Acute Respiratory Management Following Spinal Cord Injury

Viet Vu, DO
Amanda McIntyre, PhD
Carlos Cano Herrera, PhD (PT)
Matthew Querée, M.App.Psych.
Robert Teasell, MD

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Key Points

- Intubation can reduce arterial oxygen partial pressure ratios in people with acute SCI.
- Tracheostomies can reduce the number of pulmonary complications in people with acute SCI compared to those not receiving this procedure, and they may result in reduced forced vital capacity (FVC) and lower gas exchange compared to extubation.
- Tracheostomies are associated with an increase in the number of days people with acute SCI spend on ventilators.
- Diaphragm pacing in combination with mechanical ventilation (MV) can increase survival rates post SCI.
- Endotracheal (either endotracheal tube or tracheostomy tube) invasive ventilation (EIV) can lower partial pressure of CO_2 in people with acute SCI.
- Percutaneous tracheostomies may reduce rates of pneumonia when compared to surgical tracheostomies in people with acute SCI.
- Early tracheostomies may result in fewer intensive care unit (ICU) days and ventilation days; however, they may not impact in-hospital mortality, compared to late tracheostomies.
- The evidence is inconsistent regarding whether or not early tracheostomies vs. late tracheostomies reduce medical complications.
- Weaning from MV is more successful in patients who have not had a tracheostomy, and rates of decannulation and extubation are higher in patients with lower-level injuries during the acute phase post SCI.
- For MV weaning, progressive ventilator-free breathing (PVFB) may be more successful than intermittent mandatory ventilation / invasive mechanical ventilation (IMV), and using higher ventilator tidal volumes may speed up the weaning process compared to lower ventilator tidal volumes during the acute phase post SCI.
- Mechanical insufflation/exsufflation coupled with manual respiratory kinesitherapy may be effective for bronchial clearance during the acute phase post SCI.
- Inspiratory and expiratory muscle training may improve respiratory muscle function during the acute phase post SCI.
- Length of stay (LOS) in intensive care may be reduced by extubation in combination with intensive physiotherapy.
- Bronchodilator therapy with salbutamol (albuterol) may be an effective treatment for improving pulmonary function during the acute phase post SCI.

- High dose ambroxol may be an effective treatment to reduce pulmonary complications and improve oxygenation status following surgery in patients with acute cervical SCI (this is unavailable in Canada or USA).
- Specialized respiratory management programs provided in the hospital may lead to reduced procedures, ventilator days, hospital LOS, and improved respiratory and patient discharge status, in the acute phase post SCI.

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1 Executive Summary

The emphasis in respiratory acute care in people with spinal cord injury (SCI) is to maintain an open airway and diaphragm function while preventing respiratory failure, atelectasis, and pneumonia. This is a delicate balance for medical personnel as the presence of ventilation itself, despite assisting breathing, can directly lead to these pulmonary complications.

Typical Respiratory Outcomes/Issues by Level of Injury:

- C1-C3 – Complete injury above C3 usually results in paralysis and denervation of all muscles required for inspiration and expiration. Life-long ventilation usually required. (Muscles for respiration innervated at this level: sternocleidomastoid and accessory muscles)
- C3-C5 – An injury from C3-C5 results in a variable inability to inspire and expire. Often ventilated. May be able to wean from ventilation in time, depending on other factors. (Muscles for respiration innervated at this level: diaphragm and pectoralis major)
- C6-C8 - Patients experience more difficulty with expiration than inspiration. May not experience respiratory failure, but often muscle fatigue. Often ventilated initially but can usually achieve independent breathing. (Muscles for respiration innervated at this level: scalenes accessory and pectoralis major)
- T1-T12 – Patients experience more difficulty with expiration than inspiration. Patients experience a reduced ability to cough with an injury at or above this level. (Muscles for respiration innervated at this level: external and internal intercostals, abdominal muscles)

Lung function tests that may be performed to evaluate lung capacity post-SCI include forced vital capacity (FVC), tidal volume (Vt), residual volume, expiratory reserve volume, inspiratory reserve volume, forced expiratory flow, and forced expiratory volume. Arterial Blood Gas (ABG) is often performed to monitor pCO_2 while adjusting ventilator settings, notably Vt.

These measures help determine the degree to which respiration is impaired, the degree of ventilation the patient may require, and overall patient outcomes. Measurement of maximum inspiratory and expiratory pressures (MIP, MEP) can be used to estimate strength of respiratory muscles and has been used to predict pneumonia risk (Raab et al. 2016).

Pulmonary Complications During Acute SCI:

Respiratory complications occur in 36-83% of patients with acute SCI, the exact nature of which is dependent on the level of injury as this determines

which respiratory muscles are affected due to loss of innervation (Warren et al. 2014).

Impaired respiratory muscle function leads to complications such as improper bronchial secretion clearance, pneumonia, atelectasis, septicemia, pulmonary embolism, and reduced forced vital and inspiratory capacity (IC) (Warren et al. 2014).

Overall, pneumonia is the most studied associated complication with a greater incidence in patients with a higher level of injury (Cotton et al. 2005; Fishburn et al. 1990), a more severe injury (Hassid et al. 2008; Huang & Ou 2014), larger lesions (Aarabi et al. 2012), additional fractures (Chen et al. 2013; Harrop et al. 2001), no return of deep tendon reflexes after one day (Lemons & Wagner 1994), and surgical vs. percutaneous tracheostomies (Romero-Ganuza et al. 2011). Raab et al. (2016) found that maximal inspiratory pressure (MIP) was significantly associated with pneumonia risk; those with MIP at 115% above their lesion had significantly fewer instances of pneumonia (Raab et al. 2016). In addition to pneumonia, atelectasis and respiratory failure are the most common pulmonary complications following acute SCI (Berlly & Shem 2007) which often require mechanical ventilation (MV) to manage (Galeiras Vázquez et al. 2013). To confound this problem, MV puts patients at an increased risk for ventilator-assisted pneumonia, demonstrating how these complications can be difficult to control. Patients with ventilator-assisted pneumonia have an extended hospital stay and a death rate of 20-30% (Call et al. 2011; Cook 2000).

There is conflicting evidence regarding tracheostomies and their role in the development of respiratory complications. Some studies have found that patients who had tracheostomies experienced reduced respiratory complications compared to patients who did not have a tracheostomy (Leelapattana et al. 2012), whereas other studies reported the opposite (Harrop et al. 2004; Kornblith et al. 2014).

Pulmonary complications cause a significant burden to the individual and health care system, as it increases time on ventilation, hospital stay, and costs (Aarabi et al. 2012; Chen et al. 2013; Kornblith et al. 2014; Winslow et al. 2002). Furthermore, if complications cannot be managed initially, they may accumulate and put a patient at risk for more respiratory problems. For example, Huang and Ou (2014) found that the presence of respiratory failure led to a higher likelihood of developing pneumonia. Therefore, it is important that prophylactic measures be taken to prevent pulmonary complications, and that they are managed intensely. It has been suggested that the key to their prevention is intense secretion management (Claxton et al. 1998). Large volumes of mucus, or mucus staying inside the lung for extensive periods of time, encourage the growth of bacteria and subsequent development of pneumonia.

Overall, the current literature indicates that people with SCI should be screened and monitored for respiratory complications in the acute phase of SCI given their frequency as well as multifaceted origins.

Key Points

- Intubation can reduce arterial oxygen partial pressure ratios in people with acute SCI.
- Tracheostomies can reduce the number of pulmonary complications in people with acute SCI compared to those not receiving this procedure, and they may result in reduced FVC and lower gas exchange compared to extubation.
- Tracheostomies are associated with an increase in the number of days people with acute SCI spend on ventilators. Between 21% and 77% of patients with cervical SCI require a tracheostomy, with the variability of these numbers related to the influence of at least 16 other factors (e.g., severity of the injury, presence of other injuries, admission Glasgow Coma Scale score, age, etc.) (Branco et al. 2011; Como et al. 2005).
- Percutaneous tracheostomies may reduce rates of pneumonia when compared to surgical tracheostomies in people with acute SCI.
- Early tracheostomies may result in fewer intensive care unit (ICU) days and ventilation days; however, they may not impact in-hospital mortality compared to late tracheostomies. The evidence is inconsistent whether early tracheostomies reduce medical complications compared to late tracheostomies.
- Weaning from MV is more successful in patients who have not had a tracheostomy, and rates of decannulation and extubation are higher in patients with lower-level injuries during the acute phase post SCI.
- For MV weaning, progressive ventilator-free breathing (PVFB) may be more successful than intermittent mandatory ventilation / invasive mechanical ventilation (IMV), and using higher ventilator tidal volumes may speed up the weaning process compared to lower ventilator tidal volumes during the acute phase post SCI.
- Diaphragmatic pacing in combination with MV can increase survival rates post SCI.
- Endotracheal invasive ventilation (EIV) can lower partial pressure of carbon dioxide in people with acute SCI.
- Mechanical insufflation/exsufflation coupled with manual respiratory kinesitherapy may be effective for bronchial clearance during the acute phase post SCI.

- Inspiratory and expiratory muscle training may improve respiratory muscle function during the acute phase post SCI. Length of stay (LOS) in intensive care may be reduced by extubation in combination with intensive physiotherapy, may lead to fewer procedures and ventilator days, shorter hospital LOS, and improved respiratory and patient discharge status, in the acute phase post SCI.
- Bronchodilator therapy with medications (i.e., salbutamol or ambroxol), may be effective treatments for improving pulmonary function and reducing pulmonary complications during the acute phase post SCI.

Caution regarding research in acute respiratory SCI:

Fewer than ten percent of studies to date are RCTs; the majority of studies are retrospective and examine which factors on admission to acute care are associated with certain interventions and outcomes. This means that recommendations have not necessarily been established by the high standard recognized in experimental research. More prospective/match-controlled trials, or retrospective case-control reviews are required with larger samples to deliver better information regarding acute respiratory management in SCI.

2 Methods

A literature search was performed using the following databases: Cochrane Library, PubMed/MEDLINE, EMBASE, CINAHL, and Scopus. The following search terms were entered: (spinal cord injury OR paraplegia OR quadriplegia OR tetraplegia) AND respiratory, respiration, pulmonary, inspiratory muscle training, respiratory muscle strength, bronchodilators, bronchial hyperresponsiveness, ipratropium, metaproterenol, salbutamol, salmeterol, anabolic steroid, ambroxol, ventilation, ventilator, phrenic nerve stimulation, diaphragmatic stimulation, tracheostomy, atelectasis, intermittent positive pressure breathing, abdominal binder, vibration, secretion, pneumonia, lung abscess, abdominal neuromuscular electrical, or stimulation. Each search term after the brackets was added separately.

The following limits to the search were applied: the article must have been published between January 1, 2000 and December 31, 2022, in English, and included humans over the age of 18 years. The search was restricted to journal articles, reviews, and systematic reviews; grey literature, conference abstracts, case reports, study protocols, and qualitative studies were excluded. The studies had to include a minimum of three patients, of which ≥50% had spinal cord injuries, unless the results stratified injury etiology. During this process, additional studies were added as a result of cross-referencing between studies. Articles were considered to be ‘acute’ and

therefore suitable for inclusion in this chapter if the participants in each study were enrolled within approximately 1 month of their injury, or if the article did not report the time frame but made it clear that the study was conducted soon after the initial admission to hospital. For studies examining ventilator weaning and physiotherapy, the criteria was more relaxed and included studies where patients began enrollment within 1 month following injury and were included up to 4 months post-injury.

3 Introduction

The muscle groups required for respiration include the diaphragm, intercostals, abdominal muscles, and accessory muscles. A SCI that occurs in the cervical or thoracic region can affect the nerves that innervate these muscles and, as a result, impair respiration. With a complete injury above C3, paralysis of these muscles usually requires lifetime ventilation for survival. People with incomplete or lower-level injuries are not as compromised but can still experience weakness or spasticity in the muscles that reduce respiratory flow rates and lung volumes (Galeiras Vázquez et al. 2013). Developing rigorous management and prophylactic protocols for respiratory complications are key to improving patient outcomes and preventing morbidity and mortality (Berney et al. 2011). This chapter discusses the interventions available to assist with respiratory management during the acute phase post-SCI. Broadly, the interventions are categorized into mechanical ventilation (MV), non-pharmacological interventions, pharmacological interventions, and secretion management.

3.1 Neuronal Control of Breathing

Breathing is controlled by nerves that originate from the cervical and thoracic levels of the spinal cord. Due to the numerous muscles and nerves involved, the respiratory function that is affected depends on the level and severity of the injury. Table 1 outlines the associated muscles involved in inspiration and expiration that are affected by injuries at various levels; subsequent patient outcomes for these injuries are also detailed. Information for this table was adapted from Warren et al. (2014) and Mansel and Norman (1990).

Table 1. Effect of Level of Injury on Respiratory Function

<table>
<tr><th>Level</th><th>Associated Muscles for Inspiration and Pulmonary Function</th><th>Associated Muscles for Expiration</th><th>Patient Outcomes</th></tr>
<tr><td>C1</td><td rowspan="2">Sternocleidomastoid and accessory muscles (C1-C4)</td><td rowspan="2"></td><td rowspan="2">Complete injury above C3 usually results in paralysis and denervation of all muscles required for inspiration and expiration. Life-long ventilation may be required.</td></tr>
<tr><td>C2</td></tr>
<tr><td>C3</td><td rowspan="3">Diaphragm (C3-C5)

Tidal volume is reduced from injury at or above this level</td><td></td></tr>
<tr><td>C4</td><td></td><td rowspan="2">An injury from C3-C5 results in variable inability to inspire and expire. Often ventilated. May be able to wean from ventilation in time, depending on other factors.</td></tr>
<tr><td>C5</td><td rowspan="4">Pectoralis major muscle (C5-T1)</td></tr>
<tr><td>C6</td><td rowspan="3">Scalenes accessory (C4-C8)</td><td rowspan="3">Patients experience more difficulty with expiration than inspiration. May not experience respiratory failure, but often experiences muscle fatigue. Often ventilated initially but can usually achieve independent breathing.</td></tr>
<tr><td>C7</td></tr>
<tr><td>C8</td></tr>
<tr><td>T1</td><td rowspan="11">External intercostals (T1-T11)

These muscles are responsible for producing vital capacity. Vital capacity reduced by up to 53%, peak expiratory flow rate reduced by up to 42%, and forced expiratory volume is reduced up to 49% of what is seen in healthy individuals.</td><td rowspan="5">Internal intercostal muscles (T1-T11)</td><td rowspan="11">Patients experience more difficulty with expiration than inspiration. Patients have a less effective, or weaker, cough in an injury at or above this level.</td></tr>
<tr><td>T2</td></tr>
<tr><td>T3</td></tr>
<tr><td>T4</td></tr>
<tr><td>T5</td></tr>
<tr><td>T6</td><td rowspan="7">Abdominal muscles and internal intercostals (T6-T12)</td></tr>
<tr><td>T7</td></tr>
<tr><td>T8</td></tr>
<tr><td>T9</td></tr>
<tr><td>T10</td></tr>
<tr><td>T11</td></tr>
<tr><td>T12</td><td></td><td></td></tr>
</table>

3.2 Measurements for Lung Volume and Lung Capacity

Following SCI, lung function tests are performed to evaluate total lung capacity, forced vital capacity (FVC), tidal volume (Vt), residual volume, expiratory reserve volume, inspiratory reserve volume, forced expiratory flow, and forced expiratory volume. These tests help determine the degree to which respiration is impaired, the degree of ventilation the patient will require, and overall patient outcomes. A detailed explanation of these tests and their parameters is outlined in the Respiratory Management Chapter in SCIRE.

3.3 Pulmonary Complications During Acute SCI

Respiratory complications occur in 36-83% of patients with acute SCI, the exact nature of which is dependent on the level of injury as this determines which respiratory muscles are affected due to loss of innervation (Warren et al. 2014). Impaired respiratory muscle function leads to complications such as improper bronchial secretion clearance, pneumonia, atelectasis, septicemia, pulmonary embolism, and reduced vital and inspiratory capacity (IC) (Warren et al. 2014). It has been suggested that the key to their prevention is intense secretion management (Claxton et al. 1998). Hygienic behaviors, such as changing the patient's body position to promote postural draining, performing manual assisted coughing or chest percussion, and clearing bronchial secretions, are effective in reducing death from pulmonary complications (Mansel & Norman 1990). Large volumes of mucus, or mucus harboring inside the lung for extensive periods of time, encourage the growth of bacteria and subsequent development of pneumonia. Raab et al. (2016) found that maximal inspiratory pressure (MIP) less than 93.5 cm H_2O was significantly associated with pneumonia risk whereas those with MIP at 115% above their lesion-specific reference values had significantly fewer instances of pneumonia (Raab et al. 2016). In addition to pneumonia, atelectasis and respiratory failure are the most common pulmonary complications following acute SCI (Berlly & Shem 2007) which often require MV to manage (Galeiras Vázquez et al. 2013). To confound this problem, MV puts patients at an increased risk for ventilator-assisted pneumonia, demonstrating how these complications can be difficult to control. Patients with ventilator-assisted pneumonia have an extended hospital stay and a death rate of 20-30% (Call et al. 2011; Cook 2000). Other conditions such as aspiration, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), and complications related to tracheostomy and intubation, such as tracheal stenosis or stomal cellulitis, also have negative respiratory implications but these are less well studied.

The main conclusion drawn from these studies is that respiratory complications are prevalent among patients with acute SCI, and the likelihood of their development depends on a number of factors related to the initial injury on admission. Overall, pneumonia is the most studied associated complication with a greater incidence in patients with a higher level of injury (Cotton et al. 2005; Fishburn et al. 1990), a more severe injury (Hassid et al. 2008; Huang & Ou 2014), larger lesions (Aarabi et al. 2012), additional fractures (Chen et al. 2013; Harrop et al. 2001), no return of deep tendon reflexes after one day (Lemons & Wagner 1994), and surgical vs. percutaneous tracheostomies (Romero-Ganuza et al. 2011a). Regarding tracheostomies, there is conflicting evidence with respect to their role in the development of respiratory complications. Some studies have found that patients who had tracheostomies experienced reduced respiratory complications compared to patients who did not have a tracheostomy (Leelapattana et al. 2012), whereas other studies reported the opposite (Harrop et al. 2004; Kornblith et al. 2014).

The development of respiratory complications is also dependent on several other factors including the completeness of the injury (Lemons & Wagner 1994), the timing of the tracheostomy (Romero-Ganuza et al. 2011b; Romero et al. 2009) and the cause of injury (Aarabi et al. 2012). Age may play a role in the development of complications (Aarabi et al. 2012), although this finding is not always supported (Lemons & Wagner 1994). Likewise, some studies reported that receiving an early tracheostomy (ET) lowered the risk of problems (Kornblith et al. 2014; Romero-Ganuza et al. 2011b; Romero et al. 2009), but other studies found it did not matter (Choi et al. 2013). Additional data on the timing of tracheostomies can be found here. Pulmonary complications cause a significant burden to the individual and health care system, as it increases time on ventilation, hospital stay, and costs (Aarabi et al. 2012; Chen et al. 2013; Kornblith et al. 2014; Winslow et al. 2002). Furthermore, if complications cannot be managed initially, they may accumulate and put a patient at risk for additional respiratory problems. For example, Huang and Ou (2014) found that respiratory failure led to a higher likelihood of developing pneumonia. Therefore, aggressive measures should be undertaken to both prevent and treat pulmonary complications.

Other factors that have been less studied but are still shown to be associated with higher rates of respiratory complications include a history of smoking, electrolyte imbalances, and hypoalbuminemia (Chen et al. 2013). The etiology of the SCI is also a factor, specifically sports-related SCIs (Aarabi et al. 2012). There are a variety of factors, both pre-existing and related to the injury, which determine the risk of having a respiratory complication in the acute phase. Overall, the current literature indicates that all people with SCI should be screened and monitored for respiratory complications in the acute phase of SCI given their frequency as well as multifaceted origins.

4 Systematic Reviews

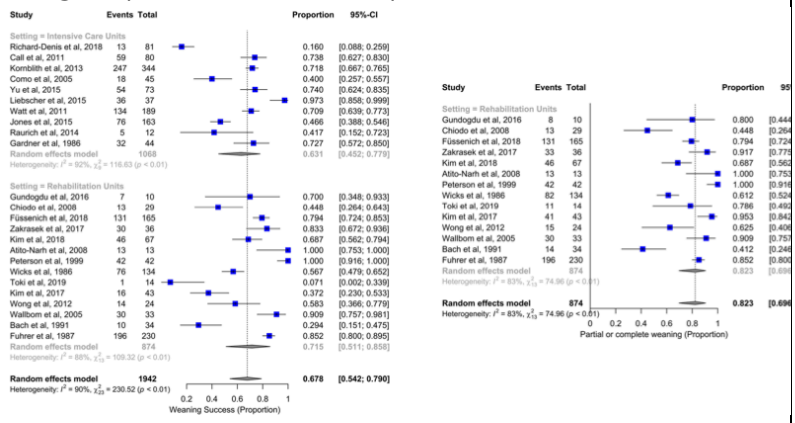
Eight systematic reviews have examined various interventions that affect respiratory function and management of people with SCI. Interventions examined include tracheostomy, respiratory muscle training (RMT), exercise training, abdominal FES, and treatment strategies for the respiratory management of acute tetraplegia. Another systematic review assessed the probability of weaning success, duration of MV, mortality, and their predictors in mechanically ventilated adult patients (Schreiber et al. 2021). These systematic reviews are outlined in Table 2 below; however, the conclusions and recommendations related to these findings are incorporated in the specific sections later in the chapter that summarizes the respective treatments.

Table 2. Systematic Reviews

Author Year **Country** **Date included in the review** **Number of articles** **Level of evidence** **Type of study** **AMSTAR Score**	**Method** **Databases**	**Conclusions**
Schreiber et al. 2021 Canada Reviewed published articles up to August 2021 N = 39 **Level of evidence:** Newcastle–Ottawa Scale **Type of study:** N/A AMSTAR: 6	**Methods:** Investigate the probability of weaning success, duration of mechanical ventilation (MV), mortality, and their predictors in mechanically ventilated adult patients with SCI. **Database:** OVID Medline, CINAHL, the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews, Ovid Embase and Scopus.	1. 14,637 patients were enrolled (13,763 in intensive care unit [ICU], 874 in rehabilitation units). 2. The mean time from injury to hospitalization was 8 h [95% CI 7–9] for studies conducted in ICU, 40 days [95% CI 29–51] for studies performed in rehabilitative units. 3. Probability of weaning from MV after SCI: a. 63% [45–78%] of the patients hospitalized in

		ICU were completely separated from the ventilator; 72% [51–86%] of the patients admitted to a rehabilitative ward were completely, and 82% [70–90%] were either completely or partially liberated from the ventilator. 4. Secondary outcomes: a. In ICU, the mean duration of MV was 27 days, LOS 23 days, hospital LOS 44 days. 81% of patients were tracheostomized and 30% of them were decannulated. Incidence of pneumonia and mortality were 40% and 8%, respectively. b. Patients hospitalized in rehabilitation centres were ventilated for a mean of 97 days (including duration of MV prior to admission and during the stay in rehabilitation) and stayed in the unit for 78 days. All patients were

		tracheostomized and 83% of them were decannulated; 36% developed pneumonia, and less than 1% died. 5. Predictors of weaning and duration of MV: a. A high number of comorbidities, high Injury Severity Score, high-level lesions (C1–C3 vs. C4–C7), elevated heart rate, and presence of tracheostomy appeared to be associated with increased odds of weaning failure. b. Shorter time to admission to a specialized SCI center, high-level lesions (C1–C4 vs. C5–C8), complete lesion, LTV and high positive end-expiratory pressure within 24 h from admission, and presence of tracheostomy were associated with a longer duration of MV.
	Figure 1. Forest plots for the outcome of complete liberation from the ventilator (left panel) and for the outcome of partial or complete weaning after rehabilitation (right panel). Studies are presented according to setting classification (intensive care	

	units vs. rehabilitation units): both overall and subgroup estimates are reported.  Figure 2. Forest plot for the outcome of duration of MV in intensive care units and rehabilitation units (upper panel). Studies are presented according to setting classification (intensive care units vs. rehabilitation units): both overall and subgroup estimates are reported. Forest plots for the outcome of duration of MV for rehabilitation units (including the time to admission to rehabilitation) (lower panels). Weight refers to the relative contribution of each study to the meta-analytic estimate and is generated using the inverse variance method.

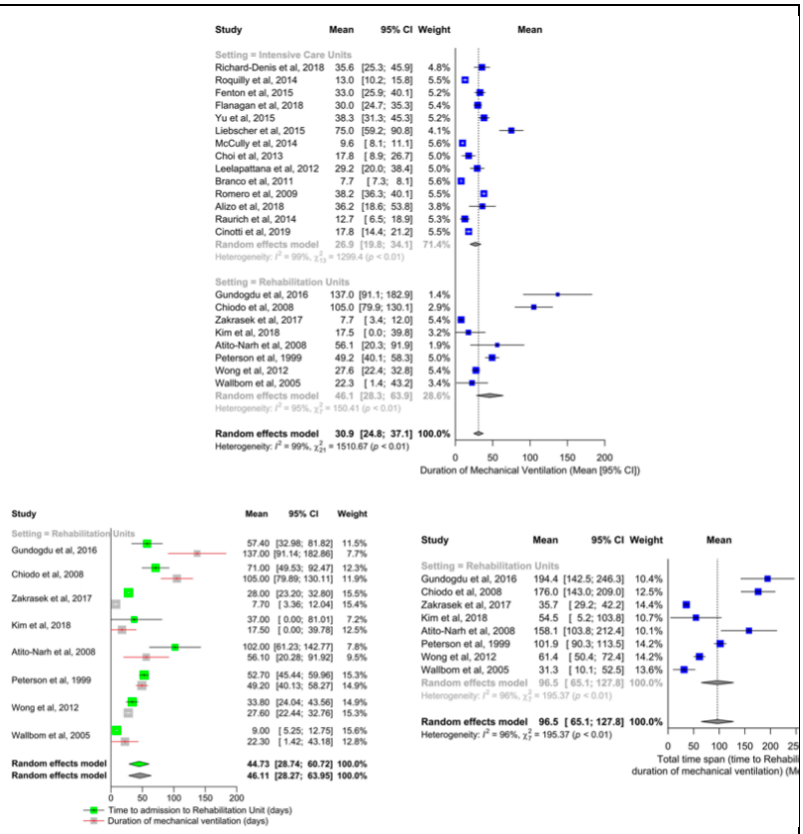
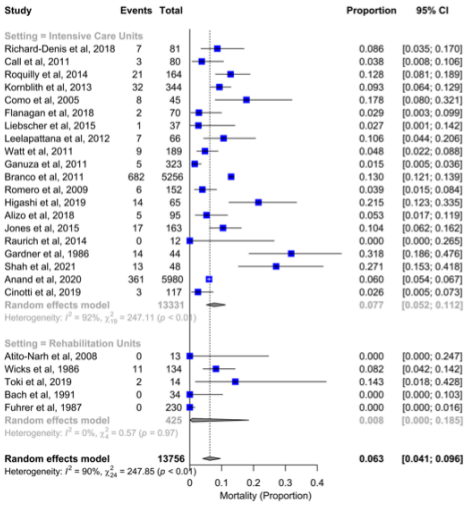


Figure 3. Forest plot for mortality. Studies are presented according to setting classification (intensive care units vs. rehabilitation units): both overall and subgroup estimates are reported.



Figures are extracted from the original article (Schreiber et al. 2021), which is licensed under Creative Commons Attribution 4.0 International License.

