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

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Abstract

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 was obtained by two independent reviewers to ensure accuracy and completeness. The quality of observational studies was evaluated using the Newcastle Ottawa Scale (NOS).

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 to 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 (ICU) 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 (VAP) and tracheostomy-related complications (RR 0.86; 95% CI 0.75 to 0.98; $p = 0.08$; $n = 2,043$ and RR 0.08; 95% CI -0.01 to -0.15; $p = 0.02$; $n = 812$ respectively). The majority of studies ranked as good methodologic quality on the NOS.

Conclusions Early tracheostomy in patients with acute traumatic SCI may reduce duration of mechanical ventilation, length of ICU 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.

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Background

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 translaryngeal intubation with placement of an endotracheal tube and initiation of invasive MV. In thoracic SCI, respiratory insufficiency and mechanical ventilation 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 [7][2]. 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 a translaryngeal intubation to a tracheostomy therefore requires anticipation of the expected duration MV and a careful assessment of the benefits and risks of the procedure.

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 non-critically ill SCI patients, and did not provide recommendations on the optimal timing of tracheostomy [18]. Although individual studies have investigated whether early (within seven days of intubation) or late (after seven days of intubation) tracheostomy improves outcomes, including mortality, ventilator-associated pneumonia, and length of hospital and intensive care unit (ICU) stay, the results remain inconclusive. Additionally, 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 PRISMA (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). The reference lists of retrieved articles were investigated to identify additional studies. Abstracts were searched from the conference proceedings listed in Supplemental Appendix 1, within the past 10 years, and the gray literature was searched using Google Scholar. A sensitivity analysis was performed utilizing 10 pre-identified studies (Supplemental Appendix 2).

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 (RCT) 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. 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 was independently extracted from included studies by two reviewers (S.J.F and S.T.) using a standardized data collection form (Supplemental Appendix 3). The Newcastle-Ottawa Scale (NOS) was used to assess the quality of included studies (Supplemental Appendix 4) [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 [22] (Table 2 and Table 3).

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 mechanical ventilation, 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, pulmonary embolus, decubitus ulcers), long term benefits (quality of life measures including Life Satisfaction Index, Beck Depression Inventory), time to swallowing and phonation, as well as time to decannulation (Supplemental Appendix 5). Analyses of the following subgroups were planned: spinal cord damage (level of injury and ASIA grade/complete versus incomplete), patients with concomitant injuries, mechanism of injury, management in a specialized SCI versus non-specialized SCI centre, patients who underwent anterior cervical spine fixation approach versus posterior approach, type of tracheostomy (percutaneous versus open surgical), patient demographics (age <18 versus >18 and <65 versus >65, smokers versus non-smokers, females versus males), timing of early tracheostomy (within 4, 7 or 10 days), year of publication (studies published within the last five years versus older publications), and type of publication (studies published in peer-reviewed journals versus 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 was analyzed using the DerSimonian and Laird random effects model to produce the effect measure as a risk ratio (RR). Continuous data was analyzed using an inverse variance random effects model and reported as the mean difference (MD). A 95% study confidence interval (CI) was utilized for the analysis of all outcomes. Heterogeneity was assessed using the I^2 statistic, the Chi-squared 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 3098 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 (Figure 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 6), although the majority utilized a range of $\leq$7 days (from either injury, intubation, or surgery) for early tracheostomy [23–33]. In one study, early and late tracheostomy were defined as $\leq$7 days and >7 days, respectively, but the time point from which tracheostomy was measured was not specified [34]. Two studies utilized a range of $\leq$10 days and >10 days [35][36]. Two studies did not report the specific timing of tracheostomy [37][38]. Patient characteristics from the included studies are reported in Supplemental Appendix 7. In one study of 344 SCI patients, 72 patients also had concomitant traumatic brain injury [34]. One study investigated outcomes of children/adolescents and thus consisted of patients <18 years old [30].

Quantitative Data Synthesis

Primary Outcome

A summary of the study results is included in Supplemental Appendix 8. Early tracheostomy was not found to be associated with short-term mortality (RR 0.84, 95% CI 0.39 to 1.79; p = 0.65; 10 studies; n = 2,072; 125 events; I^2 = 52%; Figure 2, Table 4). Flanagan et al. 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 [28]. In addition to hospital mortality, Jeon et al. also reported ICU mortality (2.6% and 4.7% for the early and late tracheostomy groups, respectively) [36].

