Combining high-frequency oscillatory ventilation and recruitment maneuvers in adults with early acute respiratory distress syndrome: The Treatment with Oscillation and an Open Lung Strategy (TOOLS) Trial pilot study*

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Objective: **To determine the safety, feasibility, and lung-recruitment efficacy of an explicit ventilation protocol combining high-frequency oscillatory ventilation and recruitment maneuvers.**

Design: **Prospective, multiple-center, single-intervention pilot study.**

Setting: **Four university-affiliated intensive care units.**

Patients: **Twenty-five patients with early acute respiratory distress syndrome and severe oxygenation failure.**

Interventions: **Patients were transitioned from standardized conventional ventilation to high-frequency oscillatory ventilation beginning with an initial cycle of up to three sustained inflation recruitment maneuvers (40 cm H_2O × 40 secs), followed by a decremental titration of F_{IO_2} and then mean airway pressure. Recruitment maneuvers were repeated for hypoxemia and routinely at least twice daily if the F_{IO_2} was >0.4. A specific protocol was used for weaning high-frequency oscillatory ventilation, for transitioning to conventional ventilation, and for judging intolerance of conventional ventilation whereby patients should be put back on high-frequency oscillatory ventilation.**

Measurements and Main Results: **Patients (median [interquartile range] Acute Physiology and Chronic Health Evaluation II, 24 [19–32]; age, 50 [41–64]) were enrolled after 13 (range, 6–51) hrs of conventional ventilation. Following the initial cycle of recruitment, the mean (±SD) Pa_{O_2}/F_{IO_2} increased significantly compared with standardized conventional ventilation (200 ± 117 vs. 92 ± 36 mm Hg, $p < .001$). After a mean of 12 hrs of high-frequency oscillatory ventilation, the mean F_{IO_2} was significantly reduced compared with prestudy levels (0.5 ± 0.2 vs. 0.9 ± 0.1, $p < .001$). A median of seven (four to 11) recruitment maneuvers was performed per patient over the study period, with only eight of 244 (3.3%) being aborted. Six of 19 patients transitioned to conventional ventilation (32%) were deemed intolerant and were switched back to high-frequency oscillatory ventilation. Protocol adherence was excellent with documented rates >90%.**

Conclusions: **The combination of high-frequency oscillatory ventilation and recruitment maneuvers resulted in rapid and sustained improvement in oxygenation, likely through lung recruitment. This explicit high-frequency oscillatory ventilation protocol appears well tolerated, feasible, and physiologically sound. (Crit Care Med 2005; 33:479–486)**

KEY WORDS: respiratory distress syndrome; adult; ventilators; mechanical; high-frequency ventilation; atelectasis

Current goals of mechanical ventilation for the patient with acute respiratory distress syndrome (ARDS) are to maintain adequate gas exchange while minimizing ventilator-induced lung injury (1, 2). In addition to a substantive body of animal data (3–5), at least two randomized trials have reported differences in outcome in adults with ARDS treated with lung-protective vs. control ventilator strategies (6, 7). These trials may not, however, represent the final answer for lung protection. Instead, they provide a reference point for future studies addressing this issue (1).

Strategies to reduce ventilator-induced lung injury include avoiding both lung overdistention and underrecruitment (1, 8, 9). High-frequency oscillatory ventilation (HFOV) is theoretically ideal for these purposes (10). HFOV provides pressure oscillations at 3–15 Hz that are greatly attenuated by the time they reach the alveoli, resulting in small tidal volumes that may be less than the anatomical deadspace (11–13). The low tidal volumes delivered should allow HFOV to be set at a mean airway pressure high enough to avoid atelectrauma (14) while still limiting volutrauma, something not always possible with conventional ventilation (CV) (15).

In adults, HFOV has been shown to be safe and effective in improving oxygenation in case series (16–18) and in one randomized trial (19). However, a number of important questions remain unanswered, including whether to use volume recruitment maneuvers with HFOV and how best to wean HFOV and transition back to CV (20). In animal studies of HFOV, recruitment maneuvers (RMs) have been shown to improve both oxygenation and lung protection (21–23). RMs (sustained inflation maneuvers with

*See also p. 667.

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30–40 cm H_2O pressures for 30–40 secs) have been found to be safe in adults on CV, but studies have shown mixed results in terms of efficacy and duration of their oxygenation effects (24–30).

Because of the lack of an appropriate surrogate end point that correlates with mortality (7, 31), a large multiple-center trial will be needed to definitively determine the relative effects of HFOV compared with CV in terms of lung-protection and mortality (19, 20). For such a trial to have the best chance of yielding a valid answer, pilot studies are needed to address the safety, feasibility, and physiologic response to a given HFOV strategy. We designed an explicit HFOV protocol using recruitment maneuvers and a standardized descending titration of mean airway pressure. Specific criteria were included for transitioning to CV and for judging intolerance of CV whereby patients would be put back on HFOV, steps necessitated by the fact that adults are unable to breathe spontaneously on the available HFOV circuit. In this article we report results of a pilot study examining the lung recruitment response (using oxygenation as a surrogate), the safety and efficacy of RMs and HFOV, and the protocol feasibility in terms of HFOV to CV transition and protocol adherence.

