Diaphragmatic Pacing in Spinal Cord Injury

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Abstract

Spinal Cord injury is a disabling condition which affects the respiratory system. The most affected neurological level is the cervical spine. Many patients with cervical spinal cord injury are unable to sustain independent ventilation and require mechanical ventilation. Long term use of mechanical ventilation is associated with poor quality of life, increased morbidity, and mortality.

In patients with intact phrenic nerve, diaphragmatic pacing can be used to help wean the patients off mechanical ventilation. In this review, we summarize the indications, contraindications, benefits, safety, and effectiveness of diaphragmatic pacing. We also report a brief case of a 62-year-old male with quadriplegia secondary to C2-C3 fracture who was intubated after drowning but was extubated with the help of diaphragmatic pacing.

Keywords: Cervical spinal injury, Diaphragmatic pacemaker, Mechanical Ventilation

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Introduction

Spinal cord injury (SCI) is a potentially disabling condition which results in significant morbidity and mortality. It affects not only motor and sensory impairment but can also cause multiple organ dysfunction.

The incidence of SCI worldwide varies between 13.0 to 163.4 per million people. [1] The most frequently affected neurological level is the cervical spine, with more than half off all SCI occurring in this area. [1,2] The percentage of cases affecting the cervical level is increasing over time. [1,3]

In addition to its impact on several other organ systems, cervical SCI can severely affect the respiratory system. Respiratory complications remain the most common cause of death following SCI. [4,5] The degree of respiratory dysfunction depends on the level and completeness of injury. [6] Cervical SCI causes interruption of the bulbospinal respiratory pathways, resulting in respiratory muscle paralysis. [7]

Currently, there is no definite treatment for respiratory paralysis. Patients who are not able to maintain independent ventilation require long term mechanical ventilatory support. [8,9] However, these patients are prone to multiple complications. [10,11,12] Ventilated patients have increased mortality compared to non-ventilated patients,[13] as well as a poorer quality of life. [14]

Several different techniques have been reported in the past to assist in liberating these patients off mechanical ventilation. [15,16,17,18] One such technique is the use of phrenic nerve stimulation, also known as diaphragmatic pacing. It is used in SCI patients who are ventilator dependent due to central respiratory paralysis but who retain functional phrenic nerves and diaphragm. [19] In this technique, the electrodes are implanted in the diaphragm, which causes diaphragmatic contraction when stimulated. [18]

Diaphragmatic pacing was used first by Glenn and associates in 1972. [20] The two main indications for this technique are patients with upper cervical spinal cord injury and central alveolar hypoventilation (either congenital or acquired). [21,22] In a multicenter trial of 29 patients, Posluszny et al demonstrated that early diaphragmatic pacing implantation in acute cervical SCI patients resulted in liberation from the ventilator in 16 of 22 (72%) cervical SCI patients. Patients who underwent diaphragmatic pacing implantation were liberated from mechanical ventilation in an average of 10.2 days. [23]

The aim of this study was to review the indications, benefits, safety, and effectiveness of diaphragmatic stimulators. We also report a brief case of a 62-year-old male with quadriplegia secondary to C2-C3 fracture who was intubated after drowning. He was then extubated after we connected him to his diaphragmatic stimulator.

Case report

A 62-year-old male with paraplegia secondary to C2-C3 fracture presented to the hospital after drowning. His CSI was due to a motor vehicle accident 30 years earlier. The exact circumstances of his drowning were unclear, but he was found to be in the water by a fisherman, who pulled him out. He was pulseless and apneic, so cardiopulmonary resuscitation (CPR) was started. Emergency medical services (EMS) found his electrocardiographic rhythm to be pulseless electrical activity. He received multiple rounds of CPR before the return of spontaneous circulation was achieved. The patient was intubated on the field. He was admitted to the medical ICU.

Chest Xray on admission showed the presence of diaphragmatic stimulators. Further history was obtained from the caregiver who reported that he had the stimulators inserted about 10 years ago (Fig.1 and 2) Once we connected him to the stimulator, we were able to wean him off the mechanical ventilator and were able to extubate him (Fig.3).

