Intensive Care Med (2006) 32:34–47
DOI 10.1007/s00134-005-2828-5

REVIEW

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Bedside waveforms interpretation as a tool to identify patient-ventilator asynchronies

Received: 24 March 2005
Accepted: 8 September 2005
Published online: 9 November 2005

Electronic Supplementary Material
Electronic supplementary material to this paper can be obtained by using the Springer Link server located at http://dx.doi.org/10.1007/s00134-005-2828-5

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Abstract *Objective:* During assisted modes of ventilatory support the ventilatory output is the final expression of the interaction between the ventilator and the patient's controller of breathing. This interaction may lead to patient-ventilator asynchrony, preventing the ventilator from achieving its goals, and may cause patient harm. Flow, volume, and airway pressure signals are significantly affected by patient-ventilator interaction and may serve as a tool to guide the physician to take the appropriate action to improve the synchrony between patient and ventilator. This review discusses the basic waveforms during assisted mechanical ventilation and how their interpretation may influence the management of ventilated patients. The discussion is limited on waveform eye interpretation of the signals without using any intervention which may interrupt the process of mechanical ventilation. *Discussion:* Flow, volume, and airway pressure may be used to (a) identify the mode of ventilator assistance, triggering delay, ineffective efforts, and autotriggering, (b) estimate qualitatively patient's respiratory efforts, and (c) recognize delayed and premature opening of exhalation valve. These signals may also serve as a tool for gross estimation of respiratory system mechanics and monitor the effects of disease progression and various therapeutic interventions. *Conclusions:* Flow, volume, and airway pressure waveforms are valuable real-time tools in identifying various aspects of patient-ventilator interaction

Keywords Assisted mechanical ventilation · Bedside waveform interpretation · Flow, volume, airway signals · Patient-ventilator interaction · Respiratory system mechanics · Ventilator triggering

Introduction

The main reasons for instituting mechanical ventilation are (a) to decrease the work of breathing, (b) to support the gas exchange, and (c) to buy time for other interventions to treat the cause of respiratory failure [1, 2]. Mechanical ventilation can be applied in patients who are or are not making respiratory efforts, using, respectively, assisted or controlled modes of support. In patients without respiratory efforts the respiratory system represents a passive structure, and thus the ventilator is the only system that controls breathing [2]. During assisted modes of ventilator support the patient's controller of breathing is under the influence of the ventilator pump. In the latter instance the ventilatory output is the final expression of the interaction between the ventilator and the patient's system of control of breathing. Thus physicians who deal with mechanically ventilated patients should know the effects of mechanical ventilation on control of breathing as well as their interaction. Ignorance of these issues may prevent the ventilator from achieving its goals and may cause patient harm [3, 4, 5, 6].

Current ventilators have the ability to display breath by breath airway pressure, flow, and volume as a function of

time. These waveforms may help the physician to understand the interaction between patient and ventilator and provide clues to identify the various problems unique to different modes of assisted mechanical ventilation. In this review we discuss the basic waveforms during assisted mechanical ventilation and how their interpretation may influence the management of ventilated patients. The discussion is limited on waveform eye interpretation of flow, volume, and airway pressure signals without using any intervention which may interrupt the process of mechanical ventilation. Such noninterventional waveform interpretation may give valuable information without imposing any harm to critically ill and often very unstable patients. Notwithstanding the usefulness of other interventions (i.e., inserting esophageal and gastric balloons, estimation of mechanics after heavy sedation, and temporary paralysis), we believe that the noninvasive aspect of bedside waveform interpretation is an attractive alternative and a skill that every practicing intensivist should possess.

Equation of motion in mechanically ventilated patients

The respiratory control system consists of a motor arm, which executes the act of breathing, a control center located in the medulla, and a number of mechanisms that convey information to the control center [7, 8, 9]. Based on the information the control center activates spinal motor neurons subserving respiratory muscles (inspiratory and expiratory muscles), with intensity and rate that varies substantially between breaths as well as between individuals. The activity of spinal motor neurons is conveyed via peripheral nerves to respiratory muscles which contract and generate pressure (Pmus). During spontaneous breathing according to equation of motion Pmus at time *t* is dissipated to overcome the resistive (Pres) and elastic (Pel) pressure of the respiratory system (inertia is assumed to be negligible) as follows:

$$\mathrm{Pmus}(t) = \mathrm{Pres}(t) + \mathrm{Pel}(t) = \mathrm{Rrs} \times \mathrm{V}'(t) + \mathrm{Ers} \times \Delta\mathrm{V}_{\mathrm{FRC}}(t) \quad (1)$$

where Rrs and Ers are resistance and elastance of respiratory system, respectively, $\Delta V_{FRC(t)}$ is instantaneous volume relative to passive functional residual capacity (FRC), and $V'(t)$ is instantaneous flow. If ΔV is related to end-expiratory lung volume (ΔV_{EE}) then:

$$\mathrm{Pmus}(t) = \mathrm{Pres}(t) + \mathrm{Pel}(t) = \mathrm{Rrs} \times \mathrm{V}'(t) + \mathrm{Ers} \times \Delta\mathrm{V}_{\mathrm{EE}}(t) + \mathrm{PEEPi} \quad (2)$$

where PEEPi is elastic recoil pressure of respiratory system at end-expiration. Equations 1 and 2 determine volume-time profile, tidal volume, and, depending on the frequency of respiratory muscles activation, ventilation.

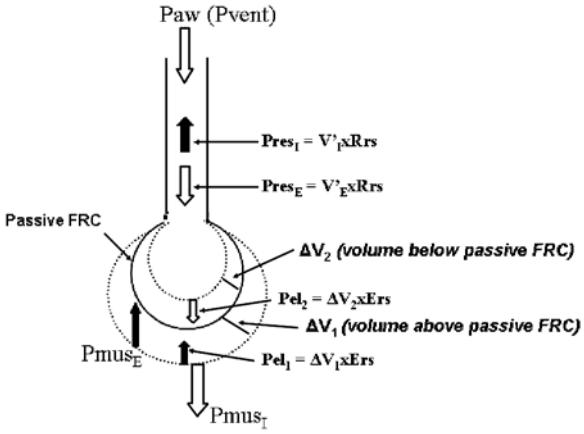

Fig. 1 Schematic representation of the respiratory system and the various applied pressures. *Arrows* indicate the direction of each pressure. Two volumes (*dashed lines*, ΔV) are shown, one above (ΔV_1) and the other below (ΔV_2) passive functional residual capacity (*FRC*). *Ers*, *Rrs* Elastance and resistance of respiratory system, respectively; *Pel*, *Pres* elastic recoil and resistive pressures, respectively; $Pmus_I$, $Pmus_E$ pressure developed by inspiratory and expiratory muscles, respectively; *Paw* airway pressure (ventilator pressure, *Pvent*); V'_I, V'_E inspiratory and expiratory flow, respectively; P_{TOT} total pressure (the sum of Paw and Pmus) applied to respiratory system; ΔV_{FRC} volume related to passive FRC. See text for further details

During mechanical ventilation the pressure provided by the ventilator (Paw) is incorporated into the system [2, 10]. Therefore in mechanically ventilated patients the total pressure applied to respiratory system at time *t* ($P_{TOT(t)}$) is the sum of Pmus(t) and Paw(t). Thus:

$$\mathrm{P_{TOT}}(t) = \mathrm{Pmus}(t) + \mathrm{Paw}(t) = \mathrm{Pres}(t) + \mathrm{Pel}(t) = \mathrm{V}'(t) \times \mathrm{Rrs} + \Delta\mathrm{V_{FRC}}(t) \times \mathrm{Ers} \quad (3)$$

and:

$$\mathrm{Paw} = \mathrm{P_{TOT}}(t) - \mathrm{Pmus}(t) = \mathrm{V}'(t) \times \mathrm{Rrs} + \Delta\mathrm{V_{FRC}}(t) \times \mathrm{Ers} - \mathrm{Pmus}(t) \quad (4)$$

