Background and Purpose. This investigation identified ventilation distribution, gas mixing, lung function, and arterial blood oxyhemoglobin saturation ($SpO_2$) physiologic responses to 2 independent airway clearance treatments, high-frequency chest wall oscillation (HFCWO) and low positive expiratory pressure (PEP) breathing, for subjects who had cystic fibrosis (CF) and who were hospitalized during acute and subacute phases of a pulmonary exacerbation. Subjects. Fifteen subjects with moderate to severe CF were included in this study. Methods. Subjects performed single-breath inert gas tests and spirometry before and immediately after HFCWO and PEP breathing at admission and discharge. Arterial blood oxyhemoglobin saturation was monitored throughout each treatment. Results. At admission and discharge, PEP breathing increased $SpO_2$ during treatment, whereas HFCWO decreased $SpO_2$ during treatment. Ventilation distribution, gas mixing, and lung function improved after HFCWO or PEP breathing. Discussion and Conclusion. High-frequency chest wall oscillation and PEP breathing are similarly efficacious in improving ventilation distribution, gas mixing, and pulmonary function in hospitalized people with CF. Because $SpO_2$ decreases during HFCWO, people who have moderate to severe CF and who use HFCWO should have $SpO_2$ monitored during an acute exacerbation. [Darbee JC, Kanga JF, Ohtake PJ. Physiologic evidence for high-frequency chest wall oscillation and positive expiratory pressure breathing in hospitalized subjects with cystic fibrosis. Phys Ther. 2005;85:1278–1289.]

Key Words: Airway clearance, Chest physical therapy, Cystic fibrosis, Gas mixing, Ventilation distribution

Joan C Darbee, Jamshed F Kanga, Patricia J Ohtake
In people with cystic fibrosis (CF), the most common lethal inherited disease affecting people of Caucasian ethnicity, the effective loosening and removal of airway mucus are crucial to enhanced life expectancy and decreased morbidity.1 Infected airway secretions contain proteases that destroy lung tissue.2 Peripheral airways, which are less than 2 mm in diameter, lose their stability secondary to lung tissue destruction and tend to collapse, trapping air and mucus.3 The collapse of smaller peripheral airways creates areas of nonhomogeneous ventilation distribution.4 As lung function continues to deteriorate, abnormalities in ventilation distribution worsen, leading to ventilation-perfusion mismatching, hypoxemia, and pulmonary hypertension5 and eventually respiratory failure and death.1,2,5 Respiratory failure accounts for greater than 80% of CF-related deaths in the United States.6 Understandably, airway clearance techniques (ACTs) are critical components of the daily regimen of care performed by people with CF.

Putative goals of ACTs are to decrease airway obstruction and airflow limitation and to improve ventilation distribution through the mobilization and removal of airway mucus.7 Two independent ACTs, high-frequency chest wall oscillation (HFCWO) and positive expiratory pressure (PEP) breathing, have been shown to be effective at loosening and removing airway mucus in hospitalized people with CF.8–10 Mucus weight was greater after HFCWO than after traditional airway clearance interventions involving postural drainage and manual percussion and vibration techniques (CPTs) when 29 subjects received each intervention 3 times a day on alternating days for 4 days.10 In contrast, mucus weights with HFCWO8,9 and PEP breathing9 were similar to sputum weights with CPTs during8,9 and up to 24 hours after8 treatment. Thus, both HFCWO and PEP breathing are effective at removing airway mucus; however, information on the concomitant effects of these 2 ACTs on ventilation distribution is scant.

To date, there have been few reports examining the effects of ACTs on ventilation distribution or gas mixing, even though it has been assumed that ACTs promote improvements in ventilation distribution.7,11 Arens et al8 assessed the phase III alveolar slope during the single-breath nitrogen (N2) washout test to discover that overall ventilation distribution improved equally for HFCWO and CPT treatment groups. Recently, Darbee and colleagues12 showed that a single PEP breathing treatment improved gas mixing, a measure of the extent to which an inspired volume of gas mixes with gas already present in the lungs, without improving ventilation distribution.

Because of the limited information regarding the effects of HFCWO and PEP breathing on ventilation distribution, it is unclear whether one of these techniques is more efficacious than the other. We decided to compare the physiologic effects of HFCWO and PEP breathing on ventilation distribution and gas mixing for people with CF by using a single-breath inert gas technique. The single-breath inert gas technique has the capacity to provide information about ventilation distribution and gas mixing. We wanted to determine the efficacy of each airway clearance intervention and to determine whether the physiologic effects of each intervention would differ in subjects during an acute phase of pulmonary disease exacerbation (within 48 hours of hospital admission) versus a subacute phase of exacerbation (within 48 hours of hospital discharge). For this study, we investigated a

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Dr Darbee provided concept/idea/research design, data collection, project management, fund procurement, and facilities/equipment. Dr Darbee and Dr Ohtake provided writing and data analysis. Dr Kanga provided subjects. Dr Darbee and Dr Kanga provided institutional liaisons. The authors thank Hill-Rom, of St Paul, Minn, for supplying The Vest airway clearance system for this study.

