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Respiratory Dysfunction in Spinal Cord Injury: Physiologic Changes and Clinically Relevant Therapeutic Applications

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Abstract

Spinal cord injury (SCI) can result in serious respiratory compromise, impaired cough ability and respiratory failure. Complications include atelectasis and pneumonia. Respiratory failure is the primary cause of morbidity and mortality in high cervical cord injuries. Various methods have been used to assist coughing in SCI, including manual and mechanical techniques. Physical therapists can apply certain exercises and maneuvers to augment tidal breathing and expiratory effort, such as respiratory muscle training. For patients with vital capacities <10 to 15 mL/kg, noninvasive methods such as abdominal binding, the pneumobelt, and face mask-applied ventilators are used to maintain adequate respiration. Phrenic nerve and diaphragmatic pacing provide increased patient mobility, comfort and lower health care costs; breathing pacemakers have increased survival and improved quality of life in individuals with upper cervical cord and brain stem lesions. Tracheostomy should be used only for those patients that have severe bulbar impairment and cannot successfully use airway clearance methods. Even patients with tracheostomy-assisted ventilation can be eventually weaned off respirators, provided they meet criteria for spontaneous breathing. Peak expiratory flows should exceed 160 L/m to assure expulsion of airway secretions and the negative inspiratory pressure should exceed -20 cm H_2O (variables measured with the tube cuff inflated) before the patient is decannulated. Appropriate vaccinations should be provided for any individual with compromised respiratory function, particularly with regularly scheduled influenza and pneumococcal pneumonia vaccines. Management of the physically impaired patient can be a major challenge for family, leading to adverse physical and psychological consequences. Long-term management requires a multidisciplinary approach that includes respiratory, physical and occupational therapists, nutritionists, social workers, psychologists, and home health agencies, all of whom contribute to key aspects of maintaining optimum respiratory function. Life satisfaction is a major consideration in this group of individuals, but it may have a more positive outlook than one would think in someone with significant physical and psychological challenges.

Keywords: Abdominal binding; Control of ventilation; Cough assist techniques; Noninvasive ventilation; Pulmonary function testing; Respiratory muscles; Spinal cord injury

Introduction

Approximately 17,000 new cases of spinal cord injury (SCI) occur each year, affecting more than 282,000 people in the U.S [1]. More than half of spinal cord-injured individuals experience an injury at the cervical level [2]. Mortality rates for individuals with cervical cord lesions are 9-18 times higher, respectively, than for those of the same age in the general population [3]. Respiratory disorders are the leading cause of death in cervical cord injuries (SCIs) [4-6], although mortality rates have decreased by as much as 79% for patients with complete tetraplegia by the 1970s [7] thanks to improved care. Respiratory illnesses comprise 20-24% of deaths during the first 15 years after injury [8,9]. Several factors adversely influence mortality, including level of SCI, older age, preexisting cardiopulmonary disease, concomitant injuries, and delayed recognition of and attention to pulmonary problems [8,9]. A prospective study found that independent predictors of all-cause mortality included diabetes mellitus, a history of heart disease, tobacco consumption, and FEV_1 at entry into the study [8]. In contrast to prior retrospective studies, level and completeness of injury, age, and injury in earlier years were not directly related to all-cause mortality. The authors concluded that as individuals with SCI survive longer, comorbid conditions and personal behavior, such as smoking, increasingly determine mortality.

Pathophysiology

The degree of respiratory impairment in patients with SCI depends on the level of injury, although partially functioning segments may contribute to improved function [10,11]. Patients with neurological complete lesions at C1 and C2 cannot breathe on their own. Individuals with complete C3 and C4 tetraplegia have impaired ventilation due to diaphragmatic paralysis and are typically ventilator dependent in the acute stage, though a significant proportion of individuals with C4 tetraplegia are ultimately able to successfully wean off the ventilator. Low cervical cord lesions (C5-C8), will impair function of the intercostal, parasternal, and scalenes, and but leave the diaphragm, trapezii, sternocleidomastoid, and the clavicular portion of the pectoralis major muscles intact. As the phrenic nerve origins are from C3 to C5, the diaphragmatic force generation will remain intact in lower cervical injuries even as other chest wall muscles lose function [12]. However, when breathing against an incremental threshold load, inspiratory muscles have limited capacity to generate pressure against the load [13]. This finding, as well as a higher tension-time index of the diaphragm compared to that of control subjects, provide evidence for diaphragm fatigue [12]. With inspiratory resistive training or phrenic stimulations, however, diaphragmatic strength and endurance may improve [14,15] along with lung function [16].

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During the acute period, forced vital capacity (FVC) in tetraplegia is markedly reduced as a result of diaphragmatic weakness, but FVC as well as other lung volume subdivisions recover over the next several weeks to months [17,18]. Linn et al. [18] reported that in subjects with complete-motor lesions, FVC ranged from near 100% of normal predicted values in the group with low paraplegia, to less than 50% in those with high tetraplegia. Incomplete lesions mitigated FVC loss in tetraplegia. For subjects with low tetraplegia (C6 - C8), a one-vertebra rise in lesion level predicted an additional nine percentage points FVC impairment. For those with paraplegia estimated effects of level were reflected as a slightly more than one percentage point FVC decrement per one- vertebra rise in level (Figure 1) Impaired function of the diaphragm in the acute stage of injury in mid-to-low cervical and high thoracic SCI is due to the mechanical inefficiency associated with paradoxical (dyssynchronous) rib cage movement and unfavorable changes in thoracoabdominal compliance. The time course of recovery of pulmonary function varies in people with SCI and may only be weakly predicted by the initial degree of impairment and the injury level [18]. Reduction in lung volume results in decreased lung and chest wall compliances [19-21], which further increase work of breathing and contribute to dyspnea and respiratory failure (Figure 2).