Foran et al. 2021 Canada Reviewed published articles up to January 2020. N = 17 **Level of evidence:** The Newcastle-Ottawa Scale (NOS) **Type of study:** Cohort studies and case series. AMSTAR: 7	**Methods:** Reviewed and evaluated evidence regarding the timing of tracheostomy in patients with acute traumatic SCI. **Database:** MEDLINE, EMBASE, CINAHL, Scopus, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL).	1. Studies differed in their definitions of ET and LT although the majority used a range of 7 days or less (from either injury, intubation, or surgery) for ET. 2. ET 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). 3. ET was found to be associated with: a. 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%). b. 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%). c. Reduced mean hospital LOS by 7.39 days (95% CI, –3.74 to –11.03; p < 0.0001; eight studies; n = 423; I^2 = 3%). d. 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%), as well as the number of

		tracheostomy-associated complications with ET (RR, 0.64; 95% CI, 0.48–0.84; p = 0.001; eight studies; n = 812; 158 events; I^2 = 0%).
Mubashir et al. 2021 USA Reviewed published articles up to October 2019. N = 8 **Level of evidence:** Study quality using the Newcastle-Ottawa Scale (NOS) for cohort studies. **Type of study:** Retrospective cohorts. AMSTAR: 9	**Method:** Reviewed the optimal timing of tracheostomy and evaluate potential subsequent beneficial effects by comparing early tracheostomy (ET) vs. late tracheostomy (LT) in patients with SCI. **Database:** Medline (Ovid), PubMed (non-Medline records only), Embase, Cochrane Central, Cochrane Database of Systematic Reviews, and PsycINFO, ClinicalTrials.gov and the International Clinical Trials Registry Platform.	1. 1220 patients among the included studies (ET, n = 441 and LT n = 779). 2. Mortality was lower among patients in the ET group compared to the LT population, but the results were not significant (OR = 0.56; 95% CI, 0.32–1.01; p = 0.054; I^2 = 0%). 3. ET was associated with reduced mean ICU LOS by 13 days (95% CI, −19.18 to −7.00; p = 0.001; I^2 = 88.8%) and mean duration of MV by 18.30 days (95% CI, −23.33 to −12.28; P = 0.001; I^2 = 85.6%). 4. There were no significant differences in total pneumonia rates between the ET and LT groups (odds ratio (OR) = 0.66; 95% CI, 0.34–1.29; p = 0.226; I^2 = 35.6%). 5. Stratified analysis demonstrated that patients with cervical SCI were twice as likely to undergo ET

		compared to thoracic SCI (OR = 2.13; 95% CI, 1.24–3.64; P = .006; I^2 = 0%). Moreover, patients with a higher cervical SCI (C1–C5 vs. C6–C8) were more likely to undergo ET, but without reaching significance (OR = 1.63; 95% CI, 0.88–3.03; P = .119; I^2 = 0%).
McCaughey et al. 2016b Australia Reviewed published articles until 23 December 2014 N = 14 **Level of evidence:** N/A **Type of study:** Self-control (randomized crossover) and RCTs AMSTAR: 7	**Methods:** Systematic review and meta-analysis made to identify whether abdominal FES is an effective intervention to improve respiratory function in both an acute and chronic manner after SCI. **Databases:** Pubmed. **Protocols of abdominal FES used:** The median maximum amplitude was 100 mA (range 100–450 mA), the mean pulsewidth (pulse duration) was 259 μs (range 25–400 μs) and almost all studies used a stimulation frequency of 50 Hz. There was a lack of homogeneity in electrode position, with a range of positions used to stimulate either or both of the rectus abdominis and external oblique muscles.	1. Low participant numbers and heterogeneity across studies reduced the power of the meta-analysis (141 participants were included in total (n = 128 receiving abdominal FES; n = 13 acting as controls). 2. 10 studies assessed acute respiratory effects of abdominal FES and showed a significant acute improvement in CPF whereas FEV_1 approached significance. 3. 4 studies assessed chronic respiratory effects of FES; showing only a significant increase and effect in FVC (P = 0.043), with a continued improvement after training; in VC (P = 0.013); and in PEF (P = 0.026).

Berlowitz and Tamplin 2013 (Tamplin & Berlowitz 2014) Australia Reviewed published articles (searches were not restricted by date, language, or publication status) N=11 **Level of evidence:** PEDro scale was used to evaluate studies **Type of study:** 11 RCT AMSTAR: 10	**Method:** Systematically review the effectiveness of RMT on pulmonary function, dyspnea, respiratory complications, respiratory muscle strength, and quality of life for people with cervical SCI. There were no date, language, or publication restrictions. Only RCTs were included. **Database:** Cochrane Injuries and Cochrane Neuromuscular Disease Groups' Specialized Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (2012, Issue 1), MEDLINE, EMBASE, CINAHL, ISI Web of Science, PubMed, and clinical trials registries (Australian New Zealand Clinical Trials Registry, Clinical Trials, Controlled Trials metaRegister), and hand searching.	1. 11 RCTs with 212 participants with cervical SCI were included. 2. Meta-analysis revealed a statistically significant effect of RMT for 3 outcomes: VC (MD mean end point 0.4L, 95% CI 0.1 to 0.7), MIP (MD mean end point 10.5 cmH_2O, 95% CI 3.4 to 17.6), and MEP (MD mean end point 10.3 cmH_2O, 95% CI 2.8 to 17.8). (Berlowitz & Tamplin 2013) 3. Meta-analysis revealed a statistically significant effect of RMT for 2 extended outcomes: MVV (MD mean end point 17.51L/min, 95% CI 5.20 to 29.81), and IC (MD mean end point 0.35L, 95% CI 0.05 to 0.65). (Tamplin & Berlowitz 2014) 4. RMT showed a combined benefit in VC & FVC (MD mean end point 0.41L, 95% CI 0.17 to 0.64) (Tamplin & Berlowitz 2014) 5. There was no effect on FEV_1 or dyspnoea. 6. The results from quality of life assessment tools could not be combined from the

		three studies for meta-analysis. 7. No adverse effects as a result of RMT were identified in cervical SCI.
Berney et al. 2011 Australia Reviewed published articles from 1950 to 2008 N= 21 **Level of Evidence:** PEDro Scale and the Newcastle–Ottawa Scale (NOS) with nine scored criteria **Type of study:** 1 RCT 3 cohort 3 case–control 14 retrospective case series reports. AMSTAR: 6	**Methods:** Literature search for English articles with quantitative study designs on the effectiveness of treatment strategies for the respiratory management of acute tetraplegia. **Databases:** MEDLINE (1950–2008), CINAHL (1982–2008), EMBASE (1980–2008), the Cochrane Library (2008), Web of Science (1900–1914–2008), http://www.guideline.gov and http://www.icord.org/scire/chapters.php on 20 October 2008.	1. A clinical pathway with a structured respiratory protocol that includes a combination of treatment techniques, provided regularly is effective in reducing respiratory complications and cost. 2. Mortality (ARR=0.4, 95% confidence interval (CI) 0.18, 0.61), the incidence of respiratory complications (ARR=0.36, 95% CI (0.08, 0.58)), and requirement for a tracheostomy (ARR=0.18, 95% CI (-0.05, 0.4)) were significantly reduced by using a respiratory protocol. 3. Overall, study quality was moderate. Further studies using specific interventions that target respiratory complications associated with specific regions of the cervical spine, using more methodologically

		rigorous designs are required.
Sheel et al. 2008 Canada Review published articles from 1980 to 2006 N=13 **Level of Evidence:** PEDro scale – RCTs Modified Downs and Black – non RCTs **Type of study:** 3 RCTs 1 pre-post 6 case series 2 cohort 1 case report AMSTAR: 6	**Methods:** Literature search for articles assessing exercise training and inspiratory muscle training (IMT) for the improved respiratory function of patients with SCI. **Databases:** MEDLINE/ PubMed, CINAHL, EMBASE, PsycINFO.	1. There is Level 2 evidence supporting exercise training as an intervention to improve respiratory strength and endurance. 2. There is Level 4 evidence to support exercise training as an intervention to improve resting and exercising respiratory function in people with SCI. 3. There is Level 4 evidence to support IMT as an intervention to decrease dyspnea and improve cardiovascular function in people with SCI.

5 Mechanical Ventilation

One of the most important avenues of respiratory management is MV. There have been increases in the incidence of high-level cervical SCI and incomplete traumatic cervical SCI, resulting in a greater percentage of ventilator-dependent patients (McCaughey et al. 2016a; Montoto-Marqués et al. 2018). Patients can be ventilated with non-invasive mask ventilation or more invasive endotracheal or transtracheal (with a tracheostomy) ventilation. Often these more invasive procedures are needed to allow for suctioning excess secretions to prevent the development of complications such as atelectasis or pneumonia (Gregoretti et al. 2005). Patients may experience more than one type of ventilation during their hospital stay as their needs adjust (i.e., they may initially be intubated with endotracheal ventilation and later proceed to transtracheal intubation to assist in ventilator weaning).

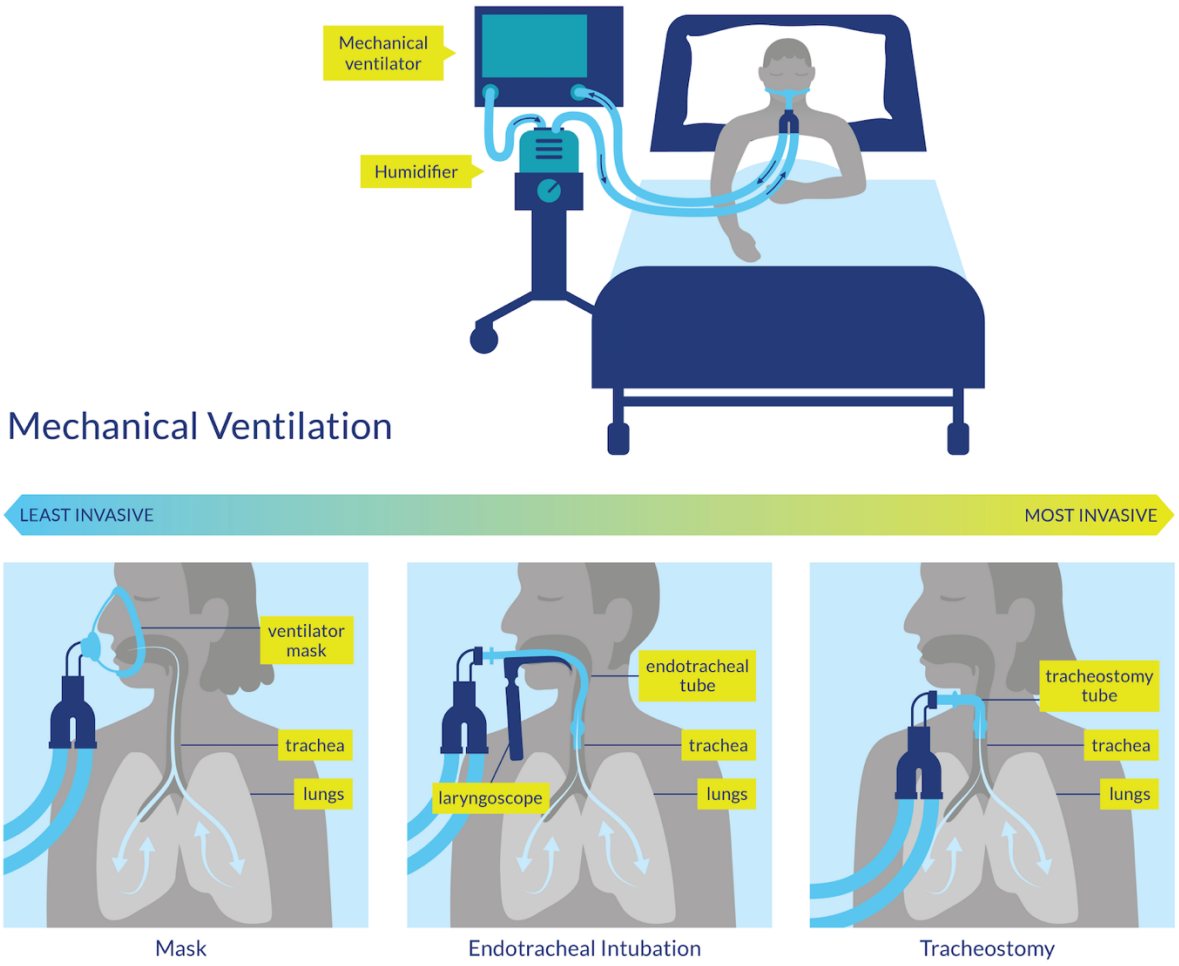


Figure 1. Mechanical ventilation procedures

There are several modes of ventilation used for patients that vary in the amount of volume or pressure controlled based on pre-set variables to maximize lung function. For example, intermittent positive pressure breathing is one of the oldest ventilation strategies in which all inspirations are provided through the application of positive pressure to the airway. Its use is common in patients with acute SCI, yet its general efficacy is still largely unknown (Denehy & Berney 2001) and is understudied in the SCI population. Intubation for MV often occurs at the time of injury to manage respiratory failure or to protect the airway in cases of complete SCI between C1 and C5 (Berney et al. 2011). In contrast, incomplete injuries lower than C5, where the airway is not immediately compromised or at risk, ventilation is often still initiated approximately four days after injury when levels of carbon dioxide rise in the blood due to difficulty expiring (Galeiras Vázquez et al. 2013). Although ventilatory needs are unique for each patient, it is useful to

determine which factors predict the need for MV in an effort to develop practice guidelines and reduce overall hospital stay (Casha & Christie 2011).

One observational study found, not unexpectedly, that patients with ASIA grades A and B were more likely to require MV, as well as those with higher injury severity scores (Montoto-Marques et al. 2018). Other factors include complete injuries, high Injury Severity Score (ISS), and compound injuries (Velmahos et al. 2003; Como et al. 2005; Seidl et al. 2010).

5.1 Intubation

Patients with acute SCI requiring ventilation are usually intubated, either in at the sight of injury or upon admission to the hospital. Intubation can either be orotracheal or nasotracheal, and both options are normally used for short periods of ventilation of less than 10 days (Shirawi & Arabi 2006). Prolonged intubation is not recommended as it can lead to the development of pneumonia, subglottic or tracheal stenosis, and increased airway resistance. In addition, it limits patients' mobility, prolongs ventilator weaning, and makes pulmonary and oral hygiene difficult (Shirawi & Arabi 2006). In cases where ventilation is required for longer than 10 days, a tracheostomy is usually performed. Intubation is safest when it is performed electively under anesthesia to reduce neurological damage experienced from neck manipulation (Durbin et al. 2014), so it often occurs before a patient is experiencing severe breathing difficulty. The risk of damage is elevated when intubation is performed urgently in the case of sudden respiratory distress.

Table 3. Evaluation of the use of Intubation for Respiratory Function During Acute SCI

Author Year Country Research Design Score Sample Size	**Methods**	**Outcome**
Iwashita et al. 2006 Japan Cohort Level 2 N = 49	**Population:** Mean age: 51 yr; Gender: male=40, female=8; Level of injury: C2-C7; Severity of injury: complete=28, incomplete=21. **Intervention:** Patients were either intubated or not intubated.	1. Patients who were intubated experienced a significantly lower PaO_2/FiO_2 (p=0.0014), a lower arterial pH (p=0.0001), and a higher $PaCO_2$ (p<0.0001), than patients who were not intubated. 2. Patients with complete injuries were intubated significantly more than

	Outcome Measures: The following retrospectively: ratio of arterial oxygen partial pressure to fractional inspired oxygen (PaO_2/FiO_2), partial pressure of carbon dioxide in arterial blood ($PaCO_2$), arterial pH, injury severity, level of injury. **Chronicity:** Time since injury not specified.	patients with incomplete injuries (p=0.011). 3. Patients with a higher level of cervical SCI were intubated significantly more than patients with a lower level of cervical SCI (p=0.002).

Discussion

A cohort study found that intubation significantly reduced the ratio of arterial oxygen partial pressure to fractional inspired oxygen (Iwashita et al. 2006), as well the need for intubation was higher in patients with complete injuries. This is significant as acute lung injury (ALI) is present when the ratio of arterial oxygen partial pressure to fractional inspired oxygen is <300, and acute respiratory distress syndrome (ARDS) is present when it is <200. Several observational studies have found similar results in terms of people with complete injuries requiring higher rates of intubation (Como et al. 2005; Velmahos et al. 2003; Seidl et al. 2010).

Conclusion

There is level 2 evidence (from one cohort study: Iwashita et al. 2006) that patients with acute SCI who are intubated may have reduced ratios of arterial oxygen partial pressure to fractional inspired oxygen compared to no intubation.

Intubation can reduce arterial oxygen partial pressure ratios in people with acute SCI.

5.2 Tracheostomy

Between 21% and 77% of patients with cervical SCI require a tracheostomy, with the variability of these numbers being due to the influence of several factors (e.g., severity of the injury, presence of other injuries, admission Glasgow Coma Scale score, age, etc.) (Branco et al. 2011; Como et al. 2005). The interactions of these other parameters make it difficult to establish clear criteria for who should receive a tracheostomy. Identifying when a tracheostomy should be performed is also important to determine, as timing

may impact a patient's recovery with regard to developing complications and weaning from ventilation. In a systematic review of non-SCI patients who required tracheostomies, Griffiths et al. (2005) concluded that patients who received an ET did not experience fewer complications but did experience a shorter duration of MV. The timing of tracheostomy following spinal fixation should also be considered. Currently, the typical time is 1-2 weeks post-surgery, but this timing lacks conclusive evidence (Galeiras Vázquez et al. 2013). In addition to who should receive a tracheostomy and when it should be performed, there is also controversy surrounding whether tracheostomies are always beneficial, effective in ventilator weaning, and result in a reduced number of pulmonary complications. In fact, complications resulting from tracheostomies, such as tracheal stenosis, occur in up to 6% of patients (Lissauer 2013), so the risks and benefits must be evaluated. Other complications have been reported to include tightness at the scar location, difficulty swallowing, and cosmetic inconveniences (Biering-Sorensen & Biering-Sorensen 1992). Several studies have retrospectively examined the predictors for needing a tracheostomy and complications associated with the procedure; these are presented in Table 4.

There are two techniques for tracheostomy: surgical (open) and percutaneous. Surgical tracheostomy (ST) is the traditional technique that requires opening the entire trachea to insert the tube. Percutaneous tracheostomy is an alternative procedure that was first developed in the late 1950s and can be performed at the patient's bedside with fewer materials (Gysin et al. 1999). Percutaneous tracheostomy is less invasive and involves inserting a tracheostomy tube through the skin without directly visualizing the trachea. Due to its less invasive nature, this procedure was thought to be associated with fewer complications and infections, although this relationship is unclear (Gysin et al. 1999). Patients who require a tracheostomy have been shown to have longer lengths of stay in hospitals and greater health care costs (Winslow et al. 2002).

Several studies have investigated factors associated with needing a tracheostomy in patients with acute SCI, such as higher injury severity and complete lesions (Leelapattana et al. 2012; Long et al. 2022; McCully et al. 2014; Menaker et al. 2013; O'Keeffe et al. 2004; Yugue et al. 2012), as well as a cervical level of injury (Biering-Sorensen & Biering-Sorensen 1992; Long et al. 2022; McCully et al. 2014; Mu & Zhang 2019; Romero-Ganuza et al. 2011a; Seidl et al. 2010; Yugue et al. 2012). Other reported factors include older age (Harrop et al. 2004; Mu & Zhang 2019; Yugue et al. 2012) and a lower ASIA motor grade upon hospital admission (Menaker et al. 2013).

Table 4. Evaluation of the use of Tracheostomy During Acute Hospitalization

Author Year Country Research Design Score Sample Size	Methods	Outcome
Sustic et al. 2002 Croatia RCT PEDro = 3 Level 2 N = 16	**Population:** Age range: 19-59 yr; Gender: male=13, female=3; Level of injury: C3-C6; Severity of injury: not specified. **Intervention:** Patients were randomized to receive either a surgical tracheostomy (ST) or an ultrasound-guided percutaneous dilational tracheostomy (PDT). **Outcome Measures:** The following post procedure: incidence of complications, duration of procedure. **Chronicity:** Time since injury not specified. Average ICU LOS=22 days (ST) and 20 days (PDT).	1. No patients experienced any major complications due to either tracheostomy procedure. 2. The duration of the PDT procedure was significantly shorter than the duration of the ST procedure ($p<0.05$).
Leelapattana et al. 2012 Canada Cohort Level 2 N = 66	**Population:** Mean age: 38 yr; Gender: male=50, female=16; Level of injury: C4-C7; Severity of injury: complete=12, incomplete=45. **Intervention:** Patients either received a tracheostomy or did not. **Outcome Measures:** The following at discharge: duration of MV, injury severity score (ISS). The following after three days of ventilation: ratio of arterial oxygen partial pressure to fractional inspired oxygen. **Chronicity:** Patients included in the study were within 24 hr of sustaining	1. Patients who had a tracheostomy had a significantly lower motor score at discharge ($p=0.04$), a longer hospital stay ($p<0.001$), a longer ICU stay ($p=0.002$), and required MV for longer ($p=0.001$) compared to patients who did not have a tracheostomy. 2. Patients who had a tracheostomy had fewer pulmonary complications ($p=0.001$) and fewer cases of death ($p=0.025$) than patients who did not have a tracheostomy. 3. ET correlated to fewer days on ventilation ($p=0.038$) and fewer days

	injury upon hospital admission.	spent in the hospital (p=0.004) compared to LT. 4. The number of days spent in hospital increased by 2.3 days for every additional day from injury to tracheostomy (p<0.001). 5. An ISS score >32, complete SCI, and a PF ratio <300 on day 3 of ventilation were predictors for requiring MV for greater than 7 days.
Romero-Ganuza et al. 2011a Spain Cohort Level 2 N = 28	**Population:** Mean age: 40 yr; Gender: male=23, female=5; Level of injury: cervical; Severity of injury: complete=21, incomplete=7; AIS A-C. **Intervention:** All patients received a percutaneous tracheostomy following anterior cervical spine fixation. **Outcome Measures:** Timing of tracheostomy, neurological deterioration, incidence of complications. **Chronicity:** The mean time from injury to fixation surgery was 2.25 days. The mean time from surgery to tracheostomy was 8.25 days.	1. Patients received a tracheostomy an average of 8.25 days after they received spinal fixation surgery. Tracheostomy was performed within 6 days or less in 42.9% (12/28) of cases. 2. No patients experienced neurological deterioration as a result of spinal surgery or tracheostomy procedure. 3. No patient experienced an infection at the cervical fixation wound, however, 10.7% (3/28) of patients experienced minor complications at the tracheostomy site. 4. The authors note that tracheostomy quickly performed after fixation surgery does not increase the rate of surgical wound infection.
McCully et al. 2014 USA Case control Level 3 N = 256	**Population:** Mean age: 46 yr; Gender: male=192, female=64; Level of injury: C1-T3; Severity of injury: complete=77, incomplete=179.	1. Patients who received a tracheostomy had more days on a ventilator than patients who did not receive a tracheostomy (p<0.05). 2. The occurrence of complete injury and

	Intervention: Patients either received a tracheostomy or did not. **Outcome Measures:** The following retrospectively: number of days on ventilator, severity of injury. **Chronicity:** Time since injury not specified. Median hospital LOS was 7 days (no tracheostomy) and 33 days (tracheostomy).	intubation was higher in patients who received a tracheostomy ($p<0.05$) than patients who did not.
Berney et al. 2011 Australia Case control Level 3 N = 114	**Population:** Mean age: 32 yr; Gender: male=86, female=28; Level of injury: C0-C8; Severity of injury: complete=72, incomplete=42; AIS A-D. **Methods:** Patients who were extubated were compared to patients who received a tracheostomy. **Outcome Measures:** The following during hospital stay: pulmonary secretion production, number of associated injuries, mental state, ASIA score, ratio of arterial oxygen partial pressure to fractional inspired oxygen, FVC. **Chronicity:** Time since injury not specified.	1. Patients with a tracheostomy produced significantly more pulmonary secretions ($p=0.003$), had significantly more associated injuries ($p=0.02$), had a more alert mental state ($p=0.005$), and had more complete injuries ($p=0.026$) compared to patients who were extubated. 2. Patients with a tracheostomy had significantly lower gas exchange ($p=0.02$) and FVC ($p<0.001$) than patients who were extubated.
Berney et al. 2008 Australia Case control Level 3 N = 71	**Population:** Mean age: 40 yr; Gender: male=46, female=25; Level of injury: C1-C8; Severity of injury: complete=45, incomplete=26; AIS A-D. **Intervention:** Patients either received tracheostomy following anterior cervical spine fixation or posterior spine fixation (control group). **Outcome Measures:** The following retrospectively: timing of the tracheostomy	1. There were no significant differences between the timing of tracheostomy in patients who received it after anterior cervical spine fixation compared to patients who received it after posterior fixation ($p=0.09$). 2. 24% (17/71) of patients developed an infection at the tracheostomy site or cervical site. Patients who

	since surgery, prevalence of infection. **Chronicity:** The median time from injury to stabilization surgery was 3 days. The mean time from surgery to tracheostomy was 3.8 days (anterior fixaton) and 3.1 days (posterior fixation).	received a tracheostomy after posterior fixation developed significantly more incision site infections than patients who received a tracheostomy after anterior fixation ($p<0.05$).
Berney et al. 2002 Australia Case control Level 3 N = 14	**Population:** Mean age 28 yr; Gender: male=11, female=3; Level of injury: cervical; Severity of injury: complete. **Intervention:** Patients who received a tracheostomy were compared to patients who were extubated and received physiotherapy. **Outcome Measures:** The following at the time of extubation/the day of tracheostomy: FVC, PaO_2/FiO_2, total number of physiotherapy treatments, number of physiotherapy treatments in ICU, LOS in ICU, days requiring MV, LOS in acute ward after discharge from ICU, days from injury to fixation. **Chronicity:** The mean time from injury to fixation was 1.9 days.	1. There was no significant difference in FVC between tracheostomized patients and physiotherapy patients ($p>0.05$). 2. There was no significant difference in PaO_2/FiO_2 ratios between tracheostomized patients and physiotherapy patients ($p>0.05$). 3. There was no significant difference in total number of physiotherapy treatments between tracheostomized patients and extubated patients. Patients who were extubated and received physiotherapy required significantly fewer treatments compared to tracheostomized patients in ICU ($p=0.047$). 4. Tracheostomized patients spent significantly more days in ICU than physiotherapy patients ($p=0.006$) and required MV for significantly longer than the physiotherapy group ($p=0.018$). 5. There was no significant difference in the LOS in the acute ward between groups ($p>0.05$).

		6. There was no significant difference in the time from injury to fixation between groups (p>0.05).
Kornblith et al. 2014 USA Case series Level 4 N = 344	**Population:** Mean age: 43 yr; Gender: male=275, female=69; Level of injury: cervical to lumbar; Severity of injury: complete=69, incomplete=275. **Intervention:** Patients either had a tracheostomy or did not. In addition, patients were either mechanically ventilated at discharge or were not. **Outcome Measures:** The following retrospectively: instances of prolonged MV, ventilator-associated pneumonia (VAP), acute lung injury (ALI), duration in ICU, duration in hospital, number of ventilator-free days, extubation attempts, ISS. **Chronicity:** Time since injury not specified. Average number of hospital days=20.	1. Patients who received a tracheostomy were associated with a 14.1-fold higher odds of requiring prolonged MV (p<0.05) compared to patients who did not receive a tracheostomy. 2. Patients who received a tracheostomy had fewer ventilator-free days (p<0.05) compared to patients who did not receive a tracheostomy. 3. Patients who had a tracheostomy required MV at discharge more often than patients who did not have a tracheostomy (p<0.05). 4. Patients who required MV at discharge had a higher ISS (p<0.05), significantly higher rates of VAP (p<0.05) and ALI (p<0.05), and longer ICU (p<0.05) and hospital stays (p<0.05) compared to patients who did not require MV at discharge.
O'Keeffe et al. 2004 USA Case series Level 4 N = 17	**Population:** Mean age 43 yr; Gender: male=12, female=5; Level of injury: cervical; Severity of injury: not specified. **Intervention:** All patients received a tracheostomy following anterior cervical spine fixation. **Outcome Measures:** The following after tracheostomy: neurologic deterioration,	Overall Analyses: 1. No patients experienced neurologic deterioration after tracheostomy following spine fixation. 2. No patients developed infections at the anterior cervical fusion site following tracheostomy. 82% (14/17) patients developed pneumonia. There were no deaths

	incidence of complications, mortalities, injury severity. **Chronicity:** Time since injury not specified.	related to airway difficulties. Analyses of entire population of patients with cervical SCI, including patients that did not receive an anterior cervical spine fixation (N=60): 3. The need for a tracheostomy correlated with injury severity ($p<0.001$) with ASIA level A and B patients requiring the most tracheostomies.
Quesnel et al. 2015 France Retrospective review Level 4 N = 108	**Population:** N=108 patients with cervical SCI and tetraplegia (86M, 22F). Mean (SD) age: 49.0 (21.1) years. 51 AIS-A, 22 AIS-B, 19 AIS-C, 10 AIS-D (out of 103 patients). **Treatment:** Tracheostomy (44/108 patients). **Outcome Measures:** Institutionalization status, decannulation status, length of treatment.	1. Out of 44 tracheotomized patients, 25 decannulated at mean of 84.1(59.1) days; 12 expired; 7 could not be weaned (3 of which expired at a mean treatment duration of 202.3(121.7) days; the others have had 727.7(283.6) days of treatment at end of study). 2. At end of study, 9 patients definitively institutionalized, 61 returned home.

Discussion

Tracheostomy is believed to facilitate weaning because it reduces the effort required to breathe (Peterson et al. 1994). Several studies examined the effect of tracheostomy on duration of MV. Among studies that did not stratify for time, tracheostomy was consistently reported to prolong MV (Berney et al. 2002; Leelapattana et al. 2012; McCully et al. 2014).

The influence of tracheostomy procedures on the development of respiratory complications has also been examined by a number of studies. Patients with tracheostomies reportedly have fewer pulmonary complications compared to patients without tracheostomies (Leelapattana et al. 2012). Regarding type of tracheostomy, Sustic et al. (2002) compared percutaneous dilatational tracheostomy (PDT) with ST, investigating the development of perioperative and postoperative complications associated with each procedure. The authors found that no patients, regardless of intervention received,

developed any major complication in relation to tracheostomy; however, the PDT was a significantly shorter procedure. Kornblith et al. (2014) found that patients who received a tracheostomy were associated with a 14-times higher odds of requiring prolonged MV compared to patients who did not receive a tracheostomy ($p<0.05$).

