MEASUREMENTS OF RESPIRATORY MECHANICS DURING MECHANICAL VENTILATION

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Preface

This handbook has been conceived for physicians and researchers who already have a basic knowledge about mechanical ventilation in anesthesia and respiratory intensive care, and enter for the first time into the wide field of the measurements of respiratory mechanics in the ventilated patient.

Most modern mechanical ventilators are provided with graphic and numeric monitoring of respiratory mechanics. Graphic monitoring generally shows graphs generated from the signals of airway pressure, gas flow and volume change of the respiratory system. Numeric monitoring results from automatic breath analysis performed on the primary signals. Stand-alone respiration monitors are also available, specialized for application in mechanically ventilated patients.

Nowadays, the information provided by respiration monitors is considered of critical importance for the correct utilization of mechanical ventilation. New ventilation modes have been, and are being developed, working with automatic adaptation of ventilator settings, based on the information provided by automatic breath analysis.

The intention of this handbook is to provide all the information necessary to understand the automatic measurements of respiratory mechanics, to perform manual measurements, and in general to exploit the potential of respiratory monitors at the best and maximum level.

Mechanical ventilation is a particular case of respiration. On one side, mechanical ventilation makes uneasy the use of the tests commonly performed in pulmonary pathophysiology, while on the other side it opens a series of opportunities not available in the conscious, spontaneously breathing subject. Thus, in the years of the recent history of mechanical ventilation, a number of methods have been developed, that are adapted and/or specialized for the particular condition of the ventilated patient. Many of these methods are presently standardized. However, the relative information is still more dispersed in a number of scientific publications, rather than organized in a modern handbook.

It is not our intention to exhaustively cover the entire field of all the proposed methods. The present handbook will deal only with those methods that are widely accepted and more commonly used. It will deal with methods already implemented in respiratory monitors as automatic measurements, or methods that can be easily put into practice by manual operations on the mechanical ventilator and the ventilator monitor, or methods that can be put into practice by means of very simple equipment.

In general, the maneuvers and the measurements of respiratory mechanics are better understood by looking at graphs. For this reason, this handbook contains a great number of figures, and a great part of the text has been written as a comment to figures. All figures are plots of the primary mechanical signals of respiration (airway pressure, gas flow, volume change, and esophageal pressure), and have been obtained from patients assisted with Galileo, the new mechanical ventilator of Hamilton Medical. Most of the plots in this handbook are similar to the plots shown by the graphic monitor of this ventilator.

The chapters of the handbook have been organized into three sections. Section A deals with the basics of mechanical ventilation and of ventilation monitoring. Section B deals with the measurements of the mechanics of the passive respiratory system: compliance, resistance, intrinsic PEEP, expiratory time constant, and static pressure-volume curve. Section C deals with the respiratory mechanics measurements that are of interest in the actively breathing patient: work of breathing, pressure-time product, maximal inspiratory pressure, and $P_{0.1}$. Approximately ten references have been selected for each chapter. The references include papers about the meaning and the use of the different measurements of respiratory mechanics, and papers dealing specifically with the methods of measurement. In several cases, interesting methodological information will be found in the Methods section of papers primarily conceived for exploring a physiological or pathological problem.

It is the authors' hope that this handbook will help the readers to improve the exploitation of the powerful means presently provided by ventilation monitors. It is also the authors' hope that a more precise, reliable and deep picture of the patient status will help to improve the treatment.

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ABBREVIATIONS, CONVENTIONS AND MATERIALS

List of Abbreviations

ARDS	Adult respiratory distress syndrome
ASV	Adaptive support ventilation
C	Compliance
C_L	Lung compliance
CMV	Volume-controlled mechanical ventilation
CO_2	Carbon dioxide
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
Crs	Respiratory system compliance
Cstart	Static compliance at 100 ml above FRC
Cstat	Static compliance
Cstat,L	Lung static compliance
Cstat,rs	Respiratory system static compliance
Cstat,w	Chest wall static compliance
Cw	Chest wall compliance
E	Elastance
Exp	Expiratory
FRC	Functional residual capacity
FRC,PEEPe	FRC artificially increased by PEEPe
I:E	Inspiratory to expiratory time ratio
Insp	Inspiratory
MIP	Maximal inspiratory pressure
Meas	Measured
NIP	Negative inspiratory pressure
P	Pressure
$P_{0.1}$	Occlusion pressure at 0.1 second
P_1	Initial elastic recoil pressure after rapid flow interruption
P_2	Static elastic recoil pressure after rapid flow interruption
PCV	Pressure-controlled ventilation
PEEP	Positive end-expiratory pressure
PEEPe	External PEEP
PEEPi	Intrinsic PEEP
PEEPtot	Total PEEP
PIMax	Maximal inspiratory pressure
PSV	Pressure support ventilation
PTP	Pressure-time product
PTPinsp,pat	Inspiratory pressure-time product for the patient

PTPinsp,vent	Inspiratory pressure-time product for the ventilator
$PaCO_2$	Carbon dioxide arterial tension
Patm	Atmospheric pressure
Paw,exp	Airway pressure at the ventilator expiratory port
Paw,insp	Airway pressure at the ventilator inspiratory port
Paw,o	Airway opening pressure
Paw,tr	Tracheal carina airway pressure
Pee,st	Static end-expiratory pressure
Pei,st	Static end-inspiratory pressure
Pel,add	Additional elastic load due to slow flow interruption
Pes	Esophageal pressure
Pes,0	Pes level of effort start
Pes,rel	Relaxed Pes
Ppause	Pause pressure
Ppeak	Peak pressure
Ppl	Pleural pressure
RCe	Expiratory time constant
RCi	Inspiratory time constant
R_L	Lung resistance
Rext	Ventilator expiratory way resistance
Rinit	Initial resistance
Rmax	Maximum resistance
Rmax,corr	Corrected maximum resistance
Rmax,L	Lung maximum resistance
Rmax,rs	Respiratory system maximum resistance
Rmax,w	Chest wall maximum resistance
Rrs	Respiratory system resistance
Rs	Respiratory system
Rw	Chest wall resistance
V	Volume
V'	Gas flow
V',exp	Gas flow in the ventilator expiratory pathway
V',insp	Gas flow in the ventilator inspiratory pathway
V'aw	Airway gas flow
V'aw,o	Airway opening gas flow
V'e,peak	Expiratory peak flow
V'ei	End-inflation flow
Vol	Respiratory system volume change
Vol,ee	End-expiratory lung volume
Vol,ei	End-inspiratory lung volume

Vt	Tidal volume
Vte	Expiratory tidal volume
Vti	Inspiratory tidal volume
Vti'	End-inflation volume
Wexp	Expiratory work of breathing
Winsp	Inspiratory work of breathing
Winsp,pat	Patient inspiratory work of breathing
Winsp,tot	Total inspiratory work of breathing
Winsp,vent	Ventilator inspiratory work of breathing
Wpat	Patient work of breathing
Wtot	Total work of breathing
Wvent	Ventilator work of breathing
ΔR	Rmax-Rinit difference
ΔVol	Volume change
ΔVol,ee,dyn	Dynamic increase in end-expiratory lung volume
ΔVol,ee,st	Static increase in end-expiratory lung volume
ΔVol,max	Maximum volume change

CONVENTIONS

The units for airway pressure and esophageal pressure are those that are commonly used in clinical practice in Italy (1 cmH_2O = 0.098 kPa). Values for airway pressure and esophageal pressure are referenced to atmospheric pressure.

A positive sign is assigned to the inspiratory flow, and a negative sign to the expiratory flow.

A value of zero is assigned to the end-expiratory lung volume of normal breaths.

MATERIALS

Most of the recordings used for the illustrations have been obtained from tests performed on patients ventilated with the Galileo ventilator (Hamilton Medical AG, Rhäzüns, Switzerland). The recordings have been performed on Apple Macintosh computers by means of the EasyDAQ software and hardware (Design Shop, Chur, Switzerland), and processed by StatView 4.5 (Abacus Concepts, Berkeley, CA). The three-dimensional plots have been generated with the Plot3D 2.1.0 plug-in module for pro Fit 5.1 (QuantumSoft, Zürich, Switzerland).

Section A

BASICS

1. PATIENT-VENTILATOR INTERACTION

The study of respiratory mechanics in ventilated patients is based on the analysis of mechanical signals of the respiratory system. Before entering in details about the methods for the qualitative and quantitative analysis of the mechanical signals of respiration, we will review some basic concepts of mechanical ventilation, about:

- how mechanical ventilators work,
- how the respiratory system can be represented by mechanical models,
- and which are the differences between passive ventilation and mechanically assisted active ventilation.

1.1. Volume-control and pressure-control mechanical ventilation

A mechanical ventilator may control either instantaneous gas flow (and hence the volume change of the respiratory system) or instantaneous airway pressure. By definition, the mechanical ventilator cannot control simultaneously both instantaneous gas flow and pressure. At any given time, the one of the two variables that is not controlled by the ventilator varies according to the active and passive forces applied by the patient.

During the expiratory phase in all ventilation modes the mechanical ventilator controls pressure, according to the set level of PEEP. Hence, during expiration the observation of airway pressure only provides information on the action of the ventilator, while the mechanical characteristics of the respiratory system are reflected by the gas flow and the volume change.

During the inspiratory phase, the mechanical ventilator may control either the gas flow or the airway pressure, according to the selected mode, respectively volume-controlled or pressure-controlled. In volume-control modes, like CMV, the inspiratory signals for gas flow and volume change provide information on the action of the ventilator, while the inspiratory airway pressure reflects the response of the respiratory system. On the contrary, in pressure-control modes like PCV and PSV, the inspiratory airway pressure reflects the action of the ventilator, while the inspiratory gas flow and volume change reflect the response of the respiratory system.

The distinction between what is controlled by the ventilator and what is a response of the patient respiratory system is essential for all the analysis of the mechanical signals of respiration. The variables that describe the respiratory system response have an obvious interest. The variables that primarily depend on the ventilator have a double interest. First, they are frequently used, in combination with variables resulting from the patient response, for respiratory system measurements. For example, the measurement of total compliance is given by the ratio between the tidal volume delivered in CMV by the ventilator, and the static pressure difference resulting in the respiratory system. Second, the variables controlled by the ventilator provide information about the condition in which a given quantitative measurement is taken, or qualitative observation is made. For example, the external PEEP level applied by the ventilator is essential to characterize a given observation of dynamic pulmonary hyperinflation of the patient, as well as PEEP and tidal volume provided by the ventilator during a CMV breath are essential to characterize a given measurement of compliance of the respiratory system.

1.2. Mechanical models of the passive respiratory system

The passive respiratory system may be represented by many different mechanical models. We will review the simplest of them.

The simplest model is represented by the linear, one-compartment model. In this model the airway is single and is connected to a single elastic balloon, representing the whole complex of the alveoli and the chest wall. Airway resistance and balloon compliance are constant at any given value for flow and volume. The product of resistance and compliance corresponds to the time constant of the system. This variable reflects the speed by which the system changes its volume in response to a change in the applied pressure. A linear one-compartment model is described by a single value for time constant. This model can be usefully applied in normal subject and in restrictive syndromes, while the application in obstructive syndromes may be more critical.

A different model is the linear two-compartment model. In this case the airway divides into two bronchi, each one connected to an elastic balloon. Each half-system has specific values for resistance and compliance, that remain constant for any given level of flow and volume. Each of the two compartments has a specific value for time constant, given by the product for its resistance and its compliance. This means that one compartment may be faster than the other one, when its resistance and/or its compliance is lower. In response to a pressure change, the fast compartment will change its volume and tend to the equilibrium before the slow compartment. This asymmetrical response means that although each of the two compartments has a linear mechanical behavior, the whole system may have a non-linear behavior. This model of a non-homogeneous respiratory system should be applied to patients presenting evident asymmetrical diseases (for instance one-lung disease, or obstruction of one stem bronchus). The two-compartment model can also be usefully applied in COPD patients, in particular for exhalation. Many COPD patients present two phases of exhalation: an initial fast phase, due to the emptying of a fast compartment, is followed by a slow phase, due to the emptying of a slow compartment. Also, this model is useful to explain the long time sometimes required for reaching a stable airway opening pressure after the start of an occlusion maneuver, i.e., after a sudden stop of flow at the airway opening. During an occlusion maneuver, some flow takes place between the fast and the slow compartment, and airway opening pressure does not stabilize until both compartments have reached the equilibrium. This phenomenon, known as "pendelluft", may be particularly evident in obstructive patients, who may present a very slow compartment due to the combination of high resistance and high compliance. However, this phenomenon may be observed also in acute restrictive patients with ARDS.

A third family of models is given by the non-linear, one-compartment models. In this case we have a single airway connected to a single elastic balloon. Airway resistance and balloon compliance may vary with values for flow and volume. An example of the non-linear, one-compartment model is given by an airway resistance that is constant, while the compliance of the balloon decreases over a given value for respiratory system volume. This model can be applied to many patients with restrictive respiratory syndrome (like ARDS or lung fibrosis), especially when they are not ventilated with subnormal tidal volumes. During the delivery of normal or high tidal volumes, the respiratory system typically responds, over a given value of volume, with a sharp rise in alveolar pressure due to overdistension of rigid structures.

Any method of measurement of respiratory mechanics is based on a given respiratory system model. Hence, the result of a given method may be more or less close to the actual value of a parameter, depending on just how close the patient respiratory system is to the model employed. In theory, in any given disease and condition, we should use only the methods based on a model that can be satisfactorily applied. In the common practice, however, the simplest methods based on the single-compartment linear model are used in a wide variety of conditions.

1.3. Passive and active breathing

Relaxed or paralyzed patients are passively ventilated by the machine. Both in volume-controlled modes and in pressure-controlled modes, during inspiration the machine increases the pressure at the airway opening, promoting an inward-directed flow through the airways and an increase in respiratory system volume. Exhalation is achieved by removal of the airway opening pressure increase that has taken place during inspiration. The elastic energy accumulated by the respiratory system during inspiration will promote an outward-directed flow through the airways and a decrease in respiratory system volume.

The simple condition of passive ventilation is the most favorable one for some measurements like airway resistance and total respiratory system compliance. Moreover, during passive ventilation important information for optimal setting of the mechanical ventilator can be easily obtained by simple observation of curves and loops of the fundamental mechanical signals, airway pressure, gas flow and volume change. The additional measurement of esophageal pressure is only required for the optional and particular purpose of partitioning the study of respiratory mechanics between the chest wall and the lungs.

However, in respiratory intensive care units, most of the patients submitted to mechanical ventilation spend most of their time in assisted modes. Patients are actively breathing, and the machine simply supports ventilation. The basis for assisted ventilation is synchronization of the ventilator on the spontaneous activity of the patient. The minimal option is to synchronize the start of the inflation phase of the ventilator on an inspiratory effort of the patient. A patient inspiratory effort normally starts at the end of a passive exhalation or during a passive exhalation. An inspiratory effort corresponds to a traction applied by the inspiratory muscles to the passive structures of the respiratory system, resulting in inward-directed flow through the airways, and in a pressure drop at the airway opening. The development either of an airway opening pressure drop, or of an airway opening inspiratory flow, is taken by the ventilator sensors as a signal from the patient to begin inspiration, according to the use of a pressure-trigger or of a flow-trigger, respectively. Once the inspiratory effort is detected, the ventilator will respond by starting its inspiratory phase. This kind of mechanism means that the inspiratory phase of the ventilator will always start with a given delay, relative to the inspiratory phase of the patient. After this delay, inspiration may proceed due to the combined action of the inspiratory musculature and the ventilator, the former pulling and the latter pushing gases into the respiratory system.

Synchronization between patient and ventilator may be lost at different times of the respiratory cycle, depending on the timing of muscle contraction and on the setting of the ventilator. When the ventilator cycling to exhalation is time-based, like during synchronized CMV or synchronized PCV, patient-ventilator synchronization after the start of the ventilator inspiratory phase is a contingent phenomenon, that may, or may not, take place. On the contrary, during PSV, synchronization is more likely to persist, due to a flow-trigger system that tends to command the machine cycling to the expiratory phase when the patient inspiratory effort ends. In any case, it may happen that the inspiratory muscles are fully relaxed before the end of the machine inspiratory phase. This means that the last part of inhalation, as well as all exhalation, will be performed only on the basis of the pressure applied (or removed) by the ventilator, and thus will be exactly the same as in a patient that is passively ventilated for the entire cycle.

The opposite phenomenon is represented by a patient who extends some contraction of the inspiratory muscles even when the machine has cycled to the expiratory phase. In this case the entire inhalation is achieved by cooperation between patient and ventilator. Later, after the start of the expiratory phase, ventilator and patient will enter into competition, the former promoting exhalation and the latter partially opposing exhalation. This kind of brake applied by the patient to the initial expiratory flow is a phenomenon known as post-inspiratory contraction of the inspiratory muscles, is commonly observed in physiological spontaneous breathing, and may be exaggerated in pathological conditions. The occurrence of this phenomenon means that the dynamics of exhalation is different from the one observed during paralysis. Namely, the expiratory flow during the first part of exhalation will be lower than in the passive condition.

The complexity of mechanically assisted, active breathing gives rise to two orders of problems. The first point is how to gather information about the passive characteristics of the respiratory system. Apparently, the simplest option is to switch off the spontaneous activity of the patient, by temporary sedation and paralysis. However, this approach is not always practical, and does not completely solve the problem, since the simple transfer of data obtained during paralysis to a condition of active breathing may not be always and entirely correct. For instance, a measurement of dynamic pulmonary hyperinflation in paralysis may not reflect the real, and worst, condition occurring during spontaneous breathing. The second point to consider is how to obtain a full picture of an actively breathing patient, who should be studied for a series of parameters that are different from those typically studied in a passive patient.

Namely, in active patients we are mainly interested in parameters that describe the activity of the respiratory muscles (like maximal inspiratory pressure, patient work of breathing, $P_{0.1}$), data that are useful for setting the mechanical ventilator and adapting the weaning process.

In the actively breathing, mechanically assisted patient, the study of respiratory mechanics is therefore more complex and difficult. The main difficulty is due to the fact that the mechanical variables of common use, airway pressure, gas flow, and volume change are not the only ones involved in the mechanism of ventilation. In order to have a full picture, the esophageal pressure should also be considered. An analysis simply based on airway pressure, gas flow, and volume change is a real challenge.

1.4. Measurements of respiratory mechanics

The most important parameters that describe the passive components of the respiratory system are resistance, compliance, and intrinsic PEEP. In the restrictive lung diseases, the static-pressure volume curve can also provide interesting information. Although not commonly used, the time constant of the respiratory system is another parameter that is simple to measure and may be useful for the setting of the mechanical ventilator.

Most commonly these measurements are taken for the entire respiratory system, on the basis of recordings of airway opening pressure, gas flow, and volume change. The partitioning of passive respiratory mechanics between the lungs and the chest wall, based on the additional recording of esophageal pressure, may be interesting, but is not common practice.

The study of the activity of the respiratory muscles can be approached by two simple parameters, maximal inspiratory pressure and $P_{0.1}$, measured from the airway opening pressure. However, a precise and full assessment of the energetics of breathing includes also the measurements of work of breathing and pressure-time product, and hence requires the recording of gas flow, volume change, airway opening pressure, and also esophageal pressure.

Several of these measurements of respiratory mechanics are automatically performed by the monitors of modern ventilators and by stand-alone respiration monitors. Other measurements, based on special maneuvers, can be easily put into practice by manual operations on the mechanical ventilator and the ventilator monitor.

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2. SIGNALS FOR RESPIRATORY MECHANICS MEASUREMENTS

2.1. Primary signals

The study of respiratory mechanics in ventilated patients is based on the recording of a few primary mechanical signals of respiration. The most commonly used primary signals are airway pressure (Paw) and gas flow (V'aw). Integration of gas flow provides a third fundamental signal, the spirogram, i.e., the volume change in time for the whole respiratory system (Vol). Eventually, the optional recording of a forth signal, the esophageal pressure (Pes), may add a great amount of information.

The primary mechanical signals from the respiratory system can be obtained with stand-alone instruments, provided with sensors for Paw and V'aw, or for Paw, V'aw, and Pes. These instruments generally calculate the spirogram from the V'aw signal, display curves on a screen, allow printouts, and provide data from the automatic analysis of the signals.

A more practical approach to the study of respiratory mechanics is based on the extended use of the mechanical ventilator. All modern mechanical ventilators include sensors for the measurement of the primary mechanical signals from the respiratory system. In particular, sensors for Paw and V'aw are used both for driving the complex functions of the ventilator and for monitoring purposes. V'aw is integrated to give the signal for Vol, the different signals are displayed on a built-in screen (or on an optional screen), and automatic breath analysis is performed and displayed. The ventilators by Hamilton Medical are also provided with an auxiliary pressure sensor, that can be used for the measurement of Pes or for other purposes.

Mechanical ventilators present major differences in the type and the location of the sensors, which may result in a more or less favorable setup for using the system for the study of respiratory mechanics. In the present chapter we will analyze these differences.

2.2. Airway pressure

The airway pressure (Paw) signal describes the forces applied by the mechanical ventilator to the respiratory system. Paw is measured with solid-state sensors, connected by means of a gas-filled line to a given point of the respiratory circuit of the ventilator.

The best location for assessing the real action of the ventilator on the respiratory system is represented by the airway opening. For the measurement of airway opening pressure (Paw,o), the Paw sensor line is connected to a port located between the external extremity of the endotracheal tube and the Y-piece of the external circuit of the ventilator. This point of measurement is typically exposed to humidity and secretions. In order to prevent obstruction of the sensor port and line, the former must be oriented upward, and the latter must be provided with a purge flow. The Hamilton Medical ventilators are provided with the measurement of Paw,o, and use for this purpose one of the pressure sensing lines of the airway opening flow sensor, namely the line that is more proximal to the patient.

For practical reasons, in most mechanical ventilators the choice is made to locate the Paw sensor port far away from the airway opening, in points where gases are clean and dry. Typically Paw is measured inside the body of the ventilator, either in the inspiratory pathway, between the inspiratory valve and the inspiratory gas outlet (Paw,insp), or in the expiratory pathway, between the expiratory gas inlet and the exhalation valve (Paw,exp). Both Paw,insp and Paw,exp are less favorable than the Paw,o for the study of respiratory mechanics. With the Paw,o approach, the mechanical ventilator makes a single unit with its external circuit, and Paw,o exactly reflects the interaction between this unit and the patient respiratory system (the latter only including the endotracheal tube as a part of the airway). On the contrary, Paw,insp and Paw,exp explore the effects of the interaction between the ventilator and a unit made of the respiratory system, the endotracheal tube, and parts of the external circuit of the ventilator.

Figure 2-1 shows the simultaneous signals for Paw,o, Paw,insp, and Paw,exp during a CMV respiratory cycle, delivered with a constant inspiratory flow and an end-inspiratory pause, in a passive patient. The effects of sampling Paw in different locations are evident. During the whole inflation phase, Paw,insp is higher than Paw,o, while Paw,exp and Paw,o are very close. During the first part of exhalation, Paw,insp is slightly lower than Paw,o, while Paw,exp is much lower than Paw,o. Only when gas flow is zero, i.e., during the end-inspiratory pause and at the end of exhalation, the differences between the three signals disappear. This means that the Paw sampling point makes no difference for static (no-flow) measurements, while it makes a lot of difference for all dynamic measurements, taken in presence of flow.

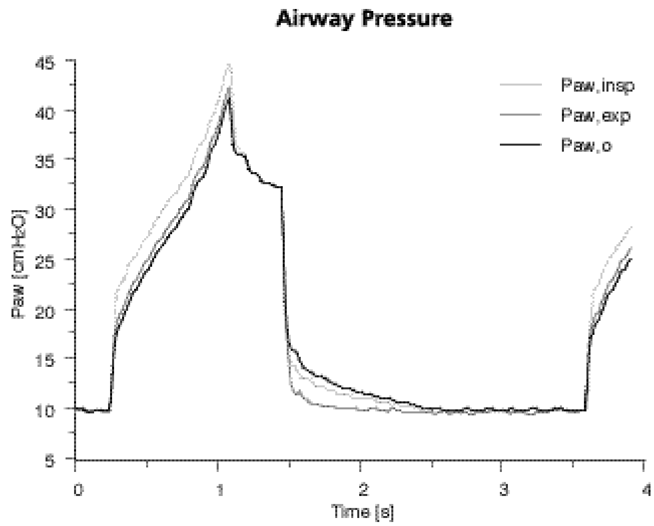

Fig. 2-1
Airway pressure recorded from three different locations: ventilator inspiratory pathway (Paw,insp), ventilator expiratory pathway (Paw,exp), and patient airway opening (Paw,o). Paralyzed patient in CMV. The same cycle is analyzed in Figs. 2-1, 2-3, 2-4, 2-5

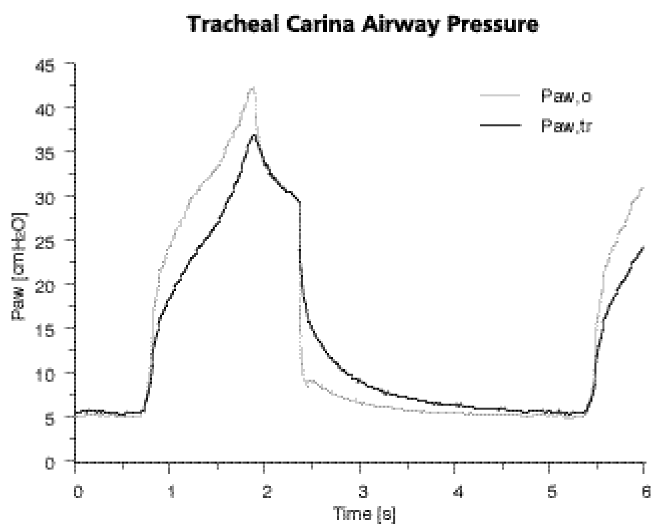

Fig. 2-2
Patient airway pressure recorded from two different locations: airway opening (Paw,o) and tracheal carina (Paw,tr). Paralyzed patient in CMV.

