Hillrom™

THE VEST® AIRWAY CLEARANCE SYSTEM

Clinical Dossier

To Support Medical Policy Review for Expanded Coverage of Neuromuscular Diseases

September 2019

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Executive Summary

CLINICAL BENEFITS

The safety and efficacy of High Frequency Chest Wall Oscillation (HFCWO) as an airway clearance modality has been demonstrated in numerous studies in patients with neuromuscular diseases including spinal muscular atrophy, amyotrophic lateral sclerosis (ALS), cerebral palsy (CP), multiple sclerosis (MS) and spinal cord injuries. A trend towards fewer hospitalizations, reduced incidence of pneumonia and reduced intravenous antibiotic use for respiratory infections have been shown.

A 2010 randomized controlled trial by *Yuan et al.* compared clinical outcomes, including duration of acute infections, adverse events, polysomnogram results, chest radiograph findings, and body mass index in a group of Neuromuscular Disease (NMD) and CP patients who were treated with standard chest physiotherapy and another group who received HFCWO over five months. There was a trend toward fewer hospitalizations for intravenous antibiotic therapy in the HFCWO group. That group also had higher maximum oxygen saturation. There were no therapy-related adverse events. Notably, a post-study caregiver survey disclosed significantly better adherence to the prescribed thrice-daily therapy in the HFCWO group, with caregivers citing difficulty with the time required and positioning involved to provide traditional chest physiotherapy.[16]

Landon et al. demonstrated that 15 NMD patients who were prescribed HFCWO for airway clearance, had significantly less hospitalization rates post initiation of HFCWO. The mean hospitalization rate was 0.37 days per therapy month during the year prior to HFCWO initiation. That rate decreased to 0.08 days per therapy month during the HFCWO intervention period (p value < 0.05), representing an 80% reduction in mean hospitalization rate. Therapy was well tolerated, with 90% of respondents considering the therapy comfortable.[17]

1.1 Spinal Muscular Atrophy

Multiple small case reports support the use of HFCWO in critically ill infants and children with Spinal Muscular Atrophy (SMA). In one 5-year-old with SMA II and Acute Respiratory Distress Syndrome (ARDS) following respiratory syncytial virus infection, HFCWO was used as the primary method of airway clearance and was well tolerated when previously, intrapulmonary percussive ventilation (IPV) combined with mechanical insufflation-exsufflation (MI-E) caused episodes of hypoxemia from presumed alveolar de-recruitment.[19]

Similarly, *Chiappeta et al.* conducted a six-week study evaluating substitution of HFCWO in place of chest physiotherapy (CPT) in a ten-year-old girl with Type II spinal muscular atrophy. The child had been hospitalized three times in past year for pneumonia, mucus retention, and pulmonary deterioration. She had received percussion and postural drainage therapy daily from her mother for four years. HFCWO

was instituted as her primary airway clearance modality for six weeks. After six weeks of HFCWO, the patient showed stronger cough function and significant improvements in FVC (25%), FEV_1 (16%), MEF (20%) and NIF (28%).[20]

1.2 Cerebral Palsy

Several small case reports support the use of HFCWO in critically ill infants and children with cerebral palsy during acute illnesses.

A retrospective outcomes review of 13 children with CP using HFCWO for at least six months prospectively compared with prior six months without the therapy showed significant aggregate reductions in hospitalizations and ER visits; pre-HFCWO documented eight hospitalizations and five ER visits vs. five hospital stays and one ER visit during HFCWO use. Caregivers also reported fewer respiratory illnesses, less antibiotic use and reduced absenteeism. High treatment adherence was also reported.[21]

1.3 Amyotrophic Lateral Sclerosis

Langford et al. demonstrated significantly improved quality of life and high rates of adherence to therapy on 47 ALS patients on HFCWO therapy.[22]

In a randomized controlled trial involving nine ALS patients, *Chaisson et al.* evaluated the effectiveness of HFCWO when added to standard of care in preventing pulmonary complication and prolonging time to death in patients concurrently receiving non-invasive ventilatory support. The addition of HFCWO coincided with a longer time to death.[23]

A retrospective chart review evaluating the effectiveness of HFCWO therapy in 18 patients with ALS demonstrated a reduction in rate of decline of FVC, MIP and PCEF. 92% of the patients reported easier breathing and feeling better after HFCWO therapy. 85% agreed that therapy eased secretion clearance and improved their quality of life.[24]

In a 12-week multi-center RCT, *Lange DJ et al.* demonstrated HFCWO patients had significantly less fatigue and breathlessness compared to the control group and 79% reported high rates of satisfaction with HFCWO treatment.[4]

1.4 Muscular Dystrophy

Respiratory disease is a leading cause of morbidity and mortality in patients with muscular dystrophy. Effective airway clearance is critical for patients with Duchenne muscular dystrophy as early intervention to improve airway clearance can prevent hospitalizations and reduce incidence of pneumonias.[2]