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A group of subjects who had moderate to severe obstructive disease and who were undergoing treatment for an acute exacerbation of their CF-related lung infections. Therefore, the purpose of this investigation was to examine the physiologic effects of HFCWO and PEP breathing on ventilation distribution, gas mixing, lung volume, expiratory airflow, and arterial blood oxyhemoglobin saturation (SpO₂) for subjects with CF at hospital admission and discharge.

**Method**

**Subjects**

From a pool of 196 subjects who had CF and who were monitored at the University of Kentucky Cystic Fibrosis Center, 112 subjects experienced 232 hospitalizations for treatment of pulmonary exacerbations during the 18-month study period. Experimental procedures were explained to 41 subjects who had CF, who were admitted to the University of Kentucky Medical Center Hospital, and who met study inclusion criteria. Fifteen subjects with CF documented by a sweat test agreed to participate and were enrolled in the study.

Subjects were eligible to participate if they were being hospitalized for treatment of an acute exacerbation of their CF-related chronic obstructive lung disease, were able to perform lung function testing according to standard guidelines, were at least 7 years of age, and were regarded as medically stable by their primary CF physician. Subjects who had a history of pneumothorax were excluded for safety reasons related to breathing against resistance. No subjects were on prescribed daytime oxygen use at the time of the study. All subjects performed HFCWO on an outpatient basis 1 to 3 times daily before admission, and no subjects performed daily PEP breathing. All subjects who had CF and who were admitted to the hospital for treatment of pulmonary exacerbations performed HFCWO 3 times daily whether or not they were study participants.

Subject characteristics at study entry are shown in Table 1. Informed consent was obtained from all study volunteers and from parents (for subjects younger than 18 years of age) before participation.

**Interventions**

For HFCWO, a model 103 Vest airway clearance system® was used while subjects were seated upright in a chair. Subjects were fitted with a nonstretch, vinyl-coated polyester inflatable vest, which was worn over the entire thorax as shown in Figure 1. The vest was closed at the front with 3 buckles and fit snugly when subjects inhaled to total lung capacity (TLC). Two ports, located on the front panels of the vest, were connected to the air-pulse generator via 2 large-bore tubes. The air-pulse generator consisted of an air blower that delivered air pressure to the inflatable vest and a rotary valve that produced alternating positive and zero pressures. During treatment, the vest was inflated so that a background air pressure was created when the setting of 5 was selected from a scale ranging between 1 and 10 (arbitrary units). A middle range for background pressure was selected because, although the volume of inspired air during spontaneous breathing has been shown to be higher during high background pressure than during low background pressure, high background pressure is known to lower end-expiratory lung volume (EELV) more than low background pressure for the same oscillation fre-

<table>
<thead>
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<th>Characteristic</th>
<th>X</th>
<th>SD</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>17.5</td>
<td>4.2</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>159</td>
<td>9.0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>46.6</td>
<td>6.9</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>18.3</td>
<td>2.0</td>
</tr>
</tbody>
</table>

**Experimental Protocol**

Each subject visited the lead author’s pulmonary laboratory located in the College of Health Sciences at the University of Kentucky on 4 separate days. Single-breath inert gas tests and spirometry were performed before and immediately after HFCWO or PEP breathing treatments to assess ventilation distribution, gas mixing, and lung function on 2 separate successive days within 48 hours of hospital admission and again on 2 separate successive days within 48 hours of hospital discharge. Because most subjects are discharged at the end of their intravenous antibiotic treatment, we were able to identify the likely discharge date and used the 2 days before discharge to study the subjects in the subacute phase.

Subjects were assigned to treatment order by numbering them consecutively, 1 through 15, at study entry. On the basis of a coin toss at admission, subject 1 and all odd-numbered subjects were randomly assigned to perform HFCWO on day 1 and PEP breathing on day 2, and even-numbered subjects performed PEP breathing on day 1 and HFCWO on day 2. At discharge, subjects received treatment in the order opposite the treatment order at admission. Three subjects were discharged while continuing to receive intravenous antibiotics. For these 3 subjects, final testing was performed within 48 hours of the time at which intravenous antibiotics were discontinued. Subjects received an average of 10 days (range=7–14) of intravenous antibiotics. The average length of hospital stay was 11 days (range=9–15).

