Effects of Inspiratory Flow Waveforms on Lung Mechanics, Gas Exchange, and Respiratory Metabolism in COPD Patients During Mechanical Ventilation*

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Study objective: **The clinical usefulness of varying inspiratory flow waveforms during mechanical ventilation has not been adequately studied. The aim of this study was to compare the effects of three different respiratory waveforms on the pulmonary mechanics, gas exchange, and respiratory metabolism of ventilated patients with COPD.**
Design: **A randomized and comparative trial of consecutive patients.**
Setting: **Medical ICUs of a 2,000-bed university hospital.**
Patients: **Fifty-four patients with COPD were enrolled.**
Interventions: **Constant, decelerating, and sine waveforms were applied to each patient in a random order.**
Measurements and results: **With tidal volume, inspiratory time, and inspiratory frequency being kept constant, the decelerating waveform produced statistically significant reductions of peak inspiratory pressure, mean airway resistance, physiologic dead space ventilation (V_D/V_T), $Paco_2$, and symptom score. There was also a significant increase in alveolar-arterial oxygen pressure difference with the decelerating flow waveform, but there were no significant changes in mean airway pressure, arterial oxygenation, heart rate, mean BP, and other hemodynamic measurements. In addition, assessment on the work of breathing (WOB) revealed that ventilator WOB values were reduced with the decelerating waveform. Oxygen consumption and carbon dioxide output were virtually not affected by changing inspiratory flow waveforms. Except for V_D/V_T, the effects of constant square and sine waveforms were similar to each other and could not be separated statistically.**
Conclusions: **The most favorable flow pattern for ventilated patients with COPD appeared to be the decelerating waveform. There are possibilities for the improvement of ventilation in these patients by selecting an appropriate inspiratory flow.** ***(CHEST 2002; 122:2096–2104)***

Key words: COPD; gas exchange; inspiratory flow waveforms; mechanical ventilation; oxygen consumption; pulmonary mechanics; work of breathing

Abbreviations: ALI = acute lung injury; Cst = static lung compliance; F_{ECO_2} = fraction of expired CO_2; F_{IO_2} = fraction of inspired oxygen; I/E = inspiratory/expiratory ratio; IPPV = intermittent positive pressure ventilation; MAP = mean airway pressure; MRaw = mean airway resistance; $P(A\text{-}a)O_2$ = alveolar-arterial oxygen pressure difference; PAO_2 = alveolar partial pressure of oxygen; PCV = pressure-controlled ventilation; PEEP = positive end-expiratory pressure; PEEPi = intrinsic positive end-expiratory pressure; PIP = peak pressure observed during mechanical inflation; PP = plateau pressure; T_I = inspiratory time; T_{TOT} = total breathing cycle time; $\dot{V}CO_2$ = carbon dioxide output; VCV = volume-controlled ventilation; V_D/V_T = physiologic dead space ventilation; $\dot{V}_E$ = minute ventilation; $\dot{V}O_2$ = oxygen consumption; V_T = tidal volume; WOB = work of breathing

Patients with COPD may require mechanical ventilation for the treatment of respiratory failure during acute exacerbations. The major physiologic defects in COPD are increased dead space, severe ventilation-perfusion maldistributions, marked airflow limitation, air trapping, and hyperinflation. Such defects frequently result in poor oxygenation and hypercapnia. Asynchronous and paradoxical breathing may be an inevitable response to the diaphragmatic flattening that is characteristic of patients with emphysematous lungs. Air trapping represents the incomplete emptying of lung units and is referred to as intrinsic positive end-expiratory pressure (PEEPi)

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during intermittent positive-pressure ventilation (IPPV). PEEPi increases the hazard of barotrauma by elevating alveolar pressure, increases the work of breathing (WOB), and decreases venous return and cardiac output.

In experimental models, the variation in inspiratory flow waveform and time during IPPV have been shown to affect physiologic variables in dogs.[1,2] However, contradictory results also have been obtained by other investigators,[3–5] both in human and animal studies. The situation is further complicated by the observation that the type of physiologic impairment and functional level of the ventilated lung may play a role in determining the magnitude of responses to various inspiratory flow waveforms.[6–9]

If a particular flow pattern was superior to others, it would be an advantage to the treatment of these patients and could facilitate the weaning of patients from mechanical ventilation. Nowadays, most of the modern microprocessor ventilators are capable of offering various waveforms options. However, the application of this technology in the clinical setting has not been well-documented. Therefore, the purpose of this study was to determine the effects of flow pattern on pulmonary mechanics, WOB, and respiratory metabolism in COPD patients who are receiving ventilatory support.

