



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg

Observational study of early diaphragm pacing in cervical spinal cord injured patients to decrease mechanical ventilation during the COVID-19 pandemic

Raymond P. Onders, MD*, MaryJo Elmo, ACNP, Brian Young, MD, Glen Tinkoff, MD

Department of Surgery, University Hospitals Cleveland Medical Center, Cleveland, OH

ARTICLE INFO

Article history:

Accepted 23 June 2022

Available online xxx

ABSTRACT

Background: Decreasing the burden of mechanical ventilation for spinal cord injuries was never more relevant than during the COVID-19 pandemic. Data have shown diaphragm pacing can replace mechanical ventilation, decrease wean times, improve respiratory mechanics, and decrease hospital costs for patients with spinal cord injuries. This is the largest report of diaphragm pacing during the pandemic.

Methods: This is a retrospective analysis of prospective Institutional Review Board approved databases of nonrandomized interventional experience at a single institution. Subgroup analysis limited to traumatic cervical spinal cord injuries that were implanted laparoscopically with diaphragm electrodes within 30 days of injury.

Results: For the study group of early implanted traumatic cervical spinal cord injuries, 13 subjects were identified from a database of 197 diaphragm pacing implantations from January 1, 2020, to December 31, 2022, for all indications. All subjects were male with an average age of 49.3 years (range, 17–70). Injury mechanisms included falls (6), motor vehicle accident (4), gunshot wound (2), and diving (1). Time from injury to diaphragm pacing averaged 11 days (range, 3–22). Two patients are deceased and neither weaned from mechanical ventilation. Nine of the remaining 11 patients weaned from mechanical ventilation. Four patients never had a tracheostomy and 3 additional patients had tracheostomy decannulation. Three of these high-risk pulmonary compromised patients survived COVID-19 infections utilizing diaphragm pacing.

Conclusion: Diaphragm pacing successfully weaned from mechanical ventilation 82% of patients surviving past 90 days. Forty-four percent of this group never underwent a tracheostomy. Only 22% of the weaned group required long term tracheostomies. Early diaphragm pacing for spinal cord injuries decreases mechanical ventilation usage and tracheostomy need which allows for earlier placement for rehabilitation.

© 2022 Elsevier Inc. All rights reserved.

Introduction

Cervical spinal cord injury (SCI) can result in catastrophic respiratory failure requiring invasive mechanical ventilation (MV) which is a leading cause of morbidity and mortality for these patients. Decreasing the burden of MV for spinal cord injuries (SCI) was never more relevant than during the COVID-19 pandemic.

Oral presentation the 79th Annual Central Surgical Meeting, Milwaukee, WI, June 2–4 2022.

* Reprint requests: Raymond P. Onders, MD, Margaret and Walter Remen Chair of Surgical Innovation, Professor of Surgery, University Hospitals Cleveland Medical Center, 11100 Euclid Ave, Cleveland, OH 44106-5047.

E-mail address: raymond.onders@uhhospitals.org (R.P. Onders);

Twitter: @OndersRay

About 75% of the approximately 17,000 new patients with SCI a year in the United States require intubation and MV acutely.^{1,2} Approximately 1,000 of these patients still require chronic MV at 1 year.³ Early reports in 2020 showed that the mortality rate of patients with SCI with COVID-19 was 19%, which was significantly higher than non-SCI patients.⁴ SCI patients are at a risk for severe COVID-19 for a number of reasons, including decreased pulmonary capacity and inability to clear secretions.⁵ In a 2020 observational study of adults with SCI during the early pandemic, 52% of participants perceived that discrimination through medical rationing was occurring and 30% reported concern of being denied access to a ventilator if hospitalized with COVID-19.⁶ After a traumatic SCI injury during some of the peaks of the pandemic, there was decreased ability to transfer to spinal cord rehabilitation centers

and long-term acute care facilities for weaning. COVID-19 leads to neurologic complications that has added strain to the rehabilitation services also used by SCI injuries.⁵

Data have consistently shown diaphragm pacing (DP; NeuRx DPS, Synapse Biomedical, Oberlin, OH) can replace MV,⁷ decrease wean times,⁸ improve survival,^{8,9} improve respiratory mechanics,¹⁰ and decrease hospital costs for SCI patients.¹¹ Our center has also reported that DP implantation within the first year of injury leads to greater odds of complete removal of MV (72.7%, 24/33 subjects) than when implanted after 2 years (51%, 22/43 subjects).⁹ A multi-center report of 29 patients who had DP implanted during the initial trauma hospitalization had a 72% success rate of complete liberation of MV.¹² This group was implanted an average of 40 days post injury (range, 3–112 days). Given the above known factors of the approaching pandemic and experience with DP, in 2020 our center became more aggressive in the early implantation of DP in SCI patients for weaning to decrease the MV rate and allow earlier transfer without tracheostomies if possible. Our objective is to report on the results of early implantation DP in SCI patients during the COVID-19 pandemic and the effect on MV weaning and tracheostomy use.

