

Effects of inspiratory flow waveforms on arterial blood gases and respiratory mechanics after open heart surgery

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ABSTRACT: The clinical usefulness of inspiratory flow pattern manipulation during mechanical ventilation remains unclear. The aim of this study was to investigate the effects of different inspiratory flow waveforms, *i.e.* constant, sinusoidal and decelerating, on arterial blood gases and respiratory mechanics, in mechanically ventilated patients.

Eight patients recovering after open heart surgery for valvular replacement and/or coronary bypass were studied. The ventilator inspiratory flow waveform was changed according to a randomized sequence, keeping constant the other variables of the ventilator settings. We measured arterial blood gases, flow, volume and pressure at the proximal (airway opening pressure (P_{ao})) and distal (P_{tr}) ends of the endotracheal tubes before and after 30 min of mechanical ventilation with each inspiratory flow waveform. We computed breathing pattern, respiratory mechanics (pressures and dynamic elastance) and inspiratory work, which was then partitioned into its elastic and resistive components.

We found that: 1) arterial oxygen tension (P_{a,O_2}) and arterial carbon dioxide tension (P_{a,CO_2}) were not affected by changes in the inspiratory flow waveform; and 2) peak P_{ao} and P_{tr} were highest with sinusoidal inspiratory flow, whilst mean P_{ao} and P_{tr} and total work of breathing were least with constant inspiratory flow, mainly because of a concomitant decrease in resistive work during constant flow inflation. The effects of the inspiratory flow profile on P_{ao} , P_{tr} and total inspiratory work performed by the ventilator were mainly due to the resistive properties of the endotracheal tubes.

We conclude that the ventilator inspiratory flow waveform can influence patients' respiratory mechanics, but has no impact on arterial oxygen and arterial carbon dioxide tension.

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During mechanical ventilation the lungs can be inflated with different pressure and flow waveforms. Originally the piston-driven mechanical ventilators generated a quasi-sinusoidal flow waveform, whereas the newer electronically controlled ventilators can also produce constant and decelerating waveforms [1, 2]. According to several theoretical [3], animal [4–7] and clinical studies [8–11], the inspiratory flow waveform affects the distribution of the inspired gas as well as respiratory mechanics and gas exchange. However, other studies failed to show any significant effect [12–14]. Thus, the clinical usefulness of inspiratory flow pattern manipulation remains unclear [2], though the capacity for selection of different inspiratory flow waveforms is provided by most modern, microprocessor-equipped ventilators [15].

The purpose of this study was to investigate the effects of constant, sinusoidal and decelerating inspiratory flow waveforms on arterial blood gases and respiratory mechanics in mechanically ventilated patients recovering from anaesthesia after cardiac surgery.

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Methods

The investigative protocol was approved by the Institutional Ethics Authorities. Informed consent was obtained from the patients or from their next of kin.

Patients

Eight mechanically ventilated patients (six males and two females), admitted to the Second Service of Anesthesia and Intensive Care of the General City and University Hospital in Verona (Italy) for recovery from anaesthesia after cardiac surgery were recruited for this study. None of the patients had a history of chronic respiratory diseases. Only the six males had a positive smoking history, though all had stopped smoking 6–12 months before surgery. All patients were intubated with a Portex cuffed endotracheal tube (ETT) (Portex, Hythe, Kent, UK) of internal diameter 7.5–9.0 mm, and were mechanically ventilated with the Puritan-Bennett 7200a (Puritan Bennett,

Table 1. – Patients' characteristics

Patient No.	Sex	Age yrs	Diagnosis	Height cm	Weight kg	ETT ID mm	F_{I,O_2}	P_{a,CO_2} kPa	P_{a,O_2} kPa	pH
1	M	38	Coronary bypass	168	66	8.5	0.35	4.48	20.6	7.37
2	F	47	Mitral stenosis	165	56	7.5	0.60	4.95	10.1	7.37
3	M	57	Aortic stenosis	180	85	9.0	0.50	4.79	12.9	7.44
4	M	63	Coronary bypass	165	72	8.5	0.40	4.31	20.2	7.38
5	M	74	Coronary bypass	170	75	8.0	0.40	4.60	17.4	7.46
6	M	67	Coronary bypass	168	72	8.0	0.40	3.90	18.0	7.43
7	M	71	Coronary bypass	165	70	8.5	0.40	4.60	21.0	7.43
8	F	46	Mitral stenosis	157	70	7.5	0.40	3.22	23.8	7.52
Mean		58		167	71		0.43	4.36	18.0	7.43
SD		13		6	8		0.08	0.56	4.5	0.05

ETT: endotracheal tube; ID: internal diameter of endotracheal tube; F_{I,O_2} : inspiratory oxygen fraction; P_{a,CO_2} : arterial carbon

Carlsbad, CA, USA) ventilator in the controlled mode (CMV) without positive end-expiratory pressure (PEEP).