Some users may be interested in collecting the Paw signal near to the tracheal carina (Paw,tr), instead of Paw,o, or additionally to Paw,o. The interest of Paw,tr is that this pressure describes the interaction between the pure respiratory system on one side, and the entire artificial apparatus on the other side, the latter including the ventilator, the external circuit of the ventilator, and also the artificial airway. The difference between Paw,o and Paw,tr is due to the resistance of the endotracheal tube and may be relevant, especially when the tube is long and/or narrow. In Fig. 2-2 we have plotted the simultaneous signals for Paw,o and Paw,tr, in a CMV cycle delivered with a constant inspiratory flow and an end-inspiratory pause, in a passive patient. The patient was ventilated through an orotracheal tube of 7.5 mm ID and of normal length. Paw,tr was measured by means of a thin catheter advanced through the endotracheal tube to the carina. Paw,tr is evidently lower than Paw,o during the whole inflation phase, while it is higher than Paw,o during exhalation, especially in the first part, when flow is maximal. At the end of the end-inspiratory pause, as well as at the end of exhalation, when gas flow is zero, Paw,tr and Paw,o are coincident.

The measurement of Paw,tr can be easily performed with stand-alone monitoring systems, as well as with the Hamilton Medical ventilators, that have a monitoring system provided with an auxiliary pressure port. Continuous monitoring of Paw,tr necessarily requires that the pressure sensing line be kept clear by a purge flow. Although the measurement of Paw,tr may be relatively easy and potentially interesting, it is not a common practice in mechanically ventilated patients.

2.3. Airway gas flow

The measurement of the flow of gas running in the patient airways (V'aw) raises problems similar to those of the measurement of Paw. Again, in most ventilators gas flow is measured in protected locations inside the machine body, where gases are clean and dry. In this case, since in the ventilator circuit the inspiratory flow pathway is different from the expiratory flow one, two different sensors are needed, one in the inspiratory pathway and one in the expiratory pathway of the circuit. At first glance, the problem of measuring V'aw can be easily solved with a simple combination of the signals coming from the two sensors, i.e., by using the former sensor for the measurement of the inspiratory V'aw, and the latter sensor for the measurement of the expiratory V'aw.

However, the problem is made more complex by the extended use of flow-by in modern ventilators. Flow-by is a given amount of gas flow that is delivered through the ventilator circuit during exhalation, ready to compensate for an inspiratory effort of the patient. Flow-by is obviously detected by the inspiratory flow sensor inside the ventilator, although it does not correspond to an inspiratory flow to the patient, except in case of patient inspiratory effort. Accordingly, flow-by is detected by the expiratory flow sensor inside the ventilator, although it does not represent an expiratory flow coming from the patient.

The problem is illustrated in Fig. 2-3, representing a CMV respiratory cycle, delivered with a constant inspiratory flow and an end-inspiratory pause. In this example the patient is passive and a flow-by is operative. In the upper panel we have plotted the gas flow simultaneously detected by two sensors inside the ventilator, respectively in the inspiratory pathway (V',insp) and in the expiratory pathway (V',exp). According to a common convention that will be used in all this book, positive values are assigned to the inspiratory flow, and negative values to the expiratory flow. In the example, V',insp rises to 800 ml/s during the inflation phase, drops to zero during the end-inspiratory pause and during the first third of the expiratory phase (when the ventilator inspiratory valve is closed), and then progressively rises to provide a flow-by of 165 ml/s (10 l/min). V',exp stays at zero during the inflation phase and during the end-inspiratory pause (when the ventilator expiratory valve is closed), then drops below zero during all the expiratory phase. The instantaneous values for V',exp correspond to patient exhalation during the first third of the expiratory phase, and to the cumulative effect of patient exhalation and flow-by during the remaining part of the expiratory phase.

In theory the problem of double flow-sensing and flow-by can be easily solved by calculating the instantaneous algebraic sum of the flow detected by the inspiratory sensor, and of the flow detected by the expiratory sensor. In practice this approach requires a very high quality of the flow-sensing system, since the two sensors must be perfectly and equally calibrated. The result of such approach is illustrated in the lower panel of Fig. 2-3, as a calculated curve of the airway opening flow (V'aw,o Calc). In the same graph, we have plotted the simultaneous curve of the flow really measured at the airway opening (V'aw,o Meas). It can be easily noticed that there are some differences between the calculated and the measured curve: V'aw,o Meas is lower during the whole inflation phase, higher than zero during the first part of the end-inspiratory pause, and presents a lower peak value at the start of exhalation. These differences are due to the effect of the compliance of the external circuit of the ventilator, and mainly to gas compression. In practice a given amount of the flow that is measured by the ventilator inspiratory sensor is compressed in the circuit, and does not reach the patient.

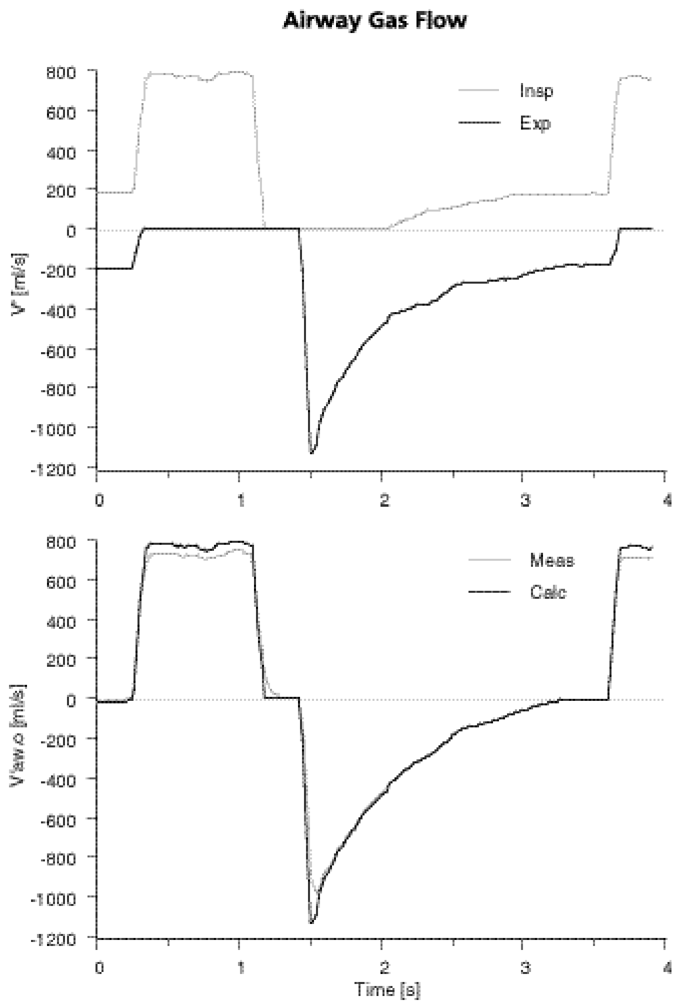

Fig. 2-3
Patient airway opening gas flow (V'aw,o), directly measured (Meas), or calculated (Calc) by combining the flow signals (V') from the ventilator inspiratory (Insp) and expiratory (Exp) pathway. Paralyzed patient in CMV.
The same cycle is analyzed in Figs. 2-1, 2-3, 2-4, 2-5

As soon as the exhalation valve opens, airway pressure drops and hence the extra volume of gas previously compressed in the circuit decompresses and takes the expiratory pathway. This generates, at the start of exhalation, an extra flow detected by the ventilator expiratory sensor, besides the flow coming from the patient airway.

All the problems due to flow-by and gas compression can be solved by a direct measurement of the airway gas flow. For this purpose, a flow sensor must be located at the airway opening, i.e., between the external extremity of the endotracheal tube and the Y-piece of the external circuit of the ventilator. However, the location of a flow sensor at the airway opening is critical from the technical standpoint, the sensing system being exposed to high humidity and secretions. Most of the available flow sensors cannot be used for prolonged measurements at the airway opening. The variable orifice Osborn-type pneumotachograph is an optimal flow sensor for this purpose. Pneumotachographs are resistive flow sensors that convert a flow signal into a differential pressure signal. In the Osborn-type pneumotachograph, the resistive element is a diaphragm with a central orifice. In order to increase the sensitivity to low flow, to reduce the resistance to high flow, and to improve the linear response of the sensor, the central orifice is partially obstructed by a flap that is passively displaced by the gas moving through the sensor. This means that the higher the flow, the larger becomes the size of the orifice. On each of the two sides of the diaphragm, the flow sensor has a pressure sensing port, for connection to a high sensitivity differential pressure transducer by means of gas-filled lines.

Only few mechanical ventilators, like the Hamilton Medical range, are equipped for flow-sensing proximal to the airway opening. The Hamilton Medical ventilators are provided with a small-size disposable Osborn-type pneumotachograph. In these machines, the performance of the flow sensor is enhanced by a purge flow for the pressure sensing lines, by an automatic system for periodical auto-zero of the differential pressure transducer, and by a digital system for the linearization of the sensor response. As already mentioned at § 2.2., of the two pressure sensing lines, the one that is proximal to the patient is also used for the measurement of Paw,o. The volume and weight of the entire airway sensor head are kept very low, at 9 ml and 11 g, respectively.

2.4. Respiratory system volume change

The direct measurement of respiratory system volume change requires the use of a spirometer, which is not practical in the setting of mechanical ventilation. However, since volume change corresponds to the time-integral of gas flow, the direct recording of a spirometric signal is unnecessary when a gas flow signal is available. The instantaneous volume change (Vol) can be easily obtained by digital integration of the signal of V'aw,o.

However, the quality of the signal of Vol will depend on the quality of the signal of V'aw,o. Fig. 2-4 represents two curves of Vol, simultaneously obtained during a CMV cycle, delivered with a constant inspiratory flow and an end-inspiratory pause, in a passive patient. One curve (Vol Calc) was obtained by integration of the V'aw,o Calc signal of Fig. 2-3, that is a flow signal obtained by combining the signals from two independent sensors, respectively near the inspiratory and near the expiratory port of the ventilator. The other curve (Vol Meas) was obtained by integration of the V'aw,o Meas signal of Fig. 2-3, that is a flow signal directly measured at the airway opening. Vol Calc overestimates the actual volume changes. During inspiration, Vol Calc becomes progressively higher than Vol Meas, reaching a maximum difference of 50 ml at the end of inspiration. Shortly after the start of exhalation, the curve of Vol Calc joins the one of Vol Meas. The overestimate typical of Vol Calc is due to the above discussed phenomenon of gas compression in the external circuit of the ventilator, meaning that the volume delivered by the ventilator during inspiration, and received back during expiration, is higher than the real volume change of the respiratory system.

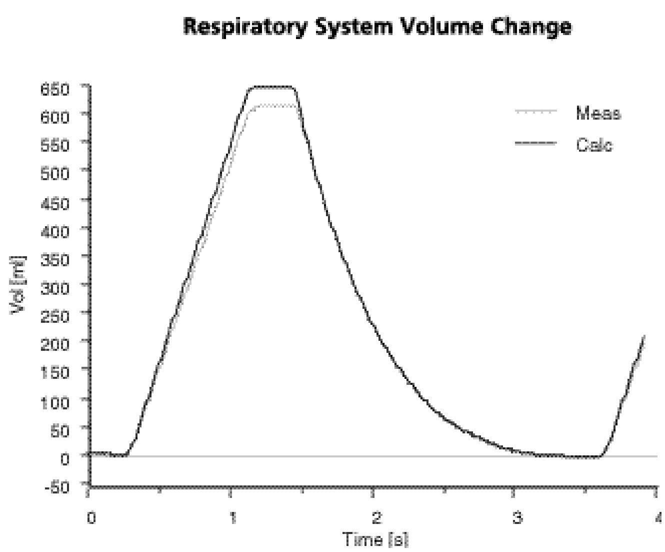

Fig. 2-4
Respiratory system volume change (Vol) obtained by integration of the gas flow directly measured at the airway opening (Meas), or calculated (Calc). Paralyzed patient in CMV.
The same cycle is analyzed in Figs. 2-1, 2-3, 2-4, 2-5

Some ventilators that make use of the double flow-sensing technique are provided with more or less sophisticated methods to compensate for the effect of compressed volume, in order to provide more reliable data of patient tidal volume. However, the calculation of exact values of instantaneous Vol with the double flow-sensing technique remains a challenge. Integration of V'aw,o from a high-quality variable orifice flow sensor is presently a much better choice for the purpose of studying respiratory mechanics.

2.5. Esophageal pressure

2.5.1. The meaning of esophageal pressure

The dynamic measurement of esophageal pressure (Pes) is not common practice in mechanically ventilated patients. However, this kind of measurement may be minimally invasive, far from difficult, and rich with information for an extended study of respiratory mechanics. In general, the changes of Pes in time accurately reflect the changes of intrapleural pressure (Ppl) in time, although the absolute values of Pes tend to overestimate the absolute values of Ppl. Since the absolute values of Ppl are unnecessary for the study of respiratory mechanics, the Pes signal is a very good substitute for the Ppl signal. Thus, the Pes signal provides information about the pressure changes in the space between the lungs and the chest wall. The pressure changes in this location depend on the elastic and the resistive load of the chest wall, as well as on the action of the respiratory muscles, while they are not directly affected by the mechanical characteristics of the lungs.

The meaning of Pes changes greatly depends on whether the patient is passively ventilated, or is actively breathing, with assisted ventilation or full spontaneous ventilation.

In Fig. 2-5 we have plotted the simultaneous signals for Paw,o and Pes in the same CMV breath that has been used for the previous figures. The patient is paralyzed and passively ventilated with CMV. The entire force promoting inspiration is applied by the machine, while the respiratory system (lungs plus chest wall) simply opposes the mechanical ventilator. It can be noticed that the profile of the Pes signal is similar to the one of the Paw,o signal: pressure rises during the inflation phase, remains stable during the end-inspiratory pause, and progressively drops toward its baseline during the expiratory phase. However, the swing of the Pes signal is much less than the swing of the Paw,o signal. This difference is due to the fact that the Paw,o changes are the result of the V'aw and Vol changes on the entire passive respiratory system, while the Pes changes are the result of the V'aw and Vol changes only on the passive chest wall. This means that, in a passive patient, Pes can be used to explore specifically the passive mechanical characteristics of the chest wall.

The condition represented by Fig. 2-6 is much different: this patient is actively breathing, while ventilation is assisted by PSV. The profile of the Pes curve is similar to the one of Fig. 2-5 only for exhalation. On the contrary, during inspiration a wide negative deflection of Pes is evident, approximately simultaneous with the positive pressure wave applied by the ventilator. This means that inspiration is promoted by the combined action of the inspiratory muscles and of the mechanical ventilator, both working against the lungs and the passive component of the chest wall, while exhalation is passive. In this condition of an actively breathing patient, the meaning of Pes changes is more complex than in paralysis, since the instantaneous Pes reflects both the passive components of the chest wall and the instantaneous result of the activity of all the respiratory muscles. Proper analysis of Pes will yield information on the activity of the respiratory muscles.

From Figs. 2-5 and 2-6, it can be noticed that the Pes signal is less clean than the above considered signals of Paw, V'aw, and Vol. This is due to that fact that Pes is measured very close to the heart. Heart activity transmits oscillations to Pes, known as cardiac artifacts.

Although the measurement of Pes is not yet common practice in mechanically ventilated patients, in this book we will make large use of Pes curves. The main reason for this is for teaching purposes, since a simultaneous plot for Pes is the only way of clarifying what is happening on the dark side of the planet represented by the many patients that are not passively ventilated. The second reason is to show how much the study of respiratory mechanics can be extended by the measurement of Pes.

2.5.2. The measurement of esophageal pressure

The measurement of Pes generally makes use of a balloon-tipped catheter, connected to a solid-state transducer by means of an air-filled line for pressure sensing. The best performance is obtained with balloons of 10-cm length and 10-ml volume. The balloon must be kept nearly empty, only filled with 0.2-1 ml of air. The balloon catheter is advanced through the nose into the mid-esophagus. Should the patient already have a naso-gastric tube in place, the balloon catheter can be placed beside the naso-gastric tube. As an alternative, we can

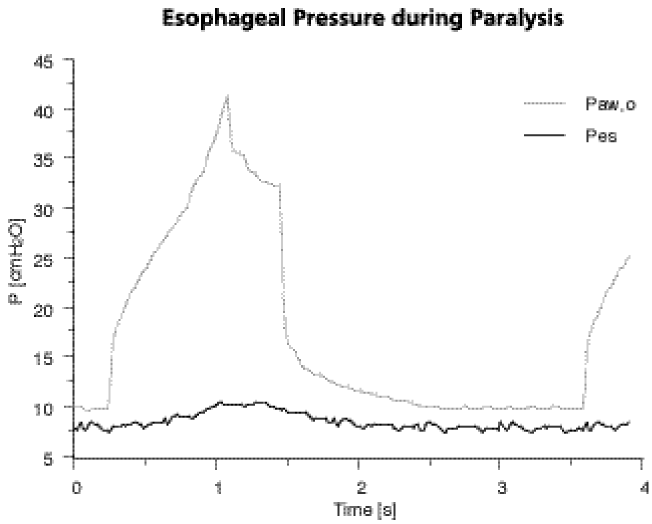

Fig. 2-5
Simultaneous recording of esophageal pressure (Pes) and airway opening pressure (Paw,o) during paralysis and CMV.
The same cycle is analyzed in Figs. 2-1, 2-3, 2-4, 2-5

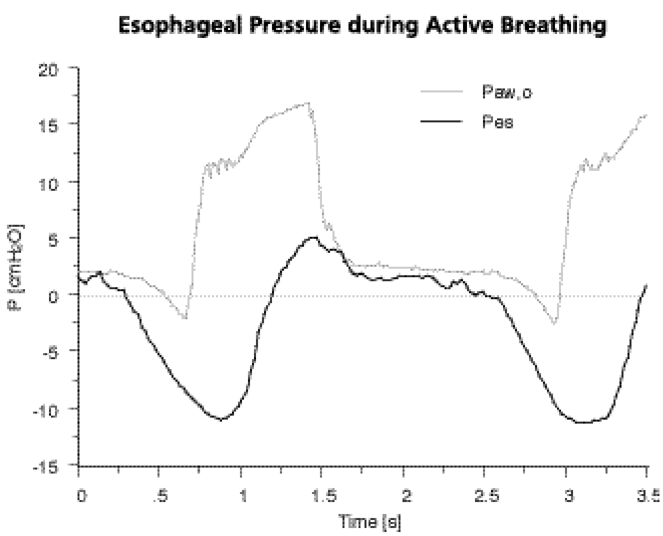

Fig. 2-6
Simultaneous recording of esophageal pressure (Pes) and airway opening pressure (Paw,o) during active breathing and PSV.

use a special naso-gastric tube, which includes an esophageal balloon together with a dedicated lumen for Pes monitoring.

In a normal adult, the tip of an esophageal balloon catheter is normally at 35 cm from the nostril. An easy way for placing the esophageal balloon into mid-esophagus in actively breathing patients is to initially advance the balloon into the stomach. Gastric location can be confirmed by inspection of the pressure curve recorded from the balloon: in the stomach no negative deflections are observed during active inspiration, unless the diaphragm is paralyzed. Then the catheter is withdrawn until the usual inspiratory deflections (Fig. 2-6) are detected: this means that a part of the balloon has entered into the chest. A further withdrawal of the catheter by 10 cm (i.e., by the balloon length) guarantees that the entire balloon is in the esophagus and inside the chest.

Patient position is important for obtaining a reliable signal of Pes. The patient should be at least in a half-sitting position. An optimal response of the esophageal balloon can be confirmed by the occlusion test. This test consists of a series of patient respiratory efforts performed against the occluded airway. Generally the occlusion is performed at end-exhalation, by means of the occlusion function that is included in the controls of modern mechanical ventilators. The occlusion test can be performed without changing the PEEP level, and in any mode of ventilation, only provided that the patient has a substantial spontaneous respiratory activity. The respiratory efforts performed against the occluded airway generate a series of swings in Paw. The principle of the test is that, during occlusion, i.e., in a condition of no flow, any change in Paw should be reflected by a simultaneous and equal change in Pes. Fig. 2-7 represents the results of a satisfactory occlusion test. The patient was actively breathing, and assisted by PSV. We have plotted the simultaneous real-time signals of V'aw, Vol, Paw, and Pes. The start of the end-expiratory occlusion period is marked by the first vertical dotted line. It can be noticed that the simultaneous changes for Pes and Paw are very similar during the entire occlusion period. The comparison between occluded Pes and Paw is made easier by observation and analysis of an X-Y graph, as the one represented in Fig. 2-8, where we have plotted all the simultaneous points of Pes and Paw included between the two vertical dotted lines of Fig. 2-7. In Fig. 2-8, linear regression and correlation have been calculated between the simultaneous values of Pes and Paw. It can be noticed that all the points of Fig. 2-8 are tightly distributed on a straight line (the correlation coefficient r^2 is very high), while the slope of the regression line is very close to 1. This confirms that the simultaneous deflections of Pes and Paw are nearly identical, and hence that the esophageal balloon

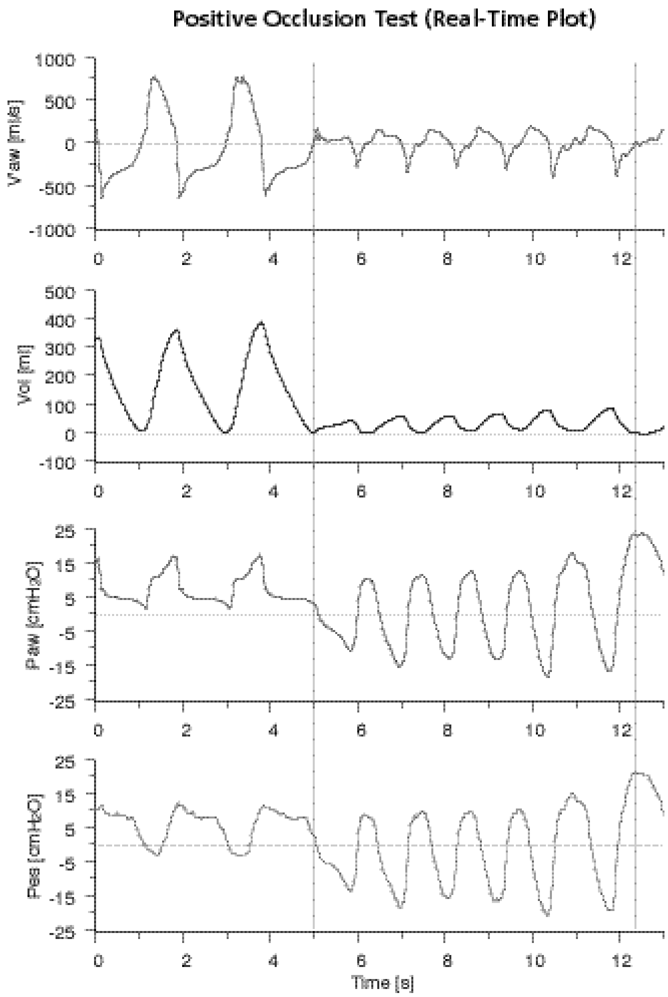

Fig. 2-7
Real-time plot of a satisfactory occlusion test for esophageal pressure validation. Actively breathing patient in PSV.
The same recording is analyzed in Figs. 2-7, 2-8

response is satisfactory. It must be noticed that the identity between the absolute values for occluded Pes and Paw is not required for judging the performance of an esophageal balloon in place. Hence, the value of the intercept of the linear regression between occluded Pes and Paw has no interest, and in particular may be different from zero. Finally, from Fig. 2-7 it can be noticed that, during the occlusion period, the V'aw and Vol changes are greatly reduced, but not perfectly suppressed. The persistence of V'aw and Vol changes is due to gas decompression and compression in the external circuit of the ventilator, in response to the respiratory efforts of the patient. Indeed, only the valves of the ventilator are closed, while the patient airway is open to the external circuit of the ventilator. This lack of occlusion proximal to the patient has no relevant effect on the esophageal balloon occlusion test.

