

Feasibility of very high-frequency ventilation in adults with acute respiratory distress syndrome*

Henry E. Fessler, MD; David N. Hager, MD; Roy G. Brower, MD

Objective: To assess the feasibility of using respiratory frequencies up to 15 Hz during high-frequency oscillatory ventilation (HFO) of adults with acute respiratory distress syndrome (ARDS).

Design: Observational study.

Setting: Medical intensive care unit at a tertiary care university hospital.

Patients: Thirty adult patients receiving HFO at the discretion of their physicians for management of severe ARDS.

Interventions: Clinical management algorithm for HFO that minimized delivered tidal volumes by encouraging the use of the highest frequency that allowed acceptable clearance of carbon dioxide. This contrasts with the typical use of HFO in adults, in which frequencies generally do not exceed 6 Hz.

Measurements and Main Results: Patients were 42 ± 15 yrs old, weighed 83 ± 25 kg, and had failed conventional lung-protective ventilation due to refractory hypoxia or respiratory

acidosis and high plateau airway pressures. During HFO, 25 of 30 patients maintained acceptable gas exchange at frequencies >6 Hz; 12 reached maximal frequencies of ≥ 10 Hz. Among patients whose maximal frequencies exceeded 6 Hz, mean maximal frequency was 9.9 ± 2.1 Hz, at a mean oscillation pressure amplitude of 81 ± 11 cm H₂O. At those settings, blood gases were pH 7.31 ± 0.06 , P_aCO₂ was 58 ± 21 mm Hg, and P_aO₂ was 82 ± 33 mm Hg. Survival to hospital discharge among this severely ill cohort was 37%.

Conclusions: Most adults can maintain adequate gas exchange using HFO frequencies well above 5–6 Hz. Use of higher frequencies should minimize tidal volume and we speculate might thereby reduce ventilator-associated lung injury. (Crit Care Med 2008; 36:1043–1048)

KEY WORDS: acute respiratory distress syndrome; respiration; artificial; high-frequency ventilation

High-frequency oscillation (HFO) is a mode of mechanical ventilation that offers the potential to maintain acceptable gas exchange while ventilating with very small tidal volumes and at relatively high mean airway pressures (MPaw) (1, 2). This approach may be more lung protective than conventional modes of ventilation for patients with acute respiratory distress syndrome (ARDS). HFO has been used for decades in neonates and small children with acute hypoxemic respiratory failure (3–7). In 2001, the U.S. Food and Drug Administration approved a pressure-cycled ventilator for HFO in adults, renewing interest

in this mode of ventilation among adult intensivists. It has now been studied in several adult case series and two small randomized trials (8–14).

During HFO, carbon dioxide clearance is controlled by adjusting the oscillation pressure amplitude (ΔP , in cm H₂O) and frequency (f , expressed in Hz). HFO tidal volumes and CO₂ clearance vary directly with ΔP . However, in contrast to the effects of respiratory rate during conventional ventilation, CO₂ clearance varies inversely with frequency. The reason for this inverse relationship is that at such rapid respiratory rates, there is insufficient time for pressure in the lungs to equilibrate with pressure at the airway opening. Increasing frequency decreases the time for air to flow, thereby decreasing tidal volume (15). During HFO, the decrease in tidal volume has a greater effect on alveolar ventilation and CO₂ clearance than does the increase in respiratory rate that causes tidal volume to decrease (16).

Current recommendations for setting frequency and ΔP appear to be designed primarily to achieve gas exchange goals rather than to maximize lung protection. For example, the operator's manual pro-

vided by the manufacturer recommends that HFO in adults begin at 5–6 Hz (17). This contrasts to HFO settings in neonatology, where higher frequencies are typically used. ΔP is initially set at about 20 cm H₂O above the arterial P_aCO₂ (measured in mm Hg) or to induce wiggling that is visible to the patient's mid-thigh. Thereafter, the primary method for changing CO₂ clearance is to adjust ΔP . According to current recommendations, frequency may be lowered to <5 Hz if needed to increase CO₂ clearance after ΔP has been maximized, but there are no recommendations to increase frequency. Adult case series and clinical trials have followed these guidelines (17).

This approach may not optimize the lung-protective potential of HFO because it results in tidal volumes that are larger than needed to achieve acceptable gas exchange. A more protective approach would use higher frequency. Although increasing frequency reduces CO₂ clearance, this can be counteracted by increasing ΔP . At any targeted P_aCO₂, the tidal volume at a high frequency and high ΔP must be smaller than at a low frequency and low ΔP . Thus, an HFO strategy designed to minimize tidal volume would

*See also p. 1358.