Anthropometric characteristics of patients, inspiratory oxygen fraction (F_{I,O_2}) and arterial blood gases prior to the experimental procedure are shown in table 1. All patients were studied within 3 h after surgery. During this period they were recovering from anaesthesia and were still under the effect of the anaesthetic drugs (fentanyl, diazepam) and muscle paralyzing agent (pancuronium). If needed, low doses of sedative and paralyzing agents were administered to keep the patients relaxed throughout the experimental period, which lasted less than 2 h. The medical treatment and fluid administration were maintained unaltered during the study. Patients were studied in the supine position, and a physician not involved in the procedure was always present to care for the patients. The electrocardiograph (ECG), systemic arterial blood pressure ($P_{a,sys}$) and pulse oximetry were monitored throughout the study. The initial ventilator settings were prescribed by the primary physicians according to conventional criteria: tidal volume (V_T) of 10–12 mL·kg⁻¹, ventilatory frequency of 12–15 breaths·min⁻¹, inspiratory to expiratory time ratio of 1:2 to 1:3. A 0.2 s end-inspiratory pause was present in all instances, and the baseline inspiratory flow pattern was, in general, decelerating. All patients had a small polyethylene catheter inserted into the radial artery, prior to the surgical procedure, to sample arterial blood gases. Another catheter was positioned into a central vein for continuous measurements of central venous pressure (P_{cv}).

Measurements

Flow (V') was measured with a heated pneumotachograph (Fleisch No. 1 (Fleisch, Lausanne, Switzerland)) inserted between the proximal tip of the endotracheal tube and the Y-junction of the ventilator tubings by means

of a flexible T-tube, and connected to a Hewlett-Packard 47304A flow transducer (Hewlett-Packard, Cupertino, CA, USA). Volume (V) was obtained by numerical integration of the flow signal. Pressure at the airway opening (P_{ao}) was measured through a side port at the Y-junction of the ventilator tubings by means of a differential pressure transducer (143PC03D; Honeywell, Freeport, IL, USA). Tracheal pressure (P_{tr}) was sampled *via* a polyethylene catheter, whose distal tip (with some spirally-arranged side holes) was positioned in the trachea, 2 cm below the distal side of the ETT. The proximal end of the catheter was connected to a differential pressure transducer (Honeywell 143PC03D) [16].

Procedure

Special care was taken to avoid gas leaks in the circuit, particularly around the tracheal cuff, which was checked frequently. Patients were suctioned before and, if needed, during the experimental procedure. After the patients were connected with the measuring equipment, a few minutes of regular baseline ventilation ensured that arterial blood gases equilibrated with the ventilatory patterns set by the primary physicians. The inspiratory flow waveform was then changed, in a randomized sequence, to one of the following modalities: 1) constant inspiratory flow; 2) decelerating inspiratory flow; and 3) sinusoidal inspiratory flow. Peak inspiratory flow was adjusted to keep the same inspiratory to expiratory ratio. All other ventilator variables (table 2) were kept constant, and corresponded to the ventilator patterns set by the primary physicians. Each inspiratory flow waveform was maintained for 30 min. During the last 3 min of this period the physiological signals were collected through the analogue/digital (A/D) converter (Data Translation DT2801/A (Malboro, MA, USA)) at 50 Hz for data analysis. The latter was performed using the

