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 USA Case control Level 3 N = 181	**Population:** 181 patients with acute SCI who were admitted to a level 1 trauma center 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);	1. Patients who received HVtV were more likely to develop VAP and require a 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.

	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.	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 = 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),	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 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

	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).	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 Case control Level 3 N = 36	**Population:** 36 patients with ventilator-dependent tetraplegia following an acute traumatic cervical SCI, history 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	1. 33/36 patients achieved 16 h VFB and 20/36 achieved 24 h VFB, representing high 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

	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.	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 N = 189	**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. **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	1. Patients aged 31-35 who were weaned from the ventilator at discharge had a significantly higher mean 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

	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.	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 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.	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 ± 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).

	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.	
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). • Group II - Pacemaker + phrenic nerve reconstruction (n = 6). • Group III - Pacemaker + diaphragm muscle replacement (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.

	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).