METHODS

The research ethics board at each participating institution approved the study, and informed consent was obtained before enrollment.

Patient Selection. Patients were recruited from four teaching hospital intensive care units (ICUs; Mount Sinai and Toronto General Hospitals, Toronto; Cochin Hospital, Paris; University Hospital of Wales, Cardiff). Patients meeting the inclusion and exclusion criteria (Table 1) were placed on standardized conventional ventilator settings, the details of which have been published previously (32). During this 30-min period, all patients were ventilated with pressure control ventilation targeting a tidal volume of 7–8 mL/kg of predicted body weight (7). F_{IO_2} was set at 1.0 and positive end-expiratory pressure at 10 cm H_2O. Patients whose Pa_{O_2}/F_{IO_2} ratio remained <200 mm Hg after 30 mins were deemed eligible for the study, and they (or their surrogates) were approached for informed consent before transitioning to HFOV.

Lung Recruitment/Oxygenation. The goals of the HFOV protocol were to recruit atelectatic lung units and then maintain lung volume at safe levels by oscillating on the deflation limb of volume-pressure curve (15). We dealt with potentially conflicting goals of both achieving lung recruitment and avoiding overdistention by initially prioritizing lung recruitment (ability to reduce F_{IO_2} below 0.6). Once this goal was achieved, we targeted a more moderate mean airway pressure of 30 cm H_2O. From this point we again focused on maintaining end-expiratory lung volume, reducing mean airway pressure to 22 cm H_2O before again lowering the F_{IO_2}.

All patients were ventilated with the 3100B high-frequency oscillatory ventilator (SensorMedics, Yorba Linda CA). Immediately on switching to HFOV, patients underwent an initial cycle of up to three sustained inflation recruitment maneuvers (Fig. 1). They then proceeded from the recruitment phase (Fig. 1, *steps 1–3*) through the maintenance and weaning phase (Fig. 1, *steps 4–6*) according to their oxygenation responses. Recruitment maneuvers were performed as indicated for persistent hypoxemia (Fig. 1, *steps 1–3*) and also at least twice daily after ventilator disconnects and/or on a routine basis as long as the F_{IO_2} was >0.4.

Ventilation. If the pH was >7.25, the oscillator was initially set at a pressure amplitude (ΔP) of 60 cm H_2O, with a frequency of 5 Hz and inspiratory/expiratory ratio of 1:2; if the pH was <7.25, then ΔP was set at 90 cm H_2O (Fig. 1). Adjustments were made, first to ΔP (range, 60–90 cm H_2O) and then to frequency (range, 3–6 Hz) to achieve a target pH of 7.30–7.45. If the pH was <7.25 despite these adjustments, a bicarbonate infusion was considered. If the pH was >7.45, ΔP was decreased in 5 cm H_2O increments until the pH was <7.45.

Switching From HFOV to CV. Patients were switched back to CV when the mean airway pressure was 22 cm H_2O with an F_{IO_2} ≤0.4 (Fig. 2). Initial settings in CV were designed to maintain the mean airway pressure at 22 cm H_2O to avoid derecruitment and were then adjusted as appropriate by the attending physician. If, during the first 48 hrs of CV, oxygenation or ventilation targets could not be met without exceeding prespecified maximal settings, patients were switched back to HFOV (Fig. 2).

Data Collection and Statistics. Demographic, baseline physiologic, laboratory, radiologic, and ventilator data were collected at enrollment. Ventilator, hemodynamic, and pulse oximetry data were collected every 8 hrs after initiation of HFOV. Once patients had successfully been managed on CV for 48 hrs, all study interventions ceased, and patient were followed only for clinical end points until ICU discharge. Other interventions throughout the study including treatment regimens for pneumonia and sepsis were not protocolized but were determined by the attending physician. Data were summarized using means and standard deviations, medians and interquartile ranges, and proportions as appropriate. Student's *t*-tests were used to compare continuous variables that were normally distributed, the Mann-Whitney U test was used

Table 1. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Age >18 yrs	Anticipated duration of ventilation <48 hrs
Endotracheal intubation and mechanical ventilation	>48 hrs elapsed since all inclusion criteria were met
Presence of one or more risk factors for ARDS[a]	Minimal chance of ICU survival as judged by attending physician
Bilateral infiltrates on seen on frontal chest radiograph	Significant heart disease[b]
Pa_{O_2}/F_{IO_2} ratio <200 mm Hg	History of significant COPD or asthma[c]
	Chronic interstitial lung disease associated with bilateral pulmonary infiltrates
	Lung biopsy or resection on current admission
	Known intracranial abnormalities[d]
	Pregnancy
	Previous lung or bone marrow transplant
	Age >75 yrs
	Inability to wean from experimental ARDS therapies[e]
	Enrollment in another interventional study

ARDS, acute respiratory distress syndrome; ICU, intensive care unit; COPD, chronic obstructive pulmonary disease.