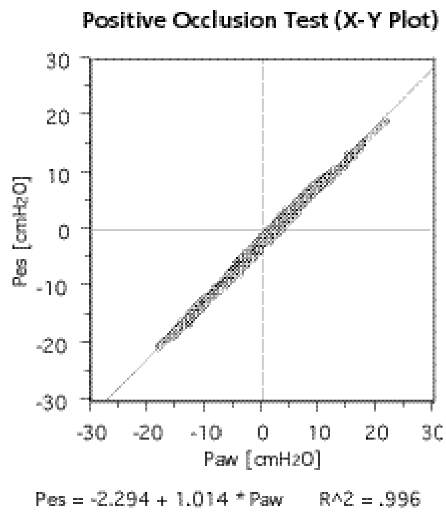

Fig. 2-8
Paw-Pes plot of a satisfactory occlusion test for esophageal pressure validation, with results of simple linear regression and correlation. Actively breathing patient in PSV.
The same recording is analyzed in Figs. 2-7, 2-8

In Figs. 2-9 and 2-10, an occlusion test that was not satisfactory is represented. The patient was actively breathing and assisted by synchronized PCV. The deflections of Pes have approximately half the amplitude of those of Paw, and the relationship between Paw and Pes is evidently non-constant. The X-Y plot results in high dispersion of the points, with a correlation coefficient much lower than 1, and a regression slope of less than 0.5. The results of this occlusion test indicate that the Pes signal is unreliable. All the measuring system should be checked, and in particular the esophageal balloon should be moved, looking for a more favorable position.

In the mechanical ventilators provided with an auxiliary pressure port, like the Hamilton Medical ones, Pes can be easily measured by connection of the esophageal balloon pressure sensing line to the auxiliary port. However, for the purpose of the Pes measurement, the user must be absolutely sure that the auxiliary pressure port is *not provided* with a purge flow. The connection of a purged pressure port to an intraesophageal balloon catheter is very dangerous, since the purge will overdistend the balloon and possibly cause an esophageal rupture.

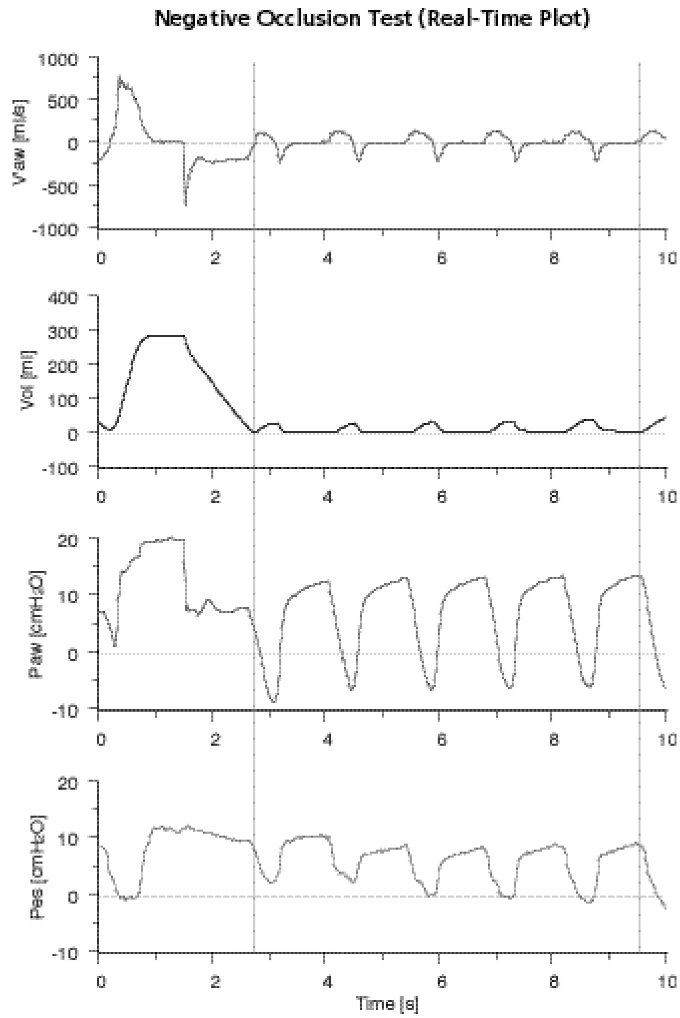

Fig. 2-9
Real-time plot of a non-satisfactory occlusion test for esophageal pressure validation. Actively breathing patient in PCV.
The same recording is analyzed in Figs. 2-9, 2-10

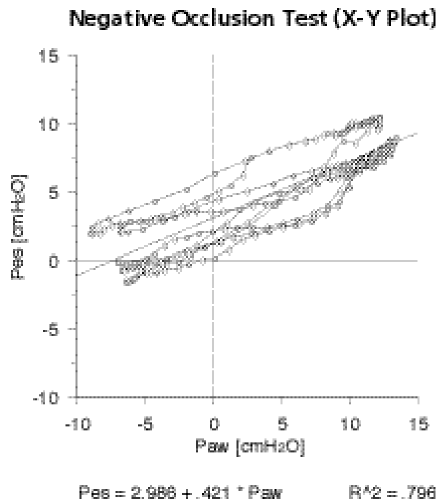

Fig. 2-10
Pes-Paw plot of a non-satisfactory occlusion test for esophageal pressure validation, with results of simple linear regression and correlation. Actively breathing patient in PCV.
The same recording is analyzed in Figs. 2-9, 2-10

2.6. Conclusions

The basic measurements of respiratory mechanics in ventilated patients are based on the recording of the instantaneous signals of Paw and V'aw. A spirometric signal is then obtained by digital integration of the V'aw signal. The most practical choice is to make use of the signals produced by the sensors of the mechanical ventilator. The best technical choice is to measure Paw and V'aw at the airway opening of the patient, by means of a variable orifice pneumotachograph and of a proximal pressure line. Advanced users will also record the instantaneous signal of Pes. This latter measurement allows the study of chest wall respiratory mechanics in the relaxed patients, and the study of the global respiratory muscle activity in the active ones.

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Section B

MECHANICS OF THE PASSIVE RESPIRATORY SYSTEM

3. DYNAMIC PULMONARY HYPERINFLATION

3.1. Dynamic pulmonary hyperinflation and intrinsic PEEP

3.1.1. Pulmonary hyperinflation

Pulmonary hyperinflation includes all the conditions in which, at the end of exhalation, the volume of the respiratory system is higher than the functional residual capacity (FRC), i.e., higher than the equilibrium volume observed when all the respiratory muscles are relaxed and both the airway opening and the surface of the thorax are exposed to the atmospheric pressure.

Pulmonary hyperinflation can be either a static or a dynamic hyperinflation. Static pulmonary hyperinflation results from a change in the static external forces applied to the respiratory system during exhalation. The resulting increase in the end-expiratory volume is still a resting equilibrium volume, although higher than FRC. In mechanically ventilated patients, the most common reason for static pulmonary hyperinflation is represented by the application of an external PEEP (PEEPe) at the airway opening, by the mechanical ventilator. The increase in the end-expiratory lung volume generated by a given PEEPe is stable, whichever is the duration of the expiratory time, and depends on the elastic characteristics of the respiratory system.

Dynamic pulmonary hyperinflation is due to a critical imbalance between the speed of exhalation and the duration of the expiratory phase of a cycle. In particular, dynamic pulmonary hyperinflation results when a new inspiration starts before full exhalation to the resting equilibrium volume is completed. The resulting increase in the end-expiratory volume is due to dynamic reasons, and not to a change in the static forces externally applied to the respiratory system. In dynamic pulmonary hyperinflation, the end-expiratory lung volume is not a resting equilibrium volume. Dynamic pulmonary hyperinflation can take place both during spontaneous or mechanically assisted breathing, and during passive mechanical ventilation. In the first two instances, full exhalation is impeded by the start of a new patient-initiated breath, while in the latter instance, it is impeded by the start of a new machine-initiated breath.

3.1.2. Terminology of pulmonary hyperinflation

Some of the terms used for the lung volumes involved in pulmonary hyperinflation have never been standardized. In order to avoid any possible misunderstanding, it may be useful to specify the terminology that will be used in this book.

The tidal volume (Vt) develops above the end-expiratory lung volume (Vol,ee), up to the end-inspiratory volume (Vol,ei). In all the graphs including volume, we shall use Vol,ee as the baseline for the volume scale, i.e., we shall assign a value of zero to Vol,ee.

Normally Vol,ee is coincident with the functional residual capacity (FRC), i.e., with the resting equilibrium volume at atmospheric pressure (Patm). However, in given conditions Vol,ee can increase above FRC, due to static and/or dynamic pulmonary hyperinflation.

In the case of application of a PEEPe by the ventilator (static hyperinflation), the resting equilibrium volume is artificially increased, and will be denoted as FRC,PEEPe. The difference between FRC,PEEPe and atmospheric pressure FRC, due to static hyperinflation, will be denoted as ΔVol,ee,st.

In the case of dynamic pulmonary hyperinflation, Vol,ee is increased above the resting equilibrium volume that corresponds to the pressure applied at the airway opening (Patm or PEEPe), i.e., is increased above FRC or FRC,PEEPe. The difference between Vol,ee and the resting equilibrium volume, due solely to dynamic hyperinflation, will be denoted as ΔVol,ee,dyn.

All these terms are reviewed in Fig. 3-1, representing the respiratory system volumes with the corresponding elastic recoil pressures: Patm corresponds to FRC, PEEPe to FRC,PEEPe, the total PEEP (PEEPtot) to Vol,ee, and the static end-inspiratory pressure (Pei,st) to Vol,ei. The difference between PEEPtot and PEEPe corresponds to the intrinsic PEEP (PEEPi), that is, the PEEP generated by dynamic pulmonary hyperinflation. PEEPi is also known as Auto-PEEP.

When we consider Fig. 3-1, we should remember that either dynamic hyperinflation, static hyperinflation, or both kinds of hyperinflation may be absent. When there is no dynamic pulmonary hyperinflation, ΔVol,ee,dyn and PEEPi are equal to zero. When there is no PEEPe application and the end-expiratory pressure corresponds to Patm, there is no static hyperinflation and hence ΔVol,ee,st is equal to zero.

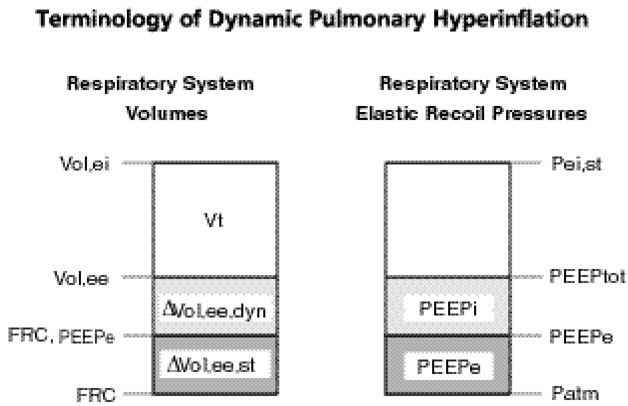

Fig. 3-1

Respiratory system volumes and corresponding elastic recoil pressures.

3.1.3. Dynamic pulmonary hyperinflation

Thus, dynamic pulmonary hyperinflation is due to an imbalance between the expiratory emptying rate of the respiratory system and the expiratory time. During a passive exhalation, the emptying rate depends on the expiratory time constant (RCe) of the system, i.e., on the product of total compliance and total resistance (see § 6.1.). In order to achieve nearly full passive exhalation (99%), the respiratory system requires an expiratory time equal to fivefold its RCe, while an expiratory time of threefold RCe allows 95% of full exhalation. For example, if we consider a total respiratory system compliance of 50 ml/cmH_2O with a total (respiratory system plus apparatus) expiratory resistance of 20 cmH_2O/l/s, RCe is 50x20 = 1000 ms = 1 s. In this example, dynamic hyperinflation is virtually absent when the expiratory time is higher than five RCe's, i.e., ≥ 5 s, and very low when it is higher than three RCe's, i.e., ≥ 3 s. On the contrary, in this example dynamic pulmonary hyperinflation becomes relevant when the expiratory time is < 3 s.

In Fig. 3-2 we present a example of severe dynamic pulmonary hyperinflation, in a patient with airway obstruction, submitted to passive mechanical ventilation, in CMV, with a PEEPe of zero. At the end of the third cycle, the ventilator is disconnected, and an additional expiratory time of 35 s is allowed. During the first 20 s of this additional expiratory time, a substantial expiratory flow is main-

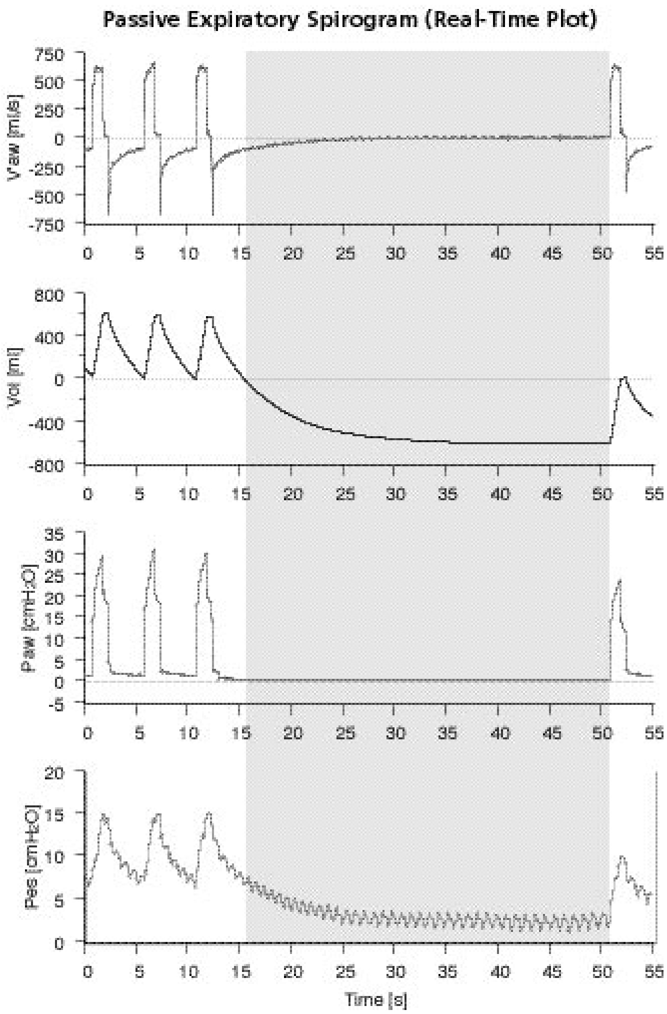

Fig. 3-2
Real-time plot of a maneuver of prolonged passive exhalation, obtained by disconnection of the mechanical ventilator in a dynamically hyperinflated paralyzed patient, ventilated in CMV with a PEEPe of zero. A ΔVol,ee,dyn of 600 ml is measured.
The same recording is analyzed in Figs. 3-2, 3-3, 3-6, 3-10, 6-2, 6-5

tained, corresponding to a decrease in the respiratory system volume by 600 ml, evident on the spirogram. Simultaneously, the internal pressure of the respiratory system decreases, as shown by the decrease in the Pes curve. In this example, the ventilator disconnection and the additional, prolonged expiratory time allow the respiratory system to attain the FRC, and reveal a Vol,ee higher than FRC by

600 ml. Since the PEEPe applied by the ventilator was zero, this elevation of Vol,ee is entirely due to dynamic hyperinflation, and hence corresponds to ΔVol,ee,dyn.

Evidently, dynamic pulmonary hyperinflation is more likely to take place when total resistance is high, and/or when total compliance is high, and/or when expiratory time is short. Dynamic pulmonary hyperinflation is typical of patients with airway obstruction and emphysema, as well as of respiratory patterns with short expiratory time (high respiratory rate, inverse I:E ratio).

3.1.4. Total PEEP and intrinsic PEEP

We have already seen that, in the presence of dynamic pulmonary hyperinflation, the average end-expiratory pressure inside the alveoli, i.e., the actual, total PEEP (PEEPtot), is higher than the PEEPe applied by the ventilator. The difference between PEEPtot and PEEPe, defined as PEEPi or Auto-PEEP, corresponds to the driving pressure of the undeveloped part of exhalation, i.e., of the part of exhalation that is impeded by the start of a new respiratory cycle.

When dynamic pulmonary hyperinflation is considered in terms of intrapulmonary end-expiratory pressure, PEEPi represents the mirror of ΔVol,ee,dyn, just as PEEPe represents the mirror of ΔVol,ee,st.

PEEPi is an important parameter of respiratory mechanics, for several reasons:

- PEEPi provides information on the amount of dynamic hyperinflation.
- PEEPi is to be summed to PEEPe in order to appreciate the real, total PEEP working on the respiratory system and on all the intrathoracic organs.
- PEEPi is to be taken into account in order to obtain a correct value for respiratory system static compliance.
- PEEPi is an inspiratory threshold load to be overcome by the patient inspiratory muscles at every patient-initiated breath, even when inspiration is mechanically assisted by the ventilator. Hence, PEEPi has important implications concerning the energetics of breathing.
- PEEPi is an additional elastic load to be overcome by the ventilator during passive ventilation. Hence, PEEPi contributes to the need for applying high inspiratory pressures in passively ventilated patients.

PEEPi has the same adverse mechanical effects of PEEPe, concerning both hemodynamics and barotrauma or volutrauma. However, PEEPe is an obvious phenomenon, being part of the ventilator setting, while PEEPi and dynamic hyperinflation may represent a hidden and inadvertent phenomenon, and hence must be actively searched for.

3.2. Detection of dynamic pulmonary hyperinflation

3.2.1. Detection of dynamic pulmonary hyperinflation in passive patients

In passive patients, dynamic hyperinflation is easily detected by simple observation of the real-time curve of V'aw, by looking at the flow rate at the point of end-exhalation. Whenever the end-expiratory flow is far from zero, it means that the respiratory system is dynamically hyperinflated. This is evident in Fig. 3-3. After its initial peak, the expiratory flow approaches the baseline by following an exponential decay, as it is normally observed during passive exhalation. However, the process of exhalation is interrupted by the time-out of the expiratory phase of the cycle, much before flow can reach a value of zero. The arrows indicate an end-expiratory flow of about 100 ml/s.

On the contrary, Fig. 3-4 is an example of lack of dynamic pulmonary hyperinflation. The exponential decay of the expiratory flow reaches the baseline before the time-out of the expiratory phase; this patient has an end-expiratory flow of zero (see the arrows).

A slightly different approach for dynamic hyperinflation detection is the observation of the flow-volume loops. Fig. 3-5 corresponds to the second respiratory cycle of Fig. 3-4 (passive ventilation in CMV), and represents a normal shape flow-volume loop indicating no dynamic hyperinflation. The loop starts from the point of zero volume and zero flow, and moves counterclockwise, as indicated by the arrows. Inspiration is on the right side (positive flow values) and exhalation is on the left one (negative flow values). In this example, the inspiratory part of the loop has a rectangular shape, due to the constant flow wave selected in the ventilator settings. On the contrary, the expiratory part of the loop has a triangular shape: after an initial peak, due to the expiratory peak flow taking place at the start of exhalation, flow decreases linearly with the

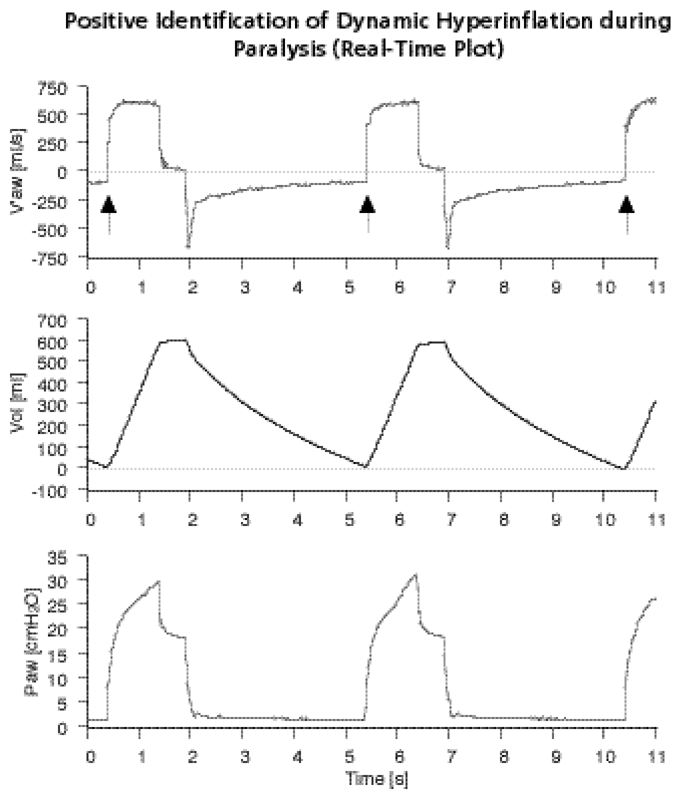

Fig. 3-3
Real-time plot of V'aw, Vol and Paw in a dynamically hyperinflated patient, paralyzed, in CMV. The arrows indicate an end-expiratory flow of 100 ml/s.
The same recording is analyzed in Figs. 3-2, 3-3, 3-6, 3-10, 6-2, 6-5

decrease of volume, and reaches a value of zero at the end of exhalation (marked by the black arrow), i.e., when volume is back to the zero baseline. This triangular shape corresponds to a linear single-compartment model with no dynamic hyperinflation (Fig. 3-7, panel a).

In turn, Fig. 3-6 corresponds to the first cycle of Fig. 3-3 (passive ventilation in CMV), and represents a pathological flow-volume loop indicating dynamic hyperinflation. Like in the previous case, the inspiratory part of the loop has a rectangular shape, due to the waveform selected in the ventilator settings. On the contrary, the expiratory part of the loop has a complex shape, with the initial peak followed by a curvilinear decrease of flow with the decrease of volume. The decrease of flow with volume is very fast immediately after the peak, then

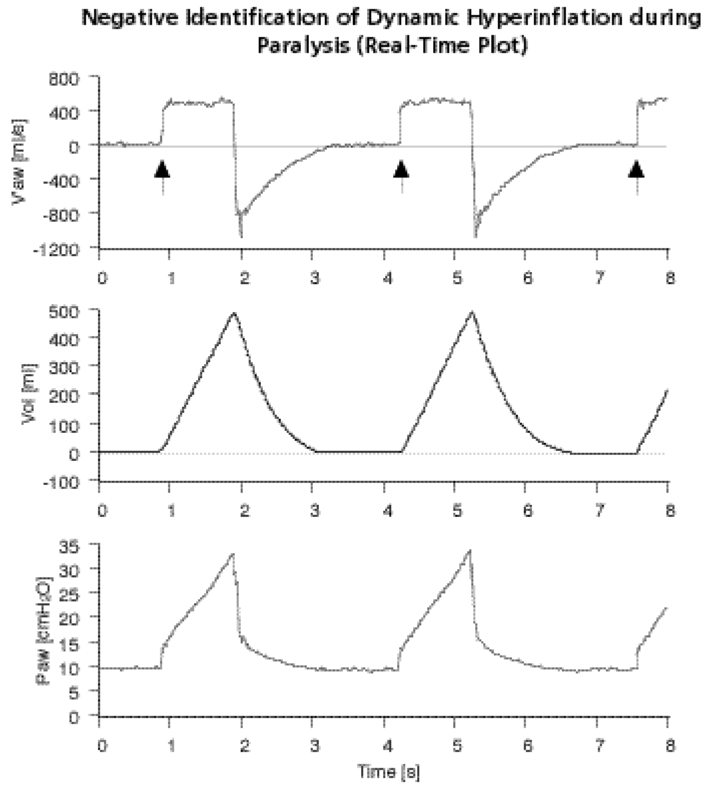

Fig. 3-4
Real-time plot of V'aw, Vol and Paw in a paralyzed patient in CMV, with no dynamic hyperinflation. The arrows indicate an end-expiratory flow of zero.
The same recording is analyzed in Figs. 3-4, 3-5, 6-1, 6-4

slows down progressively, and finally becomes virtually linear during the last part of exhalation. The expiratory flow is far from zero at the point of end-exhalation (marked by the black arrow), i.e., when volume is back to the baseline. This shape of the expiratory part of the loop is typical of COPD patients with dynamic pulmonary hyperinflation due to expiratory airway collapse, and corresponds to a linear double-compartment model (Fig. 3-7, panel b).

