-hospital mortality
Romero et al. (2009)[36]	Spain	SC (National Hospital of Paraplegics)	Traumatic SCI	152	Days 0–7 (n = 71)	>7 d (n = 81)	Subacute phase of SCI
Vitaz et al. (2001)[37]	United States	SC (University of Louisville Hospital)	Cervical/high thoracic SCI	58	Approximately postinjury Day 4 (n = 36)	NR (n = 22)	NR
Wu et al. (2013)[38]	China	SC (Third Hospital of Hebei Medical University)	Severe C4-C8 cervical SCI	54	NR (n = 11)	NR (n = 43)	Presumed hospital mortality

SC, single center; LT, late tracheostomy; NR, not reported; MC, multicenter; DDD, degenerative disc disease; TBI, traumatic brain injury; ACF/PCF; anterior cervical fusion/posterior cervical fusion.

LOS by 7.39 days (95% CI, –3.74 to –11.03; $p < 0.0001$; eight studies; n = 423; $I^2 = 3\%$; Supplemental Appendix 13, http://links.lww.com/TA/C132). Early tracheostomy was also associated with decreased incidence of VAP (RR, 0.86; 95% CI, 0.75–0.98; $p = 0.02$; 10 studies; n = 2,043; 691 events; $I^2 = 41\%$; Supplemental Appendix 14, http://links.lww.com/TA/C132), as well as the number of tracheostomy-associated complications with early tracheostomy (RR, 0.64; 95% CI, 0.48–0.84; $p = 0.001$; eight studies; n = 812; 158 events; $I^2 = 0\%$; Supplemental Appendix 15, http://links.lww.com/TA/C132). The other secondary outcomes that we were unable to find data on included long-term benefits, such as QOL measures, as well as time to phonation.

Qualitative Assessment of Additional Secondary Outcomes

Bellamy et al.[24] reported over 20 years experience at a single trauma center of respiratory complications in SCI patients with quadriplegia. Twenty-eight tracheostomies performed within 3 days of injury were associated with 39 pulmonary complications and 14 deaths, while four cases of tracheostomy performed after 3 days were associated with 24 pulmonary complications and one case of death. Mortality in this study was measured at 1 year and thus considered a long-term outcome; other than the study performed by Babu et al.,[23] which measured mortality at 1 year for the total study population, this was the only study to report long-term mortality. Only one study reported duration of sedation and found that there was no significant difference for patients who underwent early versus late tracheostomy (14.4 ± 10.4 days vs. 10.5 ± 7.1 days, respectively, $p = 0.283$).[28] The same study also found that timing of tracheostomy did not affect time to initiation of oral nutrition.[28] Vitaz et al.[37] found that implementation of a clinical pathway, including the placement of a tracheostomy approximately 4 days following injury, was associated with a decreased number of both total decubitus ulcers and stage III ulcers (25% and 0%, respectively, in the clinical pathway group compared with 54% and 14%, respectively, in the control group). In a study investigating the impact of performing tracheostomy prior to anterior cervical fusion, three patients who underwent tracheostomy within 7 days of their injury experienced a DVT, while two patients who underwent tracheostomy after 7 days experienced a DVT.[39] One patient in the late tracheostomy also experienced postoperative decubitus ulcers. In 29 patients with traumatic cervical SCI, late (>24 hours after injury) tracheostomy was associated with decreased time to decannulation compared with early (<24 hours after injury) tracheostomy (35.0 (14–46) days vs. 42.0 (23–104) days, respectively).[40] In contrast, Flanagan et al.[27] found that tracheostomy within 7 days of intubation was associated with fewer days to decannulation compared with late tracheostomy (53.0 ± 28.1 vs. 74.3 ± 45.8 days, $p < 0.05$) when ASIA Impairment Scale and level of neurological injury were controlled for.