Table 2. – Ventilatory pattern and gas exchange

Inspiratory flow waveform	$V'E$ L·min ⁻¹	V_T L	f_V b·min ⁻¹	V_T/\bar{V} L·s ⁻¹	\bar{V}/\bar{V}_{tot}	P_{a,CO_2} kPa	P_{a,O_2} kPa	pH
Constant	7.29 (1.11)	0.60 (0.11)	12.9 (1.97)	0.38 (0.06)	0.33 (0.05)	4.42 (0.48)	17.3 (3.7)	7.43 (0.04)
Decelerating	7.24 (1.01)	0.60 (0.09)	12.1 (0.84)	0.38 (0.05)	0.32 (0.02)	4.44 (0.39)	18.1 (3.3)	7.43 (0.04)
Sinusoidal	7.60* ⁺ (1.03)	0.62* (0.10)	12.3 (0.98)	0.39 (0.06)	0.33 (0.03)	4.19 (0.51)	17.2 (4.1)	7.44 (0.04)

Values are presented as mean with SD in parenthesis. $V'E$: minute ventilation; V_T : tidal volume; f_V : ventilator frequency; V_T/\bar{V} : mean inspiratory flow; \bar{V}/\bar{V}_{tot} : duty cycle. *: $p < 0.05$, sinusoidal *versus* constant; +: $p < 0.05$ sinusoidal *versus* decelerating. For further definitions see table 1.

software package ANADAT 5.1 (RHT-Infodat, Montreal, Canada). A representative experimental record is shown in figure 1. Arterial blood gases were sampled at that time and analysed by means of an ABL 330 (Radiometer, Copenhagen, Denmark) blood gas analyser.

Data analysis

Minute ventilation ($V'E$), V_T and ventilatory frequency (f_R) were computed from the volume signal. Total ventilator cycle duration (t_{tot}), inspiratory time (t_i , including the brief end-inspiratory pause of 0.2 s), expiratory time (t_E) and t_i/t_{tot} , were calculated from the flow signal. The highest values of P_{ao} and P_{tr} during inspira-

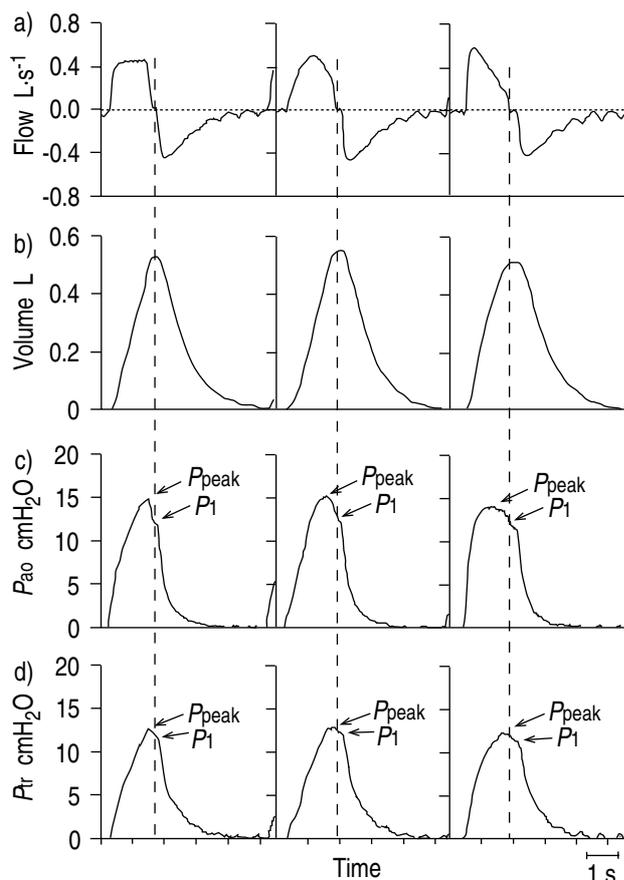


Fig. 1. — Records of: a) flow; b) volume; c) pressure at airway opening (P_{ao}); and d) tracheal pressure (P_{tr}) of a representative patient with different inspiratory flow waveforms. The horizontal dashed line on the flow tracing indicates zero flow. The vertical dashed lines indicate the onset of zero flow at end-inspiration prior to the end-inspiratory pause. P_{peak} : peak cycling pressure; P_1 : end-inspiratory value of P_{ao} and P_{tr} at zero flow.