Although very common, it is to be noticed that this shape is not the only one that denotes dynamic hyperinflation on a flow-volume loop. An alternative is represented by a trapezoidal shape, with a linear decrease of flow with volume, starting immediately from the point of peak flow (Fig. 3-7, panel c). Contrarily to the normal triangular shape (Fig. 3-7, panel a), in the trapezoidal curve the expira-

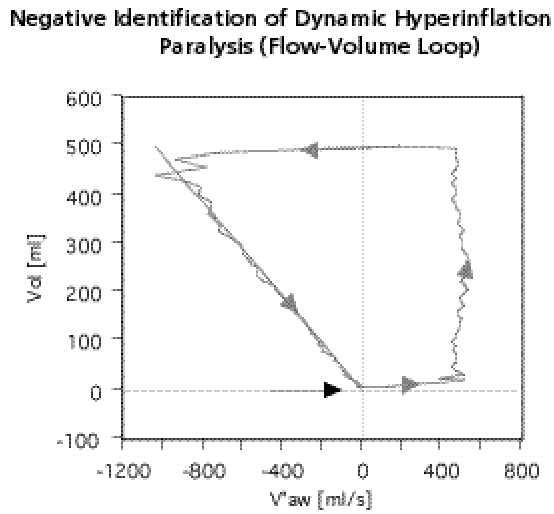

Fig. 3-5
Flow-volume loop in a paralyzed patient, in CMV, with no dynamic hyperinflation. The black arrow indicates an end-expiratory flow of zero. A straight line is fitted on the expiratory flow-volume relationship, and confirms a ΔVol,ee,dyn of zero.
The same recording is analyzed in Figs. 3-4, 3-5, 6-1, 6-4

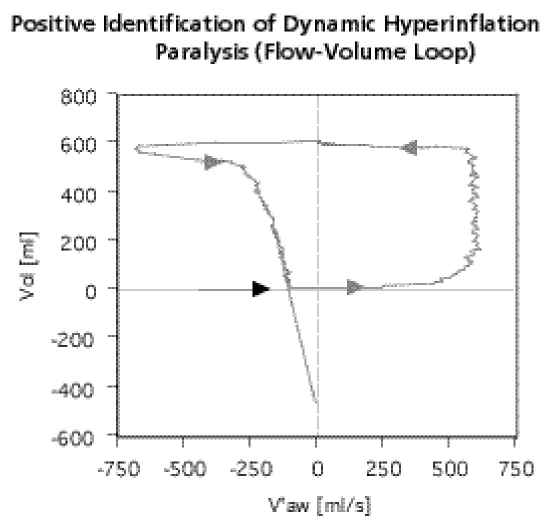

Fig. 3-6
Flow-volume loop in a dynamically hyperinflated patient, paralyzed, in CMV. The black arrow indicates an end-expiratory flow of 100 ml/s. A straight line is fitted on the second part of the expiratory flow-volume relationship, for the estimate of ΔVol,ee,dyn (500 ml).
The same recording is analyzed in Figs. 3-2, 3-3, 3-6, 3-10, 6-2, 6-5

tory flow is far from zero at the point of end-exhalation. A trapezoidal shape may result even in the absence of pathological values for resistance and compliance, when dynamic hyperinflation is simply due to the setting of a critically short expiratory time in the ventilator. Such trapezoidal shape corresponds to a linear single-compartment model.

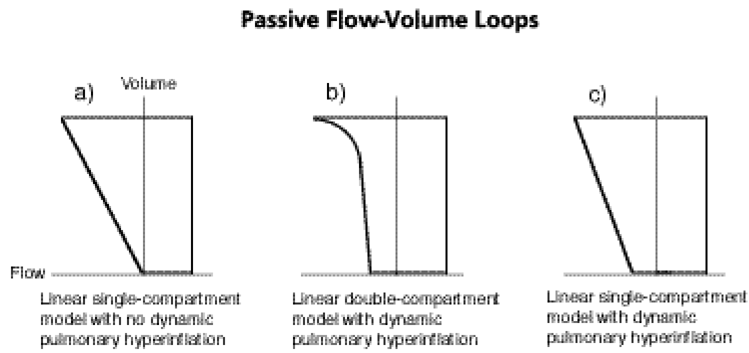

Fig. 3-7
Schematic diagrams of different passive flow-volume loops.

3.2.2. Detection of dynamic pulmonary hyperinflation in actively breathing patients

The method is based on the observation of the expiratory flow. Fig. 3-8 is a real-time recording taken in a dynamically hyperinflated patient, actively breathing, assisted by PSV. The homogeneous downward concavity of the expiratory flow profile indicates that the major part of exhalation is passive. However, just before the end of exhalation, the V'aw curve exhibits an upward inflection, marked by an arrow: starting from a value as high as 300 ml/s, the expiratory flow rapidly rises and crosses the zero line. This end-expiratory upward inflection is typically due to an inspiratory effort of the patient, as it is evident from the simultaneous drop in the Pes curve, where an arrow indicates the start of the effort. This inspiratory effort brakes and finally stops exhalation, and hence generates dynamic pulmonary hyperinflation. Even when a Pes trace is not available, the end-expiratory flow shape just described can be used to detect dynamic pulmonary hyperinflation in the actively breathing patient. The key point is an upward inflection in the end-expiratory flow, with a last passive end-expiratory flow far from zero.
The principle is similar to the one used for the passively ventilated patient, but it must be noticed that in the actively breathing patient the flow braking to zero

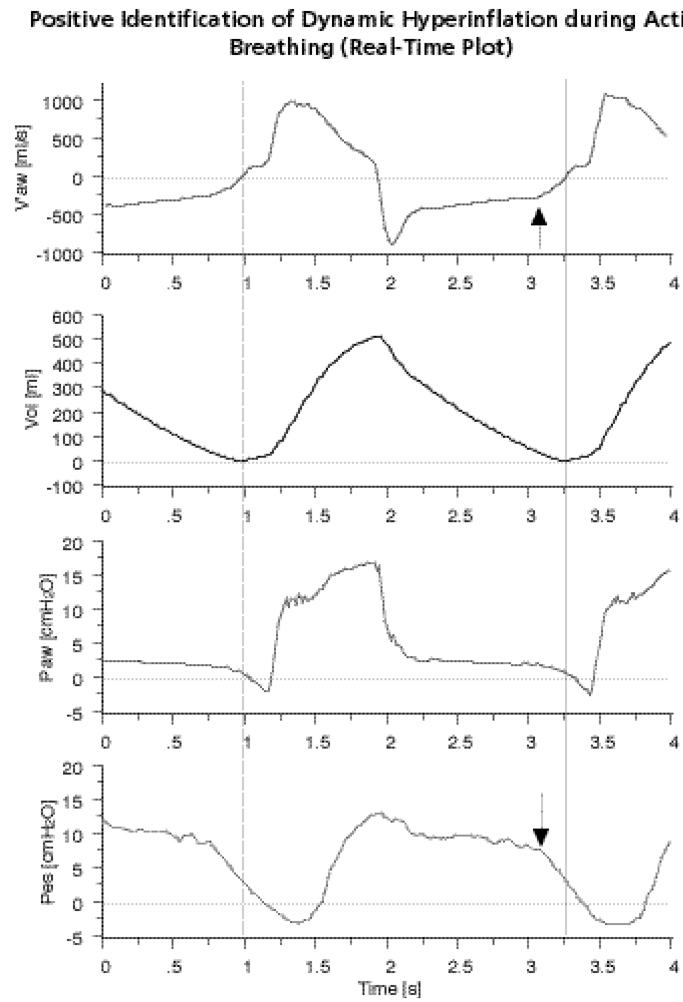

Fig. 3-8
Real-time plot of V'aw, Vol, Paw, and Pes in a dynamically hyperinflated patient, actively breathing, in PSV. The arrows indicate the start of the premature inspiratory effort, with a last passive end-expiratory flow of 300 ml/s.
The same cycle is analyzed in Figs. 3-8, 3-9, 6-3, 8-1, 8-2, 8-3, 8-5

is less fast and sharp. In the passive patient, flow braking is due to ventilator cycling to inspiration, which is a nearly instantaneous event due to a rapid closure of the expiratory valve and to a sudden pressurization by the inspiratory valve. In the active patient, expiratory flow braking is due to a progressive contraction of the inspiratory muscles, that first interrupt exhalation, and then trigger a new cycle.

Similarly to the procedure used in the passive patient, the detection of dynamic hyperinflation can be performed on a flow-volume loop, as shown in Fig. 3-9, where the same cycle considered in Fig. 3-8 is plotted. In this example, the inspiratory part of the loop has a sinus shape, typical of spontaneous or pressure supported ventilation. On the contrary, the shape of the expiratory part of the loop is similar to the one of Fig. 3-6, and hence typical of passive exhalation in a patient with expiratory airway collapse. Towards the end of exhalation, the loop exhibits a clear inflection to the right. This means that, in a given point where flow is far from zero, passive exhalation is braked and finally interrupted by a force that must be applied by the inspiratory muscles; hence, dynamic hyperinflation is generated. In the example, the inflection point, marked by the black arrow, indicates the last passive point on the expiratory part of the loop, where the expiratory flow had still a value of 300 ml/s.

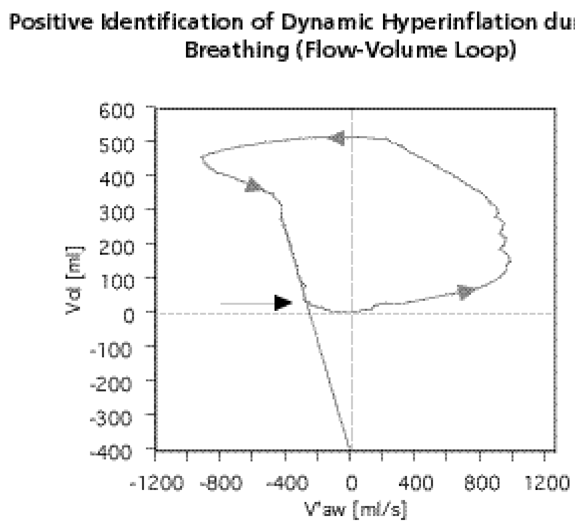

Fig. 3-9
Flow-volume loop in a dynamically hyperinflated patient, actively breathing, in PSV. The black arrow indicates the start of the premature inspiratory effort, with a last passive end-expiratory flow of 300 ml/s. A straight line is fitted on the second part of the relaxed expiratory flow-volume relationship, for the estimate of ΔVol,ee,dyn (400 ml).
The same cycle is analyzed in Figs. 3-8, 3-9, 6-3, 8-1, 8-2, 8-3, 8-5

Proper application of both the real-time and the loop method in the actively breathing patient has a necessary requirement: exhalation must be passive in the period preceding the above described inflections in the V'aw curves. The judgement about passive exhalation is based on the shape of the real-time V'aw curve, or more easily on the shape of the flow-volume curve. Some examples of the shapes typical of passive exhalation in patients with and without dynamic airway collapse are given in Figs. 3-3, 3-4, 3-5, and 3-6, and discussed at § 3.2.1. The judgement about passive exhalation may be difficult and requires training. When passive exhalation is not confirmed, the above described methods cannot be applied.

3.3. Measurement of the dynamic increase in the end-expiratory volume

3.3.1. Passive expiratory spirogram

In a paralyzed patient, the increase in Vol,ee due to dynamic pulmonary hyperinflation (ΔVol,ee,dyn) can be measured by studying the passive expiratory spirogram. The principle of this method is to use an additional, prolonged expiratory time, in order to allow full passive exhalation to FRC. The simplest application of this method is based on the disconnection of the patient from the mechanical ventilator, at any instant of an expiratory time. Besides patient paralysis, other requirements for this method are a PEEPe of zero applied by the ventilator and flow-sensing at the airway opening. Obviously, during the disconnection maneuver, the sensor head must be maintained in connection with the airway opening.

An example of the maneuver is shown in Fig. 3-2. With the ventilator disconnection, an additional and prolonged expiratory time is allowed, indicated by the shaded area. When dynamic hyperinflation is present, during this additional expiratory time the spirogram shows a prolonged drop that continues below the volume baseline corresponding to Vol,ee, and finally stabilizes at a given level, corresponding to the FRC. At this point, the ventilator can be reconnected to the patient. The time required for the respiratory system to fully empty to the resting equilibrium point is difficult to predict and sometimes may be longer than 0.5 min.

ΔVol,ee,dyn is measured on the spirogram as the difference between the spirogram baseline and the minimum volume reached during the prolonged expiratory time. In the above example, ΔVol,ee,dyn equals 600 ml. The maneuver can be analyzed either from a real-time recording or from a flow-volume loop, as shown in Fig. 3-10.

It must be noticed that a perfect calibration of the flow sensor (especially concerning the offset) is critical in order to obtain a valid measurement with the above maneuver. Indeed, due to the long time that may be necessary for reaching the FRC, a minor error in the flow sensor offset may result in a major error in the estimate of ΔVol,ee,dyn.

Moreover, it is necessary that the patient has been ventilated without PEEPe for some time previous to the start of the maneuver. Should a PEEPe level different from zero be applied, the disconnection maneuver could not distinguish which part of the additional expiratory volume is the ΔVol,ee,dyn due to dynamic hyperinflation, and which part is the ΔVol,ee,st generated by the PEEPe.

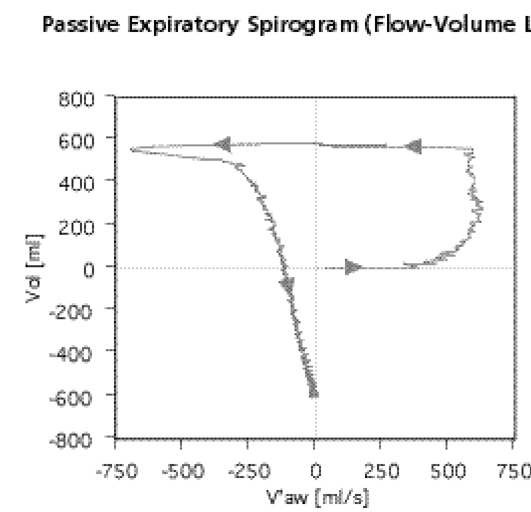

Fig. 3-10
Flow-volume loop of a breath with a prolonged passive exhalation, obtained by disconnection of the mechanical ventilator, in a dynamically hyperinflated paralyzed patient, ventilated in CMV with a PEEPe of zero. A ΔVol,ee,dyn 600 ml is measured.
The same recording is analyzed in Figs. 3-2, 3-3, 3-6, 3-10, 6-2, 6-5

3.3.2. Extrapolation of the flow-volume loop

The method is based on the assumption that, at least during the second part of exhalation, the flow-volume relationship is the expression of just one homogeneous compartment (see § 1.2.). This compartment can be either the entire respiratory system, in a linear single-compartment model, or the slow compartment, in a linear double-compartment model. For one homogeneous compartment, passive exhalation corresponds to a linear relationship between flow rate and volume change. Once it is found, either for the entire system or for the slow compartment (that is the one relevant for dynamic hyperinflation), a linear relationship can be easily used to predict the volume corresponding to an expiratory flow of zero. This level of volume corresponds either to an estimate of FRC,PEEPe, when the ventilator applies a PEEPe, or to an estimate of FRC, when exhalation is made at atmospheric pressure. Then, ΔVol,ee,dyn can be calculated as the difference between Vol,ee and either FRC,PEEPe or FRC.

The limit of this method is in the assumption of a linear relationship between flow and volume. In reality, in the last part of a passive exhalation, as well as in the part of exhalation that is impeded to develop, the flow-volume relationship may be either linear, or still curvilinear with a leftward concavity. Should the relationship be curvilinear, this method would underestimate the actual ΔVol,ee,dyn. This means that a linear extrapolation provides a measurement of the minimal possible value for ΔVol,ee,dyn. The real value cannot be lower than the estimated value, but can be higher.

The method can be applied on any respiratory cycle and does not require any maneuver. The only requirement is that exhalation be passive.

3.3.2.1. Linear extrapolation in paralyzed patients

In paralyzed patients the method is simpler, since passive exhalation is guaranteed *a priori.* Figure 3-6 is an example of the flow-volume loop of a breath in a dynamically hyperinflated patient, paralyzed and ventilated in CMV. The example has already been described at § 3.2.1. The entire expiratory flow-volume relationship is curvilinear. The second part of the expiratory flow-volume relationship looks linear, and expresses the passive emptying of the slower of two compartments, i.e., the emptying of the compartment relevant for dynamic pulmonary hyperinflation. A straight line can be fitted on this part of the loop, and extrapolated to the volume axis. The interception of this straight line on the volume axis represents an estimate of FRC,PEEPe. In the example, the interception corresponds to 500 ml below Vol,ee. Hence, the estimated value for ΔVol,ee,dyn is 500 ml. In other words, it is supposed that, should exhalation have not been interrupted by a new mechanical inflation, the respiratory system volume would have decreased to 500 ml below the actual end-expiratory level.

The fitted straight line can be obtained by simple linear regression between flow and volume, in the selected range of the loop, according to the equation:

$$Vol = (a \times V'aw) + b$$

The solution of the regression provides a value "b" of intercept, that corresponds to the volume at zero flow, and hence corresponds to the estimate of the resting equilibrium volume for the PEEPe applied by the ventilator, relative to the volume baseline. Also, the regression provides a value "a" of angular coefficient, that corresponds to the slope of the flow-volume relationship, and hence corresponds to an expiratory time constant (see § 6.).

An easy alternative is to fit a straight line by eye, just by drawing a line on a printout of the flow-volume plot.

Fig. 3-5 shows an application of the same method in a patient without dynamic hyperinflation. In this example, the expiratory flow-volume relationship looks linear from the peak to the end. The respiratory system behaves according to a single-compartment model. A straight line can be fitted from the expiratory peak to the end of exhalation. Its interception on the volume axis corresponds to a value of zero. This means that Vol,ee is coincident with FRC,PEEPe. Hence, ΔVol,ee,dyn is equal to zero.

3.3.2.2. Linear extrapolation in actively breathing patients

Many actively breathing patients present a passive exhalation. Passive exhalation can be confirmed by observation of the flow-volume loop. The expiratory part of the flow-volume loop should be considered, in the section between the initial peak and the point of start of the inspiratory effort (see § 3.2.2. for the definition of this point). In this section of the loop, when exhalation is passive, the flow-volume relationship is either linear, or curvilinear with a leftward concavity, as shown in the passive loops of Figs. 3-5 and 3-6, respectively. On the contrary, the finding of a leftward convexity indicates an active exertion of the expiratory muscles during exhalation.

When passive exhalation is confirmed, the method described at § 3.3.2.1. can be applied. The only critical point is to properly identify where in the loop the straight line must be fitted. Of course, the very last part of exhalation must be excluded, where the flow-volume relationship deviates to the right due to the inspiratory muscle contraction that will initiate the next breath. Moreover, when passive exhalation is curvilinear between the peak and the point of inspiratory effort start, only the last, steepest part of the passive flow-volume relationship should be retained, because only this part reflects the slower of two compartments.

Fig. 3-9 is an example of linear extrapolation of the passive expiratory flow-volume relationship, in a dynamically hyperinflated patient assisted by PSV. The flow-volume relationship denotes passive exhalation, except at the very end, where the relationship deviates to the right due to the inspiratory muscle contraction that terminates the present cycle and starts the next one. The passive relationship is curvilinear. A straight line is fitted on the last, steeper part of the relationship, that expresses the emptying of the slower of two compartments. The linear extrapolation results in an intercept of 400 ml below Vol,ee. Hence, it is supposed that, should exhalation have not been interrupted by a new inspiratory effort, the respiratory system volume would have decreased to 400 ml below Vol,ee. As already detailed, the straight line can be fitted either by simple linear regression or by eye. In the former case, the regression will simultaneously provide a measurement of expiratory time constant, as the value for the angular coefficient of the regression (see § 6.).

3.4. Measurement of PEEPi

3.4.1. Measurement of static PEEPi

The measurement of static PEEPi is the most common method for the assessment of PEEPi, and is based on an end-expiratory occlusion maneuver. As outlined above, PEEPtot is an alveolar pressure, namely the average pressure inside the alveoli at end-exhalation. Obviously, we have no simple way of direct measurement of the alveolar pressure during the dynamic development of a respiratory cycle. However, when the airway opening is occluded, pressures rapidly equilibrate in the entire respiratory system, and hence the alveolar pressure can be easily read at the airway opening, from the Paw curve. When we perform the occlusion maneuver at the end of an expiratory time, the pressure value on the Paw curve will correspond to PEEPtot, provided that the patient is relaxed, i.e., no force is applied by the respiratory muscles. PEEPi can then be calculated as the difference between PEEPtot and PEEPe:

$$\text{PEEPi} = \text{PEEPtot} - \text{PEEPe}$$

3.4.1.1. Static PEEPi measurement in paralyzed patients

In practice, the end-expiratory occlusion maneuver is generally achieved by the simultaneous closure of both the inspiratory and the expiratory valves of the ventilator, synchronized with the end of an expiratory time. Several mechanical

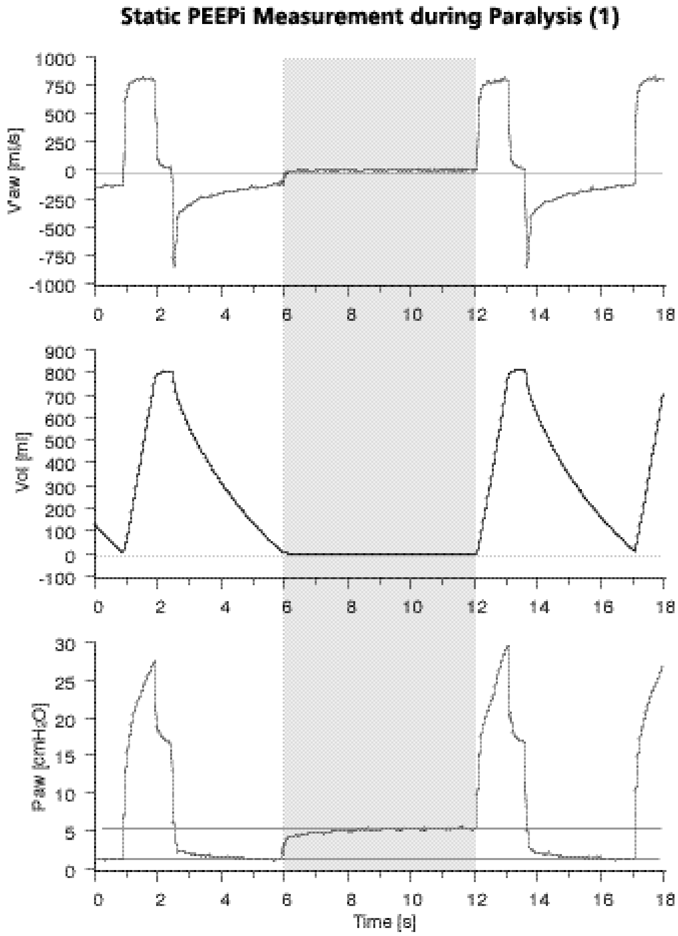

Fig. 3-11
Measurement of static PEEPi by an end-expiratory occlusion maneuver (shaded area), in a dynamically hyperinflated patient, paralyzed, in CMV.

ventilators are presently provided with a special control for this function. In order to allow a good pressure equilibration, the occlusion should be maintained for at least 4 s.

Fig. 3-11 represents the real-time curves of V'aw, Vol, and Paw during such an end-expiratory occlusion maneuver, in a paralyzed patient submitted to CMV. The V'aw curve indicates the presence of dynamic pulmonary hyperinflation in this patient: the end-expiratory flow is far from zero, and higher than 100 ml/s.

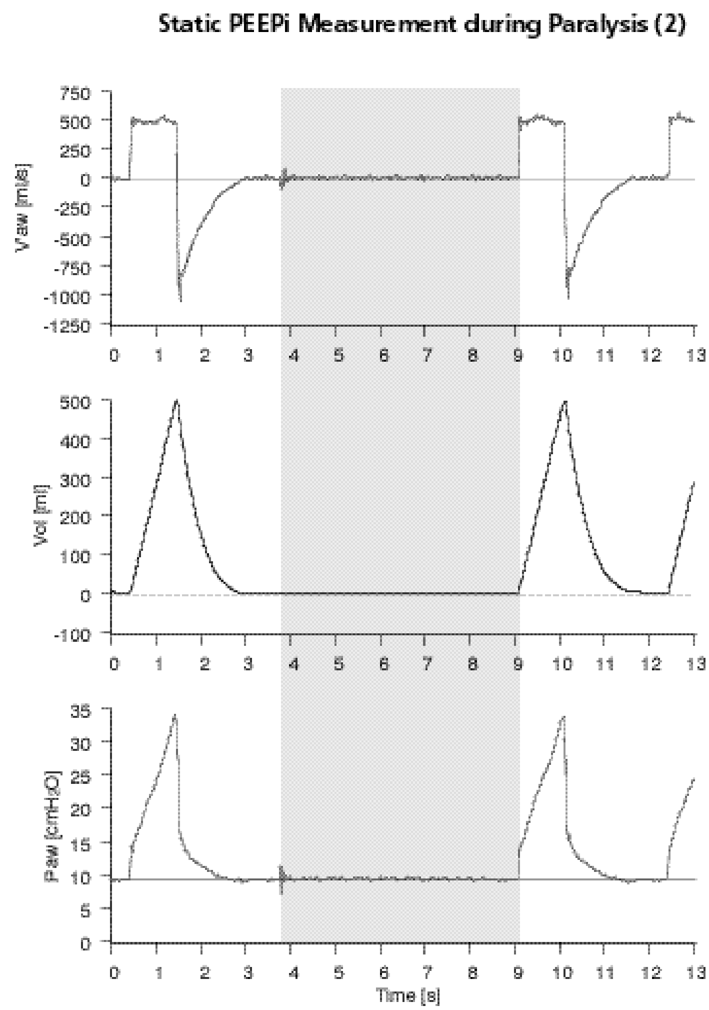

Fig. 3-12
Measurement of static PEEPi by an end-expiratory occlusion maneuver (shaded area), in a paralyzed patient, in CMV, with no dynamic hyperinflation.
The same recording is analyzed in Figs. 3-12, 5-1, 5-2, 5-3

Dynamic hyperinflation is confirmed and quantified by the end-expiratory occlusion maneuver (shaded area): as soon as V'aw is dropped to zero by the valve closure, Paw rises from the PEEPe value of 1 cmH_2O, and stabilizes at 5 cmH_2O within 3 s. Hence, in this patient PEEPtot is 5 cmH_2O and PEEPi is 4 cmH_2O.

