Functional Electrical Stimulation in Spinal Cord Injury Respiratory Care

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The management of chronic respiratory insufficiency and/or long-term inability to breathe independently has traditionally been via positive-pressure ventilation through a mechanical ventilator. Although life-sustaining, it is associated with limitations of function, lack of independence, decreased quality of life, sleep disturbance, and increased risk for infections. In addition, its mechanical and electronic complexity requires full understanding of the possible malfunctions by patients and caregivers. Ventilator-associated pneumonia, tracheal injury, and equipment malfunction account for common complications of prolonged ventilation, and respiratory infections are the most common cause of death in spinal cord–injured patients. The development of functional electric stimulation (FES) as an alternative to mechanical ventilation has been motivated by a goal to improve the quality of life of affected individuals. In this article, we will review the physiology, types, characteristics, risks and benefits, surgical techniques, and complications of the 2 commercially available FES strategies – phrenic nerve pacing (PNP) and diaphragm motor point pacing (DMPP). **Key words:** *diaphragm pacing, electric stimulation, phrenic pacing, spinal cord injury*

Background

There are an estimated 11,000 new spinal cord injuries (SCI) annually in the United States, with more than 50% of these resulting in quadriplegia.[1] For high cervical injuries, ventilation assistance is often required. Although mechanical ventilation can be life saving, it is associated with a range of complications including frequent suctioning of secretions, difficulty speaking, reduced ability to smell, and a significant burden on caregivers.[2-5] Diaphragm pacing (DP) has been shown to reduce airway pressure, increase posterior lobe ventilation, and maintain negative chest pressures.[2] DP has also been shown to improve speech, improve olfactory sensation, and eradicate ventilator noise[2,6-8] As an alternative to mechanical ventilation, DP results in a significant improvement in quality of life for individuals who would otherwise require continuous mechanical ventilation.[2] Based on current technology and available pacing systems, diaphragmatic pacing can be offered to eligible patients with SCI as a safe and effective method of ventilatory support. With diaphragm pacing via phrenic nerve pacing (PNP) or diaphragmatic motor point pacing (DMPP), mechanical ventilation may be eliminated for some or all of the day.

History

The concept of electrical stimulation to liberate patients from mechanical ventilation dates back to the 18th century.[2,8,9] In the 1940s, Sarnoff demonstrated that ventilation could be maintained with percutaneous electrodes in poliomyelitis patients.[2] Significant technologic advances were made throughout the 1960s leading to the birth of modern phrenic nerve pacing in appropriately selected patients.[10] Glenn's research led to the development of a practical phrenic nerve stimulating system and to the accumulation of long-term clinical data including surgical techniques and safety parameters for diaphragm conditioning.

In the 1980s, Mortimer demonstrated that the diaphragm can be directly stimulated at its motor points to provide ventilation. Motor points are the locations where the phrenic nerves enter the diaphragm; they can be identified by electrical stimulation from the abdominal surface of the diaphragm. The strength of diaphragm contraction

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is related to the proximity of stimulation to the motor points of the phrenic nerves. Animal results produced inspired volumes that were essentially identical to those resulting from direct phrenic nerve stimulation.[10-13] Onders' studies since the 1990s led to the current technology involving implantation of diaphragm electrodes via endoscopic surgery.

Normal physiology of respiration

Normal respiration requires the coordination of muscles innervated primarily by the cervical and thoracic spinal cord. The predominant muscle of inspiration is the diaphragm, which is innervated by the phrenic nerve from cervical levels C3, C4, and C5.[8] Contraction of the diaphragm moves the abdominal contents downwards. The abdominal contents transmit forces laterally to expand the lower rib cage during inspiration. These changes produce an increase in intrathoracic volume, which lowers intrathoracic pressure and initiates the flow of air into the lungs.[14]