From the Division of Pulmonary and Critical Care Medicine, Johns Hopkins School of Medicine, Baltimore, MD.

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For information regarding this article, E-mail: hfessler@jhmi.edu

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use a high ΔP and the highest frequency that maintains the target P_{aCO_2} (or pH) (18).

The purpose of this article is to report the feasibility of this strategy in an unselected group of adults with severe ARDS. The routine use of very high frequencies during HFO has not been reported previously in adults and represents an approach to using HFO that could be more lung protective than the current recommendations.

METHODS

This is a prospective case series of ARDS patients who received HFO in the medical intensive care unit (ICU) of a tertiary care university hospital. We maintain an institutional review board-approved utilization database of de-identified clinical data on all patients who receive HFO. Because the period of our early experience with HFO corresponded to the introduction of patient privacy (Health Insurance Portability and Accountability Act) regulations, our database was discontinued while institutional policies and procedures were developed. This report is derived from that database but is limited to the period after we modified our use of HFO, as described subsequently.

Use of HFO in this unit began shortly after U.S. Food and Drug Administration approval of the Sensormedics 3100B ventilator (Sensormedics, Loma Linda, CA) in 2001. To facilitate HFO use, we initially developed a clinical practice guideline hewing closely to the contemporary recommendations. The guideline was the product of a multidisciplinary committee of critical care physicians, nurses, and respiratory therapists. After approximately 2 yrs, we modified the guideline to emphasize the use of higher oscillation frequencies. Essential elements of this guideline are shown in Figure 1, which was provided to physicians, nurses, and respiratory therapists managing ARDS patients who were receiving HFO in this ICU. We explained the rationale for this modified HFO strategy to staff, but they were not required to follow it.

The five most salient elements of the guidelines for the purpose of this report are as follows: First, the ventilation goal was any P_{aCO_2} that would achieve a pH = 7.25–7.35. Second, ΔP was set at 90 cm H_2O , the highest value that could be consistently achieved. Third, the initial frequency was 5 Hz, but this was increased in steps to the highest level (up to 15 Hz) at which the pH goal could be maintained. Fourth, a table of suggested F_{IO_2} and MPaw combinations was provided to achieve a P_{aO_2} goal of 55–80 mm Hg, but selection of these parameters was left to the treating physicians. Fifth, use of recruitment

maneuvers or addition of an endotracheal tube cuff leak was also left to the discretion of the clinicians.

Decisions to initiate and stop HFO were made by the treating physicians. Suspected intracranial hypertension or severe obstructive lung disease was considered to be a contraindication. HFO was invariably started due to worsening gas exchange on conventional ventilation. The guidelines suggested HFO use for failure of conventional ventilation, defined as oxygenation failure (requirement for ≥ 14 cm H_2O positive end-expiratory pressure and $F_{IO_2} \geq 0.7$) or ventilation failure (inability to maintain pH ≥ 7.25 and plateau airway pressure ≤ 30 cm H_2O with tidal volume of 4–6 mL/kg predicted body weight [19]). In practice, most patients started HFO when their gas exchange was significantly worse than these thresholds. HFO was continued until either it was judged to be ineffective or gas exchange and lung mechanics improved sufficiently to allow use of lung-protective conventional ventilation. This was usually signaled by a requirement for MPaw ≤ 25 cm H_2O and $F_{IO_2} < 0.5$. Patients were then transitioned to a conventional ventilator at a tidal volume of 6 mL/kg predicted body weight and were assessed for tolerance.

This ICU also uses protocols for continuous sedation with fentanyl and midazolam in all patients, using a sedation score goal. While a patient is receiving HFO, sedation is usually titrated to suppress most respiratory effort. Neuromuscular blockade (vecuronium, by infusion or bolus) was added at the discretion of the treating physicians. Sedation was not stopped for daily arousal while patients were on HFO, but this was begun when they returned to conventional ventilation.

The database includes basic demographic data, cause of ARDS, reason for HFO (oxygenation failure, ventilation failure, both), ventilator settings, arterial blood gas results, hemodynamic variables, medications (sedatives, neuromuscular blocking agents, and vasopressors), and presence of a chest tube. Acuity of illness is recorded as the Acute Physiology and Chronic Health Evaluation II score and Multiple Organ Dysfunction Score, with normal values assumed for missing data. Respiratory, hemodynamic, and drug use data were recorded at standardized times, using the available clinical data collected as closely as possible to each time point. Patients were followed until hospital discharge for vital status.