[a]Risk factors were pneumonia, aspiration of gastric contents, inhalation injury, sepsis, major trauma, multiple transfusions, drug overdose, burn injury, acute pancreatitis, and shock; [b]significant heart disease was defined as a) left ventricular failure with either documented ejection fraction <40% or previous admission for cardiogenic pulmonary edema, b) clinician suspicion of left atrial hypertension, or c) active coronary ischemia or infarction; [c]significant COPD or asthma was defined as a) previous admissions or emergency room visits for asthma/COPD, b) history of receiving oral corticosteroids for asthma/COPD, or c) documented chronic Co_2 retention >50 mm Hg; [d]intracranial abnormalities included hemorrhage, head injury, tumor, infection, or acute stroke; [e]experimental therapies were the use of inhaled nitric oxide or prone positioning.

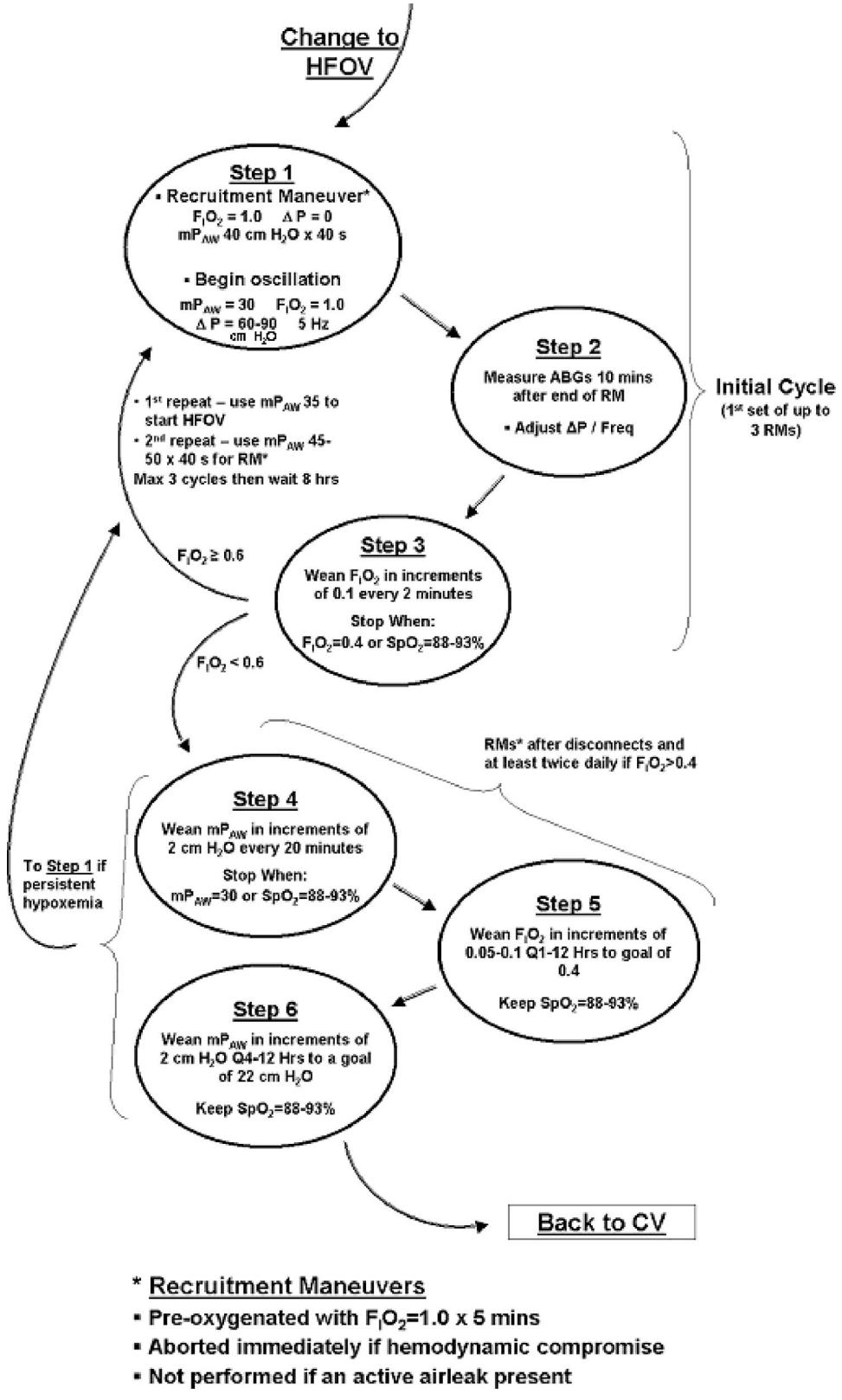

Figure 1. High-frequency oscillatory ventilation (*HFOV*) oxygenation protocol. On switching to HFOV, patients underwent an initial cycle of up to three sustained inflation recruitment maneuvers (steps 1–3). Ten minutes after the first RM, the F_{IO_2} was decreased in increments of 0.1 every 2 mins, stopping when either the F_{IO_2} was 0.4 or the arterial oxygen saturation (Spo_2) was 88–93% (step 3). If the F_{IO_2} still could not be decreased below 0.6, after a third RM at 45–50 cm H_2O, this recruitment procedure was repeated every 8 hrs. Once the F_{IO_2} could be set <0.6, the mean airway pressure was decreased in 2 cm H_2O increments until the mean airway pressure was 30 cm H_2O, keeping the Spo_2 88–93% (step 4). The F_{IO_2} was then again weaned to 0.4 before reducing the mean airway pressure below 30 cm H_2O (steps 5–6). mP_{AW}, mean airway pressure (cm H_2O); *RM*, recruitment maneuver; Δ*P*, pressure amplitude (cm H_2O); *Freq*, frequency (Hz); *CV*, conventional ventilation; *ABG*, arterial blood gas.