Conclusion

There is level 2 evidence (from one RCT: Sustic et al. 2002) that percutaneous dilatational tracheostomies have a significantly shorter procedure time and result in fewer pulmonary complications compared to surgical tracheostomies for people with acute SCI.

There is level 2 evidence (from one cohort study: Leelapattana et al. 2012) that tracheostomies can reduce the number of pulmonary complications in people with acute SCI compared to late or no tracheostomy.

There is level 2 evidence (from one cohort study: Romero-Ganuza et al. 2011a) that tracheostomies performed directly after spinal fixation surgery do not increase the rate of surgical wound infection compared to non-immediate tracheostomies in people with acute SCI.

There is level 3 evidence (from one case control study: McCully et al. 2014; and one case series: Kornblith et al. 2014) that people with acute SCI who receive a tracheostomy may spend more days on a ventilator than those who do not receive a tracheostomy.

There is level 3 evidence (from one case control study: Berney et al. 2011) that people with acute SCI who receive a tracheostomy may have more pulmonary secretions, lower gas exchange, and lower FVC compared to those who are extubated.

There is level 4 evidence (from one case series: O'Keeffe et al. 2004) that tracheostomies in people with acute SCI do not appear to increase the risk for neurologic deterioration or surgical site infection.

Tracheostomies can reduce the number of pulmonary complications in people with acute SCI compared to those not receiving this procedure, and they may result in reduced FVC and lower gas exchange compared to extubation.

Tracheostomies are associated with an increase in the number of days that people with acute SCI spend on ventilators.

5.3 Comparative or Combination Interventions

There are limited studies examining combinations of interventions for the improvement of respiratory function post SCI. However, of those that meet the SCIRE inclusion criteria, the primary focus is on the type of ventilation received by patients: multiple, singular, or none.

Table 5. Comparative or Combination Interventional Studies for Respiratory Function During Acute SCI

Author Year Country Research Design Score Sample Size	**Methods**	**Outcome**
Gregoretti et al. 2005 Italy Prospective controlled trial Level 2 N = 10	**Population:** Mean age: 34 yr; Gender: male=10, female=0; Level of injury: C4-C6; Severity of injury: not specified. **Intervention:** Patients first received endotracheal invasive ventilation (EIV) for 1-15 days and then later received transtracheal open ventilation (TOV) for 1 day. **Outcome Measures:** The following during EIV treatment, at 1-hr post TOV treatment, and 24 hrs post TOV treatment: PaO_2/FiO_2, arterial blood gas analysis in the form of partial pressure of inspired oxygen in arterial blood (PaO_2), partial pressure of carbon dioxide in arterial blood ($PaCO_2$), Respiratory rate, pressure within the distal trachea, pressure-time product of esophageal pressure. **Chronicity:** Time since injury not specified.	1. There were no significant differences between the EIV treatment and the TOV treatment with regards to PaO_2/FiO_2, PaO_2, respiratory rate, and pressure within the distal trachea ($p>0.05$). 2. Patients had a significantly lower $PaCO_2$ while receiving EIV compared to 1 hr post TOV and 24 hr post TOV ($p<0.0001$). 3. Patients had a significantly lower pressure-time product of esophageal pressure after 24 hr of receiving TOV compared to 1 hr post TOV and during EIV ($p<0.05$).
Hatton et al. 2021	**Population:** 181 patients with acute SCI who were admitted to a level 1 trauma center	1. Patients who received HVtV were more likely to develop VAP and require a

USA Case control Level 3 N = 181	receiving ventilation and were retrospectively divided in two groups based on the maximum Vt received (calculated as cc/kg of predicted body weight (PBW)): • Standard Vt (n = 159): 126 males and 33 females; median age 53 years; complete (n = 61) and incomplete SCI (n = 98); and injury level C1 (n = 11), C2 (n = 26), C3 (n = 24), C4 (n = 33), C5 (n = 42), C6 (n = 18), and C7 (n = 5). • HVtV (n = 22): 17 males and 5 females; median age 40 years; complete (n = 16) and incomplete SCI (n = 6); and injury level C1 (n = 2), C2 (n =3), C3 (n = 3), C4 (n = 6), C5 (n = 5), and C6 (n = 3). **Intervention:** Standard Vt: < 10cc/kg PBW. HVtV: >10cc/kg PBW. **Outcome Measures:** VAP, ventilator dependence at discharge, and in-hospital mortality. **Chronicity:** Acute SCI, time since injury not specified.	tracheostomy than those who received standard Vt: a. HVtV was associated with an estimated relative risk of 1.96 (95% credible interval 1.55–2.17) and a >99% posterior probability that HVtV increases VAP. b. Complete injury, high SCI level, low ISS, older age, and blunt injury mechanism were associated with increased VAP development. 2. Hospital-Free Days and Vent-Free Days were similar between groups but patients with HVtV were more likely to be discharged to a Skilled Nursing Facility or to Rehabilitation. 3. Regarding the outcome of ventilator dependence at 30 days or hospital discharge (n = 79): a. HVtV was associated with a relative risk of 2.07 (95% credible interval 1.48– 2.71) and a posterior probability of >99% that HVtV increases ventilator dependence. b. Higher injury level, complete injury, older age, higher injury severity score, and earlier year of care were associated. 4. Regarding the composite outcome of VAP or mortality (n = 97): a. On Bayesian analysis, HVtV was associated with a relative risk of 1.29

		(95% credible interval 0.86–1.71) and a posterior probability of 91% that HVtV increases VAP or mortality. b. Complete injury, high SCI level, high ISS, older age, and blunt injury mechanism were also associated. 5. Regarding to in-hospital mortality (n = 22): a. HVtV was associated with a relative risk of 1.03 (95% credible interval 0.26–2.76) for mortality, and a 52% posterior probability that HVtV increases mortality. b. Variables associated with increased mortality included high injury level, complete injury, high ISS, older age, blunt mechanism of injury, and earlier year of care.
Korupolu et al. 2021 USA Case control Level 3 N = 84	**Population:** 84 patients with acute SCI who received MV with a tracheostomy in an acute inpatient rehabilitation (AIR) facility were retrospectively divided in two groups based on the maximum Vt received (calculated as ml/kg of predicted body weight (PBW)): • Moderate Vt (MVt) (n = 50): 41 males and 9 females; median (IQR) age 33 (21-56); median (IQR) time since SCI to AIR hospital admission 22 (17-39) days; AIS A (n = 30), AIS B (n = 9), AIS C (n = 7), AIS D (n = 2), and unknown (n = 2); neurological level C1-C3 (n	1. HVt group had increased incidence (4.3 times higher, 95% CI: 1.5-12) and the risk of pneumonia compared to MVt group. 2. Higher VC at admission was associated with lower risk of pneumonia, and an increment in VC on admission by 1 ml/kg PBW was associated with 10% decreased risk of developing pneumonia (RR: 0.9, 95% CI: 0.83–0.98). 3. Incidence and odds of the composite outcome of pulmonary adverse events were higher in HVt group compared to MVt group

	= 22), C4-C6 (n = 25), T2-T4 (n = 2), and unknown (n = 1). • Higher Vt (HMt) (n = 34): 24 males and 10 females; median (IQR) age 43 (26-59); median (IQR) time since SCI to AIR hospital admission 25 (18-34) days; AIS A (n = 19), AIS B (n = 7), AIS C (n = 7), AIS D (n = 0), and unknown (n = 1); neurological level C1-C3 (n = 11), C4-C6 (n = 22), T2-T4 (n = 0), and unknown (n = 1). **Intervention:** MVt: Received <15ml/kg PBW. HVt: Received >15 ml/kg PBW. **Outcome Measures:** Incidence of pneumonia occurring at least 48h after admission to AIR or if diagnosed within 48 h of transfer from AIR to the acute care hospital due to respiratory complications, composite pulmonary adverse events, AIR preweaning days (defined as time from AIR admission to beginning of weaning), weaning days, AIR ventilator days (calculated as days on ventilator from AIR admission to discharge), the days that lapsed due to an acute care transfer for any acute emergencies during their stay in AIR facility, data on improvement in Vt, peak pressures, discharge location and AIR admission to discharge days. **Chronicity:** Mean time since injury 23.5 days).	with OR of 5.4 (95% CI: 1.8–17). 4. Regression analysis with Vt as continuous outcome revealed that for every 1 ml/kg PBW increment in Vt, risk of pneumonia increased by 28% (RR: 1.28, 95% CI: 1.1–1.6) and odds of the composite outcome of developing any pulmonary adverse events increased by 42% (OR: 1.4, 95% CI: 1.1–1.8). 5. 87% of patients were successfully weaned off MV with no significant difference between groups. Reason for failure to wean off ventilator was low VC of <12 ml/kg PBW for all except two patients in HVt group who failed to wean in spite of VC of 14 and 35 ml/kg PBW at the time of discharge from AIR, and anxiety. 6. There was no statistical difference in days from time of SCI to time of admission to AIR facility, AIR preweaning days, ventilator weaning days, AIR ventilator days, and AIR admission to discharge days between the two groups. However, higher VC at admission was associated with lower AIR preweaning and AIR ventilator days. 7. In MVt group, 80% were discharged to home compared to 65% in HVt group (p = 0.04).
Zakrasek et al. 2017 USA	**Population:** 36 patients with ventilator-dependent tetraplegia following an acute traumatic cervical SCI, history	1. 33/36 patients achieved 16 h VFB and 20/36 achieved 24 h VFB, representing high

Case control Level 3 N = 36	of tracheostomy and being weaned off ventilator support; 29 males and 7 females; AIS A (n = 30) and AIS B (n = 6); and level of injury C1 (n= 2), C2 (n = 5), C3 (n = 11), C4 (n = 14) and C5 (n = 4). **Treatment:** Patients received pulmonary management using a combination of high tidal volume (HTV) ventilation, high-frequency percussive ventilation and mechanical insufflation–exsufflation techniques (see above: Wong et al. 2012); and (recent) administration of oral theophylline during ventilator weaning. Patients were retrospectively divided into those who received theophylline (200-300 mg per day for ≥ 7 days) (n = 15) or not (n = 21). **Outcome Measures:** The ability to wean off the ventilator for all waking hours (16 h of VFB), complete liberation from the ventilator (24 h of VFB), time from injury to first attempt to breathe without ventilator support (initiation of VFB), time from injury to 16 h of VFB, time from injury to 24 h of VFB, time from injury to decannulation, change in FVC during admission, and adverse effects. **Chronicity:** Median (range) time from injury to admission 25.5 (3-54) days.	rates of successful ventilator weaning. 2. Success in ventilator liberation was strongly correlated with level of injury for 16h of VFB (P = 0.0082) and 24h of VFB (P = 0.0003), and with first FVC for 24h of VFB (P = 0.0110); and moderately associated with gender and age for 16h of VFB (P = 0.0309) and for 24h of VFB (P = 0.0383). 3. Among those treated with theophylline ≥ 7 days, medication was discontinued in six cases due to adverse events including loose stool, increased anxiety, acute interstitial nephritis, and concern of increased risk of arrhythmia. 4. Univariate analysis of theophylline's impact on ventilator weaning rates was underpowered to determine effect and did not reach statistical significance.
Watt et al. 2011 UK Case control Level 3	**Population:** Mean age: 32 yr; Gender: male=163, female=26; Level of injury: C1-S5; Severity of injury: complete=136, incomplete=53; AIS A-D.	1. Patients aged 31-35 who were weaned from the ventilator at discharge had a significantly higher mean

N = 189	**Intervention:** Patients were either weaned from ventilation at discharge or remained on ventilation at discharge. Among those who required MV, some patients also used diaphragm pacing. Patients were further stratified by age 0-30 yr, 31-45 yr, and 46+ yr. **Outcome Measures:** Mean survival time. **Chronicity:** Time since injury not specified. The date of ventilation was within a few days of injury.	survival time than patients who still required ventilation at discharge (p=0.047). There were no significant differences in survival times in the other age groups. 2. Among those who required MV at discharge, patients who used diaphragm pacing had a significantly better survival than the group who only used MV (p<0.05).
Romero-Ganuza et al. 2011b Spain Case control Level 3 N = 323	**Population:** Mean age: 42 yr; Gender: male=255, female=68; Level of injury: cervical to thoracic; Severity of injury: complete=229, incomplete=94. **Intervention:** Patients either received a tracheostomy or did not. Of those who did, they either received a ST or a percutaneous tracheostomy. They also either received an early tracheostomy (ET) (≤7 days post intubation) or a late tracheostomy (>7 days post intubation). **Outcome Measures:** The following during hospital stay: incidence of tracheostomy, incidence of complications. **Chronicity:** Mean interval from injury to admission=11.4 days.	1. There were 69 cases of perioperative complications following tracheostomy. Patients who received an ET had significantly fewer cases of tracheal stenosis than patients who received a LT (p=0.003). There were no significant differences in pneumonia (p=0.81), stomal cellulitis (p=0.45), bleeding (p=0.96), or mortality rate (p=0.22) between the two groups. 2. Patients who received a percutaneous tracheostomy experienced fewer cases of pneumonia (p=0.011) compared to patients who received a ST.
Duarte et al. 2021 Brazil Case series Level 4 N = 10	**Population:** 10 ICU patients submitted to tracheostomy due to cervical SCI (AIS A); 8 males and 2 females; and mean age 28.5 years. **Treatment:** Patients were submitted to transcutaneous electrical diaphragmatic	1. Total IMV time in the TEDS and the SWP group was 33 ± 15 and 60 ± 22 days, respectively (1.77 times shorter in TEDS than in SWP group). 2. Overall stay LOS in the TEDS and the SWP group was 60

	stimulation (TEDS) combined with standard weaning protocol (SWP) (n = 4) or SWP alone (n = 6). TEDS training consisted of two daily 20-min sessions 7 days a week. **Outcome Measures:** Time of invasive mechanical ventilation (IMV) via orotracheal tube, time of IMV via tracheostomy, ventilator WT, total IMV time, ICU LOS, overall hospital LOS, Sepsis-related Organ Failure Assessment (SOFA), and Acute Physiology and Chronic Health Evaluation (APACHE II) scores. **Chronicity:** Patients admitted in ICU; time since injury not specified.	± 32 and 81 ± 44, respectively. 3. LOS in ICU in the TEDS and the SWP group was 31 ± 18 and 63 ± 45 days, respectively (2.54 times shorter in patients in TEDS than in SWP group).
Kaufman et al. 2022 USA Pre–post Level 4 N = 10	**Population:** 10 patients with ventilator-dependent cervical tetraplegia and ASIA A, 7 males and 3 females, mean age 28 (16-47) years, average time from injury 17 (1 – 48) months, and failed prior attempts at non-invasive ventilation and weaning protocols. **Intervention:** The treatment protocol included a surgical algorithm that involved diaphragm pacing, phrenic nerve reconstruction, and diaphragm muscle replacement. Treatment selection was based upon the extent of neuromuscular dysfunction, prior failed attempts at pacemaker implantation, and duration of paralysis: • Group I - Pacemaker alone (n = 2).	1. Partial weaning (4/10) or CW (4/10) was achieved in 80% of patients whereas the remaining two patients (Group II) have demonstrated ↓VR without weaning (NC) as of the most recent follow-up (<1 year). 2. The mean duration from surgery to observed ↓VR was 4 months, and the overall mean follow-up was 23 months (range = 6–58 months). 3. Complications consisted of one patient who developed post-operative mucous plugging managed conservatively, and three patients who required pacemaker lead or receiver replacement due to malposition or malfunction.

	• Group II - Pacemaker + phrenic nerve reconstruction (n = 6). • Group III - Pacemaker + diaphragm muscle replacement (n = 2). **Outcomes Measures:** Time from surgery to observed reduction in ventilator requirements (↓VR), specific ventilatory needs as of most recent follow-up [no change (NC), partial weaning = 1–12 h/day without MV), or complete weaning (CW ≥ 12 h/day without MV)], and complications.	
Roquilly et al. 2014 France Retrospective multicenter review Level 4 N = 164	**Population:** 164 patients with acute traumatic and tetraplegic SCI from ICU (125M 76F) Median age (IQR): 44(27-59) AIS-A/B/C/D/E: 102/21/25/13/1 Median lesion level (IQR): C5(C4-C6). **Treatment:** MV. **Outcome Measures:** Duration of MV, ASIA motor score. **Chronicity:** Patients with acute traumatic SCI from ICU.	1. "The duration of MV was associated with ISS, medical history of respiratory failure, tracheal intubation, tracheotomy, hospital-acquired pneumonia, atelectasis, Vt in the first 24 hours, and PEEP (lower positive end-expiratory pressure) in the first 24 hours" (p313.e9). 2. "The duration of MV was positively associated with hospital-acquired pneumonia, lung atelectasis, and tracheotomy" (p313.e10).

Discussion

The systematic review of Berney et al. (2011) assessed 21 studies and showed reduction in mortality, respiratory complications, and need for tracheostomy when an acute SCI respiratory protocol with a combination of treatment techniques was followed. Authors cautioned that further studies using specific interventions and more rigorous research designs were required.

A case control study by Watt et al. (2011) determined that patients who used diaphragm pacing with MV compared to those who only had MV had significantly higher survival rates. Of those patients between the ages of 31-35 years, those who were weaned from a ventilator before discharge

experienced higher rates of survival compared to those that were not weaned from a ventilator before discharge (Watt et al. 2011). Duarte et al. (2021) showed that total INV duration, overall length of stay (LOS), and LOS in intensive care unit (ICU) were shorter in patients who received transcutaneous electrical diaphragmatic stimulation (TEDS), combined with a standard weaning protocol.

With respect to other respiratory parameters, when comparing endotracheal invasive ventilation (EIV) with transtracheal open ventilation (TOV), there were no significant differences in partial pressure of oxygen between the two treatment types, although patients did have a significantly lower partial pressure of carbon dioxide with EIV (Gregoretti et al. 2005).

Romero-Ganuza et al. (2011b) examined timing, type, and presence of tracheostomies in patients with acute SCI. Of those who received an ET there were fewer cases of tracheal stenosis compared to late tracheostomy (LT). The type of tracheostomy that patients received also resulted in significant differences, where patients who had a percutaneous tracheostomy experienced fewer cases of pneumonia compared to ST.

Methylxanthines such as theophylline have been used in respiratory dysfunction since the 1920s (Schultze-Werninghaus & Meier-Sydow 1982); and the earliest published use of methylxanthines for respiratory dysfunction in SCI was about 40 years later (Segal et al. 1986). Theophylline has three primary modes of action in the treatment of pulmonary dysfunction including bronchodilation, anti-inflammation and improved diaphragmatic contractility (Zakrasek et al. 2017); and specifically, in cervical SCI, theophylline has an additional proposed mechanism of improving pulmonary function, namely activation of a latent crossed phrenic pathway by adenosine receptor antagonism (Nantwi & Goshgarian 2005). Zakrasek et al. (2017) found a strong correlation of ventilator liberation in the first 24 hours with level of injury (C3-C5) and a moderate correlation with gender and age when theophylline was added as an experimental variable (though six participants had adverse events with the drug).

Kaufman et al. (2022) prospectively studied a treatment protocol using a surgical algorithm involving diaphragm pacing, phrenic nerve reconstruction, and diaphragm muscle replacement. They analyzed 10 ventilator dependent cervical ASIA A patients, who received different treatments based on the extent of neuromuscular dysfunction (pacemaker alone, pacemaker + phrenic nerve reconstruction or pacemaker + diaphragm muscle replacement), showing four patients who achieved a partial weaning and four a complete weaning (CW).

Korupolu et al. (2021) retrospectively analyzed 84 patients with acute SCI receiving MV with a tracheostomy if they underwent moderate Vt (<15ml/kg PBW) or higher Vt (>15ml/kg PBW) during their stay in an inpatient

rehabilitation facility. Overall, 87% of patients were successfully weaned off MV with no significant difference between groups. On the other hand, they showed that the HVt group had increased incidence and the risk of pneumonia and other adverse events compared to the MVt group. More precisely, for every 1 ml/kg PBW increment in Vt, risk of pneumonia increased by 28% and odds of the composite outcome of developing any pulmonary adverse events increased by 42%. In the same way, Hatton et al. (2021) retrospectively analyzed 181 patients with acute SCI receiving ventilation if they underwent standard Vt (< 10 cc/kg PBW) or HVtV (> 10 cc/kg PBW) during their stay in a level 1 trauma center. While hospital-free days and vent-free days were similar between groups, patients who received HVtV were more likely to develop VAP and require a tracheostomy than those who received standard Vt. Both Hatton et al. (2021) and Korupolu et al. (2021) highlighted that these were the first studies to investigate the association between tidal volumes on rates of VAP, pneumonia, and other undesirable respiratory outcomes in an acute inpatient as primary outcomes, reporting findings contrary to the accepted guidelines for ventilator weaning in SCI.

Conclusion

There is level 2 evidence (from one prospective controlled trial: Gregoretti et al. 2005) that EIV may lower partial pressure of carbon dioxide compared to TOV in patients with acute SCI.

There is level 3 evidence (from one case control study: Watt et al. 2011) that diaphragm pacing in combination with MV may result in higher survival than MV alone in acute SCI populations.

There is level 4 evidence (from one retrospective case series: Duarte et al. 2021) that implementation of TEDS combined with standard weaning protocol shortened the time of IMV, overall stay LOS and ICU LOS compared to the implementation of standard weaning protocol alone in tracheostomized SCI participants.

There is level 3 evidence (from one case control study: Romero-Ganuza et al. 2011b) that percutaneous tracheostomies may result in fewer cases of pneumonia compared to surgical tracheostomies in participants with acute SCI.

There is level 3 evidence (from one case control study: Korupolu et al. 2021) that administration of high Vt (> 15ml/kg PBW) increased incidence and the risk of pneumonia and pulmonary adverse events compared to administration of moderate Vt (< 15ml/kg PBW), during MV in tracheostomized participants.

There is level 3 evidence (from one case control study: Hatton et al. 2021) that administration of high Vt (> 10 cc/kg PBW) increased the risk of ventilator-

associated pneumonia (VAP) compared to administration of standard Vt (< 10 cc/kg PBW), during MV in patients with acute cervical SCI.

There is level 3 evidence (from one retrospective analysis: Zakrasek et al. 2017) that the implementation of specialized respiratory management (HVtV, HFPV, MIE) provided high rates of ventilator weaning (100% for C4 and C5 AIS-A,B, 91 % C3 AIS-A,B).

There is level 4 evidence (from one pre-post study: Kaufman et al. 2022) that the implementation of a treatment protocol which included a surgical algorithm that involved diaphragm pacing, phrenic nerve reconstruction, and diaphragm muscle replacement provided a rate of 80% of successful weaning (40% partial weaning and 80% CW) in patients with ventilator-dependent cervical tetraplegia and ASIA A.

Diaphragm pacing in combination with MV can increase survival rates post SCI.

The implementation of TEDS combined with standard protocol can shorten the time of IMV, and hospital and ICU LOS in tracheostomized patients with SCI.

The implementation of a treatment protocol which includes a surgical algorithm that involve diaphragm pacing, phrenic nerve reconstruction and diaphragm muscle replacements provides a rate of 80% of successful weaning in ventilator-dependent patients with cervical and complete tetraplegia.

EIV can lower partial pressure of carbon dioxide in people with acute SCI.

Percutaneous tracheostomies may reduce rates of pneumonia when compared to surgical tracheostomies in people with acute SCI.

5.4 Timing of Mechanical Ventilation

Many recent studies have focused on patient outcomes based on when individuals received MV (Beom & Seo 2018; Flanagan et al. 2018; Choi et al. 2013). Some studies defined ET if it was performed in the first 4 days after patient admission or after initiation of MV (Wang et al. 2021; Anand et al. 2020; Wang et al. 2020), while the majority of studies considered ET if it was performed in the first 7 days (Flanagan et al. 2018; Beom & Seo 2018; Holscher et al. 2014; Romero-Ganuza et al. 2011b; Romero et al. 2009). There has been debate as to whether early tracheostomies result in better outcomes, fewer ventilator days, decreased rates of pneumonia, and even cognitive decline.

Mubashir et al. (2021) performed a systematic review with the aim of reviewing the optimal timing of tracheostomy. Among eight studies with a total sample size of 1,220 participants with SCI, ET was associated with a reduction of ICU LOS by 13 days and of MV by 18.30 days compared to LT. There were no significant differences in total pneumonia and mortality rates between groups. The study also showed that patients with cervical SCI were twice as likely to undergo ET compared to patients with thoracic SCI, and that patients with high cervical SCI were more likely to undergo ET compared to patients with low cervical SCI. Foran et al. (2021) performed a systematic review with the same objectives as Mubashir et al. (2021) and included 17 studies with a total sample size of 2072 patients. Compared with LT, ET was associated with a reduced mean duration of MV by 13.91 days, mean ICU LOS by 10.20 days, and mean hospital LOS by 7.39, and with a decreased incidence of VAP; but ET was not associated with short-term mortality.

Table 6. Evaluation of the Use of Early vs. Late Tracheostomy During Acute SCI

Author Year Country Research Design Score Sample Size	**Methods**	**Outcome**
Anand et al. 2020 USA Case control Level 3 N = 5980	**Population:** 5980 participants with traumatic cervical SCI; 4365 males and 1615 females; mean (SD) age 46 ± 22 years, median ISS 19 (10-28); high cervical SCI (C1-C4) (48%) and lower cervical SCI (C5-C7) (52%); 17% of patients had complete injury and 2.4% had central spinal cord syndrome. **Treatment:** Participants were divided in two groups based on the timing of performing tracheostomy: • ET: Performed from 1-4 days after intubation (n = 1010). • LT: Performed from day 5 after intubation (n = 4970). **Outcome Measures:** Respiratory complications, ventilator days, in-hospital	1. Compared with patients in the LT group, ET group patients had: a. Lower rates of respiratory complications (30% vs. 46%, p = 0.01). b. Higher ventilator-free days (13 days vs. 9 days, p = 0.02). c. ICU- free days (11 days vs. 8 days, p = 0.01). d. A shorter hospital LOS (22 days vs. 29 days, p = 0.01). 2. On regression analysis, after adjusting for measurable confounding factors: a. ET was associated with lower rates of respiratory complications in patients

	mortality, and ICU and hospital LOS. **Chronicity:** Time since injury was not specified.	with high CSCI (OR, 0.55 [0.41–0.81]) and low CSCI (OR, 0.93 [0.72–0.95]). b. No association was found between time to tracheostomy and in-hospital mortality (OR, 1.04 [0.95–1.49]).
Wang et al. 2021 China Case control Level 3 N = 124	**Population:** 124 patients with cervical SCI who underwent ACFS and received percutaneous tracheotomy after surgery in the ICU; 107 males and 17 females, mean (SD) age 43.20 (± 14.68) years; AISA A (n = 72), ASIA B (n = 27) and ASIA C (n = 15). **Treatment:** Patients were divided into three groups based on the timing of tracheotomy when they received: • Early group (≤4 days from initial intubation). • Medium group (4–10 days from initial intubation). • Late group (≥10 days from initial intubation). **Outcome Measures:** Mortality, ICU LOS, duration of ventilation, incidence of pneumonia after tracheotomy, Japanese Orthopedic Association (JOA) scores, Neck Disability Index (NDI), and radiographic parameters (maximum spinal cord compression (MSCC), and lesion length (LL)). **Chronicity:** Time since injury were not specified but patients were included if they had a diagnosis of acute cervical SCI.	1. There were no intergroup differences in the radiographic parameters. 2. The late group needed significantly longer duration of MV and longer ICU LOS than the early and medium groups (p ≤ 05). 3. Significantly less ICU mortality and pneumonia after tracheotomy in the early and medium groups was observed. 4. More patients in the early (84.78%) and medium (81.58%) groups successfully weaned from MV than late group (65.00%).
Wang et al. 2020	**Population:** 45 patients with acute cervical SCI who	1. Compared with the delayed tracheotomy, the ET

China Case control Level 3 N = 45	underwent tracheostomy and cervical internal fixation; 31 males and 13 females; mean age of 50.02 years (ranging from 26 to 69 years); ASIA A (n = 24), ASIA B (n = 13), ASIA C (n = 7), and ASIA D (n = 1); and injury level C1-C2 (n = 5), C3-C5 (n = 35), and C6-C7 (n = 5). **Treatment:** Patients were retrospectively divided in two groups: • ET (immediately after spine fixation) (n = 25). • Delayed tracheotomy (3-12 days after fixation) (n = 20). **Outcome Measures:** Total duration of MV, duration of MV after tracheotomy, duration of indwelling tracheal tube, hospital LOS, pneumonia, mortality, incision infection of anterior cervical spine internal fixation, and tracheotomy complications. **Chronicity:** Time since injury were not specified but patients were included if they had a diagnosis of acute cervical SCI.	significantly reduced the total duration of MV (p = 0.001), duration of MV after tracheotomy (p = 0.011), duration of indwelling tracheal tube (p = 0.011), and hospital LOS (p = 0.001). 2. There were no significant differences in pneumonia rate (p = 0.161), mortality rate (p = 0.192) and total complications (p = 0.057) between groups.
Beom & Seo 2018 Korea Case control Level 3 N = 48	**Population:** Mean age: 53.6 yr; Gender: male=43, female=5; Level of injury: N/R; Severity of injury: Mean ASIA impairment scale score (tracheostomy)=14.1 points, mean ASIA impairment scale score (non-tracheostomy)=23.4 points. **Intervention:** Patients either received an ET (within 7 days of initial SCI surgery) or a LT (after 7 days of initial SCI surgery) or no tracheostomy. **Outcome Measures:** Length of ventilation, ICU duration.	1. There were no significant differences in the duration of post-operative ventilation between early vs. late tracheostomy patients. 2. The ET group had a significantly shorter LOS in the ICU than the LT group (p=0.03).