Descriptive statistics are reported as mean \pm sd. Changes in variables over time were analyzed by analysis of variance for repeated measures. Group comparisons were performed by paired or unpaired *t*-test for parametric data and by rank-sum testing for nonparametric data, as appropriate. Proportions were com-

pared by Fisher's exact test. We considered $p < .05$ to be statistically significant.

RESULTS

Thirty patients received HFO between April 2004 and May 2007. The mean time on mechanical ventilation before the initiation of HFO was 3.1 ± 3.0 (range 0–13) days. Twenty-two patients were ventilated with an 8-mm inner diameter endotracheal tube, 4 with a 7.5-mm inner diameter endotracheal tube, and 4 with a 7.0-mm inner diameter endotracheal tube. Patient characteristics at ICU admission and the time of HFO initiation are shown in Table 1. These patients were relatively young (42 ± 15 yrs). They weighed 83 ± 25 kg (range 52–172 kg). Pneumonia was the cause of ARDS in 16 cases (53%), with the remaining cases evenly divided among sepsis, aspiration, and other causes. Patients had very severe abnormalities of gas exchange: the mean P_{aO_2}/F_{IO_2} was 78 ± 28 on the last arterial blood gas before beginning HFO, measured on a mean $F_{IO_2} = 0.93 \pm 0.11$ and mean positive end-expiratory pressure = 13 ± 4 cm H_2O . Tidal volume immediately before initiating HFO was 5.9 ± 1.1 mL/kg predicted body weight (range 3.7–7.6).

The reasons for initiating HFO were oxygenation failure in ten patients, ventilation failure in seven, and a combination of both in 13 patients. All patients were ventilated with a 33% inspiratory time and a bias flow rate of 30–40 L/min. Subjects began HFO on an F_{IO_2} of 1.0 (one began on 0.9), which was decreased to 0.84 ± 0.15 within 4 hrs (range 0.6–1.0, $p < .001$ for initial vs. 4-hr value). Initial MPaw was 30 ± 4 cm H_2O and was unchanged at 4 hrs (31 ± 4 cm H_2O). The evolution of the oxygenation index over the first 3 days is shown in Figure 2. The changes were not statistically significant ($p = .09$).

In 25 of the 30 patients, frequency could be increased to > 5 Hz with clinically acceptable pH. The frequency was typically increased over ≥ 1 days, allowing time for renal pH compensation for hypercapnia. The maximal frequency was achieved within the first 2 days of HFO in 17 of the 25 patients able to exceed 5 Hz. In 22 of the patients, the P_{aCO_2}/pH goal could be maintained at frequency ≥ 8 Hz; in 12, frequency could be raised to ≥ 10 Hz. The heaviest patient (172 kg) achieved a P_{aCO_2} of 47 mm Hg while ventilated at 9 Hz. There was no differ-

Management of Ventilation

Overall goal: Maintain pH in the target range at the *minimum tidal volume*. This is achieved by favoring higher frequencies over lower ΔP . This goal is also promoted by accepting mild respiratory acidosis rather than attempting to normalize pH.

Monitor: Obtain ABG at least 30 minutes after each change in settings. Check ABG BID in patient on stable settings.

Target pH: 7.25-7.35
Target f: 12 Hz

Initial settings:

- f = 5 Hz
- ΔP = 90 cm H₂O

Subsequent adjustments:

pH in target range

- Increase f and increase ΔP (up to 90 cmH₂O) as follows:
 - a) Increase f in increments of 1-2 Hz q1-2 hours to max. of 15 Hz or until PaCO₂ rises and pH approaches lower limit of acceptable pH

pH too high (Correct metabolic alkalosis, if indicated)

- Increase f in increments of 1-2 Hz to max. of 15 Hz, then
- Decrease ΔP in 5 cmH₂O increments to minimum of 20.

pH too low (Correct metabolic acidosis, if indicated)

- (Consider possible pneumothorax, partial endotracheal tube occlusion, de-recruitment)
- a) Increase ΔP (up to 90 cmH₂O)
 - b) Decrease f in 1 Hz increments to minimum of 3 Hz.
 - c) Add 5 cmH₂O cuff leak¹ if f \leq 7Hz

¹ A 5 cmH₂O cuff leak is produced by increasing bias flow until mPaw rises by 5 cmH₂O, then deflating the endotracheal tube cuff to restore mPaw to initial value.

