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Ventilation for low dissipated energy achieved using flow control during both inspiration and expiration

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ABSTRACT

Mechanical or thermal stresses, which cause injury, do so essentially by dissipating energy in the tissue at a rate above some threshold at which damage occurs. This principle may also be applied to a ventilated lung. Minimizing dissipated energy is therefore a promising strategy to prevent ventilator induced lung injury (VILI) [1].

In this special interest paper, we present a qualitative argument to show that dissipated energy as determined from the area enclosed by the pressure-volume (PV) loop may be minimised during ventilation by controlling the flow to be constant during both inspiration and expiration. We then demonstrate the characteristics of the PV loop and concomitant low energy dissipation that occur with this mode of ventilation in a clinical case report. In this case, we ventilated a healthy, male, 51 year old patient undergoing elective, minor laryngeal surgery with a new, specialized ventilator, which achieves accurate control of flow during both inspiration and expiration (Evone; Ventinova Medical, Eindhoven, The Netherlands) through a small-bore (4.4 mm outer diameter), cuffed tracheal tube (Tritube; Ventinova Medical, Eindhoven, The Netherlands). This mode of ventilation is called flow-controlled ventilation (FCV). During ventilation, both inspiratory and expiratory flows were kept nearly constant at 12 ± 0.98 l/min and the I:E ratio was 1:1 with a minute volume of 6.23 ± 0.15 l/min. We recorded pressure-volume loops using pressure measured directly within the patient's trachea and calculated the energy dissipated in the patient from the hysteresis area of the PV loops.

Energy dissipation was 0.17 ± 0.02 J/l, which is close to the minimum energy dissipation achievable for this minute volume. It is lower than values quoted in the literature for spontaneous breathing (0.2–0.7 J/l) and indicative values obtained with other methods of flow control (0.32 J/l). This ventilation strategy may have implications for lung-protective ventilation.

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1. Introduction

Efforts to prevent or control ventilator induced lung injury (VILI) have evolved over several decades. During this evolution, attention has centered on several ventilation variables or phenomena in turn including: plateau pressure (addressing the risk of 'barotrauma') [2,3], tidal volume (to prevent 'volutrauma') [4–6], positive end-expiratory pressure (PEEP; to minimize 'atelectrauma' caused by the cyclic collapse and reinflation of alveoli) [7–10], and 'driving pressure' (to prevent overinflation) [11,12].

While all of these variables are in one way or another associated

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https://doi.org/10.1016/j.tacc.2018.09.003 2210-8440/© 2018 Elsevier Ltd. All rights reserved. with lung stress (for example transalveolar pressure) or strain (for example tissue extension or lung volume), it has become increasingly clear that no single variable or phenomenon is responsible for the onset and exacerbation of lung damage during mechanical ventilation. Rather, it is probable that a combination of mechanical effects, many of which are linked to ventilation strategy, contribute to the problem. In many cases the mechanical effects are exacerbated by other underlying conditions such as lung heterogenity and vascular pressure [13-15].

As the lung expands and contracts with ventilation, both stress and strain change with time. As this happens work is done on the lung system or to say it differently energy is applied. This energy is either stored and can (partially) be recovered (e.g. as the work done by elastic recoil during expiration to expel gas from the airway) or is otherwise dissipated in the airways and lung tissue.

It has been suggested that the genesis of VILI may at least in part arise from non-rupturing damage occurring at a rate faster than the body is able to repair, as a result of the energy dissipation in the tissues [16]. This may be exacerbated by - for example - visco-elastic drag, local inhomogeneities, and collagen fibre rupture under repeated cycling (analogous to material fatigue). These phenomena cause local stress amplification and the initiation of significant damage at global stress levels, which appear to be well within the tolerance of the tissue [17].