	Chronicity: Time since injury not specified, patients were treated on average 29 days after initial SCI surgical intervention.	
Flanagan et al. 2018 USA Case control Level 3 N = 70	**Population:** Mean age: 50.5 yr; Gender: male=53, female=17; Level of injury: C2=10, C3=12, C4=19, C5=9, C6=6, C7=2; Severity of injury: Mean ISS=19.6; **Intervention:** Patients either received an ET (<7 days) or late (>7 days) from their initial intubation. **Outcome Measures:** Ventilator days, tracheostomy days, ICU LOS, early pneumonia and surgical site infections, in-hospital mortality, 90-day mortality, 90-day readmission. **Chronicity:** Patients are defined as being in the acute stage.	1. ET patients had fewer ventilator days compared to LT patients (p=0.028). 2. There was no significant difference in the number of days from tracheostomy to decannulation between early and LT patients. 3. Patients with ET had significantly fewer ICU stays (p=0.021). 4. There was no significant difference in the rates of early pneumonia and surgical site infections between the two groups, although both groups had high incidences. 5. There were no significant differences between groups in terms of in-hospital mortality, 90-day mortality, and 90-day readmission.
Kornblith et al. 2014 USA Case control Level 3 N = 344	**Population:** Mean age: 43 yr; Gender: male=275, female=69; Level of injury: cervical to lumbar; Severity of injury: complete=69, incomplete=275. **Intervention:** Patients either had a tracheostomy or did not. Of those requiring a tracheostomy, patients either experienced an ET or a LT. In addition, patients were either mechanically ventilated at discharge or were not. **Outcome Measures:** The following retrospectively: instances of prolonged MV, VAP, ALI, acute respiratory distress syndrome (ARDS),	1. Patients who received a tracheostomy had higher rates of VAP (p<0.05), higher rates of ALI (p<0.01), spent significantly more days in ICU (p<0.05) and hospital (p<0.05), and had fewer ventilator-free days (p<0.05) compared to patients who did not receive a tracheostomy. 2. There were no significant differences with regards to death (p>0.05) between patients who received a tracheostomy and patients who did not.

	duration in ICU, duration in hospital, number of ventilator-free days, extubation attempts, ISS. **Chronicity:** Time since injury not specified. Average number of hospital days=20.	3. Patients who had a LT had higher rates of VAP ($p<0.05$), ALI ($p<0.05$), and ARDS ($p<0.05$) compared to patients who had an ET. 4. Patients who required MV at discharge had a higher ISS ($p<0.05$), significantly higher rates of VAP ($p<0.05$) and ALI ($p<0.05$), and longer ICU ($p<0.05$) and hospital stays ($p<0.05$) compared to patients who did not require MV at discharge.
Choi et al. 2013 Korea Case control Level 3 N = 21	**Population:** Mean age: 50 yr; Gender: male=19, female=2; Level of injury: C1-C7; Severity of injury: complete=8, incomplete=13; AIS A-D. **Intervention:** Patients either received an ET (≤10 days after injury) or a LT (>10 days after injury). **Outcome Measures:** The following retrospectively: duration of MV. **Chronicity:** Time since injury not specified. Average number of hospital days=78.	1. Patients who received an earlier tracheostomy had a significantly shorter total ICU stay than patients who received a LT ($p=0.01$). 2. Patients who received an earlier tracheostomy experienced a significantly shorter duration of MV ($p=0.009$). 3. There were no significant differences with regards to pneumonia ($p=0.283$) or tracheal stenosis ($p=0.999$) between the two groups.
Babu et al. 2013 USA Case control Level 3 N = 20	**Population:** Mean age: 47 yr; Gender: male=18, female=2; Level of injury: cervical; Severity of injury: complete=11, incomplete=9; AIS A-E. Intervention: Patients either received an ET (≤6 days after anterior cervical spine fixation) or a LT (>6 days after anterior cervical spine fixation). **Outcome Measures**: The following retrospectively: length of hospital stay, incidence of complications, incidence and risk of complications.	1. Patients who underwent an ET had a shorter hospitalization stay compared to those who received a LT, but this difference was not significant ($p=0.11$). 2. One patient developed pneumonia after tracheostomy. Patients who received a LT were at a significantly increased risk for developing pulmonary complications ($p=0.033$).

	Chronicity: Time since injury not specified. The mean time from hospital presentation to anterior cervical spine fixation was 2.8 days. The mean length of hospital stay was 39 days.	
Romero-Ganuza et al. 2011b Spain Case control Level 3 N = 323	**Population**: Mean age: 42 yr; Gender: male=255, female=68; Level of injury: cervical to thoracic; Severity of injury: complete=229, incomplete=94. **Intervention**: Patients either received a tracheostomy or did not. Of those who did, they either received ST or a percutaneous tracheostomy. They also either received an ET (≤7 days post intubation) or a LT (>7 days post intubation). **Outcome Measures**: The following during hospital stay: incidence of MV and tracheostomy, injury level, injury severity, APACHE II scores, incidence of complications, duration of MV, duration of ICU stay. **Chronicity**: Mean interval from injury to admission=11.4 days.	1. 92% (297/323) of patients required MV and 67% (215/323) required a tracheostomy. 2. Patients who received a tracheostomy had significantly higher injury levels ($p<0.001$) more severe injuries ($p<0.001$), more associated injuries ($p=0.003$), and higher APACHE II scores ($p=0.03$) than patients who did not require a tracheostomy. 3. There were 69 cases of perioperative complications following tracheostomy. Patients who received an ET had significantly fewer cases of tracheal stenosis than patients who received a LT ($p=0.003$). There were no significant differences in pneumonia ($p=0.81$), stomal cellulitis ($p=0.45$), bleeding ($p=0.96$), or mortality rate ($p=0.22$) between the two groups. 4. Patients who received an ET spent significantly fewer days on MV ($p<0.001$) and significantly fewer days in ICU ($p<0.001$) compared to patients who received a LT. 5. Patients who received a percutaneous tracheostomy spent significantly fewer days in ICU ($p=0.004$) and experienced fewer cases of pneumonia ($p=0.011$)

		compared to patients who received a ST.
Romero et al. 2009 Spain Case control Level 3 N = 152	**Population:** Mean age: 41 yr; Gender: male=122, female=30; Level of injury: cervical to thoracic; Severity of injury: complete=119, incomplete=33; AIS A-D. **Intervention:** Patients either received a tracheostomy early (≤7 days of admission) or late (>7 days of admission). **Outcome Measures:** The following retrospectively: total time of MV, time of MV post tracheostomy. **Chronicity:** Mean time interval between injury and admission=27 days.	1. Patients who received an ET had significantly fewer episodes of pneumonia during intubation than patients who received a LT ($p<0.001$). There were no significant differences in incidences of pneumonia post tracheostomy ($p=0.80$) and total incidences of pneumonia ($p=0.27$) between the two groups. 2. There were no differences in mortality between early vs. LT ($p=0.12$). 3. Patients who received an ET had significantly shorter post tracheostomy duration on MV ($p<0.005$) and total duration on MV ($p<0.001$) compared to patients who received a LT. 4. Patients who received an ET spent significantly fewer post tracheostomy days in ICU ($p<0.05$) and total days in ICU ($p<0.0010$) than patients who received a LT. 5. Patients who received an ET had significantly fewer total complications than patients who received a LT ($p<0.05$).
Binder et al. 2016 Austria Case series Level 4 N = 38	**Population:** 38 patients with cervical SCI who underwent anterior cervical spine fusion (ACSF); 32 males and 6 females; mean (SD) age 47 (± 20) years; upper cervical spine fractures (C1–4) (n = 15) and lower cervical spine fractures (C5–7) (n = 23); complete (n = 17) and incomplete (n = 22). **Treatment:** Tracheostomy. Two tracheostomies (5.3%)	1. Tracheostomy: a. There was no difference in time to tracheostomy in patients presenting initially with an ASIA score of A, B, C or D. There was a tendency for earlier tracheostomy in patients with cervical spine fractures at the level of C4 or above when compared to

	were performed simultaneously with the ACSF. The remaining 36 tracheostomies were performed after the ACSF, with an average "delay" of 15 ± 10 days. No neurological deterioration was observed after ACSF or tracheostomy. **Outcome Measures:** Initial and follow-ups neurological and clinical presentation (assessed according to the ASIA score and the Glasgow Coma Scale (GSC)); concomitant injuries related to CSI; severity of injuries (according to the ISS); X-ray follow-ups (6 and 12 weeks, and 12 and 24 months after discharge); and complications (infection, bleeding or neurological deterioration were defined as major complications). **Chronicity:** Time since injury were not specified.	patients with cervical spine fractures at the level of C5 or below. 2. Complications: a. Only 2 patients (5.3 %) exhibited infections at the site of anterior cervical fusion after placement of a tracheostomy. b. Another patient underwent revision surgery after three months, due to exhibiting oesophageal leakage. c. Six patients (15.8 %) died during their hospital stay because of multiple organ failure (n = 2), acute ischaemic stroke (n = 1) and cardiovascular failure (n = 3). d. There were no deaths directly related to airway difficulties, but 29 patients (76.3 %) exhibited culture- and X-ray-proven pneumonia, and 2 patients (5.3 %) developed ARDS.
Holscher et al. 2014 USA Retrospective chart review Level 3 N = 33	**Population:** N=91 SCI or TBI patients <18 years old who underwent tracheostomy (67M, 24F) Mean (SD) age: 13 (5) years 29 are ≤12 years old 62 are 13-18 years old **Treatment:** Early (≤7 days post-injury) vs. LT **Outcome Measures:** Number of ventilator days, ICU days, hospital days, number of patients who developed pneumonia and airway complications.	1. Significantly reduced ventilator days, ICU days, hospital days for those younger than 13 who received ET, compared to those younger than 13 who received LT. 2. The same measures are not significantly different between groups in those who are 13 or older. 3. Significantly reduced prevalence of airway complications in those who received ET (all ages).

	Chronicity: Not specified.	4. No significant between group difference in prevalence of pneumonia.
Luo et al. 2014 China Retrospective chart review Level 4 N = 21	**Population:** N=21 successfully decannulated patients with cervical SCI (17M, 4F) Mean (range) age: 44.57(12-68) years 10 tracheostomized <24h post injury 16 AIS-A, 5 AIS-B/C/D **Treatment:** Tracheostomy **Outcome Measures:** Time between tracheostomy to decannulation, time between closed tracheostomy to decannulation. **Chronicity:** Time since injury was not specified, but time to tracheostomy from injury ranged from <24 hours to > 24 hours.	1. Mean duration* (range) of tracheostomy was 40 (14-104) days. 2. Mean duration* (SD) of closed tracheostomy was 18.8 (13.5) days. 3. No significant difference in mean duration of tracheostomy or closed tracheostomy between C2-C4 and C5-C7 patients with SCI, and between AIS-A and AIS-B/C/D patients. 4. Significantly shorter duration of tracheostomy in those ventilated for <10 days (compared to >10 days), and in those tracheostomized >24h post-injury (compared to <24h). *Until decannulation.

Discussion

Generally, results favor ET over LT, based on the evidence (two systematic reviews [Foran et al. 2021; Mubashir et al. 2021] and 10 original studies [Anand et al. 2020; Babu et al. 2013; Beom & Seo 2018; Choi et al. 2013; Flanagan et al. 2018; Holscher et al. 2014; Kornblith et al. 2014; Luo et al. 2014; Romero et al. 2009; Romero-Ganuza et al. 2011b]) that showed more positive outcomes (results) if ET was performed.

Ten case control studies and two retrospective charts have examined the use of early vs. late tracheostomy during acute SCI. Beom and Seo (2018) reported no difference in the number of ventilator days between early vs. late patients, while other studies found that early patients had significantly fewer ventilator days compared to late (Anand et al. 2020; Flanagan et al. 2018; Choi et al. 2013; Holscher et al. 2014; Romero-Ganuza et al. 2011b; Romero et al. 2009; Wang et al. 2021; Wang et al. 2020). Multiple studies found that ET patients had significantly fewer ICU days than the late group (Anand et al. 2020; Beom & Seo 2018; Flanagan et al. 2018; Choi et al. 2013; Holscher et al. 2014; Romero et al. 2009; Romero-Ganuza et al. 2011b; Wang et al. 2021), except for one study with no significant results (Babu et al. 2013). Multiple studies have found conflicting results as to whether an ET results in higher rates of medical

complications in patients with SCI. Flanagan et al. (2018) found that there were no differences in the number of days to decannulation, rates of pneumonia, or in-hospital mortality between early vs. late tracheostomy patients. Choi et al. (2013) and Wang et al. (2020) found similar results, with no significant differences between groups in terms of rates of pneumonia, or tracheal stenosis. Although other case control studies (Anand et al. 2020; Babu et al. 2013; Holscher et al. 2014; Kornblith et al. 2014; Wang et al. 2021) have found an increased risk of pneumonia for LT patients. The large case control by Romero-Ganuza et al. (2011b) (N = 323) found that patients who received an ET had a significantly increased risk of tracheal stenosis, but no significant differences in rates of pneumonia. Specifically, in terms of in-hospital mortality, early tracheostomies had similar rates than LT in the majority of studies (Anand et al. 2020; Romero-Ganuza et al. 2011b; Romero et al. 2009; Flanagan et al. 2018; Wang et al. 2020); with only one study that showed significantly less ICU mortality after ET comparing to LT (Wang et al. 2021).

Conclusion

There is level 3 evidence (from 10 case control studies: Anand et al. 2020; Beom & Seo 2018; Choi et al. 2013; Flanagan et al. 2018; Romero-Ganuza et al. 2011b; Holscher et al. 2014; Kornblith et al. 2014; Romero et al. 2009; Wang et al. 2020; Wang et al. 2021) that ET could provide better outcomes (e.g., ICU mortality, respiratory complications, MV duration, hospital LOS and ICU LOS) than LT in patients with SCI.

There is level 3 evidence (from one case control study: Wang et al. 2021) that ET reduces duration of MV and ICU LOS, mortality, and pneumonia rates, and increases successful weaning rates in patients with cervical SCI who underwent anterior cervical fusion surgery (ACFS).

There is level 3 evidence (from one case control study: Wang et al. 2020) that ET in patients with acute cervical SCI who underwent cervical internal fixation reduces total duration of MV, duration of MV after tracheotomy, duration of indwelling tracheal tube, and hospital LOS.

There is level 3 evidence (from one case control study: Anand et al. 2020) that ET reduces respiratory complications and ICU LOS, and increases ventilator free days in patients with traumatic cervical SCI.

There is level 3 evidence (from one case control study: Beom & Seo 2018) that ET reduces duration of postoperative ICU hospitalization in patients with motor weakness after surgery for traumatic cervical SCI.

There is level 3 evidence (from two case control studies: Beom & Seo 2018; Flanagan et al. 2018) and level 4 evidence (from one case series study: Binder et al. 2016) that higher neurological level of injury, more severe AIS score,

cervical spine fractures at the level of C4 or above, and lower mean AIS motor impairment scale score at the time of injury are predictors for ET in patients with SCI.

Most of the evidence considers ET if it is performed in the first seven days after patient admission.

Early tracheostomies may result in fewer ICU and hospital days and ventilation days; however, they may not impact in-hospital mortality, compared to late tracheostomies.

The evidence is inconsistent whether early tracheostomies reduce medical complications associated with tracheostomies compared to late tracheostomies.

5.5 Ventilation Weaning, Extubation, and Decannulation

Some research shows that around two-thirds of mechanically ventilated patients can be weaned in ICU after SCI (Schreiber et al. 2021). Liberation from ventilator support is a primary goal for patients with SCI, but the ability to wean off the ventilator is primarily determined by the level of injury. A C1 or C2 level injury may result in lifetime ventilator dependency because there is loss of function of the phrenic nerves that control the diaphragm. A C3-C4 injury is more variable in whether independent breathing will be achieved, with approximately 40% or more of these patients are successfully weaned (Berney et al. 2011). Patients with an injury at C5 or lower often need ventilation only in the earliest stages of the injury and during spine fixation surgery but are able to wean from the ventilator soon after. The recent systematic review of Schreiber et al. (2021) included 39 studies (with a total number of 14,637 patients, which 13,763 were in ICU and found that, apart from a high-level lesions, other conditions which appear to be associated with increased odds of weaning failure were a high number of comorbidities, high Injury Severity Score, elevated heart rate, and presence of tracheostomy. Furthermore, shorter time to admission to a specialized SCI center, high-level lesions (C1-C4 vs. C5-C8), complete lesion, low tidal volume (LTV) and high positive end-expiratory pressure within 24 hours from admission, and presence of tracheostomy were associated with a longer duration of MV (Schreiber et al. 2021). Although the present review focuses on ventilator weaning, extubation, and decannulation during the first weeks and months of SCI, this process can span much longer in some cases (Galeiras Vázquez et al. 2013). For more information on long-term ventilator weaning, refer to the

section “Mechanical Ventilation and Weaning Protocols” in the Respiratory Management chapter in SCIRE.

Before a patient initiates the weaning process, extubation or decannulation, a vital capacity of 1500 mL, clear lung radiographs, stable blood gases, stable heart rate and respiratory rate, and stable excretion levels must be achieved (Chiodo et al. 2008; Peterson et al. 1999). To begin weaning, a patient is removed from the ventilator for short periods of time that progress to longer and more frequent intervals of independent breathing. There are several protocols for this process; progressive ventilator-free breathing (PVFB), intermittent mandatory ventilation / invasive mechanical ventilation (IMV), and pressure support are the most common protocols (Weinberger & Weiss 1995). Newer studies are also examining the safety of higher tidal volumes for ventilator weaning (Fenton et al. 2016). PVFB is the process whereby a patient experiences intervals of ventilator-free time that increases in length throughout the day to build muscle tone (Galeiras Vázquez et al. 2013). If PVFB is the chosen method for weaning, a patient can be weaned using either LTV or high tidal volume (HTV). Using larger ventilator volumes (greater than 20 mL/kg) is thought to be more effective than LTV and can resolve atelectasis and increase surfactant production; however, this method is also associated with more pulmonary complications in certain patient cohorts (Peterson et al. 1999; Wallbom et al. 2005). IMV is the process whereby the ventilator provides a predetermined number of breaths within a certain time frame and the patient is encouraged to spontaneously breathe in between them when they can. The number of breaths decreases as patients gain pulmonary independence. Lastly, pressure support ventilation is the technique whereby the patient must initiate every breath and the ventilator assists with the rest of the breathing process. Biphasic positive airway pressure (BiPAP) and continuous positive airway pressure (CPAP) are two systems designed for non-invasive respiratory pressure support (Tromans et al. 1998). In addition to these ventilation procedures, transition from intubation to a tracheostomy, immediate extubation, and the use of diaphragmatic pacemakers are alternatives to patients requiring full time ventilation.

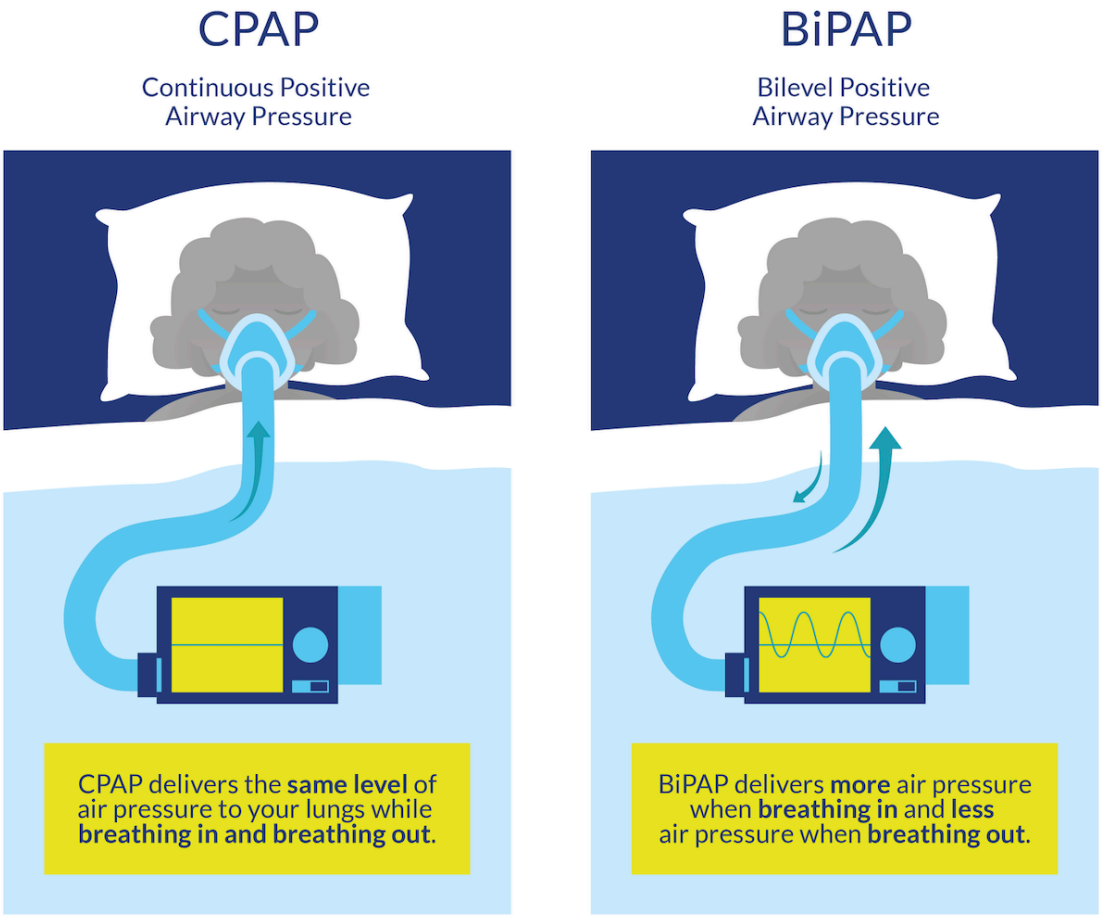


Figure 2. Description of the BiPAP and CPAP systems, designed for non-invasive respiratory pressure support

In very rare cases if lung-protective ventilation cannot be conducted, extracorporeal lung support (iLA/ECMO) can provide systemic tissue oxygenation and decarboxylation while avoiding ventilator-associated barotrauma to the lung tissue (Lotzien et al. 2017). Moreover, venovenous extracorporeal membrane oxygenation (ECMO) can be used as a salvage therapy for patients with ARDS and refractory hypoxia (Tsai et al. 2015). Venovenous ECMO primarily provides gas exchange to replace or support lung function (Lotzien et al. 2017). Blood is drained from the inferior vena cava via a femoral venous cannula or from the superior vena cava via an internal jugular venous cannula (Lotzien et al. 2017). The blood is pumped via the oxygenator back into the venous system through the internal jugular vein or through the second femoral venous cannula (Lotzien et al. 2017). Alternatively, a dual-lumen cannula can be employed for simultaneous venous drainage

and return (Lotzien et al. 2017). Venovenous ECMO can provide partial to full extracorporeal pulmonary support with blood flow up to 6 L/min (Lotzien et al. 2017). On the other hand, pumpless systems, which use the arteriovenous pressure gradient of the patient to create a shunt from the artery to the vein (interventional lung assist (iLA); facilitate extracorporeal carbon dioxide removal and can support MV by enabling a LTV and a reduced inspiratory plateau pressure (Zimmermann et al. 2009).

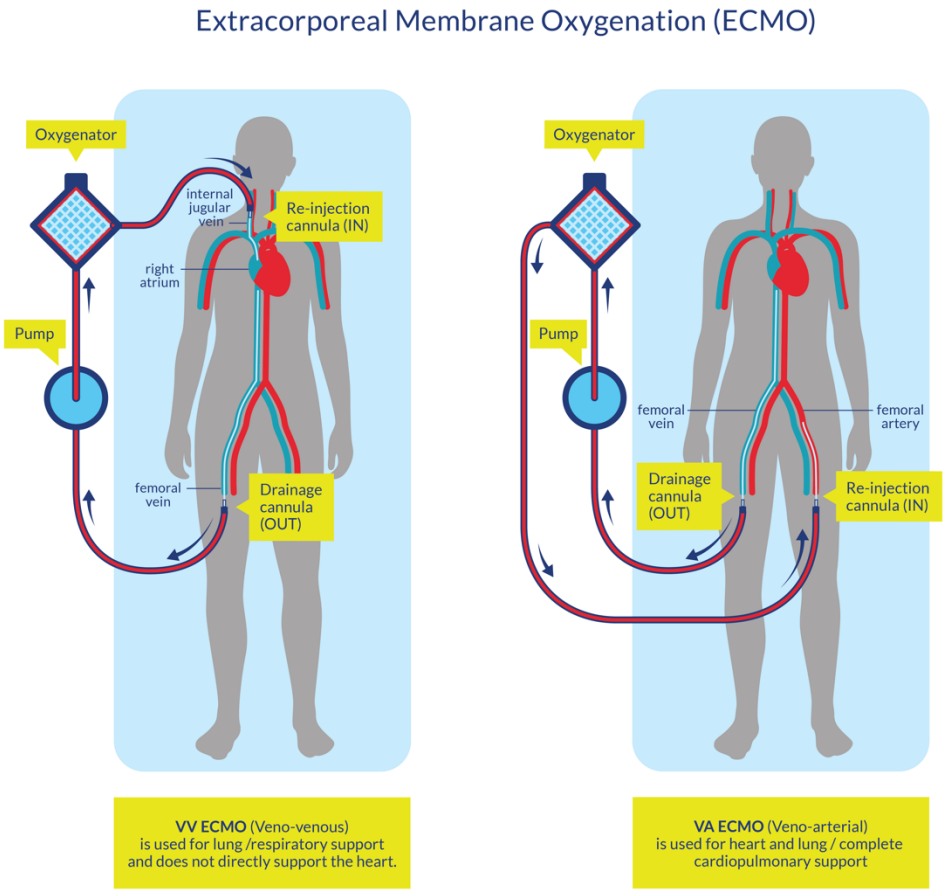


Figure 3. Characteristics of the veno-venous and veno-arterial ECMOs procedures

Decannulation, or removal of the tracheostomy, of patients with SCI is a critical milestone in their recuperation (Sun et al. 2022), but evidence for the decannulation of people with SCI is lacking. People may not meet the traditional criteria for decannulation and should be assessed on an individualized basis (Ross & White 2003; Bach & Alba 1990).