Figure 1 schematically shows all the variables of Eq. 3 (or Eq. 4), as well as the direction of various applied pressures. Contraction of inspiratory muscles generates pressure ($Pmus_I$, positive value in Eq. 3) which has the same direction with the pressure provided by the ventilator (Paw), whereas contraction of expiratory muscles generates pressure ($Pmus_E$, negative value in Eq. 3) in the opposite direction of Paw. Similarly, ΔV is assigned a positive or negative value depending on the relationship between the final volume and that of passive FRC. Finally, flow has a positive value when is inspiratory and negative when is expiratory. Because flow and ΔV_{FRC} comprise the second term of Eq. 3, the positive values of

these parameters generate pressure to the opposite direction of Paw and $Pmus_I$ (Fig. 1). We should also note that the resistance and elastance of respiratory system, particularly in the presence of lung or chest wall disease, are not constant during the breath but exhibit a considerably flow and volume dependency, complicating the schema of Fig. 1 [11, 12, 13]. Nevertheless, Eqs. 3 and 4 combined with Fig. 1 help us to interpret the basic waveforms during assisted mechanical ventilation. This review focuses on basic waveform during assisted mechanical ventilation applied mainly invasively via an endotracheal tube. Although similar principles apply during noninvasive mechanical ventilator support (NIV), specific features of the latter related principally to interface and presence of leak [14] through the interface are not reviewed here.

Basic features of positive pressure (or flow) ventilators

Three variables determine the function of a positive pressure (or flow) ventilator [15, 16] (see Electronic Supplementary Material): (a) the triggering variable (the signal of initiating the positive pressure), (b) the control variable (the algorithm that controls the delivered pressure or flow during the mechanical inspiration), and the (c) cycling off variable (the signal of terminating the pressure or flow delivery).

Trigger variable

The trigger variable may be pressure, flow, volume, and flow waveform [17]. Experimentally the activity of the diaphragm (either using electromyography or transdiaphragmatic pressure) has been also used to trigger the ventilator [18, 19].

With pressure triggering the patient in order to trigger the ventilator and initiate the inspiratory flow must decrease the pressure in the ventilator circuit to a certain extent (preset) and then open a demand valve [17, 20, 21]. With flow and volume triggering the patient triggers the ventilator when the action of respiratory muscles produces a certain inspiratory flow (preset) or volume (preset). With the flow waveform method triggering occurs either when patient effort generates inspiratory flow causing 6 ml volume to accumulate above baseline flow (volume method, similar to flow triggering), or when the patient inspiratory effort distorts the expiratory flow waveform to a certain extent (shape triggering), whichever occurs first [22].

Some ventilators have the ability to change the method of triggering breath by breath using certain algorithms [16]. For example, time triggering may change to flow or pressure triggering automatically if the patient during a certain window time makes an inspiratory effort and either decreases airway pressure or generates inspiratory flow. The reverse may also occur (pressure or flow triggering variable may change to time if during a certain window time the patient does not make an inspiratory effort). Finally some ventilators combine both flow and pressure triggering [16].

Variable that controls the pressure or flow delivery

There are several modes of assisted mechanical ventilation [15, 23]. These can be classified into three main categories based on the variable that controls the pressure or flow delivery [2, 24]: (a) assist volume control (AVC), where the ventilator, once triggered, delivers a preset tidal volume with a preset flow-time profile, (b) pressure control (PC) or pressure support (PS), where the ventilator delivers a preset pressure, and (c) proportional assist ventilation (PAV), where the ventilator delivers pressure which is proportional (the proportionality is preset) to instantaneous flow and volume. Current ventilators have the ability to combine various modes and ventilate the patients simultaneously with more than one mode, even in the same breath (dual-control modes) [25]. We should mention that although dual-control modes are not discussed specifically, the interpretation principles (see below) may be well applied to these modes.

To interpret the basic waveforms it is useful to differentiate between the dependent and independent variables in Eq. 3 during the three main modes of assisted mechanical ventilation [3]. With AVC the instantaneous volume and flow are the independent variables, and instantaneous Paw is the dependent variable. With PC and PS instantaneous Paw is the independent variable, and instantaneous volume and flow the dependent variable. Finally, with PAV instantaneous flow volume and Paw are the dependent variable. With this mode the caregiver sets the relationship between the instantaneous volume and flow and the pressure delivered by the ventilator. However, since PAV is currently under investigation, and it is not available for general use we do not discuss waveforms during this mode.

Cycling off variable

The cycling off criterion depending on the mode of support may be time, volume, airway pressure, or flow. Electronic signals have recently been used to terminate the mechanical inspiratory phase (flow-waveform and expiratory threshold methods) [22]. With AVC and PC the cycling off criterion is usually time, although depending on the ventilator it may change to flow, volume, or Paw [1, 15, 16]. When Paw is used as cycling off criterion, the ventilator terminates the pressure or flow

delivery when, due to expiratory muscle activity or abrupt relaxation of inspiratory muscles, Paw increases above a certain threshold (usually 1.5 or 3 cmH_2O, some ventilators use a threshold of 20 cmH_2O) [1, 15, 26]. When flow criterion is used cycling off occurs when inspiratory flow decreases to a preset flow criterion. This may be either a percentage of peak inspiratory flow or a fixed value of flow. Others algorithms for cycling off are the flow-waveform and expiratory threshold methods [22]. As a safety feature the ventilator may terminate the pressure or flow delivery when the duration of inspiratory flow is considerably long (i.e., above a certain time which depending on ventilation, is highly variable and may be adjustable) [26]. With PAV the ventilator inspiratory flow is driven by the inspiratory effort and pressure delivery termination occurs when inspiratory flow decreases to zero [23]. Experimentally the diaphragmatic electrical activity has been also used to control the end of mechanical expiration [18].

Ideally during assisted modes of support the end of mechanical inspiratory phase should coincide with the end of neural inspiration. However, this rarely if ever happens. Usually the termination of ventilator flow occurs either before or after the patient stops his/her inspiratory effort, a phenomenon referred to as expiratory asynchrony [27, 28, 29, 30, 31]. This is due to the fact that the algorithms used to cycle off the ventilator are far from ideal.

Waveforms during the triggering phase

During the triggering phase the basic waveforms (flow, volume, and airway pressure) are used to identify (a) triggering delay, (b) ineffective efforts, and (c) autotriggering. Under certain circumstances the waveforms may also give an estimate of respiratory drive of the patient.

Triggering delay, ineffective efforts

In several mechanically ventilated patients the respiratory system fails to reach equilibrium volume at end-expiration (passive FRC). In this instance inspiratory muscles start contracting at volumes above passive FRC where alveolar pressure is positive, a phenomenon referred to as dynamic hyperinflation. Dynamic hyperinflation is caused by several factors such as low elastic recoil of respiratory system, high tidal volume, increased resistance to expiratory flow, and short neural expiratory time [32, 33]. In the presence of dynamic hyperinflation an elastic threshold load (PEEPi) is imposed on the inspiratory muscles at the beginning of inspiration, increasing the amount of the inspiratory effort needed to trigger the ventilator [34]. Indeed, with flow or pressure triggering systems the patient must first counterbalance PEEPi in order to decrease alveolar pressure below external PEEPe and trigger the ventilator. Therefore a portion of Pmus is dissipated to counteract PEEPi (elastic threshold load) and as a consequence there is a delay between the beginning of inspiratory effort and the triggering (Fig. 2) [32, 33, 35, 36]. In some cases the inspiratory effort of the patients is not able to counterbalance PEEPi, resulting in inability to trigger the ventilator (ineffective effort; Fig. 2).

