Comparison of Conventional Mechanical Ventilation and High-frequency Ventilation

A Prospective, Randomized Trial in Patients with Respiratory Failure

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Acute respiratory failure (ARF) following trauma or sepsis has a mortality rate of 50% to 85%. The mainstays of treatment are mechanical ventilation and positive end-expiratory pressure (PEEP). In the past decade, many reports have claimed superiority of high frequency ventilation (HFV) in the treatment of ARF. We structured a prospective randomized trial of HFV *versus* conventional mechanical ventilation (CMV) in the treatment of acute respiratory failure. All patients admitted to the Surgical Intensive Care Unit (SICU) were eligible for the study. On admission patients identified for being at risk of developing acute respiratory failure were randomized to receive either HFV or CMV. Patients were treated to the same therapeutic endpoint (pH > 7.35, $PaCO_2$ 35 to 45 torr, $Pa0_2/FI0_2$ > 225). Daily ventilatory support, fluid and drug requirements, and cardiopulmonary variables were recorded. One hundred thirteen patients were entered into the study. Of these, 100 completed the study (HFV n = 52, CMV n = 48) and 60 developed acute respiratory failure (HFV n = 32, CMV n = 28). Patients on HFV reached the therapeutic endpoint at a lower level of continuous positive airway pressure and mean airway pressure; however there were no differences in mortality, SICU days, hospital days, incidence of barotrauma, number of blood gases, or cardiovascular interventions. This report suggests that HFV offers no concrete advantages over CMV when applied in a prospective fashion for the treatment of acute respiratory failure.

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THE HIGH MORBIDITY and mortality rates in patients with the adult respiratory distress syndrome (ARDS) continues to be an important consideration for surgeons caring for critically ill patients.[1,2] In the past decade, many attempts have been made to predict and prevent ARDS. Despite new insights gained during this time, mechanical ventilation and end-expiratory pressure (EEP) remain the mainstays of treatment.[3] The type of mechanical ventilation and level of EEP used, however, continue to be subjects of considerable controversy.[4-7] Regardless of the mode of ventilatory support used, approximately 10% to 15% of patients will have progressive hypoxemia and exhibit no response to EEP.[8,9] This group of patients includes those with pre-existing obstructive pulmonary disease, massive pulmonary airleaks, and viral pneumonia.[1]

During the late 1970s and early 1980s, a new type of ventilatory support was touted as a solution for the complications and failures of conventional ventilation. This technique, generically termed high-frequency ventilation (HFV), actually represented a variety of techniques as dissimilar to one another as they were to conventional ventilation. The specifics of each type of system are beyond the scope of this manuscript and have been reviewed extensively elsewhere.[10] The common characteristics of high-frequency ventilation include[1] a rate greater than three times normal,[2] tidal volumes considerably less than normal, and[3] a ventilator circuit with a negligible compressible volume.[11] High-frequency ventilation has been reported to cause less circulatory interference than conventional mechanical ventilation, reduce airleaks in bronchopleural fistulae, and create similar or improved gas exchange at lower airway pressures.[11] More than 300 manuscripts were published on HFV during the period from 1975 to 1985. Only one of these approached HFV in a prospective, randomized fashion.[12]

The present study was undertaken to examine the differences between conventional mechanical ventilation and high-frequency percussive ventilation (HFPV), applied in a random fashion to surgical patients with ARDS.

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Materials and Methods

All patients admitted to the Surgical Intensive Care Unit (SICU) from July 1985 to July 1987 who required mechanical ventilation were considered eligible for the study. Criteria for admission were determined by predictive equations identifying patients at risk for developing ARDS.[13] (Table 1) The diagnosis of ARDS was made when the following were seen concominantly: (1) diffuse, bilateral infiltrates on chest radiographs; (2) $Pa0_2$ less than 60 ($FI0_2 > 0.40$); (3) pulmonary capillary wedge pressure less than 16 torr; and (4) sufficeint injury to warrant a high index of suspicion for the disease. Patients excluded from the study included those with head injuries requiring mechanical ventilation, minors, prisoners, the mentally infirm, and pregnant women. The protocol was approved by the University of Cincinnati's Institutional Review Board.