Fig. 3-12 is an example of end-expiratory occlusion in a paralyzed patient with no dynamic hyperinflation. In the normal cycle that precedes the occlusion, the expiratory flow reaches a value of zero before the end of the expiratory time, indicating the absence of dynamic hyperinflation. This is confirmed by the occlusion maneuver (shaded area), during which Paw remains unchanged at the level of PEEPe. PEEPtot in this patient is 9 cmH_2O, and is entirely due to PEEPe, while PEEPi is zero.

3.4.1.2. Static PEEPi measurement in actively breathing patients

The end-expiratory occlusion method for the measurement of PEEPi can be used also in patients who are actively breathing through a mechanical ventilator, both with full spontaneous breathing or with assisted modes. As well as for the condition of paralysis, a qualitative and quantitative analysis of the real-time curves of V'aw, Vol and Paw is required. However, the analysis is more complex, the result is subject to a given degree of uncertainty, and the measurement is sometimes impossible. In the actively breathing patients, an occlusion maneuver synchronized with the end of the expiratory time is followed by a phasic activation of the respiratory muscles. Between two successive periods of muscular activation, periods of full relaxation may be alternated, providing adequate conditions exist for reading the PEEPtot value from the Paw curve. The problem for the operator is to judge whether or not the occlusion maneuver contains relaxation periods of acceptable duration. Fig. 3-13 provides an example of a valid end-expiratory occlusion maneuver in a patient assisted by PSV, exhibiting a fair level of static PEEPi.

The recording starts with a normal PSV cycle, followed by a 7-s end-expiratory occlusion maneuver. In order to have a full picture of what happens during the maneuver, a Pes curve has been included in the recording, although unnecessary for the purpose of the measurement. The Pes curve shows a fair drop simultaneous with the mechanical inspiration, indicating an active participation of the patient. Towards the end of inspiration, Pes rises, indicating progressive relaxation of the inspiratory muscles, while inspiration continues due to the positive pressure applied by the mechanical ventilator. During the following exhalation phase, Pes exhibits an exponential decay, indicating passive exhalation.

Just before the end of the exhalation of this cycle, the V'aw curve exhibits an upward inflection: starting from a value of expiratory flow as high as 200 ml/s, it

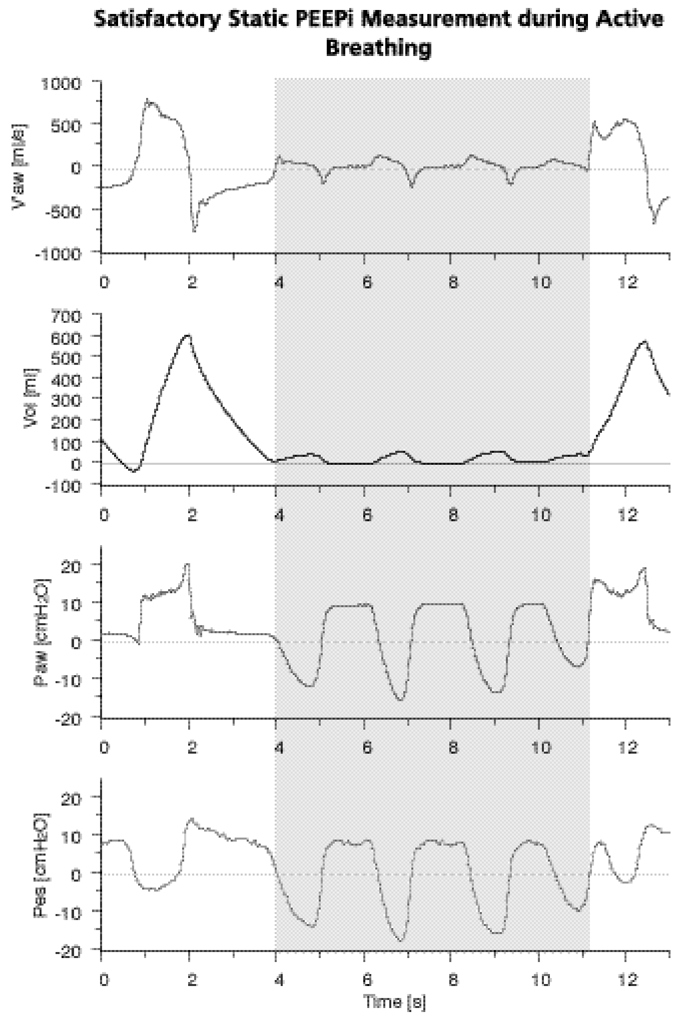

Fig. 3-13
End-expiratory occlusion maneuver in a dynamically hyperinflated patient, actively breathing, in PSV. The maneuver is valid for the PEEPi measurement.

rapidly rises and crosses the zero line. As discussed at § 3.2.2., this upward inflection following passive exhalation is due to an inspiratory effort of the patient, and indicates dynamic pulmonary hyperinflation.

If we continue the analysis of the curves, we can see that the continuing patient effort (evident on Pes) results in an initial inspiratory flow, simultaneous with a drop in Paw. Normally this initial inspiratory flow, or the simultaneous Paw drop, results in activation of the inspiratory flow-trigger or pressure-trigger of the ventilator, with consequent start of a new cycle supported by the machine. In this particular case, however, the operator has activated the ventilator function for synchronizing an occlusion maneuver with the end of exhalation. Hence, the machine operates a closure of both the inspiratory and the expiratory valve, as soon as the patient effort is detected.

During the occlusion maneuver (shaded area) we can notice:

- an evident waving in the Pes curve,
- minor wavings in the V'aw and Vol curves, and
- an evident waving in the Paw curve.

In order to understand the meaning of the Pes waving, it is important to identify, on the Pes curve, the point of start of the occluded effort. This point corresponds to the start of the downward inflection in the Pes curve, just following the slow decay that is typical of passive exhalation. The Pes level corresponding to the point of start of the occluded effort is very important, since it represents the baseline for Pes during the entire occlusion maneuver. During the occlusion period, any Pes different from the baseline reflects a contraction of the respiratory muscles (the inspiratory muscles when Pes is below the baseline, and the expiratory muscles when Pes is above the baseline). On the contrary, the finding of Pes values equal to the baseline means that the respiratory muscles are relaxed. In our example, the waving in the Pes curve is made by periods of drop below the baseline, indicating inspiratory muscle contraction, alternated with periods of return to the baseline, indicating muscle relaxation.

The waves in the flow and volume are due to minor movements of gas, to and fro between the lungs and the external circuit of the ventilator. These movements are generated by the activity of the respiratory muscles, and are allowed by the position of the closed valves, that are inside the mechanical ventilator and far from the airway opening. These minor movements of gas do not affect significantly the occlusion maneuver.

The Paw curve exhibits a waving with the same timing and amplitude as the one observed in Pes. For the purpose of the measurement of PEEPtot, the periods of drop in Paw must be discarded, indicating inspiratory muscle contraction. On the contrary, the Paw level during the periods between the drops can be considered

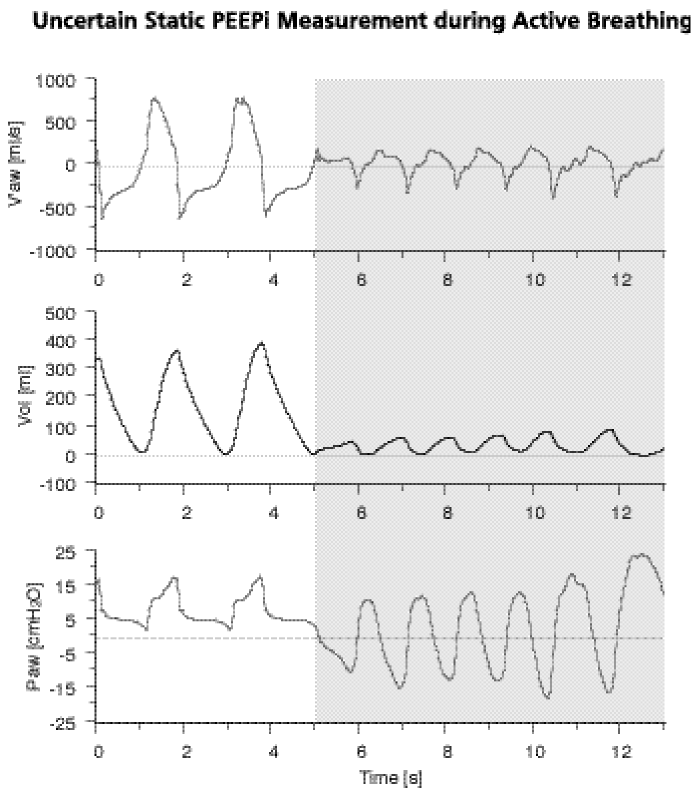

Fig. 3-14
End-expiratory occlusion maneuver in a dynamically hyperinflated patient, actively breathing, in PSV. The maneuver is not valid for the PEEPi measurement.

as an estimate of PEEPtot. In the above example, between the contraction phases, Paw indicates a PEEPtot value of 8 cmH_2O, while the PEEPe applied by the ventilator is of 2 cmH_2O. Hence a PEEPi of 6 cmH_2O can be calculated.

The quantitative analysis is very simple, but the big problem is to decide whether or not the pseudo-relaxation intervals between the Paw drops really correspond to phases of full relaxation. In the above example, relaxation is confirmed by the analysis of the Pes curve. However, in the common clinical practice, the decision should be made without the information provided by Pes. A few qualitative criteria in the analysis of the Paw curve can indicate that full relaxation is very likely:

- in the pseudo-relaxation intervals, Paw exhibits a flat profile;
- the pseudo-relaxation intervals are not too short; and
- the pseudo-relaxation intervals exhibit repetitively the same Paw level.

Fig. 3-14 is another example of the same maneuver. In this case the criteria for validating the relaxation are not entirely met: the pseudo-relaxation intervals are very short and are not flat. Hence relaxation is not guaranteed, and the measurement of the static PEEPi cannot be applied. In such cases, the alternative measurement of the dynamic PEEPi is the only way of gathering the information.

3.4.2. Measurement of dynamic PEEPi in actively breathing patients

The measurement of dynamic PEEPi in the actively breathing patient is based on the analysis of the real-time curves of V'aw, Vol, and Pes, during dynamic breathing. No occlusion maneuver is required, but an esophageal balloon in place is necessary.

The measurement is based on the principle that, in the dynamically hyperinflated, actively breathing patient, actual inspiration can start only after the inspiratory muscles have generated a drop in Pes able to offset the respiratory system elastic recoil pressure corresponding to ΔVol,ee,dyn. This means that after the start of an inspiratory effort, gas flow reverses from exhalation to inspiration only after Pes has dropped by an amount equal to PEEPi. Hence, dynamic PEEPi can be calculated as the difference between the Pes value corresponding to the start of an inspiratory effort, and the Pes value corresponding to the actual start of inspiration defined by the point of flow reversal from expiration to inspiration.

An example of measurement of dynamic PEEPi is shown in Fig. 3-15. The qualitative analysis of the flow curve indicates dynamic hyperinflation (see § 3.2.2.). In order to perform the measurement, the first task is the identification of the point of start of an inspiratory effort, on the Pes curve. The criteria for the identification of this point have been described also at § 3.4.1.2. Briefly, we should observe the Pes curve during exhalation. Normally, Pes exhibits a slow decay, with an upward concavity more or less pronounced, similar to the simultaneous shape of the spirogram. This upward concavity indicates passive exhalation. Towards the end of exhalation, a downward inflection in Pes can be noticed, indicating a contraction of the inspiratory muscles. In the example of Fig. 3-15, the start of the inspiratory effort has been identified on both cycles,

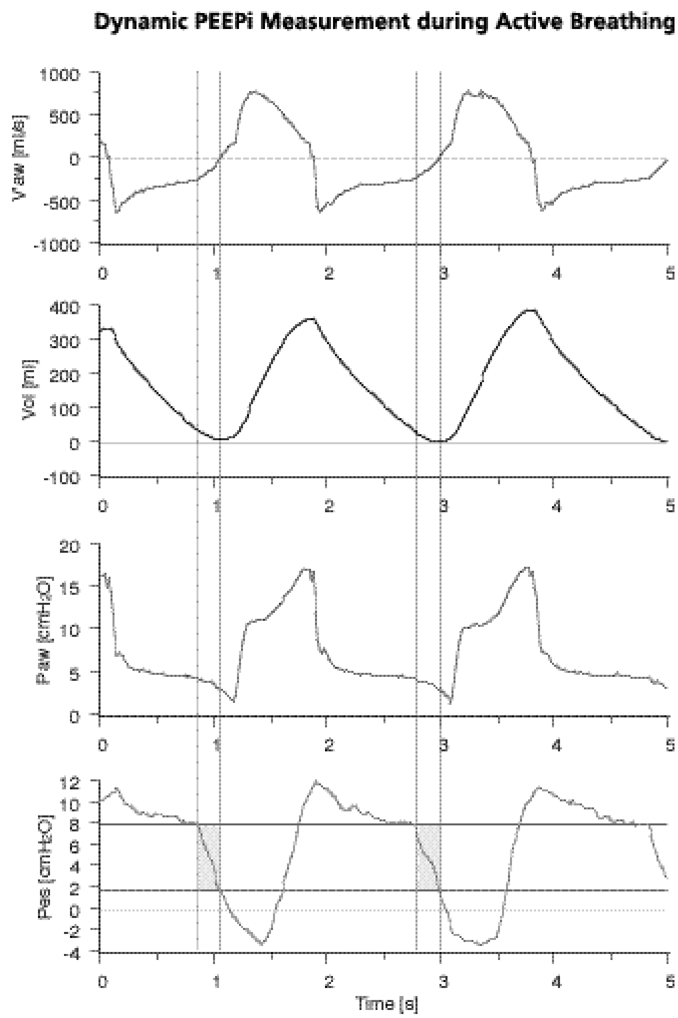

Fig. 3-15
Real-time plot of V'aw, Vol, Paw, and Pes in a dynamically hyperinflated patient, actively breathing, in PSV. The analysis for dynamic PEEPi is performed.

and marked by a first vertical line. In order to measure dynamic PEEPi, the Pes value corresponding to the start of the inspiratory effort must be read. In the example, the Pes level of inspiratory effort start has been marked by the upper horizontal line on the Pes curve, and corresponds to 8 cmH_2O. Then it is necessary to identify the point of actual start of inspiration. This corresponds to the time of flow reversal from expiratory to inspiratory values, and has been marked in the example by a second vertical line on both cycles. A second value for Pes must be read, exactly simultaneous with the flow reversal. In the example, this has been marked by the lower horizontal line on the Pes curve, corresponding to 2 cmH_2O. Dynamic PEEPi can be calculated as the difference between the first and the second Pes level, and corresponds to 6 cmH_2O in our example.

The critical point of the above described method is in the identification, on the Pes curve, of the point of start of the inspiratory effort. Identification is possible only when the inspiratory effort is preceded by a passive exhalation. Hence, when the criteria for passive exhalation are not met, the method cannot be applied, and a more complex analysis should be performed, taking advantage of a simultaneous recording of an intra-abdominal pressure.

It must be remembered that the simultaneous values for dynamic PEEPi and static PEEPi may not be the same. Typically, dynamic PEEPi exhibits values lower than static PEEPi. It is considered that the static measurement expresses an average value for PEEPi, while the dynamic measurement expresses the minimal value for the PEEPi of the different alveolar units.

3.5. Conclusions

Dynamic hyperinflation can be easily identified, most commonly by observation of the real-time curve of gas flow. The key point is the finding of an end-expiratory flow rate different from zero.

Dynamic pulmonary hyperinflation can be quantified in terms of volume, as ΔVol,ee,dyn, or in terms of pressure, as PEEPi. This measurement of PEEPi is very easy and precise when applied in the paralyzed patient, while it may be difficult and uncertain in the actively breathing patients. In such patients, the alternative measurement of the dynamic PEEPi can be proposed, but it requires an esophageal balloon catheter in place.

The quantitative assessment of dynamic hyperinflation by estimate of ΔVol,ee,dyn, i.e., of the end-expiratory lung volume above the resting equilibrium point, is not common practice. However, the estimate based on the linear extrapolation of the flow-volume loop is interesting, since it does not require any special maneuver. It only requires the monitoring system to provide a graphic representation of the flow-volume loops, and the physician to have good experience in the qualitative analysis of the curves.

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4. CLASSIC MEASUREMENTS OF PASSIVE RESPIRATORY MECHANICS

4.1. Resistance and compliance

The classic measurements of passive respiratory mechanics include all the parameters that describe the impedance of the respiratory system to ventilation: resistance, compliance, and PEEPi. The meaning of PEEPi has already been introduced at § 3.1. Here, we will introduce the concepts of resistance and compliance.

4.1.1. Resistance

Any flow of gas entering into the respiratory system during inspiration, or coming out during exhalation, is opposed by the respiratory system frictional resistance, also indicated simply as resistance. Resistance is given by the ratio between the pressure driving a given flow and the resulting flow rate. If we consider the simple case of a fluid flowing through a tube, the resistance (R) of the tube corresponds to the ratio between the pressure difference (ΔP) between the two extremities of the tube, and the flow rate (V') of the fluid :

$$R = \frac{\Delta P}{V'}$$

The dimension of resistance is pressure, divided by volume, divided by time. The unit of resistance generally employed in respiratory mechanics is $cmH_2O/l/s$.

Normally, the resistance of the respiratory system is mainly represented by the airway resistance. Tissue resistance is a second component, normally very low. Airway resistance is typically increased in the obstructive respiratory diseases. Tissue resistance may also be increased in several respiratory diseases.

It must be noted that, during mechanical ventilation, all the measurements of respiratory mechanics based on the airway opening pressure include the resistance of the endotracheal tube, as a part of lung resistance, and hence of total respiratory system resistance. The resistive effects of the endotracheal tube can be excluded only by using a tracheal carina pressure instead of the airway opening pressure (see § 2.2.).

4.1.2. Compliance

Two parameters describe the elastic resistance, or the elasticity, of the respiratory system: elastance and compliance. Elastance (E) is the ratio between a change in the static transmural pressure (ΔP) applied to the respiratory system and the resulting change in respiratory system volume (ΔVol), at the equilibrium. Compliance (C) is the reciprocal of elastance.

$$E = \frac{\Delta P}{\Delta Vol} \qquad\qquad C = \frac{\Delta Vol}{\Delta P}$$

In intensive respiratory care, elasticity is commonly assessed by means of the parameter compliance, that looks at the problem in terms of distensibility. Namely, compliance indicates how easily the respiratory system is distended by a given transmural pressure.

The dimension of compliance is volume divided by pressure, and the unit commonly used is ml/cmH_2O.

In respiratory disease, compliance is much reduced in ARDS patients, mainly due to a reduction of the number of the alveoli open to ventilation. On the opposite side, abnormally high values of compliance may be observed in advanced lung emphysema, due to reduced elastic recoil of the pulmonary parenchyma.

4.2. Principles of the classic measurements of respiratory mechanics

4.2.1. General principles

The classic measurements of respiratory mechanics are performed in paralyzed patients, ventilated in CMV with a constant inspiratory flow. For the purpose of the measurements, it is necessary to interrupt the normal ventilatory pattern with two prolonged airway occlusion maneuvers, one performed at end-exhalation, and the other one performed at end-inflation.

The classic measurements of respiratory mechanics include two different kinds of end-inspiratory resistance (the initial resistance and the maximum resistance), the static compliance, and the static PEEPi. Most commonly, the measurements are performed by an analysis of the signals of Paw, V'aw, and Vol, providing data referenced to the entire respiratory system.

When a Pes signal is available, the classic measurements of respiratory mechanics can provide data concerning separately the chest wall and the lungs. For chest wall mechanics, Pes must be used instead of Paw. For lung mechanics, the transpulmonary pressure (i.e., Paw minus Pes), must be used instead of Paw.

4.2.2. End-inspiratory occlusion maneuver

The measurement of end-inspiratory resistance is performed by two different methods: the rapid interruption and the elastic subtraction method. Both methods are based on the end-inspiratory occlusion maneuver. The same maneuver also provides data that will be used for the measurement of static compliance.

4.2.2.1. Rapid interruption method

The rapid interruption method yields the measurement of the end-inspiratory resistance known as initial resistance (Rinit). The method is based on the general principle that, when a constant-flow passive inflation is abruptly interrupted, a pressure drop is seen at the airway opening, equal to the resistive load for the interrupted flow. The end-inspiratory occlusion maneuver corresponds to a rapid interruption of the end-inflation flow (V'ei), and results in an immediate drop of Paw from the peak pressure (Ppeak) to a pressure denoted as P_1. This pressure drop correspond to the resistive load for V'ei, and hence Rinit can be calculated as:

$$\text{Rinit} = \frac{\text{Ppeak} - P_1}{\text{V'ei}}$$

P_1 is the initial elastic recoil pressure of the respiratory system, as it is observed immediately after the end-inflation flow interruption. When the flow interruption is maintained for some time, by performing a prolonged occlusion maneuver, Paw exhibits a further, slow, exponential drop below P_1. This slow pressure drop is due both to pendelluft (redistribution of volume between lung compartments with different time constants), and to stress adaptation of the respiratory system. Paw finally stabilizes at a level that is the static end-inspiratory pressure (Pei,st). In other terms, during a prolonged occlusion maneuver, the respiratory system elastic recoil pressure corresponding to the end-inspiratory volume moves from an initial dynamic value, represented by P_1, to a lower, static value, represented by Pei,st.

4.2.2.2. Elastic subtraction method

The elastic subtraction method yields a measurement of the end-inspiratory resistance based on Pei,st, and known as maximum resistance (Rmax). The method is based on the general principle that the pressure seen at the airway opening during any given point of a passive inflation is due to the sum of: a. the resistive load for the flow rate of that point, and b. the static elastic recoil pressure for the volume of that point. In the particular case of the last point of a constant flow inflation, the airway opening pressure, i.e., Ppeak, is due to the sum of the static elastic recoil pressure for the end-inspiratory volume, i.e., Pei,st, and the resistive load for the end-inflation flow (V'ei). Hence, Rmax can be calculated according to the following equation, based on the subtraction of Pei,st from Ppeak:

$$\text{Rmax} = \frac{\text{Ppeak} - \text{Pei,st}}{\text{V'ei}}$$

Since Pei,st is always lower than P_1 and Rmax is always higher that Rinit. It is considered that Rinit is mainly an expression of the pure resistive properties of the airways, while Rmax also includes the tissue resistance of the respiratory system. The difference between Rmax and Rinit, generally denoted as ΔR, is considered an expression of the tissue visco-elastic properties of the respiratory system.

4.2.3. End-expiratory occlusion maneuver

The end-expiratory occlusion maneuver is used to obtain a measurement of static PEEPtot on the signal of Paw, i.e., of the elastic recoil pressure of the respiratory system at the end-expiratory volume. The maneuver is exactly the one that has been extensively described at § 3.4.1.1. Static PEEPtot allows the measurement of static PEEPi, as difference between PEEPtot and the PEEPe applied by the ventilator, and is essential for the measurement of static compliance (Cstat).

The measurement of Cstat takes advantage of the measurements of the elastic recoil pressures of the respiratory system Pei,st and PEEPtot, respectively, obtained at the end-inspiratory volume and at the end-expiratory volume by the two occlusion maneuvers. Cstat is calculated from Pei,st, PEEPtot, and tidal volume (Vt), i.e. the volume difference between end-inspiration and end-exhalation, as:

$$\text{Cstat} = \frac{\text{Vt}}{\text{Pei,st} - \text{PEEPtot}}$$

4.3. Practice of the measurements of total respiratory system mechanics

4.3.1. General hints

For the purpose of the classic measurements of respiratory mechanics, the patient must be perfectly paralyzed and passively ventilated. A constant inspiratory flow must be used. Hence, the measurement can only be performed in CMV, delivered with a square flow pattern. The classic measurements of respiratory mechanics require two airway opening occlusion maneuvers, one at the end of an inflation, and the other one at the end of an exhalation, each occlusion lasting at least 4 seconds.

The order of execution of the two occlusion maneuvers is indifferent. On the assumption of steady state, the two maneuvers can be performed indifferently on the same respiratory cycle, on two successive cycles, or on different, noncontiguous cycles. In the example used for the next Figs. 4-1 to 4-4, the airway opening has been first occluded at the end of the exhalation of one cycle, then at the end of the inspiration of the next cycle. This is just one of the possible sequences that can be used.

In theory, the occlusion maneuvers should be performed by means of a fast interruptor placed directly at the airway opening. However, for reasons of simplicity, the maneuvers are generally performed without specialized equipment, simply by manual activation of the occlusion functions of the ventilator. Thus the occlusions are generally performed by means of the internal valves of the ventilator, and not directly on the airway opening. As it will be discussed below at § 4.3.3., lack of proximal and really fast occlusion significantly affects the values of pressure to be used for the measurements of resistance, and should be compensated for by special corrections.

It is well known that all the results of the classic measurements of respiratory mechanics vary as a function of the tidal volume and the inspiratory flow delivered by the ventilator. Hence, in order to have comparable data, especially when obtained in different times on the same patients, it is very important to standardize the ventilatory pattern set in the mechanical ventilator.