Table 7. Examination of Mechanical Ventilator Weaning, Extubation and Decannulation During Acute SCI

Author Year Country Research Design Score Sample Size	Methods	Outcome
Peterson et al. 1999 USA Cohort Level 2 N = 42	**Population:** Age range: 15-60 yr; Gender: male=37, female=5; Level of injury: C3-C4; Severity of injury: complete. **Intervention:** Patients either received HTV (20mL/kg) or low tidal volume (LTV) (15.5mL/kg) for progressive ventilator-free breathing (PVFB). **Outcome Measures:** incidence of atelectasis, lung pressure measured through centimeter of water (cmH_20). **Chronicity:** Mean duration of injury at time of hospital admission=56 days (LTV group) and 49 days (HTV group).	1. Patients who received LTV had significantly more atelectasis compared to patients who received HTV (p=0.01). 2. Patients who received HTV had significantly higher cmH_20 compared to patients who received LTV (p<0.001).
Kornblith et al. 2014 USA Case control Level 3 N = 344	**Population:** Mean age: 43 yr; Gender: male=275, female=69; Level of injury: cervical to lumbar; Severity of injury: complete=69, incomplete=275. **Intervention:** Patients either had a tracheostomy or did not. Of those requiring a tracheostomy, patients either experienced an ET or a LT. In addition, patients were either mechanically ventilated at discharge or were not.	1. Patients who received a tracheostomy had higher rates of VAP (p<0.05), higher rates of ALI (p<0.01), spent significantly more days in ICU (p<0.05) and hospital (p<0.05), and had fewer ventilator-free days (p<0.05) compared to patients who did not receive a tracheostomy. 2. There were no significant differences with regards to death (p>0.05) between patients who received a tracheostomy and patients who did not. 3. Patients who had a LT had higher rates of VAP (p<0.05), ALI

	Outcome Measures: The following retrospectively: instances of prolonged MV, VAP, ALI, ARDS, duration in ICU, duration in hospital, number of ventilator-free days, extubation attempts, ISS. **Chronicity:** Time since injury not specified. Average number of hospital days=20.	(p<0.05), and ARDS (p<0.05) compared to patients who had an ET. 4. Patients who required MV at discharge had a higher ISS (p<0.05), significantly higher rates of VAP (p<0.05) and ALI (p<0.05), and longer ICU (p<0.05) and hospital stays (p<0.05) compared to patients who did not require MV at discharge.
Nakashima et al. 2013 Japan Case control Level 3 N = 164	**Population:** Mean age: 45 yr; Gender: male=143, female=21; Level of injury: cervical; Severity of injury: complete=58, incomplete=106; AIS A-E. **Intervention:** Patients either received a tracheostomy or did not. Of those who did, they were either successfully decannulated or not. **Outcome Measures:** Proportion of patients who received a tracheostomy, proportion of patients who were successfully decannulated, level of injury, ASIA score. **Chronicity:** Mean time interval from injury to tracheostomy=5 days; Mean time interval from tracheostomy to decannulation=46 days. Time since injury not specified for patients who did not receive tracheostomy.	1. 15.2% (25/164) received a tracheostomy, 84% (21/25) of these were successfully decannulated. 2. Patients who received a tracheostomy had a history of smoking significantly more than patients who did not receive a tracheostomy (p=0.02). 3. Patients with a complete injury from C1–C4 (p=0.01) or C5–C7 (p<0.001) received a tracheostomy significantly more than patients with an incomplete injury at any level. 4. All patients with C5–7 ASIA A were successfully decannulated. Patients with C1–4 ASIA A were significantly more common in the non-decannulation group compared to patients with other injury severities and injury levels (p<0.05).
Call et al. 2011 USA Case control Level 3 N = 87	**Population:** Mean age: 39 yr; Gender: male=70, female=17; Level of injury: cervical to lumbar; Severity of injury: not specified.	Outcome of patients by degree of injury severity: 1. Patients with cervical injuries and complete motor loss had a higher rate of no attempt at

	Intervention: Patients were either discharged on ventilator support, tracheostomy collar, or natural airway. Of patients who were extubated, they were either successful on their first try, experienced 1 failure, or experienced multiple failures. **Outcome Measures:** The following during hospital stay: attempt at extubation, number of ventilator-free days, incidence of MV at discharge. The following at discharge: length of ICU stay, incidence of VAP. The following after extubation: length of ICU stay, number of ventilator-free days, length of hospital stay, incidence of VAP. **Chronicity:** Time since injury not specified. The mean time to tracheostomy=12 days. The mean length of hospital stay=33 days.	extubation (p=0.041), significantly fewer ventilator-free days (p=0.003), and higher incidence of MV at discharge (p=0.014) compared to patients without complete motor loss. Outcomes of patients at hospital discharge: 2. Patients who were discharged on positive pressure ventilation had longer ICU stays compared to extubated patients (p<0.001). Patients discharged on a tracheostomy collar had longer ICU stays than those who were extubated or decannulated (p<0.001). 3. The incidence of VAP was significantly higher in patients requiring MV (p<0.001) and those discharged on tracheostomy collar (p=0.001) compared to patients who were discharged with a natural airway. Outcome of patients who underwent extubation: 4. Of patients in whom extubation was attempted, those who extubated successfully on the first attempt had significant shorter ICU stays (p<0.001), more ventilator-free days (p<0.001), and shorter hospital stays (p=0.009) compared with patients who failed one or more weaning or extubation attempts. 5. Patients failing one or more attempts had a significantly higher incidence of VAP (p<0.001) compared to patients who were successful on their first attempt.
Peterson et al. 1994	**Population:** Mean age: 39 yr; Gender: male=80%,	1. At one month post injury, significantly more patients who

USA Case control Level 3 N = 52	female=20%; Level of injury: cervical to lumbar; Severity of injury: not specified. **Intervention:** Patients were either discharged on ventilator support, tracheostomy collar, or natural airway. Of patients who were extubated, they were either successful on their first try, experienced 1 failure, or experienced multiple failures. **Outcome Measures:** The following during hospital stay: attempt at extubation, number of ventilator-free days, incidence of MV at discharge. The following at discharge: length of ICU stay, incidence of VAP. The following after extubation: length of ICU stay, number of ventilator-free days, length of hospital stay, incidence of VAP. **Chronicity:** Time since injury not specified. The mean time to tracheostomy=12 days. The mean length of hospital stay=33 days.	received PVFB had weaned compared to patients who received IMV (p=0.01). 2. The overall ventilator weaning success rate for PVFB was significantly higher than the success rate of IMV (p=0.02). Outcome of patients by degree of injury severity: 3. Patients with cervical injuries and complete motor loss had a higher rate of no attempt at extubation (p=0.041), significantly fewer ventilator-free days (p=0.003), and higher incidence of MV at discharge (p=0.014) compared to patients without complete motor loss. Outcomes of patients at hospital discharge: 4. Patients who were discharged on positive pressure ventilation had longer ICU stays compared to extubated patients (p<0.001). Patients discharged on a tracheostomy collar had longer ICU stays than those who were extubated or decannulated (p<0.001). 5. The incidence of VAP was significantly higher in patients requiring MV (p<0.001) and those discharged on tracheostomy collar (p=0.001) compared to patients who were discharged with a natural airway. Outcome of patients who underwent extubation: 6. Of patients in whom extubation was attempted, those who extubated successfully on the first attempt had significant shorter ICU stays (p<0.001), more ventilator-free days (p<0.001), and shorter hospital stays (p=0.009) compared with

		patients who failed one or more weaning or extubation attempts. 7. Patients failing one or more attempts had a significantly higher incidence of VAP ($p<0.001$) compared to patients who were successful on their first attempt.
Kim et al. 2017 Korea Case series Level 4 N = 62	**Population:** 62 patients with cervical SCI who had received invasive acute phase respiratory management and succeed in either decannulation or extubation, mean (SD) duration from tracheostomy to decannulation 7.0 (± 14.5) months); 55 males and 7 females; mean (SD) onset age 47.6 (± 15.8) years; ASIA A (n = 49) and ASIA B (n = 13); neurological level C- (n = 1), C1 (n = 3), C2 (n = 9), C3 (n = 23), C4 (n = 20), C5 (n = 2), C6 (n = 2), C7 (n = 0), and C8 (n = 2). **Intervention**: Invasive acute phase respiratory management (including mechanically assisted coughing and non-invasive mechanical ventilation (NIV)) for patients with tracheostomy (n = 60) and endotracheal intubation (n = 2). **Outcome Measures:** Medical charts (including discharge summaries), imaging studies, and detailed pulmonary function test results (FVC in sitting and supine position, MIP, MEP, and	1. Of the 62 patients: a. 25/62 achieved transition to NIV after extubation/decannulation. b. 16/62 achieved ventilator weaning after extubation / decannulation. c. 2/62 were tracheostomy MV with re-tracheostomy after decannulation. d. 12/62 had simple decannulation without applying long-term MV. e. 7/62 were applied of NIV after decannulation. 2. For those who switched to NIV (n = 31), hours of daily need for ventilatory support gradually decreased to 5.7 ± 5.7 h at final discharge.

	unassisted and assisted PCF assessed just before each patient's decannulation) were collected before initial admission and after the intervention (mean (SD) follow-up period 21.3 (± 29.8) months).	
Lotzien et al. 2017 Germany Case series Level 4 N = 7	**Population:** 7 patients with SCI treated in ICU (paraplegia N = 2; and tetraplegia n = 5), 6 males and one female, AIS A (n = 3), AIS B (n = 2), AIS C (n = 1) and AIS D (n = 1), with ARDS. Study also used data from trauma patients (n = 49). **Intervention:** Post-traumatic lung failure treatment using extracorporeal lung support with extracorporeal membrane oxygenation (ECMO) (n = 5) or interventional lung assist (iLA) (n = 2). **Outcome Measures:** Successful weaning, ICU and hospital LOS, complications, and survival. **Chronicity:** Time since injury not specified, but patients were treated in at a level-one trauma center.	1. 6/7 patients with SCI were weaned from the extracorporeal devices (100% were successfully weaned from ECMO, and 50% was weaned from the iLA). 2. The median LOS in the ICU was 35 days, and the mean hospital LOS was 81 days, including the early phase of rehabilitation and further ventilation weaning. 3. No minor complications were observed, but severe complications occurred in two cases (dislocation of the venous cannula (iLA) during prone positioning; and oxygenator clotting and thrombosis around the dual lumen cannula). 4. In comparison with all trauma patients who received the same interventions, patients with SCI required longer ventilation periods (567 vs. 817 ventilation hours) and experienced a longer in-hospital LOS (46.7 vs. 81 days). 5. The 71.4% survival rate indicates that extracorporeal devices are a feasible treatment option for patients with SCI.
Ross & White 2003 Australia Case series Level 4	**Population:** tetraplegia (n=3) and paraplegia (n=1), level: C5-T9, AIS A (n=3) & B(n=1), age: 20-71 yrs	1. 4 participants who had evidence of aspiration were successfully decannulated after assessment by a multidisciplinary team.

N = 4	**Treatment:** Interdisciplinary evaluation and assessment **Outcome Measures:** Successful decannulation.	2. None experienced respiratory deterioration.

Discussion

In comparing methods of ventilator weaning, one case control showed that PVFB allowed patients to wean faster than IMV (Peterson et al. 1994). This finding is recommended by the Paralyzed Veterans of America Consortium for Spinal Cord Medicine (2005) and is consistent with other studies that examined non-SCI patients (Brochard et al. 1994; Esteban et al. 1995). The only study to investigate the efficacy of high vs. LTV on ventilator weaning found that HTV resulted in faster weaning and more instances of resolved atelectasis than LTV (Peterson et al. 1999). The weaning period for patients on HVtV was an average of three weeks sooner than those who received LTV ventilation.

Kim et al. (2017) retrospectively studied 62 patients with complete or sensory incomplete cervical SCI who received an invasive acute phase respiratory management (including mechanically assisted coughing and non-invasive mechanical ventilation (NIV)) for patients with tracheostomy (n = 60) and endotracheal intubation (n = 2), showing that tracheostomy decannulation was possible and non-invasive respiratory intervention, including NIV and mechanically assisted coughing, was an effective long-term alternative to tracheostomy.

Ross and White (2003) described a case series of four people with SCI who were successfully decannulated despite the presence of traditional contraindications such as evidence of aspiration. These four people were carefully selected by a multidisciplinary team who opted for decannulation after assessing the overall risks of decannulation vs. the risks of prolonged tracheostomy. Further studies examining and refining the criteria for decannulation of people with SCI are necessary.

Successful decannulation and extubation has been found to be affected by the level and severity of injury whereby a higher rate of extubation is more likely to be achieved in patients with lower spinal cord injuries (Call et al. 2011). Decannulation is performed with a higher rate of success among patients with lower-level cervical injuries compared to those with higher cervical cord injuries (Nakashima et al. 2013). The presence of a tracheostomy was found by Kornblith et al. (2014) to reduce attempts at extubation, but in cases where extubation was successful on the first attempt, patients had shorter ICU and hospital stays compared to those who have failed one or more times (Call et al. 2011). Kornblith et al. (2014) also noted that among the patients included in

their study, the majority of persons did not require MV at the time of discharge indicating that the many patients with SCI can be successfully weaned from ventilators; however, this was significantly more common in patients who did not have a tracheostomy compared to those who did require this procedure ($p < 0.05$).

Lotzien et al. (2017) described the first case series of seven patients with SCI and post-traumatic lung failure treated with lung support with ECMO or iLA devices and showed that this therapy was feasible and a life-saving procedure (71.4%).

Conclusion

There is level 3 evidence (from one case control study: Kornblith et al. 2014) that patients with acute SCI who do not require tracheostomies have a higher success rate of MV weaning compared to those who do require this procedure.

There is level 3 evidence (from two case control studies: Nakashima et al. 2013; Call et al. 2011) that higher level SCI correlates with lower rates of decannulation and extubation in patients with acute SCI.

There is level 4 evidence (from one case series study: Kim et al. 2017) that an invasive acute phase respiratory management (including mechanically assisted coughing and NIV) for patients with cervical SCI receiving tracheostomy or endotracheal intubation provides successful in tracheostomy decannulation; and noninvasive respiratory intervention, including NIV and mechanically assisted coughing, is an effective long-term alternative to tracheostomy.

There is level 4 evidence (from one case series study: Ross & White 2003) that decannulation can be successful in people with evidence of aspiration.

There is level 2 evidence (from one cohort study: Peterson et al. 1999) that higher ventilator tidal volumes may speed up the MV weaning process compared to lower ventilator tidal volumes in patients with acute SCI.

There is level 3 evidence (from one case control: Peterson et al. 1994) that PVFB is a more successful method of weaning patients with acute cervical SCI from MV than IMV.

There is level 4 evidence (from one case series: Lotzien et al. 2017) that extracorporeal lung support is a feasible therapy with a high survival rate for patients with SCI and post-traumatic lung failure.

Weaning from MV is more successful in patients who have not had a tracheostomy, and rates of decannulation and extubation are higher in patients with lower-level injuries during the acute phase post SCI.

There is some evidence that the implementation of an invasive acute phase respiratory management for patients with cervical SCI receiving tracheostomy or endotracheal intubation is successful in tracheostomy decannulation.

For MV weaning, PVFB may be more successful than IMV, and using higher ventilator tidal volumes may speed up the weaning process compared to lower ventilator tidal volumes during the acute phase post SCI.

Extracorporeal lung support could represent an option in patients with SCI and post-traumatic lung failure.

Case by case consideration should be given to tracheostomy decannulation in people with SCI. The indications and criteria for tracheostomy decannulation have not been established in SCI.

5.6 Secretion Removal Techniques

A major cause of pulmonary complications in patients with acute SCI results from an inability to clear bronchial secretions. In cervical spinal cord injuries, there is a predominance of parasympathetic drive that can lead to increased bronchial secretions. Concomitantly, nerves that innervate the diaphragm and abdominal muscles may be damaged, leading to impaired coughing ability, or a weaker less effective cough. The failure to perform deep coughing can cause pulmonary problems in two ways. First, patients can be in immediate pulmonary distress from choking or aspiration. Second, the retention of mucus, often for prolonged periods of time, can lead to respiratory infections such as bronchitis or pneumonia. For approximately 20% of people with acute tetraplegia, an excess of 1 L of mucous is produced each day (Bhaskar et al. 1991) which further demands the need for effective coughing techniques. The peak cough expiratory flow necessary to clear bronchial secretions is 3.1 L/s (Bach et al. 1993); people with SCI often test well below this threshold. Several mechanisms exist to improve coughing ability in patients with SCI. Manual assisted coughing, or “quad cough”, is an effective option whereby a caregiver applies firm and rapid pressure to the abdomen to force air out of the lungs. Mechanical assisted coughing, most commonly by mechanical insufflation-exsufflation, stimulates coughing by having a machine fill the lungs with air (insufflation) and then quickly reverse the flow to create negative pressure and push out secretions (exsufflation) (Volsko 2013). Additionally, positive expiratory pressure therapy systems are

handheld devices used to create pressure in the lungs and facilitate clearance of secretions (Volsko 2013). If needed, more invasive procedures to remove secretions can be used, such as directly "deep" suctioning the trachea with a catheter or with bronchoscopy to remove mucous plugs.

Figure 4. Manual assisted coughing ("quad cough")

Mechanical insufflation-exsufflation (e.g., using a "Cough Assist machine") is a therapy in which the device gradually inflates the lungs (insufflation), followed by an immediate and abrupt change to negative pressure, which produces a rapid exhalation (exsufflation), which simulates a cough, and helps to clear secretions.

Figure 5. Mechanical insufflation – exsufflation

Table 8. Mechanical Insufflation/Exsufflation as an Adjunctive Therapy for Bronchial Clearance during Acute SCI

Author Year Country Research Design Score Sample Size	Methods	Outcome
Pillastrini et al. 2006 Italy RCT PEDro = 3 Level 2 N = N/S	**Population:** *Control Group:* Mean Age: 52.2 yr; Gender: male=75%, female=25%; *Treatment Group:* Mean Age: 31.5 yr; Gender: male=80%, female=20%; Level of injury: cervical; Severity of injury: complete =100%; AIS A. **Intervention:** The patients were randomized to receive either mechanical insufflation/exsufflation in addition to manual kinesitherapy, or kinesitherapy only. **Outcome Measures:** Forced vital capacity (FVC), FEV_1, peak expiratory flow (PEF), (FEV_1/FVC), arterious pressure of O_2 (Pa O_2), arterious pressure of CO_2 (Pa CO_2), (pH), saturation of oxygen (SaO_2). **Chronicity:** Time since injury not specified.	1. Among patients who received mechanical insufflation/exsufflation, FVC and $FEV_1$was significantly higher at the end of treatment compared to the beginning (p=0.0001). 2. Among patients who received mechanical insufflation/exsufflation, PEF was significantly higher at the end of treatment compared to the beginning (p=0.0093). 3. Among patients in the control group, there was no significant improvement in FVC, FEV_1, or PEF (p>0.05) between the end of treatment and the beginning. 4. There were no significant differences in FEV_1/FVC, Pa O_2, Pa CO_2, pH, and SaO_2 in either of the groups (p>0.05 in all cases).
Garstang et al. 2000 USA Pre-post Level 4 N = 18	**Population**: 18 patients with SCI (C1-T3), 88% were C5 or higher. **Methods:** Surveyed preference for: suctioning or maximal in/exsufflation (MI-E). **Outcome Measures:** Not Specified. **Chronicity:** Time since injury was up to 3 years post-injury; patients originated from	1. MI-E was less irritating, less painful, less tiring, less uncomfortable. All were clinically significant changes (except less tiring). 2. 16 of 18 patients preferred MI-E and one preferred suctioning; 1 patient had no preference. 3. When surveyed, average time from MI-E was 146

	several different acute care hospitals.	days and from suctioning was 253 days.

Discussion

A single RCT found that mechanical insufflation/exsufflation is more effective at restoring cough than manual techniques alone (Pillastrini et al. 2006). This study did not test the efficacy of removing secretions directly, but instead tested them indirectly by measuring coughing ability through measurements such as FVC, forced expiratory volume, and peak cough expiratory flow. These measures were significantly improved with the addition of mechanical insufflation/exsufflation, demonstrating that these devices can enhance cough in patients with acute SCI. A pre-post study by Garstang et al. (2000) surveyed the preference for suctioning or maximal in/exsufflation in 18 patients with SCI; the majority of patients (16/18) reportedly preferred maximal in/exsufflation.

Conclusion

There is level 2 evidence (from one RCT: Pillastrini et al. 2006) in support of mechanical insufflation/exsufflation as an effective adjunctive therapy to the use of respiratory kinesitherapy for bronchial clearance in patients with acute SCI.

There is level 4 evidence (from one pre-post study: Garstang et al. 2000) that patients with SCI prefer maximal in/exsufflation over suctioning.

Mechanical insufflation/exsufflation coupled with manual respiratory kinesitherapy may be effective for bronchial clearance during the acute phase post-SCI.

Table 9. Other Techniques to Cough Assist and Remove Secretions During Acute SCI

Author Year Country Research Design Score Sample Size	Methods	Outcome
Kluayhomthong et al. 2019 Thailand RCT (crossover) PEDro = 5 Level 2 N = 13	**Population:** 13 intubated patients with cervical SCI referred to physical therapy for secretion clearance, 12 males and one female, mean age 51 (28 – 70) years, and AIS C. **Treatment:** Patients received 3 interventions carried out on consecutive days, devices used for breathing exercise were based on the threshold incentive spirometry device: • Oscillated positive expiratory pressure breathing (OPEP) intervention. • Oscillated incentive spirometry (OIS) + OPEP. • Sham intervention: Patient undertook the intervention as for OIS+OPEP but with no oscillation or humidification of the air flow because there was no water in either bottle. The patient was disconnected from the ventilator and the tracheostomy or endotracheal tube was connected to the device and performed 10 sets of active breathing with 10 breaths/set and one minute of rest (patient reconnected to the ventilator) between sets. **Outcomes Measures:** Airway secretions; spontaneous VE; VT; slow vital capacity (SVC); physical effort (RPE) and sensation of dyspnea (RPB) during breathing exercises; adverse events; oxygen	1. Patients had no difficulties with the interventions and there were no adverse events. 2. The median interquartile range (IQR) secretion wet weight in the 3 h before the interventions was 2.61 g (2.21, 3.85) and this increased following each of the interventions; showing OPEP+OIS was more effective than OPEP (p = 0.006) and Sham (p = 0.006), while OPEP was more effective than Sham (p = 0.019). 3. RPE and RPB during intervention were not statistically significant between groups.

	saturation; heart rate; and spontaneous breathing frequency were collected before and after each treatment session (day). **Chronicity:** 23 days since injury.	
Torres-Castro et al. 2014 Chile Pre-post Level 4 N = 15	**Population:** 15 in-patients with complete tetraplegia (C4–C6, AIS A) were included. Median age was 33 years (16–56). **Treatment:** PCF was measured during four different interventions: spontaneous maximal expiratory effort (MEE); MEE while receiving Assisted Cough (MEE-AC); MEE after Air Stacking with a manual resuscitation bag (AS-MEE); and MEE with AS and AC (AS-MEE-AC). **Outcome Measures:** PCF. **Chronicity:** The inclusion criteria was SCI within 1 year of injury. Patients included had an average of 3 months since injury.	1. We observed significant differences in PCF while applying MEE-AC and AS-MEE compared with MEE. 2. The difference in PCF value was greatest using the AS-MEE-AC techniques combined. 3. Application of combined techniques (AS-MEE-AC) can reach near normal PCF values and be a low-cost and easily applied intervention for people with tetraplegia.

Discussion

There is one RCT that showed that oscillated incentive spirometry (OIS) plus oscillated positive expiratory pressure (OPEP) breathing in a single-day intervention was more effective in the removal of secretions in intubated patients with cervical SCI for secretion clearance than OPEP and placebo interventions (Kluaythomthong et al. 2019).

A pre-post study of Torres-Castro et al. (2014) compared the application of different interventions to increase peak cough flow (PCF) in patients with complete tetraplegia. The authors reported that the combined technique of maximal expiratory effort while receiving assisted cough after air stacking with a manual resuscitation bag (AS-MEE-AC) provided the best values of PCF.

Conclusion

There is level 2 evidence (from one RCT: Kluaythomthong et al. 2019) that OPEP plus OIS intervention facilitates secretion removal in patients with acute SCI.

There is level 4 evidence (from one pre-post study: Torres-Castro et al. 2014) that the combined technique of maximal expiratory effort while receiving assisted cough after air stacking with a manual resuscitation bag (AS-MEE-AC) reaches near normal PCF values.

> Interventions like OPEP breathing plus OIS, or the combined technique of maximal expiratory effort while receiving assisted cough after air stacking with a manual resuscitation bag (AS-MEE-AC) facilitates secretion removal and reaches near normal PCF values in patients with SCI.

5.7 Other Surgery

The trapezius muscles, dominated by spinal accessory nerves, can have an important role in reconstructing the respiratory function of patients with cervical SCI (Yang et al. 2011). The trapezius muscles (mainly innervated by the first and second levels of spinal cord, C1–2) have auxiliary inspiration function with the coordination of the muscles that attach the scapula to the rib cage (Yang et al. 2014). When extensive muscle paralysis is caused by cervical SCI, the scapula will slide up along the rib cage when the trapezius muscle contracts, limiting additional anatomical help with breathing (Yang et al. 2014). An innovative surgical technique using the trapezius muscles was developed and called “rib suspension surgery” (or thoracic breathing reconstruction); as the trapezius muscle strength is preserved in patients with injuries below C2 level, they can be surgically transferred to the rib cage through the scapula to recover the lost thoracic breathing, thus improving respiratory function (Yang et al. 2014).

Table 10. Other Surgery

Author Year Country Research Design Score Sample Size	Methods	Outcome
Yang et al. 2014 China Pre-post Level 4 N = 6	**Population:** N=6 participants with SCI (4M 2F) Mean age (SD): 41.7(16.2) Mean DOI* (SD): 84(26.7) days All with limited diaphragmatic function, dyspnea, and good trapezius muscle strength All cervical SCI, AIS-A *At time of surgery **Treatment**: Rib suspension surgery. **Outcome Measures:** Vital capacity (VC), Vt, cough & expectoration assessment, ventilator & oxygen dependence, diaphragmatic activity (fluoroscopy), phonation ability, electromyography, arterial blood gas analysis and development of complications. **Chronicity:** Mean time since injury was 84 (± 26.7) days.	1. Patients reported improved breathing, cough and expectoration 1 day post-surgery. 2. Increased range of diaphragmatic activity 2-3 weeks post-surgery. 3. Extubation completed in all patients within 4 weeks post-surgery. 4. Significantly increased VC post-surgery. 5. No significant change in TV.

Discussion

A pre-post study by Yang et al. (2014) used rib suspension surgery; in which the trapezius muscle strength was surgically transferred to the rib cage through the scapula to recover the lost thoracic breathing. They found that people reported significantly increased VC post-surgery, improved breathing, cough, and expectoration 1-day post-surgery, and increased range of diaphragmatic activity 2-3 weeks post-surgery.

Conclusion

There is level 4 evidence (from one pre-post study: Yang et al. 2014) that used rib suspension surgery and found an improvement in breathing, cough and expectoration 1 day post-surgery, an increased range of diaphragmatic

activity 2-3 weeks post-surgery, and a significantly increased VC post-surgery in patients with complete high cervical SCI.

6 Non-pharmacological Interventions for Pulmonary Function Improvement During Acute SCI

6.1 Respiratory Muscle Training

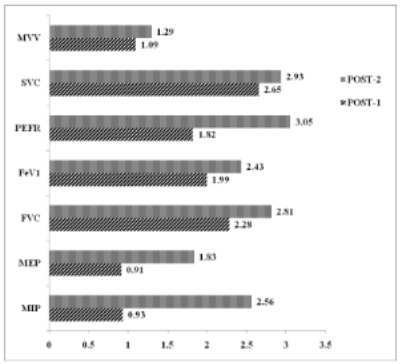
Acute physiotherapy is an emerging non-invasive option to help patients resume normal pulmonary functioning and timely discharge. Early prophylactic treatment in the form of physiotherapy has been shown to improve diaphragm function and reduce secretions in patients with acute SCI (McMichan et al. 1980). Assisted coughing, intermittent positive pressure breathing, and regular changes in body positioning are some of the techniques used to help keep patients' airways clear and breathing independently (Berney et al. 2002). In addition, breathing exercises and diaphragm strengthening can also improve lung functioning and assist in weaning from MV. Resistive inspiratory muscle training (RIMT) and abdominal weights (AbWts) training (Gross et al. 1980; Lin et al. 1999) as well as cough training combined with functional electrical stimulation (McBain et al. 2013) are techniques that have been implemented for physiotherapy in chronic patients with SCI. RIMT (Derrickson et al. 1992; Postma et al. 2014; Raab et al. 2019), expiratory resistive muscle training (Roth et al. 2010), respiratory (inspiratory and expiratory) muscle training (Boswell-Ruys et al. 2020; Sikka et al. 2021), AbWts training (Derrickson et al. 1992), normocapnic hyperpnea training (Van Houtte et al. 2008), isocapnic hyperpnea (Mueller et al. 2012; 2013), and complex interventions (self-directed RMT consisting in glossopharyngeal breathing exercises, inspiratory muscle training (IMT) using incentive spirometry, and air stacking exercises with a resuscitation bag) (Shin et al. 2019) have been studied in the acute SCI population and are reviewed below.