Patients with tetraplegia exhibit a rapid, shallow breathing pattern [22]. Rib cage motion is paradoxical because of a reduced anteroposterior diameter of the upper rib cage [23-26]. This paradoxical rib cage motion is caused by paralysis of the rib cage inspiratory muscles, particularly the parasternals and external intercostals which ordinarily provide stability to the rib cage.

Ventilatory drive in individuals with SCI can be assessed by recording the airway occlusion pressure (P0.1 or P100) response to hypercapnia during CO_2 rebreathing. The occlusion pressure is the airway or mouth pressure measured 0.1 seconds after the subject initiates an inspiratory

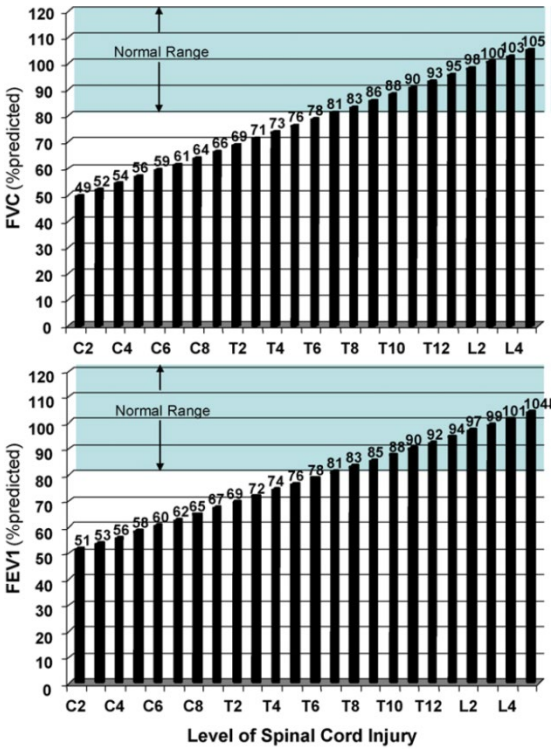

Figure 1: Correlation of forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) with level of spinal cord injury [18].

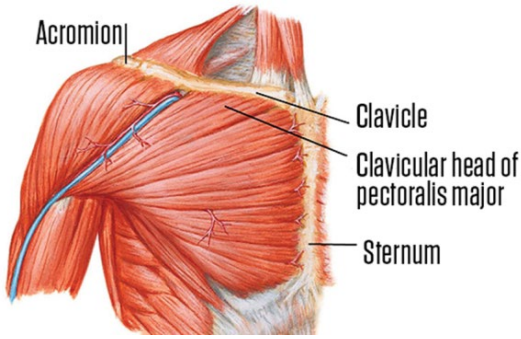

Figure 2: Diagram illustrating the expiratory action of the clavicular portion of the pectoralis major. The muscle fibers run caudally and laterally from the medial half of the clavicle to the humerus. Consequently, if the arms are fixed, contraction of these fibers on both sides of the chest displaces the clavicles and the manubrium sterni in the caudal direction. As a result, the upper part of the rib cage moves caudally as well and compresses the upper rib cage. Exercising this portion of the clavicle augments the cough effort and may increase inspiratory capacity.

effort against an occluded airway, and is referred to as the P0.1. It reflects neuromuscular drive, and is unaffected by cortical input, as the subject is unaware that the airway is blocked until (relatively) long after the airway has been occluded. Because there is no flow at the time of occlusion, P0.1 is unaffected by airway resistance, but is influenced by lung and chest wall volume and compliance. Neuromuscular drive as measured by P0.1 increases with CO_2 rebreathing. In this regard, studies have shown conflicting results in persons with quadriplegia, with some demonstrating ventilatory response to hypercapnia in SCI to be the same as in able-bodied controls [25], but most others showing blunted responses [26,27], Despite the blunted response to hypercapnia, normoxemic tetraplegic individuals exhibit the ability to compensate for an increased mechanical load, such as breathing against an inspiratory resistance, as shown by an increase in P0.1 [25]. Neural inspiratory drive (Edi) as defined by the moving integrated average of the diaphragmatic electromyogram, and measured by esophageal electrode, also increases with added inspiratory load [27]. Similarly, ventilatory and P0.1 responses to hypercapnia do not change with assumption of posture from supine to semi-recumbent or seated in which a shortening of the resting length of the diaphragm would reduce its force-generating ability [28-32]. The rate of rise of the Edi response to hypercapnia is significantly higher in seated SCI patients, a change not seen in control subjects [33]. Under loaded conditions, the intensity of central neural output in SCI patients is preserved to achieve adequate tidal volume (Vt) as in healthy controls, but the inspiratory duration is markedly shortened, perhaps in an attempt to minimize energy requirements [34].