Subgroup 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 versus older) was performed (p = 0.58; 10 studies; n = 2,072; 125 events; I^2 = 0%). Further planned subgroup analyses could not be completed due to insufficient data.

Secondary Outcomes

Secondary outcomes are reported in Table 4. Early tracheostomy was found to be associated with reduced mean duration of mechanical ventilation by 13.91 days (95% CI -6.70 to -21.11; p = 0.0002; 10 studies; n = 855; I^2 = 96%; Supplemental Appendix 10), 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%; Supplemental Appendix 11), as well as reduced mean hospital LOS by 7.39 days (95% CI -3.74 to -11.03; p < 0.0001; 8 studies; n = 423; I^2 = 3%; Supplemental Appendix 12). Early tracheostomy was also associated with decreased incidence of VAP (RR 0.86, 95% CI 0.75 to 0.98; p = 0.08; 10 studies; n = 2,043; 691 events; I^2 = 41%; Supplemental Appendix 13) as well as the number of tracheostomy-associated complications with early tracheostomy (RR 0.08, 95% CI -0.01 to -0.15; p = 0.02; 8 studies; n = 812; 158 events; I^2 = 60%; Supplemental Appendix 14). The other secondary outcomes that we were unable to find data on included long-term benefits such as quality of life measures as well as time to phonation.

Qualitative Assessment of Additional Secondary Outcomes

Bellamy et el. reported over 20 years experience at a single trauma centre 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 4 cases of tracheostomy performed after 3 days were associated with 24 pulmonary complications and 1 case of death [26]. 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., which measured mortality at 1 year for the total study population, this was the only study to report long-term mortality [24]. Only 1 study reported duration of sedation and found that there was no significant difference for patients who underwent early versus late tracheostomy (14.4 $\pm$ 10.4 days vs. 10.5 $\pm$ 7.1 days, respectively, p = 0.283) [25]. The same study also found that timing of tracheostomy did not affect time to initiation of oral nutrition [25]. Vitaz et al. 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 decubitus ulcers and stage III ulcers (25% and 0%, respectively, in the clinical pathway group compared to 54% and 14%, respectively, in the control group) [33]. 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 deep vein thrombosis (DVT), while two patients who underwent tracheostomy after 7 days experienced a DVT [39]. One patient in the late tracheostomy also experienced post-operative decubitus ulcers. In 29 patients with traumatic cervical SCI, late (>24 hours after injury) tracheostomy was associated with decreased time to decannulation compared to early (<24 hours after injury) tracheostomy (35.0 (14-46) days vs. 42.0 (23-104) days, respectively) [40]. In contrast, Flanagan et al. found that early tracheostomy was associated with fewer days to decannulation compared to late tracheostomy (53.0 $\pm$ 28.1 vs. 74.3 $\pm$ 45.8 days, p < 0.05) when ASIA Impairment Scale and level of neurological injury were controlled for [28].

Patient and surgical factors associated with timing of tracheostomy

Analysis of spinal cord injury level and timing of tracheostomy found earlier tracheostomy was more likely performed in patients with a thoracic SCI compared to cervical SCI (RR 1.56, 95% CI 1.10 to 2.21; p = 0.01; 2 studies; n = 367; 172 events; $I^2 = 0\%$). Evaluating specific SCI levels, there was a trend towards early tracheostomy in patients with a SCI at or below C5, compared with a SCI above C5 (RR 1.29, 95% CI 0.97 to 1.72; p = 0.08; 4 studies; n = 1,243; 352 events; $I^2 = 43\%$). There was a trend towards male sex associated with early tracheostomy (RR 1.12; 95% CI 0.98 to 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 to percutaneous tracheostomy (RR 1.09, 95% CI 0.90 to 1.32; p = 0.36; 5 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 to an anterior fixation (RR 1.14, 95% CI 0.60 to 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 to late tracheostomy, is not associated with improvements in short-term mortality, however it is associated with a decreased duration of mechanical ventilation, 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 randomized controlled trials 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 mechanical ventilation or intensive care stay in a general critical care population [46–48]. conflicting results regarding the incidence of VAP and duration of sedation [46–48]. The indications for endotracheal intubation, mechanical ventilation 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 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 mechanical ventilation 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 mechanical ventilation or respiratory care for pulmonary hygiene which may favour early tracheostomy, but also have specific surgical and anatomic considerations which impact the ability to perform this procedure promptly due to 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 due to the perceived risk of cross-contamination between the two incision sites [39][51]. However, we found that early tracheostomy prior to, 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 14) [39][52–55]. It should be noted that one study found that patients were more likely to develop a posterior incision site infection compared to an anterior one (OR 18.97, 95% CI 2.31 to 155.54)[53]. However, this study appears to be very small with wide confidence intervals, single center and possibly not generalizable. Additionally, there has 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 spinal cord injury 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 due to 1) patient selection of ASIA Impairment Scale and illness severity scores (e.g., APACHE II or SOFA), 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 co-interventions in SCI patients include protocols or algorithms for liberation from mechanical ventilation. The use of mechanical insufflation-exsufflation in the liberation process, venous thromboembolism 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 co-interventions 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 centre studies, percutaneous and surgical techniques, different timings of early tracheostomy (all within 10 days of intubation), and mixed cervical and thoracic level SCI populations. 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.