In able-bodied individuals, the diaphragm accounts for approximately 65% of the vital capacity. The accessory muscles of inspiration include the sternocleidomastoid, trapezius, scalene, and external intercostal muscles.[8] The sternocleidomastoid and trapezius are innervated by the spinal accessory nerve, which is infrequently disrupted in SCI as it originates from the superior segments of the spinal cord and the brain stem. The scalene muscles are innervated by the cervical nerve roots C3 through C8. The external intercostal muscles are innervated by the thoracic spinal cord. Together, these accessory muscles work to lift the rib cage and expand the lungs.[15]

Expiration is normally a passive process in which inspiratory muscles relax and air is driven out of the lungs by the reverse pressure gradient between the lungs and the atmosphere until the system reaches its equilibrium point again. The muscles of expiration consist of the rectus abdominus, transversus abdominus, internal and external obliques, pectoralis major, and internal intercostal muscles. The abdominal muscles are innervated by the thoracic and upper lumbar spinal cord. The pectoralis major is innervated by the medial and lateral pectoral nerves from C5 to T1. These muscles become more important to facilitate high minute ventilation in the presence of exertion or to generate expulsive forces necessary for effective cough when secretions increase airway resistance. Attempts have been made to restore many of the normal processes mentioned above, including restoration of both breathing and coughing through the use of FES devices.

Changes in physiology of respiration after SCI

Chronic SCI results in a restrictive impairment with changes in spirometry that reflect a decrease in total lung capacity. There is an inverse relationship between forced vital capacity and higher levels of injury. The functional residual capacity decreases at the expense of expiratory reserve volume with a compensatory increase in residual volume.[16] This is due to an increase in lung recoil pressure and a decrease in chest wall recoil forces. It has been thought that most changes in pressure-volume curves are due to loss of gas-containing alveoli (ie, atelectasis); but according to one study, reduced lung distensibility is not due to microatelectasis but may be related to changes in elasticity of lung tissue.[17] DP offers the ability to prevent some of these changes by maintaining more normal mechanics of ventilation.

Cough is impaired by paralysis of expiratory muscles in persons with tetraplegia and in many individuals with paraplegia. During cough, the abdominal muscles normally work to compress the abdominal cavity and push the diaphragm upward while the internal intercostal muscles pull the ribs downward and inward.[14] The pattern of activation and mechanical action of the diaphragm has been studied by Estenne and colleagues, who have demonstrated that after SCI there is actually a paradoxical movement of the abdomen and lower rib cage during the compressive phase of coughing. This occurs because contraction of the pectoralis major reduces the size of the upper ribcage, which increases intrathoracic pressure and results in dynamic airway collapse. The effectiveness of coughing in patients with tetraplegia may be improved with specific muscle training of the pectoralis major and abdominal binding.[18] In addition, current research is developing FES devices that can facilitate coordination of the

diaphragm and intercostal and abdominal muscles to produce more forceful cough.[19]

Indications for diaphragm pacing

Potential DP candidates need to be carefully screened and to meet specific criteria.[20] Both PNP and DMPP require intact phrenic nerves. Patients need to be free of chest wall deformity and be medically stable. In addition, they should be highly motivated to improve overall function, and they and their caregivers should have appropriate expectations for the benefits of DP.[21,22]

During the natural history of recovery after SCI, phrenic nerve function may improve and patients can sometimes be weaned from mechanical ventilation. Therefore, DP is usually implanted 12 months post injury.[1,23] Recently, there has been debate over the optimal timing of DP in individuals with high complete tetraplegia. One study concluded that FES of only 30 minutes a day could suppress pathologic diaphragmatic attenuation and preserve diaphragm thickness and function.[24] In addition, pacing may lead to neuroplasticity; in rare instances, it has resulted in the recovery of volitional control of breathing.[25,26] Some reports indicate that pacing has potential to lead to phrenic nerve reinnervation as demonstrated by nerve conduction studies.[27]