Crescimanno et al. documented a case study of two young boys with Duchenne muscular dystrophy hospitalized with pandemic A H1/N1 influenza who failed to respond to standard care. CT scans showed extensive pulmonary bilateral segmental atelectasis. Following institution of a sequential respiratory therapy protocol that included multiple sessions of HFCWO therapy augmented with mechanically assisted

cough maneuvers, both boys showed rapid clinical and radiological improvement and recovered fully. Treatments were well tolerated even by one boy with severe scoliosis.[18]

Gomez et al. demonstrated effective mobilization of distal airway secretions resulting in significant clinical improvement after initiation of HFCWO therapy in a 16 year old patients with Duchenne muscular dystrophy and profound kyphoscoliosis.[31]

ECONOMIC BENEFITS

Health economic studies evaluating HFCWO therapy have established total medical costs, hospitalizations, and pneumonia claims were less after initiation of HFCWO than before in a broad group of patients with NMD resulting in significant cost savings. The reductions in health-care utilization and claim costs were the result of a proactive airway clearance regimen utilizing HFCWO therapy. These findings lend support to the routine use of HFCWO therapy in the care of patients with NMDs.

In 2016, *Lechtzin et al.* compared health-care claims of 426 patients with NMD receiving The Vest® Airway Clearance System from two large commercial insurance claim databases before and after initiation of HFCWO. The majority of these patients were documented to have muscular dystrophy (150) and Quadriplegia (171).[25]

- Total medical costs per member per month decreased 18.6% after HFCWO use (p value .002)
- In-patient admission costs decreased by 41.7% (p value .001)
- Costs related to treatment of pneumonia decreased by 18.1% (p value .02)
- Average length of stay decreased from 11.6 days to 9.1 days

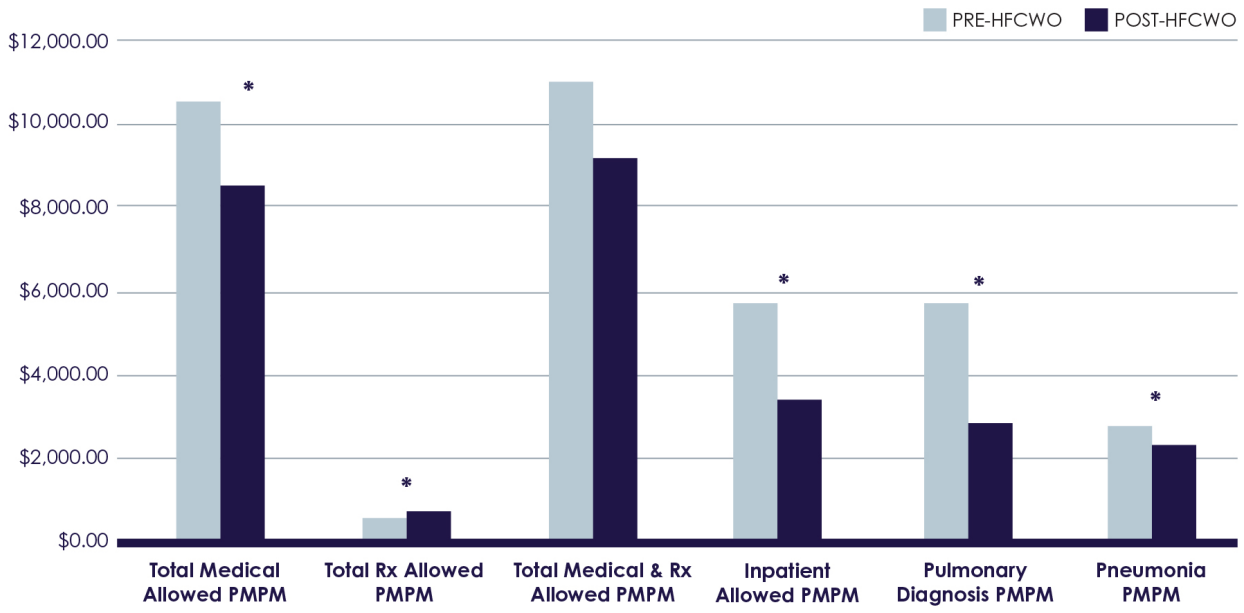

Figure 1: Healthcare costs before and after prescription of HFCWO. Costs are shown in U.S. dollars. *P,0.05. PMPM = per member per month; RX = prescription.

In a 2018 UK based NICE cost effectiveness analysis, assessed the cost-effectiveness of The Vest® Airway Clearance System compared to chest physical therapy for airway clearance in patients with NMD. A decision-analytic Markov model was developed to estimate the cost and effectiveness of each airway clearance strategy over 5- and 10-year time horizons. Costs were estimated from a UK NHS and personal social services perspective. The main input parameters in the model were the rates of incidence of respiratory infection, respiratory-related hospitalization and antibiotic use due to respiratory infections, and the cost of The Vest® System and NHS resource use for treatment of the respiratory infection.

The study demonstrates that over 5- and 10-year time horizons, usage of The Vest® System as a primary airway clearance modality results in fewer costs and more quality-adjusted life-years gained per patient. Results also indicate that this intervention has a high probability of being cost-effective (>98%) at willingness-to-pay thresholds £20,000 and £30,000.