During the study period, 135 patients were eligible for the investigation. Twenty-two patients could not be randomized because informed consent could not be obtained within the first 6 hours. After entry criteria were met, the patients (n = 113) were assigned to receive conventional mechanical ventilation or HFV according to a table of random numbers.

Ventilator Descriptions

Conventional mechanical ventilation was provided by a time-cycled ventilator (IMV Bird, Palm Springs, CA). All patients were ventilated in the intermittent mandatory ventilation (IMV) mode at a measured tidal volume (V_T) of 12 to 15 cc/Kg and a respiratory rate (f) sufficient to maintain a pH of more than 7.35, normocarbia, and a spontaneous f of less than 30 BPM. Inspired oxygen concentration was maintained at 0.45, unless the clinical situation mandated an increased $FI0_2$. Continuous positive airway pressure (CPAP) was begun at 5 cmH_2O and increased in 2- to 3-cmH_2O increments until the therapeutic endpoint was reached. Inspiratory time (I_T) was set between 1.5 and 2.5 seconds (depending on f). I:E ratio was maintained at least at 1:2 Peak (PIP), mean (Paw), and end-expiratory (CPAP) airway pressures were measured at the proximal airway by a commercially available pressure monitor (Bunnell Ventilator Monitor, Mallinkrodt Critical Care, Glen Falls, NY). Humidification was provided with a wick humidifier (Conchatherm II, RCI, Arlington, IL) set to deliver a temperature of 32 C at the proximal endotracheal tube.

High-frequency Ventilator

High-frequency percussive ventilation (HFPV) was delivered by a high-frequency pulse generator (HFPG) (Bird Space Technologies, Percussionaire Corp., Sandpoint, ID). The high-frequency percussive ventilator system consists of a time-cycled, pressure-limited ventilator (pulse generator) connected to a sliding venturi at the airway. The ventilator allows control of inspiratory and expiratory time, peak airway pressure, CPAP, and percussive frequency. The resulting airway pressure waveform resembles interrupted high-frequency jet ventilation. A comparison of a single breath with each ventilation system is shown in Figure 1 for clarification. Inspiratory and expiratory times were manipulated, along with PIP, to maintain pH of more than 7.35, normocarbia, and a spontaneous f less than 30 BPM. Continuous positive airway pressure was started at 5 cmH_2O and increased in 2- to 3-cmH_2O increments until the therapeutic endpoint was achieved. Percussive frequency was increased to improve oxygenation and decreased to improve CO_2 elimination. The optimal range of the frequency used was 200 to 600 BPM, as described previously.[10] Airway pressures were measured at the patient airway, approximately 8 cm distal from the injector of the venturi, thus preventing artifacts in pressure measurements from entrainment of gases. Humidification was provided in the same manner as with conventional mechanical ventilation. The unique part of the HFV system is the sliding venturi that serves as inspiratory and expiratory valve, as well as the source of CPAP. Figure 2 depicts operation of the sliding venturi in inspiration and expiration.

TABLE 1. *Patient Demographics*

Demographics	Conventional	High Frequency	Total
Total number of patients	48	52	100
Number of trauma patients	33 (69%)	34 (65%)	67 (67%)
Number of surgery patients	15 (31%)	18 (35%)	33 (33%)
Number of patients with ARDS	28/48 (60%)	32/52 (61.5%)	60 (60%)
Number of ARDS/trauma	17/33 (51%)	21/34 (62%)	38/67 (56%)
Number of ARDS/surgery	11/15 (73%)	12/18 (67%)	23/33 (70%)
Total mortality	10/48 (21%)	10/52 (19%)	20/100 (20%)
Mortality with ARDS	10/28 (36%)	10/32 (31%)	20/60 (33%)
Mortality with ARDS/trauma	3/17 (18%)	4/21 (19%)	7/38 (18%)
Mortality with ARDS/surgery	7/11 (64%)	6/12 (50%)	13/23 (56.5%)