Table 3. — Respiratory mechanics

Inspiratory flow waveform	$P_{ao,peak}$ cmH ₂ O	$P_{tr,peak}$ cmH ₂ O	\bar{P}_{ao} cmH ₂ O	\bar{P}_{tr} cmH ₂ O	P_1 cmH ₂ O	W_{tot} J·L ⁻¹	W_{ETT} J·L ⁻¹	W_{rs} J·L ⁻¹	W_{el} J·L ⁻¹	W_{res} J·L ⁻¹
Constant	22.2 [†] (8.0)	17.1 [†] (6.3)	6.13* (2.50)	5.56* (2.21)	15.4 (5.4)	1.614 ^{†+} (0.655)	0.463 ^{†+} (0.161)	1.151 [†] (0.523)	0.838 (0.370)	0.313 (0.185)
Decelerating	20.9* (8.3)	16.1** (6.3)	6.50 (2.86)	6.03 (2.54)	15.4 (5.7)	1.821 (0.733)	0.632 (0.229)	1.188 (0.593)	0.796 (0.312)	0.392 (0.316)
Sinusoidal	23.8 (9.3)	18.0 (6.4)	6.67 (2.70)	6.07 (2.45)	16.4 (4.9)	1.840 (0.770)	0.596 (0.252)	1.244 (0.552)	0.889 (0.403)	0.355 (0.174)

$P_{ao,peak}$: peak airway pressure; $P_{tr,peak}$: peak tracheal pressure; \bar{P}_{ao} : mean airway pressure; \bar{P}_{tr} : mean tracheal pressure; P_1 : end-inspiratory value of P_{ao} and P_{tr} at zero flow. W_{tot} : total inflation work; W_{ETT} : resistive work to overcome resistance of the endotracheal tube; W_{rs} : work to inflate respiratory system; W_{el} : elastic work; W_{res} : resistive work of the respiratory system; *: p,0.05, decelerating versus sinusoidal; †: p<0.05, constant versus decelerating; †: p<0.05, constant versus sinusoidal.

tion were termed, $P_{ao,peak}$ and $P_{tr,peak}$, respectively. Dynamic intrinsic PEEP ($PEEP_{i,dyn}$) was measured from the positive change in P_{ao} , relative to the atmosphere, prior to the onset of inspiratory flow [17]. The dynamic elastance of the total respiratory system (E_{dyn}) was computed from the ratio of change in (Δ) P_{ao} measured between the onset and the end of inspiratory flow over V_T [16]. The end-inspiratory values of P_{ao} and P_{tr} at zero flow were equal and were termed P_1 [16, 18]. As described previously [16, 19], the inspiratory P_{ao} and P_{tr} signals were integrated with respect to the corresponding volume changes, to obtain, respectively, the total work done by the ventilator (W_{tot}), and the work done on the respiratory system (W_{rs}) excluding the ETT. The difference between W_{tot} and W_{rs} yielded the work done by the ventilator to overcome the flow resistance of the endotracheal tube (W_{ETT}). W_{rs} was further divided into the elastic (W_{el}) and resistive (W_{res}) work. To obtain W_{el} , the relationship between the elastic recoil pressure of the total respiratory system ($P_{el,rs}$) and lung volume was assumed to be linear, and was computed as $0.5 \times E_{dyn} \times V_T^2$.

The difference between W_{rs} and W_{el} provided the work done by the ventilator to overcome the flow resistance of the total respiratory system (W_{res}). Work was also divided by V_T to obtain the work per litre of ventilation. We also computed the mean airway and tracheal pressures by integrating P_{ao} and P_{tr} over the entire ventilatory cycle and then dividing that integral by t_{tot} . For all variables of respiratory mechanics, the average values from seven mechanical inflations were used for further analysis.

Statistical analysis was performed using the non-parametric analysis of variance (Friedman's ANOVA). If the ANOVA was significant, the Wilcoxon rank test for paired observations was used. A p-value of less than 0.05 was accepted as significant.

Results

The average values of the ventilatory variables are shown in table 2. Although great care was taken to keep the ventilatory variables constant, there was, on average, a slight increase in V_T (+3%) and $V'E$ (+4%) with the sinusoidal inspiratory flow waveform compared to both constant and decelerating flow patterns. Table 2 also shows that the mean values of P_{a,O_2} and P_{a,CO_2} did not change.