**Table 1.**

Demographics of Participants (8 Male, 7 Female)

* Hill-Rom, 1020 West County Rd F, St Paul, MN 55126.
frequency. In addition, there were no differences in the volumes of expired air between the low and the high background pressure settings during spontaneous breathing for the same oscillation frequency. 

Oscillation frequency was set at 10 Hz for the initial 15 minutes and was increased to 15 Hz during the last 15 minutes of treatment. Oscillation frequencies of 10 and 15 Hz were selected because these 2 frequencies were previously identified to generate peak airflow during spontaneous tidal volume breathing, which is the movement of air in and out of the lungs during resting, has been shown to decrease during expiration as oscillation frequency increases beyond 15 Hz.

A hand-foot switch, controlled by the subjects, activated and deactivated oscillations. Every 5 minutes, subjects deactivated the oscillations, inhaled to TLC, activated the oscillations at 10 or 15 Hz, and performed a forced expiratory maneuver to a low lung volume, which resulted in coughing, in order to clear airway secretions. Each subject determined how many forced expiratory maneuvers, followed by coughing, were necessary in order to clear airway secretions at each 5-minute interval. Six cycles consisting of 5 minutes of treatment followed by forced expiratory maneuvers and coughing were completed by all subjects.

Low PEP was generated by breathing through a face mask fitted with a 1-way valve, an expiratory resistor, and a pressure manometer as shown in Figure 2. During low-PEP breathing, a resistor with an internal diameter that provided a steady PEP of 10 to 20 cm H2O during expiration, while the subject was breathing through the PEP mask, was used. On the basis of clinical observations made by the lead author, low PEP as opposed to high PEP (>20 cm H2O) was selected for use in the present study because high-PEP breathing is not well tolerated and cannot easily be performed by people experiencing an acute pulmonary exacerbation. The pressure manometer provided visual feedback so that a steady PEP of 10 to 20 cm H2O was maintained during tidal exhalations and exhalations were slightly active. 

Expiratory resistor internal diameters and mean sustained expiratory pressures generated during low-PEP breathing for each subject are shown in Table 2. Subjects breathed against the expiratory resistance for 8 breaths, removed the PEP mask, and were encouraged to perform a forced expiratory maneuver to a low lung volume, which resulted in coughing, in order to clear airway secretions. Each subject determined how many forced expiratory maneuvers, followed by coughing, were necessary in order to clear airway secretions. A total of 8 to 10 cycles consisting of 8 breaths were performed over 30 minutes.

Subjects inhaled an aerosolized solution containing 0.5 mL of albuterol and normal saline by using a PARI Master nebulizer during the HFCWO and PEP breathing treatment interventions. The nebulizer was interfaced with the inspiratory port of the one-way valve during PEP breathing so that the aerosol was inhaled through the PEP mask. Subjects held the nebulizer in their hand during HFCWO treatment. Nebulized albuterol was administered during both ACTs in an effort to duplicate treatments routinely performed by our subjects during hospitalizations and at home. Subjects at our CF center perform bronchodilator therapy during HFCWO treatment.

Measurements

The distribution of ventilation (phase III N2 slope data expressed as percentages of predicted values) and gas mixing (dilution index values expressed at an absolute lung volume [DLx]) were measured by use of a single-breath inert gas test in accordance with standard guidelines. Subjects were prompted to perform a slow inhalation of a test gas mixture containing 5% helium (He), 5% sulfur hexafluoride (SF6), and 90% oxygen gases, from residual volume (RV) to TLC, followed by a slow controlled expiration back to RV. Figure 3 shows the distribution of ventilation depicted by single-breath

figure 1. Vest airway clearance system used to deliver high-frequency chest wall oscillations. Note the air compressor connected by tubing to the vest.
washout curves of exhaled N₂ gas concentrations plotted against exhaled lung volume for a subject without CF (top panel) and a subject with CF (bottom panel).

A regression test was performed on the N₂ data versus the lung volume data between the onset of phase III and the onset of phase IV of the single-breath curve. The slope of the regression line represented the N₂ /volume slope of phase III, which served as a measure of the uniformity of the distribution of ventilation and which was the result of incomplete gas mixing. The closer the phase III slope was to horizontal, the more uniform was the distribution of ventilation. Upward sloping of the line away from horizontal represented an increase in the phase III slope and a poorer distribution of ventilation. Phase III alveolar slope data for expired N₂ were expressed as percentages of predicted values. The greater the percentage of the predicted value for the N₂ slope, the poorer the distribution of ventilation.