Materials and Methods

Patients

A group of 54 patients with COPD, consisting of 32 men and 22 women and with an age range of 48 to 72 years (mean [± SD] age, 60 ± 9 years) was studied. These patients had been regularly followed up at the outpatients clinic of a teaching hospital in the past 3 months before entry into the study. The diagnosis of pulmonary emphysema and/or chronic bronchitis fulfilled the criteria established by the American Thoracic Society.[10] The duration of COPD ranged from 2 to 10 years. The pulmonary functional status of each patient was assessed during hospital visits using an automated spirometer (model HI-501; CHEST MI Inc; Tokyo, Japan). A current (*ie*, within 2 months prior to hospital admission) value for FEV_1/FVC was used in the final analysis.

Patient characteristics are given in Table 1. Patients were in respiratory failure (*ie*, arterial $Po_2 < 50$ mm Hg and/or $Pco_2 > 50$ mm Hg), had been admitted to the medical ICU of the hospital, were intubated, and required IPPV as part of their therapy because of secondary infections and/or acute exacerbations of COPD. Patients were maintained on regimens of their usual medications, as they would have been in clinical practice. The baseline evaluation included a clinical examination, chest radiographs, an ECG, and arterial blood gas measurements. The study was approved by the local institutional human ethics committee, and informed consent was obtained from each patient after the nature of the procedures had been explained.

Table 1—*Patient Characteristics*

Characteristics	Patients, No.	Mean ± SD	Range
Clinical diagnosis			
Emphysema	23		
Chronic bronchitis	23		
Mixed*	8		
Indications for ventilator support			
Respiratory tract infections	14		
Pneumonia	19		
Acute respiratory failure	21		
Male gender	32 (60%)		
Smokers	42 (78%)		
Age, yr		60 ± 9	48–72
Duration of COPD, yr		5 ± 2	2–10
Duration of respiratory distress prior to entering study, d		5.2 ± 2.4	1–8
FEV_1/FVC, %†		44.3 ± 6.9	36.1–54.5

*Patient had both pulmonary emphysema and chronic bronchitis.
†Based upon the results of a current measurement during visits to the clinic.

Ventilator Settings

All patients received ventilation with a microprocessor ventilator (model PB-7200; Puritan-Bennett Corp; Carlsbad, CA), which allowed variations in inspiratory flow waveform. Standard connections and tubing were used, including a heated humidifier (Cascade II; Puritan-Bennett Corp). Each patient received ventilatory support in the assist-control mode. Low doses of sedatives and paralyzing agents were administered to keep the agitated patients relaxed during the initiation of mechanical ventilation, if needed. The drugs were discontinued at least 6 h before the beginning of this study.

The study was started within 12 h after the patient's presentation to the hospital. Appropriate ventilator parameters were estimated to provide adequate oxygenation and a desired minute ventilation ($\dot{V}E$) in each patient. The estimated $\dot{V}E$ depended on body surface area and oxygen consumption ($\dot{V}o_2$) level. A tidal volume (VT) of 10 to 15 mL/kg ideal body weight was initially used and then was adjusted to produce an end-tidal carbon dioxide concentration of 4 to 5%. The fraction of inspired oxygen (FIo_2) was determined by the clinical state of the patient. The inspiratory/expiratory ratio (I/E) was 1:2.5 to 3.0. Ventilatory parameters including VT, FIo_2, inspiratory time (TI), and frequency (15 to 24 breaths/min) were then kept constant throughout the entire study period. Since the mean flow is lower than the peak flow with a decelerating waveform, it was necessary to increase the peak flow setting when this flow pattern was in use, for the purpose of diminishing the lengthening of TI.

External positive end-expiratory pressure (PEEP) was added whenever necessary. The presence and level of PEEPi (*ie*, auto-PEEP) were determined by a respiratory mechanics monitor (model CP-100; Bicore Inc; Irvine, CA), which had a flow transducer that was connected between ventilator tubing circuits and the endotracheal tube. In addition, an esophageal balloon catheter was placed into the patient's esophagus via the nostril for the measurement of esophageal pressure. Once PEEPi was detected, aggressive bronchodilation, secretion removal, and an external PEEP level of ≤ 85% of the measured PEEPi were applied for the purpose of reducing the PEEPi to < 1.5 cm H_2O. The external PEEP then was held constant throughout the entire study period.