Methods

This is a cohort observational report of consecutive SCI patients implanted with DP to decrease MV and tracheostomy use. It is a retrospective analysis of prospective Institutional Review Board (IRB) approved databases of nonrandomized interventional experience at a single institution. Subgroup analysis was limited to traumatic cervical SCI with respiratory compromise implanted laparoscopically with diaphragm electrodes within 30 days of injury. This analysis encompassed all patients involved in 14 different prospective IRB approved protocols at University Hospitals Cleveland Medical Center that included patients from January 2020 through December of 2021. Final status of implanted patients occurred in April of 2022. All patients gave informed consent for both the evaluation and subsequent operative mapping and implantation of DP. Health Insurance Portability and Accountability Act of 1996 compliance was met. Demographic data, operative data, assessment of diaphragm's ability to be stimulated electrically, and postoperative data were collected prospectively then analyzed retrospectively. Key data included date of injury, cervical spine injury level, date of surgical implant, weaning location and success, tracheostomy data and final utilization of DP during this study period. The injury level was identified by both radiologic imaging and neurologic exam. Successful weaning from mechanical ventilation was considered extubation or tracheostomy collar with no pressure support for 24 hours continuously. Subjects that were extubated without tracheostomy and those extubated with tracheostomies were compared.

Traumatic SCI patients are managed by our institution's Level 1 trauma center team. All patients are cared for in our trauma intensive care unit (ICU). Standard assessment for weaning from mechanical ventilation is performed by the trauma ICU team. When weaning is unsuccessful or predicted to be difficult, diaphragm pacing is considered and performed by a separate surgical team. No other preoperative test is performed to assess the integrity of the phrenic motor neurons or phrenic nerve. We have previously published that preoperative phrenic nerve conduction tests have a significant false positive and false negative incidence.¹³ Every patient underwent laparoscopic evaluation to assess the potential for successful diaphragm stimulation in each diaphragm. If a patient had a severe injury or infarction of C3, C4, and C5 there is significant risk of having destroyed phrenic motor neurons thus rendering the diaphragm non-stimulable. Additionally, if the phrenic nerve or

phrenic nerve roots are irreparably damaged the diaphragm muscle cannot be stimulated and DP would not work. We did not include any patients that did not have some stimuable diaphragms for this analysis and with our experience patients with nonstimulable diaphragms were considered unweanable from MV.

The surgical technique of diaphragm pacing has been described previously but will be reviewed briefly here.¹⁴ A supraumbilical, midline access port is placed to visualize both diaphragms. Two 5 mm, lateral, subcostal trocars are then placed to assess the diaphragms. The falciform ligament is divided, and a 12 mm epigastric trocar is placed to accommodate the 11 mm diameter implant instrument. A standard laparoscopic dissector was attached to an external clinical station that provides electrical stimulation to map the diaphragms. Mapping identifies the motor point where maximal contraction occurs and then 2 electrodes are implanted in each diaphragm. The electrodes are tunneled from the epigastric port to an exit site along with a subcutaneous ground electrode.

Postoperatively, the external DP pulse generator is programmed to maximize the electrical stimulation through each electrode with pulse width, amplitude, frequency, and breaths per minute while maintaining patient comfort. DP is begun once the patient is stable in the ICU usually the same day of surgery. DP is begun continuously with setting being increased based on patient tolerance. This is different than is used in patients with a chronic SCI injury on the ventilator where DP is done intermittently while the diaphragm is being reconditioned. A pressure support wean is then begun on the ventilator. How fast the patient can be weaned also depends on other physiologic events from their initial trauma such as autonomic dysreflexia or post spinal cord injury bradycardia. If a patient can be weaned off MV without the use of a tracheostomy our ICU liberally uses mechanical insufflation-exsufflation (cough assist) to promote secretion clearance.¹⁵ The decision to perform a tracheostomy was done by the ICU team depending on the injury pattern such as facial trauma, secretions, other co-existing injuries that would affect weaning and surgical finding of strength of diaphragm. Patients with weaker diaphragms from nerve root injury would require a longer time to wean and then would receive a tracheostomy earlier.