Table 3 shows the average values for respiratory mechanics. A small $PEEP_{i,dyn}$ (about 1 cmH₂O) was observed in almost all instances. The values of $P_{ao,peak}$ and $P_{tr,peak}$ (fig. 1 and table 3) with sinusoidal flow were slightly, though significantly, higher than with the decelerating

and constant inflation flows. The $P_{tr, peak}$ with decelerating flow was the lowest. As illustrated by figure 1, with both sinusoidal and decelerating flow, the peak cycling pressure did not occur at the end of the mechanical lung inflation, but preceded it. Therefore, in this case $(P_{peak}-P_1)/V\dot{V}$ cannot be used to calculate interrupter resistance [18].

Table 3 also shows that the mean values of P_{ao} and P_{tr} were slightly different, the lowest values occurring during constant flow. The value of P_1 was, on average, independent of inspiratory flow waveform. E_{dyn} , amounted to 26.2 ± 9.6 cmH₂O·L⁻¹, with constant flow inflation and did not change. As also shown in table 3, the passive work of breathing (W_{tot}) was lowest during constant flow inflation; the difference been due substantially to the contribution of the ETT; on average, W_{ETT} amounted to about 30% of W_{tot} with all inspiratory flow waveforms.

Mean systemic arterial pressure (81 ± 12 mmHg), central venous pressure (8 ± 4 mmHg) and cardiac frequency (101 ± 29 beats·min⁻¹) did not change.

Discussion

This study shows that, in mechanically ventilated patients recovering from anaesthesia after cardiac surgery, the arterial blood gases and haemodynamics were not significantly influenced by the inspiratory flow waveform, whereas differences in respiratory mechanics were observed.

Respiratory mechanics

A small intrinsic PEEP (PEEP_i) and an increased elastance were found in the present patients recovering from cardiac surgery, in agreement with VALTA *et al.* [20] although, in the present study, the values of PEEP_i were lower and those of the elastance higher. However, we measured dynamic elastance and not static elastance as in the study of VALTA *et al.* [20]. In patients recovering from cardiac surgery the elastance of the respiratory system may increase as a result of: 1) reduced functional residual capacity (FRC) due to the supine position and the effect of anaesthesia [1, 21, 22]; and 2) modifications in the elastic properties of the chest wall following surgery and lung atelectasis [20, 23]. Neither E_{dyn} nor PEEP_i were influenced by the variation of the inspiratory flow waveform. In contrast, $P_{ao, peak}$ was lowest with decelerating flow and highest with sinusoidal flow (table 3). However, $P_{ao, peak}$ does not reflect the actual changes in alveolar pressure [24] because it includes the flow-dependent resistive pressure dissipated in the endotracheal tube [16] and it can be out of phase with end-inflation volume (fig. 1). In contrast P_1 , which reflects the end-inspiratory alveolar pressure [25] remained the same with different inflation flow waveforms, suggesting that a potential risk of alveolar overdistention is not modified by changes in inspiratory flow profile. On average, the changes of $P_{tr, peak}$ with different inspiratory flow profiles essentially paralleled those of $P_{ao, peak}$, except that the values of $P_{tr, peak}$ were smaller because they reflected only the resistive pressure dissipated within the conducting airways of the patients.

Measurements of the "passive" work of breathing during controlled mechanical ventilation provide the only

way to measure the work done on the total respiratory system (*i.e.* lungs and chest wall) as well as to assess the impact of different inspiratory flow profiles because the other ventilatory parameters may be kept constant. In this connection it should be noted that modifications in the ventilator settings may also occur if one changes the inspiratory flow profile without adjusting the other variables to keep the ventilator pattern constant. The total work of breathing was significantly lower with constant flow inflation than with the other two inspiratory flow patterns studied. In line with our previous study [16], we found here that about 30% of the total inspiratory work was required to overcome the resistance of the endotracheal tube. In the present patients, recovering from cardiac surgery both W_{rs} and W_{ETT} were least with constant flow inflation. This is in agreement with theoretical predictions [26].

JOHANSSON and co-workers [12, 13] failed to find significant differences in the total inspiratory work of breathing between constant flow and decreasing flow waveform. In contrast, AL-SAADY and BENNETT [10] found a significant reduction of the passive inspiratory work of breathing with decelerating flow compared to constant flow. Whether these differences reflect a different patient population and/or different ventilator technology, cannot be stated.