Future research could look more specifically at quality of life (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 group [25]. 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 [59]. It also found that those patients with dysphagia experienced a higher rate of VAP compared to those without dysphagia (58% vs. 9%). In another study included in this review, one case of vocal cord dysfunction was noted [30]. Additionally, 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 to late tracheostomy had higher scores on the questionnaire [60]. Further investigation into QOL measures, and factors that impact those measures including the ability to phonate and swallow, should be conducted. Additionally, the long-term effects of early versus late tracheostomy remains unclear, with only one study found that investigated long-term mortality [26].

Conclusions

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 short-term mortality. The impact of tracheostomy timing on long-term outcomes in SCI patients, including mortality, patient comfort and quality of life, 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.

Supplemental Digital Content

Supplemental Appendix 1 – Search Strategy

Supplemental Appendix 2 – Sensitivity Analysis of Database Search

Supplemental Appendix 3 – Data Extraction Sheet

Supplemental Appendix 4 – Data Quality Analysis

Supplemental Appendix 5 – Definitions of Outcome Measures

Supplemental Appendix 6 – Summary of 'Timing' Definitions

Supplemental Appendix 7 – Patient Characteristics of Included Studies

Supplemental Appendix 8 – Summary of Results

Supplemental Appendix 9 – Subgroup Analysis Short-Term Mortality

Supplemental Appendix 10 – Duration of Mechanical Ventilation

Supplemental Appendix 11 – ICU Length-of-Stay

Supplemental Appendix 12 – Hospital Length-of-Stay

Supplemental Appendix 13 – Incidence of Ventilator-Associated Pneumonia

Supplemental Appendix 14 – Tracheostomy-Related Complications

Supplemental Appendix 15 – References

List Of Abbreviations

SCI = spinal cord injury; MV = mechanical ventilation; RR = risk ratio; CI = confidence interval; MD = mean difference; NOS = Newcastle-Ottawa Scale; ICU = intensive care unit; VAP = ventilator-associated pneumonia; RISMA = Preferred Reporting Items for Systematic Reviews and Meta-Analyses; CENTRAL = Cochrane Central Register of Controlled Trials; RTC = randomized controlled trial; LOS = length of stay; DVT = deep vein thrombosis; ASIA: American Spinal Cord Injury Association; APACHE II = Acute Physiology and Chronic Health Evaluation II; SOFA = Sequential Organ Failure Assessment

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

All data generated or analysed during this study are included in this published article [and its supplementary information files]