Fig 1: Power source of the diaphragmatic pacing

Fig 2: Receiver implant of the diaphragmatic pacing attached to patients' body

Fig 3: Patient on spontaneous ventilation and able to trigger ventilator after connecting to the diaphragmatic pacing (red arrow). Respiratory rate of 14

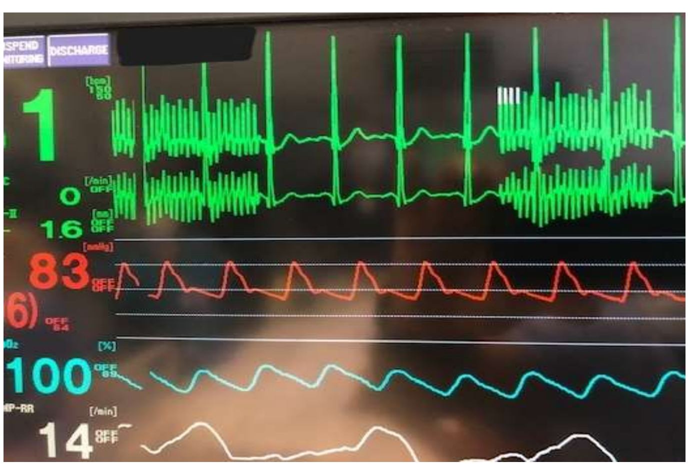

Figure 4: Monitor screen shot showing the artificat effect of the diaphragmatic stimular corresponding to the respiratory rate (white)

Normal physiology of breathing and dysfunction in spinal cord injury

The normal physiology of breathing involves the utilization of oxygen in order to provide for respiration on a cellular level, while exhaling carbon dioxide. Respiration and respiratory organs synchronously facilitate gas exchange via the lungs, bronchi, trachea, throat, oral cavity, and nose. The primary muscle of inspiration is the diaphragm. The diaphragm along with the external intercostal muscles contract during inspiration, which creates a negative-pressure vacuum within the lungs and draws air into the thoracic cavity through the respiratory system as the diaphragm flattens. When the muscles of respiration relax, the diaphragm returns to its domed shape. Air is forced out and exhaled due to the elastic recoil of the lung. The diaphragm is innervated by the phrenic nerve, which is supplied by cervical spinal nerves C3, C4, and C5.

Impairment in spinal cord injury is greatest following cervical spinal injuries. [24] The respiratory dysfunction in cervical SCI is multifactorial. Directly following traumatic SCI, a temporary spinal shock may result in flaccid paralysis of muscles lower than the injury level, a condition that lasts on the order of weeks to months. [25] When intercostal muscles are paralyzed, the chest wall is not stable; thus, during inspiration, negative intrathoracic pressure leads to the paradoxical depression of the ribs. [26] Ventilation does not occur in an efficient manner and the work of breathing increases, leading to airway collapse and atelectasis. [11]

In cervical and high thoracic injuries above T6, a decreased amount of sympathetic nervous system activity occurs with increased parasympathetic vagal nerve activity predominating, resulting in increased reactivity of the bronchioles. [27,28,29] Due to impaired cough, secretions accumulate throughout the lungs. [30] Also in cervical SCI, there is direct damage of the respiratory bulbospinal pathway that can lead to muscle paralysis. In the weeks to months following SCI, the paralysis of muscles may lead to intubation or tracheostomy as the need for respiratory support increases.

Indications and contraindications for pacing

Diaphragmatic pacing is a technique initially developed for the treatment of respiratory muscle weakness in patients with SCI. [31] Despite the lack of randomized control trials, there are 2 indications that account for most of the cases of diaphragmatic pacing: reliance on mechanical ventilation in either central hypoventilation syndromes (CHS), [32] or high-level SCI.