Expired He, N₂, and SF₆ concentrations were expressed as DIVL to determine whether there were any changes in expired gas concentrations after treatment. Higher DIVL for He, N₂, and SF₆ gases after treatment than before treatment would indicate improved mixing of the inspired test gas with gas already present in the lungs.

Vital capacity and expiratory flow measurements were obtained by simple spirometry according to standard methods by use of a MedGraphics PC SpiroCard interfaced with the Office Medic software program and a computer. The measurements were expressed as percentages of predicted values.

Noninvasive, continuous-pulse oximetry (Nellcor N-200) was performed with a finger probe attached to the right index finger to estimate SpO₂. Arterial blood oxyhemoglobin saturation was measured before treatment, continuously throughout treatment, and for several minutes after treatment until heart rate and SpO₂ stabilized. Arterial blood oxyhemoglobin saturation measurements were obtained during both ACTs because HFCWO-induced decreases in EELV have the potential to decrease SpO₂, and low-PEP breathing has the potential to increase SpO₂ during and after treatment.

Table 2.
Expiratory Resistor Internal Diameters (IDs) and Mean Sustained Expiratory Pressures (SEPs) Generated During Low Positive Expiratory Pressure (PEP) Breathing

| Subject No. | Admission | | Discharge | |
|-------------|-----------|-----------|-----------|
| | Resistor ID (mm) | SEP (H₂O) | Resistor ID (mm) | SEP (H₂O) |
| 1 | 2.5 | 20 | 2.0 | 20 |
| 2 | 2.0 | 18-20 | 2.0 | 20 |
| 3 | 2.0 | 15-18 | 2.0 | 20 |
| 4 | 2.0 | 18-20 | 2.0 | 18-20 |
| 5 | 2.0 | 18-20 | 1.5 | 18-20 |
| 6 | 2.0 | 20 | 2.0 | 20 |
| 7 | 1.5 | 20 | 1.5 | 20 |
| 8 | 1.5 | 20 | 1.5 | 20 |
| 9 | 1.5 | 15 | 1.5 | 18 |
| 10 | 1.5 | 18 | 1.5 | 18-20 |
| 11 | 2.0 | 20 | 1.5 | 20 |
| 12 | 1.5 | 10 | 1.5 | 15 |
| 13 | 2.0 | 15 | 2.0 | 20 |
| 14 | 1.5 | 20 | 1.5 | 20 |
| 15 | 1.5 | 18 | 1.5 | 20 |

Data Analysis
To ensure that this study had adequate power, a power analysis was conducted. The results of the power analysis indicated that for a large effect size at an alpha level of .05, the study required 15 subjects per treatment group.
Group means and standard deviations were calculated for demographic data, for percentages of predicted N2 /volume slope data, for DI\textsubscript{VL} for He, N2, and SF\textsubscript{6}, for Spo\textsubscript{2}, and for percentages of predicted forced vital capacity (FVC), forced expiratory volume in 1 second (FEV\textsubscript{1}), and forced expiratory flow between 25% and 75% vital capacity (FEF\textsubscript{25%–75%}) at study enrollment. To determine acute changes during treatment sessions and differences in treatment at hospital admission and discharge, a 3-way repeated-measures analysis of variance was performed (treatment [HFCWO or PEP breathing] \times time [before or after treatment] \times hospital status [admission or discharge]) with time and hospital status as the repeated variables (Statistica 6.1 software package\textsuperscript{1}). Analysis of Spo\textsubscript{2} data was performed as for the other variables, with the exception that because Spo\textsubscript{2} was measured continuously throughout the airway clearance treatment, the high and low Spo\textsubscript{2} values during treatment were identified, thus yielding 4 levels for time (before, high, low, and after) but 2 levels for the other variables. Significant F ratios were followed up with Tukey honestly significant difference post hoc methods to identify specific differences. Significance was set at a P value of <.05.

**Results**

**Effects of Airway Clearance on Pulmonary Function at Hospital Admission and Discharge**

Pulmonary function was measured before and after airway clearance treatments at admission to and discharge from the hospital (Tab. 3). At admission to the hospital, pulmonary function values measured before airway clearance treatments were not different on the 2 testing days (Tab. 3).

Airway clearance treatments were associated with changes in FVC and FEV\textsubscript{1}. Specifically, a significant interaction between time and hospital status was observed for FVC. This interaction demonstrated that both HFCWO and PEP breathing resulted in average improvements in FVC of 13% (P<.0002) during the acute stage of exacerbation (admission) but not during the subacute stage (discharge) (Tab. 3). A significant main effect of time was observed for FEV\textsubscript{1}, indicating that during both the acute stage of exacerbation and the subacute stage, HFCWO and PEP breathing treatments resulted in improvements in FEV\textsubscript{1} (P<.0002) (Tab. 3).