Figure 6. The Breather® Respiratory Muscle Trainer

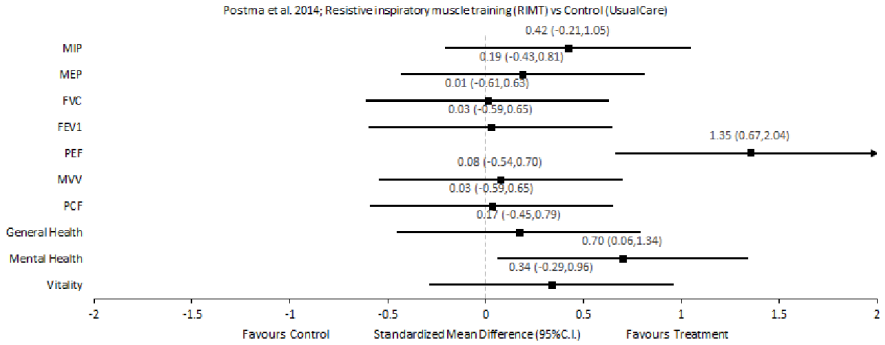
Table 11. Effect of Respiratory Muscle Training on Pulmonary Function During Acute SCI

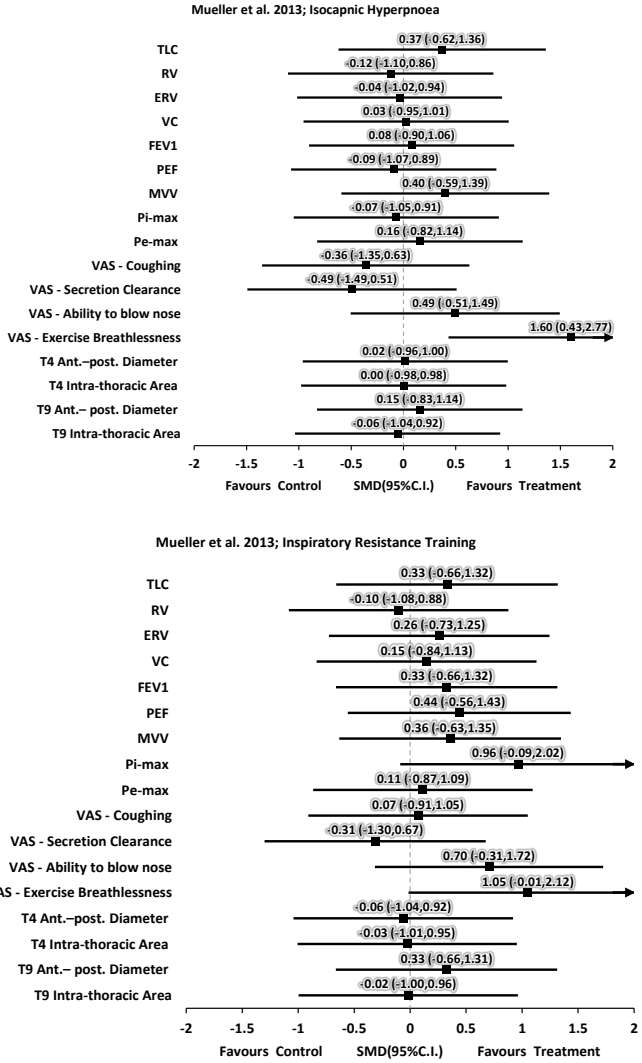
Author Year Country Research Design Score Sample Size	**Methods**	**Outcome**
Boswell-Ruys et al. 2020 Australia RCT PEDro = 10 Level 1b N = 62	**Population:** 62 patients with tetraplegia (C4-C8) with related respiratory deficits; 58 males and 4 females; mean age 53,6 years; level of injury C4 (n = 21), C5 (n = 12), C6 (n = 16) and C7 (n = 13); AIS A (n = 32), AIS B (n = 9), and AIS C (n = 21). **Treatment:** Participants were allocated to sham (n = 32) or active (n = 30) treatment. All participants performed supervised RMT with a single threshold RMT device (the sham device was modified to hold the pressure valve permanently open). 3 to 5 sets of 12 breaths (IMT and EMT, separated by quiet breathing for 2 min) were performed twice daily, 5 days a week for 6 weeks, increasing 10% weekly of each participant's baseline PImax and PEmax if	1. After 6 weeks of RMT PImax was significantly greater in the active group compared with the sham group; SGRQ score improved more in the active group compared with the sham group (mean between-group difference 10.3 points, 95% CI 0.01 to 20.65, p = 0.046); Borg scores for breathlessness during 10 inspiratory loaded breaths reduced more in the active group compared with the sham group (mean

	tolerated. **Outcome Measures:** PImax, (IC), VC, FVC, FEV_1, peak expiratory flow while coughing (PEFc), TLC, PEmax at TLC, perceived breathlessness, respiratory-related morbidity, respiratory health (the St George Respiratory Questionnaire (SGRQ)) and quality of life (the Short Form Health Survey: walk/ wheel (SF-36ww) and the EuroQol-Five Dimensional Visual Analogue Scale (EQ-5D VAS)) were collected at baseline, 6 weeks and 1 year. **Chronicity:** Patients were included if they had acute (< 6 months since injury) or chronic SCI.	between-group difference 0.96, 95%CI 0.01 to 1.91, p = 0.049); and Borg scores at rest were greater in the sham group (mean between-group difference 0.64, 95% CI 0.11 to 1.17, p = 0.021). 2. After one year of unsupervised training, in comparison of baseline data, there was no significant difference between active and sham groups in any outcome measures except for the incidence of respiratory complications (there was a greater total number of respiratory complications in the sham group (n = 10) compared with the active group (n = 3), p = 0.017).
Sikka et al. 2021 India RCT PEDro = 4 Level 2 N = 96	**Population:** 96 patients within first week (mean time post injury 1.05 days) of traumatic cervical SCI; 72 males and 24 females; mean age 40.98 years; AIS A (n = 57) and AIS B (n = 49); and level of injury C4-C5 (n = 16), C5-C6 (n = 50), and C6-C7 (n = 30). **Treatment:** Patients were divided to: • Resistive IMT (RIMT) group (n = 48) received an IMT and EMT twice daily, 5 days per week, with 3 sets of 12 inspirations and then 3 sets of 12 expiration for four weeks with an IMT	1. The pre-training and post-training mean values of all outcome measures revealed significant differences within groups (P < 0.05). 2. RIMT, compared to control group, resulted in a highly significant positive effect on all measures, recorded after 2 and 4 weeks of training (P < 0.01).

	Threshold trainer. Training intensity began at 30% PImax and 30% PEmax; and was increased on alternate days by 10% (if tolerated) and was capped at 70% of the very best weekly MIP or MEP. Conventional intervention, including deep breathing exercises, huffing and cough assisting, postural drainage, percussion, vibration, and other rehabilitative programs like passive range of motion exercises, MAT exercise, sitting balance and upper limb functional training were administered. • Control group (n = 48) received only the conventional intervention. **Outcome Measures:** Pulmonary function testing / Spirometry (FVC, FEV_1, PEFR, SVC (slow vital capacity) and MVV (Minute ventilation volume)) and respiratory muscle strength (MIP and MEP) were obtained before intervention; and after two and four weeks of intervention. **Chronicity:** Patients were included within the first week after injury.	3. The effect size difference between RIMT and control group for all the outcome measures was large.
	Comparison of Effect Sizes ("Cohen -d values") for pre to post training changes between RIMT and Control Group:  Effect size, "d≥0.8" indicates a large clinically significant effect. POST-1 (after two weeks training), POST-2(after four weeks of training).	

	Figures are extracted from the original article (Sikka et al. 2021), which is licensed under Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.	
Postma et al. 2014 The Netherlands RCT PEDro = 7 Level 1b N = 40	**Population:** *Resistive inspiratory muscle training group (RIMT):* Mean age: 47.1 yr; Gender: male=20, female=1; *Control Group:* Mean age: 46.6 yr; Gender: male=15, female=4; Level of injury: T12 and above; Severity of injury: complete=24, incomplete=16. **Intervention:** Patients were randomly assigned to receive usual rehabilitation care plus RIMT with a threshold trainer (RIMT group), or usual rehabilitation care only (control group). **Outcome Measures:** The following at baseline, after 8 weeks of intervention, 8 weeks after intervention, 1 yr after discharge from inpatient rehabilitation: maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), FVC, FEV_1, peak expiratory flow (PEF) rate, maximum ventilation volume, health-related quality of life (HRQoL), and 36-item short-form health survey (SF-36). **Chronicity:** Median number of days since injury was 74 (RIMT group) and 88 (control group).	1. MIP improved more in the RIMT group compared with the control group 1 week after the intervention period (mean difference=11.67 cm H_2O, p=0.002); this difference was no longer significant 8 weeks after the intervention period (p=0.065) or at 1 yr after discharge from inpatient rehabilitation (p=0.271). 2. No other between-group differences were found in any of the other measures of respiratory function. 3. The RIMT group improved more in mental health compared with the control group 1 week after the intervention period (p=0.006).

	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data.  	
Mueller et al. 2012 & 2013 Switzerland RCT PEDro = 5 Level 2 N = 24	**Population:** N=24 participants with traumatic complete tetraplegia (C5-C8, AIS A) were randomly assigned to 1 of 3 groups. *Placebo group*: 6M 2F; mean (SD) age: 41.6(17.0) yrs; DOI: 6.6(1.4) months. *Isocapnic hyperpnea (IH) group*: 6M 2F; mean (SD) age: 33.5(11.7) yrs; DOI: 6.6(0.9) months. *Inspiratory resistive training (IRT) group:* 6M 2F; mean (SD) age: 35.2(12.7) yrs; DOI: 6.0(0.0) months. **Treatment:** All participants completed 32 supervised training sessions over 8 weeks. **Outcome Measures:** inspiratory and expiratory muscle strength. **Chronicity:** 6.6 (± 0.9) months since injury.	1. Compared to placebo training, IRT showed high effect sizes for inspiratory muscle strength (d=1.19), VAS values of “cleaning the nose” (d=0.99), and the physical component of subjective quality of life (d=0.84). 2. IH compared with placebo showed a high effect size for breathlessness during exercise (d=0.81). 3. Friedman analysis showed a significant effect for IRT vs. placebo and vs. IH on inspiratory muscle strength.

	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention (IH and IRT respectively) data. 	
[Van Houtte et al. 2008](#) Belgium RCT PEDro = 8 Level 1b N = 14	**Population:** C4-T11 AIS A, B, or C; 2-6 months since injury. **Treatment:** sham or normocapnic hyperpnea training for 15-30 min x 8 wks; average of 27 sham and 28 training sessions. **Outcome Measures:** MIP, VC, MVV, respiratory muscle endurance, respiratory infections. **Chronicity:** Time since injury ranged from 2 to 6 months since injury.	1. Significant increase in MIP, VC, MVV, and respiratory muscle endurance. and lung volumes after IMT. 2. Number of respiratory infections was less in the training than the sham group (1 vs. 14).

Roth et al. 2010 USA RCT PEDro = 4 Level 2 N = 29	**Population:** *Resistance Training Group*: Mean age: 31.1 yr; Gender: male=81%, female=19%; *Sham Training Group:* Mean age: 28.9 yr; Gender: male=69%, female=31%; Level of injury: C4-C7, T1; Severity of injury: complete. **Intervention:** Patients were randomly assigned to either expiratory muscle resistance training or sham training for a total of 6 weeks. **Outcome Measures:** The following before and after the training program: FVC, FEV_1, maximum expiratory pressure (MEP), maximum inspiratory pressure (MIP), IC, expiratory reserve volume (ERV), total lung capacity (TLC), functional residual capacity (FRC), and residual volume (RV). **Chronicity:** Patients were invited to participate in the study if the SCI was recent and had occurred within 6 months' time. No further information regarding time since injury was provided.	1. Multivariate analysis did not reveal any significant differences between the resistance training and sham training groups for any of the pulmonary function tests (p=0.22). 2. Univariate analysis revealed significant improvements in FVC (p=0.02), FEV_1 (p=0.02), ERV (p=0.04), MIP (p=0.002), and MEP (p<0.001) in the resistance training group. 3. Univariate analysis revealed significant improvements in FVC (p=0.04), FEV_1 (p=0.01) and ERV (p<0.01) in the sham training group.
Liaw et al. 2000 Taiwan RCT PEDro = 4 Level 2 N = 30	**Population:** N=30 participants with SCI (C4-C7, 30-134 post-injury); 20 participants completed (13 control,17 IMT group), 8M:2F in each group, mean (SD) age RIMT:30.9(11.6) yrs; control: 36.5(11.5) yrs. **Treatment:** Target resistive IMT or control; 15-20min 2x/day × 6wks; other rehab activities continued. **Outcome Measures:** Spirometry, MIP. **Chronicity:** Mean time since injury (53.1) days.	1. Pre-post % change of VC and TLC in IMT group was greater compared to change in control values. 2. MIP improved in both groups which might be due to natural progression of improvement from SCI, learning to do the maneuver, and/or insufficient length of training.
	Population: Age range: 16-41 yr; Gender: male=6, female=5; Level of injury: C4-5 to C7; Severity of injury: complete.	Between group comparison: 1. There were no significant

Derrickson et al. 1992 USA RCT PEDro = 3 Level 2 N = 11	**Intervention:** Patients were randomly assigned to receive resistive inspiratory muscle training (RIMT) or abdominal weights (AbWts) training for 7 weeks. Training sessions consisted of two 15-minute treatments each day, 5 days a week. **Outcome Measures:** The following after one week and seven weeks: FVC, IC, maximal voluntary ventilation (MVV), PEF rate, and increased inspiratory mouth pressure (PImax). **Chronicity:** Time since injury was an average of 12 days (RIMT group) and 25 days (AbWts group).	differences in FVC, MVV, PEFR, PImax, and IC between patients who received RIMT training and those who received AbWts training ($p>0.05$ in all cases). Within group comparison: 2. After 7 weeks, patients who received RIMT training experienced a significantly larger FVC ($p<0.001$), a larger MVV ($p<0.05$), a higher PEF ($p<0.01$), a lower PImax ($p<0.001$), and a higher IC ($p<0.05$) compared to these measures after 1 week. 3. After 7 weeks, patients who received AbWts training experienced a significantly larger FVC ($p<0.001$), a larger MVV ($p<0.001$), a higher PEF ($p<0.001$), and a lower PImax ($p<0.001$) compared to these measures after 1 week.

Raab et al. 2019 Switzerland Case control Level 3 N = 67	**Population:** 67 patients with traumatic (n = 59) or non-traumatic (n = 8) SCI; motor lesion level from C4 to T12; 55 males and 12 females; mean age 50 (35 to 66) years; mean time post injury 1.9 (1.2-2.9) months; AIS A/B (n = 41) and AIS C/D (n = 26). **Treatment:** IMT with a training device for isolated inspiratory resistance with the valve calibrated and adjusted (9–41 cmH_2O) according to the participant's PImax. IMT started about 6 weeks after injury and lasted for a period of about 6 consecutive weeks with 3–5 training sessions per week and with up to 90 repetitions per training session (according to the individual capacity, and individually and gradually increased). All participants received standard physiotherapy as part of the comprehensive in-patient rehabilitation program. **Outcome Measures:** Respiratory muscle strength (PImax and PEmax), repetitions per session, number of training sessions, and training intensity (% resistance of the individual baseline value of PImax). **Chronicity:** Mean time post injury 1.9 (1.2 – 2.9) months.	1. Effect size of 7% (95% confidence interval (CI) 2.8–11.6%) increase in PImax per 10 units (cmH_2O) of increase in training intensity. The association of PImax with training intensity was independent of AIS (test of interaction: chi^2 = 0.18, d.f. = 1, p = 0.67) and lesion level (chi^2 = 0.00, d.f. = 1, p = 0.99). 2. The effect of training intensity on PEmax was conditional on AIS (test of interaction: p < 0.021). While participants with motor complete lesions (AIS A/B) showed a 6.8% (95% CI 2.1 to 11.7%) increase in PEmax per 10 units (cmH_2O) of increase in training intensity, the corresponding adjusted effect size in the group with motor incomplete lesions (AIS C/D) was 0.1% (95% CI −4.3 to 4.5%).

Shin et al. 2019 Republic of Korea Case control Level 3 N = 104	**Population:** 104 patients with acute (n = 14), subacute (n = 42), and chronic (n = 48) SCI; 78 males and 26 females; mean (SD) age 48.7 (± 17.5) years; AIS A (n = 21), AIS B (n = 7), AIS C (n = 30) and AIS D (n = 46); injury severity (complete, n = 21 and incomplete, n = 83); level of injury (tetraplegia, n = 65, paraplegia, n = 39); and mean (SD) disease duration 97.4 (± 139.2) days. **Treatment:** Self-directed RMT and care for 4 weeks (more than 5 days a week) consisting in glossopharyngeal breathing exercises, IMT using incentive spirometry, and air stacking exercises with a resuscitation bag. Patients were subgrouped by injury severity, level of injury and disease duration for analysis. **Outcome Measures:** Pulmonary function evaluation (FVC in sitting position (ΔFVCsit), FVC in supine (ΔFVCsup), and PCF (ΔPCF)) before and after the short-term rehabilitation therapy. **Chronicity:** Time since injury not specified. Patients were included if they had an acute, subacute, or chronic SCI.	1. FVCsup, FVCsit, and PCF were more severely affected in the tetraplegic group compared to the paraplegic group (P < 0.01) at baseline. 2. The absolute value of FVCsup was significantly higher compared with that of FVCsit at the initial and final assessment in all subgroups, except for the acute group. 3. After treatment protocol, the absolute values of FVCsup, FVCsit, and PCF had significantly improved in all subgroups regardless of the injury level and severity, as well as disease duration. 4. The subacute group showed the highest improvement in ΔFVCsit and ΔPCF, compared with the acute and chronic groups (P < 0.05); and a greater ΔFVCsup compared with the chronic group (P = 0.002) and a higher tendency compared with the acute group (P = 0.056).

McDonald & Stiller 2019 Australia Pre–post Level 4 N = 7	**Population:** 7 male patients with acute complete (AIS A) SCI, mean age 33.6 (22-62) years; level of injury C4 (n = 1), C6 (n = 3), C7-T1 (n = 1), T4 (n = 1), and T6 (n = 1); and time since injury 10.1 (5-17) days. **Treatment:** IMT protocol consisting in a high-resistance, low-repetition, using a hand-held electronic IMT device. Each session comprised 3-6 sets of 6 breaths, with rest allowed between sets as desired and a total session time less than 10 minutes. Training load was set at 50% of PImax (RPE of 6-8) and once the participant's RPE was < 6 and/or they were able to complete the entire IMT session, training pressure was increased by 10% per week to a maximum of 90% PImax. Training frequency was once per day for 4–5 days/week, with 2–3 rest days/week. IMT sessions continued for the duration of each participant's stay at the hospital to an arbitrary maximum of four weeks. **Outcome Measures:** Feasibility (number of sessions when the criteria to participate in IMT were met/not met, and reasons why), safety, and efficacy (PImax, FVC and PEF rate) were collected before, during and after intervention. **Chronicity:** Time since injury was 10.1 (5 – 17) days.	1. A mean (range) of 7.1 (3–11) IMT sessions per participant delivered over 10.7 (4–17) days were performed. The variability in the number of IMT sessions and days over which it was delivered resulted from the variability in participants' hospital LOS. 2. No adverse safety outcomes were identified. 3. Lung function parameters were variable both between and within participants (improvements in lung function were seen for 4 of the 7 participants over the duration of their IMT sessions).
Raab et al. 2018 Switzerland Case control Level 3 N = 79	**Population:** *Inspiratory Muscle Training Group – AIS A/B:* Mean age: 48 yr; Gender: male=10, female=5; Level of injury: N/R; Injury severity: tetraplegia=7, paraplegia=8. *Inspiratory Muscle Training Group – AIS C/D:* Mean age: 63 yr; Gender: male=22, female=5; Level of injury: N/R;	1. PImax was seen to significantly increase for those treated with combined muscle training, regardless of AIS score ($p<0.001$) and for those treated with inspiratory

	Injury severity: tetraplegia=22, paraplegia=5. *Combined In- and Expiratory Muscle Training Group – AIS A/B:* Mean age: 44.5 yr; Gender: male=14, female=2; Level of injury: N/R; Injury severity: tetraplegia=7, paraplegia=9. *Combined In- and Expiratory Muscle Training Group – AIS C/D:* Mean age: 60 yr; Gender: male=18, female=3; Level of injury: N/R; Injury severity: tetraplegia=18, paraplegia=3. **Intervention:** Participants had up to 5 training sessions per week of either inspiratory muscle training or combined in- and expiratory muscle training. **Outcome Measures:** PImax, PEmax, FVC, forced expiratory volume, sniff nasal inspiratory pressure, and PEF. Results were stratified by AIS groups A/B and C/D. **Chronicity:** On average patients were 2.4 months post injury.	muscle training only (p=0.008). 2. PEmax was seen to significantly increase for those treated with combined muscle training, regardless of AIS score (p<0.001) and for those with AIS scores of C or D treated with inspiratory only muscle training (p<0.001). 3. FVC was seen to significantly increase in those who were treated with combined muscle training, regardless of AIS score (p<0.001). The same trends were observed for those in the inspiratory only muscle training groups (p<0.05). 4. Forced expiratory volume was found to significantly increase in participants treated with combined muscle training, regardless of AIS score (p<0.05), while the same trend was observed for those treated with inspiratory only muscle training (p<0.05). 5. Sniff nasal inspiratory pressure was found to significantly increase in those treated with combined muscle

		training ($p<0.001$), regardless of AIS score. No significant improvements were observed in the inspiratory only muscle training group. 6. PEF was only seen to improve significantly in the AIS C and D groups regardless of type of intervention ($p<0.05$), but not the AIS A/B groups.
Berney et al. 2002 Australia Case control Level 3 N = 14	**Population:** Mean age: 28 yr; Gender: male=11, female=3; Level of injury: C5-C7; Severity of injury: complete. **Intervention:** Patients who received a tracheostomy were compared to patients who were extubated and received physiotherapy. **Outcome Measures:** The following at the time of extubation/the day of tracheostomy: FVC, PaO_2/FiO_2, total number of physiotherapy treatments, number of physiotherapy treatments in ICU, LOS in ICU, days requiring MV, LOS in acute ward after discharge from ICU, days from injury to fixation. **Chronicity:** Patients were studied beginning within 24 hr of injury.	1. There was no significant difference in FVC between tracheostomized patients and physiotherapy patients ($p>0.05$). 2. There was no significant difference in PaO_2/FiO_2 ratios between tracheostomized patients and physiotherapy patients ($p>0.05$). 3. There was no significant difference in total number of physiotherapy treatments between tracheostomized patients and extubated patients. Patients who were extubated and received physiotherapy required significantly fewer treatments compared to tracheostomized

		patients in ICU (p=0.047). 4. Tracheostomized patients spent significantly more days in ICU than physiotherapy patients (p=0.006) and required MV significantly longer than the physiotherapy group (p=0.018). 5. There was no significant difference in the LOS in the acute ward between groups (p>0.05). 6. There was no significant difference in the time from injury to fixation between groups (p>0.05).

Discussion

A Cochrane review and meta-analysis demonstrated that RMT training in the hospital (including IMT, expiratory muscle training [EMT], isocapnic hyperpnea, among other types of respiratory training) can significantly improve respiratory muscle strength, function, and endurance for people with tetraplegia (as measured by vital capacity, maximal voluntary ventilation (MVV), IC, MIP, and MEP). (Berlowitz & Tamplin 2013; Tamplin & Berlowitz 2014).

Eight RCTs have examined the effectiveness of physiotherapy techniques on the pulmonary function of patients with SCI. Boswell-Ruys et al. (2020) found that RMT (IMT and EMT) provided more improvements in MIP, respiratory health, and Borg scores for breathlessness during 10 inspiratory loaded breaths compared to the same exercises using a sham device in 62 patients with acute or chronic tetraplegia. A study of 96 patients by Sikka et al. (2021) suggested that resistive IMT (using a threshold trainer imposing resistance to inspiration and expiration) resulted in a significant positive effect on pulmonary function and on respiratory muscle strength compared to the control group. Mueller et al. (2012 & 2013) evaluated 24 participants with complete tetraplegia in three groups (sham, isocapnic hyperpnea and

inspiratory resistive training). After eight weeks of training, patients who performed isocapnic hyperpnea and inspiratory resistive training obtained significantly better results in inspiratory muscle strength and different components of quality of life, compared to those who were training with placebo. Liaw et al. (2000) studied 30 participants with acute SCI and found that the group who performed a target resistive inspiratory muscle training twice a day for 6 weeks showed a greater change in VC and TLC in the IMT group compared to the change in control values, whereas MIP improved in both groups. Postma et al. (2014) investigated the effect of RIMT in people with SCI during inpatient rehabilitation. This technique was found to have a positive short-term effect on inspiratory muscle function one week following the intervention period; however, this effect was no longer significant eight weeks post muscle training. Finally, Roth et al. (2010) assessed the effectiveness of expiratory muscle training compared to sham training in patients with acute SCI. Multivariate analysis did not reveal any significant between-group differences for any pulmonary function tests conducted after the 6-week training period.

A case-control study also found positive results with both inspiratory and combination in- and expiratory muscle training regardless of AIS score (Raab et al. 2018). Measures of inspiratory and expiratory pressure significantly increased, as well as FVC regardless of muscle training group (Raab et al. 2018). Another study with patients with acute SCI found that IMT, starting about six weeks after injury for six consecutive weeks with a gradual increase in the intensity, provided an increase in MIP and MEP. The association of MIP with training intensity was independent of AIS and lesion level, whereas the effect of training intensity on MEP showed differences between groups; participants with motor complete lesions (AIS A/B) showed a 6.8% (95% CI 2.1 to 11.7%) increase in MEP per 10 units (cmH_2O) of increase in training intensity, compared with participants with motor incomplete lesions (AIS C/D) who the increase was 0.1% (95% CI −4.3 to 4.5%) (Raab et al. 2019). The pre-post study of McDonald & Stiller (2019) assessed 7 patients with acute SCI who performed a protocol of IMT consisting of a high-resistance and low repetition, with progressive increase of training load (until 90% MIP) for 4 weeks. They showed no adverse safety outcomes and improvements in lung function in four of the seven participants.

A case control study (Berney et al. 2002) has shown that extubation along with initiation of intensive physiotherapy can improve lung function, reduce the rate of pulmonary complications and decrease the LOS in intensive care for patients with acute tetraplegia. It should be noted that patients who have been extubated or who have had a tracheostomy are able to receive physiotherapy, if treatment occurs once the patient is in stable condition.

Physiotherapy treatments during acute SCI would be useful for stable patients and in hospitals that have the resources for on-call physiotherapists.

Prospective large-scale RCTs should continue to be conducted to confirm these findings that physiotherapy is an effective adjuvant to improve acute pulmonary functioning.

Conclusion

There is level 1b evidence (from four RCTs: Mueller et al. 2012 & 2013; Postma et al. 2014; Liaw et al. 2000; Derrickson et al. 1992), level 3 evidence (from three case-control studies: Raab et al. 2019; Raab et al. 2018; Shin et al. 2019), and level 4 evidence (from one pre-post study: McDonald & Stiller 2019) in support of inspiratory muscle training as an effective means to improve respiratory muscle function compared to usual care in patients with acute SCI regardless of AIS score.

There is level 1a evidence (from two RCTs: Boswell-Ruys et al. 2020; Sikka et al. 2021) that respiratory muscular training (imposing resistance to inspiration and expiration) improves respiratory muscle strength and pulmonary function in patients with acute SCI.

There is level 1b (from one RCT: Van Houtte et al. 2008) that normocapnic hyperpnea training provided a significant increase in respiratory muscle strength and endurance, pulmonary function, and decrease the rate of respiratory infections in patients with acute SCI.

There is level 3 evidence (from one case control: Berney et al. 2002) that extubation and intensive physiotherapy reduces LOS in intensive care in patients with acute SCI.

Inspiratory and expiratory muscle training may improve respiratory muscle function during the acute phase post SCI.

LOS in intensive care may be reduced by extubation in combination with intensive physiotherapy.

6.2 Abdominal Neuromuscular Electrical Stimulation (NMES)

Abdominal neuromuscular electrical stimulation (NMES) can be used in conjunction with voluntary efforts (depending on the level of SCI) to improve forced expiratory maneuvers including cough.

Table 12. Abdominal Neuromuscular Electrical Stimulation (NMES)

Author Year Country Research Design Score Sample Size	Methods	Outcome
McCaughey et al. 2015 USA Cohort Level 2 N = 10	**Population:** 10* patients ventilator-dependent with SCI and tetraplegia (8M, 2F) & N=9 retrospectively matched control patients (8M, 1F) Mean (SD) age: 48.2 (18.0) years *1 male excluded in analysis **Applicable to intervention group only **Treatment:** Abdominal FES. **Outcome Measures:** V_T, VC, time to ventilation weaning. **Chronicity:** Median (SD) DOI: 22.2 (12.0) days.	1. Significantly greater V_T in abdominal FES group compared to control group in 1 of 9 sessions, but not significant longitudinally. 2. Significantly greater VC in final 2 sessions (abdominal FES) or 3 sessions (control), compared to respective first session; no significant between-group difference. 3. No significant difference between groups in change of V_T and VC per week. 4. No significant between group difference in time to wean.
McBain et al. 2013 Australia RCT (crossover) PEDro = 5 Level 2 N = 15	**Population:** N=15 males with SCI (C4-T5); mean (SD) age: 45(4); DOI: 11.9(4.3) yrs. **Treatment:** All participants trained for 6 weeks, 5 days per week (5 sets of 10 coughs per day). Participants coughed voluntarily at the same time as a train of electrical stimulation was delivered over the abdominal muscles via posterolaterally positioned electrodes (50Hz, 3s).	1. During voluntary coughs, FES cough stimulation improved Pga, Pes, and Pescough acutely, 20-fold, 4-fold, and 50%, respectively. 2. Six weeks of cough training caused further improvements. It significantly increased Pga (SD) from 37.1 (2.0) to 46.5 (2.9)

	Outcome Measures: Pes and Pga expiratory pressures, peak expiratory flow (PEFcough) produced before, during, and after the training. **Chronicity:** Mean (± SD) time since injury was 1.4 (± 2.2) (from 0.2 to 7.8 years).	cmH2O, Pes from 35.4 (2.7) to 48.1 (2.9)cm H2O, and PEFcough from 3.1 (0.1) to 3.6 (0.1) L/s. 3. Cough training also improved pressures and flow during voluntary unstimulated coughs.
Cheng et al. 2006 Taiwan RCT PEDro = 5 Level 2 N = 26	**Population:** N = 26 participants with traumatic cervical SCI; 21 males and 5 females; mean age 36.8 years; AIS A or B; and level of injury between C4 and C7. **Treatment:** Participants were randomly assigned to: • Control group (n = 13): Participants received a conventional rehabilitation program (which included passive range of motion, mattress exercise, sitting balance or upper extremity functional training). • NMES therapy group (n = 13): Patients underwent the conventional program plus NMES therapy (which consisted in NMES applied to the clavicular portion of the pectoralis major and abdominal muscle stimulation for 30 minutes daily, 5 days a week for 4 weeks). **Outcome Measures:** VC, FVC, FEV_1, PEF, MIP, MEP, and pulmonary complications were assessed before and after the	1. Significant improvements were found in the NMES therapy group vs. The control in VC, FVC, FEVi, PEF, MIP, and MEP at 4 weeks, at 3-month and 6-month follow-up testing, $p < 0.05$. 2. Six (46.1%) of the 13 patients in the control group suffered pulmonary complications in the follow-up period, while only 1 (7.7%) of the 13 patients in the NMES therapy group had pulmonary complications during this period ($p < 0.05$).