In this connection, patients with high SCI exhibit an intact sensation of "air hunger" to hypercapnia or reduced Vt. Manning and coworkers showed that "air hunger" correlated significantly with Vt and end-tidal partial pressure of carbon dioxide ($PetCO_2$) independent of each other, suggesting that the sensation of "air hunger" is independent of afferent information from the chest wall [28].

The diaphragm and other skeletal muscles serve purposes other than respiration. In patients with low cervical injury, in addition to serving as the major inspiratory muscle, the diaphragm functions also as a trunk extensor [35]. When performing forward trunk flexion, these patients exhibit continuous and augmented diaphragm electrical activity and abdominal pressures [36]. Thus, during posture imbalance the diaphragm may fatigue as a result of overriding its inspiratory

function [35]. Paralysis of the abdominal muscles results in ineffective cough and clearance of secretions. To assist in cough, during forced expiration, tetraplegic individuals can recruit the clavicular portion of the pectoralis major (motor innervation C5 to C7) to compress the rib cage [37], with enough force to even cause dynamic airway collapse, as in able-bodied persons (Figure 2). Both repetitive isometric contractions of the pectoralis conducted over several weeks [38,39] and paired magnetic stimulation of abdominal muscles [40] improve or retain abdominal muscle force generation. With paralysis of the major respiratory muscles, individuals with tetraplegia can use the sternocleidomastoid and other accessory neck muscles (trapezii, platysma, mylohyoid) to sustain brief periods of spontaneous breathing [37].

Secondary immune deficiency is a serious complication that may lead to chronic and recurrent infections after SCI [41]. Immune dysfunction and infectious complications are more prevalent than in persons with paraplegia. The role of autonomic dysreflexia is an intriguing neurogenic mechanism contributing to post-traumatic immune suppression, thought to be related to the release of immunomodulatory glucocorticoids and norepinephrine into the blood and immune organs with each dysreflexic episode [42]. These authors and others showed previously that splenic B-cell numbers and antibody production were reduced early after high level SCI [43,44]. It has been suggested that assessment of heart variability by Holter monitoring can predict infectious complications [45,46], although this concept requires additional research.

Respiratory Impairment- Clinical Aspects

As respiratory complications are among the most common adverse systemic events following cervical SCI, identification of factors that would predict morbidity, mortality and increased length of stay is important. In a study of 109 patients (motor injury complete in nearly 60%) Aarabi et al. [47] found associations between pulmonary complications and younger age, sports injuries, the American Spinal Injury Association (ASIA) Impairment Scale (AIS) grade at admission [47], ascending neurological level, and lesion length on MRI studies. Patients with AIS grades A, B, and C were 10, 2.6, and 1.7 times as likely to have a moderate to severe pulmonary complication compared to those with AIS grade D injury.

Bronchial hyperresponsiveness

Individuals with cervical SCI exhibit bronchial hyperresponsiveness to histamine that can be blocked with ipratropium chloride [48,49] and oxybutynin chloride, an antimuscarinic agent administered to reduce urinary frequency due to bladder spasticity [50]. Airway hyperresponsiveness reflects unopposed cholinergic bronchoconstrictor tone resulting from disruption of upper thoracic ganglia. As a result of these changes, patients with high SCI benefit from nebulized β2-agonist bronchodilator therapy. As in able-bodied individuals, smoking adversely affects lung function as reflected by reduced values of forced expiratory volume in one second (FEV_1) and peak expiratory flow (PEF) [51].

Acute respiratory distress syndrome

Acute respiratory distress syndrome (ARDS) and acute lung injury (ALI) are common complications after acute SCI. A large database assessment of more than 37,000 admissions with SCI conducted between 1988 and 2008 evaluated the relationship between SCI and ARDS [52]. ARDS was observed in 32% of more than 12,000 admissions of SCI with evidence of open vertebral column fractures (VCF), in 21% in those with closed VCF, in 9% of patients without fracture, and in 2.4% in patients with closed fracture but no SCI. The overall prevalence of SCI ARDS or ALI in all SCI patients was 17% and 11% in patients with cervical cord injuries. SCI was a greater risk factor for ARDS and acute lung injury (ALI) and was significantly greater than in patients with spinal trauma without SCI [odds ratio (OR) 4.9], although the study was completed just before the new Berlin classification of ARDS which no longer includes ALI as a subcategory of the condition [53]. The presence of sepsis or cardiac arrest further increased risk of ARDS (OR 8.6). As expected, in-hospital mortality rates were much higher in patients with ARDS/ALI than in those without (OR 6.5). Mean hospital length of stay was 4 times as long in SCI patients than in those without SCI. Hispanic and native American males were at a higher risk of developing ARDS/ALI, findings similar to that in traumatic brain injuries [54].