Management of Oxygenation

Overall goal: Increase lung recruitment while avoiding overdistension; balance risks of overdistension versus oxygen toxicity. Mean airway pressure (mPaw) is used to recruit lung. Increased mPaw is favored over increased FiO₂ unless patients have circulatory failure. Threshold for overdistension is unknown, but it may be more likely at mPaw > 35 cmH₂O.

Monitor: SpO₂ or PaO₂; Observe SpO₂ changes 5-10 minutes after a change in ventilator settings. Check ABG twice daily.

Target: PaO₂ 55-80 mmHg or SpO₂ 88-95%; use PaO₂ for decisions if only one is out of target range.

Initial settings and adjustments:

- mPaw = mPaw on conventional ventilator + 5 cmH₂O, but do not exceed 35 cmH₂O
- FiO₂ = 1.0
- If oxygenation is below target, increase mPaw in 2-5 cmH₂O increments to maximum of 45 cmH₂O. Consider 1-2 recruitment maneuvers.²
- If oxygenation is above target, decrease FiO₂ to reach a FiO₂/ mPaw combination on scale

Subsequent adjustments:

Oxygenation in target range

- No change required

Oxygenation above the target range

- Decrease down FiO₂/ mPaw scale in 1-2 step increments

Oxygenation below target range

- Increase up FiO₂/ mPaw scale in 1-2 step increments (Consider recruitment maneuvers) (Higher MAPs may depress venous return; assure adequate volume.) (At MAP > 35 or FiO₂ > 0.9, consider prone positioning or NO)

² A recruitment maneuver consists of stopping oscillator and elevating MAP to 45 cmH₂O. Maintain for 40-60 seconds. Monitor closely for hypotension or desaturation. Return to desired settings and restart oscillator.

B mPaw /FiO₂ Scale for HFOV

Adjust FiO₂ or mPaw according to the scale to maintain oxygenation in target range
 SpO₂ 88-95% or PaO₂ 55-80 mmHg

<i>Step</i>	FiO₂	mPaw	<i>Step</i>	FiO₂	mPaw
1	0.4	24	9	0.8	32
2	0.5	24	10	0.9	32
3	0.5	26	11	1.0	32
4	0.6	26	12	1.0	34
5	0.6	28	13	1.0	36
6	0.7	28	14	1.0	38
7	0.7	30	15	1.0	40
8	0.8	30	16	1.0	42
			17	1.0	45

Figure 1. Guide used for patients receiving high-frequency oscillatory ventilation (HFOV). This chart is posted at the bedside to facilitate the approach to HFO described in this article. A, management of ventilation and oxygenation. B, suggested mean airway pressure (mPaw) and FiO₂ combinations. ΔP , oscillation pressure amplitude; ABG, arterial blood gases; BID, twice a day; f, frequency; SpO₂, oxyhemoglobin saturation by pulse oximetry; MAP, mean arterial pressure.

Table 1. Patient characteristics (mean \pm SD)

Age, yrs	42 \pm 15
Gender, M/F	12/18
Actual weight, kg	83 \pm 25
APACHE II, day of ICU admission	25 \pm 7
APACHE II, day of HFO initiation	26 \pm 7
MODS, day of HFO initiation	8 \pm 3
Respiratory variables immediately prior to HFO	
Respiratory rate	34 \pm 3
Tidal volume, mL/kg PBW	5.9 \pm 1.1
Plateau airway pressure, cm H ₂ O	32 \pm 7
FiO ₂	0.93 \pm 0.10
PEEP, cm H ₂ O	13.3 \pm 4.1
pH	7.22 \pm 0.13
Paco ₂	70 \pm 33
Pao ₂	71 \pm 21

APACHE, Acute Physiology and Chronic Health Evaluation; ICU, intensive care unit; HFO, high-frequency oscillation; MODS, Multiple Organ Dysfunction Score; PBW, predicted body weight; PEEP, positive end-expiratory pressure.