Patient and Surgical Factors Associated With Timing of Tracheostomy

Analysis of SCI level and timing of tracheostomy found earlier tracheostomy was more likely performed in patients with a thoracic SCI compared with cervical SCI (RR, 1.56; 95% CI, 1.10–2.21; $p = 0.01$; two studies; n = 367; 172 events; $I^2 = 0\%$). Evaluating specific SCI levels, there was no difference in timing of tracheostomy in patients with a SCI at or below C5, compared

Study	Early Tracheostomy Events	Early Tracheostomy Total	Late Tracheostomy Events	Late Tracheostomy Total	Weight	Risk Ratio M-H, Random, 95% CI
Flanagan[27]	1	37	1	33	5.6%	0.89 [0.06, 13.70]
Galeiras[28]	8	31	2	25	12.0%	3.23 [0.75, 13.85]
Ganuza[6]	1	101	4	114	7.7%	0.28 [0.03, 2.48]
Guirgis[29]	2	32	5	13	11.6%	0.16 [0.04, 0.73]
Jeon[31]	2	39	6	86	11.3%	0.74 [0.16, 3.48]
Khan[32]	12	280	49	859	18.8%	0.75 [0.41, 1.39]
Kornblith[33]	7	57	1	61	8.3%	7.49 [0.95, 59.01]
Lozano[35]	4	39	1	59	7.8%	6.05 [0.70, 52.14]
Romero[36]	1	71	5	81	8.0%	0.23 [0.03, 1.91]
Wu[38]	1	11	12	43	9.0%	0.33 [0.05, 2.24]
Total (95% CI)		**698**		**1374**	**100.0%**	**0.84 [0.39, 1.79]**
Total events	39		86			

Heterogeneity: Tau² = 0.69; Chi² = 18.94, df = 9 (P = 0.03); I² = 52%
Test for overall effect: Z = 0.45 (P = 0.65)

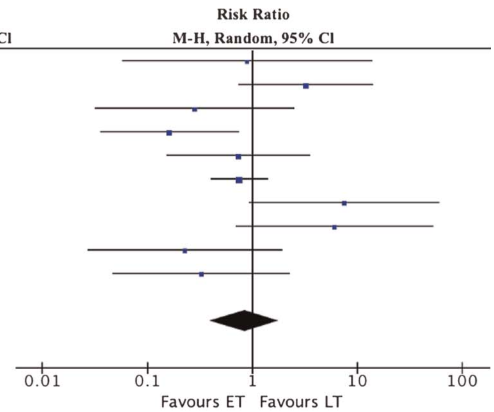

Figure 2. Random effects meta-analysis on short-term mortality, expressed as the RR. The blue box represents the point estimate of the study result, the black horizontal line represents the 95% confidence interval of the study result, and the black diamond represents the mean point estimate and mean confidence interval of all the studies. Flanagan et al.[27] measured mortality at admission (ICU). Galeiras et al.[28] measured mortality during admission. Ganuza et al.,[6] Kornblith et al.,[33] Romero et al.,[36] and Wu et al.,[38] did not specify the time at which mortality was measured. Guirgis et al.[29] measured ICU mortality. Khan et al.[32] measured in-hospital mortality. Jeon measured in-hospital mortality.[31] Lozano measured in-hospital mortality.[35] ET, early tracheostomy, LT, late tracheostomy.

with a SCI above C5 (RR, 1.29; 95% CI, 0.97–1.72; p = 0.08; four studies; n = 1,243; 352 events; I^2 = 43%). There was no difference in timing of tracheostomy in men versus women (RR, 1.12; 95% CI, 0.98–1.29; p = 0.10; 11 studies; n = 2106; 732 events; I^2 = 12%). In terms of type of tracheostomy procedure, there was no difference in the timing of tracheostomy when performing a surgical tracheostomy compared with percutaneous tracheostomy (RR, 1.09; 95% CI, 0.90–1.32; p = 0.36; five studies; n = 609; 284 events; I^2 = 0%). Finally, there was no difference in the timing of tracheostomy in patients that received a posterior spine fixation compared with an anterior fixation (RR, 1.14; 95% CI, 0.60–2.14; p = 0.69; 2 studies; n = 320; 95 events; I^2 = 6%).

DISCUSSION

In this systematic review and meta-analysis of patients with acute cervical or thoracic traumatic SCI, we found that early tracheostomy, as compared with late tracheostomy, is not associated with improvements in short-term mortality; however, it is associated with a decreased duration of MV, ICU LOS, and hospital LOS. Early tracheostomy was also associated with a reduced incidence of ventilator-associated pneumonia and tracheostomy-related complications.