The airway clearance treatments at admission and discharge had no effect on FEV\textsubscript{1}/FVC and FEF\textsubscript{25%–75%}. Additionally, there were no differences in the responses of any of the pulmonary function measures between the

\textsuperscript{1} StatSoft Inc, 2300 E 14th St, Tulsa, OK 74104.
HFCWO and the PEP breathing treatments at either admission or discharge (Tab. 3).

**Effects of Airway Clearance on Ventilation Distribution and Gas Mixing at Hospital Admission and Discharge**

Ventilation distribution and gas mixing were measured before and after airway clearance treatments during both the acute stage (admission to the hospital) of exacerbation and the subacute stage (just before discharge from the hospital) (Tab. 4, Figs. 4 and 5). At admission to and discharge from the hospital, the values for N₂ slope, which provides an index of overall ventilation distribution homogeneity, were not different before either airway clearance treatment (Tab. 4, Fig. 4).

A main effect of time was observed for N₂ slope, indicating that treatment with either HFCWO or PEP breathing at both admission and discharge was associated with a reduction in N₂ slope (P=.011) (Tab. 4, Fig. 4). This reduction indicates that ventilation was more uniformly distributed throughout the lungs after either airway clearance treatment during both the acute exacerbation stage and the subacute stage (Tab. 4, Fig. 4).

The DI<sub>VL</sub> for the 3 test gases (He, N₂, and SF₆) measure how well an inspired test gas mixes with gas already present in the lungs. At admission to and discharge from the hospital, the DI<sub>VL</sub> for He, N₂, and SF₆ were not different before either airway clearance treatment (Tab. 4, Fig. 5).

There were main effects of time for the DI<sub>VL</sub> for He, N₂, and SF₆ (Tab. 4, Fig. 5). This finding indicates that treatment with either HFCWO or PEP breathing at both admission and discharge was associated with improvements in gas mixing. The DI<sub>VL</sub> for He, N₂, and SF₆ increased, on average, 8% (P<.0004), 9% (P<.0002), and 10% (P<.0003), respectively (Tab. 4, Fig. 5).

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**Table 3.** Lung Function at Admission and Discharge<sup>a</sup>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HFCWO</th>
<th>PEP Breathing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Admission</td>
<td>Discharge</td>
</tr>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>FVC (% predicted)</td>
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<td>18</td>
</tr>
<tr>
<td>FEV₁ (% predicted)</td>
<td>54</td>
<td>20</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
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<td>0.15</td>
</tr>
<tr>
<td>FEF₂₅₋₇₅% (% predicted)</td>
<td>38</td>
<td>32</td>
</tr>
</tbody>
</table>

<sup>a</sup>HFCWO=high-frequency chest wall oscillation, PEP=low positive expiratory pressure, Pre=before treatment, Post=after treatment, FVC=forced vital capacity, FEV₁=forced expiratory volume in 1 second, FEF₂₅₋₇₅%=forced expiratory flow between 25% and 75% vital capacity.

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**Table 4.** Single-Breath Data<sup>a</sup>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HFCWO</th>
<th>PEP Breathing</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Admission</td>
<td>Discharge</td>
</tr>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td>N₂ slope (% predicted)</td>
<td>922</td>
<td>631</td>
</tr>
<tr>
<td>DI&lt;sub&gt;VL&lt;/sub&gt; for He</td>
<td>3.6</td>
<td>1.3</td>
</tr>
<tr>
<td>DI&lt;sub&gt;VL&lt;/sub&gt; for N₂</td>
<td>3.2</td>
<td>1.4</td>
</tr>
<tr>
<td>DI&lt;sub&gt;VL&lt;/sub&gt; for SF₆</td>
<td>3.6</td>
<td>1.5</td>
</tr>
</tbody>
</table>

<sup>a</sup>HFCWO=high-frequency chest wall oscillation, PEP=low positive expiratory pressure, Pre=before treatment, Post=after treatment, N₂=nitrogen, DI<sub>VL</sub>=dilution index values expressed at an absolute lung volume, He=helium, SF₆=sulfur hexafluoride.

<sup>b</sup>Significant change between pretreatment and posttreatment values.
Effects of Airway Clearance on SpO₂ at Hospital Admission and Discharge

Arterial blood oxyhemoglobin saturation was measured before, during, and after airway clearance treatments at both admission to and discharge from the hospital. There were no differences in SpO₂ before either treatment at admission to and discharge from the hospital (Fig. 6).