Competing interests

The authors declare that they have no competing interests

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Tables

Table 1: Summary of characteristics of included studies

Study	Country	Centres	Study population/ type of ICU	N (SCI)	Timing of Early tracheostomy	Timing of Late tracheostomy or prolonged intubation	Time of primary mortality endpoint
Babu **2013**	USA	SC (Duke University Medical Center)	Anterior cervical spine fixation and trach in same hospitalization (SCI (18), DDD (2))	20	≤6 days (n=9)	LT Days 7-12 (n=9)	Hospital and median follow-up of 12.5 months
Bellamy 1973	USA	SC (Los Angeles County Hospital)	Cervical spine fractures resulting in quadriplegia	54 (30 patients with complete and 24 patients with incomplete quadriplegia)	Within 3 days of injury (n=28)	After 3 days of injury (n=4)	Within first year of injury * Within 14 days 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 2018	South Korea	SC (Chonnam National University Hospital)	Surgery for traumatic cervical SCI w/ motor weakness	49 (22 w/ trach) (27 in non-trach group, intubation removed within 4 days of surgery)	≤7 days (n=10)	LT >7 days (n=12)	NR
Choi **2013**	South Korea	SC (Neurosurgery department at Busan Paik Hospital)	Traumatic cervical spinal cord injury	21	Day 1-10 (n=10)	LT >10 days (n=11)	NR
Flanagan 2018	USA	SC (single one trauma center)	Traumatic cervical SCI	70	≤7days (n=37)	LT >7 days (n=33)	In-hospital mortality and 90-day mortality
Galeiras 2018	Spain	SC (specialized hospital w spinal cord injury unit)	Adults with SCI above level D1	56	Before cervical surgery or <4 days after surgery (n= 31)	LT >4 days (n=25)	Mortality during admission
Ganuza 2011	Spain	SC (National Hospital of Paraplegics de Toledo)	Traumatic SCI at cervical or thoracic level	297 (required MV) 215 (underwent trach)	<7 days after orotracheal intubation (n=101)	LT ≥ 7 days (n=114)	Mortality at post-cervical stabilization surgery
Guirgis 2016	Oman	SC (ICU of Khoula Hospital)	Adult patients w/ cervical SCI	69	≤7 days (n=51)	LT >7 days (n=18)	ICU mortality
Holscher 2014	USA	MC (two academic level I trauma centers	Traumatic injury, <18 years	91	≤7 days (n=43)	LT >7 days (n=48)	In-hospital mortality
Jeon 2014	South Korea	SC (Seoul National University Hospital)	Mechanically ventilated neurosurgical patients admitted to surgical ICU, underwent	166 (125 included in data analysis)	<10 days from MV (n=39)	≥ 10 days from MV (n=86)	ICU and in-hospital mortality

			tracheostomy, and had MV >7 days				
Khan 2020	USA	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 days after injury (n=280)	>7 days after injury (n=859)	In-hospital mortality
Kornblith 2013	USA	MC (14 major trauma centers)	SCI requiring MV (72 patients also had TBI)	344	<7 days (48%) (n=57)	>7 days (52%) (n=61)	Death due to respiratory complications and overall mortality (unclear at what time)
Leelapattana 2012	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) days		>7 days after admission
Lozano 2018	USA	SC (regional SCI center)	Trauma patients with cervical spine trauma + treated with ACF/PCF	98	≤4 days (after ACF) (n=39)	LT >4 days (after ACF) (n=59)	In-hospital mortality
Romero 2009	Spain	SC (National Hospital of Paraplegics)	Traumatic SCI	152	Days 0-7 (n=71)	>7 days (n=81)	Subacute phase of SCI
Vitaz 2001	USA	SC (University of Louisville Hospital)	Cervical/ high thoracic SCI	58	Approximately postinjury day 4 (n=36)	NR (n=22)	NR
Wu, 2013	China	SC (Third Hospital of Hebei Medical University)	Severe C4-C8 cervical SCI	54	NR (n=11)	NR (n=43)	Presumed hospital mortality

SCI=spinal cord injury, SC=single-center, LT=late tracheostomy, NR=not reported, MV=mechanical ventilation, MC=multicenter

Table 2. Newcastle-Ottawa Scale – Cohort studies

Study	Selection				Comparability	Outcome			Total Score
	Representativeness of intervention cohort	Selection of non-intervention cohort	Ascertainment of intervention	Outcome not present at start	Comparability of cohorts based on design/analysis	Assessment of outcome	Time to follow-up	Adequacy of follow-up	
Babu 2013	*	*	0	*	*	0	*	*	**6/9**
Choi 2013	*	*	0	*	**	0	0	*	**6/9**
Flanagan 2018	*	*	0	*	**	0	*	*	**7/9**
Galeiras 2018	*	*	*	*	**	0	*	*	**8/9**
Ganuza 2011	*	*	*	*	**	*	0	*	**8/9**
Guirgis 2016	*	*	*	*	*	*	0	*	**7/9**
Holscher 2014	0	*	*	*	0	*	0	*	**5/9**
Jeon 2015	*	*	*	*	**	*	0	*	**8/9**
Khan 2020	*	*	*	*	**	*	0	*	**8/9**
Kornblith 2013	*	*	*	*	*	*	0	*	**7/9**
Leelapattana 2012	*	*	*	*	*	*	0	*	**7/9**
Lozano 2018	*	*	*	*	*	*	0	*	**7/9**
Romero 2009	*	*	*	*	**	*	0	*	**8/9**
Vitaz 2001	*	0	*	*	0	*	0	*	**5/9**
Wu 2013*	**N/A**								