Arterial blood gases

The effects of inspiratory flow waveform on arterial blood gases have been investigated by several authors with conflicting results [2]. A decelerating flow profile was found to elicit a significant improvement in P_{a, O_2} compared to other inflation flow waveforms in anaesthetized animals [4–6], and patients with acute respiratory failure [10]. The same was found in patients with acute respiratory failure during pressure controlled ventilation [11].

Several mechanisms were invoked to explain the possible effects of different inspiratory flow waveform on arterial blood gases. First, the decelerating flow profile can generate a more uniform distribution of ventilation in relation to perfusion [27]. Second, the decelerating flow pattern results in an increased mean lung volume and, hence, in higher mean intrapulmonary pressure, which is similar to positive end-expiratory pressure [6]. Third, if flow decreases during lung inflation, the bulk of the VT is delivered early in inspiration allowing a longer residence time for the fresh gas in the alveoli, favouring gas diffusion. In addition, the decreasing pattern allows more time for gas to enter the alveoli with long time constants [10]. Finally, airway pressure is maintained at a higher level throughout the inspiratory phase, whereas with constant flow, pressure increases gradually to the preset volume [11]. Despite all of these potential advantages with the decelerating flow profile, neither this study nor that of LAVOIE *et al.* [14] found any significant improvement in P_{a, O_2} with modifications of the inspiratory flow waveform. Also, JOHANSON and co-workers [12, 13] found that P_{a, O_2} was not affected by changes of the inspiratory flow profile (accelerating, constant, and decelerating), although P_{a, CO_2} was lowest with constant flow and highest with the decelerating flow. In patients with acute respiratory failure, the modification of the inspiratory flow waveform (accelerating,

constant and decelerating flow profiles) had negligible effects on both P_{a,O_2} and P_{a,CO_2} [13].

In this connection, it should be mentioned that the ventilator settings in the present study included a brief end-inspiratory pause (0.2 s) with all three inspiratory flow waveforms used. It has been suggested that such a pause may improve the distribution of ventilation in the presence of regional differences in airway disease. Therefore, the presence of the end-inspiratory pause may have attenuated, at least in part, the potential differences in the distribution of the inspired gas generated by the different inspiratory flow patterns [15]. We kept the end-inspiratory pause because it is commonly used in many intensive care units, including our own. However, FULEIHAN *et al.* [28] showed that end-inspiratory pauses ranging 0–1.2 s resulted in no improvement of oxygenation in patients with acute respiratory failure, although P_{a,CO_2} was decreased because of a smaller dead space with the slow flow patterns but not with the fast flow patterns. In the present study the mean inspiratory flow, *i.e.* the V_T/\bar{t}_I , was rather slow ($0.38 \text{ L}\cdot\text{s}^{-1}$), such that it seems unlikely that the brief end-inspiratory pause could entirely offset the effects of different inspiratory flow waveforms, if any were present [28].

In conclusion, in patients recovering from cardiac surgery, the inspiratory flow waveform had no effect on arterial oxygen and carbon dioxide tensions during controlled mechanical ventilation. The resistive work dissipated in the endotracheal tube was significantly influenced by the inspiratory flow waveform, being lowest with constant flow.