PBW for males = 50 + (0.91 \times [height in cm - 152.4]), for females = 45.5 + (0.91 \times [height in cm - 152.4]).

ence in the maximal frequency achieved among the eight patients intubated with a 7.0 to 7.5-mm endotracheal tube (mean 8.8 Hz) and the 22 patients intubated with an 8.0-mm endotracheal tube (8.9 Hz). Similarly, there was no significant difference in the proportion of patients with smaller or larger endotracheal tubes who were not increased to >5 Hz (2 of 8 vs. 3 of 22). The maximal frequencies achieved are shown in Figure 3, used in association with a Δ P of 81 \pm 11 cm H₂O. The mean arterial blood gas values at the time of this maximal frequencies were pH 7.31 \pm 0.06 (range 7.23–7.48), Paco₂ 58 \pm 21 mm Hg (range 34–124 mm Hg), and Pao₂ 82 \pm 33 mm Hg (range 54–223 mm Hg). In patients who later deteriorated, frequency typically had to be lowered as gas exchange or metabolic acidosis worsened. An endotracheal tube cuff leak was also used to assist CO₂ clearance in nine patients at some point in their course on HFO. Despite the recommendation that

cuff leak be applied whenever frequency could not be raised to >7 Hz, it was first added at 3–5 Hz in all patients except one who had a cuff leak added while still at 11 Hz. The addition of a cuff leak immediately reduced Paco₂ by 13 \pm 17 mm Hg (range +7 to -47, p = .04). In only five patients, frequency was not increased to >5 Hz at any time because of acidosis. In four of these, frequency had to be reduced to 3–4 Hz.

Patients were divided into those who achieved a maximal frequency >8 Hz (18 patients) and those whose maximal frequency was \leq 8 Hz. Comparing these two groups, there were no differences in baseline weight, endotracheal tube size, pH, Paco₂, Pao₂, respiratory system compliance, or minute ventilation at their last measurement before beginning HFO.

The mean duration of HFO was 152 \pm 139 hrs (median 88 hrs). Relatively high doses of sedatives were administered to suppress respiratory efforts (13 \pm 7 mg/hr of midazolam and 387 \pm 211 mm/hr of fentanyl at 24 hrs). Thirteen of the 30 patients received neuromuscular blockade, either as a continuous infusion or as an occasional bolus, at some time during their period on HFO. Six patients developed a pneumothorax requiring chest tube placement while on HFO. Mean length of ICU stay was 19 \pm 12 days (median 15.5 days). Eleven patients (37%) survived to hospital discharge. ICU length of stay tended to be longer in survivors than nonsurvivors (25 \pm 12 vs. 16 \pm 12 days, p = .06).

DISCUSSION

Even when used at typical frequencies of 3–6 Hz, HFO in adults provides tidal volumes smaller than the 6 mL/kg predicted body weight advocated for lung-protective ventilation with conventional modes (15, 20). However, HFO is also used at quite high MPaw (9–11, 13). These pressures at the midpoint of the HFO respiratory cycle are at or above plateau pressures believed to reflect injurious degrees of lung distension on conventional ventilator modes. The rationale for attempting to further reduce the already small HFO tidal volumes is twofold: first, to minimize tidal changes in lung volume at any MPaw, and second, to attenuate potential overdistension injury during HFO at the high MPaw often used in patients with severe ARDS.

We have demonstrated that HFO with the SensorMedics 3100B can provide ac-

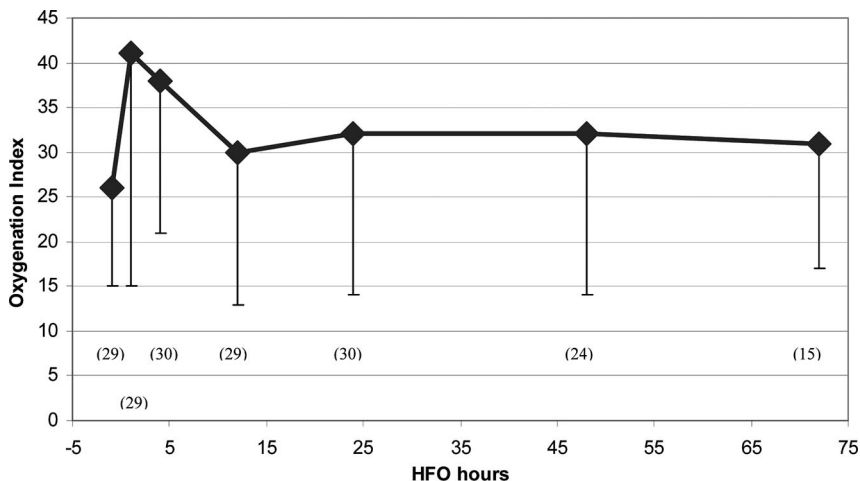


Figure 2. Oxygenation index over the first 72 hrs of high-frequency oscillation (HFO). Numbers in parentheses indicate the number of subjects with data available; fewer patients at 48–72 hrs are due to death or recovery. Oxygenation index = (FiO₂/Pao₂) \times mean airway pressure \times 100.