For any material, the area under the stress-strain curve is the energy per unit volume applied in stretching the material [18]. If the material is subject to cyclic stress, the stress-strain curve traces out a loop and the energy dissipated in the material is proportional to the area within the loop (arising from the hysteresis) [19]. This is analogous to the pressure-volume (PV) loop during respiration, where for spontaneous breathing the work of breathing is simply the area within the loop [20,21]. For a ventilated patient, when the measured pressure is corrected for pressure drop in the ventilation system to give the intratracheal pressure, the area within the loop (when intratracheal pressure is used) is the work done by the ventilator on the patient's respiratory system. It is the energy dissipated in the patient during one breath (= respiratory cycle). This energy comes from the ventilator.

In recent years, there has been increasing interest in the potential contribution to VILI from energy applied to the patient by the ventilator during the inspiration phase of ventilation [1,22], with some evidence from work in animals to suggest that the rate at which energy is applied is indeed related to the onset of damage [23–25].

Part of the energy applied to the patient by the ventilator during inspiration is dissipated in the patient and part is stored as potential energy by the extension of the elastic components of the lung parenchyma and the chest. On expiration, this potential energy is released — and now, part of this stored energy is dissipated in the patient during expiration and part is dissipated outside the patient in the ventilator, it's associated tubing, and the atmosphere. It is possible that the energy dissipated in the patient (during both inspiration and expiration) that is related to lung injury.

If energy dissipation is indeed eventually shown to be a contributor to lung damage during ventilation, then it is worth asking the question: 'How should we ventilate to minimise energy dissipation in the patient airway?'.

1.1. Ventilation for minimum energy dissipation

This question is easily answered by considering PV loops arising from pressure-controlled (PCV) and volume-controlled ventilation (VCV).

Illustrative, idealised, PV loops for a system consisting of a compliant reservoir (the compliant lung) fed via a resistance (the airway resistance) are shown in Fig. 1. Note that the pressure in this plot is the pressure at the circuit end of the airway resistance.

In PCV, the pressure applied to the proximal end of the patient circuit is essentially switched between the plateau pressure (Pplat) during inspiration and the PEEP during expiration. The flow varies substantially, is highly dynamic, and is not truly controlled in either phase. This gives rise to the PV loop of classic PCV shown in red in Fig. 1. The horizontal (pressure) deviation of the plot from a static compliance curve joining the PEEP and Pplat is related to the airway resistance and the flow rate. The (decelerating) flow is very high (typically greater than 40 l/min) just after the beginning of both inspiration and expiration phases, and so the pressure deviations from the static compliance curve are largest here.

The blue curve in Fig. 1 is an idealised PV loop that would be obtained for the same patient using (classical) VCV. Here, the flow is

controlled at a constant value throughout the (major part of the) inspiration phase (until the tidal volume set is insufflated, followed by a Pplat-phase with almost no flow), but is uncontrolled during expiration. The flow during inspiration is substantially lower than the peak flow that occurred with PCV, and so there is a constant pressure difference between airway pressure and the static compliance curve (joining PEEP and Pplat) throughout inspiration. This appears as a horizontal displacement of the inspiratory part of the curve to the right, relative to the static compliance curve.

In both cases, the energy dissipated in the patient per respiratory cycle is proportional to the hysteresis area of the PV loop. For the same PEEP, Pplat, and respiratory rate, the energy dissipated during VCV is lower than that during PCV. The energy during the inspiration phase is minimized, if the flow is kept constant throughout inspiration.

Clearly, the energy dissipation can be reduced further by also controlling the flow to be constant during expiration and thereby minimising the energy dissipated in the patient during this phase too. This would change the expiration part of the PV loop of VCV to the shape shown in the green trace. This is analogous to the curve optimally obtainable during inspiration under VCV, but with the pressure on the low pressure side of the static compliance curve due to the change in direction of flow.

Finally, if flow is controlled during both inspiration and expiration, then the lowest overall flow (and therefore the lowest overall energy dissipation) for a given minute volume is obtained, provided that inspiration and expiration flows are made equal. For a respiratory exchange ratio (RER) of unity, the I:E ratio then necessarily becomes 1:1. It is worth noting that RER has only small effect on the optimum I:E ratio. For example, if oxygen uptake is 300 ml/min and a carbon dioxide release is 210 ml/min (a RER of 0.7), the total expiratory volume over 1 min would be only 90 ml/ min less than the inspiratory volume over 1 min. This difference is very small compared to typical minute volumes of 5 or 6 l/min.