Results indicate that The Vest® System is a cost-effective strategy, with significant cost savings being made primarily due to a reduction in the number of hospitalizations that treated patients experience and a reduced length of stay in hospital.[26]

Figure 2: Base-case probabilistic results over a 5-years' time horizon

Strategy	Average Cost Per Patient (£)	Incremental Cost (£)	Average QALYs Per Patient (£)	Incremental QALYs	ICER (£) (ΔCost/ ΔQALYs)	Probability Cost-Effective for Different WPT Thresholds (%)	
						£20,000	30,000
Base-case analysis – Informing the clinical effectiveness input parameters using results from the UK based study- 5 years' Time horizon							
MCWP	20,211	-	1.65	-	-	-	-
The Vest® System	14,176	-6,035	1.72	+0.07	Dominant	98%	99%
Base-case analysis – Informing the clinical effectiveness input parameters using results from the UK based study- 10 years' Time horizon							
MCWP	£34,632	-	3.03	-	-	-	-
The Vest® System	£24,108	-10,524	3.23	0.19	Dominant	98%	100%
Sensitivity analysis- Informing the clinical effectiveness input parameters using results from study by Yuan et al. 2010- 5 years' Time horizon							
MCWP	£14,835	-	1.77	-	-	-	-
The Vest® System	££9,108	-£5,727	1.90	0.14	Dominant	100%	100%
Sensitivity analysis- Informing the clinical effectiveness input parameters using results from study by Lechtzin et al. 2016- 5 years' Time horizon							
MCWP	£20,211	-	1.65	-	-	-	-
The Vest® System	£17,618	-£2,593	1.69	0.03	Dominant	100%	100%

MCWP: Manual Chest Wall Physiotherapy; QALY: Quality Adjusted Life Years

Figure 3: Total health resource use saved over 5 years' time horizon

Health Resource Use	Pre-Vest® System	Post-Vest® System	Difference
Intervention cost per 1,000 patients	£230,580	£7,820,998	£7,590,418
Total cost of hospital admissions per 1,000 patients	£19,487,088	£6,016,681	-£13,470,407
Total cost of outpatient treatment per 1,000 patients	£493,269	£338,594	-£154,675
Total cost per 1,000 patients	£20,210,937	£14,176,272	-£6,034,665

Health Resource Use	Pre-Vest® System	Post-Vest® System	Difference
Intervention cost per 1,000 patients	5,071	2,630	-2,442
Total cost of hospital admissions per 1,000 patients	59,729	9,861	-49,868
Total cost of outpatient treatment per 1,000 patients	5.07	2.63	-2.4
Total cost per 1,000 patients	59.73	9.86	-49.9

In a retrospective chart review of 44 patients with NMD including muscular dystrophy, SMA and CP, *Rayabhari et al.* demonstrated a reduction in healthcare resource utilization with a change in average days of hospitalization from 10.5 days pre-HFCWO compared to 4.1 days post-HFCWO (p value 0.01). Another retrospective outcomes review demonstrated statistically significant aggregate reductions in hospitalization, ER visits and antibiotic use six months post- initiation of HFCWO therapy in pediatric CP patients.[27]

Smaller studies in children with a variety of neuromuscular or neurological diseases have compared healthcare utilization before and after HFCWO use.[28-39] Seven subjects with quadriplegic CP demonstrated a significant reduction in episodes of pneumonia and more effective airway suctioning, defined as suctioning attempts in which sputum was recovered, in the 12 months after use of HFCWO compared with the 12 months before. Seizure events fell from 267 to 43 after initiation of HFCWO therapy.[29] Furthermore, none of the subjects experienced adverse events resulting from HFCWO use.

Similarly, 15 children and young adults with familial dysautonomia in a retrospective/ prospective study comparing 12 months of CPT pre-initiation of HFCWO at initiation and exit, pulmonary function tests (PFT), chest radiographs and blood tests were performed. Daily logs provided information on parameters including respiratory illnesses, doctor visits and hospitalizations. At the end of 12 months, data comparison showed clinically and statistically significant improvements with HFCWO in all measured health outcomes including: pneumonias, hospitalizations, antibiotic courses, antibiotic days, doctor visits and FVC and PEFR demonstrated sustained improvement and days of school absence.[30]

Another 2014 prospective study involving 22 neurologically impaired children also demonstrated a significant reduction in hospitalization rates from 45% before HFCWO use to 36% and 13% in the first and second years after its use.[28]

CONCLUSION

There is a typical progression of respiratory complications in patients with NMDs that begins with respiratory and bulbar muscle weakness and proceeds to sleep-disordered breathing with the eventual development of nocturnal and then diurnal hypercapnia, recurrent respiratory infection and hospitalizations. These predictable problems form the framework for determining which assessments and interventions are necessary. Early interventions in this patient population aimed at overcoming impaired airway clearance utilizing HFCWO has been demonstrably safe, clinically effective and result in significant costs savings, disease specific and all cause related health care resource utilization.