A significant interaction between time and treatment was observed for SpO₂. This interaction demonstrated that during both the acute stage of exacerbation and the subacute stage, SpO₂ responses differed between HFCWO and PEP breathing airway clearance treatments. Specifically, HFCWO resulted in decreases in SpO₂ during treatment at both admission and discharge (P<.00004) (Fig. 6). Immediately after treatment, SpO₂ returned to pretreatment levels. Conversely, airway clearance with PEP breathing at both admission and discharge was associated with increases in SpO₂ during treatment (P<.00004) (Fig. 6). These increases were not sustained after treatment.

Discussion

In this investigation, we evaluated the physiologic responses to 2 airway clearance interventions, HFCWO and low-PEP breathing, in subjects who had moderate to severe CF and who required hospitalization because of an exacerbation of their chronic lung disease. The goal of this investigation was to use the physiologic response data obtained during the application of HFCWO and low-PEP breathing to improve the prescription of airway clearance treatment in this patient population. The most important finding in this investigation was that both the HFCWO and the PEP breathing interventions were similarly efficacious in improving pulmonary function, ventilation distribution, and gas mixing in subjects who had CF and who were experiencing an exacerbation. However, distinct differences in the underlying physiologic mechanisms between the 2 treatments were identified, and

Figure 4.
Ventilation distribution depicted by the phase III alveolar nitrogen (N₂) slope expressed as a percentage of predicted values for high-frequency chest wall oscillation (HFCWO) and low positive expiratory pressure (PEP) breathing interventions before treatment (Pre) and after treatment (Post) at hospital admission and discharge. Values are means±SDs. * = significant change between pretreatment and posttreatment values.

Figure 5.
Gas mixing for helium expressed in dilution index format for high-frequency chest wall oscillation (HFCWO) and low positive expiratory pressure (PEP) breathing interventions before treatment (Pre) and after treatment (Post) at hospital admission and discharge. Values are means±SDs. * = significant change between pretreatment and posttreatment values.
these differences may affect clinical decision making during prescription of an airway clearance treatment intervention in this patient population.

Effects on \( \text{SpO}_2 \)
The most striking difference between the HFCWO and the PEP breathing treatments was the observation that the HFCWO treatment was associated with decreases in \( \text{SpO}_2 \) during treatment, whereas the PEP breathing treatment produced modest, but significant, increases in \( \text{SpO}_2 \) during treatment (Fig. 6). When subject \( \text{SpO}_2 \) values are 94% or above, values that correspond to partial pressures for oxygen in the low to middle 70s, as we observed in our study subjects, the decreases in \( \text{SpO}_2 \) with HFCWO are likely to be clinically insignificant. However, the observed decreases in \( \text{SpO}_2 \) may be important to note, because the lower a subject’s pretreatment \( \text{SpO}_2 \), the more likely desaturation will occur and the

Figure 6.
Percent arterial blood oxyhemoglobin saturation (\( \text{SpO}_2 \)) values for high-frequency chest wall oscillation (HFCWO) and low positive expiratory pressure (PEP) breathing interventions before treatment (Pre), during treatment, and after treatment (Post) at hospital admission and discharge. Note the low and high \( \text{SpO}_2 \) values during each intervention. Values are means±SDs. **=significantly different from values for HFCWO-Pre, HFCWO-High, HFCWO-Post, and PEP-High. ***=significantly different from values for PEP-Pre, PEP-Low, PEP-Post, and HFCWO-Low.

more likely the subject will experience hypoxia during HFCWO treatment.

Among reports of HFCWO use by subjects with CF,\(^8\)–10,15 only Arens et al\(^8\) measured and reported subject \( \text{SpO}_2 \) responses. In contrast to the findings in the present study, improvements in \( \text{SpO}_2 \) occurred during and up to 1 hour after treatment on days 7 and 14 of hospitalization for a pulmonary exacerbation in both the CPT and the HFCWO groups, but there were no differences in \( \text{SpO}_2 \) between the 2 treatment interventions.\(^8\) Interestingly, at enrollment, our subjects had less central and peripheral airway obstruction than subjects in the study of Arens et al,\(^8\) as indicated by the percentages of the predicted FEV\(_1\) (X\(\pm\)SD: 55±21 versus 33.8±2.4) and FEF\(_{25\%–75\%}\) (37±29 versus 13.5±2.0) values, yet the mean \( \text{SpO}_2 \) was slightly lower in our study subjects. In addition, our study subjects exhibited more ventilation distribution inhomogeneity, as indicated by the percent predicted \( N_2 \) slope values (X\(\pm\)SD: 914±567) in the present study compared with the percent predicted \( N_2 \) slope values in the study of Arens et al\(^8\) (X\(\pm\)SD: 601±75).