Contraindications for diaphragm pacing

Absent or significantly reduced phrenic nerve function is a contraindication for DP. Other contraindications include significant lung, chest wall, or primary muscle diseases. Surface EMG and phrenic nerve stimulation are sometimes employed to confirm phrenic nerve integrity. Owing to technical difficulty and decreased compound motor action potentials (CMAP) resulting from variable degrees of diaphragm atrophy, CMAP and latency may be unreliable in assessing the integrity of the phrenic nerves. Due to these difficulties, some centers utilize ultrasound or fluoroscopic examination of the diaphragm during electrical stimulation.[28] Stimulation of the phrenic nerve at the manubrium sterni by surface or needle electrode should result in diaphragm descend of 4 cm or more in adults.[29] Alternatively for DMPP systems, integrity of the phrenic nerves can be assessed by stimulation at the time of laparoscopy.

Surgical Considerations for Diaphragm Pacing

Implantation of DP technology requires precise understanding of the anatomy specific to the procedure. Paralyzing anesthetic agents are avoided as they interfere with the response of the diaphragm to test stimulation during surgery. All surgical procedures, particularly those involving implantation of a foreign body, carry some risk of infection. To reduce the risk of infection of the implant, presurgical surveillance cultures are often used as well as prophylactic antibiotics at the time of surgery. Previous reports[13,23,30] have indicated infection rates of approximately 3%; although with modern surgical technique, this rate may be significantly lower. Infection is a serious complication, because its occurrence often dictates removal of all implanted components.

Phrenic nerve pacing systems

Currently, there are 3 phrenic nerve stimulation systems available worldwide: Avery Biomedical Devices, Atrotech, and Medimplant systems. The Avery device is commercially available in the United States, the Atrotech device has been available in the United States only through clinical trials, and the Medimplant system is available in Europe. Each of these systems is designed for lifetime use with long-term technical support. The Avery Mark IV device has a unique optional interface that allows biofeedback control from pulse oximetry and CO_2 monitoring.[31,32] In addition, trans-telephonic monitoring is available, allowing the electronic output and phrenic nerve-diaphragm neurophysiologic response to be monitored by telephone.[31]

Atrotech (Tampere, Finland) and Medimplant (Vienna, Austria) systems differ from the Avery system in the electrode technology.[11,20,33,34] The Atrotech system has the ability to stimulate different portions of the nerve each time with the intention of reducing muscle fatigue. The Vienna phrenic pacer (Medimplant, Vienna, Austria) system also has multiple electrode contacts with the phrenic nerve.

Despite their differences, the 3 available PNP systems share a number of features. In all cases, the electrodes are directly attached to the phrenic nerve and contraction of the diaphragm occurs via excitation of the nerve.

Surgical approach for phrenic nerve pacing

Surgical implantation of the PNP can be done via the cervical and thoracic approach. The thoracic approach carries higher risks and surgical costs. Video-assisted thoracoscopic surgery (VATS) can minimize the morbidity of the thoracotomy and allow appropriate nerve stimulation. The cervical approach, although less invasive, is associated with a specific set of complications including incomplete diaphragm activation or stimulation of other nerves in proximity to the phrenic nerve resulting in pain and/or undesirable movement. Neck movement may place a significant mechanical stress on the nerve-electrode interface, increasing the risk for nerve injury. In both approaches, the phrenic nerve is directly manipulated with potential iatrogenic, mechanical, and/or ischemic injury to the nerve during placement, which can lead to failure. The electrodes are connected to a radiofrequency receiver, which is normally positioned superficially over the anterior chest wall.[1]

Diaphragm motor point pacing systems

Mortimer, DiMarco, and Onders have demonstrated a method by which the phrenic nerves can be activated via intramuscular diaphragm electrodes. The intramuscular diaphragm electrodes can be placed via a laparoscopic procedure as an outpatient. Laparoscopic implantation of intramuscular diaphragm electrodes provides a less invasive and less costly alternative to conventional PNP. At the time of writing, there is only one commercially available DMPP system, the NeuRx RA/4 external stimulator.[9,20] This is a 4-channel percutaneous neuromuscular stimulation system that requires leads tunneled subcutaneously to an exit site in the skin connected to an external stimulating device.