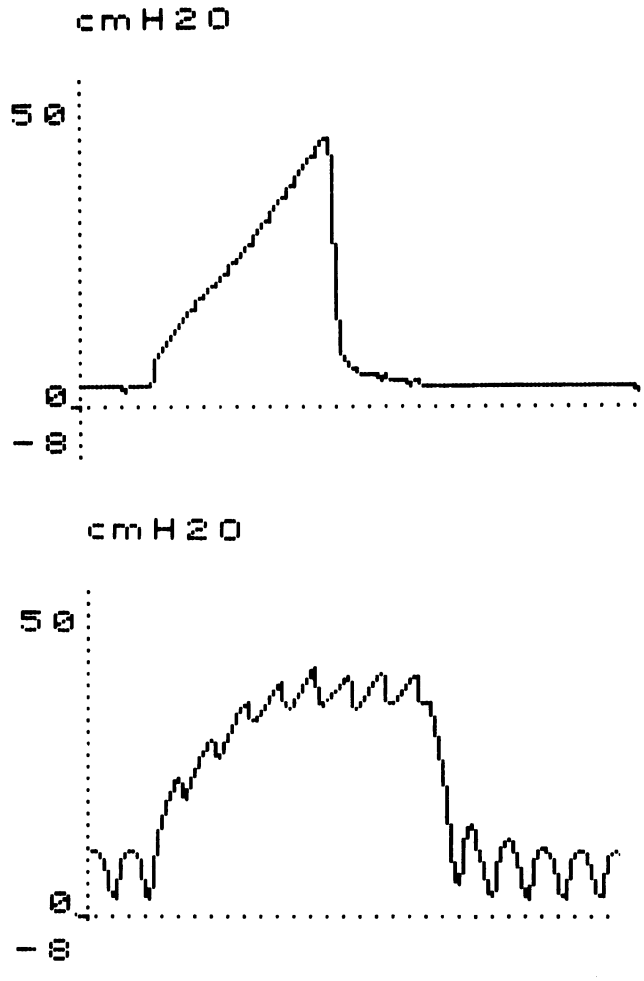

FIG. 1. The pressure tracing during a single breath with conventional and HFPV.

Monitoring

All patients were monitored by standard Intensive Care Unit practices. Vital signs were recorded at least hourly, and the electrocardiogram was monitored continuously. Continuous arterial blood pressure monitoring by indwelling arterial line was standard. Flow-directed, pulmonary artery catheters (Edwards Lab, Santa Anna, CA) were placed when clinically indicated. No lines were placed solely for the purpose of the study. Arterial and mixed venous blood for analysis of blood gases and pH were made several times daily in stable patients, after each ventilator change, and when clinical examination suggested a deterioration in the patient's condition. Blood gas analysis was performed immediately after sampling and was corrected for the patient's body temperature. Oxygen saturation was also measured for each blood gas analysis (OSM-2, Radiometer, Copenhagen, Denmark). Thermodilution cardiac output determinations were measured at least three times daily and were performed in triplicate. Pressure monitoring information recorded with each ventilator change, along with blood gas information and cardiac output, were used to calculate stroke volume, stroke volume index, left ventricular stroke work, left ventricular stroke work index, right ventricular stroke work, pulmonary vascular resistance, cardiac index, systemic vascular resistance, systemic vascular resistance index, arterial oxygen content (CaO_2), and mixed venous oxygen content (CVO_2), oxygen content, arterial-mixed venous oxygen difference, intrapulmonary shunt ($\dot{Q}sp/\dot{Q}t$), oxygen delivery ($\dot{D}O_2$), and oxygen consumption ($\dot{V}O_2$). PaO_2/FIO_2 ratios were calculated from arterial PaO_2 and ventilator FIO_2.

Ventilator Care

All ventilators were checked by the staff respiratory therapist every 2 hours. The checklist consisted of measuring and recording ventilator settings (FIO_2, f, CPAP, V_T, inspiratory, and expiratory time) and patient-related variables (PIP, Paw, spontaneous f, and spontaneous V_T). After each use ventilators were cleaned according to standard infection control policies and checked to verify appropriate function. Ventilator failures were recorded and the cause determined.