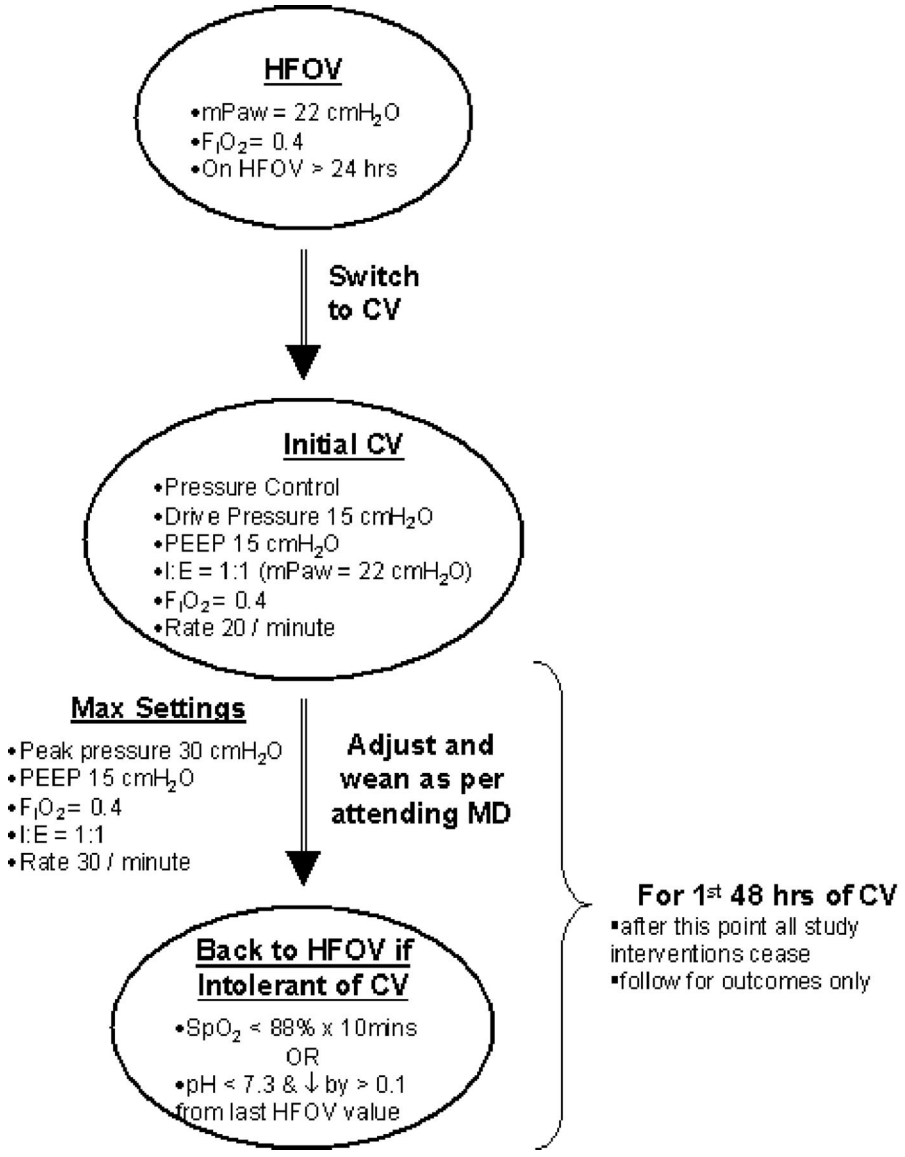

Figure 2. High-frequency oscillatory ventilation (*HFOV*) to conventional ventilation (*CV*) transition. Patients were switched back to CV when the mean airway pressure was weaned to 22 cm H_2O with an $F_{IO_2} \leq 0.4$ and the duration of HFOV was > 24 hrs. If the patient was deemed intolerant of CV, he or she was switched back to HFOV. If this intolerance occurred within 2 hrs, then HFOV was restarted with a standard recruitment maneuver and then returned to its most recent settings before switching to CV. If the intolerance criteria were met after 2 hrs, HFOV was restarted at the beginning of the protocol (Fig. 1). mP_{AW}, mean airway pressure (cm H_2O); Spo_2, arterial oxygen saturation (%); *PEEP*, positive end-expiratory pressure (cm H_2O); *I:E*, inspiratory/expiratory ratio.

for nonparametric continuous variables, and dichotomous outcomes were compared with Fisher's exact test. All analyses were performed using SAS (SAS Institute, Cary NC).

RESULTS

A total of 25 patients (Toronto 14, Paris 8, Cardiff 3) were included after having met all inclusion and exclusion criteria and remaining eligible after screening with standardized ventilator settings. Their demographic and baseline conventional ventilator data are shown in Tables 2 and 3.

Oxygenation and Recruitment Effects. Patients progressed through the initial recruitment cycle (Fig. 1), requiring a mean of 2.4 RMs applied over a mean of 1.5 hrs. The mean (±SD) Pa_{O_2}/F_{IO_2} increased significantly compared with standardized conventional ventilation following this initial cycle (200 ± 117 vs. 92 ± 36 mm Hg, $p < .001$, Fig. 3*A*), and in ten of 25 patients (40%) the Pa_{O_2}/F_{IO_2} more than doubled after the initial RM cycle (Fig. 3*B*). After a mean of 12 hrs of HFOV, the mean F_{IO_2} was significantly reduced compared with prestudy levels (0.5 ± 0.2 vs. 0.9 ± 0.1, $p < .001$). Despite a large increase in mean airway pressure (22 ± 4.1 cm H_2O CV to 32 ± 3.9 cm H_2O HFOV, $p < .001$), the oxygenation index (100 × mean airway pressure × F_{IO_2}/Pa_{O_2}) decreased significantly over this same interval from its prestudy level of 30 ± 14.9 to 21 ± 11.0 ($p = .04$). The F_{IO_2} was reduced below 0.6 in 17 of 25 patients (68%) after this initial cycle of RMs, and these patients immediately entered the maintenance and weaning phase of the HFOV protocol (Fig. 1).