Triggering delay and ineffective efforts can be easily detected by recording esophageal pressure (Fig. 2). Inserting an esophageal catheter is, however, a relatively invasive procedure and may not be suitable for everyday practice. In addition, the esophageal pressure may be altered by body position, heart beats, swallowing, and displacement of the balloon, thus complicating the signal interpretation. Finally, esophageal waveform may not precisely follow neural events [37]. Inspection of flow tracings may be an alternative [38]. An abrupt decrease in expiratory flow from the flow trajectory established earlier indicates either the beginning of inspiratory muscle contraction and/or relaxation of expiratory muscle if expiration is active. In either case the point of expiratory flow deviation signifies the beginning of triggering phase (Fig. 2). The time lag between this point and the point at which Paw starts to increase is the triggering delay (Fig. 2). If the abrupt decrease in expiratory flow is not followed by mechanical breath ineffective effort occurs (Fig. 2). Flow distortion due to cardiac oscillation may be confused with ineffective efforts, particularly if the stroke volume of the patient is relatively high [39]. The short duration (<0.3 s) and the rapid frequency (close to heart rate) of flow distortion suggest cardiac oscillation rather than ineffective efforts [38].

Paw signal may be also used to identify an ineffective effort, although its sensitivity is lower than that of flow waveform (Fig. 3). This is because during expiration the amount of Paw above PEEP depends on the product of the small resistance of expiratory circuit ($Rexp_{circuit}$) and expiratory flow (V'_E):

$$Paw = V'_E \times Rexp_{circuit} \quad (5)$$

To the extent that $Rexp_{circuit}$ is small (ideally should be zero) [40, 41], the decrease in Paw (ΔPaw) induced by contraction of inspiratory muscles (or relaxation of expiratory muscles) is also small as dictated by the following equation:

$$\Delta Paw = \Delta V'_E \times Rexp_{circuit} \quad (6)$$

We should mention, however, that if Paw is measured distal to a heat and moisture exchange filter (i.e., close to the patient), the relatively high resistance of the filter will cause a clear signal of Paw as a result of flow distortion. Similarly, in some ventilators expiratory and PEEP valves may impose a significant resistance to expiratory circuit. In this case ineffective efforts may be detected using Paw waveform (Fig. 4).

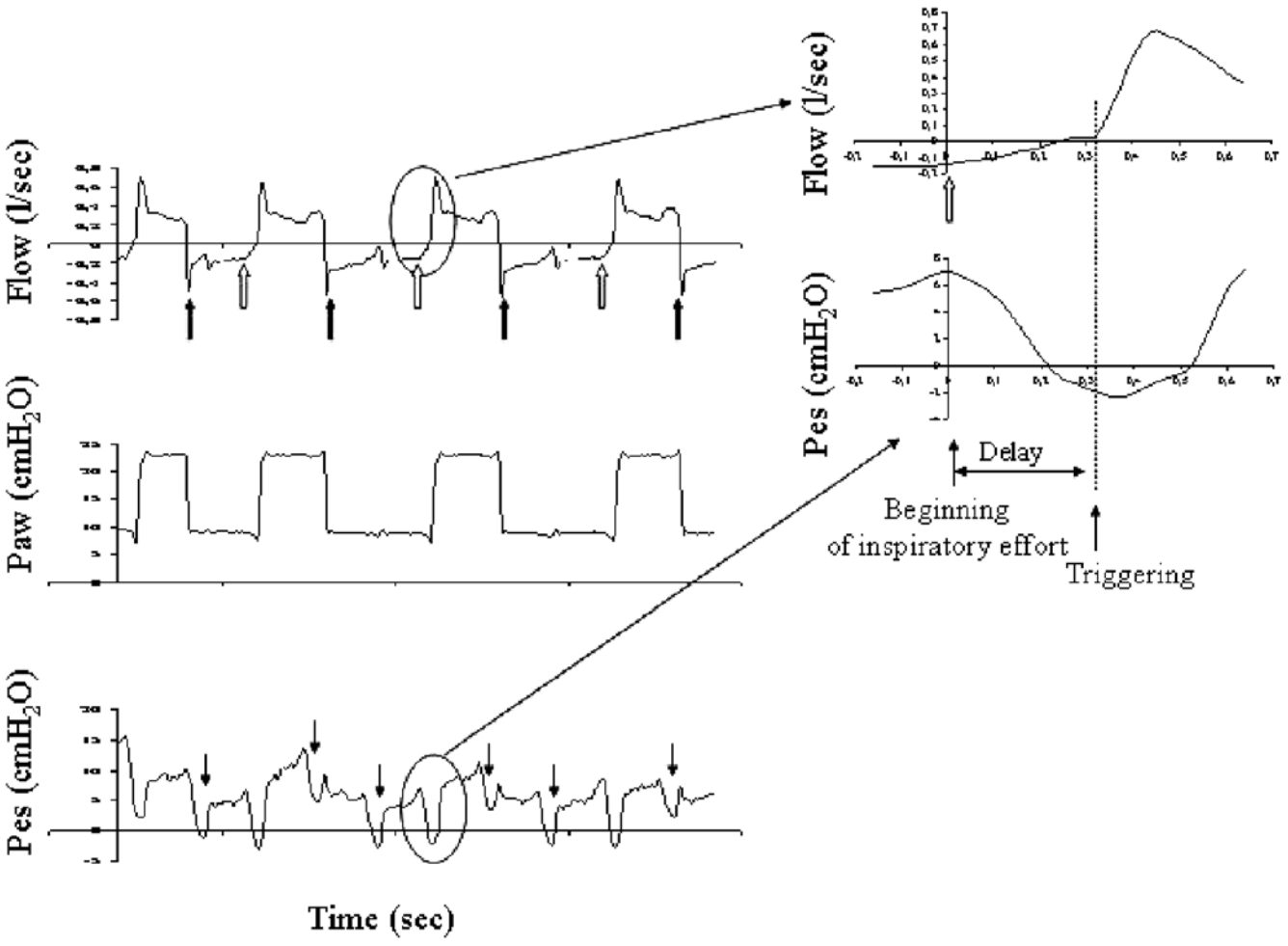

Fig. 2 Airflow (inspiration up), airway pressure (*Paw*), and esophageal pressure (*Pes*) in a patient with obstructive lung disease ventilated on pressure support. Observe the triggering delay in every mechanical breath. In some breaths almost all inspiratory effort is dissipated to trigger the ventilator (see the magnified tracing of flow and Pes). Observe also the ineffective efforts (*small arrows*). These can be detected by careful inspection of flow tracing. The ventilator rate is 12 breaths/min, while the patient's breathing frequency is 35 breaths/min. *Open arrows* indicate the abrupt decrease in expiratory flow from the flow trajectory established earlier signifying the beginning of inspiratory muscle contraction. Note finally that expiratory flow exhibits an initial spike (*thick arrows*), a sign of considerably increased airflow resistance and flow limitation. See text for further details

Ineffective effort is not a phenomenon limited to mechanical expiratory phase, but it may be also observed during mechanical inspiratory phase (Figs. 2, 5). Ineffective efforts during mechanical inspiratory phase may be identified using the flow or Paw waveform depending on the mode of support. With AVC inspiratory flow is the independent variable, and thus Paw is the signal which is distorted by the inspiratory effort [3]. Ineffective effort decreases transiently the Paw, although this distortion is not always easy to recognize [26, 42] (Fig. 5). With PS flow is the dependent, variable and this should be examined for ineffective efforts; an abrupt increase in inspiratory flow suggests ineffective effort (Fig. 2). However, we should emphasize that if PC modes are used which permit spontaneous efforts even if the ventilator delivers a constant pressure (i.e., bilevel intermittent positive airway pressure), the abrupt increase in inspiratory effort signifies spontaneous breaths and not ineffective efforts [25].

Finally, we should also note that the independent variable (pressure with PC and PS or flow with assist-volume) may be affected by rapid changes in respiratory muscle pressure [26], since the ventilator is not able to precisely follow these changes (Fig. 5).