As of January 1, 2019, all jurisdictions of the Centers for Medicare and Medicaid Services (CMS) revised the Local Coverage Determination (LCD ID L33785) for HFCWO to include the following neuromuscular diagnoses:

ICD-10 CODE	DESCRIPTION
B91	Sequelae of poliomyelitis
D81.810	Biotinidase deficiency
G12.0	Infantile spinal muscular atrophy, type I [Werdnig-Hoffman]
G12.1	Other inherited spinal muscular atrophy
G12.20	Motor neuron disease, unspecified
G12.21	Amyotrophic lateral sclerosis
G12.22	Progressive bulbar palsy
G12.23	Primary lateral sclerosis
G12.24	Familial motor neuron disease
G12.25	Progressive spinal muscle atrophy
G12.29	Other motor neuron disease
G12.8	Other spinal muscular atrophies and related syndromes
G12.9	Spinal muscular atrophy, unspecified
G14	Postpolio syndrome
G35	Multiple sclerosis
G71.00	Muscular dystrophy, unspecified
G71.01	Duchenne or Becker muscular dystrophy
G71.02	Facioscapulohumeral muscular dystrophy
G71.09	Other specified muscular dystrophies
G71.11	Myotonic muscular dystrophy
G71.12	Myotonia congenita
G71.13	Myotonic chondrodystrophy
G71.14	Drug induced myotonia
G71.19	Other specified myotonic disorders
G71.2	Congenital myopathies
G71.3	Mitochondrial myopathy, not elsewhere classified
G71.8	Other primary disorders of muscles

G72.0	Drug-induced myopathy
G72.1	Alcoholic myopathy
G72.2	Myopathy due to other toxic agents
G72.89	Other specified myopathies
G73.7	Myopathy in diseases classified elsewhere
G82.50	Quadriplegia, unspecified
G82.51	Quadriplegia, C1-C4 complete
G82.52	Quadriplegia, C1-C4 incomplete
G82.53	Quadriplegia, C5-C7 complete
G82.54	Quadriplegia, C5-C7 incomplete
J98.6	Disorders of diaphragm
M33.02	Juvenile dermatomyositis with myopathy
M33.12	Other dermatomyositis with myopathy
M33.22	Polymyositis with myopathy
M33.92	Dermatopolymyositis, unspecified with myopathy
M34.82	Systemic sclerosis with myopathy
M35.03	Sicca syndrome with myopathy

The Vest® Airway Clearance System is established as a safe, effective and efficient airway clearance modality. It is a more consistent therapy compared to CPT and may be the ideal choice of treatment for patients whose respiratory function is compromised by NMD and who are unable to tolerate other modalities of airway clearance.

PRODUCT DESCRIPTION

2.1 The Vest® Airway Clearance System[32]

HFCWO technology is based on the principle that rapid compression and relaxation (oscillation) of the chest wall generates increased airflow velocities, thus creating brief changes in lung airflow patterns similar to coughing. The percussive effects of chest wall oscillation also loosens sticky secretions, making them easier to clear. No special positioning or breathing techniques are required, making it ideal for the NMD patient population.

The Vest® System administers HFCWO therapy by means of an inflatable vest attached by hoses to an air pulse generator. The Vest® System inflates and deflates rapidly, gently compressing and releasing the chest wall 5-20 times per second. The oscillations can be adjusted to different frequencies and pressures. During therapy with The Vest® System, oscillating compressive forces are distributed evenly over the thorax surrounding the area of the lungs. This extensive contact area results in a large total oscillatory force applied to the thorax. The Vest® System HFCWO therapy does not require specific positioning for postural drainage; it is not technique dependent; and often can be administered without a caregiver or with minimal caregiver supervision. HFCWO therapy has been shown to be effective, safe and cost effective.

All lobes of the lungs are treated at the same time and the patient can sit in any position throughout the entire treatment. The Vest® System treatment is typically 10-30 minutes, depending on physician's order.

The Vest® System was developed in the 1980s and is:

- Prescribed as a peripheral airway clearance therapy.
- Used in conformity to clinical practice guidelines for Postural Drainage established by the American Association for Respiratory Care.
- The Vest® System is 510(K) cleared to promote airway clearance or improve bronchial drainage in situations where physicians recommend external manipulation of the thorax.

2.2 The Monarch® Airway Clearance System[33]

The Monarch® Airway Clearance System is a high frequency chest wall oscillation therapeutic device with revolutionary new technology combining mobility with targeted kinetic energy and air flow to thin and mobilize secretions from the airways. By allowing patients to move about freely during therapy it enables them to take control of their therapy.

The Monarch® System is used to aid mobilization of secretions from the airway to help improve airway clearance. This is achieved by the placement of eight pulmonary oscillating disks (PODs) containing magnets over the upper and lower lobes of the lungs. The PODs provide a targeted kinetic energy to the lungs. This therapy generates

airflow to help thin and mobilize mucus from the small airways to the large airways where it can be coughed out or suctioned.

Expiratory airflow bias is important and kinetic energy transferred through the chest wall to the lungs is believed to help loosen secretions adhering to lung tissue. This creates kinetic energy designed to increase airflow to help mobilize secretions from the airways.