*Quality assessment not performed

Table 3. Newcastle – Ottawa Scale – Case Series

Study	Selection				Comparability	Outcome			Total Score
	Adequacy of case definition	Representativeness of cases	Selection of controls	Definition on controls	Comparability of case/controls based on design/analysis	Ascertainment of exposure	Same method ascertainment for cases/controls	Non-response rate	
Bellamy 1973	0	0	0	*	0	*	*	*	**4/9**
Beom 2018	*	*	0	*	0	0	*	*	**5/9**

Table 4. Primary and Secondary Outcomes

Outcomes	Number of studies	Number of patients providing data	Effect estimate [95% CI]	P value for effect estimate	I^2 (%)
Primary outcome					
Short-Term Mortality[1]	10	2,072	0.84 [0.39, 1.79]	0.65	52
Secondary outcomes					
Duration of MV	10	855	-13.91 [-21.11, -6.70]	0.0002	96
ICU LOS	10	855	-10.20 [-15.74, -4.66]	0.0003	90
Hospital LOS	8	423	-7.39 [-11.03, -3.74]	<0.0001	3
Incidence of VAP	10	2,043	0.86 [0.75, 0.98]	0.02	41
Tracheostomy-Related Complications[2]	8	812	-.08 [-0.15, -0.01]	0.02	60

[1]Short-term mortality is defined as mortality occurring in-hospital and reported as either ICU or hospital mortality

[2]Trachesotomy-related complications consisted of tracheal stenosis, peri-/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

MV=mechanical ventilation, LOS=length of stay, VAP=ventilator-associated pneumonia, CI=Confidence interval, I^2=Study heterogeneity