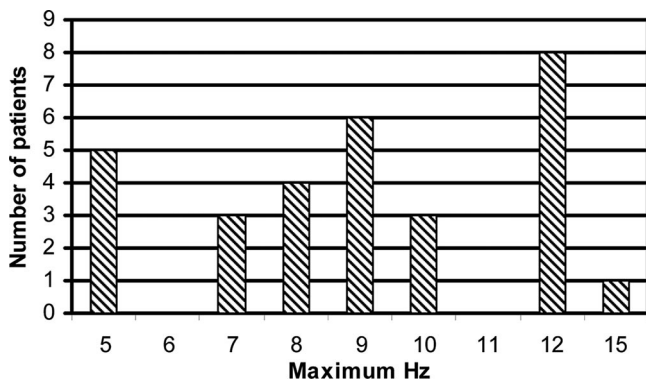


Figure 3. Histogram of the highest frequency achieved in each patient. The five patients who could not exceed 5 Hz due to refractory hypercarbia are all plotted at 5 Hz.

ceptable gas exchange in most adults with severe ARDS at frequencies higher than the typically recommended range of 5–6 Hz (17). This is facilitated by the use of higher ΔP s than are typically used with lower frequencies. These settings provide tidal volumes that are smaller than those that result from the settings recommended by the manufacturer and used in most reports of HFO in adults (15). These smaller tidal volumes may be less likely to cause ventilator-induced lung injury.

There have been a few case series reporting ventilation in adults with ARDS using frequencies up to 20 Hz. However, these have used either custom-built piston-driven ventilators (21) or a jet ventilator that is no longer manufactured (22). While these case series lend support to the feasibility of very high-frequency ventilation in adults, the technology differed greatly from the currently available ventilator. Furthermore, such high frequencies never became routine practice in any form of ventilation in adults with ARDS.

Some investigators have suggested that high-frequency ventilation should be conducted at the resonant frequency of the respiratory system (23). Frequencies near the resonant frequency would transfer energy more efficiently to the lungs and chest wall in a manner analogous to pushing a playground swing at its resonant frequency. Resonant frequencies are variable, and as high as 22 Hz, when measured in neonates receiving HFO (24). The resonant frequency of the respiratory system in healthy adults has been estimated between 6 and 9 Hz (25). We are unaware of measurements of resonant frequency in adults with ARDS. Moreover, the goal of oscillating at the resonant frequency may be inconsistent with the goals of lung-protective ventilation. Maximizing energy transfer will increase the tidal volume at a given ΔP . This would be useful if the goal were to maintain acceptable pH and P_{aCO_2} while setting the ΔP as low as possible. To maximize the lung-protective value of HFO, we suggest the goal should be to minimize tidal volume.

The Sensormedics 3100A and B ventilators provide no measurement of tidal volume. However, numerous studies in neonates, large and small animals, and lung models (20, 26–29) demonstrate the inverse relationship between tidal volume and frequency. We measured tidal volume in seven adults receiving HFO (all of whom are also included in this report) as part of a separate study (15). Measure-

ments were made at the baseline settings that had been selected by the managing physicians and at eight additional combinations of ΔP and frequency values centered on the baseline settings. Tidal volume was strongly dependent on frequency within and between patients. On the clinician-selected settings that provided acceptable gas exchange, tidal volume was as high as 156 mL in a patient ventilated at 5 Hz and $\Delta P = 90$, and as low as 58 mL in a patient ventilated at 12 Hz and $\Delta P = 60$. These measurements in a subset of our patients confirm the concepts that have guided our recommendations.

In addition to the use of small tidal volumes, optimal lung recruitment is another important element of a protective strategy of mechanical ventilation (18, 30). When we instituted our guidelines, we focused on the new approach to managing frequency. We provided an oxygenation goal and suggested combinations of F_{IO_2} and $MPaw$ (Fig. 1B) for the convenience of house staff unfamiliar with HFO but neither emphasized the use of those particular combinations nor prescribed the use of recruitment maneuvers. Therefore, in this observational study we cannot comment on how or why clinicians chose $MPaw$ or F_{IO_2} . We believe this issue is very important to provide the most lung-protective use of HFO, but the details remain unsettled. There are tradeoffs inherent in the use of higher pressure ($MPaw$ or recruitment maneuvers) vs. higher F_{IO_2} to support oxygenation. In a recent roundtable discussion, we were unable to reach consensus on this issue among a group of clinicians and researchers experienced with HFO (31). The most protective approach to oxygenation awaits experimental verification. The feasibility of using high $MPaw$ and recruitment maneuvers has been reported (11). The current report shows only the feasibility of use of higher frequencies, an element of the lung-protective approach to HFO about which there was general agreement (31).