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References

- Nunn JF. Applied Respiratory Physiology. London, Butterworth & Co., 1987; pp. 392–422.
- Kacmarek RM, Hess D. Basic principles of ventilator machinery. In: Tobin MJ, ed. Principles and Practice of Mechanical Ventilation. New York, McGraw Hill, 1934; pp. 65–110.
- Otis AB, McKerrow CB, Bartlett RA, *et al.* Mechanical factors in distribution of pulmonary ventilation. *J Appl Physiol* 1956; 8: 427–443.
- Baker AB, Babington PCB, Colliss JE, Cowie RW. Effects of varying inspiratory flow waveform and time in intermittent positive pressure ventilation I: introduction and methods. *Br J Anaesth* 1977; 49: 1207–1220.
- Baker AB, Colliss JE, Cowie RW. Effects of varying inspiratory flow waveform and time in intermittent positive pressure ventilation II: various physiological variables. *Br J Anaesth* 1977; 49: 1221–1234.
- Modell HI, Cheney FW. Effects of inspiratory flow pattern on gas exchange in normal and abnormal lungs. *J Appl Physiol* 1979; 46: 1103–1107.
- Baker AB, Thompson JB, Turner J, Hansen P. Effects of varying inspiratory flow waveform and time in intermittent positive pressure ventilation: pulmonary oedema. *Br J Anaesth* 1982; 54: 539–546.
- Lyager S. Influence of flow pattern on the distribution of respiratory air during intermittent positive-pressure ventilation. *Acta Anaesth Scand* 1968; 12: 191–211.
- Dammen JF, Crawford T, McAslan TC, Maffeo CJ. Optimal flow pattern for mechanical ventilation of the lung. 2. The effect of a sine *versus* square wave flow pattern with and without an end-inspiratory pause on patients. *Crit Care Med* 1978; 6: 293–310.
- Al-Saady N, Bennett ED. Decelerating inspiratory flow waveform improves lung mechanics and gas exchange in patients on intermittent positive-pressure ventilation. *Int Care Med* 1985; 11: 68–75.
- Abraham E, Yoshihara G. Cardiorespiratory effects of pressure controlled ventilation in severe respiratory failure. *Chest* 1990; 98: 1445–1449.
- Johansson H, Lofstrom JB. Effect on breathing mechanics and gas exchange of different inspiratory gas flow patterns during anaesthesia. *Acta Anaesth Scand* 1975; 19: 8–18.
- Johansson H. Effect on breathing mechanics and gas exchange of different inspiratory gas flow patterns in patients undergoing respirator treatment. *Acta Anaesth Scand* 1975; 19: 19–27.
- Lavoie A, Valta P, Corbeil C, *et al.* Effect of different inspiratory flow patterns on gas exchange and hemodynamics during mechanical ventilation. *Am Rev Respir Dis* 1993; 147: A893.
- Kallet R. The effects of flow patterns on pulmonary gas exchange, lung-thorax mechanics, and circulation. *Respir Care* 1996; 41: 611–624.
- Polese G, Rossi A, Appendini L, Brandi G, Bates JHT, Brandolese R. Partitioning of respiratory mechanics in mechanically ventilated patients. *J Appl Physiol* 1991; 71: 2425–2433.
- Rossi A, Gottfried SB, Zocchi L, *et al.* Measurement of static compliance of the total respiratory system in patients with acute respiratory failure during mechanical ventilation: the effect of "intrinsic" PEEP. *Am Rev Respir Dis* 1985; 131: 672–677.
- Bates JHT, Rossi A, Milic-Emili J. Analysis of the behaviour of the respiratory system with constant inspiratory flow. *J Appl Physiol* 1985; 58: 1840–1848.
- Coussa ML, Guérin C, Eissa NT, *et al.* Partitioning of work of breathing in mechanically ventilated patients. *J Appl Physiol* 1993; 75: 1711–1719.
- Valta P, Takala J, Eissa NT, Milic-Emili J. Effects of PEEP on respiratory mechanics after open heart surgery. *Chest* 1992; 102: 227–233.
- Behrakis PK, Higgs BD, Bevan DR, Milic-Emili J. Partitioning of respiratory mechanics in halothane-anesthetized humans. *J Appl Physiol* 1985; 58: 285–289.
- D'Angelo E, Robatto FM, Calderini E, *et al.* Pulmonary and chest wall mechanics in anesthetized paralyzed humans. *J Appl Physiol* 1991; 70: 2602–2610.
- Wilcox P, Baile EM, Hards J, *et al.* Phrenic nerve function and its relationship to atelectasis after coronary artery bypass surgery. *Chest* 1988; 93: 693–698.
- Valta P, Corbeil C, Chassè M, Braidy J, Milic-Emili J. Mean airway pressure as an index of mean alveolar pressure: effect of expiratory flow limitation. *Am J Respir Crit Care Med* 1996; 6: 1825–1830.
- Milic-Emili J, Robatto FM, Bates JHT. Respiratory mechanics in anaesthesia. *Br J Anaesthesia* 1990; 65: 4–12.
- Milic-Emili J. Work of breathing. In: Crystal RG, West JB, eds. The Lung: Scientific Foundations. New York, Raven Press Ltd, 1991; pp. 1065–1075.
- Hedenstierna G, Johansson H. Different flow patterns and their effect on gas distribution in a lung model study. *Acta Anaesth Scand* 1973; 17: 190–196.
- Fuleihan SF, Wilson RS, Pontoppidan H. Effect of mechanical ventilation with end-inspiratory pause on blood-gas exchange. *Anesth Analg* 1976; 55: 122–130.