We emphasise that the PV loops in Fig. 1 are for illustration only. Their detailed shape is affected by the effects of multiple compartments in the lung, and viscoelasticity. However, the conclusion that energy dissipation is minimised if the flow is kept constant remains valid.

A simple form of flow control during expiration by a passive, dynamic resistor has been used in both animals and patients [26–28]. In these investigations, the expiratory flow still varied substantially. For example, in the experiments described by Goebel et al. [27] flow varied during expiration from a peak flow of 244 ml/ sec to zero with approximately constant flow for roughly 40% of the expiration phase. Further, the I:E ratios were 1:2 (based on flow phases), so energy dissipation was not minimised. Nonetheless, even with such imperfect flow control, the effect of expiratory flow control in partially narrowing the PV loop and therefore reducing energy dissipation can be seen in Fig. 3 of the paper by Schumann et al. [26].

Flow-controlled ventilation (FCV) was developed from an earlier concept: Expiratory ventilation assistance (EVA) [29–33] where suction is applied to the proximal end of a high resistance tubing connected to the patient. In FCV, the suction pressure is continuously controlled to provide substantially constant flow during expiration. Intratracheal pressure is monitored as part of the control schema, and to ensure that patient pressure never goes below the set PEEP.

The recently CE-certified, Evone ventilator (Ventinova Medical, Eindhoven, The Netherlands) implements FCV by an ejector-based gas flow reversing element (GFRE), which applies Bernoulli's principle to extract and control gas flow from the patient during expiration [34] and ventilates with continuous flows during both inspiration and expiration.

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Fig. 1. Idealised PV loops (the enclosed area of each loop is the dissipated energy) during PCV (red line), VCV (blue line) and FCV (blue line during inspiration, green line during expiration). The dashed line is the static compliance curve of the lung/chest system in this example.

The Evone ventilator uses the intratracheal pressure together with a servo system to control the flow (measured by mass flowmeters) during both inspiration and expiration to achieve a closely linear variation of intratracheal pressure with time.

The ventilator allows the operator to set the end expiratory pressure (PEEP), the peak inspiratory pressure (PIP), and the inspiratory and expiratory flow rates (these are usually set to be equal, with an I:E ratio of 1:1). At the start of each inspiration, the intratracheal pressure is the PEEP set at the ventilator. The ventilator then provides the set inspiratory flow to the patient and the intratracheal pressure rises as the lungs fill. When the intratracheal pressure reaches the set PIP, the ventilator stops inspiratory flow and immediately switches to expiration. It then extracts gas from the patient. The intratracheal pressure now falls as the lungs empty and the ventilator adjusts the flow to achieve a linear fall in pressure with time – thereby achieving a nearly constant expiratory flow. When the intratracheal pressure reaches the PEEP, the ventilator stops expiration, switches to inspiration, and the ventilation cycle is repeated.

The result is that the patient is ventilated with nearly constant and continuous flow during both inspiration and expiration. The ventilator provides comprehensive data output, including readings of flow and intratracheal pressure at 0.01 sec intervals during the respiratory cycle, and measurements of PIP, PEEP, tidal volume, minute volume, and respiratory rate at the end of each cycle.

The volume of the entire ventilation system (ejector-cartridge, main-stream capnometry cuvette, HME-filter, non-compliant connecting tubing (1.5 m long, 4 mm inner diameter), and the Tritube is less than 60 ml. This gives a very non-compliant ventilation system

compared to conventional ventilators, which allows precise measurement and control of flow and intratracheal pressure.

In this case study described below, we present flow and pressure profiles with time obtained when FCV was used on a healthy patient during a minor microscopic laryngeal procedure, together with PV loops and estimations of energy dissipation.