Three inspiratory flow waveforms were compared (*ie*, constant square, decelerating, and sine) [Fig 1]. All experiments commenced with the constant square waveform. Each waveform was applied for 30 min, and readings were made at the end of this stabilization period. Respiratory rate, heart rate, and BP were also recorded. Breathing sounds were monitored by chest auscultation. After completing the first set of readings, another waveform was randomly selected by the primary physicians who were responsible for care of the patients but were not involved in the investigations. Readings for the remaining waveform were similarly obtained. Finally, the sequence went back to constant square. In 29 patients, the sequence of the waveforms studied was constant, decelerating, sine, and back to constant. In 25 further patients, the sequence was constant, sine, decelerating, and then constant. The physiologic data were collected and analyzed by investigators who were blind to the sequence of waveforms.

Measurements of Pulmonary Mechanics

All the patients were studied in the supine position. Pulmonary mechanics were assessed in terms of exhaled VT, peak pressure observed during mechanical inflation (PIP), mean airway pressure (MAP), plateau pressure (PP), static lung compliance (Cst), and mean airway resistance (MRaw). The magnitude of PIP, MAP, and PP were obtained directly from the digital readout of the ventilator and then the PEEP level was subtracted from that value. The accuracy of the airway pressure measurement by the ventilator was checked periodically with a pressure transducer connected between the Y-piece of the breathing tubes and the endotracheal tube. The exhaled VT, Cst, and MRaw values, and the ratio of TI to total breathing cycle time (TTOT) were measured using the monitor (model CP-100; Bicore). MRaw is the difference in transpulmonary pressure divided by the difference in flow taken at the same volume during both inspiration and expiration. Cst was calculated automatically by the monitor as follows:

$$\text{Cst} = \frac{\text{exhaled } V_T}{\text{PP} - \text{PEEP}}$$

In the presence of PEEPi, since the externally applied PEEP and concomitant use of bronchodilators caused the almost complete disappearance of the PEEPi, this method would not significantly underestimate the Cst.

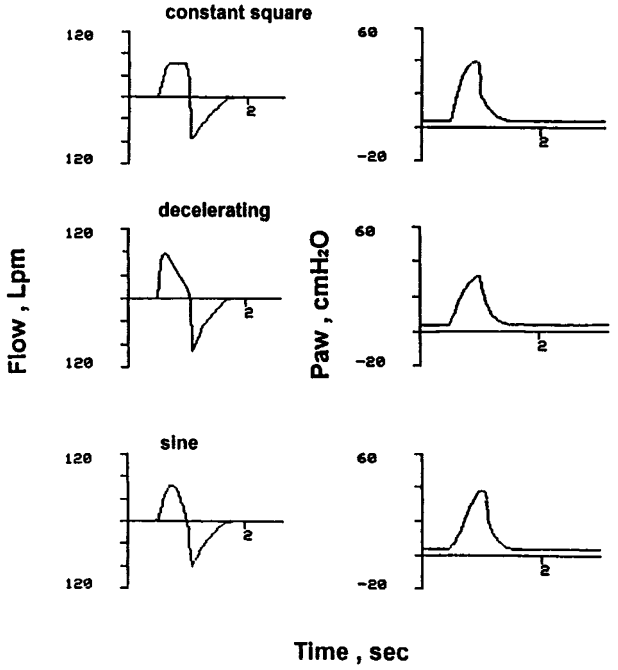

FIGURE 1. The three types of inspiratory flow waveforms studied (left panels). The right panels show airway pressure tracings of each corresponding waveform. The ventilator was connected to a lung model with PEEP set at 5 cm H_2O. It is of note that with the decelerating waveform, the peak flow setting had to be increased to diminish TI, in order to maintain a similar I/E as those achieved with the other waveforms.

Determination of Breathing Work and Respiratory Metabolism

Mechanical WOB was calculated by the integration of values for pressure and volume. This is equivalent to determining the area under a pressure-volume curve of the lung, which was displayed by the same respiratory monitor. For all variables of respiratory mechanics and the total WOB performed by the ventilator, the average values from 10 controlled breaths were used for the final analysis. Abnormal cycles caused by coughing or small VT were excluded.