We routinely analyzed diaphragm electromyography (dEMG) to assess for respiratory activity that the patient may have volitionally or spontaneous brain stem-controlled respiration. This technique has previously been reported.¹⁶ Briefly, a polysomnography unit (Crystal PSG, CleveMed, Cleveland, OH) is used to record dEMG measurements by assessing the spatial summation between 9 mm of exposed intramuscular electrodes in each hemidiaphragm using the implanted remote subcutaneous electrode as the ground. The dEMG allows continuous evaluation of epochs of diaphragm activity when the patients are on positive pressure ventilation and during the weaning process. Analysis of dEMG was one of the modes of assessing recovery and function of the diaphragm and for eventual removal of the DP electrode. Prior to removal of the DP electrodes, we also perform 24-hour oxygen saturation testing with DP to make sure the patient is not having apneas or desaturations. There is a significant prevalence of sleep disordered breathing in SCI patients in the first months after injury which does improve chronically.¹⁷ DP can overcome apneas and sleep disordered breathing. If any of the patients recover volitional breathing during the day but were identified as having apneas during sleep, then DP is continued to prevent this from occurring.

Results

The database included 197 patients with DP implantations from January 1, 2020, to December 31, 2022, for all indications. Within

Table 1
Demographic data and results of diaphragm pacing in the analyzed cohort of subjects

Subject	Injury date	Age, y	Mechanism	ISS	Level	Days to DP	Days to trach	Wean MV and days	Hospital days	Trach decannulation	DP Status
1	7/4/20	54	Fall	25	C5	6	N/A	N	14 expired	N/A	N/A died
2	7/19/20	60	MVA	38	C5–6	22	3	Y >30 d*	31	N	Still DP
3	8/9/20	41	MVA	17	C-5	22	19	Y 1 d	38	Y	Weaned off
4	9/10/20	55	Fall	21	C3–4	15	N/A	Y 5 d	27	N/A	Weaned off
5	10/6/20	17	MVA	N/A	C4–5	8	27	Y >30 d*	33	Y	Weaned off
6	10/8/20	47	Fall	30	C6–7	6	15	N	21	N	Stopped DP
7	12/18/20	60	MVA	26	C2	12	19	N expired 86 d	31	N	N/A died
8	1/11/21	26	GSW	50	C6	7	11	N	23	N	Stopped DP
9	2/2/21	70	Fall	25	C3–6	14	N/A	Y 1 d	16	N/A	Still DP
10	3/14/21	70	Fall	26	C3	12	16	Y > 30d *	32	N	Still DP
11	4/30/21	62	Fall	26	C3–4	4	N/A	Y 3 d	16	N/A	Still DP
12	6/13/21	29	Diving	32	C3–5	3	15	Y 21 d	42	Y	Weaned off
13	8/8/21	50	GSW	30	C5–7	10	N/A	Y 1 d	18	N/A	Weaned off

C, cervical; DP, diaphragm pacing surgery; GSW, gunshot wound; ISS, injury severity score; MV, mechanical ventilation; MVA, motor vehicle accident; N/A, not applicable; N, no; Trach, tracheostomy; Y, yes.

* Was weaned after discharge from the intensive care unit into spinal cord rehabilitation or long-term acute care hospital and exact date of wean unknown but it was greater than 30 days.

this group, 13 patients with SCI secondary to trauma and implantation within 30 days of their injury were identified. These patients were accrued from these 2 IRB protocols: (1) IRB #07-08-26 Humanitarian Device Exemption Protocol for The Diaphragm Pacing System for Ventilatory Assist in Spinal Cord Injury (12 patients); and (2) IRB #11-08-27 Protocol for Compassionate Use of the Diaphragm Pacing System for Ventilatory Assist in Spinal Cord Injured Pediatric Patients (1 patient).

Table 1 provides the data for each subject. All the subjects were male with an average age at implant 49.3 years (range, 17–70). The predominant mechanism of injury was blunt (11 out of 13) and included falls,⁶ motor vehicle accident,⁴ gunshot wound,² and diving.¹ The cervical SCI level was considered high (C1–4) in 7 patients and low (C5–7) in 6 patients. Injury Severity Score averaged 28.8 with the one pediatric trauma excluded because of lack of data (range, 17–50). Time from injury to DP averaged 11 days (range, 3–22). There were no complications from the DP procedure. Operative finding showed good stimulatable diaphragms with no lower motor neuron involvement of phrenic nerve injuries in 9 of 13 subjects. Subjects 1, 2, 7, and 10 had one hemidiaphragm that was significantly weaker either from pre-existing unilateral diaphragm dysfunction or phrenic nerve injury from the traumatic event. When this is found at surgery, the ability to rapidly wean from MV will be limited because nerve recovery and subsequent diaphragm function with electrical stimulation can take up to 18 months.¹⁶ Two of these patients (subjects 1 and 7) both died and never weaned from MV. Subject 1 one withdrew care 14 days post injury and subject 7 withdrew care after decubitus ulcer sepsis in rehabilitation center day 86 post injury. Subjects 2 and 10 did successfully wean from MV but they took greater than 30 days and occurred at outside facilities. During this 2-year period there were no acute SCI patients who went for laparoscopic evaluation and did not have stimulatable diaphragms and were not implanted. It has previously reported that up to 24% of SCI patients may have non stimulatable diaphragms and do not get implanted.¹²