This report has several weaknesses. This series is too small to draw conclusions about the safety of our approach. Our high mortality rate was not unexpected, given that HFO was chosen for ARDS patients with the most severe gas exchange abnormalities. Our rate of gross barotrauma was similar to other case series of ARDS or HFO (10, 11, 13, 19). This is also an observational series in which no attempt was made, beyond education, to constrain the decisions of the treating

physician team. Clinicians were not required to follow our guidelines and did so to varying degrees. Before we introduced our guidelines, most attending staff had some experience managing patients with HFO using more traditional settings and gas exchange goals. Acceptance and use of the modified guidelines improved over the time span of this case series. The maximum frequency in the first ten patients was 7.3 ± 3.3 , while in the last ten it was 10.8 ± 2.1 ($p = .012$ for comparison). This likely reflects greater familiarity with and confidence in the use of such high rates and pressures. The guidelines recommend increasing frequency even though gas exchange may have been in a range considered acceptable by most clinicians. There may have been little inclination to respond by further increasing the frequency setting when pH and P_{aCO_2} were adequate. Therefore, the data in Figure 3 may underestimate the frequencies that could be achieved in most ARDS patients. On the other hand, critically ill patients are dynamic. Ventilator settings varied in all patients as their condition changed. Even patients who achieved the high frequency shown in Figure 3 during some part of their course may have had it reduced at other times when lung mechanics or metabolic acidosis worsened. Unfortunately, because of the disruption of routine database maintenance following Health Insurance Portability and Accountability Act regulations, we do not have a large database of earlier patients managed at our institution using typical HFO guidelines for comparison.

CONCLUSION

Most adults with severe ARDS can maintain acceptable gas exchange with HFO frequencies substantially higher than 5 Hz. This approach will yield tidal volumes that are smaller, and possibly less injurious, than the currently recommended approach. Clinical trials comparing lung-protective conventional ventilation to HFO are needed before HFO should be considered for routine treatment of ARDS. However, extrapolating from proven principles of lung-protective ventilation, we recommend that adults be managed on the highest tolerated frequency; use of a high ΔP is often necessary with this approach. A trial directly comparing these very high frequencies to more traditional high frequencies would be needed to definitively determine which approach is advantageous. However, in

the absence of such confirmation, we suggest that clinical trials of HFO use the very high-frequency approach to take best advantage of its lung-protective characteristics.