Ventilator settings and blood gas values taken while patients were managed with HFOV are shown in Table 4. A median of seven (range, four to 11) recruitment maneuvers was performed per patient. Only eight of 244 (3.3%) total RMs were aborted in six patients, six because of hypotension that recovered quickly with abolition of the RM, with no reason specified or apparent in the other two cases. Of the six patients who were intolerant of RMs, four successfully tolerated subsequent RMs. Oxygenation effects of RMs were more prominent during the initial days of HFOV (Fig. 4); however, even at days 5 and 6, the mean increase in Pa_{O_2}/F_{IO_2} 10 mins after the RM was >25%.

Switching From HFOV to CV. Nineteen patients were transitioned to CV after a median of 3.3 (interquartile range, 1.6–5.5) days. Six of these patients (31.6%) could not be managed within the constraints placed on CV settings (all because of hypoxemia) and were switched back to HFOV in a median of 20 (interquartile range, 9.2–26.3) hrs. This second round of HFOV lasted for a median of 1.9 (interquartile range, 1.2–3.4) days. ICU mortality was not different between those who did (two of six, 33%) or did not (three of 13, 23.1%) switch back to HFOV. Among these 19 patients who were switched to CV, the percentage of total ventilatory time spent on HFOV was 41.2% (interquartile range, 21.6–75.1%).

Safety and Protocol Adherence. Clinically significant gross barotrauma (necessitating the insertion of a chest tube) was reported in two patients (8%) during HFOV. These episodes occurred on HFOV day 2 in one case and day 9 in the other, while patients were receiving mean airway pressures of 35 and 22 cm H_2O. The times from the most recent RM to the

Table 2. Demographic and baseline information

	Patients
No.	25
Age	49.6 (41.3–64.1)
Gender, % male	56.5
APACHE II	24.0 (19.0–32.0)
MODS	6.0 (5.0–10.0)
No. of organ failures	1.0 (1.0–2.0)
ARDS risk factors, %[a]	
Pneumonia	59.1
Aspiration of gastric contents	22.7
Sepsis	27.3
Shock	13.6
Multiple transfusions	13.6
Inhalation injury	13.6
Duration of ventilation prior to enrollment, hrs	13 (5.8–50.5)

APACHE, Acute Physiology and Chronic Health Evaluation; MODS, multiple organ dysfunction syndrome; ARDS, acute respiratory distress syndrome.