$\dot{V}O_2$ and carbon dioxide output ($\dot{V}CO_2$) were measured with an integrated and automated unit (MMC Horizon System; SensorMedics Corp; Yorba Linda, CA) that was positioned at the end of the expiratory limb of the ventilatory circuit. Pulmonary gas analyzers consisting of a polarographic oxygen sensor and an infrared CO_2 analyzer were used to measure the concentrations of the expired gases. The values for mean expired O_2 fraction and mean fraction of expired CO_2 ($FECO_2$) then were used to calculate other physiologic variables. For example, $\dot{V}CO_2$ was calculated as a product of $FECO_2$ and $\dot{V}E$, and physiological dead space ventilation (VD/VT) was derived from the Enghoff modification of the Bohr equation,[11] as follows:

$$\frac{V_D}{V_T} = \frac{PaCO_2 - PECO_2}{PaCO_2}$$

In order to derive the alveolar-arterial oxygen pressure difference ($P[A\text{-}a]O_2$), PAO_2 was calculated using the ideal alveolar equation[12] as follows:

$$PAO_2 = PIO_2 - [1 - (1 - R)FIO_2] \times \frac{PaCO_2}{R},$$

where PIO_2 is the inspiratory oxygen tension and R is the respiratory quotient (*ie*, of $\dot{V}CO_2/\dot{V}O_2$). The instruments were calibrated periodically. The accuracy of the gas analyzers was checked on a weekly basis.

Arterial Blood Gas Analysis

Samples for blood gas analysis were taken through the radial artery catheter and analyzed (model ABL-3 blood gas analyzer; Radiometer; Copenhagen, Denmark). The arterial PO_2 was corrected for the FIO_2 used for the particular patient.

Assessment of Respiratory Symptoms

Symptom status after applying each waveform was assessed according to the scoring system, as previously described.[13] Cough, wheezing, dyspnea, chest pain and tightness, substernal irritation, headache, and fatigue were recorded. The frequency of cough and the severity of dyspnea and wheezing were assessed by

an attending physician. The presence, improvement, or progression of the other symptoms also were reported by patients through handwritten communications. Each symptom was scored as follows for the reporting period: 0, not present; 5, minimal (not noticeable unless asked about); 10, mild (noticeable but not bothersome); 20, moderate; 30, severe; and 40, incapacitating. For each patient, the same physician performed all measurements for ascertaining the symptom scores throughout the study. The overall respiratory symptom status was expressed by the sum of all the individual scores recorded.

Statistical Analysis

All data were coded, entered into an IBM-compatible computer, and analyzed using appropriate software (SAS; SAS Institute; Cary, NC). Statistical analysis was performed by using repeated-measures analysis of variance, and multiple pairwise comparisons between groups were performed by *t* test with Bonferroni correction, when appropriate. Respiratory symptom score data were analyzed by the Friedman test, followed by use of an adaptation of the Student-Newman-Keuls test for use in multiple comparisons. p Values of $\leqq 0.05$ were regarded as being significant.

Results

Ventilator Variable

Table 2 shows the mean values of ventilator variables after varying the inspiratory flow waveform to each modality. It is evident from this table that both VT and tidal frequency, and thus the $\dot{V}E$, did not change throughout the entire study period. The average values of the ventilatory pattern during initial and final constant square flows were similar, verifying the reproducibility of the system. There also was no significant difference in TI/TTOT ratio in all instances. Although the decelerating waveform was associated with a slightly higher mean inspiratory flow compared to both constant square and sine flow patterns, this was statistically insignificant ($p = 0.647$ [analysis of variance]).

Breathing Mechanics

In regard to airway pressure, the decelerating waveform produced a significantly lower PIP than did those of the constant square and sine waveforms. There was no significant difference in this variable between the constant square and sine waveforms (Table 3). Although the decelerating waveform was associated with a slightly higher MAP than the other two flow patterns, this difference did not achieve statistical significance. In addition, alteration in the inspiratory flow waveforms had no impact on PP and Cst. For VD/VT, the highest ratio was found with constant square flow, and the lowest was found with decelerating flow ($p < 0.001$). A decrease in VD/VT by 17% was found when the flow was changed from constant square to decelerating, while it increased by 18% on returning to constant square. The effects of sine flow on VD/VT could be separated statistically from those of the decelerating and constant square waveforms ($p < 0.001$ and $p < 0.01$, respectively), with values for sine flow falling between the latter two. There were no significant changes in breathing mechanics between the periods when the initial and final constant square waveforms were applied.