Nine of the 13 patients were completely weaned off MV (69%). Excluding the 2 deceased patients with early deaths less than 90 days from injury who never weaned from MV, 9 of the remaining 11 patients weaned from MV. All 9 of the patients are free from MV 24 hours a day. The 2 who failed to wean (subjects 6 and 8) had good stimulatable diaphragms at surgery but had significant difficulty with long-term care facilities for weaning with no family support. They both have stopped pacing. Three patients were transferred to spinal cord rehabilitation centers or long-term acute care hospitals

and were successfully weaned. For these patients we do not have the exact dates for complete weaning. During and after transfer there is always a delay in weaning with DP as the new center must be trained and accustomed to DP. In the 6 patients who weaned from MV in our ICU the average days to wean was 5 days after DP (range, 1–21 days).

Four subjects never had a tracheostomy and were successfully weaned from MV with DP alone. For the 8 subjects with tracheostomy the average time from injury to tracheostomy was 15.6 days (range, 3–27). One patient withdrew life support on hospital day 14 while still intubated. Two of the tracheostomies occurred before DP with no success in weaning from MV until DP. The 2 patients who did not wean from MV still have tracheostomies. Excluding the one patient who withdrew life support at day 14, the average hospital days for the remaining 12 patients was 27 days (range, 16–42). The average duration of stay for the subjects weaned without tracheostomy (4 subjects) was 19 days (range, 16–27) versus those with a tracheostomy (8 subjects), which was 31 days (range, 21–42). The 3 subjects with the unilateral weak diaphragm identified at surgery (excluded the 1 patient with a weak diaphragm who withdrew life support) all required tracheostomies.

The long-term follow-up of the 11 remaining cohort is an average of 15.5 months from injury (range, 8–21 months). There were no additional patient deaths. The 2 patients who did not wean are not doing DP presently although their DP wires are still place. In the long term, 3 patients were able to have their tracheostomy decannulated. Three of the cohort of these high-risk pulmonary compromised patients post discharge had symptomatic COVID 19 infections and survived utilizing DP (subjects 5, 9, and 12). Five patients had full recovery of automatic breathing with subsequent DP removal. This was confirmed by recovery of diaphragm EMG that is routinely performed on our patients. Because the DP system is percutaneous, the DP electrodes can be removed with gentle traction in the outpatient settings. Three patients use DP 24 hours a day for ventilation. One patient (subject 9) without a tracheostomy still uses DP but only at night because of sleep disordered breathing that DP helps overcome.

Discussion

The objective of early use of DP to improve weaning from MV with decreased tracheostomy rates to allow more efficient discharge during the COVID-19 pandemic was met. Early DP successfully weaned from MV 50% of the SCI patients before discharge

(6 of 12) and in 82% of patients surviving past 90 days (9 of 11). Of the rapid weaning group 66% (4 of 6) did not require a tracheostomy. This group of no tracheostomy rapid weaning patients with catastrophic SCI injury on average had only 19-day hospital stays. Long term, only 22% of the weaned group of quadriplegics required tracheostomies for secretions and both had initial unilateral hemidiaphragm weakness. Obstacles to weaning with early DP were not related to DP but involved patient withdrawal of care and long-term care issues. Decreased MV and tracheostomy use allowed earlier and easier placement for rehabilitation.

There have been increasing publications outlining the success of DP in SCI recently leading the American College of Surgeons trauma quality program in March of 2022 to update their best practices guidelines for spine injury and listed, as a key point to consider, stimulation of the diaphragm to become ventilator free.¹⁸ A 2022 publication of the results of the initial FDA IDE study showed 96.2% of patients could use DP to support ventilation at least 4 hours a day.⁷ They also report a meta-analysis cohort of 196 patients exhibited a similar results of 92.2% of patients successfully using DP a minimum of 4 hours. Kerwin et al reported statistically significant saving of \$144,444 ($P = .003$) in average hospital charges with the use of DP compared with a propensity matched group. They also report a more rapid wean from MV of 10.1 days as opposed to 29.2 days ($P < .001$).¹¹ A European registry concluded that DP is a good alternative to MV.¹⁹ A 2018 report showed that early mortality rate decreased from 15% to 3% with the use of DP early in the hospital course.⁸ The duration of hospitalization was also decreased in the DP group (65 ± 61 vs 43 ± 24 days for the control and DP groups, respectively $P = .03$). Although the patient groups may be different, with aggressive early implantation our duration of stay average was only 29 days.