Provided that the ventilator is functioning properly, the strategies for decreasing the triggering delay and the number of ineffective efforts are (a) measures that decrease the magnitude of dynamic hyperinflation (low tidal volume, long expiratory time, decrease the expiratory resistance), (b) interventions which increase Pmus during the triggering phase (i.e., decrease in sedation level), (c) application of external PEEP, and (d) decrease the

threshold for triggering (Fig. 4). In addition, the triggering system may also affect the response of the ventilator. It has been shown that in the presence of dynamic hyperinflation the flow-waveform method of triggering compared to flow triggering decreases the triggering delay and the number of ineffective efforts [22]. Theoretically, decreasing the resistance to inspiratory flow by using large bore endotracheal tube and bronchodilators drugs might be of importance in flow triggering systems. This, however, needs to be studied.

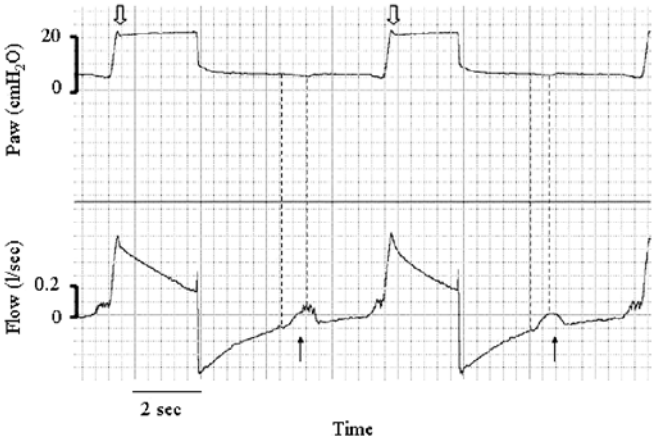

Fig. 3 Airway pressure (*Paw*) and air flow in a patient with obstructive lung disease ventilated on pressure support. Observe the flow distortion during expiration (*arrows*) which is not followed by mechanical breath signifying the presence of ineffective efforts. Note also that the signal of flow distortion is much clearer than the corresponding Paw change; flow changes by approx. 150% while the corresponding change in Paw is in the range of 10% (*vertical dotted lines*). Observe finally the small overshoot in Paw (*open arrows*) due to high pressurization rate

Autotriggering

Autotriggering refers to the phenomenon of the ventilator being triggered in the absence of patient effort (Fig. 6) [22, 39, 43]. This phenomenon may be caused by low threshold (pressure or flow) for triggering and by flow or Paw distortion due to circuit leaks, presence of water in the circuit and cardiogenic oscillators. Hiccups may also trigger the ventilator. Autotriggering is recognized in all currently used methods of triggering and usually is associated with low respiratory drive and breathing frequency and absence of dynamic hyperinflation [22, 39, 43]. These factors maintain zero end-expiratory flow for some time before the next inspiration, making the system vulnerable to autotriggering caused by any distortion of airway pressure which is not due to inspiratory effort (Fig. 6). Nevertheless, circuit leaks may cause autotriggering even in patients with dynamic hyperinflation.

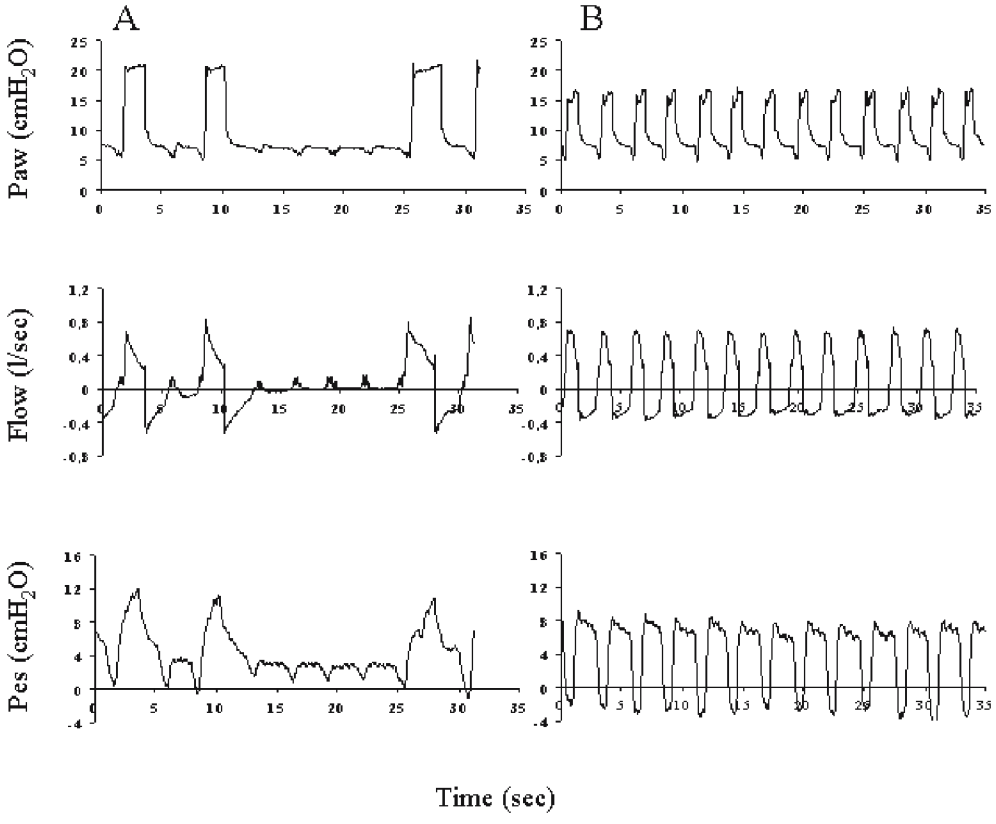

Fig. 4 Airway pressure (*Paw*), flow, and esophageal pressure in a patient with obstructive lung disease ventilated on pressure support mode (*PS*) at two levels of pressure assist using a flow triggering system. **A** PS 20 cmH_2O, flow threshold for triggering 5 l/min. **B** PS 15 cmH_2O, flow threshold for triggering 2 l/min. Note that decreasing PS and the threshold for triggering eliminates the ineffective efforts (*arrows*). Observe also the minimal inspiratory effort with high PS as indicated by the relatively small Pes deflections, which should contribute to inability of the patient to trigger the ventilator. The ineffective efforts can be detected using both the flow and Paw tracings

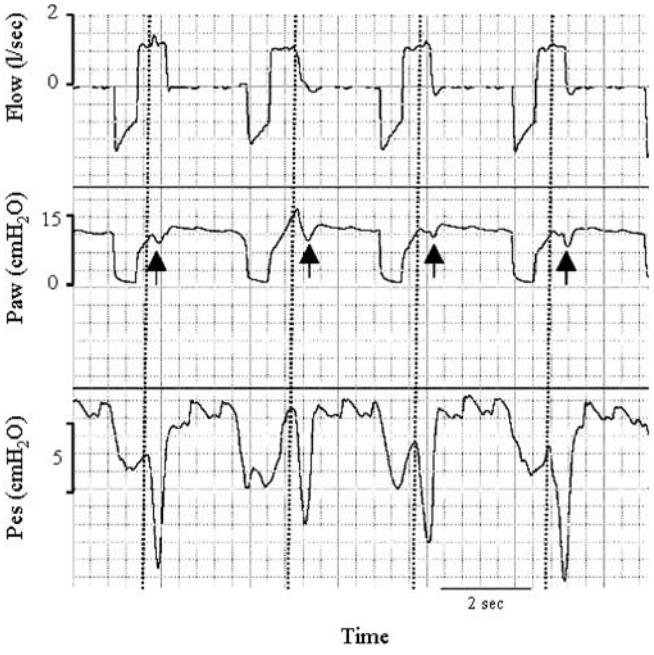

Fig. 5 Airflow and airway and esophageal pressures in a patient ventilated on assist volume control with a relative high back up rate, long inspiratory pause time, and tidal volume of 0.5 l (not shown). These settings are not recommended for patients with active respiratory efforts. Note that none of the mechanical breaths are triggered by the patient inspiratory effort which begins (*dashed vertical lines*) at different time during the mechanical inspiration. These represent ineffective efforts during mechanical inspiration and results in Paw distortion (*arrows*). Observe the similar flow-time (independent variable) and the different Paw-time (dependent variable) waveforms between breaths. Because in the second breath the inspiratory effort started at the end of inspiratory flow Paw-time waveform exhibit the pattern of passive respiratory system inflation at constant inspiratory flow. The high end-expiratory flow indicates dynamic hyperinflation caused by the short expiratory time