2. Methods

We illustrate FCV in operation below using a case study which FCV was used to ventilate a healthy, 51 year old man scheduled for elective, minor microscopic laryngeal surgery. The patient had no medical history of pulmonary disorder or related comorbidities. The patient weighed 80 kg with a height of 182 cm. The case was well-suited to the demonstration of FCV because there were no additional manipulations during surgery and so the probability of artefacts affecting the measurements was minimised, In order to have optimal working conditions, the surgeon requested that intubation was undertaken with a narrow bore tracheal tube (Tritube, Ventinova Medical, Eindhoven, The Netherlands). The Tritube is a CE-certified, 40 cm long, small-bore (4.4 mm outer diameter), cuffed tracheal tube (TT), which has a ventilation lumen of 2.3 mm and a pressure measurement lumen allowing direct measurement of intratracheal pressure. The Evone ventilator was used to ventilate through the Tritube.

Ventilation data was logged as part of the quality/reliability evaluation of the ventilation system. The patient gave informed, written, consent for use and publication of anonymised data derived from the ventilation data logs. 4

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Pressure and Flow obtained 12.9 minutes into the procedure







Fig. 2. Flow and intratracheal pressure readings obtained during the procedure. Flows are typically constant to better than 20% over the whole of both inspiration and expiration phases, with an I:E ratio of 1:1.

The patient was preoxygenated by face mask for 3 min before induction of anaesthesia, which was carried out by intravenous administration of 200 μ g remifentanil over 60 sec followed by an induction dose of 2.4 mg/kg propofol over 30 sec. An intravenous bolus of 25 mg rocuronium was administered after loss of consciousness to provide neuromuscular blockade for intubation. Anaesthesia was maintained with a continuous infusion of propofol (5 mg/kg/h) and remifentanil (12 μ g/kg/h) at an FiO₂ in the range 0.22–0.4.

The patient was intubated with the Tritube using videolaryngoscopy and the cuff was inflated to a pressure of 30 mbar. The flow rate (for both inspiration and expiration) set for the majority of the procedure was 12 l/min. From the ventilation log, data groups of four successive respiratory cycles during 'steady state' normoventilation of the patient (based on mainstream capnometry) were retrospectively chosen as representative samples to illustrate the characteristics of the ventilation. Data groups were selected in the early part of the procedure (12.9 minutes after the start of ventilation), near-mid-procedure (26.5 minutes after the start of ventilation), and after the major part of the surgery was completed (49 minutes after the start of ventilation).

2.1. Determination of PV loops with constant flow ventilation

We recorded intratracheal pressure and input flow to the gas flow reversing element (GFRE) in the Evone ventilator at 0.01 sec intervals throughout the procedure and used this information to reconstruct PV loops for the ventilation.

During inspiration, all of the input flow from the Evone is directed to the patient. We were therefore able to integrate that flow to find both the volume variation in the lungs during inspiration and also the overall tidal volume supplied to the patient for each breath. During expiration, the input flow to the GFRE is used to generate negative pressure (by Bernoulli's principle), which extracts gas from the patient. The flow of gas from the patient during expiration is related to the input flow to the GFRE, and the ventilator continues expiration until the intratracheal pressure has reached the set PEEP (which was the pressure that the preceding inspiration started from).

We were therefore able to estimate the expiratory flow from (and therefore the volume change in the lungs of) the patient during expiration by processing the measurement of flow supplied to the GFRE so that the calculated volume extracted from the patient during expiration was equal to the volume supplied during the previous inspiration.

The Evone ventilator also outputs the intratracheal pressure (measured via the pressure measurement lumen in the Tritube) (simultaneously with the flow readings) at 0.01 sec intervals throughout the ventilation cycle. We were therefore able to plot intratracheal pressure against lung volume through each ventilation cycle to produced a PV loop. We then separately numerically integrated the areas under the expiration and inspiration phases of the resultant PV plot, and subtracted the area under the inspiration segment from the area under the expiration segment to obtain the area enclosed by the PV loop. From this we were able to estimate the energy dissipation in the patient over each respiratory cycle.

2.2. Statistical analysis

Data are reported as mean \pm standard deviation where appropriate.