4.3.2. Measurement of Cstat, Rmax and PEEPtot

Fig. 4-1 is a real-time recording of V'aw, Vol, Paw and Pes, with the occlusion maneuvers (shaded areas) necessary for the classic measurements of respiratory mechanics. CMV was set to deliver a constant inspiratory flow. In the example, an optional end-inspiratory pause was also set, equal to 10% of the duration of the cycle. A PEEPe of 5 cmH_2O was set. The recording starts with a CMV cycle with normal inflation, end-inspiratory pause, and exhalation. At the last point of the expiratory time, the airway opening is occluded. The occlusion is maintained for 5 s, then it is released and a normal inflation takes place. At the end of this inflation, the airway opening is occluded again for 5 s. Then the occlusion is released, a normal exhalation takes place, and the normal respiratory pattern is resumed. In this example, the occlusion maneuvers have been performed distally from the patient, by the occlusion functions of the ventilator.

Fig. 4-2 is a zoom of Fig. 4-1, limited to V'aw, Vol, and Paw, showing in detail the occlusion periods, together with the inflation interposed between the two occlusion maneuvers. The last Paw before the start of the end-expiratory occlusion represents the PEEPe applied by the ventilator. It can be noticed that, with the start of the end-expiratory occlusion, Paw rises from PEEPe, and within a few seconds stabilizes at a level that represents PEEPtot. This behavior is typical of dynamically hyperinflated patients with significant PEEPi (see § 3.4.1.1. and Fig. 3-11). In patients without dynamic hyperinflation, during the expiratory occlusion, Paw does not move from the level of PEEPe (see § 3.4.1.1. and Fig. 3-12). In Fig. 4-2, it can also be noticed that, with the start of the end-inspiratory occlusion, Paw exhibits a fast drop from Ppeak, and within few seconds stabilizes at a level that represents Pei,st.

In this figure, we have marked all the measurements necessary for the calculation of Rmax, Cstat, and PEEPi, namely:

- V'ei, the gas flow at the end of inflation,
- Vti, the inspiratory Vt, from zero, at the start of inflation, to the maximal level that is exhibited at end of the end-inspiratory occlusion maneuver,
- Ppeak, the Paw at the end of inflation,
- Pei,st, the Paw at the end of the end-inspiratory occlusion maneuver,
- PEEPtot, the Paw at the end of the end-expiratory occlusion maneuver,
- PEEPe, the Paw at the end of the expiratory time preceding the end-expiratory occlusion maneuver.

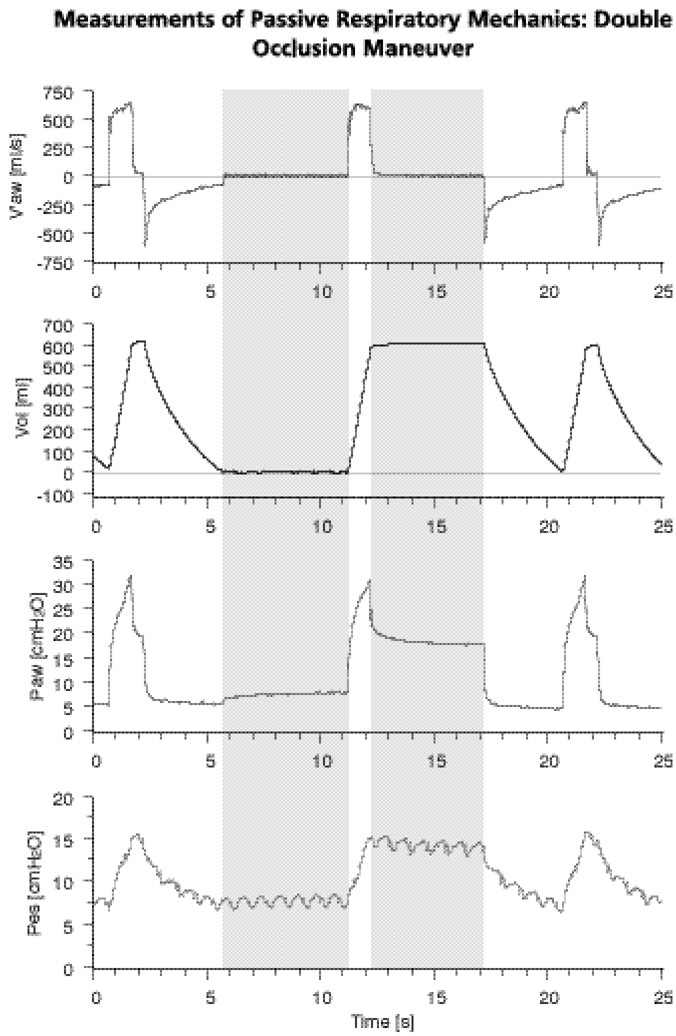

Fig. 4-1
Real-time curves of V'aw, Vol, Paw, and Pes during CMV with constant inspiratory flow, in a paralyzed patient with dynamic pulmonary hyperinflation. Prolonged occlusion maneuvers are performed at end-expiration and end-inspiration (shaded areas) by means of the mechanical ventilator, for the purpose of the classic measurements of passive respiratory mechanics.
The same recording is analyzed in Figs. 4-1, 4-2, 4-3, 4-4

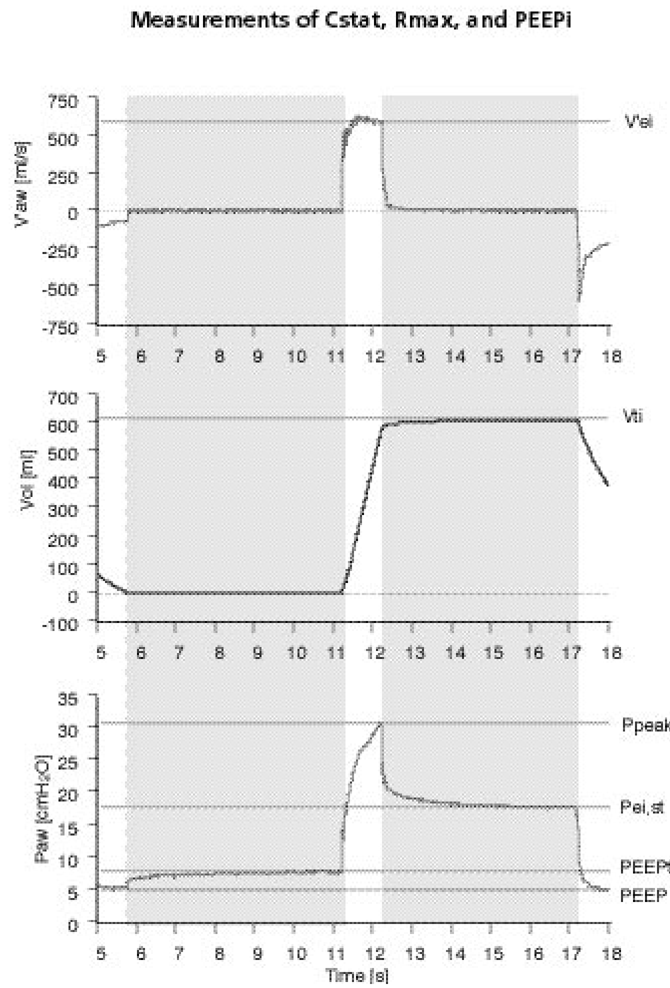

Fig. 4-2
Real-time curves of V'aw, Vol, and Paw during CMV with constant inspiratory flow, in a paralyzed patient with dynamic pulmonary hyperinflation (taken from Fig. 4-1, with the time-axis zoomed on the occlusion periods, marked by the shaded areas). The horizontal markers indicate the readings necessary for the measurements of Cstat, Rmax and PEEPi.
The same recording is analyzed in Figs. 4-1, 4-2, 4-3, 4-4

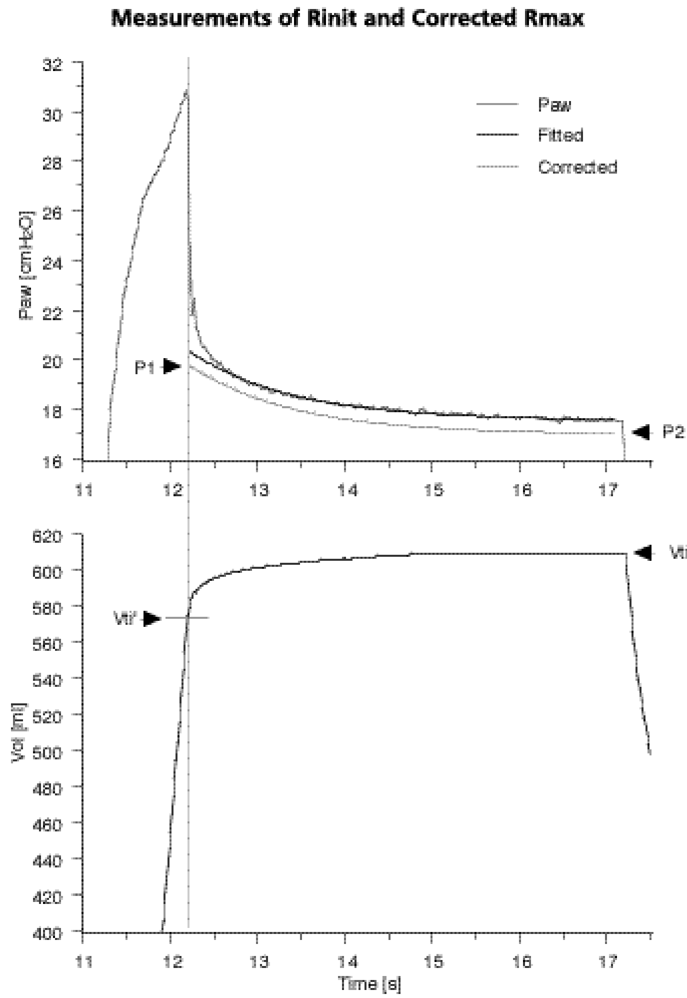

Fig. 4-3
Real-time curves of Paw and Vol during CMV with constant inspiratory flow, in a paralyzed patient (taken from Fig. 4-1, with the time-axis zoomed on the inspiratory occlusion period, and amplified Y-axis). On the Paw graph, we have plotted the fitted curve and the corrected curve that are used for the reading of P_1 and P_2. The Vol plot shows the effect of slow interruption of flow: volume increases from the point of end-inflation (Vti') to the point of end-inspiration (Vti). These data allow the calculation of Rinit and of corrected Rmax.
The same recording is analyzed in Figs. 4-1, 4-2, 4-3, 4-4

The respective data are:

V'ei	0.6	l/s
Vti	610	ml
Ppeak	31	cmH_2O
Pei,st	17.5	cmH_2O
PEEPtot	7.5	cmH_2O
PEEPe	5	cmH_2O

Based on these data, we can calculate Rmax, Cstat, and PEEPi according to the formulas of § 4.2., as follows :

Cstat	610 / (17.5 - 7.5)	=	61	ml/cmH_2O
Rmax	(31 - 17.5) / 0.6	=	22.5	$cmH_2O/l/s$
PEEPi	7.5 - 5	=	2.5	cmH_2O

4.3.3. Measurement of Rinit and of corrected Rmax

In order to correctly calculate Rmax and identify P_1 for the calculation of Rinit, we should use a fast interruptor, located very close to the airway opening. Even with this technique, the identification of P_1 may be difficult, due to the noise generated by the interruptor.

As described above, usually the occlusion maneuvers are performed by means of the valves of the ventilator. These valves can operate very fast, but their distance from the patient means that, at the airway opening, flow interruption is always relatively slow. A slow interruption has no effect on the measurement of compliance, but affects the measurements of resistance.

Fig. 4-3 is a further zoom of Fig. 4-1, concerning the inspiratory occlusion maneuver, with amplified curves of Paw and Vol. As already mentioned, in this example the occlusion is obtained by the ventilator valves. This impedes the fast interruption of V'aw (not shown in the picture) since, as soon as Paw drops, a transfer of pressurized gas takes place from the external circuit of the ventilator into the respiratory system. Fig. 4-3 shows the effects of this transfer of gas in terms of volume: after the occlusion start, marked by a dotted vertical line and corresponding to an end-inflation volume (Vti') of 575 ml, the respiratory system volume continues to increase for a few seconds, finally reaching the level corresponding to the complete inspiratory tidal volume (Vti) of 610 ml. This means that, after the start of the inspiratory occlusion maneuver, an additional inspiratory volume of 35 ml is delivered to the patient.

In practice, the profile of Paw between the start and the end of an inspiratory occlusion maneuver operated by the ventilator valves depends on the interaction of three different phenomena:

- fast interruption of the flow delivered by the ventilator, that should give an immediate and stable drop in Paw;
- pendelluft and stress adaptation, that should give a further slow exponential drop in Paw;
- slow transfer of gas from the ventilator circuit to the respiratory system, that partially counteracts the Paw drops due to the interruption of the flow delivered by the ventilator, to the pendelluft, and to the stress adaptation.

A slow interruption has two different effects :

a. The value of P_1 cannot be read directly on the Paw curve, since the profile of the curve during the former part of the occlusion maneuver is altered by the persistent transfer of gas from the ventilator circuit to the respiratory system.

b. The value of Pei,st directly read on the Paw curve is to be referred to a lung volume higher than the one that was present at the end of inflation. Pei,st corresponds to the end-inspiratory volume Vti, while the static elastic recoil pressure to be subtracted from Ppeak for a correct calculation of Rmax should correspond to the end-inflation volume Vti', i.e., to a volume lower than Vti by 35 ml in our example. On the contrary, Pei,st remains the good measurement for the calculation of compliance, since it corresponds to Vti.

The effects of slow interruption can be corrected, but a relatively complex mathematical processing of Paw is required. In particular, the correct identification of P_1 cannot be performed by eye or by hand. Briefly, we must fit a single exponential curve on the slow decay of Paw during the inspiratory occlusion. The fitted curve must be extrapolated backwards in time (Fitted curve, in Fig. 4-3). Then we must subtract the effect of the additional elastic load (Pel,add) due to the additional volume transfer that takes place during the inspiratory occlusion. Pel,add is a function of static compliance, and can be calculated as:

$$\text{Pel,add} = \frac{(\text{Vti} - \text{Vti'})}{\text{Cstat}}$$

Therefore, all the fitted curve must be lowered by a value equal to Pel,add (Corrected curve, in Fig. 4-3). Then P_1 is read on the corrected curve at the time zero of the occlusion maneuver, i.e., at the point that has the same time as Ppeak.

Rinit can be calculated from P_1, according to the formula of § 4.2. In turn, corrected Rmax (Rmax,corr) can be calculated from a pressure denoted as P_2 and corresponding to Pei,st diminished by Pel,add:

$$P_2 = Pei,st - Pel,add \qquad Rmax,corr = \frac{Ppeak - P_2}{V'ei}$$

In the example of Figs. 4-1 to 4-3, the following data have been read for the purpose of the calculation of Rinit and corrected Rmax :

V'ei	0.6	l/s
Vti	610	ml
Vti'	575	ml
Ppeak	31	cmH_2O
Pei,st	17.5	cmH_2O

By means of the above described procedures, the following data have been calculated:

Pel,add	(610 - 575) / 61	=	0.6	cmH_2O
P_1			19.8	cmH_2O
P_2	17.5 - 0.6	=	16.9	cmH_2O
Rinit	(31 - 19.8) / 0.6	=	18.7	$cmH_2O/l/s$
Rmax,corr	(31 - 16.9) / 0.6	=	23.5	$cmH_2O/l/s$
ΔR	23.5 -18.3	=	5.2	$cmH_2O/l/s$

4.4. Measurements of separate chest wall and lung mechanics

The same procedures used for total respiratory system mechanics can be used for separate chest wall and lung mechanics, provided that a Pes signal is available.

The measurements of chest wall mechanics are based on the signals of V'aw, Vol, and Pes. An example is given in Fig. 4-4, that is, a zoom of Fig. 4-1, with real-time curves of V'aw, Vol, and Pes during the double occlusion. In theory, the signal can be processed exactly by the same procedures described at § 4.3.2. and 4.3.3. However, as it can be noticed in the example, the Pes signal is typically affected by noise due to cardiac activity. For this reason, the identification of P_1 is extremely difficult and uncertain. Moreover, the chest wall values for resistance (and particularly for Rinit) are very low. Finally, the measurements of both resistance and dynamic hyperinflation on the chest wall are of no clinical use.

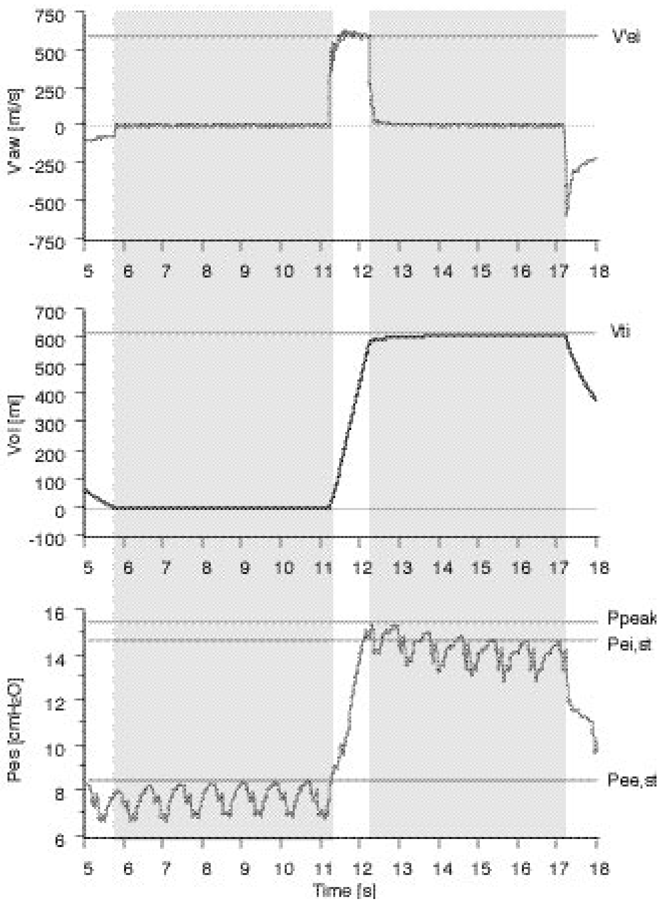

Fig. 4-4
Real-time curves of V'aw, Vol, and Pes during CMV, in a paralyzed patient with dynamic pulmonary hyperinflation (taken from Fig. 4-1, with the time-axis zoomed on the occlusion periods, marked by the shaded areas). The horizontal markers indicate the readings necessary for the classic measurements of the passive respiratory mechanics of the chest wall.
The same recording is analyzed in Figs. 4-1, 4-2, 4-3, 4-4

Hence, the data collection for the measurements of chest wall mechanics can be simplified, and limited to the following points (marked in Fig. 4-4):

- V'ei, the gas flow at the end of inflation,
- Vti, the inspiratory Vt, from zero, at the start of inflation, to the maximal level, exhibited at end of the inspiratory occlusion maneuver,
- Ppeak, the Pes at the end of inflation,
- Pei,st, the Pes at the end of the inspiratory occlusion maneuver,
- Pee,st, the Pes at the end of the expiratory occlusion maneuver.

The respective data are :

V'ei	0.6	l/s
Vti	610	ml
Ppeak	15.5	cmH_2O
Pei,st	14.5	cmH_2O
Pee,st	8.5	cmH_2O

Based on these data, we can calculate Cstat and Rmax for the chest wall, according to the following equations:

$$\text{Cstat} = \frac{\text{Vti}}{\text{Pei,st} - \text{Pee,st}} \qquad \text{Rmax} = \frac{\text{Ppeak} - \text{Pei,st}}{\text{V'ei}}$$

as follows :

Cstat	610 / (14.5 - 8.5)	=	102	ml/cmH_2O
Rmax	(15.5 - 14.5) / 0.6	=	1.7	$cmH_2O/l/s$

Concerning the measurements of lung mechanics, these can be performed by analysis of V'aw, Vol, and transpulmonary pressure, i.e., Paw minus Pes. However, once the measurements of total respiratory system mechanics and chest wall mechanics have been performed, it is easier to calculate lung data from the following equations:

$$\text{Cstat,L} = \frac{1}{\frac{1}{\text{Cstat,rs}} - \frac{1}{\text{Cstat, w}}} \qquad \text{Rmax,L} = \text{Rmax,rs} - \text{Rmax,w}$$

where L denotes the lung, rs the total respiratory system, and w the chest wall. In the above example, Cstat,L is 152 ml/cmH_2O and Rmax,L is 21.8 $cmH_2O/l/s$. These data denote airway obstruction and lung emphysema.

4.5. Simplified approaches to the measurement of total respiratory system mechanics

The full and precise approach to the classic measurements of passive respiratory mechanics is more suitable for scientific purposes than for common clinical practice. For these reasons, simplified methods have been developed, based on the same principles of the classic methods.

One simplified approach is based on :

- patient paralysis,
- CMV delivered with a square wave inspiratory flow,
- end-inspiratory pause of 10-20% of cycle duration,
- no end-expiratory occlusion.

These conditions are used by several ventilator monitors in order to provide data for total respiratory system compliance (calculated as Cstat) and resistance (calculated as Rmax). An end-inspiratory pause of 10-20% of total cycle time corresponds to an end-inspiratory occlusion maneuver, but may not guarantee that a real static condition is achieved. The advantage of such a short occlusion is that it may be included in the respiratory pattern set in the mechanical ventilator, thus allowing breath-by-breath monitoring of respiratory mechanics. However, the major limit of this simplified approach is the lack of an end-expiratory occlusion. The method postulates lack of dynamic hyperinflation, and uses the value read for PEEPe as an estimate of the end-expiratory elastic recoil pressure of the respiratory system.

With this approach, the measurements of both Rmax and Cstat may be underestimated, due to insufficient pressure equilibration during the inspiratory pause, resulting in an inspiratory pause pressure (Ppause) higher than the static end-inspiratory elastic recoil pressure. However, the results may be acceptable in patients with short respiratory system time constant, such as the ARDS patients. On the contrary, in the COPD patients, and in general in the dynamically hyperinflated patients, a significant underestimate results in Rmax, and especially a major underestimate results in Cstat. The latter is mainly due to an end-expiratory elastic recoil pressure higher than PEEPe. For this reason, the physician should check the flow signal curve for dynamic hyperinflation (see § 3.2.1.), and retain the monitor results only when lack of dynamic hyperinflation is confirmed.

Should the physician detect dynamic hyperinflation, a manual end-expiratory occlusion maneuver is to be performed, by means of the occlusion function of the ventilator. This will allow the measurement of PEEPtot, and hence the manual calculation of PEEPi, and the better estimate of Cstat, as Vt divided by Ppause minus PEEPtot.

As a third alternative, the physician can decide to perform the full, double occlusion maneuver, but to limit the measurements to Cstat, Rmax, and PEEPi, and avoid the correction for the slow interruption of flow as well as the measurement of Rinit. In this case, the measurements are simple and fast, and do not require specialized equipment.

4.6. Conclusions

The classic measurements can provide a deep picture of the passive mechanics of the respiratory system, including separate measurements for airway and tissue resistance, and also, when Pes is available, separate measurement for the chest wall and the lungs. However, the classic measurements require a double, prolonged occlusion maneuver. Moreover, in order to obtain the full panel of data and precise results, a complicated and time-consuming analysis is necessary.

In the common clinical practice, the measurements are limited to the calculation of Cstat, Rmax, and PEEPi for the entire respiratory system.

Automatic breath-by-breath analysis of Cstat and Rmax based on the classic principles strictly requires patient paralysis and a ventilator setting including a square waveform and an end-inspiratory pause. The results for Cstat will be completely unreliable in the presence of dynamic pulmonary hyperinflation.

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5. RESPIRATORY MECHANICS BY LEAST SQUARE FITTING

5.1. Mathematical approach

The least square fit method for the assessment of respiratory mechanics is based on the equations of motion of the relaxed respiratory system, developed by Rohrer. Most commonly, the method is applied to the entire respiratory system. The equation for the entire relaxed respiratory system is:

$$Paw(t) = (V'aw(t) \times Rrs) + \left(\frac{Vol(t)}{Crs}\right) + PEEPtot$$

This equation tells that, at any time t of a relaxed respiratory cycle generated by a mechanical ventilator, instantaneous Paw equals the sum of the resistive load, of the elastic load, and of a constant. The resistive load corresponds to the product of instantaneous flow and total resistance (Rrs). The elastic load corresponds to the ratio between the instantaneous volume above the end-expiratory volume and the total compliance (Crs). The constant corresponds to the elastic load of total intrapulmonary PEEP (PEEPtot).

In theory, when we know at least three sets of simultaneous data for Paw(t), V'aw(t), and Vol(t), we can solve the equation for the three unknowns represented by Rrs, Crs, and PEEPtot. However, due to the noise normally included in the signals, a good estimate of the actual values of the unknowns can be obtained only when a large number of sets of data is processed.

The most common application of the least square fit method uses data of Paw, V'aw, and Vol taken from an entire respiratory cycle, by sampling the signals at high rate. For example, a sampling rate of 60 Hz is used. This means that, at a respiratory rate of 20 breaths/min, 180 sets of data are used for each respiratory cycle.