REFERENCES

1. Krishnan J, Brower RG: High-frequency ventilation for acute lung injury and ARDS. *Chest* 2000; 118:795–807
2. Derdak S: High-frequency oscillatory ventilation for acute respiratory distress syndrome in adult patients. *Crit Care Med* 2003; 31(4 Suppl):S317–S323
3. Bollen CW, Uiterwaal SPM, vanVught AJ: Cumulative meta-analysis of high-frequency versus conventional ventilation in premature neonates. *Am J Respir Crit Care Med* 2003; 168:1150–1155
4. Clark RH, Gerstmann DR, Null DM Jr, et al: Prospective randomized comparison of high-frequency oscillatory and conventional ventilation in respiratory distress syndrome. *Pediatrics* 1992; 89:5–12
5. Courtney SE, Durand DJ, Asselin JM, et al: High-frequency oscillatory ventilation versus conventional mechanical ventilation for very-low-birth-weight infants. *N Engl J Med* 2002; 347:643–652
6. Gerstmann DR, Minton SD, Stoddard RA, et al: The Provo multicenter early high-frequency oscillatory ventilation trial: Improved pulmonary and clinical outcome in respiratory distress syndrome. *Pediatrics* 1996; 98:1044–1057
7. Ogawa Y, Miyasaka K, Kawano T, et al: A multicenter randomized trial of high frequency oscillatory ventilation as compared with conventional mechanical ventilation in preterm infants with respiratory failure. *Early Hum Dev* 1993; 32:1–10
8. Bollen CW, van Well GT, Sherry T, et al: High frequency oscillatory ventilation compared with conventional mechanical ventilation in adult respiratory distress syndrome: A randomized controlled trial. *Crit Care* 2005; 9:R430–R439
9. David M, Weiler N, Heinrichs W, et al: High-frequency oscillatory ventilation in adult acute respiratory distress syndrome. *Intensive Care Med* 2003; 29:1656–1665
10. Derdak S, Mehta S, Stewart TE, et al: High-frequency oscillatory ventilation for acute respiratory distress syndrome in adults: A randomized, controlled trial. *Am J Respir Crit Care Med* 2002; 166:801–808
11. Ferguson ND, Chiche JD, Kacmarek RM, et al: Combining high-frequency oscillatory ventilation and recruitment maneuvers in adults with early acute respiratory distress syndrome: The Treatment with Oscillation and Open Lung Strategy (TOOLS) pilot study. *Crit Care Med* 2005; 33:479–486
12. Fort P, Farmer C, Westerman J, et al: High-frequency oscillatory ventilation for adult respiratory distress syndrome—A pilot study. *Crit Care Med* 1997; 25:937–947
13. Mehta S, Lapinsky SE, Hallett DC, et al: Prospective trial of high-frequency oscillation in adults with acute respiratory distress syndrome. *Crit Care Med* 2001; 29: 1360–1369
14. Mehta S, Granton J, MacDonald RJ, et al: High-frequency oscillatory ventilation in adults: The Toronto experience. *Chest* 2004; 126:518–527
15. Hager DN, Fessler HE, Simon BA, et al: Tidal volume delivery during high frequency oscillatory ventilation in adults with acute respiratory distress syndrome. *Crit Care Med* 2007; 35:1522–1529
16. Rossing TH, Slutsky AS, Lehr JL, et al: Tidal volume and frequency dependence of carbon dioxide elimination by high frequency ventilation. *N Engl J Med* 1981; 305:1375–1379
17. 3100B Operator's Manual. Yorba Linda, CA, SensorMedics Corporation, 1999
18. Froese AB: High-frequency oscillatory ventilation for adult respiratory distress syndrome: Let's get it right this time! *Crit Care Med* 1997; 25:906–908
19. ARDS Network Investigators: Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med* 2000; 342: 1301–1308
20. Sedeek KA, Takeuchi M, Suchodolski K, et al: Determinants of tidal volume during high-frequency oscillation. *Crit Care Med* 2003; 31:227–231
21. Butler WJ, Bohn DJ, Bryan AC, et al: Ventilation by high-frequency oscillation in humans. *Anesth Analg* 1980; 59:577–584
22. Gluck E, Heard S, Patel C, et al: Use of ultrahigh frequency ventilation in patients with ARDS—A preliminary report. *Chest* 1993; 103:1413–1420
23. Venegas JG, Fredberg JJ: Understanding the pressure cost of ventilation: Why does high-frequency ventilation work? *Crit Care Med* 1994; 22(9 Suppl):S49–S57
24. Lee S, Alexander J, Blowes R, et al: Determination of resonance frequency of the respiratory system in respiratory distress syndrome. *Arch Dis Child Fetal Neonatal Ed* 1999; 80:F198–F202
25. DuBois A, Brody A, Lewis D, et al: Oscillation mechanics of lungs and chest in man. *J Appl Physiol* 1956; 8:587–594
26. Dimitriou G, Greenough A, Kavvadia V, et al: Volume delivery during high frequency oscillation. *Arch Dis Child Fetal Neonatal Ed* 1998; 78:F148–F150
27. Hager DN, Fuld M, Kaczka DW, et al: Four methods of measuring tidal volume during high frequency oscillatory ventilation. *Crit Care Med* 2006; 34:751–757
28. Pillow JJ, Wilkinson MH, Neil HL, et al: In vitro performance characteristics of high-frequency oscillatory ventilators. *Am J Respir Crit Care Med* 2001; 164:1019–1024
29. Scalfaro P, Pillow JJ, Sly PD, et al: Reliable tidal volume estimates at the airway opening with an infant monitor during high-frequency oscillatory ventilation. *Crit Care Med* 2001; 29:1925–1930
30. Rimensberger PC, Pristine G, Mullen JBM, et al: Lung recruitment during small tidal volume ventilation allows minimal positive end-expiratory pressure without augmenting lung injury. *Crit Care Med* 1999; 27: 1940–1945
31. Fessler HE, Derdak S, Ferguson ND, et al: A protocol for high-frequency oscillatory ventilation in adults: Results from a roundtable discussion. *Crit Care Med* 2007; 35: 1649–1654