Recovery of respiratory function after SCI

Recovery of respiratory function has been studied in monkey models [55]. Destructive changes in the anterolateral columns as well as the phrenic motoneurons contributed to the apneas. A delayed form or respiratory paralysis within 30 to 60 minutes was caused by edema and centrifugal pressure from the expanding central cord lesion leading to secondary ischemia as seen on photomicrography. Durotomy performed within 2 hours after injury reversed respiratory dysfunction as long as respiratory pathways remained viable. Nevertheless, many of the animals still exhibited impaired breathing as noted by irregular and paradoxical breathing patterns

Recovery of respiratory function in humans, at least to some degree, may occur within months after SCI. Ledsome and Sharp [17] found that in patients with functionally complete transection of the cord between segments C5 and C6, the VC was 30% of predicted one week following injury. Patients with an FVC of <25% predicted had a high incidence of respiratory failure requiring assisted ventilation, particularly seen with C5 or higher injuries. The VC increased significantly within 5 weeks of injury and had approximately doubled after 3 months. An incidental finding was that of a high incidence of hypoxemia, even in the absence of hypercapnia. This can be attributed to an elevated diaphragm with resultant increase in closing volume, de-recruitment of alveoli and ventilation-perfusion mismatching [56]. Axen and colleagues [57] found that VC increased by an average of 29% in 36 tetraplegic individuals after 10 months following injury. The improvement in lung function was attributed to at least partial recovery of phrenic nerve function. These authors observed simultaneous improvement in shoulder and upper arm muscles with some segmental innervation in common with the diaphragm. Brown et al. [58] serially measured lung volume subdivisions in 5 complete persons with quadriplegia over the course of one year: mean inspiratory capacity and expiratory reserve volume increased by 47% and 245%, respectively. A concomitant improvement in transdiaphragmatic pressure indicated some spontaneous recovery of diaphragm innervation, a conclusion similar to that of Axen et al. [57]. Bluechardt and colleagues [19] found that FEV_1 and FVC increased by 40% and 33%, respectively, between 3 and 7 months, changes attributed to improved diaphragmatic and accessory respiratory muscle function [58-63]. As might be expected, approximately 80% of SCI patients (65% of those with complete cervical motor injuries) meet testing standards for acceptability and reproducibility according to American Thoracic Society guidelines [64,65].

Following high cervical cord injury, ipsilateral excitatory input to the phrenic motoneurons from the medulla is removed and rhythmic phrenic activity ceases on the side of injury. However, latent contralateral excitatory premotor input to phrenic motoneurons can be strengthened

over time after cord hemisection leading to functional recovery of activity. This neuroplasticity can mediated through neurotrophins such as brain-derived neurotrophic factor (BDNF) acting through tropomyosin related kinase receptors (TrkB). One group is currently conducting a study to determine if functional recovery of rhythmic phrenic activity is enhanced by an increase in TrkB.FL signaling in phrenic motoneurons and to determine whether time-dependent changes in TrkB signaling following cord hemisection mediate the acute enhancing effect of intrathecally and intrapleurally administered BDNF on functional recovery [66]. Unfortunately, intrathecal BDNF has been associated with significant adverse effects that preclude its therapeutic use. As an alternative, the group is also studying locally implanted mesenchymal stem cells genetically engineered to produce BDNF, combined with a novel targeted approach to increase expression of TrkB in phrenic motor neurons using adeno-associated virus designed to promote functional recovery after spinal cord injury.

Management of Respiratory Complications Following SCI

Tracheostomy-assisted ventilation

Patients with acute SCI should be monitored in the intensive care unit because of the potential for cardiorespiratory complications. Patients with complete SCI at the C5 level and above typically require airway protection and assisted ventilation at least initially [5,67,68]. Even as many as 79% patients following acute complete injuries at C6 or below may require intubation and half of them may progress to tracheostomy [67], the purpose of which is to facilitate removal of airway secretions to prevent atelectasis, hypoxemia and pneumonia. Mechanical ventilation corrects hypercapnia and hypoxemia resulting from weak respiratory muscles. Because several months may pass before recovery of neurological function is sufficient enough to sustain spontaneous breathing, most patients with cervical SCI will require a tracheostomy shortly after injury. In a retrospective study of 69 individuals with cervical SCI (65% with high SCI), Guirgis et al. [69] found that early tracheostomy was found to significantly reduce the duration of mechanical ventilation in patients with both high and low cervical spinal cord injuries Patients with a low cervical SCI spent a longer time in the ICU on average. Mortality was significantly lower among high CSCI patients who underwent an early tracheostomy, although this was not the case for patients with low CSCIs.

Impaired bulbar function, which when coupled with absent abdominal muscle contractility, may lead to poor cough generation, retained airway secretions, atelectasis and pneumonia, although this finding is rare in high SCI individuals, unlike in other neuromuscular disorders such as amyotrophic lateral sclerosis. Retrospective studies suggest that early application of tracheostomy (prior to day 7 following SCI) facilitates respiratory management, shorter time on mechanical ventilation, fewer airway complications (related to prolonged intubation), and earlier discharge from the intensive care unit [70,71]. Tracheostomy also appears to reduce the working of breathing during weaning trials [72], particularly when the cuff is deflated [73], and shortens time to decannulation. Cuff deflation may also reduce respiratory infections and improve swallowing function.