The mathematical method used for solving the motion equation for such a big number of sets of data is the least square fit. This method is better known in the statistics field, where it is used for the multiple linear regression procedure. The general equation for the analysis is:

$$y = (x_1 \times a) + (x_2 \times b) + k$$

This kind of analysis must be necessarily performed by a computer, working on digital signals for Paw, V'aw, and Vol.

5.2. Graphic approach

Although the least square fit method is a mathematical procedure, some readers might better understand the principle by looking at the problem from a graphic standpoint.

When we consider the simultaneous signals of V'aw, Vol, and Paw, a relaxed respiratory cycle generated by a mechanical ventilator corresponds to a three-dimensional loop. In Fig. 5-1, the points of such a loop have been plotted by assigning V'aw to the X-variable axis, Vol to the Y-variable axis, and Paw to the Z-variable axis. Plotted data are taken from a CMV cycle, with a constant inspiratory flow and a PEEPe of 9 cmH_2O. The reader can see the corresponding real-time plots as the second cycle of Fig. 3-12.

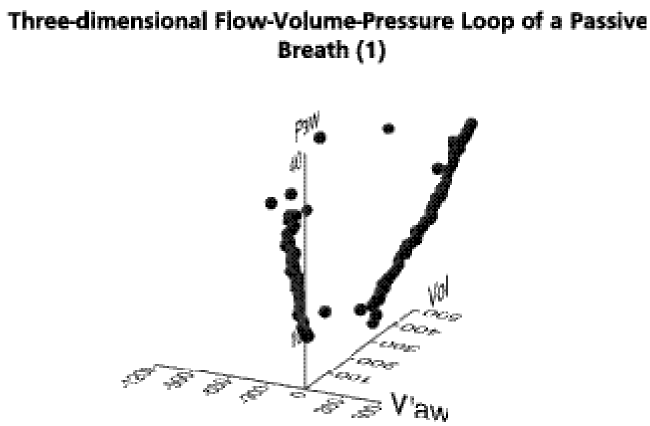

Fig. 5-1
3-D loop of V'aw, Vol, and Paw during a single respiratory cycle in CMV, with a PEEPe of 9 cmH_2O, in a paralyzed patient. Data points are sampled at 60 Hz. Based on these data, the least square fit procedure allows the calculation of Rrs, Crs, and PEEPtot.
The same cycle is analyzed in Figs. 3-12, 5-1, 5-2, 5-3

For better visualization, in Fig. 5-2 the surface enclosed by the loop has been filled. By looking at the graph from different angles (Figs. 5-2 and 5-3), it can be noted that the surface enclosed by the loop is nearly flat. Hence, the loop tends to run on a single plane. This plane can be described by a slope relative to the V'aw-axis, a slope relative to the Vol-axis, and an intercept on the Paw-axis. According to the equation of motion of the relaxed respiratory system (see above), the slope relative to the V'aw-axis corresponds to Rrs, while the slope relative to the Vol-axis corresponds to 1/Crs, and the intercept on the Paw-axis corresponds to PEEPtot.

Three-Dimensional Flow-Volume-Pressure Loop of a Passive Breath (2)

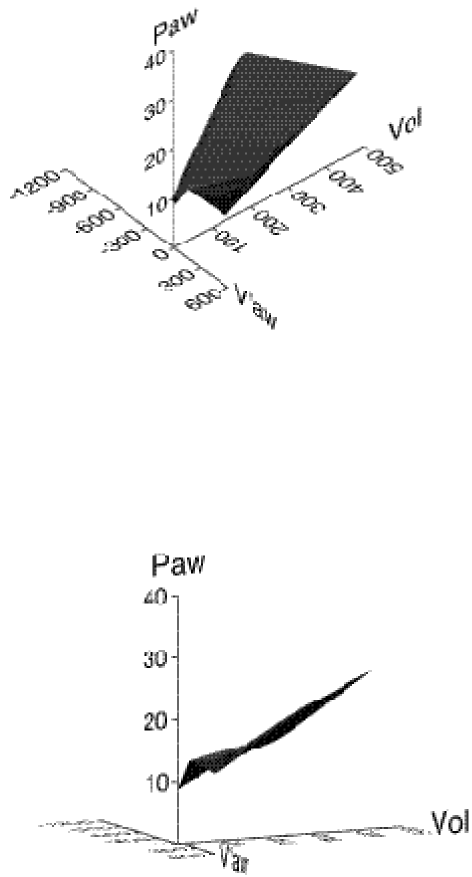

Fig. 5-2
The surface enclosed by the 3-D loop of Fig. 5-1 has been filled. The different views show that the surface is nearly flat. The least square fit procedure identifies slopes and intercept of the corresponding plane. The slope relative to the V'aw-axis corresponds to Rrs, while the slope relative to the Vol-axis corresponds to 1/Crs, and the intercept on the Paw-axis corresponds to PEEPtot.
The same cycle is analyzed in Figs. 3-12, 5-1, 5-2, 5-3

From a graphic standpoint, the least square fit method is nothing else than a statistical approach for the identification of the plane that best fits with the loop described by the data points. Identifying the plane means to obtain slopes and intercept, and hence Rrs, 1/Crs, and PEEPtot.

Three-Dimensional Flow-Volume-Pressure Loop of a Passive Breath (3)

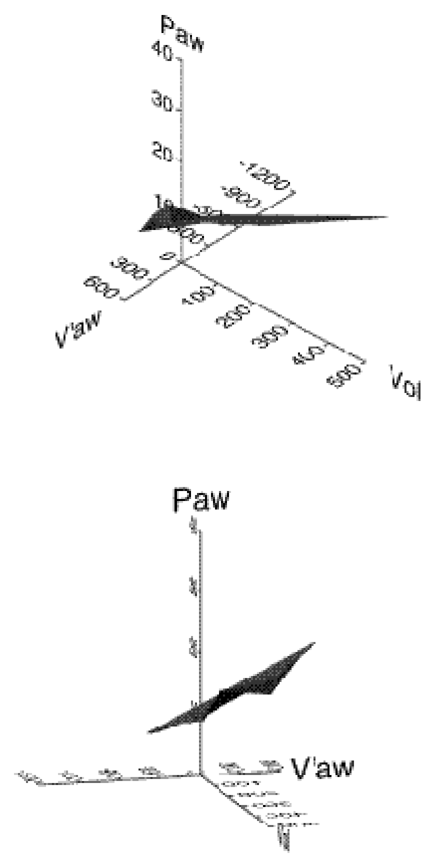

Fig. 5-3
The surface enclosed by the 3-D loop of Fig. 5-1 has been filled. The different views show that the surface is nearly flat. The least square fit procedure identifies slopes and intercept of the corresponding plane. The slope relative to the V'aw-axis corresponds to Rrs, while the slope relative to the Vol-axis corresponds to 1/Crs, and the intercept on the Paw-axis corresponds to PEEPtot.
The same cycle is analyzed in Figs. 3-12, 5-1, 5-2, 5-3

5.3. Results, advantages and limits

In contrast to the classic approach to respiratory mechanics, the least square fit method requires no special respiratory pattern and no occlusion maneuver. Hence, it can be applied on a breath-by-breath basis, in any ventilation mode, with any inspiratory flow pattern, only provided that the patient is relaxed. For example, the least square fit method can be applied indifferently in CMV and in PCV.

In theory, the least square fit method requires perfect patient relaxation. However, it has been shown that it can be applied satisfactorily also in patients in PSV, provided that the patient respiratory activity is very low. In this condition, we can obtain at least a good estimate of compliance, while some underestimate in resistance is generally observed.

The equation of motion described above postulates a linear single-compartment model for the respiratory system. In other words, the respiratory system is described by single values of resistance and compliance, valid for at any point of the respiratory cycle, and during both inspiration and expiration. Thus, the results of the least square fit approach are weighted on the entire cycle, and may exhibit some differences when compared with the results of the classic approach to respiratory mechanics (see § 4.). The classic approach calculates resistance on just one point of the cycle, end-inspiration, and compliance from data of just two points, end-inspiration and end-exhalation.

The least square fit method provides an estimate of PEEPtot, simultaneously to the estimate of Rrs and Crs. An estimate of PEEPtot is particularly interesting in the COPD patient with dynamic pulmonary hyperinflation, since it allows the calculation of PEEPi as difference between PEEPtot and PEEPe. However, in the dynamically hyperinflated COPD patient, the PEEPi calculated by the least square fit method greatly underestimates the static PEEPi measured with the classic approach (see § 3.4.1.1.). Hence, the evaluation of PEEPi seems to be the weakest point of the least square fit method, the worst results being provided exactly in those cases in which an assessment of dynamic hyperinflation would be more interesting. This is probably due to the fact that the least square fit method relies on a linear single-compartment model, while the respiratory system of a COPD patient is better described by other models.

5.4. Variants of the least square fit method

The least square fit method has been originally proposed for the application on an entire respiratory cycle. However, it can be applied also on selected periods of a cycle. For instance, for the purpose of the measurement of resistance, it can be applied separately on inspiration and on exhalation. In this case the method will provide a measurement for inspiratory resistance, weighted on the entire inspiration, and a measurement for expiratory resistance, weighted on the entire exhalation. The limit of the least square fit method applied on periods shorter than one cycle is that, when the period of analysis is too short, few sets of data are available, and hence the results may be less precise due to the effect of noise.

Another variant is the application of the method on single components of the respiratory system, namely the chest wall and the lungs. When applied to the chest wall, the method relies on the equation of motion of the relaxed chest wall:

$$Pes(t) = (V'aw(t) \times Rw) + \left(\frac{Vol(t)}{Cw}\right) + k$$

In this case, the Pes signal is used instead of the Paw one, and the results of the analysis are chest wall resistance (Rw) and chest wall compliance (Cw).

Another alternative is to apply the least square method to the equation of motion of the lungs:

$$Paw(t) - Pes(t) = V'aw(t) \times R_L + \left(\frac{Vol(t)}{C_L}\right) + k$$

In this case, transpulmonary pressure (Paw minus Pes) must be used instead of Paw, and the results are lung resistance (R_L) and lung compliance (C_L). It must be noticed that the equation of motion of the lungs is valid both in the relaxed patient and in the actively breathing one.

5.5. Practical applications

The least square fit method is particularly suitable for on-line automatic breath-by-breath analysis of respiratory mechanics, performed by a digital monitoring system. On the contrary, a simple manual application of the method is impossible. The only choice for manual application of the method is to import the numeric signals of Paw, V'aw and Vol into a computer. The data can then be analyzed off-line, by taking advantage of any software able to perform a multiple linear regression.

The least square fit method is presently used by the monitoring system of the ventilator Galileo (Hamilton Medical). At any breath, the system provides data of total compliance, inspiratory resistance, expiratory resistance, and PEEPi. Normally the data are obtained by processing Paw, and hence are relative to the entire respiratory system. However, the monitoring system of the ventilator Galileo also supports an esophageal balloon catheter. When this is in use, the user can switch the analysis from Paw to Pes, and thus obtain data relative to the chest wall. Obviously, when considering the least square fit data provided by the monitor, the user should judge whether or not the necessary conditions are met for obtaining valid data, i.e., patient relaxation or at least near-relaxation.

5.6. Conclusions

The least square fit method is a mathematical approach based on the equation of motion of the relaxed respiratory system, and on the assumption of a linear single-compartment model. The method requires simultaneous digital sampling of the signals of Paw, V'aw, and Vol, and computer processing. The most common application of the least square fit method takes into account an entire respiratory cycle, and can provide breath-by-breath data for total resistance, total compliance, and PEEPtot.

The advantages of the method include no need for occlusion maneuvers and for special flow patterns. Hence, it can be applied on a breath-by-breath basis in any mode of ventilation, provided that the patient is relaxed, or at least near-relaxed.

If a signal of esophageal pressure is available, variants of the method include the assessment of separate chest wall and lung mechanics. For the assessment of lung mechanics, patient relaxation is unnecessary.

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6. RESPIRATORY SYSTEM TIME CONSTANTS

6.1. Time constants

6.1.1. Ventilation and exponential functions

When a step change in the pressure applied to the respiratory system (ΔP) takes place, a change in volume (ΔVol) results. Any given step change in pressure can generate just one maximum change in volume ($\Delta Vol,max$), as a function of total respiratory system compliance (Crs), according to the equation:

$$\Delta Vol,max = \Delta P \times Crs$$

However, volume change requires time to take place. Thus, it may happen that the potential $\Delta Vol,max$ is never reached, due to the step change in pressure to be removed before the attainment of the new equilibrium. When a step change in pressure is applied, the instantaneous change in volume follows an exponential curve, which means that, formerly faster, it slows down progressively while it approaches the new equilibrium.

The speed of the entire process is described by the time constant. This parameter has the dimension of time. The exponential function tells that any given duration of a step change in pressure corresponds to a change in volume equal to a given % of $\Delta Vol,max$, as a function of the time constant of the system. Some examples of the results of different durations of a step change in pressure are given in the following table:

Duration of step change in pressure (s)	Resulting change in volume (% of $\Delta Vol,max$)
1 x Time Constant	63
2 x Time Constant	86.5
3 x Time Constant	95
4 x Time Constant	98
5 x Time Constant	99
Infinite x Time Constant	100

During ventilation, many processes follow the exponential function. Some examples are:

- inspiration during paralysis and PCV (upward step change in Paw);
- exhalation during paralysis, in any mode (downward step change in Paw);
- passive exhalation during spontaneous or assisted breathing (downward step change in the pressures that have generated the previous inspiration).

Hence, the time constant is an interesting parameter for setting the inspiratory time in PCV: if we want the inspiratory pressure applied by the ventilator to result in a substantial change in volume, we must avoid inspiratory times too short, namely lower than 2, or at least 1, time constant.

The time constant is even more interesting for exhalation. This parameter allows us to predict the expiratory time that is necessary to allow full exhalation to the resting equilibrium point. As it has been discussed in § 3., if we want to avoid substantial dynamic pulmonary hyperinflation, we must allow an expiratory time of 4, or at least 3, time constants.

6.1.2. Respiratory disease and time constants

The time constant describes how fast the passive respiratory system responds to an external mechanical perturbation. Short time constant means fast response, while long time constant means slow response and delayed attainment of the new equilibrium. The time constant is not really a parameter that describes the impedance of the respiratory system, by it depends on the impedance parameter's resistance and compliance. Namely, the time constant of the respiratory system corresponds to the product of resistance and compliance. This means that, the higher the compliance and/or resistance, the later an equilibrium will be reached. In some way, this is intuitive. If we consider, for instance, passive exhalation, high compliance means that the elastic recoil pressure that pushes the expiratory flow is low. Also, high resistance means that the expiratory flow is opposed by relevant friction. Hence, both high compliance and high resistance independently slow down the process of exhalation.

ARDS patients typically have a respiratory system time constant lower than normal, due to greatly reduced compliance (resistance is normal, or only moderately increased). When an inspiratory step change in pressure is applied, like during PCV, ΔVol,max may be rapidly attained. In the severe ARDS patient a long inspiratory time can be used just to increase the mean airway pressure, but is of no use for the development of tidal ventilation. Also during exhalation, the equilibrium is attained very rapidly, and dynamic pulmonary hyperinflation is only observed when the expiratory time is extremely short. Hence, ARDS patients can be ventilated at a high respiratory rate, and/or at a high I:E ratio, without major adverse mechanical effects.

A long time constant is typical of patients with acute asthma (due to high airway resistance) or with pulmonary emphysema (due to high compliance), and especially of patients with emphysema combined with bronchial obstruction (due to high compliance and high resistance). In these patients, during PCV the inspiratory volume is necessarily much lower than ΔVol,max, at the end of a normal inspiratory time. Moreover, during exhalation the equilibrium is never attained within a normal expiratory time, which results in dynamic pulmonary hyperinflation (see § 3.). Hence, these patients take advantage of a respiratory rate lower than normal, which allows a prolongation of both the inspiratory and the expiratory time. With a lower rate, at the same I:E ratio, a given inspiratory pressure results in higher tidal volume, while dynamic hyperinflation is reduced.

The above examples introduce the item of the relationship between respiratory system time constant and optimal respiratory rate. It is well known that, for any given level of alveolar ventilation and dead space, there is one value of respiratory rate that corresponds to the minimal total work of breathing. Any different rate, lower or higher, corresponds to a less advantageous energetic condition, and requires a higher pressure to be developed by the respiratory muscles during spontaneous breathing, as well as a higher pressure to be applied by the mechanical ventilator during passive ventilation. The value of optimal respiratory rate depends on the value of the respiratory system time constant. The longer the time constant, the lower the optimal respiratory rate. For these reasons, a measurement of time constant is used by the new, closed-loop controlled ventilation mode Adaptive Support Ventilation (ASV) provided by the ventilator Galileo (Hamilton Medical). On the basis of the monitoring of the expiratory time constant, the ASV mode automatically selects, and continuously updates, the setting of the mechanical respiratory rate in order to constantly maintain the most favorable energetic condition.

6.1.3. Different time constants

Let us suppose that we are mainly interested in the measurement of the expiratory time constant (RCe), for the purpose of predicting which expiratory time should be set in the mechanical ventilator in order to avoid, or limit, dynamic hyperinflation. At first glance, one may think that the problem is extremely simple, since the parameter corresponds to the product of respiratory system resistance (Rrs) and compliance (Crs).

Nonetheless, a first problem to face is which resistance should be considered for the calculation. When the respiratory system of a patient corresponds to a linear single-compartment model, resistance has the same value during inspiration and expiration, and during the entire cycle (see § 1.2.). However, we know:

a. that the respiratory system of many obstructive patients may be better described by a double-compartment model, with a fast compartment (and a short time constant) and a slow compartment (and a long time constant);
b. that, during exhalation, the respiratory system of many obstructive patients behaves differently than during inspiration, due to the occurrence of airway collapse.

When we calculate the time constant from the classic measurements of respiratory mechanics, for instance as a product of Cstat and Rmax, we use a measurement of resistance taken at end-inspiration, and hence we calculate an inspiratory time constant (RCi). In obstructive patients with collapsing airways, it is very likely for this RCi to be much lower than the slow-compartment RCe, i.e., than the RCe that is more relevant for the generation of dynamic hyperinflation.

A second problem is that RCe must include the effect of the resistance of the entire expiratory pathway of the ventilator circuit (Rext), according to the equation:

$$RCe = (Rrs + Rext) \times Crs$$

Hence, a time constant simply calculated from Rrs and Crs necessarily underestimates the actual RCe. For an accurate assessment of RCe, the Rext should also be measured and taken into account.

A third problem is that data for Rrs and Crs may not be available on a breath-by-breath basis (for instance, due to lack of patient relaxation). Hence, a breath-by-breath assessment of RCe by simple calculation from resistance and compliance is not always possible.

For all these reasons, methods have been developed for measurements of time constant independent from the measurements of resistance and compliance.

6.2. Measurement of the expiratory time constant

6.2.1. Principle of measurement of the expiratory time constant

The respiratory system time constant can be assessed, on a single breath and independently from measurements of resistance and compliance, from the analysis of the flow-volume loop. The inspiratory section of the loop can provide information on RCi, while the expiratory section provides information on RCe. The analysis is based on the principle that, for one linear compartment, passive inflation, as well as passive exhalation, corresponds to a linear relationship between flow rate and volume change. The time constant is the slope of this linear relationship.

Our attention will be focused on RCe for two reasons:

- when RCi and RCe are different, the expiratory value reflects better the likelihood of dynamic hyperinflation;
- the relaxation condition necessary for the measurement is more likely to be found during exhalation than during inspiration. In actively breathing patients, inspiration can never be used for the measurement of time constant. On the contrary, it is likely that at least one part of exhalation is performed in relaxation. Hence, a method of analysis aimed to RCe has a fair chance to produce acceptable measurements in all conditions.

6.2.2. Manual measurement of the expiratory time constant

Fig. 6-1 shows a flow-volume loop with a normal shape, representing a breath of a paralyzed patient with no dynamic hyperinflation. Exhalation has a triangular shape: after an initial peak, due to the expiratory peak flow taking place at the start of exhalation, flow decreases linearly with the decrease of volume and reaches a value of zero at the end of exhalation, i.e., when volume is back to the baseline. The triangular shape denotes lack of dynamic hyperinflation, since it corresponds to a flow of zero at the volume of end-exhalation.

The linear relationship between flow and volume after the point of peak is typical of a single-compartment model, i.e., of a model described by a single RCe. The value for RCe corresponds to the slope of the flow-volume relationship. In this particular case (linear single-compartment with no dynamic hyperinflation), the slope, and hence RCe, can be indifferently calculated from any couple of data of Vol and V'aw, starting from the point of peak. For instance, a Vol of 300 ml corresponds to an expiratory V'aw of 600 ml/s. Hence RCe is equal to 300 / 600 = 0.5 s.

Fig. 6-2 is a different example, taken from a paralyzed patient with dynamic hyperinflation due to expiratory airway collapse. Exhalation has a complex shape: after the point of initial peak, flow exhibits a curvilinear decrease with volume. Moreover, the expiratory flow does not reach a value of zero at the end, when volume is back to the baseline. The value of the end-expiratory flow, different from zero, denotes dynamic hyperinflation. The curvilinear flow-volume relationship, with a leftward concavity, is typical of passive exhalation for two different compartments. The initial slope of the flow-volume relationship expresses a small fast compartment, with short RCe. Then, rapidly the slope becomes steeper and stabilizes in a wide segment, that expresses a wide slow compartment, with long RCe. The latter compartment is the one that is relevant for the generation of dynamic hyperinflation. The RCe of the slow compartment can be measured as the slope of the steeper segment. The slope can be calculated from two couples of data of Vol and V'aw, taken anywhere in the segment. RCe will correspond to the ratio between the difference in Vol and the difference in V'aw, for the two points considered. For instance, we can read a difference in Vol of 300 ml, corresponding to a difference in V'aw of 85 ml/s. An RCe of 3.5 s results for the slow compartment.

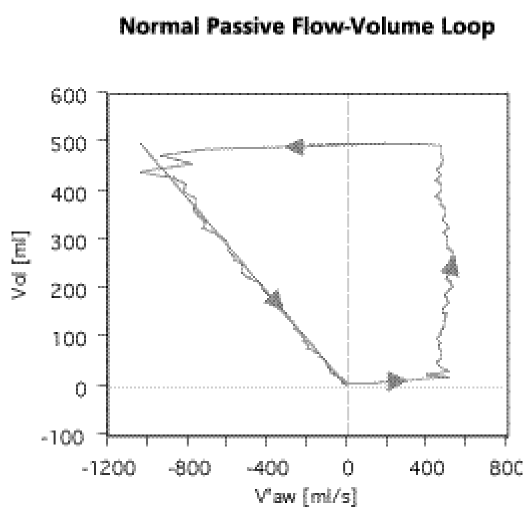

Fig. 6-1
Flow-volume loop in a paralyzed patient, in CMV, with no dynamic hyperinflation. The straight line represents the expiratory flow-volume relationship for the entire respiratory system. The slope of the straight line corresponds to the expiratory time constant.
The same recording is analyzed in Figs. 3-4, 3-5, 6-1, 6-4

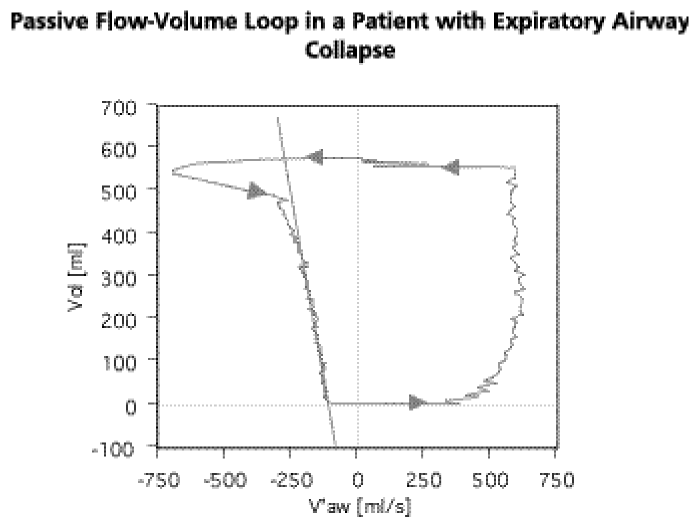

Fig. 6-2
Flow-volume loop in a dynamically hyperinflated patient, paralyzed, in CMV. The slope of the straight line represents the expiratory time constant of the slow compartment.
The same recording is analyzed in Figs. 3-2, 3-3, 3-6, 3-10, 6-2, 6-5

Different alternatives can be adopted to reduce the effect of noise and improve the measurement :

- data points can be taken far from each other (e.g., one near to the start of the segment, and one near to the end);
- a line can be fitted by eye on the graph, and data points far from each other are taken on the fitted line, instead of on the actual curve;
- a linear regression can be performed between Vol and V'aw, for the range corresponding to the segment to analyze. RCe will correspond to the angular coefficient of the regression.

Fig. 6-3 is an example of a flow-volume loop of a breath of an actively breathing patient in PSV, with dynamic hyperinflation due to expiratory airway collapse. Exhalation has a shape similar to the previous example: the initial peak is followed by a curvilinear decrease of flow with the decrease of volume, with a leftward concavity, typical of passive exhalation for two different compartments.