There are some significant limitations to this report. This is a single site report at an institution with a long history of DP utilization and experience, but other centers have reported similar results with early implantation.^{8,11} This report did not analyze all SCI admissions which may have included deaths before consideration of diaphragm pacing. It did not include those that were weaned of MV without DP or were not even deemed to be a candidate for diaphragm pacing. There was no randomization of patients to DP or not DP; there was no control group. There were also no female patients with SCI that were implanted during this period. In our previous report 20% of the 92 patients implanted over 17 years were females with no difference in outcomes.⁹ In our previous report the average time to implantation was 47.5 months with the median time 1.58 years with only 6 patients implanted in the first 30 days from injury.⁹ Four of those 6 (66%) were weaned with 1 early death from malignant hyperthermia. The 66% success rate is similar to this report of 69% (9 of 13). This report did not specifically look at the role of noninvasive ventilation (NIV) in extubating patients with SCI without the use of DP. NIV does have a role in patients with traumatic SCI who struggle postextubation, in weaning from tracheostomy MV¹ and is used in our center. Conversion of a patient with SCI dependent on tracheostomy MV to NIV is usually not performed in the first 30 days post injury.²⁰ Given the concern of the lack of intensive care unit beds and the lack of ventilators during the pandemic with the authors experience the process was to provide DP as soon as the patient was stable and with their consent. The IRB Humanitarian Device Exemption consent process is performed separate from the ICU team and was the same consent form and process before the COVID-19 pandemic with explanations of all the options for ventilation.

The management of tracheostomies is significant during the COVID-19 pandemic since a tracheostomy is an aerosol generating procedure.²¹ Health care workers are at risk of infection both during the initial insertion and subsequent care of the patient.

Decreasing the need for tracheostomy can be significant in decreasing the risk for healthcare workers along with the continuous need for appropriate personal protective equipment in managing a tracheostomy. Overall, we were able to prevent tracheostomy in 4 of the 12 patients (33%). Three of these patients had unilateral diaphragm weakness at surgery and would have required a tracheostomy based on those finding, so the weaning success without tracheostomy could be considered at 44% (4 of 9) for this subgroup. In our previous report on 92 patients,⁹ only one patient was weaned without a tracheostomy so this much earlier use of DP has increased this success rate up to 44% of patients. Although tracheostomies are recommended early in SCI,¹⁸ they are not without risks which include dislodgement, occlusion, hemorrhage, tracheomalacia, infections, mucous production, pneumonias, granulation tissue, stenosis, and death. Tracheostomy tube obstruction and dislodgement are the most common adverse events but account for a significant proportion of airway related deaths and hypoxic brain damage.²² Some of these risks to the trachea were increased during the COVID-19 pandemic because of the more aggressive cuff overinflation to try to decrease aerosolization.

SCI associated with MV drastically decreases life expectancy. A 40-year SCI patient with the same level of injury but is on MV is only expected to live 8.8 years compared with 20.7 years if the patient was not on MV.² The leading cause of death is pneumonia. Long-term use of DP has been shown to improve survival⁹ and early use of DP has been shown to decrease early mortality.⁸ The 13 patients in this report are comparable to the 750 annual SCI patients that have stimulative diaphragms who historically have been on MV at the 1-year mark. Additional research can be done to show the use of DP to decrease the time spent on MV for those patients who had historically been weaned by the 1 year mark. Our aggressive use of DP with no tracheostomy should only be recommended at centers experienced with insufflation-exsufflation assisted coughing therapy or the lack of secretion management could lead to pneumonia because of the poor cough in these patients. Even if a tracheostomy is performed early in the SCI course, if a patient can be weaned off MV with DP, the patient should be evaluated in the future for decannulation of the tracheostomy. Removal of a tracheostomy improves a patient's quality of life and physical function, in addition to perceived physical appearance.¹

Patients with SCI have an increased risk of developing respiratory complications²³ and they frequently have comorbidities such as hypertension, cardiovascular disease, diabetes, and obesity, which has been linked to worse prognosis of COVID-19.⁵ Although 3 of our patients suffered from COVID-19 infections, fortunately none of them died even though their predicted mortality rate is elevated.⁴ Liberation from MV increases the possibility of a patient's return home, rather than residence in a long term care facility which is historically associated with higher COVID-19 mortality rates.