	4 weeks therapy and at 3- and 6-month follow-up. **Chronicity:** Mean time since was injury 2.45 months.	
McLachlan et al. 2013 UK Pre–post Level 4 N = 12	**Population:** N=12 participants with tetraplegia (11M;1F); median age: 31 yrs (range: 18-73); 7 AIS A, 5 AIS C; median DOI: 5 months (range: 2-94). **Treatment:** 3 weeks of abdominal muscle conditioning using transcutaneous abdominal functional electrical stimulation (AFES). **Outcome Measures:** FVC, FEV_1, PEFR, MEP. **Chronicity:** Median time since injury was 5 months, ranging from 2 to 94.	1. Mean (SD) FVC increased by 0.36(0.23) L during training. 2. No significant changes were found in mean FEV_1 and PEF. 3. No significant change was found in the outcome measures during a 1-week pre-training control phase and during a 3-week post-training phase.
Zupan et al. 1997 Slovenia Pre-Post Level 4 N=13	**Population:** 13 patients with tetraplegia; 11 men and 2 women; mean age 26.9 years; injury level C4 (n = 2), C5 (n = 2), C6 (n = 6), and C7 (n = 3); complete SCI (n = 10) and incomplete SCI (n = 3); and mean time between injury 7 months. *One patient with cavernoma had a history of disease for 10 years. **Treatment:** Each patient was subjected randomly for three periods: • Inspiratory muscle training, consisting of inspiratory muscles exercises for training both strength and endurance. • Expiratory muscle training, consisting of expiratory muscle	1. During condition 1, the measured RT in both positions (sitting and lying) revealed statistically significant increase (P<0.05) after the inspiratory muscle training; however, at the conclusion of expiratory muscle training, the measured RT revealed no statistically significant changes in sitting position but statistically significant changes in lying position. 2. During condition 2 and 4, the measured RT in both positions revealed statistically significant increase (P<0.05) following both kinds of training.

	exercises accompanied by electrical stimulation of the abdominal muscles. • 1-month without training. Both programs of respiratory muscle training consisted of seven different exercises and each one was repeated ten times. Each training session lasted 20 ± 30 min and was conducted twice a day six days a week for a period of 4 weeks. **Outcome Measures:** Respiratory tests (RT) (FVC and FEV_1) were conducted in sitting and lying positions at baseline and at the conclusion of each 1-month period. RT were conducted under four sets of conditions: • Condition 1: The patient's unassisted effort. • Condition 2: The patient's effort combined with pressure manually applied by a therapist to the upper part of their abdomen. • Condition 3 and 4: The patient's effort accompanied by electrical stimulation of the abdominal muscles during the early phase of expirium, once triggered by the therapist (3) and once by the patients themselves (4).	3. During condition 3, there was a significant increase ($P<0.05$) in measured RT in both positions after the period of inspiratory muscle training but no significant increase after the expiratory muscle training. 4. After the period without training no one measurement showed significant increase in RT. 5. The patient's voluntary effort combined with electrical stimulation (conditions 3 and 4) was more effective than voluntary effort alone. 6. Two patients complained of experiencing more spasms during the expiratory muscle training combined with electrical stimulation, and during measurements where patients voluntary effort was combined with the therapist's manual assistance or electrical stimulation.

Discussion

The systematic review and meta-analysis of McCaughey et al. (2016b) showed that abdominal functional electric stimulation is an effective technique for improving respiratory function in both an acute (as measured by cough peak flow) and chronic manner (as measured by FVC, vital capacity, and peak expiratory flow [PEF]) in people with SCI. However, low participant numbers and heterogeneity of participants and outcomes across studies reduced the power of the meta-analysis and the establishment of the clinical efficacy of this technique.

To date, there are only two studies assessing abdominal (and pectoralis major) NMES in patients with SCI in the acute phase. McCaughey et al. (2015) showed that a program of abdominal FES applied for between 20 and 40 minutes per day, five times per week on four alternate weeks provided improvements in VT and VC and faster weaning rates from mechanical ventilation in patients with ventilator-dependent tetraplegia (mean time since injury 22.0 days) in comparison with their matched-controls. Cheng et al. (2006) showed that a conventional therapy program plus NMES to the clavicular portion of the pectoralis major and abdominal muscle (30 minutes daily, 5 days a week for 4 weeks) provided significant improvements in pulmonary function (as measured by vital capacity, FVC, FEV_1, PEF, MIP, and MEP) immediately after the intervention, at 3-month, and at 6-month follow-up. Pulmonary complication rates were also assessed at 6 months, and it was shown that patients in the intervention group had fewer complications than patients in the control group ($p < 0.05$) (Cheng et al. 2006). Zupan et al. (1997) studied 13 participants with tetraplegia with a mean time since injury of 1.3 years; each participant completed one month of inspiratory muscle training, expiratory muscle training, and a period without training (Zupan et al. 1997). Both programs of respiratory muscle training consisted of seven different exercises; with sessions of 20 ± 30 min conducted twice a day, six days a week (Zupan et al. 1997). Electrical stimulation of the abdominal muscles was only delivered for the expiratory muscle training sessions; and only for eight repetitions of one of the exercises (i.e., tries to reach maximal expiration on Wrights peak flow meter) (Zupan et al. 1997). The authors showed that the respiratory tests (FVC and FEV_1, in sitting and lying positions) were slightly superior after the inspiratory program than after the expiratory (plus electrical stimulation) program (Zupan et al. 1997). It is important to consider that measurements were taken under four sets of conditions: the patients' unassisted efforts, their efforts combined with pressure manually applied by a therapist to the upper part of their abdomen, and their efforts accompanied by electrical stimulation of the abdominal muscles during the early phase of expirium, once triggered by the therapist and once by the patients themselves (Zupan et al. 1997). After one month of training, the patient's voluntary effort combined with electrical stimulation (when the stimulation

was triggered by the therapist and when it was triggered by the patient himself) was more effective than voluntary effort alone (Zupan et al. 1997).

Conclusion

There is level 2 evidence (from one RCT: Cheng et al. 2006) that a conventional training program and additional NMES sessions for the clavicular portion of the pectoralis major and abdominal muscle provides significant improvements in pulmonary function both short-term and long-term, and reduces the respiratory complication rates at 6 months follow-up; compared with a conventional training intervention alone in patients with acute SCI.

There is level 2 evidence (from one cohort study: McCaughey et al. 2015) that a program of abdominal FES provides improvements in VT and VC and faster weaning rates from mechanical ventilation in patients with ventilator-dependent tetraplegia in comparison with their matched-controls.

Neuromuscular abdominal electrical stimulation could provide an improvement in pulmonary function at short-term and long-term, could accelerate the weaning from the mechanical ventilation, and could reduce the respiratory complication rates during a 6-month follow-up in patients with acute SCI.

6.3 Diaphragm Pacing

The diaphragm is primarily controlled by the phrenic nerve. Diaphragm pacing involves surgically implanted electrodes onto the diaphragm that stimulates intact phrenic nerves to contract the diaphragm muscle (Madden 2016). In 2008 the Food and Drug Administration approved the use of the NeuRx Diaphragm Pacing System (DPS) for humanitarian-use for patients with SCI (Madden 2016).

Table 13. Effect of Diaphragm Pacing on Respiration During Acute SCI

Author Year Country Research Design Score Sample Size	**Methods**	**Outcome**
Kerwin et al. 2020b USA Case control	**Population:** 101 patients with acute cervical SCI and requiring MV and tracheostomy for respiratory failure, 83 males and	1. 97% of patients in the DPS group survived, while 82% survived in the NO DPS group. This difference was

Level 3 N = 101	18 females; mean age 42 years; level of injury high (C1-C4) (n = 34) and low (C5-C7) (n = 57); complete injury (n = 85) and incomplete injury (n = 14). **Treatment:** Patients were divided in two groups: • DPS group (n = 40): Underwent laparoscopic DPS. • No DPS group (n = 61): Case matching patients with similar injuries. **Outcome Measures:** Ventilator liberation before discharge, days to liberation from ventilator, VT change before discharge, and mortality. **Chronicity:** Patient population defined as acute.	statistically significant on bivariate analysis (p = 0.05) but was not significant on multivariate models that included age, sex, race, injury severity, and injury year (p = 0.69). 2. The DPS group had a mean increase in VT of 88 ± 22 mL within 72 hours of DPS implantation, while the NO DPS group patients had a mean decrease in VT of 14 ± 32 mL at postinjury day 14. This difference was statistically different on multivariate linear regression analysis controlling for age, sex, race, injury severity, and injury year (p = 0.008). 3. The mean time to liberation in the DPS group was 10.1 ± 1.7 days as compared with 29.2 ± 3 days in the NO DPS group. This difference was statistically significant on multivariate linear regression analysis, including age, sex, race, injury severity, and injury year as covariates (p < 0.001). 4. Hospital LOS was significantly longer in the NO DPS group (65 ± 61 days vs. 43 ± 24 days, p = 0.03).
Kerwin et al. 2020a USA Case control Level 3 N = 101	**Population:** 101 patients with acute cervical SCI and requiring MV and tracheostomy for respiratory failure, 83 males and 18 females; mean age 42 years; level of injury high (C1-C4) (n = 34) and low (C5-C7) (n = 57);	1. Following DPS implantation, there was a statistically significant increase in spontaneous Vt compared with NO DPS (+88 mL vs. −13 mL; 95% CI

	complete injury (n = 85) and incomplete injury (n = 14). **Treatment:** Patients were divided in two groups: • DPS group (n = 40): Underwent laparoscopic DPS. • No DPS group (n = 61): Case matching patients with similar injuries. **Outcome Measures:** Adjusted hospital charges. **Chronicity:** Patient population defined as acute.	46 to 131 vs. −78 to 51 mL, respectively; p = 0.004). 2. Median time to liberation after DPS was significantly shorter (10 vs. 29 days; 95% CI 6.5 to 13.6 vs. 23.1 to 35.3 days; p < 0.001). 3. Adjusted hospital charges were significantly lower for DPS on multivariate linear regression models controlling for year of injury, sex, race, injury severity, and age (p = 0.003).
Kerwin et al. 2018 USA Case control Level 3 N = 101	**Population:** *DPS Group, n=40*: Mean age: 45 yr; Gender: male=29, female=11; Level of injury: C1-C4= 35%, C5-C7= 65%; Severity of injury: complete=88%, incomplete=12%. *No DPS Group, n=61*: Mean age: 39 yr; Gender: male=54, female=7; Level of injury: C1-C4=33%, C5-C7=67%; Severity of injury: complete= 82%, incomplete= 15%. **Intervention:** Patients either underwent diaphragm pacing system implantation or did not. **Outcome Measures:** Ventilator days, VAP. **Chronicity:** Patient population defined as acute.	1. There were no significant differences between groups in terms of the number of days spent on ventilators. 2. There were no significant differences between groups in terms of the rates of VAP.
Duarte et al. 2021 Brazil Case control Level 3 N = 10	**Population:** 10 ICU patients submitted to tracheostomy due to cervical SCI (AIS A); 8 males and 2 females; mean age 28.5 years. **Intervention:** TEDS combined with standard weaning protocol (SWP) or SWP alone (n = 4). TEDS training consisted of two daily 20-min sessions 7 days a week. Electrical stimulation device was triggered manually	1. Total IMV time was 1.77 times shorter in patients in the TEDS relative to patients in the SWP group. 2. LOS in ICU was 2.54 times shorter in patients in the TEDS group relative to patients in the SWP group. 3. Weaning time in the TEDS and the SWP group was 28 ± 15 and 50 ± 19 days, respectively.

	once every two breaths using verbal cues. A dual channel unit with self-adhesive electrodes (attached to the left and right midaxillary line at the level of the sixth, seventh, and eighth intercostal spaces, and to the paraxiphoid region) was used. **Outcome Measures:** Time of IMV via orotracheal tube, time of IMV via tracheostomy, ventilator WT, total IMV time, ICU LOS, overall hospital LOS, Sepsis-related Organ Failure Assessment (SOFA), and APACHE II scores. **Chronicity:** Time since injury not specified but patients were included at ICU.	4. The mean number of training sessions (in the TEDS group) required for ventilator withdrawal was 47, spread across 23 days on average.
Esclarin et al. 1994 Spain Case control Level 3 N = 22	**Population:** 22 participants with either: diaphragmatic pacemaker (DP) (n=9) or MV (n=13); mean (SD) age: 10.6(2.5) years (DP group) and 35(5.5) years (MV group); Injury level: C1 (n=10), C2 (n=9) or C3 (n=3). **Treatment:** Diaphragmatic pacemaker or MV. Retrospective study with follow up information from last clinical examination or by telephone call. **Outcome Measures**: Respiratory complications (atelectasis and pneumonia); functional status (ability to remain seated at 50-90°, skill to drive electric wheelchair, use of phonetic language); satisfaction with treatment; cost of maintenance materials; cause of death. **Chronicity:** Time from the lesion to admission was 225 ± 49 days in the pacemaker	1. Respiratory problems: DP group produced less bronchial secretions; type of organisms found similar for both groups. 2. No significant differences between groups with respect to functional status. 3. Satisfaction with treatment significantly better for the DP group. 4. Mean yearly cost of materials higher for MV group. 5. Deaths: 4 deaths in DP group: pneumonia (n=2), cardiogenic shock (n=1), unknown (n=1). 1 death in MV group, presumably due to inappropriate home care.

	group and 328 ± 87 in the ventilator group.	
Nakajima & Sharkey 1990 Japan Case series Level 4 N = 15	**Population:** n = 15, C1-C3, brainstem tetraplegia. **Intervention:** Phrenic nerve (14 – neck, 1 – thorax) stimulation. **Chronicity:** Interval from injury to implantation was 3 to 35 months.	1. 11/15 achieved full time pacing. 2. 2/15 achieved half-time pacing. 3. 2/15 showed no response: a. One developed perineural fibrosis around the phrenic nerve thereby inhibiting stimulation. b. The other (a four-year-old child) showed loss of nerve viability.
Sharkey et al. 1989 USA Case series Level 4 N = 15	**Population:** N = 15, high cervical tetraplegia. **Intervention:** Phrenic nerve (14/15 neck and 1/15 thoracic) stimulation. **Chronicity:** Interval from injury to implantation was 3 to 35 months; with a mean interval being 13 months.	1. 13/15 achieved full time pacing (including 1 who at the time of follow up did so for 16 years). 2. 2/15 achieved half-time pacing. 3. Complications: a. Equipment failures, in one case. b. Fibrosis around the electrode resulted in failure to stimulate the nerve, in another case. c. Infection required the removal of the system.
Posluszny et al. 2013 USA Case series Level 4 N = 29	**Population:** N=29 (27M, 2F); of which N=7 were non-stimulable (7M); mean (range) age: 31.4 (17-65). **Intervention:** Diaphragm pacer implantation. **Chronicity:** Elapsed time from injury to surgery was 40 days (range from 3 to 112).	1. 16/22 completely weaned within a mean of 10.2 days, 18/22 within 180 days. 2. 3/22 partially weaned (mixture of MV and pacer). 3. 8/22 complete recovery of respiration and pacer removal. 4. One patient successfully implanted but had life-prolonging measures withdrawn.

Elefteriades et al. 2002 USA Case series Level 4 N = 12	**Population:** N = 12, C1 - C2 tetraplegia. **Intervention:** Bilateral phrenic nerve stimulation and diaphragm conditioning. **Chronicity:** Time after injury to pacing ranged from 3 to 32 months.	1. Long-term follow up outcomes. a. 6/12 paced full-time (mean 14.8 years). b. 1/12 paced full-time for 6.5 years before lapsing to part time. c. 3/12 paced for an average of 1.8 years before stopping. d. 2/12 were deceased: 1 paced for 10 years. 2. Patients who stopped pacing full-time did so due to inadequate financial or social support, or because they were institutionalized.

Discussion

In 1972, the first tetraplegic patient underwent phrenic nerve pacing (PNP). This technology was widely used in the 1980s and 1990s, but had considerable risks from thoracotomy, phrenic nerve damage with electrode placement, and perineural fibrosis (scarring) around the phrenic nerve. Then in 2002, DiMarco and Onders described placement of electrodes into the diaphragm muscle itself, positioning the leads near the motor points of the phrenic nerve without compromising the nerve or its sheath. The diaphragm pacing system (DPS) is gaining acceptance as an alternative to MV in centers that are capable of implanting these systems.

To date only a few studies have examined diaphragm pacing during the acute SCI phase. Diaphragm pacing is one of the newer approved interventions for respiratory function post SCI. There are three cohort studies that have compared patients with acute and cervical SCI who received DPS (n = 40) and those who didn't receive DPS (n = 61) (Kerwin et al. 2020a; Kerwin et al. 2020b; Kerwin et al. 2018). Studies showed that DPS implantation produced significant improvements in spontaneous Vt, and reduced hospital LOS, time to liberation from MV and hospital charges, compared with no receive DPS (Kerwin et al. 2020a; Kerwin et al. 2020b). In the case of development of VAP, the DPS patients had significantly shorter vent days compared with the No DPS patients (mean = 8.7 days less) (Kerwin et al. 2018). However, DPS implantation did not demonstrate any significant improvement in outcome measures (hospital LOS, ICU LOS, vent days, or VAP) when examined in multivariable linear regression models (controlling for confounders such as age, sex, race, insurance status, and injury year)

(Kerwin et al. 2018). In the previous study by Kerwin et al. (2018), diaphragm pacing was found to have no significant influence on the rates of VAP. However, its efficacy as an intervention for improving respiratory outcomes needs to be further examined as there were no significant effects of diaphragm pacing on the number of days spent on a ventilator. As only one respiratory outcome and one complication were examined in this sole study, more research needs to be conducted to make conclusions about the value of diaphragm pacing for patients with acute SCI. In another retrospective case control study, Esclarin et al. (1994) reported higher rates of power wheelchair management, phonation success, patient satisfaction and hospital discharge in paced participants compared to mechanically ventilated participants. A basic cost analysis in that study suggested that costs were 50 hours per year for ventilatory management in the mechanically ventilated group (Esclarin et al. 1994). However, caution in data interpretation is warranted given small sample sizes, lack of baseline statistics between groups, potential for selection bias in participants receiving pacemakers, and overall high rate of death in the high lesion SCI population. Prospective comparison studies looking at morbidity, mortality, quality of life and costs related to phrenic and diaphragmatic pacing are lacking. There are several small level 4 studies to show that bilateral phrenic nerve pacing and bilateral diaphragmatic pacing can be used successfully for the ventilation of people with SCI (Posluszny et al. 2013; Elefteriades et al. 2002; Nakajima & Sharkey 1990).

A recent case-control retrospectively analyzed 10 patients with tracheostomy and cervical SCI and showed that those who received TEDS training in combination with a standard weaning protocol had a shorter duration of IMV and ICU LOS compared who received only the standard weaning protocol (Duarte et al. 2021).

Conclusion

There is level 3 evidence (from one case control study; Kerwin et al. 2018) that diaphragm pacing may not increase the risk of VAP or reduce the number of ventilator days compared to no implantation for patients acute SCI. There is level 3 evidence (from 2 case control studies: Kerwin et al. 2020a; Kerwin et al. 2020b) that DPS implantation produced significant improvements in spontaneous Vt and reduced hospital charges, hospital LOS and time to liberation from MV compared with those who did not receive DPS in patients with acute cervical SCI.

There is level 3 evidence (from one case control study: Esclarin et al. 1994) that suggests better power wheelchair management, phonation success, patient satisfaction and hospital discharge in phrenic paced participants compared to mechanically ventilated participants.

There is level 4 evidence (from three case series: Posluszny et al. 2013; Elefteriades et al. 2002; Nakajima & Sharkey 1990) that phrenic nerve stimulation can be used as a long-term alternative to MV for people with injuries at C2 or above.

There is level 3 evidence (from one case control study: Duarte et al. 2021) that patients submitted to tracheostomy due to cervical SCI who received TEDS training in combination with a standard weaning protocol have a shorter duration of IMV and ICU LOS compared with who received only a standard weaning protocol.

While diaphragm pacing may not reduce the number of days spent on a ventilator, it does not appear to increase the risk of VAP in patients with acute SCI.

There is some evidence that suggests a higher survival rate, as well as better power wheelchair management, phonation success, and patient satisfaction in phrenic paced participants compared to mechanically ventilated participants.

Phrenic nerve or diaphragmatic stimulation may be used as a long-term alternative to MV for people with injuries at C1 or C2.

6.4 Intermittent Positive Pressure Breathing

Intermittent positive pressure breathing (IPPB) is a respiratory therapy that is used to expand the lungs and induce hyperinflation (Laffont et al. 2008). Little is known about the effects of IPPB in patients with SCI, and very little literature is published for patients with acute SCI. The limited studies that do exist examining IPPB among participants with tetraplegia demonstrate very few complications after treatment (Laffont et al. 2008).

Table 14. Intermittent Positive Pressure Breathing (IPPB) for Patients with Acute SCI

Author Year Country Research Design Score Sample Size	**Methods**	**Outcome**
Laffont et al. 2008 France RCT	**Population:** 14 traumatic SCI participants (C5-T6, AIS A or B), injured within the last 6	1. IPPB had no short-term or long-term effects on VC, lung compliance, or work of breathing.

PEDro = 5 Level 2 N = 14	months with no thoracic injuries. **Treatment:** Intermittent positive-pressure breathing (IPPB), at least 20 minutes twice daily for 5 days a week; patients treated with 2 months IPPB treatment and 2 months without IPPB, in random cross-over design. **Outcome Measures:** Lung function tests; lung compliance; work of breathing. **Chronicity:** Mean time since injury was not specified, but patients were included if they were injured in the last 6 months.	
Stiller et al. 1992 Australia Pre-post Level 4 N = 5	**Population:** Mean age: 34 yr; Gender: male=3, female=2; Level of injury: C5-C7; Severity of injury: not specified. **Intervention:** All patients received IPPB. **Outcome Measures:** Lung volume, vital capacity, Vt. **Chronicity:** Patients were studied beginning within 24 hr of sustaining injury.	1. On admission, patients had significantly reduced resting vital capacity compared to normal values ($p<0.001$). 2. Lung volume was significantly higher during IPPB compared to resting values ($p<0.001$). 3. Immediately after receiving IPPB, vital capacity ($p<0.02$), but not Vt ($p>0.05$), was significantly higher compared to resting levels.

Discussion

In a pre-post study by Stiller et al. (1992), the effectiveness of IPPB on lung capacity was studied. The authors found that this style of MV significantly increased lung volume, as well as vital capacity (Stiller et al. 1992). More recently, a RCT by Laffont et al. (2008) found that IPPB had no short-term or long-term effects on pulmonary function, lung compliance or work of breathing in patients within 6 months of SCI who were not in respiratory failure. The authors reported that IPPB requires significant resources with respect to staff and equipment and is reported as unpleasant by many people with SCI.

While IPPB does not appear to be effective on lung function and compliance, further studies that explore the effect of IPPB on atelectasis, secretion management, and in acute respiratory failure following SCI are needed.

Conclusion

There is level 2 evidence (from one RCT: Laffont et al. 2008) that IPPB has no short-term or long-term effects on lung function within one year of SCI.

There is level 4 evidence (from one pre-post study: Stiller et al. 1992) that intermittent positive pressure breathing may increase lung volume as well as vital lung capacity in people with acute SCI.

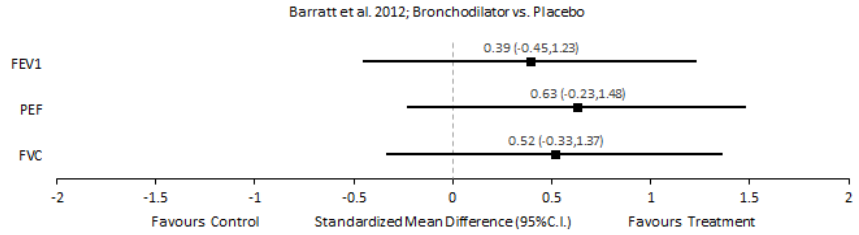
IPPB may increase lung volume and vital lung capacity in persons with acute SCI.

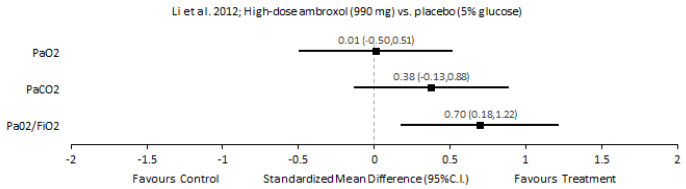
7 Pharmacological Interventions for Pulmonary Function Improvement During Acute SCI

Pharmacological treatments for pulmonary function in patients with SCI aim to improve breathing and coughing. This area of research has been explored largely in patients with chronic SCI, where bronchodilators and anabolic steroids have shown varying degrees of success (see the rehabilitation chapter on Respiratory Management in SCIRE version 6.0).

Table 15. Pharmacological Interventions for Pulmonary Function During Acute SCI

Author Year Country Research Design Score Sample Size	**Methods**	**Outcome**
Barratt et al. 2012 Australia RCT PEDro = 9 Level 1b N = 12	**Population:** Age range: 25-37 yr; Gender: male=9, female=3; Level of injury: C5-C7; Severity of injury: complete=10, incomplete=2; AIS A-B. **Intervention:** Patients were randomized to receive either bronchodilator therapy	1. After 10 minutes, patients who received the bronchodilator therapy experienced a significant improvement in FVC ($p<0.05$), FEV_1 ($p<0.05$), and PEF ($p<0.05$) compared to patients who received the placebo.

	(inhaler, 100 µg salbutamol) or placebo (propellant only). **Outcome Measures:** The following at 10 minutes and 30 minutes after inhalation: FVC, FEV_1, and peak expiratory flow (PEF) rate. **Chronicity:** The median time since injury was 24 (18-35) days.	2. After 30 minutes, patients who received the bronchodilator therapy experienced a significant improvement in FVC ($p<0.05$) and FEV_1 ($p<0.05$) compared to patients who received the placebo. There were no significant differences between groups with regard to PEF ($p>0.05$).
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- (baseline) and post-intervention (after 10 minutes) data. 	
Li et al. 2012 China RCT PEDro = 6 Level 1b N = 61	**Population:** Age range: 39-67 yr; Gender: male=40, female=21; Level of injury: cervical; Severity of injury: complete=27, incomplete=34 AIS A-B. **Intervention:** Patients were randomized to receive either high-dose ambroxol (990 mg/day for 5 days) or placebo (5% glucose in 500 mL saline for 5 days) after spinal fixation surgery. **Outcome Measures:** The following during hospital stay: post-operative pulmonary complications in the form of pulmonary infection, atelectasis, and hypoxemia. The following after 3 and 5 days in the ICU: arterial blood gas analysis in the form of partial pressure of inspired	1. Patients who received high dose ambroxol experienced significantly fewer episodes of pneumonia ($p=0.027$) and hypoxemia ($p=0.047$) than patients who received placebo. There were no significant differences with regards to atelectasis between groups ($p=0.430$). 2. After 3 days in ICU, patients who received high dose ambroxol had a significantly higher oxygenation index than patients who received placebo ($p=0.049$). There were no significant differences in PaO_2 ($p=0.683$) and $PaCO_2$ ($p=0.847$) between groups. 3. After 5 days in ICU, patients who received

	oxygen in arterial blood (PaO_2), partial pressure of carbon dioxide in arterial blood ($PaCO_2$), and ratio of arterial oxygen partial pressure to fractional inspired oxygen. **Chronicity:** Time since injury not specified.	high dose ambroxol had a significantly higher oxygenation index than patients who received placebo (p=0.032). There were no significant differences in PaO_2 (p=0.193) and $PaCO_2$ (p=0.928) between groups.
	Effect Sizes: Forest plot of standardized mean differences (SMD ± 95%C.I.) as calculated from pre- and post-intervention data. 	

Discussion

For cervical SCI, the imbalance of parasympathetic drive leads to bronchoconstriction and bronchosecretion. Medications such as salbutamol (albuterol in the USA) and ipratropium are commonly used during acute hospitalization. Other medications that are commonly used are mucolytics for secretion management, such as scopolamine, atropine, glycopyrrolate, N-Acetylcysteine, hypertonic saline. There is not any evidence in acute SCI.

Other medications that have been piloted is the anabolic steroid called Oxandralone (Halstead et al. 2010) and theophylline (Tzelepis et al. 2006) to improve respiratory function; but these studies were done in patients with chronic SCI.