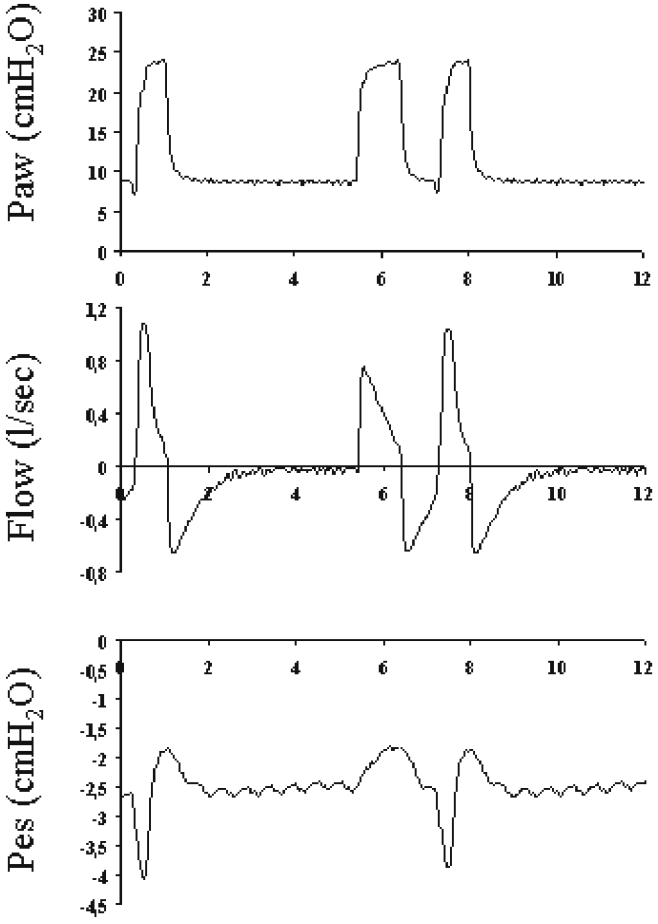

Fig. 6 Airway pressure, airflow (inspiration up), and esophageal pressure in a patient ventilated on pressure support. Observe that the second breath is triggered in the absence of patient's inspiratory effort (no abrupt decrease in Paw and Pes). Note also the flow distortion due to cardiogenic oscillation and/or secretions (clearly detected in Pes tracing), and that before autotriggering flow remains to zero for some time. Observe finally the different flow-time profile between triggered and autotriggered breaths, a feature which characterizes the pressure support ventilation

Autotriggering is obviously not an issue with PAV since with this mode inspiratory muscle effort is necessary for pressure delivery.

Inspection of pressure and flow waveforms may help to identify autotriggering. The absence of the initial pressure drop below end-expiratory pressure is indicative of autotriggering. With flow triggering systems, however, the pressure drop before the mechanical breath may be minimal if the resistance upstream to the Paw measurement is very low, making the signal less clear. Triggering occurring synchronously with cardiogenic oscillations also suggests autotriggered breaths. This is particularly true in young patients with relatively high stroke volume [39]. With PC and PS considerable variation in peak inspiratory flow or the duration of mechanical inspiration in patients with absence of dynamic hyperinflation may also be a clue of autotriggering (Fig. 6).

We should mention that, in contrast to AVC mode (where the ventilator once triggered provides a preset tidal volume with a preset flow time profile), with PC, PS and PAV events during the triggering phase may considerably influence the subsequently delivery of flow and volume by the ventilator. For example, breath-by-breath variability in tidal volume may be the cause of corresponding variability in the magnitude of dynamic hyperinflation in the face of constant patient's respiratory effort [44]. Also, the flow-time waveform of autotriggered breaths may differ substantial from that of breaths triggered by the patient's inspiratory effort (Fig. 6, see also theoretical consideration in the Electronic Supplementary Material).

Respiratory drive

With pressure triggering system the patient in order to open the demand valve contracts his/her inspiratory

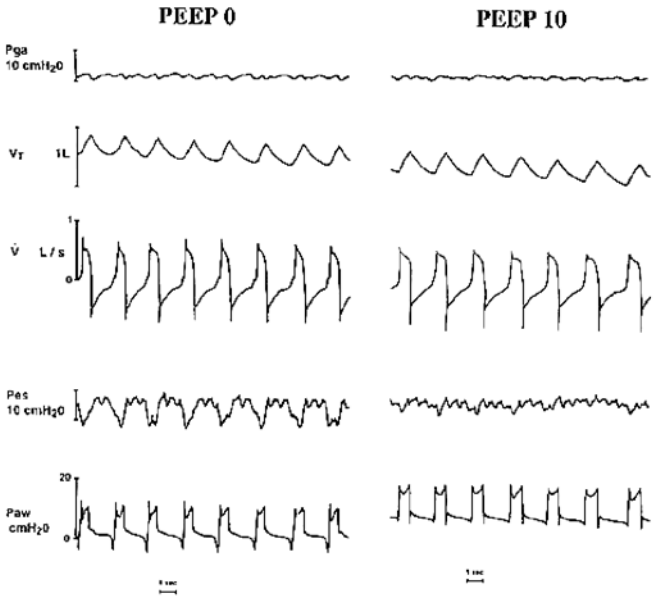

Fig. 7 Gastric pressure (*Pga*), tidal volume (V_T), flow (V'), esophageal pressure (*Pes*) and airway pressure in a patient with obstructive lung disease ventilated with pressure support without and with PEEP using a pressure triggering system. Note that application of PEEP decreases patient respiratory effort, as indicated by the decrease in Pes excursion. This decrease is reflected in Paw decrease before triggering. (With permission from [46])

muscles isometrically. As a result the rate of Paw decrease should be similar to that of alveolar pressure which reflects the rate of Pmus increase, which is an index of respiratory drive. Measuring the rate of Paw decrease during the zero flow interval provides an estimate of respiratory drive. Studies have shown that the rate of Paw during the interval of zero flow with pressure triggering system gives similar information with $P_{0.1}$ obtained by airway occlusion for 100 ms [45, 46]. In the presence of high respiratory drive the ventilator may not respond in an adequately timely manner to the rapid drop of Paw before triggering, and as a result Paw significantly decreases below the threshold for triggering (Fig. 7) [46, 47]. Similar to $P_{0.1}$, several factors should be taken into consideration before the rate of Paw decrease during the triggering time is interpreted as reflecting the respiratory drive. Dynamic hyperinflation and the shape of the rising phase of Pmus may influence the measurement independent on the respiratory drive [48].

The above principles should not be applied when flow or flow-waveform methods of triggering are used since with these systems there is no airflow obstruction and thus the decrease in Paw before triggering depends solely on the inspiratory resistance of ventilator circuit and instantaneous flow [16]. Considering that the new generation ventilators impose a minimal inspiratory resistance (close to zero) the decrease in Paw as a result of inspiratory flow generated by inspiratory muscle contraction is very small.