Surgical approach for diaphragm motor point pacing

The DMPP procedure involves implanting intramuscular electrodes in the diaphragm near the points where the phrenic nerves enter the muscle. The phrenic nerve motor points are not visible from the abdominal surface of the diaphragm, and it is critical to locate the motor points correctly in DMPP for adequate diaphragmatic activation.[30] During laparoscopy, electrical stimulation is applied systematically to various locations on the diaphragm to identify the location of the motor points. Because DMPP avoids the need to mobilize a section of the nerve, the risk of nerve injury is reduced compared with PNP.[1,13,30,35] During the procedure, caution must be taken when identifying motor points as the liver can sometimes be attached to the right hemidiaphragm. An electrocardiogram is recorded during the procedure to be sure that there is no capture of the cardiac rhythm.[13,20,24,30] Research over the last 20 years with SCI patients indicates that the likelihood of a skin infection at percutaneous electrode sites is extremely low.[1,18]

Transition from Mechanical Ventilation to Pacing

Because of the changes in respiratory physiology that occur soon after an SCI, conditioning of the respiratory muscles is an integral part of the patient's rehabilitative process. Reduced diaphragm work during mechanical ventilation leads to disuse atrophy and lowered resistance to fatigue. The extent of atrophy has been shown to be affected by physical condition prior to injury, rehabilitation after injury, and the time from injury to the implant of a pacer.[12,36] Levine et al showed that as little as 18 hours on mechanical ventilation can lead to atrophy of the diaphragm with conversion of type I to less fatigue resistant type IIb muscle fibers.[27,37-39] For these reasons, full-time pacing systems support cannot be achieved immediately, but rather should be attempted in a systematic progression. Advancement of pacing time should be correlated with improvement in diaphragm strength and endurance. Age and time since injury directly affect the conditioning time needed to achieve 4 continuous hours with DP. The reported conditioning times range from less

than 1 week for 18- to 20-year-olds who have been ventilated for less than 1 year to up to 4 weeks for 40- to 50-year-olds who have been ventilated for longer than 5 years.[10] One study found that patients younger than 25 years of age took the least amount of time to achieve 4 hours of ventilator independence, with a median of 19 days compared to 54 days in older subjects.[40] Patients who are older than 65 years of age may need up to 21 weeks to meet their conditioning goal,[10] and patients with significant scoliosis may require increased time for diaphragm conditioning.[1]

Initiation of diaphragm conditioning

Prior to the initiation of diaphragmatic conditioning, the patient should be medically stable and free of pneumonia or other infections, excessive secretions, acute pulmonary pathology, or hemodynamic instability. It is imperative to optimize the physiologic reserve of the individual in order to set the stage for success. For example, it has been suggested that malnutrition may contribute to lack of success with postoperative conditioning.[41]

Long-term mechanical ventilation often leads to chronic hyperventilation and reduction of bicarbonate stores. Pacing systems are designed to maintain physiologic levels of CO_2; therefore, patients may initially experience sensations of dyspnea during pacing. Dyspnea results from acidosis as CO_2 levels rise to normal despite eucapnea. Acidosis can be minimized by gradually adjusting the ventilator to restore near-normal levels of PCO_2 prior to the initiation of pacing.[1,8,35] Initial diaphragm pacing goals should be set to provide tidal volumes approximately 15% above the basal needs of the patient (5-7 mL/kg).[42] The early phase of conditioning can be implemented with the patient still on mechanical ventilation, as it may be difficult to achieve adequate inspired volumes in the beginning of the process.[10] While on assist control mode, the ventilator can be triggered by the negative inspiratory pressure generated at the tracheal opening.