3. Results

The procedure lasted 80 minutes. The patient was mechanically ventilated with the Evone ventilator, and was stable throughout. Extubation was uneventful.

The I:E ratio was 1:1.01 \pm 0.05 and the flow was 12 l/min for the respiratory cycles for which PV loops are presented here. The respiratory rate was 10 \pm 0.3 per min. Standard deviations of the flow rate during inspiration and expiration were 0.09 l/min and 0.98 l/min, respectively. For the respiratory cycles presented here, peak inspiratory pressure was 18.09 ± 0.11 mbar (18.45 ± 0.11 cmH₂O) with a PEEP of 5.04 ± 0.15 mbar (5.14 ± 0.15 cmH₂O) resulting in an inspiratory tidal volume of 615.4 ± 12.6 ml. Compliance reported by the ventilator was 43.7 ± 2.1 ml/mbar (42.85 ± 2.06 ml/cmH₂O). Patient airway resistance reported by the ventilator during these measurements was 4 mbar/l/sec (4.08 cmH₂O/l/sec).

Fig. 2 shows the flow and intratracheal pressure for groups of four successive breaths at 12 l/min average flow, at 12.9, 26.5, and 49 minutes after the start of ventilation with Evone under otherwise stable conditions with no surgical or other manipulations undertaken.

Fig. 3 shows PV loops obtained for each of these cycles. Pressure and volume are referenced to PEEP in this diagram.

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Table 1

Respiratory cycle parameters for PV loops.

Time into procedure (min)	Resp. cycle	Tidal volume (ml)	Peak pressure (mbar)	PEEP (mbar)	Energy dissipation (J)	Energy dissipation per minute at 10/min (J/min)	Minute volume (l/min)	Energy dissipation per ventilated volume (J/l)
12.9	1	606.6	18.2	5.16	0.11	1.2	6.07	0.19
	2	629.2	18.0	5.16	0.12	1.2	6.29	0.19
	3	601.8	18.2	5.16	0.10	1.0	6.02	0.17
	4	625.0	18.0	5.16	0.097	0.97	6.25	0.16
	Mean	615.5	18.1	5.16	0.11	1.1	6.16	0.17
	Standard deviation	13.7	0.12	0	0.01	0.1	0.13	0.016
26.5	1	631.8	18.1	4.80	0.12	1.2	6.32	0.18
	2	629.3	18.1	4.90	0.10	1.0	6.29	0.16
	3	631.3	18.3	4.90	0.09	0.9	6.31	0.15
	4	600.3	18.0	4.80	0.11	1.1	6.00	0.18
	Mean	623.2	18.08	4.85	0.107	1.07	6.23	0.17
	Standard deviation	15.3	0.12	0.06	0.013	0.13	0.15	0.022
49.0	1	605.9	18.2	5.18	0.093	0.93	6.06	0.15
	2	608.0	18.0	5.07	0.11	1.1	6.08	0.18
	3	609.1	18.0	5.06	0.11	1.1	6.09	0.18
	4	606.1	18.0	5.07	0.098	0.98	6.06	0.16
	Mean	607.3	18.05	5.1	0.103	1.03	6.07	0.17
	Standard	1.54	0.1	0.06	0.009	0.09	0.015	0.015
	deviation							
	Overall mean	615.4	18.09	5.04	0.105	1.05	6.15	0.17
	Overall standard deviation	12.6	0.11	0.15	0.01	0.11	0.013	0.014

The PIP, PEEP, and energy dissipation estimated from the area enclosed by the PV loops as described above are given in Table 1. Table 2 shows the haemodynamic parameters taken from the anaesthetic record and the end tidal CO_2 readings measured during each group of breaths.

4. Discussion

The shape of the PV loops recorded using intratracheal pressure with accurate control of both inspiratory and expiratory flow is substantially different to curves normally shown for patients ventilated under PCV or VCV.