Gas Exchange

Varing inspiratory flow had no effect on arterial pH and oxygenation (Table 4). There was no difference in $PaCO_2$ between the constant square and sine waveforms. However, the decelerating waveform produced a significantly higher $P(A\text{-}a)O_2$ and significantly lower $PaCO_2$ than did either the constant square or sine waveforms ($p < 0.01$). There was no difference in $P(A\text{-}a)O_2$ when the constant square waveform was compared to the sine waveform. On the other hand, analysis of the hemodynamic data showed that heart rate and mean BP were apparently not affected by changing the inspiratory flow patterns (Table 4).

WOB

As shown in Table 5, the average values for MRaw and ventilator WOB were lowest with decelerating flow. On returning to the constant square waveform, these two variables increased by 12% ($p < 0.05$) and 23% ($p < 0.001$), respectively. The mean values of WOB were similar between measurements of the initial and final constant square waveforms. More-

Table 2—*Group Mean Ventilator Variable Data by Inspiratory Flow Waveforms*

Ventilator Variable	Waveforms (mean ± SD)			
	Constant Square (Initial)	Sine	Decelerating	Constant Square (Final)
VT, mL	562 ± 67	558 ± 65	566 ± 59	571 ± 72
Frequency, breaths/min	18.2 ± 1.7	18.6 ± 1.4	18.4 ± 1.9	18.5 ± 1.3
$\dot{V}E$, L/min	10.4 ± 1.6	10.3 ± 1.5	10.6 ± 1.6	10.7 ± 1.8
TI/TTOT	0.29 ± 0.04	0.28 ± 0.03	0.29 ± 0.04	0.28 ± 0.03
Inspiratory flow, L/min	38 ± 5	37 ± 7	39 ± 7	38 ± 6

Table 3—*Effects of Alteration in Inspiratory Flow Waveforms on Breathing Mechanics in COPD Patients*

Variable	Waveforms (mean ± SD)			
	Constant Square (Initial)	Sine	Decelerating	Constant Square (Final)
PIP, cm H_2O	47.1 ± 11.5	47.8 ± 10.8	39.5 ± 9.7*	46.6 ± 11.0
MAP, cm H_2O	7.6 ± 4.2	7.2 ± 4.8	8.4 ± 4.5	8.1 ± 3.9
PP, cm H_2O	20.2 ± 9.1	19.6 ± 10.6	18.9 ± 8.8	21.4 ± 10.4
VD/VT, %	58.4 ± 5.2	54.5 ± 6.3†	48.6 ± 5.5*	57.6 ± 4.9
Cst, mL/cm H_2O	35.3 ± 8.9	35.8 ± 11.2	36.6 ± 9.3	37.2 ± 9.7

*Values of the variables are compared to those of either constant square or sine waveform by Bonferroni *t* test ($p < 0.001$).
†Values of the variable are compared to those of constant square waveform by Bonferroni *t* test ($p < 0.01$).

over, the symptom score improved to a greater extent with decelerating flow than during the other two flow inflations.

Respiratory Metabolism

Neither $\dot{V}O_2$ nor CO_2 production were affected by varying the inspiratory flow waveforms. There were no significant changes between the beginning and the end sets of measurements for $\dot{V}O_2$ and $\dot{V}CO_2$ with the constant square flow.

Discussion

Our findings revealed that in patients with chronic airflow limitation, the decelerating waveform significantly reduced PIP and, although not statistically significant, tended to increase MAP if VT, respiratory rate, and I/E were kept constant. The results are consistent with those of some other investigations,[6–9,14] either on human subjects or in animal models, although in the latter cases the underlying physiologic impairment of the subjects or animals studied was not necessarily obstructive[7–9,14] and a fixed VT might not have been used.[8,9]

Overdistension of the lung has been advocated as an important factor predisposing the patient to barotrauma. Hyperinflation may result from large VT values and high airway pressure and PEEP values. Our data demonstrated a lower PIP with decelerating flow. In fact, this is a relatively consistent finding across all studies, with even flows applied by employing modern pressure-controlled ventilation (PCV) or volume-controlled ventilation (VCV).[15–17] However, the relationship between PIP and barotrauma is questionable in the setting of significantly increased airway resistance. Since PP remained the same, this suggests that the high flow meeting the endotracheal tube during use of the constant square and sine waveforms is the cause of the elevated PIP. Therefore, it is still too early to conclude that decelerating flow can reduce the risk of barotrauma in patients with COPD.