Waveforms during the pressurization and cycling off phases

Firstly the pressurization phase should be examined for the presence of ineffective efforts, as described above. Then signs indicative of patient's respiratory effort and of expiratory asynchrony should be sought. Finally, particularly with PS the pressurization rate should be also examined since it may considerably influence the waveforms.

Estimation of patient's respiratory effort

Assist volume control

As noted above, with AVC instantaneous flow and volume are the independent variables and instantaneous pressure the dependent variable in Eqs. 3 and 4. Thus Paw bears a negative relationship with Pmus, and the slope of this relationship is theoretically −1. Some ventilators, however, do not permit Paw to decrease below PEEP (the amount of Paw decrease is dictated by the variables of Eq. 4), and as a result flow and volume may be higher than the predetermined value. Under these circumstances the slope of Paw-Pmus relationship is greater than −1. With this mode the cycling off variable is time (or volume) whereas the ventilator delivers flow with a preset flow-time profile which is usually square-wave (i.e., constant) or decelerating [1, 15, 16].

By inspection of Paw the caregiver may estimate the patient's respiratory effort [42]. Equations 3 and 4 dictate that for a given preset volume-time and flow-time profiles Paw decreases with increasing inspiratory effort (Pmus is positive) and increases with increasing expiratory effort (Pmus is negative; Fig. 8). Therefore any deviation of Paw from that obtained with zero Pmus (i.e., absence of inspiratory effort during the pressurization) should be due to Pmus (Fig. 8). Despite the difficulty in obtaining a passive Paw waveform gross deviation of Paw from the expected contour of Paw during passive ventilation may give a qualitatively accurate estimation of patient's respiratory effort (Fig. 8) and guide the physician in choosing the settings (flow, volume) which are associated with minimal work of breathing.

Pressure support, pressure control

With PS and PC the dependent variables in Eq. 3 are instantaneous flow and volume, and independent variable is instantaneous Paw [15, 49]. Thus with this mode there is no relationship between Paw and Pmus. For this reason Paw waveform does not reflect the patient's inspiratory effort, and the caregiver should examine the independent variables such as flow and, to a much lesser

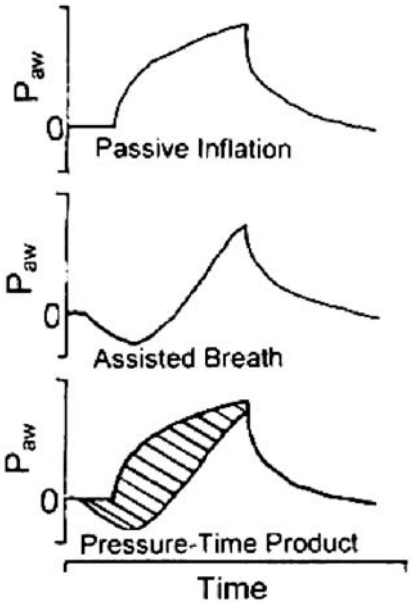

Fig. 8 Airway pressure (*Paw*) waveforms during controlled mechanical ventilation in a completely relaxed patient (*top*) and during a triggered breath (*middle*). The *shaded area* in the bottom waveform is the pressure-time product of the inspiratory muscles calculated as the difference in area subtended by the Paw-time curve in the presence (*middle*) and absence (*top*) of inspiratory muscle activity. The *shaded area* may be used as an index of inspiratory effort (large area indicates high inspiratory effort). (With permission from [42])

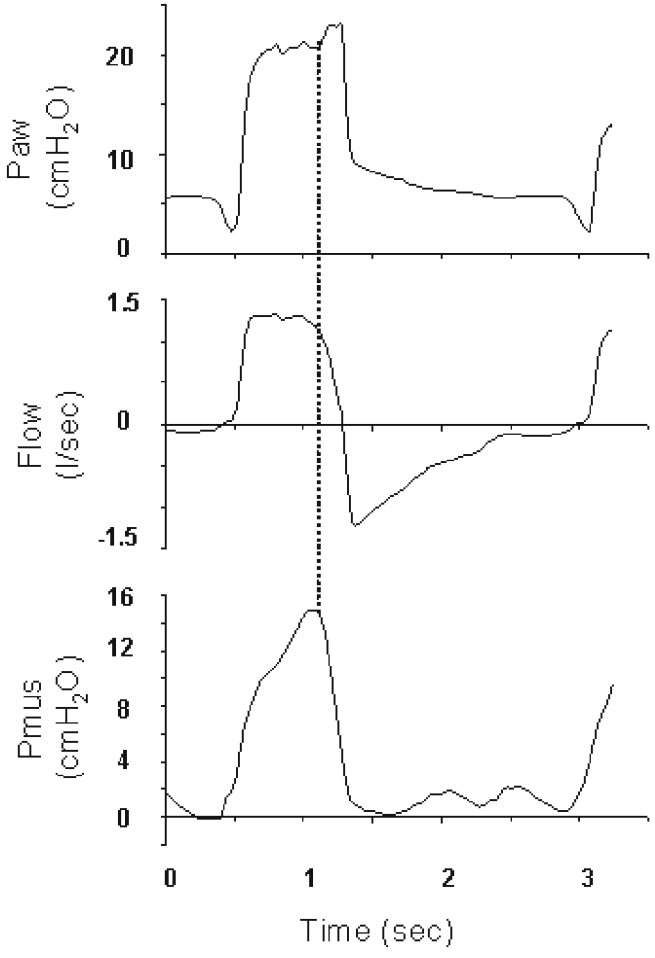

Fig. 9 Airway pressure (*Paw*), flow, and total pressure developed by respiratory muscles (*Pmus*) in a patient ventilated on pressure support. Observe that Pmus (calculated using esophageal pressure and taking into account passive elastic and resistive properties of chest wall, Campbell diagram) progressively increases toward the end of mechanical inspiration. The magnitude of this increase is considerable, indicating a vigorous contraction of inspiratory muscles. As a result inspiratory flow remains relatively constant throughout inspiration (because the progressive increase in inspiratory muscle pressure is able to counterbalance the progressive increase in elastic recoil pressure). Note finally that when Pmus starts to decrease rapidly (i.e., beginning of neural expiration, dotted line) Paw increases slightly due to the fact that the ventilator is not able to precisely follow the rapid Pmus change and maintain constant pressure in the circuit

extent, volume in order to estimate the patient's breathing effort. In addition because the interaction between Pmus and cycling off criteria has significant impact on the duration of pressurization phase, its examination may reveal information about the patient's respiratory effort. With PS, if the patient relaxes all respiratory muscles immediately after triggering, the duration of pressurization phase should be determined by the time taken for the exponential declining flow to reach the flow threshold (V'_{th}) for cycling off (a percentage of peak inspiratory flow or a fixed value). This depends on (a) the time constant of respiratory system (τ) and (b) V'_{th}; this increases with increasing τ and decreasing V'_{th} [50]. If the patient does not relax, the respiratory muscles (inspiratory and expiratory) after triggering the resulting flow and volume, as well as the duration of inspiration, is rather unpredictable since Pmus may vary from breath to breath and from time to time. Nevertheless, inspection of flow-time waveform provides information on the patient's respiratory effort. Any deviation of flow waveform from that achieved during passive conditions (an exponential declining pattern) indicates respiratory muscle effort (inspiratory or expiratory) [51, 52]. For example, rounded or constant flow suggests significant inspiratory effort and might be due to inadequate PS (Fig. 9). On the other hand, a rapid decrease in inspiratory flow to V'_{th} in a patient with relatively long time constant is a sign of expiratory muscle contraction and considerable asynchrony between patient and ventilator (Fig. 10) [53].