The Monarch® System is intended to provide airway clearance therapy and promote bronchial drainage where external manipulation of the thorax is the physician's choice of treatment. It is indicated for patients having difficulty with secretion clearance or the presence of atelectasis caused by mucus plugging. It is intended to be used in the home care environment by patients 15 years and older.

The Monarch® System PODs create a magnetic field which is present whether the device is turned on or off. Due to the presence of this magnetic field, people who have an active implantable medical device, such as any of the following, are contraindicated:

- Pacemakers
- Neuro stimulators
- Infusion pumps including insulin pumps
- Circulatory support devices
- Implantable cardioverter defibrillators
- Head and or neck injury that has not yet been stabilized
- Active hemorrhage with hemodynamic instability

The Monarch® System warnings state patients who may have difficulty clearing secretions from the upper airway, such as those with DMD or other advanced neuromuscular or neurological disorders, may require specialized therapy regimens involving manually or mechanically assisted coughing or other in conjunction with The Monarch® System.

DISEASE DESCRIPTION

3.1 Introduction

Patients diagnosed with NMD often share a common problem – impaired airway clearance resulting from any, or a combination of, the following pulmonary risk factors:

- Recurrent respiratory infections
- Mucus plugging and atelectasis
- Secretion hyperproduction
- Abnormally thick, sticky secretions
- Ineffective cough
- Respiratory muscle weakness
- Increased risk of aspiration
- Immobility
- Restrictive lung disease
- Artificial airway

NMDs are characterized by progressive weakness of skeletal muscle, skeletal and spinal deformities, spinal contractures and restrictive lung disease leading to poor respiratory function.[1] These include illnesses such as muscular dystrophies[2,3] and amyotrophic lateral sclerosis.[4] They may be hereditary or acquired, and differ markedly in prevalence, age of onset and involvement of affected muscles, and rate of progression.[5-7] Among patients with severe NMD, respiratory failure ranks as the primary cause of death. Recurrent pulmonary infection is the leading cause of morbidity among NMD patients, and places them at high risk for progressive lung damage and ultimately, respiratory failure.[6-8]

3.2 Airway clearance and lung defense mechanism

In healthy individuals, mucociliary clearance and cough mechanisms are effective and efficient in defending against infections. Mucus is transported under normal circumstances from the lower respiratory tract into the pharynx by cephalad bias airflow and the mucociliary escalator mechanism. These mechanisms may become ineffective if the mucociliary system malfunctions and/or in the presence of excessive bronchial secretions, as occurs in patients with NMDs.[5]

An effective cough is essential to clear airway secretions from the more proximal airways. For an effective cough, one needs firstly to take a sufficiently deep breath and the glottis needs to close briefly to allow an increase in intrathoracic pressure. Explosive glottic opening together with abdominal contraction which results in air being forcibly expelled the cough expiatory air flow can be measured and is known as peak call flow (PCF).[9-10]

3.3 Respiratory complications in NMD

Individuals with NMD have weak or impaired strength of expiratory muscles, with or without glottic closure issues, resulting in decreased PCF. This constellation of pathological changes results in difficulty clearing the airways, necessitating institution of artificial airway clearance techniques.[11]

Weakness of the inspiratory muscles leads to a progressive decrease in vital capacity and PCF. The long volume changes that appear in some patients with NMD are

attributable to a combination of muscle weakness and alterations of the mechanical properties of the lungs and chest wall. Reduced ability to cough leads to secretion retention, predisposing to progressive respiratory morbidity. [11]

Severe bulbar dysfunction and glottic dysfunction most commonly occurs in patients with ALS, SMA type 1 and other neuromuscular disorders such as X-linked myotubular myopathy and pseudobulbar palsy of central nervous system origin.[12] Inability to close the glottis and vocal cords results in complete loss of the ability to cough and swallow. Difficulty swallowing liquids may result in pooling of saliva and mucus in the pharynx especially in the vallecula and pyriform sinus. These predispose to recurrent respiratory infections. [12]

Alterations in alveolar ventilation, atelectasis, mucus plugging, and recurrent respiratory tract infections are also a consequence of an ineffective cough in NMD patients. Recurrent respiratory tract infections lead to further respiratory muscle weakness, with the resulting vicious cycle of respiratory disease.[11]

3.4 Clinical and economic implications of respiratory complications and airway clearance therapy in NMD patients

Hypoventilation and managing secretions are among the most important problems from patients' perspective and presents respiratory physiotherapist with unique management challenges in the care of patients with NMDs. Despite the clear implications, the problem of managing secretions in the care of patients with NMD has received little attention.[13]

Patients with NMDs are living longer and consequently we are seeing more complex ventilator dependent and independent patients. Respiratory physiotherapy is an essential part of the multidisciplinary management of these individuals but owing to the heterogeneity of the condition and the growing number of available airway clearance techniques and associated technological developments, it is challenging for physiotherapist to understand what assessments are required and what treatment options are available and appropriate for patients with NMD.[13-15]

As in other chronic disorders, the home organization of patients with chronic respiratory disorders is challenging and time consuming. The cost and availability of respiratory experts in primary care, the geographic location of patients, lack of engagement practitioners and care coordination may lead to poor quality of care.