There is an extensive array of literature investigating the timing of tracheostomy in general critically ill populations. Although multiple cohort studies have shown that early tracheostomy may reduce the duration of MV and LOS, shorten the duration of sedation, and lower the incidence of VAP, larger RCTs have established that a strategy of routinely performing early tracheostomies confers no survival benefit and may result in excess procedures.[41–45] Several recent systematic reviews also found that early tracheostomy (within 7–10 days) does not reduce mortality, in addition to finding no effect on the duration of MV or intensive care stay in a general critical care population.[46–48] However, meta-analyses found conflicting results regarding the incidence of VAP and duration of sedation.[46–48] The indications for endotracheal intubation, MV, and the need for a tracheostomy vary considerably between the heterogeneous mix of critically ill patients included in these studies. Early tracheostomy may help specific subgroups of critically ill populations. For example, patients with acute brain injury typically require airway protection for depressed airway reflexes, rather than respiratory failure. A recent meta-analysis of RCTs, including only patients with severe

TABLE 2. Primary and Secondary Outcomes

Outcomes	No. Studies	No. Patients Providing Data	Effect Estimate [95% CI]	p Value for Effect Estimate	I^2 (%)
Primary outcome					
Short-term mortality*	10	2,072	0.84 [0.39–1.79]	0.65	52
Secondary outcomes					
Duration of MV	10	855	−13.91 [−21.11 to −6.70]	0.0002	96
ICU LOS	10	855	−10.20 [−15.74 to −4.66]	0.0003	90
Hospital LOS	8	423	−7.39 [−11.03 to −3.74]	<0.0001	3
Incidence of VAP	10	2,043	0.86 [0.75–0.98]	0.02	41
Tracheostomy-related complications**	8	812	0.64 [0.48–0.84]	0.001	0

*Short-term mortality is defined as mortality occurring in-hospital and reported as either ICU or hospital mortality.

**Tracheostomy-related complications consisted of tracheal stenosis, perivertebral/paravertebral abscess, tracheoesophageal abscess, mediastinal abscess bleeding, stomal cellulitis, tracheitis, subglottic stenosis, endotracheal granuloma, glottis granuloma, tracheomalacia, arytenoid dislocation, vocal cord dysfunction, tracheostomy site infection, cervical fusion site infection, esophagocutaneous fistula, suture dehiscence.

Study	Early Tracheostomy Events	SD	Total	Late Tracheostomy Events	SD	Total	Weight	Risk Ratio M-H, Random, 95% CI
Beom[25]	6.0	0.0	10	6.9	0.0	12		Not estimable
Choi[26]	5.2	6.5	10	29.2	22.9	11	8.3%	-24.00 [-38.12, -9.88]
Flanagan[27]	23.9	16.5	37	36.9	26.7	33	10.1%	-13.00 [-23.55, -2.45]
Galeiras[28]	66.0	68.7	31	66.4	61.9	25	2.9%	-0.40 [-34.66, 33.86]
Ganuza[6]	26.1	11.7	101	48.8	13.5	114	13.2%	-22.70 [-26.07, -19.33]
Guirgis[29]	9.3	7.2	32	13.7	3.2	13	13.3%	-4.40 [-7.44, -1.36]
Holscher[30]	14.0	0.0	43	21.0	0.0	48		Not estimable
Jeon[31]	11.4	5.6	39	21.5	15.5	86	13.1%	-10.10 [-13.82, -6.38]
Romero[36]	26.07	1.69	71	48.75	3.45	81	13.6%	-22.68 [-23.53, -21.83]
Vitaz[37]	12.8	11.6	36	18.8	12.9	22	12.0%	-6.00 [-12.59, 0.59]
Total (95% CI)			**410**			**445**	**100.0%**	**-13.91 [-21.11, -6.70]**

Heterogeneity: Tau² = 86.15; Chi² = 186.61, df = 7 (P < 0.00001); I² = 96%
Test for overall effect: Z = 3.78 (P = 0.0002)

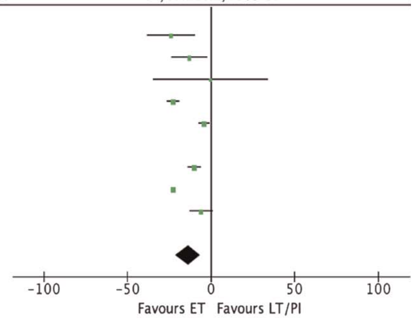

Figure 3. Random-effects meta-analysis on duration of MV, expressed as the MD in days. The green box represents the point estimate of the study result, the black horizontal line represents the 95% confidence interval of the study result, and the black diamond represents the mean point estimate and mean confidence interval of all the studies. MD, mean difference.