In this report, 5 of the 11 surviving patients (45%) were able to be weaned off DP because of complete recovery of respiration which is greater than the 5 patients out of 92 we had previously reported (5%).⁹ In our previous report, the only patients who recovered breathing were implanted less than 6 months from injury.⁹ We are now implanting much earlier after injury which may be the reason for the increase in complete recovery. Functional electrical stimulation and physical therapy has been shown to have a positive trophic effect in helping recovery from SCI and DP is aggressive physical therapy and functional electrical stimulation for the diaphragm.^{24,25} Future work could investigate whether DP has a role in not only weaning from MV but also some recovery from the SCI.

Early DP has been associated with rapid weaning from MV and avoidance of tracheostomy with a favorable safety profile. In

conclusion, early DP for SCI, once the patient is stabilized, is a strategy to decrease MV usage, especially when faced with critical needs of MV during future disasters or pandemics.

Funding/Support

There was no payment or involvement from Synapse Biomedical in funding or preparation of this article. MaryJo Elmo, ACNP, Brian Young, MD, and Glen Tinkoff MD have no financial disclosures.

Conflict of interest/Disclosure

Dr Raymond Onders, University Hospitals of Cleveland and Case Western Reserve University School of Medicine have intellectual property rights involved with the diaphragm pacing system and equity in Synapse Biomedical who manufactures the device. Dr Raymond Onders is also Chief Medical Officer and is on the board of Synapse Biomedical.