Factors contributing to the shape difference include:

- 1. Our curves are based on directly measured intratracheal pressure, rather than airway pressure. PV loops recorded using airway pressure have additional and substantial flow-dependent pressure drop incorporated into them, which arise from the resistance of the TT [35]. Curves based on airway pressure are therefore wider than those based on intratracheal pressure due to the extra energy dissipation in the TT [36]. These effects are not present in our measurements because of the direct measurement of intratracheal pressure.
- 2. Viscoelastic effects in the airway [37,38] also modify the PV loop, tending to smooth out the effect of sudden flow changes on pressure variations. If airway pressure is used for the PV loop, these effects are partially masked by the pressure drop across the TT resistance, but here we are using intratracheal pressure

and, consequently, the viscoelastic smoothing results in relatively slow variation of pressure, when the flow changes direction between inspiration and expiration phases.

3. Lung heterogeneity has effects similar to viscoelasticity. Gas swapping between lung compartments of different time constants also smooths out pressure variations in response to sudden flow changes [39]. Again, these effects are partially masked by the effect of the TT resistance, when using airway pressure for the PV loop rather than intratracheal pressure as we have done.

We report a case involving a single surgical procedure here simply to illustrate the characteristics of FCV in a clinical setting, rather than to compare FCV with other ventilation modes. Comparison of FCV with other modes in the clinical setting will be the subject of future work. We therefore confine ourselves here to comparisons with data available from the literature.

Because we were using directly measured rather than mathematically estimated intratracheal pressure, the hysteresis area within the PV loops directly mirrored the energy losses in the patient during ventilation. The value we measured of 0.17 ± 0.014 J/l of ventilated volume compares to typical work of breathing reported for healthy adults during spontaneous ventilation of 0.2-0.7 J/l [40,41]. Our remarkably low values (for mechanical ventilation) may be due to the fact that work of breathing measurements using the Campbell diagram usually also take into account the energy applied to extending the elastic elements of the airway [42], whereas we are measuring only the dissipated (component of)

Table 2

Haemodynamic parameters and End Tidal CO₂ measurements during the periods when the respiratory cycles shown in this paper were logged.

Time into procedure (min)	Heart Rate (BPM)	SpO ₂ (%)	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)	End Tidal CO ₂ (%)
12.9	40	97	108	40	5.4
26.5	44	96	120	60	4.2
49.0	40	99	110	50	6.3
Mean	41.3	97.3	112.7	50	5.3
Standard deviation	2.3	1.5	6.4	10	1.1

energy.

However, even values obtained by simply integrating the hysteresis area of the PV loop as in Levy et al. [43] (so that only energy dissipated in the patient was measured) are in the range of 0.1-4.09 J/l for successfully extubated patients, recovering from conditions such as COPD, pneumonia, and ARDS.

The pressure difference between PIP and PEEP (the so-called 'driving pressure') was 13 mbar for this patient – towards the upper end of, but within, the range normally expected for ventilation of a patient without pulmonary complications. We set this as follows:

With the Evone ventilator operating at an I:E ratio of 1:1, the minute volume is equal to half the set flow rate - and is in fact independent of the respiratory rate. However, in order to minimise the rate of energy dissipation, it is advantageous to have the respiratory rate as low as possible in addition to ensuring the flow is constant. Respiratory rate is determined by the PEEP, PIP, and the flow rate (at the same flow rate, a lower PEEP and a higher PIP will give a lower respiratory rate). At the same time, it is important that the lungs are not overinflated (this limits the PIP that can be used) and that cyclic collapse and reinflation of alveoli is minimised (this limits the PEEP) – that is, that the lungs are ventilated at optimal compliance. We therefore started with a PEEP of 5 mbar, a driving pressure of 10 mbar, and a flow of 12 l/min - values which are in an acceptable range for most patients. We then determined the 'best' PEEP by adjusting PEEP to achieve the best compliance with that driving pressure. Following that we adjusted the driving pressure (by changing the PIP in small increments) - again to optimise the compliance. By this means we could be assured we were operating at optimal compliance while avoiding overinflation (which would have manifest as a decrease in compliance with increasing PIP). Finally the flow was set to achieve the desired amount of CO₂ elimination - and this was the 'best' flow which necessarily results in the lowest respiratory rate for the required CO₂ elimination – and therefore energy dissipation rate.