With respect to tracheostomy-assisted mechanical ventilation, tidal volumes between 15 and 20 mL/kg are generally recommended, for the purpose of relieving air hunger and preventing atelectasis [74,75]. The assumption is based on the concept that high volumes improve the production of surfactant, prevent the collapse of the airway, promote recruitment, and are better tolerated by the patient, although the evidence for this recommendation is based on retrospective studies and case series [76,77]. Peterson [78] reviewed 42 patients with SCI and found that those who were ventilated with >20 mL/kg were weaned 3 weeks earlier than those ventilated with smaller tidal volumes. Higher tidal volumes have been safely utilized during weaning of patients with tetraplegia [79], although larger randomized controlled trials are needed to determine whether higher Vts translate to improved outcomes in this unique patient population. In the absence of acute lung injury from other causes, higher tidal volumes don't seem to cause ventilator-associated lung injury in people with tetraplegia, possibly because lung volumes and compliance are already reduced and are likely to reverse with application of high tidal volumes. Nevertheless, the peak airway pressure must be kept below 40 cm H_2O to avoid volutrauma. In addition, high airway volumes and pressures could potentially lead to hemodynamic instability in patients with autonomic dysfunction and hypotension. In the case of non-invasively ventilated patients, breath stacking is another way to prevent or reverse atelectasis (see below).

Airway protection becomes necessary when the SCI has occurred with traumatic brain injury and the Glasgow Coma Score is 8 or less. Variables considered important in determining the need for airway management include the FVC, volume of respiratory secretions and gas exchange, which allow accurate prediction of such management in 80% or more of patients [80]. Table 1 summarizes important clinical and physiologic variables to consider in this regard. Tracheostomy facilitates suctioning for caregivers, and reduces dead space physiology and hypercapnia. Of course, it has its own associated complications, including suction trauma, granulation tissue, stomal infections, tracheal stenosis, tracheomalacia, and probably the most devastating of all (while rare), tracheovascular fistulas that may result in catastrophic hemorrhage. Other issues include hypocapnea related to bypassing of anatomic dead space of the upper airway. The resultant respiratory alkalosis may result in hypokalemia, cerebral vasoconstriction and ischemia, and seizures which may complicate associated head injury. Later on, to the extent that there is recovery of respiratory muscle function, the patient may be bridged on to noninvasive ventilation. When used in conjunction with manual and machine-generated cough-assist techniques, or phrenic nerve and/or abdominal muscle stimulation, the patient may get by without a tracheostomy entirely [81].

Noninvasive ventilation

Bach and colleagues [82-84] have published their experience describing the eventual decannulation of tetraplegic patients for conversion to full-time support with noninvasive positive pressure ventilation (NIPPV) after initial intubation for mechanical ventilation. In one of their series, 7 of 23 patients who initially had been supported

Guidelines for weaning from assisted ventilation
• Patient is cooperative and not agitated or delirious; no need for use of sedation.
• Afebrile, stable vital signs.
• Arterial oxygen saturation > 95% and paCO2 < 40–45 mm Hg, while breathing room air.
• Fraction of inspired oxygen no more than 25% and PEEP < 5 cm H2O.
• Chest imaging with no or resolving abnormalities
• Minimal airway secretions.
• Negative inspiratory pressure <−20 cm H2O.
• Vital capacity > 10–15 mL/kg of ideal weight.
• Stable hemodynamic status (that is, normal intravascular volume balance and not requiring inotropic agents or vasopressor
• Ability to tolerate physical therapy or use of noninvasive mechanical ventilation

Table 1: Guidelines for weaning from assisted ventilation.

with tracheostomy-assisted ventilation were converted to using continuous NIPPV (with no free time) for a mean of 7.4 years (range 1 to 22 years) [73]. Determinants for initiation of NIPPV included younger age, intact bulbar function and mental status, and absence of parenchymal disease such as pneumonia. NIPPV would also be indicated in SCI patients with obstructive sleep apnea syndrome, particularly in those with high cord injuries. Bach and his group [82-88] have continued to manage neuromuscular patients with unmeasurable VC without tracheostomies for many decades. Patients have generally preferred NIPPV to tracheostomy-assisted ventilation for comfort, safety, swallowing, speech, and aesthetic reasons. Absence or resolution of bulbar impairment, however, is a requisite for NIPPV.

Another method that has been used is glossopharyngeal breathing ("frog breathing"), a technique that was initially devised for and taught to patients with acute poliomyelitis with respiratory compromise in the 1950s and 1960s [89]. In this method, the patient gulps small amounts of air (40 to 200 mL) into the lungs in sequences of 6-9 breaths in a row, and then exhales or coughs. This method is a substitute for sighing, and can be used to augment tidal breathing, prevent atelectasis, and clear airway secretions.

Pneumobelts (cyclically inflatable abdominal binders) may have certain advantages as a choice for interim or permanent ventilation of individuals with high SCI without severe bulbar impairment. During inflation the device displaces the diaphragm cephalad, allowing it to become mechanically more efficient. Placing its upper border two fingerbreadths below the costophrenic junction avoids paradoxical expansion of the chest cause by enclosure of the lower thorax [90]. Miller [91] described 12 of 21 patients with high tetraplegia who were able to progress within days up to 4 hours of continuous use of a pneumobelt, and thereafter to 12-hour or all day use. This enabled independence and mobility, safety and health, improved speech, and general appearance (no tracheostomy). Disadvantages included pump noise, stomach gas, and position difficulties. Use of the pneumobelt requires that the individual be sitting up.