STUDY SUMMARIES

I. **Castagnino M., Vojtova J., Kaminski S., Fink R. Safety of High Frequency Chest Wall Oscillation in patients with respiratory muscle weakness. Chest 1996; 110: S65.**
In this controlled short-term evaluation of safety, efficacy and acceptance of HFCWO eight patients with respiratory muscle weakness (vital capacities of 30 ml/kg or less; age > 10 years, able to perform PFTs) received a single therapy session in a sitting position at frequencies of 5, 15, and 20 Hz for five minutes each. Measures of patient comfort, pulmonary function and other physiological parameters including but not limited to vital capacity, peak expiratory flow, arterial oxygen saturation and heart rate were collected and evaluated as mean percent change from baseline. No clinically relevant changes occurred in physiological values; all patients found HFCWO acceptable without complaint of pain or discomfort. No adverse events were noted.

II. **Chiappetta A. Beckerman R. High Frequency Chest Wall Oscillation in spinal muscular atrophy (SMA). RT J Respir Care Pract 1995; 8(4): 112-114.**
This Case Report presents results of a six-week trial replacing percussion and postural drainage (PD&D) with HFCWO treatments in a ten-year-old girl with spinal muscular atrophy, type II (SMA II). Before the study, she had been treated for four years with twice daily P&PD administered by her mother. Her condition had worsened significantly in the previous year requiring three hospitalizations for pneumonia, mucus retention, and pulmonary deterioration. Protocol for her six-week trial of HFCWO included two, 30-minute daily treatments for five minutes at each of six frequencies. Each five-minute session was followed by one or two cough maneuvers. After six weeks of HFCWO, clinically significant improvements included stronger cough function and gains in pulmonary function. FVC, FEV1, MEF and NIF improved 25%, 16%, 20%, and 28% respectively.

III. **Chaisson K.M., Walsh S., Simmons Z., Vender R.L. A clinical pilot study: High frequency chest wall oscillation airway clearance in patients with amyotrophic lateral sclerosis. ALS 2006; 7 (2): 107-111.**
This single center study performed at the Penn State Milton S. Hershey Medical Center (HMC) evaluates the effectiveness of high frequency chest compression (HFCWC) when added to standard care in preventing pulmonary complications and prolonging the time to death in patients with ALS. Nine patients with a diagnosis of ALS and concurrently receiving non-invasive ventilatory support with bi-level positive airway pressure (BiPAP) were randomized to receive standard care (four patients) or standard care plus the addition of HFCWO (five patients) twice-daily for 15 minutes. Longitudinal assessments of oxyhemoglobin saturation, forced vital capacity (FVC), and adverse events were obtained until time of death. Pulmonary complications of atelectasis, pneumonia, hospitalization for a respiratory-related abnormality, and tracheostomy with mechanical ventilation were monitored throughout the study duration. The addition of HFCWO coincided with longer time to death numerically but short of statistical significance compared to standard treatment alone (340 days +/- 247 vs. 470

days +/- 241; p value 0.26); effects on pulmonary function were also non-significant. Investigators comment that this study does not exclude the potential benefit of HFCWO in select patients with ALS who have co-existent pulmonary diseases, pre-existent mucus-related pulmonary complications, or less severe levels of respiratory muscle weakness.

IV. **Crescimanno G., Marrone O. High-frequency chest wall oscillation plus mechanical in-exsufflation in Duchenne muscular dystrophy with respiratory complications related to pandemic influenza /H1N1. Rev Port Pneumonol 2010; 16 (6): 912-916.**
Two young boys with Duchenne muscular dystrophy (DMD) and hospitalized with pandemic A H1/N1 influenza failed to respond to standard care. CT scans showed extensive pulmonary bilateral segmental atelectasis. Following institution of a sequential respiratory therapy protocol that included multiple sessions of HFCWO therapy augmented with mechanically assisted cough maneuvers, both boys showed rapid clinical and radiological improvement and recovered fully. Treatments were well tolerated even by one boy with severe scoliosis.

V. **Fitzgerald, K., et al. (2014). "High-frequency chest wall compression therapy in neurologically impaired children." Respir Care 59(1): 107-112.**
In this single center, investigator-initiated prospective study to assess the clinical feasibility of high frequency chest wall compression (HFCWC) therapy in neurologically impaired children with respiratory symptoms 22 subjects were studied for 12 months before and 12 months after initiation of HFCWC therapy. Fifteen subjects were followed for an additional 12 months. The threshold of adherence to HFCWC therapy was 70%. The number of pulmonary exacerbations requiring hospitalization were recorded. Data analysis showed that 45% percent of the subjects required hospital admission before initiation of HFCWC therapy. This rate decreased to 36% after the first year with HFCWC, and to 13% after the second year with HFCWC. Relative to pre-treatment, there was a statistically significant reduction of the number of hospital days and costs of care at follow-up. Outcomes suggest that regular HFCWC therapy may reduce the number of hospitalizations in neurologically impaired children.