In patients with high airway resistance mechanically ventilated on PS, inspiratory flow after an initial peak may decrease abruptly, generating a flow spike (see Electronic Supplementary Material, Fig. S33). This is a sign of severe obstructive lung disease, the initial peak inspiratory flow representing the air displacement from

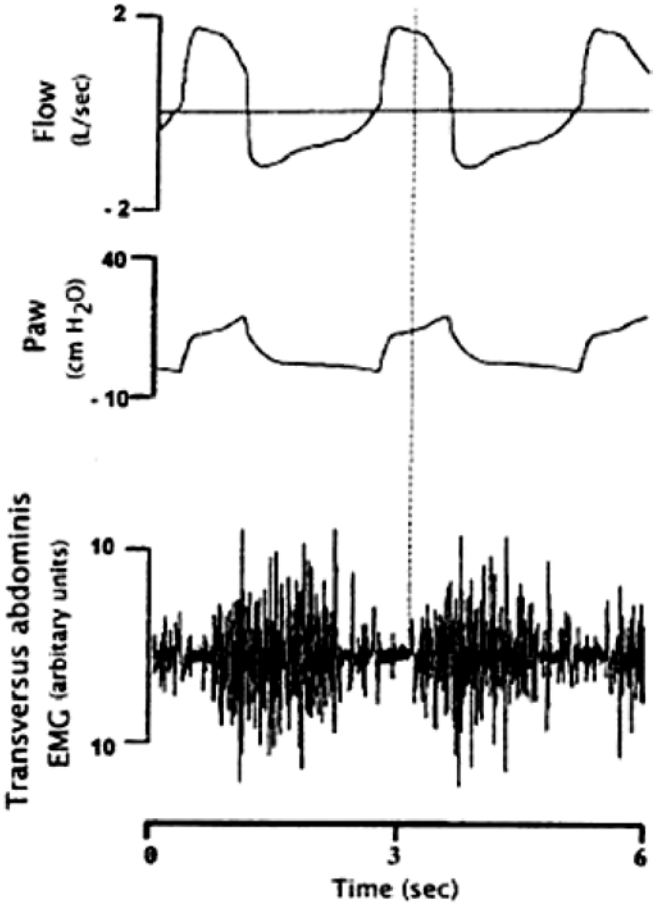

Fig. 10 Flow, airway pressure (*Paw*), and expiratory muscle activity (*EMG*) in a patient ventilated with pressure support. Note the rapid decrease in inspiratory flow and the slight increase in Paw at the onset of expiratory muscle contraction (*dotted line*). (With permission from [27])

the endotracheal tube and large airways [54]. However, we should note that a similar pattern can be observed if the patient relaxes his/her inspiratory muscle or contracts his/her expiratory muscles. Inspection of esophageal pressure and clinical examination may differentiate between these two causes (Fig. 2). A similar pattern may be observed during expiration, although it is not unique to PS (see below) (Fig. 2).

Rising time

With the new generation ventilators the caregiver may modify the time in which pressure delivered by the ventilator reaches the preset value (rising time) [21, 47, 55, 56]. Equation 3 predicts that the rising time has a profound effect on flow-time waveform [57]. An instantaneous increase in pressure to desired level (rising time 0) should be associated with a sharp increase in inspiratory flow as dictated by the interaction between Paw, Pmus, and elastic recoil pressure at end-expiration [31, 58, 59]. In some ventilators a very high pressurization rate is associated with pressure overshoot (Fig. 3) and increased sense of dyspnea. On the other hand, a slower increase in rising time eliminates the sharp increase in inspiratory flow because when pressure achieves its final value, the opposing effect of elastic recoil (due to volume increase during the rising time) decreases the driving pressure (i.e., Paw+Pmus-Pel) for flow [31, 58, 59, 60]. Very low rising time may cause a rounded shape of inspiratory flow. We should note that a similar pattern (rounded shape) may be observed if the patient continues to increase his/her inspiratory muscle pressure during mechanical inspiration.

Expiratory asynchrony

It has been shown that expiratory asynchrony is a common phenomenon during all modes of assisted mechanical ventilation [2, 28, 30, 56, 61, 62, 63]. As note above, expiratory asynchrony occurs when the end of mechanical inspiration precedes or follows the end of neural inspiration [2, 27, 61]. With AVC the duration of mechanical inspiration is preset, and expiratory asynchrony is the rule. Although with PS the various algorithms to terminate the pressurization phase were designed to synchronize the end of mechanical inflation with that of neural inspiration, in reality this rarely if ever occurs [27]. To overcome this problem in the new generation ventilator the caregiver has the option to modify the flow criterion for cycling off [29, 30]. Indeed by changing V'_{th} and all else being similar, the duration of mechanical inspiration changes [31, 60]. Thus it is important for the physician to recognize this expiratory asynchrony during PS ventilation. With PAV expiratory asynchrony is greatly minimized since with this mode there is a link between Paw and Pmus. Nevertheless technical features of ventilator function may delay for a few milliseconds the end of mechanical inspiration [63].

Premature termination of mechanical inspiration

With all modes of ventilatory support in passive condition the opening of the exhalation valve reverses flow from inspiratory to expiratory due to positive elastic recoil at end inspiration [21, 26, 30]. Expiratory flow instantly achieves its highest value as dictated by the elastic recoil pressure at end-inspiration, airway pressure (i.e., PEEP), and expiratory resistance (respiratory system + ventilator circuit). Thereafter flow decreases exponentially to zero following the corresponding decrease in elastic recoil pressure. If the patient continues to generate inspiratory muscle pressure, this expiratory flow pattern will be af-

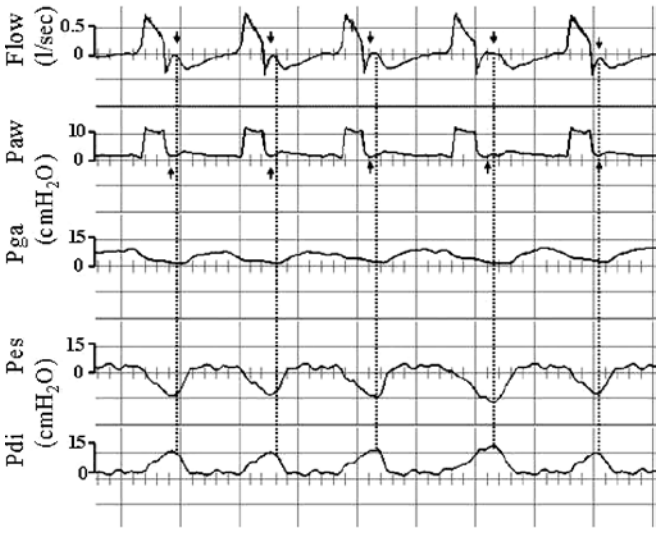

Fig. 11 Flow, airway pressure (*Paw*), gastric pressure (*Pga*), esophageal pressure (*Pes*), and transdiaphragmatic pressure (*Pdi*) as a function of time in a patient ventilated with pressure support. Observe the flow and Paw distortion early in expiration (*arrows*) caused by continuing contraction of inspiratory muscles. The end of neural inspiration is the point at which Pdi started to decline rapidly (*dotted vertical line*). This type of expiratory asynchrony is due to premature opening of exhalation valve (premature termination of mechanical inspiration)