acute brain injury, showed that early tracheostomy results in decreased long-term mortality, duration of MV and ICU LOS.[49]

The ongoing respiratory care needs for the homogeneous critically ill population with acute SCI are unique. They require a tracheostomy for the provision of prolonged MV due to the high incidence of respiratory complications, including atelectasis, pneumonia, and ventilatory failure following an SCI.[1] They also require an airway conduit to maintain pulmonary hygiene and suctioning due to the accumulation of secretions from the combined loss of sympathetic innervation, resulting in increased bronchial tone and mucous secretions, and expiratory musculature and ability to cough.[50] Our meta-analysis included data from only critically ill patients with cervical and high thoracic SCI. This patient population may have unique and competing considerations regarding tracheostomy that impact the timing of tracheostomy, as well as subsequent outcomes. These patients often required prolonged MV or respiratory care for pulmonary hygiene, which may not only favor early tracheostomy but also have specific surgical and anatomic considerations, which impact the ability to perform this procedure promptly because of concerns over surgical site infection.

Multiple factors may contribute to the lack of consensus regarding the timing of tracheostomy in patients with acute SCI. The necessity of cervical spine fixation surgery in cases of SCI has historically resulted in delayed tracheostomy because of the perceived risk of cross-contamination between the two incision sites.[39,51] However, we found that early tracheostomy before, or just after, anterior cervical spine fixation surgery did not result in an increased rate of tracheostomy-associated complications, including wound infection (stoma cellulitis and cervical site wound infection) (Supplemental Appendix 15, http://links.lww.com/TA/C132).[39,52–55] In addition, there have been limited published data regarding optimal timing of tracheostomy in SCI patients, with single studies reporting on various different outcomes; several studies have only briefly explored tracheostomy timing within the broader context of identifying factors that predict the need for tracheostomy.[56,57] In the most recent clinical practice guidelines for management of SCI published in 2005, there is no recommendation of the optimal timing of tracheostomy in patients expected to require prolonged MV. Thus, the timing of tracheostomy remains highly variable, with it often being delayed until ventilator weaning and extubation have been attempted (although a primary tracheostomy as opposed to a secondary tracheostomy following extubation failure may decrease ICU mortality and LOS).[58]

The interpretation of these findings must consider the heterogeneity between studies. Clinical heterogeneity likely exists because of (1) patient selection of ASIA Impairment Scale and illness severity scores (e.g., acute physiology and chronic health evaluation II or sequential organ failure assessment), and age, which is known to be associated with duration of MV and ICU stay in SCI patients, and (2) variability in cointerventions between studies. Important cointerventions in SCI patients include protocols or algorithms for liberation from MV. The use of mechanical insufflation-exsufflation in the liberation process, venous thromboembolism

Study	Early Tracheostomy Events	SD	Total	Late Tracheostomy Events	SD	Total	Weight	Risk Ratio M-H, Random, 95% CI
Beom[25]	11.4	0.0	10	19.7	0.0	12		Not estimable
Choi[26]	20.8	6.0	10	38.0	18.5	11	7.0%	-17.20 [-28.75, -5.65]
Flanagan[27]	20.7	6.5	37	26.0	11.4	33	12.8%	-5.30 [-9.72, -0.88]
Galeiras[28]	32.9	11.0	31	35.2	19.4	25	9.2%	-2.30 [-10.83, 6.23]
Ganuza[6]	36.5	21.6	101	54.6	24.9	114	11.3%	-18.10 [-24.32, -11.88]
Guirgis[29]	19.1	32.7	32	18.2	5.2	13	6.9%	0.90 [-10.78, 12.58]
Holscher[30]	19.0	0.0	43	27.0	0.0	48		Not estimable
Jeon[31]	19.9	10.6	39	31.1	18.2	86	12.3%	-11.20 [-16.29, -6.11]
Romero[36]	36.52	1.59	71	54.58	2.92	81	14.9%	-18.06 [-18.80, -17.32]
Vitaz[37]	21.2	12.7	36	28.0	13.1	22	10.7%	-6.80 [-13.67, 0.07]
Total (95% CI)			**410**			**445**	**100.0%**	**-10.20 [-15.74, -4.66]**