Therapeutic Endpoints

Both groups were treated to the same therapeutic endpoint. Oxygenation endpoints were a PaO_2/FIO_2 of more than 225 in patients without pulmonary artery catheters and a Qsp/Qt less than 20% in those with pulmonary artery catheters. Ventilation was adjusted as described above. FIO_2 was only increased when an increase in CPAP to more than 20 cmH_2O could not meet oxygenation cri-

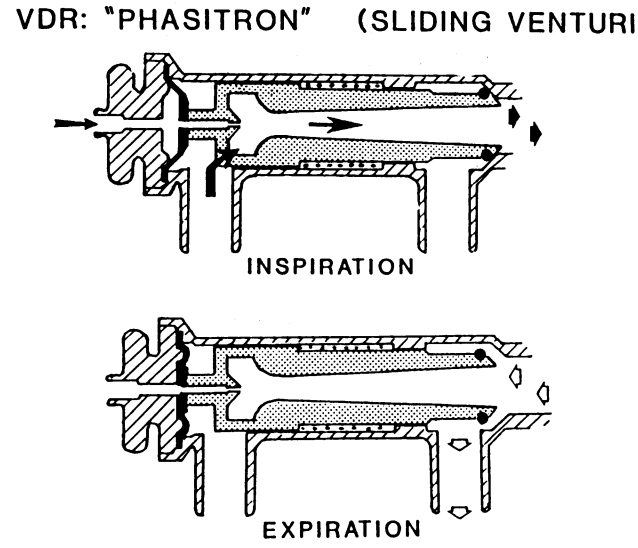

FIG. 2. The sliding venturi used with HFPV. During inspiration (top), gas pushes the venturi forward and flow is delivered to the patient. During expiration, the venturi releases backward, allowing for passive expiration.

teria. Cardiac index was supported with volume loading and/or inotropic agents, as the clinical situation indicated, to a minimum of 3.0 L/minute/m^2. Hemoglobin was maintained at more than 12 g/dL by appropriate administration of blood products.

Discontinuation of Mechanical Ventilation

All patients were weaned from mechanical ventilation using established criteria.[14,15] When CPAP was 5 cmH_2O, $FIO_2 \leq 0.45$, and spontaneous f less than 30 BPM, patients were placed on room air (0.21), and 5 cmH_2O CPAP, through the ventilator, for 20 minutes. At the end of the trial, arterial blood was drawn for analysis and the patient was returned to the original settings. If PaO_2 was more than 55, spontaneous f was less than 30 BPM, $PaCO_2$ was normal for that patient, and pH was more than 7.35, an attempt at extubation was made.

Crossover

If any patient failed to reach the therapeutic endpoint within 24 hours, the alternate mode of ventilation was attempted. After another 24 hours, the ventilatory mode, which maintained the best PaO_2/FIO_2 or Qsp/Qt, was used throughout the patient's hospital course.

Results

During the study period, 113 patients were entered into the investigation. Of these, 13 patients were removed from the study, two for insufficient data collection and 11 for failure to adhere to the protocol. Table 2 depicts the number of patients in each arm of the study, the number of trauma and surgery patients, the incidence of ARDS, and number of deaths. There were no statistically significant differences in any of these variables.

Data were tabulated for all patients. Patients were stratified into four categories: (1) all patients ventilated with CMV; (2) all patients ventilated with HFV; (3) patients ventilated with CMV who developed ARDS; and (4) patients ventilated with HFV who developed ARDS.

Analysis of pretreatment variables including age, Therapeutic Intervention Scoring System, Glasgow Coma Scale, age, and Trauma Score demonstrated no appreciable differences (Table 3).

TABLE 2. *Patient Population*

	CMV (Total)	HFV (Total)	CMV (ARDS)	HFV (ARDS)
Age	45 ± 20	41 ± 16	49 ± 21	42 ± 18
Sex	18/30	17/35	10/18	11/21
TISS (admission)	41 ± 6	42 ± 7	47 ± 6	47 ± 8
GCS (admission)	12 ± 3	12 ± 3	11 ± 3	12 ± 2
TS	11 ± 2	11 ± 3	9 ± 1.6	8 ± 1.7