Cough assist techniques

Assisted coughing can replace the function of the paralyzed expiratory muscles by increasing the pressure below the diaphragm. This is usually performed by an assistant working with the patient, although some lower SCI patients with intact hand function can learn to perform the technique on themselves. It consists of a sharp inward and upward application of pressure to the upper abdomen just below the diaphragm, designed to expel large airway secretions, much like a Heimlich maneuver. It is most effective in the supine position. Assisted coughing is indicated when the cough effort is noted to be ineffective [88]; a good index to monitor is when the peak expiratory flow (PEF) falls below 160 L/m [83,86,88]. Other indications include retained secretions heard on auscultation, radiographic evidence of atelectasis, postoperatively when the patient is recovering from anesthesia, and a reduction for the need of tracheal suctioning to reduce suction trauma. Absolute contraindications to manual assisted coughing include unstable angina or acute myocardial infarction, extensive chest trauma, including broken ribs and flail chest, elevated intracranial pressure or known intracranial aneurysm, cystic or bullous lung disease which could potentially result in pneumothorax from sudden increases in intrathoracic pressure. Relative contraindications include spinal misalignment, abdominal injury or ileus, skin hypersensitivity and poor integrity, bronchospasm and chest drain. Staff and/or family members should be trained in and be assessed for competence for the procedure before performing the technique unsupervised. Factors to consider before applying manual assisted cough techniques include spinal stability, size of the patient's chest, whether the patient is in bed or wheelchair, thickness and quantity of airway secretions, the experience of available staff, and the upper body strength of the staff member [92].

Many techniques have been devised to assist a patient's cough, and experienced staff may modify these methods according to their expertise and for maximum effectiveness [92]. These techniques have the advantage of achieving airway clearance in patients who do not have tracheostomies; indeed, use of these methods may avoid the need for tracheostomies, even in patients with low or unmeasurable vital capacities and poor cough effort. Cough procedures may be performed as often as needed, and if available, in conjunction with chest insufflation and mechanical cough devices. Patients should be monitored for dyspnea, pain, sputum appearance and quantity, breath sounds, and presence of any change in neurological signs and hemodynamic compromise (cardiac arrhythmias or hypotension). To assess the effects of the manual cough assist, measurements of FVC and PEF should provide useful information. The assisted cough is considered to be effective if the patient can generate a PEF of 270-360 L/min or more, the patient expresses relief of dyspnea and congestion, the cough sounds are stronger than an unassisted cough, and the patient is able to swallow or expectorate secretions, or the latter can be removed with just shallow tracheal suctioning [92].

The use of an abdominal binder is also used to augment the cough effort. Julia et al. [93] found that depending on the number of straps in an abdominal binder, the peak expiratory flow increased by 19% to 28% in supine tetraplegic patients. In 13 seated patients with C5-C7 SCI, West and colleagues [94] found increases in VC, inspiratory capacity, maximal expiratory mouth pressure, transdiaphragmatic pressure (Pdi, difference between esophageal and gastric pressures), and cardiac output, while decreases occurred in residual volume and functional residual capacity (Figure 3).

Glossopharyngeal breathing and air stacking are additional approaches in which breaths are stacked, usually 3 to 6 in a row, before exhalation or coughing.

Mechanically assisted coughing (insufflation-exsufflation) employs a technical respiratory method (cough-assist device) by which air is blown into the lungs and then suctioned out rapidly (Figure 4). The insufflation-exsufflation pressures are adjusted to a range of positive

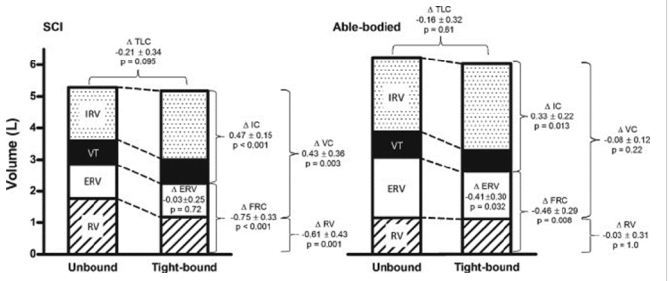

Figure 3: Static lung volumes and capacities in unbound and tight-bound conditions in abdominal binding for SCI (left panel; n=13) and able-bodied (right panel; n=8). TLC=total lung volume; IRV, inspiratory reserve volume; VT, tidal volume; ERV, expiratory reserve volume; RV, residual volume; IC, inspiratory capacity; FRC, functional residual capacity; VC, vital capacity; Δ, binding-induced change (i.e., mean difference ± SD between values in unbound and tight-bound). Note the decrease in RV and FRC, and the consequent increase in IC and VC in tight-bound vs. unbound for the SCI group. Also note the decrease in FRC and increase in IC in tight bound vs. unbound in the able-bodied group; the increase in IC, however, was at the expense of a decrease in ERV, such that VC remained unchanged [94].

Figure 4: Cough assist machines used to clear airway secretions and to help expand the chest to maintain compliance of the chest wall and prevent loss of lung volume (courtesy of Respironics, Murrysville, PA).

and negative 30-40 cm H_2O and are applied alternatively in sequence. Expiratory flows generated can reach 600 L/min [88]. In effect, this method is a form of suctioning out airway secretions without resorting to intubation or tracheostomy. The cough device can be applied through a face mask or (in those patents that require an airway) tracheostomy.