VI. **Giarraffa P., Berger K.I., Chaikin A.A., et al. Assessing efficacy of high-frequency chest wall oscillation (HFCWO) in patients with familial dysautonomia. Chest 2006; 128:3377-3381.**
In this one-year clinical trial to evaluate the benefits of high frequency chest wall oscillation (HFCWO) therapy, 15 patients (seven female and eight male; age range, 11 to 33 years) with familial dysautonomia (FD) and a history of lung disease requiring daily inhalation therapy were enrolled in a one-year, self-controlled clinical trial of HFCWO. Two subjects withdrew, one after three months and one after six months. Medical charts were reviewed for 12 retrospective months during which patients had received chest physiotherapy (CPT and compared with data obtained during 12 months of HFCWO therapy. At initiation and exit, pulmonary function tests (PFT), chest radiographs and blood tests were performed. Daily logs provided information on parameters including respiratory illnesses, doctor visits, hospitalizations, etc. and reviewed at one-, three-, six-,

nine- and 12-month intervals. Spirometry and pulse oximetry values were obtained on the same schedule. At the end of 12 months, data comparison showed clinically and/or statistically significant improvements with HFCWO in all measured health outcomes including: pneumonias (p value 0.056); hospitalizations (p value 0.0156); antibiotic courses (p value 0.0005); antibiotic days (p value 0.0002); doctor visits (p value 0.0005) and; absenteeism (p value 0.0002). FVC and PEFR were the pulmonary function measures demonstrating sustained improvement.

VII. **Gomez A., Elisan I., Hardy K. High frequency chest wall oscillation: video documentation of effect on a patient with Duchenne muscular dystrophy and severe scoliosis. Poster presentation at the 46th International Respiratory Congress of the American Association for Respiratory Care, October 7, 2000, Cincinnati, Ohio, USA.**
A 16-year-old Duchenne muscular dystrophy patient with severe kyphoscoliosis and deteriorating respiratory health had persistent atelectasis and mucus plugging unresponsive to both manual chest physiotherapy (CPT) and therapeutic bronchoscopy. A subsequent bronchoscopy performed while the patient simultaneously received HFCWO therapy successfully cleared large volumes of secretions. A follow-up videotaped bronchoscopy with HFCWO showed healing bronchial mucosa, minimal secretions and significant mobilization for mucus from peripheral lung regions.

VIII. **Jackson C.E., Moore D., Kittrell P., Ensrud E. High-frequency chest wall oscillation in amyotrophic lateral sclerosis. J Neuromusc Dis 2006; 8 (2): 60-64.**
In this three-month retrospective chart review to evaluate the effectiveness of HFCWO therapy in 18 patients with ALS, pre-treatment and post-treatment data including ALS Functional Rating Scale-Revised (ALSFRS-R), forced vital capacity (FVC), maximal inspiratory pressure (MIP), peak cough expiratory flow (PCEF), and daytime oximetry were compared. Daytime oximetry increased for eight of 18 patients; none of the other measures changed significantly although the change in slope of FVC, MIP, and PCEF following initiation of treatment suggested a reduction in the rate of decline of each measure. Patient survey results reported that 92% felt better after HFCWO therapy and breathing was easier; 85% agreed that HFCWO eased secretion clearance and improved their quality of life. Early intervention with effective airway clearance therapy (ACT) may improve quality of life for patients with ALS.

IX. **Keating J.M., Collins N., Bush A., et al. High-frequency chest-wall oscillation in a noninvasive-ventilation-dependent patient with type 1 spinal muscular atrophy. Respir Care 2011; 56(11): 1840-1843.**
This is the first case report of the use of HFCWO for secretion clearance in a severely weak young child with type 1 SMA who was dependent on noninvasive ventilation, and in whom conventional secretion-clearance physiotherapy alone was no longer effective. HFCWO was added to her respiratory treatment regimen as a rescue therapy. Shortly after initiation of treatment, her self-ventilation time improved significantly. This experience suggests that HFCWO can be used safely in combination

with conventional secretion-clearance techniques in patients with severe respiratory infection and compromise secondary to NMD.

X. **Landon C., Goldie W. and Evans J.R. Airway clearance therapy utilizing high frequency chest wall oscillation (HFCWO) for medically fragile children [Abstract/Poster]. J Am Med Dir Assoc 2002; 3(2):A17.**
In this conference presentation of outcomes of 15 medically fragile children with various neuromotor/neuromuscular/neurological diagnoses and who were prescribed HFCWO for airway clearance, medical records were retrospectively reviewed to assess hospitalization events for pulmonary complications after initiation of HFCWO compared with the previous year during which patients received standard CPT. The mean hospitalization rate was 0.37 days per therapy month during the year prior to HFCWO initiation. That rate decreased to 0.08 days per therapy month during the HFCWO intervention period (p value < 0.05). Therapy was well tolerated and 90% of respondents considered the therapy comfortable.