Increases in MAP appeared to be directly related to increases in oxygenation.[18,19] Moreover, MAP may tend to be inversely related to PIP.[20] However, the elevation of MAP is not a universal consequence with decelerating flow. It has been suggested that during decelerating flow inflation, $\dot{V}E$ profoundly influences MAP at specific peak flow rates.[21] Increasing $\dot{V}E$ with low peak flow rates (*ie*, < 50 L/min) are more likely to produce a significant increase in MAP. In consideration of the finding that those patients in our sample had a relatively low $\dot{V}E$ (approximately 10 L/min) and peak flow rates frequently exceeding 50 L/min, MAP is not anticipated to be definitely increased. It is not surprising, therefore, that the decelerating waveform produced no

Table 4—*Effects of Alteration in Inspiratory Flow Waveforms on Gas Exchange and Cardiovascular Data in COPD Patients*

Variable	Waveforms (mean ± SD)			
	Constant Square (Initial)	Sine	Decelerating	Constant Square (Final)
Arterial pH	7.44 ± 0.04	7.44 ± 0.07	7.43 ± 0.06	7.44 ± 0.04
PaO_2/FIO_2, mm Hg	236 ± 73	231 ± 65	223 ± 70	227 ± 67
$PaCO_2$, mm Hg	45 ± 10	45 ± 10	37 ± 9*	46 ± 12
$P(A\text{-}a)O_2$, mm Hg	133.1 ± 36.5	136.4 ± 34.2	156.3 ± 33.7*	134.4 ± 35.3
Heart rate, beats/min	106.1 ± 18.1	108.3 ± 20.2	105.3 ± 18.9	109.9 ± 20.5
BP, mm Hg	92 ± 23	88 ± 18	88 ± 21	90 ± 19

*Values of the variables are compared to those of either constant square or sine waveform by Bonferroni *t* test ($p < 0.01$).

Table 5—*Effects of Alteration in Inspiratory Flow Waveforms on WOB, Respiratory Metabolism, and Symptom Score in COPD Patients*

Variables	Waveforms (mean ± SD)			
	Constant Square (Initial)	Sine	Decelerating	Constant Square (Final)
WOB, J/L	0.92 ± 0.16	0.88 ± 0.18	0.75 ± 0.15*	0.92 ± 0.18
MRaw, cm H_2O/L/s	12.6 ± 3.1	12.4 ± 3.6	11.2 ± 2.4†	12.5 ± 3.3
$\dot{V}O_2$, mL/min	384 ± 53	389 ± 60	377 ± 49	382 ± 52
$\dot{V}CO_2$, mL/min	274 ± 52	280 ± 47	273 ± 56	276 ± 55
Symptom score	54.5 ± 13.4	58.6 ± 11.9	42.7 ± 12.3‡	56.1 ± 12.8

*Values of the variables are compared to those of either constant square or sine waveform by Bonferroni *t* test ($p < 0.001$).
†Values of the variables are compared to those of either the constant square or sine waveform ($p < 0.05$).
‡Values of the variable are compared to those of either constant square or sine waveform by Friedman test ($p < 0.05$).

significantly higher PaO_2 values in this study, when compared to those of other waveforms.

Total mechanical WOB can be measured during controlled artificial ventilation. Our data revealed that the work of inspiration performed by the ventilator was significantly decreased with the decelerating waveform in patients with acute exacerbations of COPD. Similar results were obtained by Cinnella et al[22] who found that at specific VT and low flow rates, PCV reduced the respiratory work rate more effectively than did VCV. Kallet et al[15] demonstrated that in the setting of acute lung injury (ALI) and ARDS, PCV significantly reduced patient WOB relative to VCV during assisted ventilation. Since around 11 to 30% of the total inspiratory work is required to overcome the resistance of the endotracheal tube, depending on tube size and $\dot{V}E$, a reduced WOB is certainly a clinical advantage to those patients receiving ventilatory support. The patients may become more comfortable and may require much less sedation.