It is important to strive for the lowest stimulus frequencies and respiratory rates necessary to maintain adequate ventilation and patient comfort. Individual stimulus parameters to be adjusted include pulse amplitude, width, rate, and frequency to maintain a comfortable level of stimulation for the conditioning session.

Diaphragm conditioning in practice

Diaphragm conditioning is usually initiated at least 2 weeks after surgery in order to allow adequate time for healing of the surgical incisions and resolution of inflammation and edema at the interface of the electrode and the site of stimulation.[32] Pacing should occur in a closely monitored setting under physician supervision and should involve a respiratory therapist. Once the conditioning process has been implemented, it should be progressed in a stepwise fashion with close monitoring of objective and subjective data before, during, and after pacing.[43] Higher levels of stimulation may be required in the seated versus supine position due to the anatomical and force-generating effects of gravity as discussed previously.

Objective measures of baseline respiratory function should be obtained as well as a subjective measure of dyspnea, such as the Borg Rating of Perceived Exertion Scale (RPE). Objective measurements may include pulse oximetry, respiratory rate, tidal volume, vital capacity, FEV1, negative inspiratory pressure, end-tidal CO_2 correlation with arterial blood gas, and baseline chest x-ray. The integrity of the pacing system should be assessed initially and monitored frequently based on one or more of the following parameters. For example, the stimulus threshold is the minimum stimulus amplitude that results in visible or palpable diaphragm contraction. The magnitude of diaphragm force generation can be assessed by measuring the changes in airway pressure during tracheal occlusion and is useful in the presence of significant airway secretions or atelectasis.

In practice, the goal is to eventually achieve full-time pacing without significant fatigue of the diaphragm. There are no standards of care regarding progression of diaphragmatic pacing, but a popular approach is to determine the time to onset of fatigue as derived from objective and subjective monitoring parameters. Conditioning can begin with a short period of pacing, such as 5 minutes, every waking hour of the day for the first

week. The amount of time per hour can be slowly advanced until the patient is comfortably pacing continuously during waking hours. At this time, pacing can be advanced through sleeping hours. Upper airway obstruction may occur due to the lack of synchronous activation of the upper airway muscles in relation to the diaphragm.[8] During nocturnal pacing, the plug is often removed from the tracheostomy to prevent the development of upper airway obstruction.

Future Directions

A totally implantable system similar to cardiac pacemakers would eliminate the need to attach materials to the body surface and connect to an external transmitter. This would further improve patient convenience, but would also require periodic surgical replacement or recharging of an implanted battery.[22]

The diaphragm motor point pacing system currently uses percutaneous wire electrodes that exit the skin and are attached to an external stimulator. This system is reliable, but in the future an implanted stimulator may be used as with phrenic pacing systems.

All current systems are of the open-loop design. Electrical signals from the pacer activate the diaphragm independent of signals from the central nervous system. Consequently, upper airway muscle activation can occur independent of diaphragm activation, placing patients at risk for upper airway obstruction during sleep.[8,16,22,25,42] One possible solution would be the use of an upper airway muscle signal to trigger diaphragm activation. This type of device would potentially eliminate the need for a tracheostomy and provide a mechanism for ventilatory adjustment to speech and changes in ventilatory requirements.

Many patients have suffered significant injury to both phrenic nerves and therefore cannot be offered DP. If only one hemidiaphragm can be activated, combined intercostal pacing and unilateral diaphragm pacing with plication of the noncontracting diaphragm may prove successful. Further development of surgical transfer of intercostal to phrenic nerves may allow these patients the possibility of DP.[24]

Finally, the use of electrical stimulation to activate the expiratory muscles to restore a cough mechanism in patients with SCI is being studied. Cough initiation can be combined with traditional DP, because stimulated cough is brief, lasting less than one second, and applied intermittently. Recent advances in FES for cough have recently been reported.[19]

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