High frequency chest wall oscillation (HFCWO) has been shown to be effective in helping to clear secretions from the lungs of patients with cystic fibrosis, bronchiectasis, COPD, blunt chest trauma and some neuromuscular disorders. Individuals with SCI are at increased risk for development of pulmonary complications related to airway clearance and may benefit from this device. HFCWO uses a pressurized vest to transmit high frequency oscillations to the chest (Figure 5). This action mobilizes secretions which can be cleared by cough or by suction in the case of intubated patients. HFCWO treatment has been shown to be safe in patients with lung and chest wall injuries [95].

Respiratory muscle training

Various regimens of respiratory muscle training (RMT) are available to improve respiratory function in individuals with cervical SCI. Studies evaluating the outcomes on respiratory function and quality of life are of different designs accounting for variable outcomes. Most investigations have assessed the effects of RMT on maximal inspiratory and expiratory muscle strength (MIP and MEP, respectively); surprisingly, only a few have reported changes in the VC and none have reported on the effects on FEV_1. An extensive Cochrane meta-analysis by Berlowitz and Tamplin [96] provided details on 11 randomized studies with 212 individuals studied [19,97-105]. Different types of RMT were reviewed, including inspiratory muscle training, expiratory muscle training, combinations of both, isocapnic hyperpnea and therapeutic singing. Training was compared to control conditions, including no training, sham training, and alternate interventions. Eight of the 11 studies were conducted in seated position, 2 in seated and supine postures, and one in supine position only. Risk bias was assessed by a number of domains: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. Only 4 studies reported the method of randomization, and 4 studies described allocation concealment or blinding, or both. The meta-analysis of the 11 studies showed statistically significant effects of RMT for 3 outcomes: VC, MIP and MEP, with mean differences of 0.4 L, 10.5 cm H_2O and 10.3 cm H_2O, respectively. There was a high coefficient of variation for all 3 measurements in both able-bodied controls and even more so in the cervical SCI cohort with differing injury levels and severity [106], reducing the power of smaller studies to find statistically significant treatment effects.

A more recent study investigated the effects of RMT combined with abdominal drawing-in maneuver (integrated training group, ITG) on pulmonary function in 37 patients with SCI (level: C4-T6) over a 8-week

Figures 5: Examples of commercially available thoracic vests that provide vibratory action through the chest wall to help mobilize secretions. Panel C shows an intubated patient being fitted for HFCWO treatment. The vest type being fitted is the "wrap type" of vest. This allows for positioning of the vest so it does not interfere with chest tubes or lines (panels A-C courtesy of Hill-Rom, Chicago, Illinois, Vest® airway clearance systems; panel D courtesy of RespirTech inCourage Airway Clearance System, St. Paul, MN).

period [107]. By the end of the study, in the ITG, FVC had increased by more than 3 times as much as in the RMT alone group (0.47 L *vs.* 0.15 L), suggesting another technique for augmenting breathing in such patients.

Effects of body position and selective muscle stimulation to enhance respiratory function; phrenic nerve pacing

The association between body position and respiratory performance is a significant one, with implications for improved lung expansion, improved cough and reduction in dyspnea [108-110]. Supine posture produces the highest spirometric values [29,110]. Because individuals with SCI spend much of their time seated in a wheelchair, how variation of seated posture affects respiratory function is also important, particularly with respect to rehabilitation and patient comfort. To simulate standing position, a seating arrangement designed to simulate standing position by eliminating ischial support on the back part of the seat resulted in increases of 12% and 25% in the FVC and peak expiratory flow, respectively [111]. An increase in lumbar lordosis induces a decrease in thoracic kyphosis, enabling the thoracic cage to expand more during inspiratory efforts [30], in turn resulting in greater cough effort. In the seated position, abdominal contents displace the diaphragm cephalad, placing it at a mechanical disadvantage [112-114], quite the opposite of what is observed in able-bodied persons. Trendelenburg positioning, when used in conjunction with other components of multimodal chest physiotherapy (referred to as chest optimization), is associated with increases in duration of spontaneously breathing trial, alveolar ventilation, cardiac output, CO_2 elimination and respiratory compliance [115].

The reduction in FVC and associated dyspnea in sitting position can be reversed with an abdominal binder that forces the diaphragm cephalad, increases its resting length and appositional zone along the abdominal wall, thereby increasing its force generation. These actions result from expansion of the lower portion of the rib cage during inspiration is greater when a passive mechanical support is applied to the abdomen by the binder [116,117]. Because the binder opposes shortening of diaphragmatic fibers, it places them in a more advantageous position of their length-tension curve and thereby exerts a greater force on the lower ribs. A meta-analysis of 11 studies

concerning the effects of abdominal binding on lung function suggested that VC usually increases, especially in the seated posture, while functional residual capacity decreases (Figure 5) [118]. Chest vests can also be used for airway clearance for patients experiencing airway clearance dysfunction, secretion retention and/or ineffective cough due to immobility, deconditioning or muscle weakness.