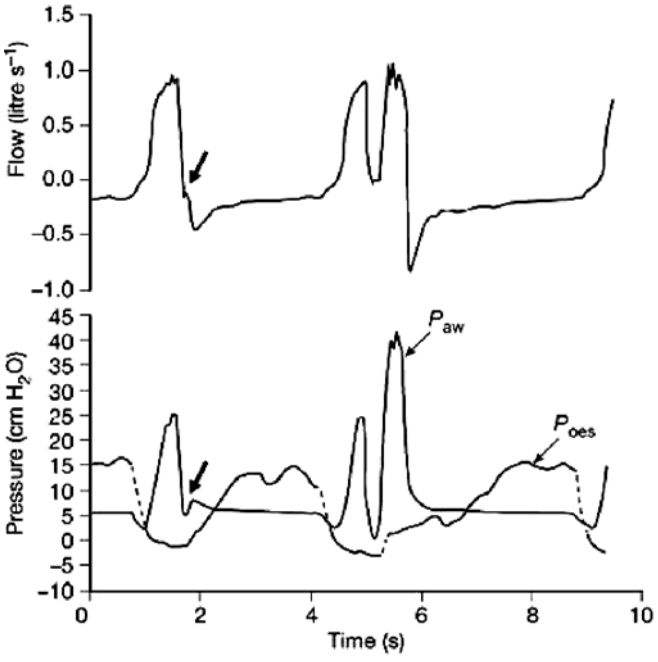

Fig. 12 Flow, airway pressure (*Paw*), and esophageal (*Pes*) pressure in a patient recovering from acute lung injury and ventilated on assist volume control with constant inspiratory flow. In the first breath the retardation of early expiratory flow and the distortion of Paw after opening of exhalation valve (*thick arrows*) are signs of premature termination of mechanical inspiration. This is clearly shown in the second breath in which tidal volume (volume was not shown) is decreased at the same inspiratory flow. As a result mechanical inflation time is further reduced, exaggerating the premature termination of mechanical inspiration. Because inspiratory muscles continue to contract with open exhalation valve, they develop pressure which overcame the elastic recoil at the end of inspiration. As a result Paw decreases below the triggering threshold, and thus the ventilator delivers a new mechanical breath. The ventilator is triggered three times by the two inspiratory efforts. Observe the high Paw of the third mechanical breath due to high lung volume (the volume of the third breath was added to that of the second). Note also that total breath duration of the second respiratory effort of the patient was considerably longer than that of the first one, owing to activation of Hering-Breuer reflex by the high volume

fected depending on the variables of Eq. 3. Zero or small inspiratory flow for some time after opening the exhalation valve indicates that inspiratory muscles continue to contract after the end of mechanical inspiration. In some cases there is a sharp decrease from the peak expiratory flow which lasts few milliseconds followed by an increase and then decreases gradually to zero toward the end of expiration [30, 31] (Fig. 11). The later flow-time waveform is due to the fact that when ventilation cycles off end-inspiratory elastic recoil pressure is higher than inspiratory muscle pressure and as a result alveolar pressure is positive creating expiratory flow. Because volume (and thus elastic recoil pressure) decreases while inspiratory muscles continue to contract, a progressively increasing opposing pressure to expiratory flow ensues, causing a corresponding decrease in expiratory flow and retardation of volume decline. Relaxation of inspiratory muscles eliminates this opposing pressure and expiratory flow increases as determined by the elastic recoil pressure and resistive properties of the patient and expiratory circuit. In some breaths inspiratory effort is adequate to decrease expiratory flow to zero and initiate the triggering process (Fig. 12). In these cases one inspiratory effort triggers the ventilator more than once [30, 64]. With PS the duration of the second breath is usually relatively short because the inflation of the lung starts at lung volumes well above the passive FRC and as a result the driving pressure for inspiratory flow is relatively low. On the other hand, with AVC the ventilator, once triggered, delivers the preset volume which adds to the remaining volume from the previous breath in the cost of high airway pressure (Fig. 12).

With PS premature termination of pressure delivery is caused by low levels of PS, short time constant of respiratory system, relatively high V'_{th}, and dynamic hyperinflation which reduces the driving pressure for flow [30, 31]. With AVC settings which decrease the duration of inflation phase promotes this type of expiratory asynchrony.

Delayed opening of exhalation valve

Identification of delayed opening of exhalation valve in relation to neural inspiration using the basic waveform is difficult, particularly if the patient does not contract his/her expiratory muscles. Relaxation of inspiratory muscles before the end of mechanical inspiration results in pressure, flow, and volume waveforms similar to these obtained with passive inflation. To the extent that passive contour waveforms are not known recognizing this type of expiratory asynchrony imposes significant difficulty. Despite such difficulty with PS a rather sharp decrease in inspiratory flow followed by an exponential decline toward the end of mechanical inspiration indicates that neural inspiration ends well before the exhalation valve opens. In some cases the end of neural inspiration (i.e., Pmus starts to decline rapidly after its peak) causes, similar to the case with expiratory muscle contraction, a small increase in airway pressure. Thus during PS Paw may increase either by abrupt relaxation of inspiratory muscles or contraction of expiratory muscles. In either case this Paw increase is an indication of delayed opening of expiratory valve (Fig. 9). We should note that if this increase is higher than a certain threshold (1.5–3 cmH_2O), the pressure delivery is terminated. With AVC a linear increase in airway pressure is a sign of termination of neural inspiration before the end of mechanical inflation (see Electronic Supplementary Material, Fig. S36).

With PS excessive support, long time constant of respiratory system of the patient, and relatively low V'_{th} are the main causes of this type of expiratory asynchrony [2]. With AVC ventilator settings that result in long mechanical inflation time, such as high tidal volume, low inspiratory flow, and application of end-inspiratory pause may cause delayed opening of exhalation valve [2].

Waveforms during mechanical expiration

Inspection of Paw-time waveform during mechanical expiration may give information about the resistance of expiratory circuit. This is because during expiration Paw depends on the resistance of expiratory circuit (from the point at which Paw is measured to the PEEP valve) and expiratory flow ($Paw=V'_E \times Rexp_{circuit} - PEEP$). Ideally $Rexp_{circuit}$ should be zero and thus when the ventilator cycles off Paw should decrease immediately to PEEP, remaining at this level throughout expiration independently on Palv. In real life, however, expiratory circuit exhibits a finite resistance which is flow dependent and in new generation ventilators ranges between 2–5 cmH_2O/l per second [40, 41]. It follows that Paw immediately in the beginning of expiration decreases abruptly from end-inspiratory Paw to a lower level as dictated by the Eq. 3 and followed by a gradual decline to PEEP which is reached when expiratory flow decreases to zero. Therefore during expiration the difference between PEEP and Paw is a reflection of the resistance of expiratory circuit. PEEP valve malfunction and kinking of expiratory tube may increase the resistance of expiratory circuit, and as a result the difference between PEEP and Paw increases throughout expiration. A similar pattern may be observed if a heat and moisture exchange filter placed upstream of the site of Paw measurement is obstructed by secretions. In this case the expiratory circuit resistance is higher than 2–5 cmH_2O/l per second.

In patients with flow limitation during tidal expiration inspection of expiratory flow-time waveform may reveal a pattern consisting of an expiratory flow which after an initial spike after the opening of the exhalation valve decreases abruptly to much lower values (Fig. 2). The initial expiratory flow spike is due to dynamic compression of central airways with expulsion of their air content at the beginning of expiration [65, 66]. Thereafter expiratory flow decreases since the high resistance to flow and the driving pressure from alveoli to choke point determine the value of flow. Interventions that limit the magnitude of flow limitation affect this pattern.

As note above, inspection of expiratory flow-time waveform is a sensitive method to detect the beginning of triggering phase. If the beginning of this phase occurs when flow is still expiratory, dynamic hyperinflation or relaxation of expiratory muscle should be suspected [67]. Clinical examination including palpation of the abdomen may differentiate between these two possibilities since relaxation of expiratory muscle requires active expiration.

Conclusion

The flow, volume, and airway pressure signals displayed in the monitor of new-generation ventilators are of great help in identifying several aspects of patient-ventilator interaction. A careful inspection of these signals helps the caregiver to recognize triggering delay, ineffective efforts, and autotriggering and gives an estimate of patient's respiratory efforts. Based on these signals delayed and premature opening of exhalation valve may be recognized and guide the ventilator settings. Finally, these signals may serve as a tool for gross estimation of respiratory system mechanics and monitor the effects of disease progression and various therapeutic interventions.

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