Improvements in \( \text{SpO}_2 \) during low-PEP breathing in the present study were similar to improvements in \( \text{SpO}_2 \) reported by other authors.\(^17\) Arterial blood oxyhemoglobin saturation increased after a 20-minute low-PEP breathing treatment, peaked at 35 minutes after treatment, and never dropped below baseline for a group of subjects who had CF and who had considerably more central airway obstruction, as indicated by an FEV\(_1\) that was 34% of the predicted value,\(^17\) than the subjects in our study, who had an FEV\(_1\) that was 55% of the predicted value.

Different Mechanisms Leading to Improved Ventilation Distribution and Gas Mixing
Although there were no differences between the effects of the HFCWO and PEP breathing treatments on ventilation distribution and gas mixing in our study, there were differences in the underlying physiologic mechanisms of the 2 treatments that led to the improvements, and these differences warrant further discussion. The decreases in the phase III alveolar slopes after both airway clearance treatments resulted from more complete gas mixing and led to improvements in ventilation
obstructive pulmonary disease, such as CF secondary to volume, is commonly elevated in subjects with chronic dynamic and constantly changing breath-by-breath lung oscillation frequencies potentially leads to small-airway closure and deterioration in gas exchange for subjects who already have expiratory airflow limitations. The time constant for a lung unit is defined as the time required for a lung unit to empty or fill and is equal to the product of its resistance to airflow and its compliance. Thus, air movement within the lungs is dependent on airway diameter and tissue elasticity. Time constants are slow when lung units have low distensibility and high airway resistance, such as in CF-related lung disease. Parallel lung units, present in the same lung region, normally fill and empty at about the same rates. However, in obstructive lung disease, parallel lung units frequently fill and empty at different rates. During HFCWO, pendelluft may increase the recirculation of air, thereby increasing alveolar ventilation for previously closed or underventilated lung units. The results are improvements in gas mixing and homogenization of expired gas concentrations from these neighboring lung units.

High-frequency chest wall oscillation delivered at 10 and 15 Hz has been shown to decrease functional residual capacity (FRC) and to increase tidal volume and airflow in subjects who were healthy and in subjects with obstructive lung disease. Functional residual capacity, or EELV (the volume of gas remaining in the lungs at the end of expiration), decreased during HFCWO, pendelluft may increase the recirculation of air, thereby increasing alveolar ventilation for previously closed or underventilated lung units. The results are improvements in gas mixing and homogenization of expired gas concentrations from these neighboring lung units.

During HFCWO intervention, we purposefully selected lower oscillation frequencies, of 10 and 15 Hz, and a midrange background pressure in order to maximize oscillated airflow and oscillated tidal volume and to minimize reductions in EELV. In this regard, Jones et al reported reductions in EELV to 90% of baseline pre-HFCWO values. Although reductions in EELV were observed, no deterioration in SpO₂ occurred during or after HFCWO treatment because the subjects were breathing 50% supplemental oxygen. The authors speculated, however, that hypoxia could occur for subjects with CF during a 30-minute HFCWO treatment while breathing room air because of the reductions in EELV associated with HFCWO. Therefore, the observed decreases in SpO₂ during HFCWO treatment in the present study may be important because the lower the subject’s pretreatment SpO₂, the more likely desaturation is to occur.

In light of the small decreases in SpO₂ during HFCWO, it is possible that some small-airway closure occurred and may have reduced the contribution made by small-airway inhomogeneities to the phase III alveolar slope during single-breath testing and caused the phase III slope to move downward toward horizontal. However, the effects of any decreases in lung volume likely were offset by the effects of improved gas mixing during HFCWO, which preserved gas exchange in our subjects in both the admission and the discharge HFCWO treatment sessions.