Phrenic nerve and diaphragmatic pacing provide increased patient mobility, comfort and lower health care costs [119,120]. Breathing pacemakers have increased survival and improved quality of life in individuals with upper cervical cord and brain stem lesions [121-126]. Electrical stimulation of abdominal muscles by radio frequency generator has been shown to be effective in augmenting respiratory function. In a study of 10 upright individuals with injury level of C5-T7, Langbein et al. [125] showed that during electrical stimulation through surface electrodes, spirometric values increased by 11% to 15%. Subjects with the lowest FVC and FEV1 values exhibited the greatest improvement when electrical stimulation was applied during forced expiration. The authors suggested that subjects with spirometric values of >80% predicted were not likely to benefit from this procedure. DiMarco and colleagues [126] described the outcome in a 52-year-old man with C5-6 incomplete tetraplegia who had epidural electrodes implanted at the time of hemilaminectomies at the T9, T11 and L1 levels. During combined stimulation of T9 and L1 levels, the patient was able to generate airway pressure and PEFR to 132 cm H_2O and 7.4 L/s, respectively. His caregiver requirements for airway clearance were eliminated as he was able to trigger the device independently.

Weaning off mechanical ventilation

The success rate in weaning off tracheostomy-assisted mechanical ventilation (with the ultimate goal of decannulation) is approximately 40% in patients with cervical injuries above C4, and more so in injuries below C5 [127]. Respiratory assessment before and during weaning includes arterial blood gases to evaluate oxygenation and carbon dioxide elimination, VC and effectiveness of cough and ability to expel airway secretions [128]. Peak expiratory flows should exceed 160 L/m to assure expulsion of airway secretions and the negative inspiratory pressure should exceed -20 cm H2O (both variables measured with the tube cuff inflated) [88]. In a study of 26 ventilator-dependent tetraplegic patients, Chiodo et al. [129] found that failure to wean off the ventilator could be predicted by diaphragm needle electromyography (EMG) recorded during negative inspiration force generation. Fluoroscopic examination of the diaphragm and bedside spirometry were not as good predictors of weaning ability, failing to predict accurately in 44% and 19% of cases, respectively. Any outliers that may have been expected to wean based on ASIA examination (i.e. C4 or lower neurological levels) were also predicted not to wean by needle EMG.

Before the weaning trial, tracheal secretions should be cleared (either by gentle suctioning or use of cough assist devices), the patient should be positioned in the supine or Trendelenburg position, and bronchodilators delivered by nebulization [115]. Methods used in weaning have included spontaneous breathing or T-tube trials, pressure support and synchronized intermittent mandatory ventilation (SIMV) [71,130-133], of which the T-tube has shown the greatest success with weaning [131-132]. The majority of these weaning trials have been performed in able-bodied individuals. During spontaneous breathing trials the patient gradually spends more time breathing on his own as respiratory muscle function slowly improves. Patient should be able to breathe spontaneously for at least 48 hours before being discontinued from assisted ventilation. Other criteria that should be fulfilled before extubation are listed in the Table 1. Once these precautions are taken into consideration, patients with SCI make take weeks to months to successfully come off assisted ventilation [134,135].

Long-term respiratory management

For patients with compromised or limited respiratory function, deep breath generating methods have been advocated to prevent atelectasis and maintain normal chest wall and lung mechanics. Application of sighs with noninvasive ventilation and use of insufflation-exsufflation devices to "stretch" lung and thoracic cage volumes have been useful in this regard [83,86,88]. Cough assist devices, both manual and mechanical, are useful in promoting airway clearance in patients both with and without tracheostomies. Methods used to augment inspiratory effort, such as strengthening of chest wall muscles, RMT training, phrenic nerve stimulation have all been used with varying degrees of success in the prevention of respiratory complications, and have been summarized above.

Appropriate vaccinations should be provided for any individual with compromised respiratory function, particularly with regularly scheduled influenza and pneumococcal pneumonia vaccines. The latest recommended immunization schedule for adults aged 19 years or older, including those with potential immune compromise related to chronic respiratory disorders, have been approved by the Advisory Committee on Immunization Practices (ACIP), as well as several other professional organizations [136]. Changes in the 2018 adult immunization schedule from the previous year's schedule include the use of recombinant zoster vaccine (RZV) for individuals aged 50 years or older, and the use of an additional dose of measles, mumps, and rubella vaccine (MMR) in a mumps outbreak setting.

Conclusion

It is vital that patients have sufficient social and caregiver support to provide optimum respiratory care in the community. Management of the physically impaired patient can be a major challenge for family, leading to adverse physical and psychological consequences. Long-term management requires a multidisciplinary approach that includes respiratory, physical and occupational therapists, nutritionists, social workers, psychologists, and home health agencies, all of whom contribute to key aspects of maintaining optimum respiratory function. Life satisfaction is a major consideration in this group of individuals, but it may have a more positive outlook than one would think in someone with significant physical and psychological challenges. Bach and Tilton [137] found that the majority of ventilator-assisted persons with tetraplegia were significantly more satisfied with their housing, family life and employment than were spontaneously breathing tetraplegic individuals. Krause [138] found that, over a 15-year period, life satisfaction in SCI individuals improved starting at least 2 years after injury.

Ventilator-dependent individuals with more limited functional abilities than spontaneously breathing SCI seem to appreciate that their quality of life is closely tied to family lives and personal relationships; then use of a ventilator takes on a positive aspect in permitting maintenance of social ties.

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