[a]Patients could have more than one risk factor; risk factor data were missing in three cases. Median values (interquartile range) or proportion (%) are presented.

Table 3. Hemodynamic and ventilator data prior to high-frequency oscillatory ventilation

	Standardized Conventional Ventilation	
Ventilator		
Rate	24	(20–26)
V_T	515	(449–582)
V_T/kg IBW	8.8	(8.4–9.4)
F_{IO_2}	1.0	(1.0–1.0)
PEEP	10	(10–15)
PIP	32	(30–34)
Paw	20	(18–23)
Hemodynamics		
HR	110	(104–129)
MAP	74	(70–82)
ABGs		
pH	7.28	(7.25–7.31)
$Paco_2$	44	(37–50)
Pao_2	96	(66–115)
HCO_3	21	(17–23)
Sao_2	94	(91–98)
Pao_2/F_{IO_2}	96	(66–115)
OI	23	(16–35)

V_T, tidal volume (mL); IBW, ideal body weight; PEEP, positive-end expiratory pressure (cm H_2O); PIP, peak inspiratory pressure (cm H_2O); Paw, mean airway pressure (cm H_2O); HR, heart rate (beats/min); MAP, mean arterial pressure (mm Hg); ABG, arterial blood gas; HCO_3, arterial bicarbonate concentration (mmol/L); Sao_2, percent oxygen saturation; OI, oxygenation index ($OI = P_{AW} \cdot F_{IO_2} \cdot 100/Pao_2$).

Median values (interquartile range).

documentation of barotrauma were 11 and 70 hrs. Isolated pneumomediastinum, pneumopericardium, and subcutaneous emyphysema not requiring chest tubes were reported in three further patients (two survived, one died >2 wks after this finding).

The ICU mortality rate was 44%, with the primary cause of death being multiple organ failure or sepsis in ten patients and brain death following a cardiac arrest in one patient. Life-sustaining treatment was withdrawn in six of 11 deaths. Patients remained on HFOV for a median total of 4.6 (interquartile range, 2.1–6.2) days and had a total duration of ventilatory support of 8.8 (interquartile range, 4.9–20.4) days.

Three patients were withdrawn from the protocol after meeting a predefined threshold, one for uncontrolled barotrauma (with *Pneumocystis* pneumonia), one for refractory acidosis, and one because the attending physician believed the patient needed conventional ventilation and bronchoscopy for pulmonary toilet. The first two of these patients died, whereas the third survived to ICU discharge.

Determining the degree of protocol adherence was not straightforward because the HFOV protocol was written as a dynamic tool to be responsive to the needs of each individual patient. Depending on their responses, patients may have had a great many appropriate combinations of mean airway pressure and F_{IO_2} and of pressure amplitude, $Paco_2$, and frequency. We therefore examined three definite protocol demands. First, the number of RMs performed during the initial recruitment cycle was dependent on the oxygenation response. No patients who received fewer than three RMs should have had an $F_{IO_2} \geq 0.6$ after the initial cycle. Of 11 patients who received only one or two initial cycle RMs, ten (90.9%) had an $F_{IO_2} < 0.6$ following the initial cycle. Second, no patients requiring an $F_{IO_2} \geq 0.6$ should have had a mean airway pressure <30 for more than a 10-min period. Of the 88 time points on HFOV with a recorded $F_{IO_2} > 0.6$, eight (9.1%) were >1 cm H_2O below the threshold of 30, and only two (2.3%) were >2 cm H_2O below this target. Finally, specific constraints were placed on patients who were transitioned to CV, including a peak pressure limit of 30 cm H_2O and an F_{IO_2} limit of 0.4. Of the 19 patients transitioned to CV, only one (5.2%) had major violations of these constraints and should have been, but was not, placed back on HFOV. Four patients (21.1%) had minor CV protocol violations, defined as the use of an F_{IO_2} of 0.5 or peak pressures up to 35 cm H_2O.

DISCUSSION

The major finding of this study was that the combination of this HFOV protocol and RMs was well tolerated and resulted in rapid and sustained improvement in oxygenation, likely through lung recruitment. Furthermore, the protocol for weaning HFOV and transitioning to CV appeared practical and safe. Finally, adherence to our explicit patient-responsive HFOV protocol appeared very good.