References

- Sun GH, Chen SW, MacEachern Wang J. Successful decannulation of patients with traumatic spinal cord injury: a scoping review. *J Spinal Cord Med.* 2020; 1–12.
- National Spinal Cord Injury Statistical Center. Spinal cord injury facts and figures at a glance: 2022 SCI data sheet. Available from: <https://msktc.org/sites/default/files/SCI-Facts-Figs-2022-Eng-508.pdf>. Accessed May 5, 2022.
- Monden KR, Coker J, Charlifue S, Bennett SJ, Draganich C, Coons D, Marino RJ, Berliner J. Long-term follow-up of patients with ventilator-dependent high tetraplegia managed with diaphragmatic pacing systems. *Arch Phys Med Rehabil.* 2022;103:773–778.
- Burns SP, Eberhart AC, Sippel JL, Wilson GM, Evans CT. Case-fatality with coronavirus disease 2019 (COVID-19) in United States Veterans with spinal cord injuries and disorders. *Spinal Cord.* 2020;58:1–2.
- Hoogenes B, Queree M, Townson A, Willms R, Eng JJ. COVID-19 and spinal cord injury: clinical presentation, clinical course and clinical outcomes: a rapid systematic review. *J Neurotrauma.* 2021;38:1242–1250.
- Monden KR, Andrews E, Pilarski C, Hearn J, Wudlick R, Morse LR. COVID-19 and the spinal cord injury community: concerns about medical rationing and social isolation. *Rehabilitation Psychology.* 2021;66:373–379.
- Onders RP, Khansarinia S, Ingvarsson PE, Road J, Yee J, Dunkin B, Ignangi AR. Diaphragm pacing in spinal cord injury can significantly decrease mechanical ventilation in multicenter prospective evaluation. *Artif Organs.* 2022;46(10):1980–1987.
- Kerwin A, Yorkgitis B, Ebler D, Madbak F, Hsu A, Crandall M. Use of diaphragm pacing in the management of acute cervical spinal cord injury. *J Trauma Acute Care Surg.* 2018;85:928–931.
- Onders RP, Elmo MJ, Kaplan C, Schilz R, Katirji B, Tinkoff G. Long-term experience with diaphragm pacing for traumatic spinal cord injury: early implantation should be considered. *Surgery.* 164:705–711.
- Kerwin AJ, Zuniga YD, Yorkgitis BK, et al. Diaphragm pacing improves respiratory mechanics in acute cervical spinal cord injury. *J Trauma Acute Care Surg.* 2020;89:423–428.
- Kerwin AJ, Diaz Zuniga Y, Yorkgitis BK, et al. Diaphragm pacing decreases hospital charges for patients with acute cervical spinal cord injury. *Trauma Surgery Acute Care Open.* 2020;5.
- Posluszny JA, Onders R, Kerwin AJ, et al. Multicenter review of diaphragm pacing in spinal cord injury: successful not only in weaning from ventilators but also in bridging to independent respiration. *J Trauma Acute Care Surg.* 2014;76:303–310.
- Onders RP, Elmo M, Stepien C, Katirji B. Spinal cord injury level and phrenic nerve conduction studies do not predict diaphragm pacing success or failure: all patients should undergo diagnostic laparoscopy. *Am J Surg.* 2021;221: 585–588.
- Onders RP, Ignagni AI, DeMarco AF, Mortimer JT. The learning curve of investigational surgery: lessons learned from the first series of laparoscopic diaphragm pacing for chronic ventilator dependence. *Surgical Endoscopy.* 2005;19: 633–637.
- Reyes MR, Elmo MJ, Manachem B, Granda SM. A primary care provider's guide to managing respiratory health in subacute and chronic spinal cord injury. *Top Spinal Cord Inj Rehabil.* 2020;26:116–122.
- Onders R, Elmo MJ, Kaplan C, Katirji B, Schilz R. Extended use of diaphragm pacing in patients with unilateral or bilateral diaphragm dysfunction: a new therapeutic option. *Surgery.* 2014;156:772–786.
- Chiodo AE, Siltrini RG, Bauman KA. Sleep disordered breathing in spinal cord injury: a systematic review. *J Spinal Cord Med.* 2016;39:374–382.
- American College of Surgeons. American College of Surgeons trauma quality programs best practice guidelines spine injury. Available from: https://www.facs.org/-/media/files/quality-programs/trauma/tqip/spine_injury_guidelines.ashx. Accessed May 5, 2022.
- Wijkstra PJ, van der Aa H, Hofker HS, Curto F, et al. Diaphragm pacing in patients with spinal cord injury: a European experience. *Respiration.* 2022;101: 18–24.
- Toki A, Nakamura T, Nishimura Y, Sumida M, Tajima F. Clinical introduction and benefits of non-invasive ventilation for above C3 cervical spinal cord injury. *J Spinal Cord Med.* 2021;44:70–76.
- Meister KD, Pandian V, Hillel AT, et al. Multidisciplinary safety recommendations after tracheostomy during COVID-19 pandemic: state of the art review. *Otolaryngol Head Neck Surg.* 2021;164:984–1000.
- Brenner MJ, Pandian V, Milliren CE, et al. Trach-related complications: Global Tracheostomy Collaborative: data-driven improvements in patient safety through multidisciplinary teamwork, standardisation, education, and patient partnership. *Anaesth.* 2020;125:e104–e118.
- Sampol J, Golzalez-Viejo MA, Gomez A, et al. Predictors of respiratory complications in patients with C5–T5 spinal cord injuries. *Spinal Cord.* 2020;58: 1249–1254.
- Lorenz J, Datta S, Harkema S. Longitudinal patterns of functional recover in patients with incomplete spinal cord injury receiving activity based rehabilitation. *Arch Phys Med Rehabil.* 2012;93:1541–1552.
- Benito-Panalva J, Edwards D, Opisso E, et al. Gait training in human spinal cord injury using electromechanical systems: effect of device type and patient characteristics. *Arch Phys Med Rehabil.* 2012;93:404–412.

Discussion

Invited Discussant: Jana Hambley

Jana Hambley (Cincinnati, OH): I am Jana Hambley from Cincinnati, Ohio. Your paper has a large amount of discussion on whether patients need a tracheostomy and the outcomes of these patients. Could you please elaborate on the decision process for tracheostomy patients in this program? Is it based primarily on injury pattern, for instance, facial fractures, or on their subsequent diaphragm function or another assessment?

Raymond Onders: There is actually a separate team that chooses the tracheostomy, not me, and so we do know, and 2 of our patients had tracheostomies prior to diaphragm pacing because you are exactly right, because of their facial fractures and other injuries that they had the tracheostomy early on. And we do know on the patients that we have great diaphragm signs that we are going to be able to probably get them off the ventilator,

and so the surgical assessment is key. The 4 patients or the 3 patients that survived with the weak hemidiaphragms all had tracheostomies, so we utilized those 2 facts along with secretions as we do know there is almost a universal pneumonia rate in these high quadriplegics, and if they have severe secretions, they will get their tracheostomy for that management, so we do utilize all those facts for it.

The decision to perform a tracheostomy was done by the ICU team depending on the injury pattern such as facial trauma, secretions, other co-existing injuries that would affect weaning. Two of the patients had tracheostomy before diaphragm pacing. The surgical finding of strength of diaphragm also affected when we would do tracheostomy. Patients with weaker diaphragms from nerve root injury would require a longer time to wean and then would receive a tracheostomy earlier.