Because our patients were in acute respiratory failure and were depending totally on ventilators for breathing, the situation was quite different from that of patients with stable respiration during periods of weaning from the ventilator. Therefore, ventilator WOB instead of patient WOB was measured. However, ventilator WOB remains a helpful parameter for the assessment of ventilator settings, and as a reference value for patient WOB later on during assisted ventilation when effort is required for triggering and maintaining adequate inspiratory flows.

So far as we are aware, the effects of varying inspiratory flow waveforms on metabolic WOB in ventilated patients with COPD have been reported sparsely in the literature. In the present study, we were unable to demonstrate a significant change in both $\dot{V}O_2$ and $\dot{V}CO_2$ by altering the flow patterns. Since the ventilators of all patients were put on the assist-control mode, it is unlikely that their metabolic WOB would be influenced by the reduced ventilator work of inspiration.

Our observation is that improved symptom scores with the decelerating waveform may be explained by the physiologic consequences related to this flow pattern. In patients with COPD and hypercapnic respiratory failure, a decreased VD/VT would cause $PaCO_2$ to fall, and thus would reduce the level of dyspnea. Consequently, chest pain relative to overexertion of the respiratory muscles may be improved. In addition, a lower MRaw may be of benefit to those patients with severe airflow limitation by lessening manifestations such as paroxysmal cough and wheezing respirations. Thus, an improvement in airway clearance of secretions also can be expected. Obviously, all of these factors may facilitate patients' recovery from fatigue.

Conflicting results have been obtained, from both animal models and clinical observations, as to the relative effectiveness of different inspiratory flow patterns during mechanical ventilation (Table 6). Johansson and Löfström[9] demonstrated in anesthetized patients with normal lung function that the decelerating waveform increased VD/VT and $PaCO_2$ when compared to the constant square and sine waveforms. Baker et al[6] showed in dogs with pulmonary emphysema induced by papain inhalation that with the decelerating flow waveform VD/VT and $PaCO_2$ decreased, $P(A\text{-}a)O_2$ increased, while Cst remained unchanged when compared with values obtained using the constant square and sine waveforms. In a sheep model of ALI,[23] no differences were observed in pulmonary gas exchange function between the constant square and decelerating waveforms. In the clinical setting, Al-Saady and Bennett[14] were able to demonstrate that relative to flow with the constant square waveform, the decelerating waveform in patients on IPPV for various reasons significantly decreased VD/VT, lowered $P(A\text{-}a)O_2$, improved PaO_2, and increased Cst. However, it had no effect on $PaCO_2$. In several studies[24,25] of ventilated patients, PaO_2 and $PaCO_2$ were found not to be influenced by changing the inspiratory flow waveform.

Table 6—*Comparison of Results in Studies on Pulmonary Effects of Varying Inspiratory Flow Waveforms in Mechanical Ventilation

Study	Subjects and Type of Physiologic Impairment	Variables							
		PIP	MAP	Pa_{O_2}	Pa_{CO_2}	V_D/V_T	Cst	$P(A\text{-}a)O_2$	WOB
Present study	COPD patients	D < CS and S	ND	ND	D < CS and S	D < S < CS	ND	D > CS and S	D < CS and S
Kallet et al[15]	Patients with ALI or ARDS, R	PCV < VCV							PCV < VCV
Polese et al[24]	Surgical patients, R	D and CS < S	S > CS, S = D	ND	ND				CS < D and S
Cinnella et al[22]	Patients on IPPV, both O and R	APCV < ACV	APCV > ACV	ND	ND				APCV < ACV
Mang et al[23]	Sheep with ALI	PCV = VCV (I/E = 1:2)	Kept constant	ND	ND				
Lessard et al[25]	Patients with ARDS, R	PCV < VCV (I/E = 1:2)	ND	ND	ND				
Rappaport et al[17]	Patients with ARDS, R	PCV < VCV	ND	ND	ND		ND		
Rau and Shelledy[20]	Lung model	D < S < CS	D > S > CS						
Abraham and Yoshihara[16]	Patients with ARDS, R	PCV < VCV	ND	PCV > VCV	ND				
Johansson and Löfström[9]	Anesthetized patients, normal lung	D < CS		ND	D > CS	D > CS			D = CS
Al-Saady and Bennett[14]	Patients on IPPV, both O and R	D < CS	D = CS	D > CS	ND	D < CS	D > CS	D < CS	D < CS
Johansson[8]	Patients on IPPV, both O and R	D < CS		D = CS	D = CS	ND			D = CS
Baker et al[6]	Emphysematous dogs, O		D > CS and S	ND	D < CS and S	D < S < CS	ND	D > CS and S	
Baker et al[7]	Dogs with pulmonary edema, R		D > CS and S	ND	D < CS and S	ND	ND	ND	

*D = decelerating waveform; CS = constant square waveform; S = sine waveform; O = obstructive; R = restrictive; APCV = assisted pressure-control ventilation (decelerating flow pattern); ACV = assist control ventilation (constant square flow pattern); ND = no difference.