The pressure and flow measurements with the Evone system are not easily directly compared with those obtained using a standard ventilator because of the quite different way in which measurements of flow and pressure are made in the two systems. The entire ventilation system of Evone (including narrow-bore connecting tubing and the Tritube) has a volume of less than 60 ml. Therefore, it has very low compliance compared to conventional ventilators with standard 22-25 mm diameter compliant tubing. The combination of the low compliance and the use of mass flowmeters to measure flow in the Evone ventilator enables precise measurement of flow into the patient – and therefore the inspired volume of gas. In addition, the Evone system uses direct measurement of intratracheal pressure, whereas conventional ventilators usually measure airway pressure (i.e. a pressure proximally from the tracheal tube) and then - if at all - estimate intratracheal pressure from the measured airway pressure using the measured flow and resistance coefficients of the tracheal tube and associated circuit components determined in vitro. In situations where the variation of flow is large (as in conventional PCV and VCV scenarios) this approach can potentially give rise to substantial errors in the estimated intratracheal pressure at key points in the ventilation cycle, and thereby affect the measured respiratory mechanics in a way that does not occur with the Evone system. The low-compliance, flow-controlled ventilation system with direct measurement of intratracheal pressure (rather than relying on airway pressure) provided by Evone enables accurate measurement of pressure and flow and allows a precise view of respiratory mechanics of a ventilated patient.

It is worth noting that the static compliance curve is a convenient construct, but does not properly reflect the mechanical properties of the lung-chest-system during the dynamic situation, which pertains during ventilation. Given the direct nature of our measurement of pressure and the precision afforded by the low compliance ventilation system in our ventilations, the PV loops given here probably represent a more accurate view of (individual) inspiratory and expiratory intratidal compliance than those currently used, and demonstration of this will be the subject of future investigations.

It is also worth noting that the 'static' PV loops obtained with intermittent step-by-step insufflation and desufflation of gas from the lungs in the super-syringe method [44] are affected by continuous oxygen resorption coupled with limited carbon dioxide release into the alveoli occurring during the measurement. This is also true of 'semi-static' PV loops obtained by insufflating gas into the lungs at very low flow rates.

However, the Evone system enables direct measurement of PV loops and compliance at normal respiratory rates because of the combination of flow control, a low compliance gas feed system, and direct intratracheal pressure measurement.

Finally, we were able to (very) roughly estimate the energy dissipations in the first experiment in pigs with so-called flow-controlled expiration (FLEX) reported by Schumann et al. [26; Fig. 3]. For (classical) VCV (used as control in this study) we obtained a value of 0.39 J/l, and for partially flow-controlled expiration we calculated a value of 0.32 J/l. Clearly the provided figures are subject to substantial uncertainty and are in a porcine model rather than in humans, so any comparison should be undertaken with caution. Nonetheless, the factor of two difference between these values and the (lower) values we found in our first analysis of mechanical, automated ventilation with the Evone using FCV indicate that further trials of this technique to minimise energy dissipation in ventilated patients are warranted.

5. Conclusion

We have reported measurements of ventilation parameters obtained in a healthy patient with an unaffected airway using a recently launched new type of ventilator providing full control of both inspiration and expiration. We maintained inspiratory as well as expiratory flow rates accurately constant with an I:E ratio of very close to 1:1 in order to minimise energy dissipation during ventilation. We calculated energy dissipation from PV loops obtained using direct, continuous measurement of intratracheal pressure. Energy dissipation was $0.17 \text{ J/l} - \text{lower than values normally quoted for spontaneous breathing, or found in experiments on pigs using methods with less accurate flow control.$

Conflicts of interests

T. Barnes: patent application on calculating and displaying dissipated energy, (paid) consultant to Ventinova Medical.

D. Enk: inventor of EVA technology (Ventrain, Tritube, Evone), royalties for EVA technology (Ventrain, Tritube, Evone), patent applications on minimising dissipated energy and on calculating and displaying dissipated energy, (paid) consultant to Ventinova Medical.

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