Although several types of bronchodilators and secretolytic agents exist, only two have been tested within the acute SCI population. Based on one study alone, bronchodilator therapy with salbutamol provided effective short-term improvements in lung function (Barratt et al. 2012). Barratt et al. (2012) showed that salbutamol increased FVC and forced expiratory volume; these improvements were maintained for half an hour. Peak cough expiratory flow also improved, but this effect deteriorated after ten minutes (Barratt et al. 2012).

The second RCT by Li et al. (2012) studied the secretolytic agent, ambroxol, after surgical spinal cord decompression and stabilization and demonstrated more long-term improvements in pulmonary functioning. Oxygenation indexes remained elevated after five days, and patients had fewer episodes of pneumonia and hypoxemia overall (Li et al. 2012). These two studies showed

that pharmacological interventions may be helpful in improving breathing and reducing infection, but long-term treatments (>1 month) and the efficacy of alternative drugs remain unknown (Barratt et al. 2012; Li et al. 2012).

Conclusion

There is level 1b evidence (from one RCT: Barratt et al. 2012) that bronchodilator therapy with salbutamol may improve pulmonary function compared to placebo in patients with acute SCI.

There is level 1b evidence (from one RCT: Li et al. 2012) that high dose ambroxol may reduce postoperative respiratory complications and increase blood oxygenation following surgical spinal cord decompression and stabilization compared to placebo in patients with acute cervical SCI.

Bronchodilator therapy with salbutamol may be an effective treatment for improving pulmonary function during the acute phase post SCI.

Ambroxol may be an effective treatment to reduce pulmonary complications and improve oxygenation status following surgery in patients with acute cervical SCI.

8 Hospital Programs for Respiratory Management in SCI

Respiratory management for patients with SCI is thought to be most effective when the care extends beyond the individual to incorporate specialized hospital programs (Parker et al. 2010). Studies have examined the effect of respiratory management programs on enhancing patient recovery and decreasing hospital stay compared to regular hospital treatment that may differ for each person.

Table 16. Effects of Hospital Programs for Respiratory Management During Acute SCI

Author Year Country Research Design Score Sample Size	Methods	Outcome
Richard-Denis et al. 2018 Canada Case control Level 3 N = 81	**Population:** (*Group 1*): Mean age: 43.6 yr; Gender: male=75.4%, female=24.6%; Injury severity: Mean ISS= 35.3. (*Group 2*): Mean age; 42.5yr; Gender: male=83.3%, female=16.7%; Injury severity: Mean ISS=42.7%. **Intervention:** Patients in group 1 were transferred early to a level-1 trauma center for surgical management of SCI. Patients in Group 2 were transferred late (post-operatively) to the same SCI trauma center for care. **Outcome Measures:** Tracheostomy requirement, MV requirement, ventilation and support duration. **Chronicity:** Patient population was defined as acute SCI.	1. Group 2 had significantly higher rates of required tracheostomies (p=0.004). 2. There were no significant differences between groups in terms of the number of patients who required MV support. 3. There was a significant difference between groups for the number of days spent on ventilation, with Group 2 spending on average 50 more days on ventilation (p=0.006).
Cinotti et al. 2019 France Pre-post Level 4 N = 117	**Population:** 117 patients with a traumatic cervical SCI admitted in the ICU in the first 48 hours; 81 males and 36 females; mean age 46.5 years; AIS A (n = 67), AIS B (n = 16), AIS C (n = 18), and AIS D (n = 16); and clinical motor level (ASIA score) C2 (n = 4), C3 (n = 2), C4 (n = 22), C5 (n = 36), C6 (n = 20), C7 (n = 15), and T1 (n = 3). **Intervention:** Study was divided in two periods (where patients were analyzed	1. During the intervention period, overall bundle compliance* was achieved in 0 patients in the control group and 5 (8.3%) patients after the rehabilitation program implementation. 2. Median ICU LOS was not statistically different between the two periods (26 [16–47] vs. 29 [11.00–46.75] days; p=0.9). 3. During the control period, the Delta ASIA motor score

	receiving different intervention protocols): • Control phase (n = 57): Consisted of all consecutive patients who were admitted to ICUs receiving general care according with local protocol and French guidelines. • Intervention phase (n = 60): Involved all consecutive patients receiving an early rehabilitation strategy with an ET in case of upper injury (> C6), bronchial drainage physiotherapy, assisted cough with mechanical insufflator/exsufflator in atelectasis and aerosol therapy based on beta-2 mimetics, among other techniques. *Some of the interventions remained similar in the two intervention phases. **Outcome Measures:** The Delta ASIA motor score (ASIA motor score variation between ICU admission and ICU discharge) in the subgroup of patients with AIS grade A; compliance with rehabilitation program; the number of respiratory complications; in-ICU LOS; hospital LOS; ASIA score at 1 year; and 1-year mortality. **Chronicity:** Patients were admitted in the ICU in the first 48 hours.	between ICU discharge and admission was +6 [0–14], as compared to +16 [4–32] with the rehabilitation program ($p < 0.05$). In a multi-variate linear regression model, the intervention period was significantly associated with a higher Delta ASIA motor score (β coefficient, 11.4; CI_{95} [1.9–21.0]; $p = 0.01$). In the subgroup of patients with AIS Grade A patients, the Delta ASIA motor scale was +1 [0–10] in the control period, and +10 [3–24]; $p = 0.02$) in the intervention period. 4. One year after SCI, the Delta ASIA motor score between 1-year follow-up and ICU admission remained higher in the intervention phase than in the control period (+34 [15–60] vs. +11 [0–33]; $p < 0.05$). * Overall bundle compliance is defined by the association of ET as recommended in the 7 days after ICU admission, protective ventilation (6–8 mL/kg^{-1}), PEEP >0 cmH_2O, early enteral nutrition, early mobilization, and early active perineal care, within 48 h after ICU admission.
Romero-Ganuza et al. 2015 Spain Pre-post Level 4 N = 68	**Population:** Mean age: 53.8 yr; Gender: male=49, female=19; Level of SCI: C1-C4=44, C5-C8=11, thoracic=13. **Intervention:** Patients were treated with a specific	1. Five patients died in hospital. 2. The average LOS for survivors was 195.6 days. 3. 63/68 of patients were discharged to the community, 47 patients

	respiratory care comprehensive rehabilitation program. **Outcome Measures:** Hospital mortality, LOS, discharged to community, discharged home, discharge to extended care facilities, discharge to acute care hospital, weaned from ventilation, patients with permanent respiratory support. **Chronicity:** Patients were admitted within 3 months of injury.	were discharged home, 13 were discharged to extended-care facilities, and 3 were sent to an acute care hospital setting. 4. 23 patients were weaned at the hospital. 5. 20 patients had permanent respiratory support.
Wong et al. 2012 USA Post-test Level 4 N = 24	**Population:** Mean age: 33 yr; Gender: male=22, female=2; Level of injury: C1-C4; Severity of injury: complete=79%, incomplete=21%; AIS A-D. **Intervention:** Retrospective analysis of patients who received a hospital program at an SCI specialty unit of HVtV, high frequency percussive ventilation, and mechanical insufflation-exsufflation were compared before and after the program. **Outcome Measures:** Occurrence of high tidal ventilation, high frequency percussive ventilation, mechanical insufflation-exsufflation, initiating a speaking valve, ventilator weaning attempts, time from admission to ventilator wean. **Chronicity:** Average time from injury to transfer to the SCI unit was 33.8 days.	1. In 14 patients who were weaned off the ventilator, the average day to be weaned from the time of admission was 27.6 days (*SD* 12.9 days). 2. Three participants with C3 AIS A were ventilator weaned in 24 to 62 days (average 43.67 days). Eight participants with C4 AIS A were ventilator weaned in 14 to 31 days (average 22.13 days). Two participants with C4 AIS B were weaned from the ventilator in 19 to 22 days (average 20.5 days). One participants with C4 AIS C was weaned in 37 days. 3. Six participants were decannulated prior to discharge to home, and the average days to be decannulated after admission was 42.0 days (*SD* 16.6 days).
Cameron et al. 2009 Australia Cohort Level 2 N = 102	**Population:** Age range: 24-52 yr; Gender: male=78, female=24; Level of injury: C4-C8. T1-T5, T6 and below; Severity of injury: complete=44, incomplete=58; AIS A-D.	1. There were no significant differences with regards to hours mechanically ventilated (p=0.71) and hours in ICU (p=0.60) between pre-TRAMS

	Intervention: Patients either received tracheostomy review and management services (post-TRAMS group, 2003-2006) or did not receive tracheostomy review and management services (pre-TRAMS group, 1991-2001). **Outcome Measures:** Hours mechanically ventilated, hours in ICU, length of hospital stay, duration of cannulation, initiation of communication through a one-way speaking valve, deaths. **Chronicity:** Length of acute hospital stay was a median of 60 days (pre-TRAMS group) and 41.5 days (post-TRAMS group); time since injury was not specified.	patients and post-TRAMS patients. 2. Post-TRAMS patients had a significantly shorter hospital stay compared to pre-TRAMS patients (p=0.03). 3. Post-TRAMS patients had a significantly shorter duration of cannulation compared to pre-TRAMS patients (p=0.03). 4. Post-TRAMS patients began using one-way speaking valves significantly earlier than pre-TRAMS patients (p<0.01). 5. There were no tracheostomy-related deaths in either group.
Vitaz et al. 2001 USA Cohort Level 2 N = 58	**Population:** Mean age: 33 yr; Gender: not specified; Level of injury: C1-T5; Severity of injury: not specified. **Intervention:** Patients either received treatment according to the clinical care pathway (Group 1) or received regular treatment (Group 2; control). **Outcome Measures:** The following during hospital stay: episodes of pneumonia, length of hospital stay, length of ICU stay, days on ventilator. **Chronicity:** Average overall length of hospital stay was 36 days and 24 days for Group 1 and Group 2 patients, respectively; time since injury was not specified.	1. Patients in Group 1 experienced significantly fewer episodes of pneumonia compared to patients in the control group (p<0.05). 2. Patients in Group 1 experienced a significantly shorter stay in the hospital (p<0.05) and ICU (p<0.05) and required significantly fewer days on the ventilator (p<0.05) compared to patients in the control group.

Discussion

Overall, specialized respiratory management programs provided in the hospital for respiratory management have been shown to benefit individuals

more than traditional hospital care. These programs reduce the length of hospital stay and ventilator days (Cameron et al. 2009; Vitaz et al. 2001; Richard-Denis et al. 2018), help individuals gain independence by initiating speaking valves sooner (Wong et al. 2012) and reduce the incidence of pulmonary complications (Vitaz et al. 2001). Although Wong et al. (2012) did not perform statistical analyses to compare the efficacy of their program, the patients who received all three respiratory management therapies (HVtV, high frequency percussive ventilation, and mechanical insufflation-exsufflation) had fewer complications than those who did not.

Cinotti et al. (2019) prospectively studied 117 patients with traumatic cervical SCI admitted to the ICU in the first 48 hours and compared outcomes between a control phase (where treatment was administered following standard hospital protocols) and an intervention phase (based on a multiple-disciplinary rehabilitation program protocol which included, among other techniques, ET) observing that a higher Delta ASIA motor score was associated with the intervention phase compared to the control phase between ICU discharge and admission and between ICU admission and 1 year follow up.

Another moderate sized case control study found that patients admitted early to a specialized level-1 trauma center overall had fewer procedures and complications compared to who? (Richard-Denis et al. 2018). Early admission to this center significantly decreased the rates of tracheostomies, as well as the total number of days in hospital. Early admitted patients spent on average 50 fewer days on ventilation (Richard-Denis et al. 2018). Another study examining specialized care by Romero-Ganuza et al. (2015) found that a third of patients were able to be weaned at the hospital, and 63/68 participants were discharged to the community and not to long-term care. More research is needed to determine how this level of specialized care compares to other standards of care.

Conclusion

There is level 4 evidence (from one post-test: Wong et al. 2012) that the implementation of specialized respiratory management results in stabilization and improvement of respiratory status in patients with acute SCI.

There is level 2 evidence (from one cohort study: Cameron et al. 2009) that the tracheostomy review and management service reduces length of hospital stay and duration of cannulation while increasing speech valve usage compared to those who do not receive tracheostomy review and management in patients with acute SCI.

There is level 2 evidence (from one cohort study: Vitaz et al. 2001) that the use of a clinical care pathway reduces length of hospital stay and results in fewer

complications compared to those who received regular care in patients with acute SCI.

There is level 3 evidence (from one case control study: Richard-Denis et al. 2018) that early admission to a level-1 trauma center results in lower rates of tracheostomies, as well as fewer ventilator days for patients with acute SCI, compared to late admission.

There is level 4 evidence (from one pre-post test: Romero-Ganuza et al. 2015) that specialized respiratory care results in a high number of community discharges in patients with acute SCI.

There is level 4 evidence (from one pre-post study: Cinotti et al. 2019) that a multiple-disciplinary rehabilitation protocol which included, among other techniques, ET, provides a higher Delta ASIA motor score between ICU discharge and admission and between ICU admission and 1 year follow up in patients with traumatic cervical SCI who were admitted in the ICU in the first 48 hours.

Specialized respiratory management programs provided in the hospital may lead to reduced procedures, ventilator days, hospital LOS, and improved respiratory and patient discharge status, in the acute phase post SCI.

9 Sleep Disordered Breathing (SDB) in SCI

Sleep disordered breathing (SDB) is a term used to describe a broad spectrum of breathing disorders during sleep. The most commonly known disorder is obstructive sleep apnea (OSA). It is a disease characterized by recurrent collapse of the upper airway during sleep leading to nocturnal hypoxemia and sleep fragmentation. Characteristic symptoms include loud snoring, excessive daytime sleepiness, and nocturnal choking. Risk factors for this disease include alcohol use, sedatives, obesity, increased age, and male gender. Because of activation of systemic inflammation and the sympathetic nervous system, sleep apnea may be an independent risk factor for the development of cardiovascular disease. In the able-bodied, sleep apnea is relatively common and under-diagnosed.

Generally, the first line treatment of sleep apnea is lifestyle counseling (i.e., weight loss, avoidance of alcohol). There are different types of sleep apnea and they require different treatment approaches; OSA occurs when throat muscles relax, and central sleep apnea occurs when the brain does not send proper signals to the muscles that control breathing. OSA can be treated with CPAP therapy, considered to be first-line therapy. This consists of a mask

placed on the face attached to an air compressor via plastic tubing. CPAP devices establish a positive pressure in the upper airway preventing its collapse during sleep. Studies of CPAP in people without SCI demonstrate significant benefits in terms of reducing sleepiness and preventing motor vehicle crashes. Other therapies that have been used to treat OSA include mandibular advancement devices (dental splints) and upper airway surgery. Central sleep apnea requires a back-up rate, and sleep-related hypoventilation and a pressure differential between inspiration and expiration (a treatment called Bi-level PAP) (Chiodo et al. 2016). Research shows that central apnea is more common in patients with tetraplegia than in patients with paraplegia (Chiodo et al. 2016).

9.1 Prevalence and Risk Factors

SDB, including sleep apnea appear to have a higher prevalence in people after SCI than those without, with some researchers estimating it is present in 60% of motor complete persons with tetraplegia (Proserpio et al. 2015; Chiodo et al. 2016). In general, the studies that examined the prevalence of OSA were limited by small sample sizes and by experimental designs that lacked a non-SCI control group that could be directly compared to the patients with SCI. Both overnight oximetry and full polysomnography were used to diagnose the disorder. The prevalence rate ranged from 9.1% to 83% (Short et al. 1992; Burns et al. 2000; Burns et al. 2001; Stockhammer et al. 2002; Berlowitz et al. 2005). Obesity was identified as a risk factor for sleep apnea in most studies. The use of muscle relaxants was identified as a potential risk factor for SDB in some but not all studies (Short et al. 1992; Ayas et al. 2001; Burns et al. 2001; Berlowitz et al. 2005).

Table 17. Treatment of Sleep Disordered Breathing (SDB)

Author Year Country Score Research Design Sample Size	**Methods**	**Outcome**
Berlowitz et al. 2019 Australia RCT PEDro = 8 Level 1b N = 149	**Population:** 149 Patients with traumatic quadriplegia and SDB - OSA; 134 males and 15 females; mean (SD) age 47 (± 15); injury level C2-C4 (n = 74) and C5-T1 (n = 75); AIS A (n = 55); and mean time since injury 73 days.	1. Study participants improved on the PASAT by an average (SD) of 17.0 (± 28.1) over the 3 months; however, no significant difference was observed between groups.

	Treatment: All participants with an apnea hypopnea index (AHI) >10 events per hour were trialed on an auto titrating CPAP for up to 3 nights and if tolerated the treatment for at least 4 hours on one of three nights were randomized to: • CPAP + usual care (n = 73), received auto titrating CPAP immediately during 3 months. • Usual care only (n = 76), wait for 3 months. **Outcome Measures:** Neurocognitive test battery (attention and information processing as measure with the Paced Auditory Serial Addition TASK (PASAT), the Rey Auditory Verbal Learning Test (RAVLT), the Digit Span subtest of the Wechsler Adult Intelligence Scale IV, Symbol Digit Modalities Test and North American Adult Reading Test (NAART)); sleep disorder symptoms and state sleepiness (the Basic Nordic Sleep Questionnaire (BNSQ) and the Karolinska Sleepiness Scale (KSS)); health-related quality of life (the Assessment of Quality of Life Scale); mental health and mood (the Hospital Anxiety and Depression Scale and the Profile of Mood States (POMS); non-blinded measures of sleepiness (KSS); autonomic dysfunction; CPAP adherence; medication; troubleshooting of any mask or device issues; and spirometry (FVC and FEV_1) were administered at	2. Sleepiness measured by the KSS was significantly improved by auto titrating CPAP on intention- to-treat analysis ($p < 0.01$, mean difference in improvement of −1.26, 95% CI −2.2 to –0.32), after controlling for baseline predictors (−0.65, 95% CI −1.3 to –0.01) and in each week in which participants were classified as adherent ($p = 0.004$, −0.45, 95% CI −0.77 to –0.14). The BNSQ measure of sleepiness was non-significantly improved by CPAP on intention to treat ($p = 0.16$; −2.86, 95% CI −0.11 to 6.84) but significantly improved after controlling for baseline predictors (−3.42, 95% CI −6.67 to –0.16) and on *per protocol* (p=0.003; −9.09, 95% CI −3.2 to –15). The POMS Fatigue score improved overall (−1.37, 95% CI −2.2 to –0.44) but was not different between groups ($p = 0.57$). 3. 10 of the 27 outcome measures significantly improved within group over time. The intention-to-treat, linear regression models and the per protocol comparisons, found no between-group differences in any of the outcome measures other than sleepiness (KSS). 4. Baclofen prescription increased at study conclusion but proportionally less in the

	baseline and at study completion. **Chronicity:** Mean time since injury was 73 days.	CPAP group (52% vs. 75%, p = 0.03). 5. No differences were observed between groups in the frequency of autonomic dysreflexia events per week (p = 0.37; −0.17, 95% CI −0.55 to –0.21), serious adverse events or measures of heart rate variability.
Graco et al. 2019 Australia Secondary analysis of CPAP data from RCT Level 3 N = 79	**Population:** 79 patients with traumatic tetraplegia and OSA; 72 males and 67 females; mean (SD) age 46.2 (± 15.9) years; injury level C2-C4 (n = 43) and C5-T1 (n = 36); AIS A (n = 33); and mean (SD) time since injury 77.7 (± 64.3) days. **Intervention:** Secondary analysis of the 79 patients who were enrolled in a previous study (Berlowitz et al. 2019; see above). **Outcome Measures:** Adherence within (mean nightly hours of use), adherent (recorded device use of at least 4 hours average per night throughout the study), baseline factors (age, sex, injury severity, time since injury, OSA severity (AHI, Arousal Index, number of awakenings, and 4% oxygen desaturation), quality of life, premorbid intelligence (the North American Adult Reading Test [NAART]), anxiety and depression, mood, daytime sleepiness, waist circumference, neck circumference, BMI, and CPAP use in the first week),	1. Mean daily CPAP use was low (2.9 ± 2.3 hours). 2. 33% of the participants receiving CPAP (n = 26) were adherent over the 3-month study with mean daily use of >4 hours; about 43% (n = 34) used CPAP for <2 hours per night; and 24% (n =19) used CPAP for between 2 and 4 hours per night on average. 3. Greater CPAP use over the 13-week trial was associated (P < 0.01) with CPAP use in the first week, higher premorbid intelligence, higher abdominal girth, increasing age, and more severe OSA. 4. Higher 95th percentile pressure (cmH_2O) was significantly associated with greater daily hours of CPAP use (coefficient = 0.20; 95% confidence interval, 0.16 - 0.25; P < 0.001). Baseline AHI (coefficient = 0.01; P = 0.08) and 95th percentile leak (coefficient = 0.001; P =

	CPAP device pressure and leak. **Chronicity:** Mean (SD) time since injury was 77.7 (± 64.3) days.	0.68) were not associated with daily usage.
Proserpio et al. 2015 Italy Prospective observational study Level 5 N = 35	**Population:** Thirty-five (15 tetraplegic and 20 paraplegic) patients were enrolled. Nine patients (25.7%) had an obstructive sleep-disordered breathing (SDB) and 10 (28.6%) had periodic leg movements during sleep (PLMS). **Treatment:** Each patient underwent a clinical assessment, full polysomnography, and arterial blood gas analysis before and immediately after sleep. **Outcome Measures:** Multiple logistic regressions were applied to evaluate factors associated with SDB and PLMS. **Chronicity:** Mean (SD) time since injury was 77 (± 68) days.	1. The frequency of SDB in the first year following injury was higher in tetraplegic than in paraplegic participants whereas PLMs were significantly more frequent in participants with an incomplete motor lesion than in participants with a complete motor lesion. 2. Multiple regression shows that the level and the completeness of the spinal cord lesion are the main factors associated with an early development of SDB and PLMS.

Discussion

SDB is common in people with SCI; obesity appears to be a consistent risk factor. The prospective observational study of Proserpio et al. (2015) with 35 patients with acute SCI found that SDB in the first year following injury was more frequent in tetraplegic than in paraplegic patients, and periodic leg movements during sleep (PLMS) were more frequent in participants with an incomplete motor lesion than in those with complete motor lesions. Moreover, they showed that level and completeness of the spinal cord lesion were the main factors associated with an early development of SDB and PLMS.

There are few studies that have assessed the impact of sleep apnea therapy in patients with SCI. Berlowitz et al. (2019) showed in an RCT that CPAP plus usual care reduced sleepiness when patients with acute SCI were adherent to the therapy during the 3-month study period. Graco et al. (2019) showed that

greater usage of CPAP was associated with higher abdominal girth, increased age, and more severe OSA. A limited number of studies have examined the impact of sleep apnea therapy on health and quality of life outcomes in SCI; future investigations should examine these and other questions with larger sample sizes to determine more accurate effects of CPAP therapy.

Conclusion

There is level 1b (from one RCT: Berlowitz et al. 2019) to support CPAP therapy therapies to treat SDB in people with acute SCI.

People with SCI have a high prevalence of SDB, and therapy may improve quality of life and other outcomes. Signs and symptoms (e.g., snoring, obesity, witnessed apneas, daytime sleepiness) should be monitored and sleep apnea testing should be conducted (i.e., overnight oximetry or polysomnography).

10 Summary

It is important to note that despite the evidence presented in this chapter, less than ten percent of all studies to date in acute SCI are RCTs. As such, most evidence in this field has been determined retrospectively.

Most of the research in acute respiratory management for people with SCI is centered on re-establishing ventilation (e.g., tracheostomy, intubation, extubation, or secretion removal techniques) and preventing and treating pulmonary complications. It is of vital importance to maintain an open airway and diaphragm functioning while preventing respiratory failure, atelectasis, and pneumonia. This is a delicate balance for medical personnel as the process of ventilation itself (despite assisting breathing) can directly lead to these pulmonary complications.

There is some evidence that tracheostomies can reduce the number of pulmonary complications in people with acute SCI compared to those not receiving this procedure (Leelapattana et al. 2012). There is also some consensus that early tracheostomies provide fewer intensive care unit (ICU), hospital, and ventilation days in comparison with late tracheostomies; however, more evidence is still needed to elucidate if early tracheostomies may decrease the rates of mortality and other complications in patients with acute SCI (Anand et al. 2020; Beom & Seo 2018; Choi et al. 2013; Flanagan et al. 2018; Romero-Ganuza et al. 2011b; Holscher et al. 2014; Kornblith et al. 2014; Romero et al. 2009; Wang et al. 2020; Wang et al. 2021). Predictors of early tracheostomy (ET) in people with SCI include: higher injury level, more severe AIS score, cervical spine fractures at C4 or above, and lower mean AIS motor impairment score at the time of injury (Beom & Seo 2018; Flanagan et al. 2018; Binder et al. 2016).

The inability to clear bronchial secretions is a major cause of pulmonary complications in patients with acute SCI; unfortunately, only a few high-quality studies show that techniques such as mechanical insufflation/exsufflation and oscillated positive expiratory pressure (OPEP) breathing plus oscillated incentive spirometry (OIS) facilitate secretion removal in the acute phase of SCI (Pillastrini et al. 2006; Kluaythomthong et al. 2019).

There is good evidence to show that non-pharmacological interventions, such as respiratory muscle training, have positive effects on lung function in people with acute SCI, regardless of AIS status (Boswell-Ruys et al. 2020; Sikka et al. 2021; Mueller et al. 2012 & 2013; Postma et al. 2014; Liaw et al. 2000; Derrickson et al. 1992; Raab et al. 2019; Raab et al. 2018; Shin et al. 2019; McDonald & Stiller 2019).

Some evidence suggests that diaphragmatic pacing system (DPS) implantation and/or phrenic nerve stimulation can produce significant

improvements in ventilation, reduce hospital LOS, and be an alternative to mechanical ventilation (MV) for people with acute SCI (Kerwin et al. 2018; Kerwin et al. 2020a; Kerwin et al. 2020b; Posluszny et al. 2013; Elefteriades et al. 2002; Nakajima & Sharkey 1990).

Two RCTs have demonstrated that adding medications such as salbutamol or high-dose ambroxol to bronchodilator therapy or post-surgery can improve pulmonary function and minimize post-operative complications in people with acute SCI (Barratt et al. 2012; Li et al. 2012).

Further, evidence suggests that specialized respiratory management programs delivered in the hospital, implementation of a clinical care pathway, and/or early admission to a level 1 trauma center can result in better respiratory outcomes and higher rate of discharge to the community Wong et al. 2012; Cameron et al. 2009; Vitaz et al. 2001; Richard-Denis et al. 2018; Romero-Ganuza et al. 2015).

Sleep disordered breathing (SDB), more specifically obstructive sleep apnea (OSA), is common in people with SCI. Though there are few studies in this area, in an RCT, Berlowitz et al. (2019) found that continuous positive airway pressure (CPAP) therapy was effective in treating OSA in people with acute SCI.

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Abbreviations

%VC	percentage of vital capacity
AbWts	abdominal weights
ACSF	anterior cervical spine fusion
AIR	acute inpatient rehabilitation
AIS	ASIA Impairment Scale
ALI	acute lung injury
APACHE II	Acute Physiology and Chronic Health Evaluation II
ARDS	acute respiratory distress syndrome
ASIA	American Spinal Injury Association
BiPAP	biphasic positive airway pressure
CW	complete weaning
CPAP	continuous positive airway pressure
DPS	diaphragmatic pacing system
ECMO	extracorporeal membrane oxygenation
EIV	endotracheal invasive ventilation
EMT	expiratory muscle training
ET	early tracheostomy
FEV_1	forced expiratory volume in one second
FVC	forced vital capacity
HTV/HVtV	high tidal volume (ventilation)
IC	inspiratory capacity
ICU	intensive care unit
iLA	interventional lung assist
IMV	intermittent mandatory ventilation / invasive mechanical ventilation
IMT	inspiratory muscle training
IPPB	intermittent positive pressure breathing
ISS	Injury Severity Score
LOS	length of stay
LT	late tracheostomy

LTV	low tidal volume
MV	mechanical ventilation
MVV	maximal voluntary ventilation
NMES	neuromuscular electrical stimulation
OIS	oscillated incentive spirometry
OPEP	oscillated positive expiratory pressure
OSA	obstructive sleep apnea
PCF	peak cough flow
$PaCO_2$	partial pressure of carbon dioxide in arterial blood
PaO_2	partial pressure of inspired oxygen in arterial blood
PaO_2/FiO_2	ratio of arterial oxygen partial pressure to fractional inspired oxygen
PDT	percutaneous dilational tracheostomy
PEF	peak expiratory flow
PEmax/MEP	maximal expiratory pressure
PImax/MIP	maximal inspiratory pressure
PLMS	periodic leg movements during sleep
PVFB	progressive ventilator-free breathing
RCT	randomized controlled trial
RIMT	resistive inspiratory muscle training
SaO_2	saturation of oxygen
SDB	sleep disordered breathing
SCI	spinal cord injury
ST	surgical tracheostomy
TEDS	transcutaneous electrical diaphragmatic stimulation
TOV	transtracheal open ventilation
TRAMS	Tracheostomy Review and Management Services
VAP	ventilator-associated pneumonia
VFB	ventilator-free breathing
Vt	tidal volume