Because of the small tidal volumes generated with HFOV, there is very little tidal recruitment of the injured lung, creating a more compelling rationale for RMs in this setting (20, 21, 33–35). In animal models, RMs on HFOV were needed to improve oxygenation, histologic appearance, and even mortality in more severe forms of lung injury (23, 36). To our knowledge, ours is the first report on the use of RMs in adults on HFOV. By design, our protocol combined the use of RMs with high mean airway pressures that were then titrated in a decremental fashion (37). It is therefore impossible to completely separate the roles of increased mean airway pressure on HFOV vs. the RMs on the oxygenation response. The fact that dramatic oxygenation improvements were seen very early (within 1.5 hrs, Fig. 3) compared with other HFOV series (16, 17, 19), and the persistent demonstrable pre-and-post effect (Fig. 4) both point toward an added contribution of RMs. It is important to note that we enrolled patients early in their course of ARDS, and if necessary we applied a series of RMs and increased mean airway pressure following an RM to achieve and maintain a response (25, 26). Perhaps be-

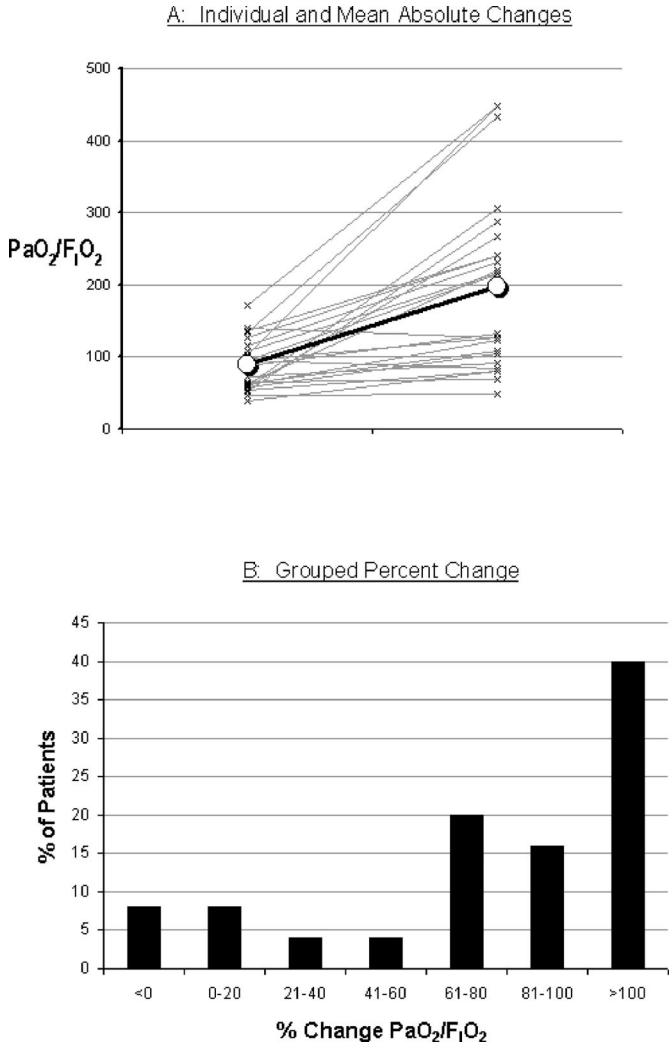

Figure 3. Early oxygenation effects. *A*, individual (*gray lines*) and mean (*solid line*) changes in Pao_2/Fio_2 ratio from standardized conventional settings to completion of the initial recruitment cycle (high-frequency oscillatory ventilation with one to three recruitment maneuvers). *B*, same data, displaying the percentage of patients in each of the Pao_2/Fio_2 ratio percentage change categories.

Table 4. High-frequency oscillatory ventilation settings

Variables, Mean (SD)	Days 1–2 (n = 25[a])	Days 3–4 (n = 18[a])	Days 5–6 (n = 12[a])
Mean airway pressure, cm H_2O	31 (3.4)	28 (3.9)	26 (4.2)
Frequency, Hz	5 (1.9)	5 (0.8)	5 (1.2)
Pressure amplitude, cm H_2O	71 (10.4)	68 (9.5)	73 (11.5)
Fio_2	0.53 (0.13)	0.50 (0.11)	0.50 (0.14)
Arterial pH	7.35 (0.09)	7.36 (0.07)	7.36 (0.10)
$Paco_2$, mm Hg	42 (9.6)	46 (10.5)	47 (8.9)
Pao_2, mm Hg	95 (27.9)	79 (16.5)	85 (18.9)

[a]Number of patients still receiving high-frequency oscillatory ventilation on given days. Mean values (SD) are shown.

cause of the ongoing high mean airway pressures, these positive responses were seen despite the fact that the majority of our patients had ARDS of pulmonary origin (25, 29). Like previous investigators who used CV (24, 28, 29), we found that RMs were well tolerated on HFOV, with only 3% being aborted. We did observe barotrauma in five patients (although pneumothoraces were seen in only two), but barotrauma was not temporally related to RMs (occurring 31 hrs later on average) and did not occur at uniformly high mean airway pressures. These findings, combined with the variability inherent to our small sample size and the previously demonstrated low rates of barotrauma with HFOV (19), do not lead us to conclude that our observed rate was unacceptably high; rather, we conclude that this will need to be observed closely in larger studies.