The discrepancies in the various studies may be explained by the following reasons. (1) TI, VT, and frequency were not always kept constant in some of these studies. If a fixed VT is employed with a volume-cycled ventilator, changing the inspiratory flow waveform produces secondary changes in TI, and this may significantly alter VD/VT, PaO_2, $PaCO_2$, and MAP.[26–29] (2) Findings based on observations of healthy anesthetized patients might not be applicable to patients with significant pulmonary disease. It is very likely that a definite improvement in certain parameters with the use of a particular waveform in healthy subjects may not be observed in patients with COPD, or vice versa. (3) The nature (obstructive or restrictive) and severity of lung functional impairment of the patients receiving mechanical ventilation might influence the overall assessment of the effectiveness of altering inspiratory flow patterns. The response of a patient with a restrictive type of lung disease such as pulmonary edema, which is characterized by a large amount of shunting, small VT, and diffusion impairment, to varying inspiratory waveforms also may be different from that of a patient with an obstructive lung disease. Furthermore, just as in any other treatment modality, the improvements obtained after applying a particular inspiratory flow pattern become obscured when the disease is aggravated.

The use of decelerating flow in patients with COPD requiring IPPV was found to significantly decrease VD/VT and, thus, to decrease $PaCO_2$. It is postulated that the respiratory improvement obtained with a decelerating waveform resulted from the early delivery of VT by a high initial peak flow that is followed by a slow decline in flow. This sequence allows more time for gas to stay in the alveoli and results in a lower PIP.[14] A more even distribution of ventilation may be achieved under such a circumstance. Consequently, alveoli with prolonged time constants can be filled with more gas. Although a prolonged TI also can affect gas distribution and alveolar ventilation,[30,31] the findings associated with the decelerating waveform observed in this study cannot be entirely attributed to a longer TI, since it was diminished and TI/Ttot remained the same compared to other waveforms. The decreased $PaCO_2$ was best explained by the reduced VD/VT because $\dot{V}CO_2$ did not change.

It is of interest to note that the rise in $P(A\text{-}a)O_2$ was greater than the magnitude of the fall in $PaCO_2$ in this study. Obviously, the decrease in $PaCO_2$ contributed an increase in the alveolar partial pressure of oxygen (PAO_2), but it would not account entirely for the incremental increase in $P(A\text{-}a)O_2$. According to the alveolar air equation, PAO_2 rises when $PaCO_2$ falls, while FIO_2 is kept constant. However, the PaO_2 does not change linearly with PAO_2. In fact, PaO_2 may actually tend to decrease in response to the elevated PAO_2 in the clinical setting of COPD. This may further increase $P(A\text{-}a)O_2$. The following two possible mechanisms are suggested to explain this phenomenon: (1) increased shunting due to absorption atelectasis[32,33]; and (2) altered ventilation-perfusion relationships secondary to the redistribution of blood flow caused by vascular autoregulatory mechanisms.[34] Indeed, although statistically insignificant, PaO_2 tended to decrease with decelerating flow in this study.

In conclusion, our data indicate that the decelerating waveform should be recommended as a beneficial breathing pattern in patients with COPD requiring IPPV. The application of decelerating flow produced detectable improvement in pulmonary mechanics, gas distribution, and respiratory symptom scores. The total ventilator WOB was reduced. With careful monitoring of the ventilator variables, this modality did not provoke systemic side effects since there was no significant change in heart rate and BP compared to those obtained with the constant square or sine waveform. The lower PIP obtained with the decelerating waveform most probably can be explained by the decrease in MRaw. However, since clinical outcomes are quite sensitive to the other ventilator settings used by the primary physician, we suggest that comprehensive cardiopulmonary monitoring be performed at the same time as the application of various inspiratory flow waveforms.

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