XI. **Lange D.J., Lechtzin N., Davey C., David D., Heiman-Patterson T., Gelinas D., Becker B., Mitsumoto H. and the HFCEO Study Group. High-frequency chest wall oscillation in ALS: An exploratory randomized controlled trial. Neurology 2006; 67:991-997.**
This 12-week, multicenter randomized controlled trial (RCT) evaluated changes in pulmonary function (PFT) parameters in ALS patients after treatment with HFCWO. Forty-six patients were enrolled (58.0 +/- 9.8 years; 21 men, 25 women) and 35 completed the study. Baseline PFTs were similar. After 12 weeks, data were analyzed for patients who completed the study; (19 randomized to HFCWO and 16 control (untreated) participants). Results showed that HFCWO users had less fatigue and breathlessness (p value 0.021) and coughed more at night (p value 0.048) compared to baseline. HFCWO users reported a decline in breathlessness (p value 0.048); nonusers reported more noise when breathing (p value 0.027). There were no significant intra-group differences in FVC change, peak expiratory flow, capnography, oxygen saturation values or transitional dyspnea index. Analysis of data for patients with FVC between 40 and 70% predicted showed a significant mean FVC decrease in untreated control patients but not in HFCWO patients. Seventy-nine percent of HFCWO users rated the treatment as satisfactory.

XII. **Langford V., Brooks B.R., Ward A., et al. High frequency chest wall oscillation therapy adherence on quality of life in patients with ALS/MND [Abstract]. The 21st International Symposium on ALS/MND, Orlando, FL, December 11-13, 2010; [CW240]**
In this survey study to evaluate quality-of-life (QOL) and adherence outcomes following one year of in-home HFCWO therapy, 47 ALS clinic patients agreed to participate. At regular intervals, patients/caregivers were asked to respond to items on a QOL questionnaire and to report average daily usage. Results showed high rates of adherence (18.8 minutes per day). Participants also reported better

QOL, rating a mean of 4.2 on all indicators out of a possible 5 points. National average scores on the QOL instrument used is 3.8.

XIII. **Overgaard P.M., Radford P.J. High frequency chest wall oscillation improves outcomes in children with cerebral palsy. Chest 2005; 128 (4): 354S.**
A retrospective quality assurance review of 13 children with CP using HFCWO for airway clearance therapy for at least six months (seven for 6+ months; six for 1+ years) showed significant aggregate reductions in hospitalizations and emergency room (ER) visits. Chart review for the year prior to HFCWO use compared prospectively with six or more months of HFCWO therapy documented eight hospitalizations and five ER visits vs. five hospitalizations and one ER visit. Parents reported fewer respiratory illnesses, less antibiotic use, and reduced absenteeism. Treatment adherence (measured by hourly use meter) and parental satisfaction were high.

XIV. **Plioplys A.V., Lewis S., Kasnicka I. Pulmonary vest therapy in pediatric long-term care. J Am Med Dir Assoc 2002; 3:318-321.**
In this retrospective/prospective study to evaluate the use of HFCWC in institutionalized quadriplegic CP patients with lung disease, seven subjects (age range 7-28, median age 19) received HFCWO for 12 months. All subjects had histories of frequent pulmonary infections, were fed by G-tube and were treated retrospectively with CPT; five had tracheostomies, three had active seizure disorder. Prospective data was collected and compared with 12-month retrospective data from nursing records maintained daily according to facility protocol. Improvements were shown in all outcome measures after 12 months of HFCWO: 1) fewer pneumonias (p value 0.025); 2) fewer hospitalizations (p value 0.16) and; 3) increased effective suctioning interventions (p value 0.008). Unexpectedly, seizures fell from 267 events retrospectively to only 43 during the HFCWO year (p value 0.125). HFCWO was well tolerated; no complications or side effects were noted.

XV. **Yuan N., Kane P., Shelton K., Matel J., Becker B., Moss R.B. Safety, tolerability, and efficacy of high-frequency chest wall oscillation in pediatric patients with cerebral palsy and neuromuscular diseases: An exploratory randomized controlled trial. J Child Neurol 2010 (25 (7): 815-821. 2010; 25(7):815-821.**
This is a prospective randomized controlled trial (RCT) comparing HFCWO to standard CPT in participants with CP or NMD. Among 28 participants enrolled, 23 completed the study (11 randomized to HFCWO; 12 to CPT). The mean study period five was months; no adverse events were reported. Outcome measures included respiratory-related hospitalizations, antibiotic therapy, chest radiographs, and polysomnography. Analysis of data, including caregiver adherence reports, showed a trend toward fewer hospitalizations requiring IV antibiotics in the HFCWO group compared to the CPT group (p value 0.09). Tolerability and adherence to HFCWO was significantly higher than with standard CPT (p value 0.036). Results suggest that improvements in airway clearance in this patient population may reduce the frequency of hospitalization.

List of Review Articles

An expanding volume of clinical and research literature is advancing awareness of secretion-related respiratory complications in patients with NMDs. Increasingly, as this problem is described in the review literature, newer interventional strategies are being discussed and explored. Several relevant articles and commentaries are cited below:

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