The combination of high-frequency oscillatory ventilation and recruitment maneuvers resulted in rapid and sustained improvement in oxygenation, likely through lung recruitment.

Oxygenation was not used as a surrogate marker for mortality in this study. Although a lower Pao_2/Fio_2 may be associated with higher mortality (38), improving oxygenation may also be associated with worse outcomes (7). Improving oxygenation, however, is not inherently detrimental, but rather its effect is dependent on the method used to achieve it. In this study we used oxygenation as a surrogate for lung recruitment and used RMs, high mean airway pressures, and very small tidal volumes to achieve this. As such, our pilot results are promising because we were able to improve oxygenation and maintain a lower Fio_2 in the majority of patients, likely through lung recruitment. Whether this will translate into improved clinical outcomes needs to be tested in future comparative studies.

This HFOV protocol differs significantly from those used in previous adult HFOV studies. In addition to using RMs, we provided a uniformly high initial mean airway pressure across patients and then titrated this in a decremental and timely fashion according to the patient's oxygenation response. This is in contrast to the usual method of setting mean airway pressure relative to variable conventional ventilator settings and titrating upward over an indefinite time period (16, 17, 19, 39). In addition, we provided explicit instructions on the timing and or-

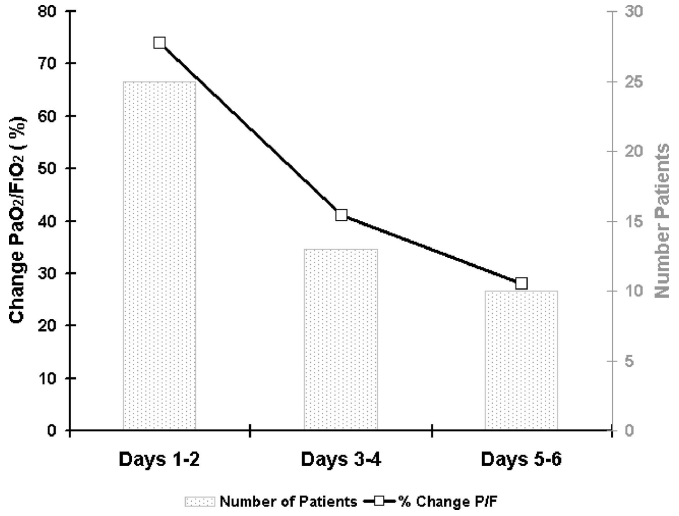

Figure 4. Recruitment maneuver effects over time. Mean percentage (*solid line*) changes in Pao_2/FIo_2 (*P/F*) ratio from immediately before to 10 mins after each recruitment maneuver are displayed according to the day of high-frequency oscillatory ventilation (HFOV) treatment. Columns depict the total number of patients receiving HFOV during each time period.

der of weaning mean airway pressure and FIo_2 (Fig. 1). Finally we included a protocol for converting back to CV and monitoring the success of this transition. Protocol adherence in our study appeared excellent judging by the benchmark points that we were able to analyze, with demonstrated compliance >90%. All of these steps should increase the standardization of HFOV use across clinicians and centers. This standardization and reproducibility are key not only for the generalizability of future trials but also for their validity given the inevitable unblinded nature of such trials.

The issue of converting patients back to CV is an important one for future studies because the HFOV circuit does not allow adults to breathe spontaneously and wean (20). If one is not aggressive at weaning HFOV and transitioning to CV, then duration of ventilation will be adversely affected, with potential ramifications on outcome. Conversely, if patients are converted to CV too early and then spend the majority of their active ventilation time on this mode, HFOV is unlikely to affect outcome (20). Our application of strict criteria for transitioning to CV and then observing for intolerance (Fig. 2) appears to be a practical approach to this problem. The CV intolerance rate of 32% seems to strike a balance between aggressive weaning and delays in transitioning, especially since the need to go back on HFOV did not appear to be harmful.

CONCLUSIONS

HFOV and recruitment maneuvers can be combined in adults with ARDS to provide significant sustained improvements in lung recruitment and oxygenation. The feasibility of our dynamic HFOV protocol appears promising, including its method for transitioning back to CV. This ventilation protocol was generally well tolerated, but the incidence of barotrauma will need to be observed closely in larger studies. Consideration should be given to employing many of these techniques in future trials comparing HFOV to conventional ventilation.

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