TABLE 3. *Ventilator Variables at the Time the Therapeutic Endpoint Was Reached*

Respiratory Parameter	CMV (Total)	HFV (Total)	CMV (ARDS)	HFV (ARDS)
Time to reach therapeutic endpoint	0.41 ± 0.02	0.39 ± 0.2	0.53 ± 0.2	0.49 ± 0.2
FIO_2	0.48 ± 1	0.46 ± 1	0.51 ± 0.1	0.47 ± 1.2
PIP	43 ± 15	38 ± 11	60 ± 13	45 ± 12*
CPAP	11 ± 3	9 ± 4	16.5 ± 4	13 ± 3†
Paw	14 ± 2	12 ± 2	22 ± 5	17 ± 5†
I_T	1.6 ± 0.4	2.3 ± 0.6	1.7 ± 0.3	2.5 ± 0.7†

* $p < 0.05$ CMV-ARDS *vs.* HFV-ARDS.
† $p < 0.01$ CMV-ARDS *vs.* HFV-ARDS.

The therapeutic endpoint was reached in 45 of 48 patients in the CMV group and in 51 of 52 patients in the HFV group. There was no difference in the time to reach the therapeutic endpoint. When the groups as a whole were compared, there were no statistically significant differences in ventilator parameters at the time the therapeutic endpoint was reached. When the ARDS groups were compared, however, the HFV group demonstrated significantly lower peak, mean, and end-expiratory pressures and a longer inspiratory time than the CMV group (Table 4).

We also compared the raw values for blood gas and cardiovascular parameters between the groups. These were expressed as a function of ventilator days. There were no statistically significant differences in hospital days, ICU days, or ventilator days between the groups. Also there was no difference in the total number of blood gases obtained or the number of cardiac output determinations (Table 5).

The incidence of pulmonary barotrauma for all patients was 3% (3 of 100 patients). There were two pneumothora-

TABLE 4. *Study Parameters*

	CMV	HFV	p
SICU (days)	13 ± 5	14 ± 7	NS
VENT (days)	10 ± 4.2	11 ± 7	NS
HOSPITAL (days)	25 ± 17	25 ± 13	NS
ABG (total)	100 ± 52	98 ± 67	NS
ABG (day)	8.5 ± 3	8.4 ± 6	NS
VBG (total)	54 ± 44	66 ± 43	NS
VBG (day)	4.6 ± 3	5 ± 2.8	NS
CO (total)	63 ± 45	72 ± 47	NS
CO (day)	5.2 ± 3	5.4 ± 2.7	NS
PaO (torr)	15 ± 4.2	18 ± 2.6	NS
CVP (torr)	14 ± 3.6	16 ± 3	NS
CO (L/minute)	7.5 ± 2.1	7.5 ± 2	NS
CI (L/minute/m^2)	3.7 ± 1	4.1 ± 1	NS
Qsp/Qt (%)	15 ± 4	15 ± 2	NS
PaO_2 (torr)	86 ± 14	87 ± 11	NS
$PaCO_2$ (torr)	41 ± 3	40 ± 2	NS

NS, not significant.

TABLE 5. *Changes in Oxygenation and Ventilation After Crossing Over from One Ventilator to Another*

Study Parameters	CMV to HFV	HFV to CMV
Number	3	1
Change in PaO_2	+12 ± 4	+18
Change in $PaCO_2$	−4 ± 1	−2
Change in CPAP	−3 ± 2	+4
Change in PIP	−8 ± 3	+14
Change in Qsp/Qt		
Number surviving	1	0
Number reaching therapeutic endpoint	0	0

ces in the CMV and ARDS group (7%) and one in the HFV and ARDS group (3%). There were no ventilator failures in either group, although several air/oxygen blenders failed after becoming plugged with moisture from contaminated air lines.

Four patients failed to reach the therapeutic endpoint and were transferred to the alternate mode of ventilatory support. Three patients were switched from CMV to HFV and one from HFV to CMV. Of these patients none reached the therapeutic endpoint and three died. The one patient switched from HFV to CMV improved initially, but over the course of 4 hours deteriorated with blood gases reaching pretransition levels.

Discussion

Ventilatory support of the patient with acute respiratory failure is largely supportive. The goals of ventilatory support are to insure adequate oxygen delivery to the tissues and maintain normal acid-base balance while the underlying cause (sepsis, trauma, and so on) is identified and, if possible, treated. As such, mechanical ventilation itself is not life saving. Yet a myriad of ventilatory techniques have been developed during the past 10 years that have been touted as superior to conventional ventilatory support. Perhaps the most promising of these techniques is HFV.