The phrenic nerve cell bodies are in the anterior horns of C3 to C5. Thus, ideal candidates with SCI are those with injury above the C3 level as there is no impairment of the phrenic nerve. It has allowed patients to reduce their time on mechanical ventilation or even eliminate the need for mechanical ventilation. [33,34,35] Other unusual conditions with successful application includes brain stem infarction, [36] Syringomyelia, [37] Pompe Disease, [38] intractable hiccups, [39] severe COPD. [40] (Table 1)

Diaphragm pacing is contraindicated for patients with trauma at the mid cervical spine or direct trauma to the phrenic nerve including nerve tumors and neuropathies in that location as the phrenic nerve cannot be stimulated in those patients. In addition, patients with a nonfunctioning diaphragm also not candidates for diaphragm pacing stimulation. Therefore, evaluation of phrenic nerve function needs to be performed in each patient undergoing diaphragmatic pacing. [41] In addition, patients with amyotrophic lateral sclerosis (ALS) are not suitable candidates for diaphragmatic stimulation. Randomized trials have shown unclear benefit or potential harm in this condition. [42,43,44]

Indications	**Contraindications**
SCI above C3 level	Trauma at the mid cervical spine (C3-C5)
Congenital central alveolar hypoventilation	Direct trauma to the phrenic nerve
Brain stem infarction and tumors	Nonfunctional phrenic nerve
Basilar meningitis	Phrenic nerve tumor
Arnold-Chiari malformations	Phrenic nerve neuropathies
Pompe Disease	Nonfunctional diaphragm
Syringomyelia	
Lower motor neuron diseases like Charcot Marie Tooth, polio disease, spinal muscular atrophy, diaphragmatic flutter, and acute flaccid myelitis	
Intractable Hiccups	
Severe COPD	
Meningomyelocele	
Cerebrovascular accidents	
Accidental unilateral phrenic nerve injuries	
Amyotrophic lateral sclerosis (ALS)? Some research has shown benefit whereas some have shown some potential harm	

Table1: Indications and Contraindications of diaphragmatic pacing

Type of surgical technique

There are three locations for phrenic nerve stimulation: the cervical, thoracic, and diaphragmatic approach, also known as diaphragmatic pacing stimulation (DPS)

1. The cervical approach is an option for ventilator-dependent patients from brainstem and high cervical cord lesions. It has several advantages over a traditional thoracic approach including a minimally invasive approach with low morbidity, compared to chest surgery required in a thoracic approach. The procedure can be performed during a single operation and can be performed in an outpatient setting. [45,18] There are some disadvantages of the cervical approach. Inadequate stimulation of the phrenic nerve intraoperatively may occur from stimulation of an accessory branch of the phrenic nerve or from prior damage to the phrenic nerve. Postoperative complications include irritation of the surrounding brachial plexus structure and hardware malfunction. [45]
2. The thoracic approach is the oldest technique for diaphragmatic pacing. The technique has higher morbidity and mortality. [46] Implantation of the phrenic nerve pacemaker needs to be performed via either video-assisted thoracoscopic surgery (VATS) or open thoracotomy. The advantage of this technique is to avoid brachial plexus stimulation. Additionally, this technique may stimulate a larger portion of the phrenic nerve as it joins the main nerve trunk after entering the thoracic cavity. [47] However, no randomized control trials have compared the effectiveness of these 2 techniques.

3. The diaphragmatic approach, or intraperitoneal diaphragm pacing, is a more recent technique that is also a minimally invasive surgical technique. The procedure is performed laparoscopically to implant electrodes into the diaphragm. The device implantation can be performed in one procedure. The main advantages of an intraperitoneal approach are to avoid brachial plexus stimulation and avoid potential phrenic nerve damage. [48,49]

In every type of surgical approach, diaphragmatic pacemakers contain both internal and external electrodes. An internal electrode is placed on the phrenic nerve in the cervical and thoracic approach. In the diaphragmatic approach, they are implanted to diaphragmatic muscle at the point of insertion to the phrenic nerve.

For the external component, a stimulus transmitter is connected to an antenna on the skin surface above a subcutaneous radio frequency receiver. The transmitter controls pulse frequency, amplitude of the current, respiratory rate and inspiratory time. [21]

Benefits, complications, and outcomes

In non-severe trauma, slowly progressive/reversible neuromuscular disease, and minor stretch injuries to the phrenic nerve, mild respiratory insufficiency can be supported with intermittent non-invasive ventilation. However, in complete spinal cord injuries, patients largely require mechanical ventilation. High transection of the spinal cord proximal to or at the origin the phrenic nerve at cervical levels C3-C5 largely results in quadriplegia and complete apnea, and thus patients become permanently dependent on invasive positive pressure to support respiration. However, in patients with bilaterally patent phrenic nerves that remain innervated and intact with the diaphragm, pacing is an option to allow decreased dependence, or even liberation from mechanical ventilation [50]. Even in the midst of unilateral injury to the phrenic nerve, patients may still benefit from diaphragmatic stimulation when combined with techniques such as surgical phrenic nerve repair and intercostal nerve stimulation [51,52]