Figures

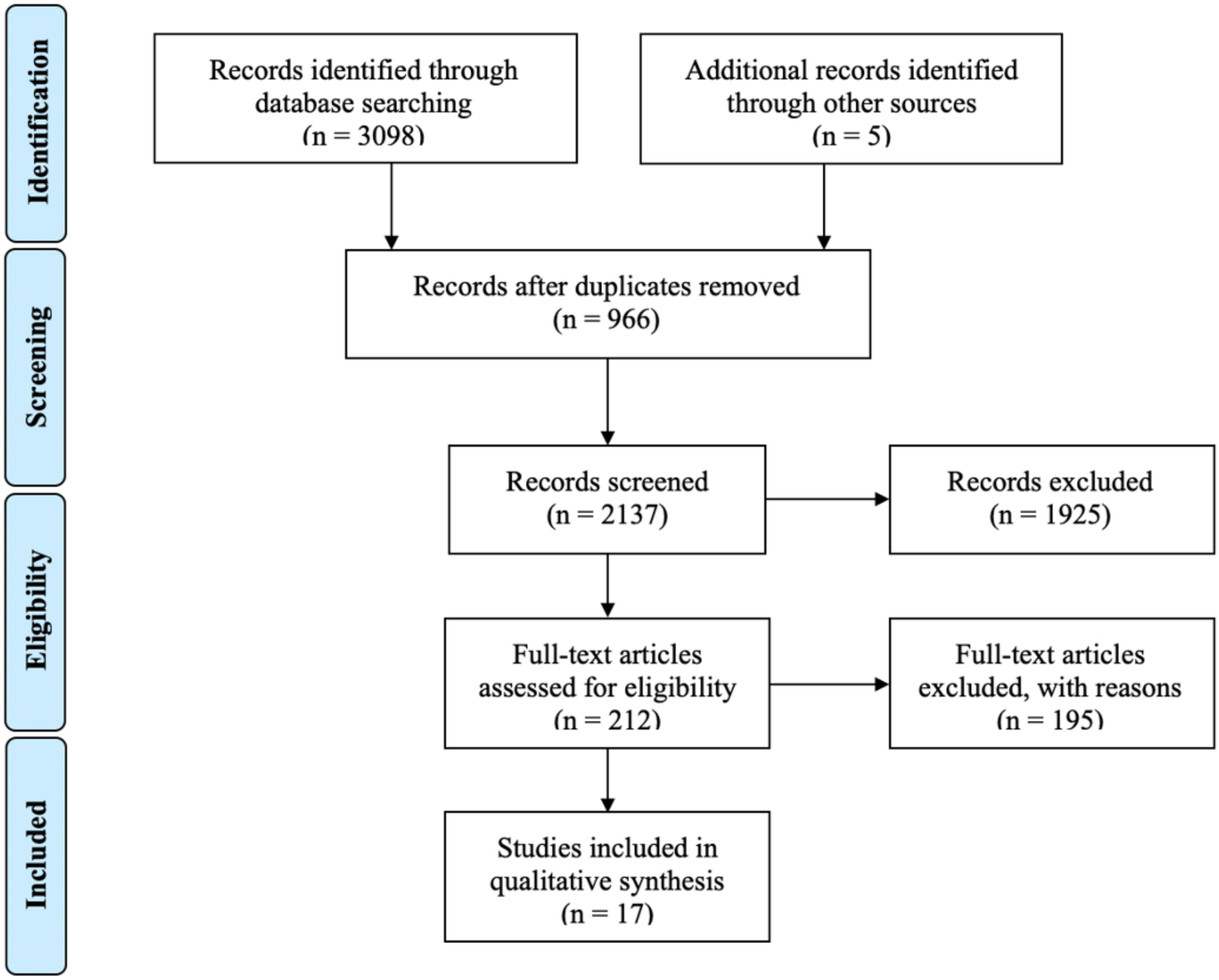

Figure 1

PRSIMA flow diagram [19]

	Early Tracheostomy		Late Tracheostomy			Risk Ratio
Study	**Events**	**Total**	**Events**	**Total**	**Weight**	**M-H, Random, 95% CI**
Flanagan 2018	1	37	1	33	5.6%	0.89 [0.06, 13.70]
Galeiras 2018	8	31	2	25	12.0%	3.23 [0.75, 13.85]
Ganuza 2011	1	101	4	114	7.7%	0.28 [0.03, 2.48]
Guirgis 2016	2	32	5	13	11.6%	0.16 [0.04, 0.73]
Jeon 2014	2	39	6	86	11.3%	0.74 [0.16, 3.48]
Khan 2019	12	280	49	859	18.8%	0.75 [0.41, 1.39]
Kornblith 2013	7	57	1	61	8.3%	7.49 [0.95, 59.01]
Lozano 2018	4	39	1	59	7.8%	6.05 [0.70, 52.14]
Romero 2009	1	71	5	81	8.0%	0.23 [0.03, 1.91]
Wu 2013	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: $Tau^2 = 0.69$; $Chi^2 = 18.94$, df = 9 (P = 0.03); $I^2 = 52\%$

Test for overall effect: Z = 0.45 (P = 0.65)

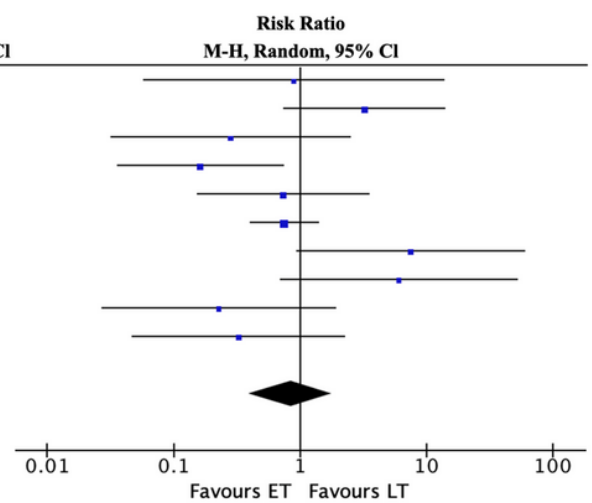

Figure 2

Random effects meta-analysis on short-term mortality, expressed as the risk ratio (RR). The blue box represents the point estimate of the study result, the black horizonal 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. measured mortality at admission (ICU). Galeiras et a. measured mortality during admission. Ganuza et al., Kornblith et al., Romero et al., and Wu et al., did not specify the time at which mortality was measured. Guirgis et al. measured ICU mortality. Khan et al. measured in-hospital mortality. Jeon measured in-hospital mortality. Lozano measured in-hospital mortality. ET=Early tracheostomy, LT=Late tracheostomy, CI=Confidence interval, I2=Study heterogeneity

Supplementary Files

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