Jana Hambley: Secondly, you discuss in your paper that there is no preoperative testing done on these patients. Could you provide more information on the numbers of patients that are taken to the operating room for diaphragm pacing assessment but who are not ultimately implanted? What are these patient outcomes, and are there any associated complications with the investigational procedure?

Raymond Onders: Historically, we used to get phrenic nerve studies to see if they are suitable for this, to see if they had intact lower motor neurons, but 2 years ago I published a paper that showed that there is a high false-negative rate, so therefore we just go directly to laparoscopy for all these patients. In this 2-year time period, we just had no patients that we could not stimulate.

Now the interesting factor in those 4 with hemidiaphragms that were weaker, if I would have waited 3 months, would that diaphragm have been denervated and not been stimlatable? That is what we do not know. Historically, in our 2014 paper, our multicenter paper, 24% of patients we would take to surgery with spinal cord injury had nonstimulatable diaphragms, so in all centers it is probably about 24%. We do realize earlier implantation may allow that nerve to recover. I just came from the Spinal Cord Injury Association trial. Early electrostimulation has really become critical for spinal-cord-injured patients on their long-term recovery. We as trauma or general surgeons can provide that for these high patients. Electrostimulation changes the milieu of the spinal cord that will help these patients recover. Perhaps by doing this earlier, we might be seeing that benefit. Again, with a small patient population, there is no way I could prove that, but that is a great point.

During this two year time period there were no acute SCI patients who went for laparoscopic evaluation and did not have stimlatable diaphragms and were not implanted. There were 4 patients that had partially denervated diaphragms. We do not know if these patients through wallerian nerve degeneration if that diaphragm in the future would not be stimulated. It has previously reported that up to 24% of SCI patients may have non stimlatable diaphragms in a previous published multicenter publication. We do realize that earlier implantation may allow the phrenic nerve to recover. In a recent spinal cord meeting there were multiple presentations discussing how early electrical stimulation can help in recovery for spinal cord injured patients. Electrical stimulation changes the milieu of the spinal cord that can help these patients recover. Perhaps by doing this earlier, we might be seeing this benefit. Again with a small patient population there is no way we can prove that, but that is a great point you bring up.

Jana Hambley: Your paper says there are 2 patients who underwent an implantation of a diaphragm pacer but ultimately were

not able to use it because of difficult social situations. Do you anticipate a way to evaluate these patients in the future so that you have a better idea of who may be able to have a social situation to continue to use the pacer?

Raymond Onders: I think this is one of the sad aspects about spinal-cord-injured quadriplegics on ventilators. There is no disease I know of that in 2020 has a worse survival than in 2010 except for a 20-year-old on a ventilator with a spinal cord injury. Their survival, again, you are going to die from something because of that catastrophic injury. In 2019 before the pandemic, the survival, and again, there is a great spinal cord statistical site that keeps all this data from federal grants; we have very good numbers on this. In 2010, a 20-year-old, which is an otherwise perfectly healthy spinal-cord-injured patient would live 22 years after a spinal cord injury on a ventilator. By 2019, that had gone down to 10 years, and we know why that is because we know that in many states, there are no longer any nursing homes that will take ventilators. We know that long-term acute care facilities do not provide good care. We know that the support system for a patient on a ventilator is one, very expensive, averages almost \$200,000 a year to be on a ventilator, and the care in these facilities, which is even worse now after the pandemic—as we know, there are 600 nursing homes closing across the country, and nobody will take a ventilator patient these days—is only going to be worse.

Kerwin actually showed in his database of cohorts that he looked at that the early mortality rate of 15% that he had before he instituted diaphragm pacing in everybody in Jacksonville went down to 3% by just getting people off the ventilator, so I am not sure what is going to happen to these young patients that we still in the United States do not provide good long-term care for because I do a lot of research on overseas. Most other countries, if a patient chooses to be on a ventilator, has much better care and facilities for them than we have in the United States. I do not know what we are going to do for that, and I do not know how we can predict that in these patients, but it is a very difficult problem that we have in the United States for these patients.

This is a significant problem. Even prior to the pandemic the National Spinal Cord Injury Statistical Center showed that the survival for a 20 year old SCI patient on a ventilator had significantly decreased from 20 years in 2010 to 11 years in 2020. There is no disease that I know of that has had such a drastic decrease in survival. Most likely this is because of a decrease in facilities that can handle a patient chronically on a ventilator. Kerwin et al has shown already that there is a decrease in the early mortality rate from 15% to 3% with routine use of diaphragm pacing. In this orphan rare disease of SCI patients on the ventilator we need to have more centers using all the available technology.