Low-PEP breathing also was associated with marked improvements in ventilation distribution (Tab. 4, Fig. 4) and gas mixing (Tab. 4, Fig. 5), but through physiologic mechanisms different from those of HFCWO. Improvements in gas mixing after low-PEP breathing in the present study were similar to findings reported previously from our laboratory. Our data suggest that the improvements in gas mixing and FVC likely were attributable to a decrease in the partial or complete obstruction of smaller, peripheral airways. The low expired He, N₂, and SF₆ concentrations (Tab. 4, Fig. 5) and the N₂ phase III alveolar slope values (Tab. 4, Fig. 4) measured before the interventions reflected heterogeneity of time constants within the peripheral airways of our subjects with CF, confirming the presence of fast and slow time constants. During 30 minutes of resistance breathing during PEP treatment, peripheral airways were dilated, facilitating the ongoing exhalation of RV gas. The ongoing exhalation of RV gas generated airflow through the smaller airways and facilitated faster filling and emptying times for lung units, but particularly for slow lung units. Gas mixing improved because time constants for lung units, which are dependent on airway diameter and tissue elasticity, became faster and additional gas volume could be
indexes reflecting airway clearance, such as SpO₂ clearance treatment, it is important to consider other
study.12 We believe that, in the evaluation of an airway
low-PEP, and high-PEP conditions in our previous
increases in sputum amounts observed during control,
removal of sputum, which led to the cumulative
longed, forceful exhalations performed during pulmo-
believe that deep breathing, coughing, and the pro-
 interventions, reflects only the efficacy of an ACT. We
attribute this finding to the high
diffusivity of He, which permitted the gas to diffuse into
poorly ventilated regions before PEP breathing treat-
ment and therefore minimized our ability to measure
any changes in ventilation distribution that might have
occurred as a result of the PEP breathing treatment. In
the present study, we used heavier, resident N₂ gas
which, in contrast to He gas, had unequal concentra-
throughout the lungs due to poorly ventilated
regions before treatment. During PEP breathing treat-
ment, airways were opened and N₂ gas likely diffused
into previously closed regions as a result of breathing
against positive pressure.12,35 The improvements in the
homogeneity of ventilation distribution were reflected
by the decreased N₂ phase III alveolar slopes after PEP
breathing treatment.

Role of Sputum Collection in Studies of Airway Clearance
Treatments
Sputum collection was not performed in this study. Based
on our previous findings,12 we do not believe that
sputum collection, within the context of repeated pul-
monary function testing and airway clearance treatment
interventions, reflects only the efficacy of an ACT. We
believe that deep breathing, coughing, and the pro-
longed, forceful exhalations performed during pulmo-
nary function testing facilitated the loosening and
removal of sputum, which led to the cumulative
increases in sputum amounts observed during control,
low-PEP, and high-PEP conditions in our previous
study.12 We believe that, in the evaluation of an airway
clearance treatment, it is important to consider other
indexes reflecting airway clearance, such as SpO₂, venti-
lation distribution, and gas mixing, which are physiolog-
ically meaningful and have important implications for
physical therapist clinical practice.

Limitations
In the present study, the subjects used bronchodilator
therapy during both airway clearance treatments. Because PEP breathing transmits a back pressure to the
airways, it is conceivable that the administration of the
bronchodilator will be altered during this treatment and
thus may affect results. However, a previous study that
examined the effect of PEP breathing on the delivery of
metered-dose inhaled albuterol showed that there were
no differences in total drug dosages with PEP breathing
and without PEP breathing.18 Additionally, in another
study,19 an inhaled bronchodilator was administered
with PEP breathing and without PEP breathing; the
authors found that peak expiratory flow increased simi-
larly with the administration of the bronchodilator with
PEP breathing and without PEP breathing.19 These
findings suggest that the administration of albuterol with
PEP breathing or without PEP breathing is unlikely to be
a major confounding variable.

Conclusion
The results of this investigation indicated that both
HFCWO and low-PEP breathing airway clearance inter-
ventions were similarly efficacious in improving pulmo-
nary function, ventilation distribution, and gas mixing
for subjects who had CF and who were experiencing an
acute exacerbation of their pulmonary disease. These
improvements in ventilation distribution and gas mixing
were associated with small, yet significant, increases in
SpO₂ during PEP breathing. Alternatively, the use of
HFCWO was associated with improvements in ventila-
tion distribution and gas mixing and small decreases in
SpO₂. These findings led to our recommendation that,
for people who have moderate to severe CF-related lung
disease and who are experiencing an acute exacerbation
requiring hospital admission, it is essential to monitor
SpO₂ during airway clearance treatments. People who
have low pretreatment SpO₂ levels could desaturate to
unacceptable levels during HFCWO therapy. These indi-
viduals may benefit from the use of low-PEP breathing
therapy during an acute exacerbation of their lung
disease. Both HFCWO and low-PEP breathing interven-
tions were associated with improvements in ventilation
distribution and gas mixing. Therefore, we recommend
either HFCWO or low-PEP breathing for people stable
CF-related lung disease because, once the acute lung
infection has been treated and lung function improves,
it may be possible to maintain SpO₂ at acceptable levels
with either treatment and still experience the benefits of
improved gas mixing. For people in whom HFCWO
results in desaturation and who find that low-PEP breath-
ing is too fatiguing to perform during the early stages of
treatment for an acute exacerbation, CPT may be indi-
cated because it has been shown that CPT and low-PEP
breathing are equally effective at secretion removal in
subjects with CF.9 For people with stable lung function,
both HFCWO and low-PEP breathing are associated with
similar improvements in pulmonary function, ventila-
tion distribution, and gas mixing; thus, patient prefer-
ence should be considered in the prescription of a
specific airway clearance treatment.

References