Heterogeneity: Tau² = 50.63; Chi² = 68.21, df = 7 (P < 0.00001); I² = 90%
Test for overall effect: Z = 3.61 (P = 0.0003)

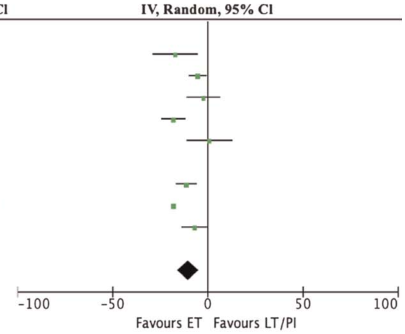

Figure 4. Random effects meta-analysis on ICU LOS, expressed as the MD in days. The green box represents the point estimate of the study result, the black horizontal line represents the 95% confidence interval of the study result, and the black diamond represents the mean point estimate and mean confidence interval of all the studies.

prophylaxis, and adherence to repositioning protocols to prevent the development of decubitus ulcers, which are known to be associated with duration of MV and ICU/hospital LOS and mortality in SCI patients. We were not able to complete a sensitivity analysis to adjust for these factors in the included studies to determine whether such cointerventions impacted on the pooled estimate of effects on duration of MV and ICU/hospital LOS.

This systematic review synthesizes the current data regarding optimal timing of tracheostomy in acute SCI patients. Strengths of this review include the comprehensive study protocol, rigorous methodology, and transparent reporting process. Data were individually collected by two reviewers to limit bias, and the quality of studies was analyzed using a validated quality assessment tool. Limitations of this study include the heterogeneity between studies, the inclusion of small single-center studies, mixed cervical and thoracic level SCI populations, and lack of a comparator "no tracheostomy" cohort in the included studies (which may have helped to evaluate the presence of a bias with regard to the SCI patients' stability and overall clinical status). In addition, the studies in this systematic review included both percutaneous and surgical techniques, as well as different timings of early tracheostomy (all within 10 days of intubation). However, it should be noted that the effect of percutaneous versus open would likely not bias the estimates as most of the duration of MV and ICU/hospital LOS would be driven by compromised ventilatory mechanics and VAP development. In addition, in terms of the variability in the point of reference from which duration of tracheostomy was measured, we postulate that because of the high C-spine injury, the day of injury is likely also the day of MV initiation as breathing would have typically been affected instantly or over hours because of decreased ventilation efficacy, increased work of breathing, and secretion burden.[59–61]

Future research could look more specifically at QOL or other patient-reported outcome measures following tracheostomy in patients with SCI. One study included in this systematic review investigated QOL outcomes and found that the number of days until initiation of oral nutrition was not significantly different between the early and late tracheostomy groups.[28] A prior study examining dysphagia in SCI patients found that those patients without dysphagia experienced a mean orotracheal intubation duration prior to tracheostomy of 10.0 days versus 16.9 days for those with dysphagia.[62] It also found that those patients with dysphagia experienced a higher rate of VAP compared with those without dysphagia (58% vs. 9%). In another study included in this review, one case of vocal cord dysfunction was noted.[30] In addition, researchers at the Johns Hopkins Hospital developed a validated QOL questionnaire for mechanically ventilated ICU patients and found that those who underwent early tracheostomy compared with late tracheostomy had higher scores on the questionnaire.[63] Further investigation into QOL measures, and factors that impact those measures including the ability to phonate and swallow, should be conducted. In addition, the long-term effects of early versus late tracheostomy remains unclear, with only one study found that investigated long-term mortality.[24]

CONCLUSION

This systematic review suggests early tracheostomy (within 7 days of injury, intubation, or surgery) in acute SCI patients reduces MV duration, ICU and hospital LOS, VAP, and tracheostomy-related complications. However, early tracheostomy was not associated with a decrease in short-term mortality. The impact of tracheostomy timing on long-term outcomes in SCI patients, including mortality, patient comfort, and QOL, warrants further study. Randomized controlled trials are necessary to establish the optimal timing of tracheostomy, understand patient selection considering the injury level and severity, and inform evidence-based guidelines for critically ill patients with acute SCI.

AUTHORSHIP

All authors contributed equally to the work.

DISCLOSURE

The authors declare no conflicts of interest.
Availability of data and materials: All data generated or analyzed during this study are included in this published article (and its supplementary information files).

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