During the late 1970s and early 1980s, HFV was said to have the following advantages over conventional ventilation: (1) lower airway pressures, (2) reduced circulatory interference, (3) improved oxygenation due to enhanced diffusion and gas mixing, (4) reduced barotraumatic potential, and (5) reduced airflow through a bronchopleural fistula. Unfortunately most of this information was obtained from descriptive studies and anecdotal reports in which HFV was substituted for CMV as a salvage treatment. As such the true advantages of HFV are difficult to determine.

In 1983, Carlon et al.[12] published the results of a randomized trial comparing high-frequency jet ventilation (HFJV) to conventional ventilation in 309 postoperative patients. They concluded that HFJV was as safe and reliable as CMV but provided no significant benefits. A criticism of this study is that the therapeutic end-points were different for each group.

Our study is the first, to our knowledge, to prospectively compare a method of HFV to CMV using the same therapeutic endpoints. As such, each proposed advantage of HFV will be discussed in light of the results.

This study shows that HFV provides equal oxygenation and ventilation at lower peak, mean, and end-expiratory pressures, as compared to CMV in patients with ARDS. We also found that inspiratory time tended to be longer with HFV than with CMV and hence, I:E was shorter. We believe this occurs because more attention is given to setting inspiratory and expiratory time with pressure-limited ventilation than during volume-oriented ventilation. In no situation was I:E reversed, although this has been suggested, by Gurevitch et al.,[16] as another alternative to ventilating patients with ARDS.

These reductions in airway pressures are beneficial if they reduce circulatory interference and barotrauma. Our data suggest that despite lower airway pressures, the incidence of barotrauma was unchanged and no appreciable differences were seen in cardiovascular variables.

The fact that similar oxygenation and ventilation were achieved at lower airway pressures with HFV suggests that intrapulmonary gas mixing is improved. There are several gas transport theories that appear to be active during HFV that are not present during CMV. These include radial and axial diffusion (Taylor-type dispersion), a pendeluft effect between adjacent alveolar units and enhanced diffusion created by the high-frequency percussions increasing kinetic energy of the gases. All these theories are plausible and have been shown to occur in models of the tracheobrochial tree and in animals.[17,18] Their contribution to gas exchange in patients with ARDS is speculative, but does offer some explanation of the results obtained in our study.

Our study did not address the effects of HFV on bronchopleural airleaks. However this is the one indication for HFV approved by the Food and Drug Administration.

Perhaps the most important variables in comparing treatments is outcome. Our study did not demonstrate any significant differences in mortality, hospital days, days on the ventilator, or days in the intensive care unit. There were also no differences in the number of blood gases drawn or cardiac output determinations made per day. As such, no changes in cost could be expected between groups. Four patients failed to reach the therapeutic endpoint, three in the CMV group and one in the HFV group. The three patients switched to HFV had an improvement in oxygenation and ventilation at a lower airway pressure, but none reached the therapeutic endpoint. Of these three, only one survived. The one patient switched from HFV

to CMV had an improvement in PaO_2 but required an increase in PIP of 14 cmH_2O and in CPAP of 4 cmH_2O. This patient also did not reach the therapeutic endpoint and he did not survive.

The use of HFV appears to have waned during the past few years, partly due to the fact that the initial enthusiasm has died and given way to more practical decision making. Our results demonstrate that HFV provides comparable oxygenation and ventilation to CMV at lower airway pressures. Despite lower airway pressures, however, we did not demonstrate any differences in pulmonary barotrauma or any improvement in cardiovascular performance (as judged by the requirements for fluids or iontropes). The equality of oxygenation and ventilation at lower airway pressures suggests that HFV may enhance pulmonary gas distribution when compared to CMV. These results suggest that HFV may be advantageous in a small group of patients with some hemodynamic embarrassment in which positive airway pressure impairs venous return. Other possible uses are in patients with previous barotrauma requiring excessively high airway pressures during CMV, as a method of reducing further airleaks.

When used in a prospective fashion in patients with ARDS, HFV offers no clear advantage over CMV with respect to morbidity and mortality rates. The use of HFV should be restricted to that small group of patients refractory to conventional ventilatory techniques.

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