Efficacy, defined as being able to maintain an unassisted tidal volume 15% greater than a patient's weight adjusted basal requirement, has been demonstrated in up to 98% of patients who receive pacing. [50] Up to 72% of patients receiving successful diaphragmatic pacing have been able to sustain complete weaning from the ventilator at an average of 10 days postoperatively, [53] with a range of 40-72% reported in prospective and retrospective reviews. [54] When including patients who can tolerate significant periods off the ventilator on a daily basis, this percentage increased to up to 96%, with some additional evidence suggesting reductions in hospital length of stay and mortality. [49]

Effective implantation of diaphragmatic pacing has been accomplished across a wide range of delays in surgery, spanning on average between 40 days to 9.7 years since the time of initial CSI. [54] Some observational evidence has demonstrated that a shorter interval between the time of implantation and time of injury resulted in high rates of ventilator liberation [23]. While ideal candidates are those with ventilator dependence due to spinal cord injury proximal to cervical level C3, it has successfully been implemented in patients sustaining low cord injury to levels C4-C7. [49]

Diaphragmatic pacing stimulation is a minimally invasive laparoscopic procedure with perioperative mortality as low as less than 1%, and infrequent risk of infection as low as 2%. [49] Capnothorax is a relatively common complication of implantation, in which carbon dioxide gas from laparoscopic abdominal insufflation transverses into the pleural space and forms a pneumothorax. While typically managed with observation alone when asymptomatic and small in non-tetraplegic patients, patients with tetraplegia may require temporary increases in ventilator-provided tidal volume to adequately expand the lungs, fill the pleural space, and resorb the gas. If recalcitrant, insertion of either chest tube or thoracentesis needle is often needed. [49] Other theoretic complications include diaphragmatic and viscus perforation related to laparoscopic surgery; however these are infrequently reported.

Clinical significance and future direction

Diaphragmatic pacing is an alternative to mechanical ventilation in patients with central hypoventilation syndrome [55] and cervical SCI, [56] however other indications have been explored, including amyotrophic lateral sclerosis (ALS) and heart failure.

Randomized controlled trials in patients with ALS demonstrated decreased survivability in two separate studies despite the theoretical benefit of delaying progression of diaphragmatic weakness. [42,43] A pilot study in heart failure showed that diaphragmatic pacing in addition to cardiac resynchronization therapy helped to improve symptoms of dyspnea, work capacity, and left ventricular ejection fraction over 3 weeks. However, this study only included 24 patients and further trials need to be completed. [57]

Other potential indications to consider are early diaphragm pacing to facilitate weaning from the ventilator in select patients, e.g., ventilator induced diaphragmatic dysfunction. [21] More studies are needed regarding risks and benefits of such an approach as well as cost effectiveness measures, as the initial cost of diaphragm pacing may be quite high.

In conclusion, diaphragmatic pacing in ventilator dependent SCI can dramatically improve not only mortality, but quality of life as well. Recipients of diaphragmatic pacing benefit from increased survivability, likely related to decreased incidence of ventilator associated respiratory infections. [58] Ventilator-free quadriplegics demonstrate a post-injury life expectancy of 35 years, while those requiring chronic mechanical ventilation have a life expectancy of only 18 years. [21] Furthermore, gradual independence from mechanical ventilation leads to increased patient mobility, comfort, and speech ability.

Despite these potential benefits, current data and clinical outcomes are limited. The definition of successful pacing is not standardized, varies between studies, and ranges anywhere as low as 50%, to as high as 98%. The degree of mechanical ventilation liberation also varies widely, ranging from complete independence to a few hours a day. [47,55,59]

While future trials should aim to be larger, more robust, and better defined, diaphragmatic pacing represents a promising and powerful therapeutic option for CSI patients who often have very few. In the appropriate candidate, it should strongly be considered a means of not only improving morbidity and mortality, but also a way of returning a sense of control and freedom to patients often feeling like they have none.

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