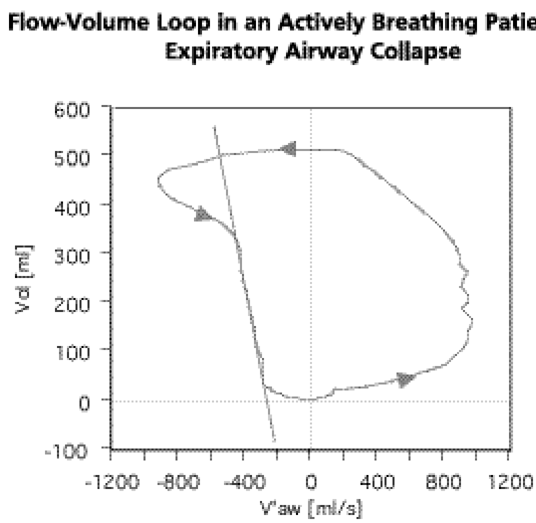

Fig. 6-3
Flow-volume loop in a dynamically hyperinflated patient, actively breathing, in PSV.
The slope of the straight line represents the expiratory time constant of the slow compartment.
The same cycle is analyzed in Figs. 3-8, 3-9, 6-3, 8-1, 8-2, 8-3, 8-5

The main difference from the previous example is represented by a final rightward inflection of the curve, denoting an active inspiratory effort that brakes exhalation and terminates the cycle. This inspiratory effort, combined with the long RCe of the slow compartment, generates dynamic hyperinflation. The RCe of the slow compartment can be measured as the slope of the steeper segment of the passive expiratory flow-volume relationship, by taking two couples of data of Vol and V'aw, as detailed above. For instance, a difference in Vol of 200 ml can be read against a difference in V'aw of 110 ml/s, resulting in an RCe of 1.8 s for the slow compartment.

The measurement of RCe from the flow-volume relationship postulates passive exhalation, at least in the section that is considered for the measurement. In the actively breathing patient, exhalation may be affected by the respiratory muscles in various ways:

- persistent contraction of the inspiratory muscles, and/or inefficacious inspiratory efforts, brake exhalation and shift the curve rightwards;
- contraction of the expiratory muscles forces exhalation and shifts the curve leftward.

In order to obtain reliable results, we should formerly observe the loop, and formulate a judgement about relaxation, based on the profile of the loop. The loop may be distorted by muscular activity. The method described is applicable only when a significant segment is identified as corresponding to relaxation.

6.2.3. Simplified automatic measurement of the expiratory time constant

The interest of the time constant as a parameter for driving advanced mechanical ventilation modes, based on closed-loop control, has stimulated the research of robust, simplified methods for the measurement of RCe. The aim was to provide acceptable information under any condition.

A first method simply calculates RCe as the ratio between the expiratory tidal volume (Vte) and the expiratory peak flow (V'e,peak). This method assumes a triangular shape for the expiratory section of the flow-volume loop. Hence, it assumes a linear single-compartment model, relaxation, and lack of dynamic hyperinflation. This method generally provides good results in patients with normal lungs and in patients with restrictive syndromes, like ARDS. An example is

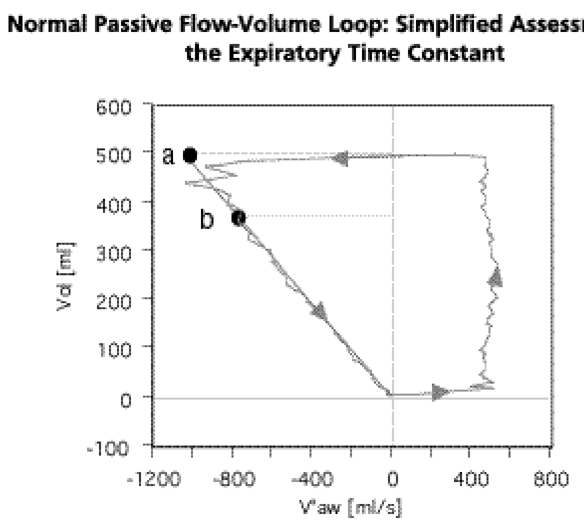

Fig. 6-4
Flow-volume loop in a paralyzed patient, in CMV, with no dynamic hyperinflation. Point **a** represents the expiratory tidal volume (Vte) and the expiratory peak flow (V'e, peak). Point **b** represents the 75% of Vte and the corresponding expiratory flow.
The same recording is analyzed in Figs. 3-4, 3-5, 6-1, 6-4

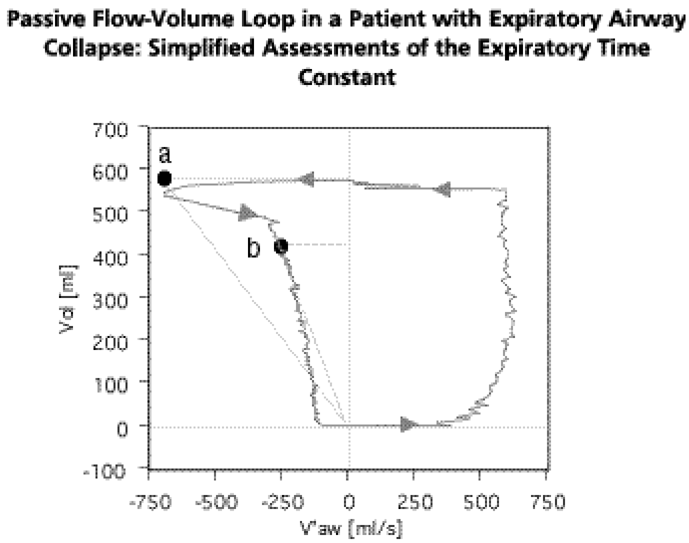

Fig. 6-5
Flow-volume loop in a dynamically hyperinflated patient, paralyzed, in CMV. Point **a** represents the expiratory tidal volume (Vte) and the expiratory peak flow (V'e,peak). Point **b** represents the 75% of Vte and the corresponding expiratory flow.
The same recording is analyzed in Figs. 3-2, 3-3, 3-6, 3-10, 6-2, 6-5

represented by Fig. 6-4, where Vte / V'e,peak (point a) corresponds to 500/1000 = 0.5 s. This value is an accurate estimate of the actual RCe.

The worst condition for the application of this method is represented by the COPD patients with expiratory airway collapse. As we have already considered, in these cases, the relevant time constant is the one of the slow compartment. Unfortunately, the ratio between Vte and V'e,peak cannot provide any information about the slow compartment. The RCe estimated by the ratio between Vte and V'e,peak is always much lower than the slow-compartment time constant. An example is represented by Fig. 6-5, where Vte / V'e,peak (point a) corresponds to 580/700 = 0.83 s, while the actual RCe of the slow compartment is of 3.5 s.

This original method has been improved on the basis of the observation that, in the COPD patients with expiratory airway collapse, the expiratory flow-volume relationship exhibits an inflection. This inflection represents the junction between the prevalent emptying of the fast compartment and the prevalent emptying of the slow compartment, and generally takes place within the first 25% of the exhaled volume. The idea has been to move the calculation of the volume/flow ratio from the point corresponding to the entire tidal volume, to a point corresponding to the 75% of tidal volume. Thus, the flow-volume curve section that mainly expresses the fast compartment is discarded, while the section that mainly expresses the slow compartment is explored. By moving the point of measurement to the 75% of tidal volume, the simplified assessment of RCe has been selectively improved for the COPD patients with collapsing airways, while left unchanged for the other conditions, where the performance was already good.

Examples of the improved method are provided by Figs. 6-4 and 6-5 (points b). If we consider the COPD patient of Fig. 6-5, the volume/flow ratio at the 75% of the tidal volume (point b) corresponds to an RCe of 435/250 = 1.74 s. Although this value still underestimates the actual RCe of the slow compartment, it is more than the double of the result provided by the original method. If we consider the normal subject of Fig. 6-4, the volume/ratio at 75% of the tidal volume (point b) corresponds to an RCe of 375/750 = 0.5 s. Hence, in this case the result is the same as the one provided by the original method and perfectly reflects the actual RCe.

The weak points of the simplified method remain the assumptions of relaxed exhalation and of lack of dynamic hyperinflation. Nonetheless, even with the limits outlined above, the improved simplified method seems able to provide an estimate of respiratory system time constant that is able at least to classify patients with short, normal, or long time constant, and to indicate the direction of a time constant change in dynamic conditions. The improved simplified method for the measurement of RCe is presently included in the monitoring system of the Galileo ventilator (Hamilton Medical). In the same ventilator, the data of RCe are used by the closed-loop control mode ASV for the automatic selection of the respiratory rate and of the duty cycle for the mechanical breaths.

6.3. Conclusions

The measurement of the respiratory system time constant is not yet common practice in respiratory mechanics. However this parameter has a great importance for decision making about the settings for respiratory rate and duty cycle in the mechanical ventilator.

The time constant can be either calculated as a product of total system resistance and compliance, or directly measured by analysis of the flow-volume loop.

A simplified method for the assessment of the expiratory time constant is based on the calculation of the ratio between the volume above the baseline and the simultaneous expiratory flow, taken at a level corresponding to the 75% of the tidal volume. Although its results may lack perfect accuracy, this method is suitable for working in a wide variety of conditions, and for breath-by-breath monitoring of the parameter.

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7. RESPIRATORY SYSTEM STATIC PRESSURE-VOLUME CURVE

7.1. Static pressure-volume curve

Most of the measurements performed in the mechanically ventilated patient assume, as we have seen, the linear single-compartment model. In this simple model, the static pressure-volume (P-V) relationship corresponds to a straight line, and a single value describes the respiratory system compliance. In other words, the ratio between a change in volume (ΔVol) and the corresponding change in transmural pressure (ΔP) is always the same, and independent from the level of start for the volume change, from the magnitude of the volume change, and from the kind of volume change, indifferently represented by an increase or by a decrease of volume.

However, in respiratory physiology, the static P-V relationship of the respiratory system is linear only within a limited range of volumes. Rather, the entire relationship is curvilinear, presenting a lower slope (and hence a lower compliance) at low and high volumes, and a steeper slope (and hence a higher, better compliance) in between. The low section of the curve, where the compliance is less favorable, corresponds to a condition in which a given number of alveolar units are collapsed. When the volume is progressively increased by higher transmural pressures, these collapsed alveolar units are progressively recruited for ventilation. Hence, the intermediate section of the curve, where the best compliance is exhibited, corresponds to a range of volumes in which all alveolar units are recruited. The high section of the curve, where the compliance progressively decreases again, corresponds to the progressive over distension of the respiratory system.

The curvilinear shape of the P-V curve is not evident in the normal subject, unless volumes below the functional residual capacity (FRC), or very high volumes, are considered. The P-V curve of the normal subject is linear in a wide range. This is not the case with most ARDS patients. The respiratory system of these patients is more rigid than normal, mainly due to a great number of alveolar units collapsed or filled with fluid, and hence lost for ventilation. The phenomenon of progressive recruitment with progressive increase in transmural pressure may be very evident. However, many alveolar units remain not recruitable. For this reason, over distension will start at volumes much lower than normal.

It is well known that, in the same ARDS patient, the compliance may vary, depending on the section of the entire P-V relationship where tidal ventilation takes place. In particular, the compliance may be influenced by changes in the end-expiratory volume (due to changes in the PEEPe applied by the ventilator, and/or in the PEEPi generated by dynamic hyperinflation), as well as by changes in tidal volume.

Therefore, the study of the static P-V relationship of the respiratory system can provide extremely useful information for the optimal setting of the mechanical ventilator, especially for what concerns the choice of PEEPe and of tidal volume in the ARDS patients. If we can maintain tidal ventilation within the P-V relationship section that corresponds to the best compliance, by means of suitable choices of PEEPe and tidal volume, we should obtain the maximal alveolar recruitment while avoiding lung over distension. Simultaneously, we should minimize the elastic work required for the development of the tidal volume.

7.2. Measurement of the static pressure-volume curve

7.2.1. Different methods of measurement

Several methods have been proposed for obtaining the static P-V curve of the respiratory system in mechanically ventilated patients. All methods require the paralysis of the patient. The common feature is the measurement of the elastic recoil pressure of the entire respiratory system at different volumes above FRC. In a paralyzed patient, the elastic recoil pressure can be measured from the airway opening pressure, provided that flow is interrupted by an occlusion maneuver. In order to obtain the curve, the elastic recoil pressure must be measured at different known volumes above FRC, taken in a wide range. All the measurements are then plotted on a graph, most commonly with pressure on the X-axis and volume on the Y-axis.

The oldest method for the measurement of the static P-V curve makes use of a super-syringe. The respiratory system is inflated to a given volume by sequential steps of 100 ml, starting from FRC. The pressure reached at the equilibrium of each step inflation is recorded. Optionally, the procedure can be continued backwards, in order to explore the respiratory system also during deflation. The super-syringe can be operated by hand, or by a motor.

The opposite approach is based on a regular pressure ramp. The respiratory system is inflated to a given pressure by small sequential pressure steps, regularly delivered at the airway opening, starting from FRC. The volume actually reached at the equilibrium of each pressure step is measured by a pneumotachograph at the airway opening. After full inflation, the procedure can be continued backwards, for deflation. The method can be implemented in a mechanical ventilator, as a special function for the measurement of the static P-V curve.

Another method is based on passive inflation by a low, constant flow. The respiratory system is inflated by a very low flow of oxygen, fixed at a given known value. It is more difficult to apply this method for deflation. In theory, this method cannot provide an exact measurement of the elastic recoil pressures. However, if the flow selected is very low, the effect of the respiratory system resistance is irrelevant, and hence, a good estimate of the elastic recoil pressures can be read at the airway opening, even in a dynamic state.

A completely different method is based on the delivery of a wide range of different tidal volumes, during CMV. At each cycle, the elastic recoil pressure is measured by an end-inspiratory occlusion maneuver.

The different methods based on steps allow a plot made of a series of separated points. The apparent P-V curve is then interpolated by drawing a line through the points. In other words, the curves provided by the step methods may not be very well defined. On the contrary, the low constant flow method directly provides a continuous curve, highly defined, without need for interpolations.

7.2.2. Inflation and deflation P-V curve

When the static P-V relationship is studied simultaneously for inflation and deflation, major differences can be seen between the two curves. Also, a part of the volume delivered during the inflation phase will not be recovered at the end of the deflation phase. A lot has been written about the meaning of the hysteresis between the inflation and the deflation curve, as well as of the unrecovered volume.

Finally, it has been concluded that both hysteresis and unrecovered volume are mostly due to artifacts, depending on the prolonged duration of the entire maneuver. A full maneuver of step-by-step inflation and deflation can last even much more than one minute, and represents a condition similar to apnea. During the time of the maneuver, a fair volume of oxygen is absorbed by the blood that crosses the lungs, while the volume of the CO_2 discharged into the alveoli is much less. This phenomenon means that, while the maneuver is proceeding in time, the volume measurements taken at the airway opening result in a progressively increasing underestimate of the actual volume changes of the respiratory system.

This underestimate of the real volume changes is difficult to correct. The use of alternative instruments for the assessment of the volume changes is effective, but complicated. For these reasons, we have chosen to reduce the errors just by reducing as much as possible the duration of the maneuver. We limit the study to the inflation curve, and use a relatively fast method, the constant flow method applied with a flow of oxygen of 50 ml/s.

7.2.3. Static P-V curve by the low constant flow method

In our practice, the inflation is performed by means of a precise oxygen flowmeter, set to deliver exactly 50 ml/s for an adult subject. The flowmeter is directly connected to the endotracheal tube, by means of a tube of 1-meter length and 4-mm inner diameter. The connector for the endotracheal tube is a T-connector with a lateral port for the measurement of the airway opening pressure. Before the measurement, the patient must be paralyzed, and the tightness of the endotracheal tube must be checked. The measurement is generally performed in the supine position. After disconnection of the patient from the mechanical ventilator, a prolonged expiratory time must be allowed, in order to ensure that the inflation maneuver will start from the FRC. Then the oxygen flowmeter, already set at 50 ml/s, is connected to the endotracheal tube. The inflation must be performed under strict monitoring of the airway pressure, and should be interrupted as soon as a Paw of 30-45 cmH_2O is reached. For maximum safety, the gas delivery system can be equipped with a pressure-limiting valve. Once the inflation maneuver is terminated, a prolonged exhalation is allowed before reconnecting the patient to the mechanical ventilator.

The method is very simple and fast. The duration of the inflation maneuver is around 30 s in a normal subject, and may be even shorter than 10 s in a restrictive patient. The short duration of the maneuver greatly limits the errors in the estimate of the volume change of the respiratory system.

As already mentioned, in theory, the entire pressure curve obtained with this method overestimates the actual values of elastic recoil pressure, due to the resistive load opposed by the respiratory system. In practice, however, this overestimate is irrelevant, an inspiratory resistance as high as 20 $cmH_2O/l/s$ accounting for a constant overestimate of just 1 cmH_2O.

Fig. 7-1 illustrates the real-time curves of V'aw, Vol, and Paw during the inflation maneuver, performed in a subject with a nearly normal respiratory system. Time zero corresponds to the start of inflation. The inflation was terminated after a pressure of 30 cmH_2O was overcome, and corresponded to a volume of gas of 1750 ml, delivered in 35 s. The tiny irregularities of the Paw curve correspond to cardiac oscillations, and typically increase with the increase of pressure.

In the example of Fig. 7-1, for the purpose of documentation, we have measured the flow of oxygen delivered by the flowmeter, and we have obtained a volume signal by integration of flow. In common practice, however, we can skip the measurement of flow, and simply consider the real-time curve of Paw during the inflation maneuver. The upper panel of Fig. 7-2 is the Paw graph of Fig. 7-1, limited to the inflation maneuver. If we trust the performance of the flowmeter, on the basis of the delivered flow of 50 ml/s, we can overwrite a volume scale on the time-axis. Thus, a volume-pressure (V-P) curve is easily obtained, ready for interpretation, with the calculated volume on the X-axis and the pressure on the Y-axis. In this example, the V-P curve is nearly normal. The curve starts with a gentle inflection, then becomes linear for a wide range of volumes, and finally exhibits an upper inflection at the highest values for volume. We have drawn the straight line that corresponds to the intermediate, linear section of the V-P relationship. The comparison between the actual curve and the straight line allows us to easily identify the lower inflection zone, possibly corresponding to alveolar recruitment, and the upper inflection zone, corresponding to alveolar over distension.

When the maneuver is recorded by a digital system, the V-P curve can be easily converted into the conventional P-V presentation, with the pressure on the X-axis and the calculated volume on the Y-axis, as shown in the lower panel of Fig. 7-2. The interpretation of the convention P-V curve and of the less conventional V-P curve is exactly the same.

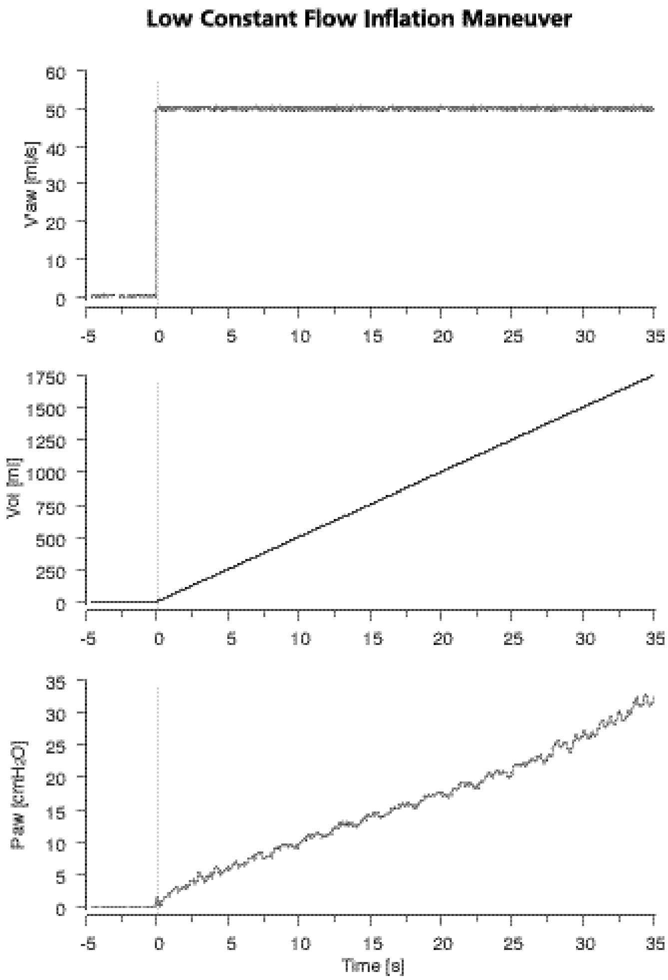

Fig. 7-1
Real-time curves of V'aw, Vol, and Paw during a low constant flow inflation maneuver for the measurement of the static pressure-volume curve.
The same recording is analyzed in Figs. 7-1, 7-2

Static Volume-Pressure Curve and Pressure-Volume Curve

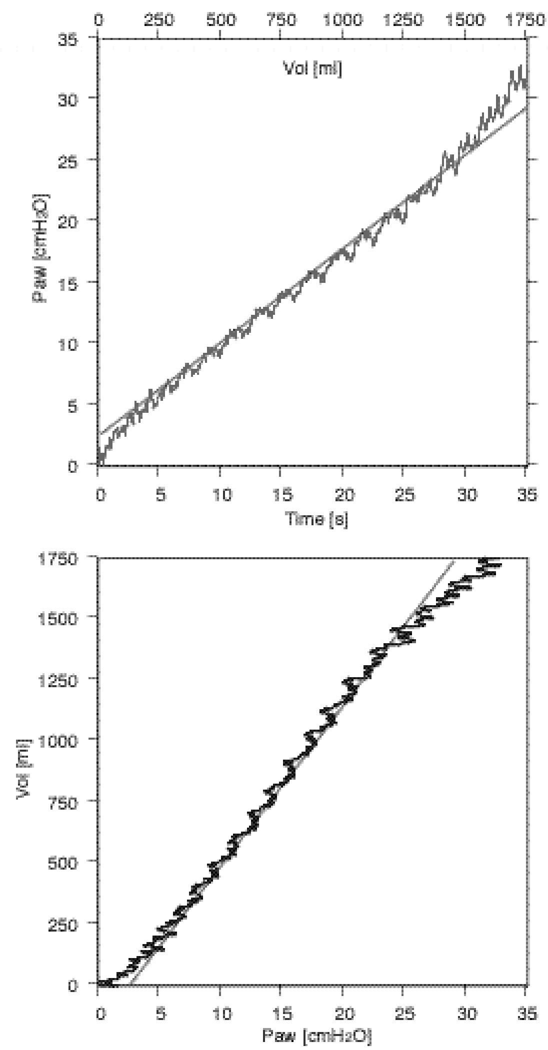

Fig. 7-2
Upper panel: Real-time curve of Paw during a constant flow inflation maneuver at 50 ml/s. A volume-pressure curve is obtained by transfer of the calculated volume above FRC on the time-axis. Lower anel: A conventional pressure-volume curve is obtained from the same data, by exchanging the axes.
The same recording is analyzed in Figs. 7-1, 7-2

7.3. Interpretation of the static P-V curve

Fig. 7-3 shows a P-V curve obtained by the low constant flow method in an ARDS patient. The P-V relationship is much less favorable than in the example of Fig. 7-2, as it can be noted from the big difference in the volume-axis scale, indicating that respiratory system compliance is much lower. The shape of the curve is similar, but the double inflection is more pronounced.

A straight line, drawn through the linear, intermediate section of the curve, allows the identification of a wide lower inflection zone, that represents recruitment. The upper point of the lower inflection zone, identified in Fig. 7-3 as point a, corresponds to a pressure of 11 cmH_2O and a volume of 130 ml above FRC. This point has been defined as the "best PEEP point," since it should correspond to the pressure that allows the mechanical recruitment of the maximal number of recruitable alveoli.

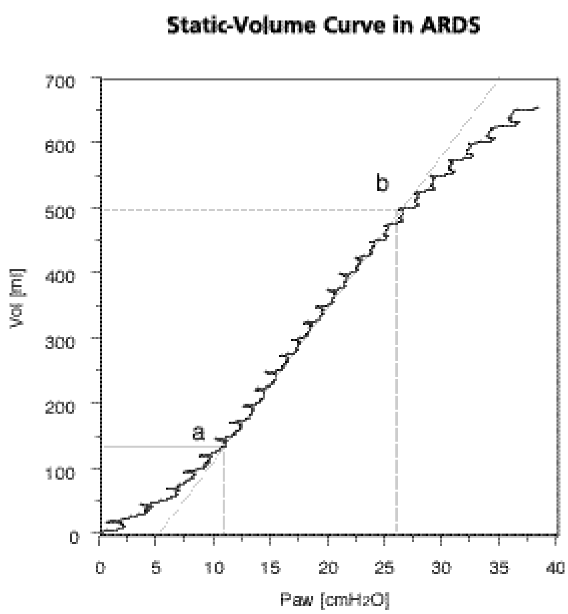

Fig. 7-3
Typical static pressure-volume curve of a severe ARDS patient. Point **a** corresponds to the "best PEEP point", while point **b** corresponds to the start of the upper inflection zone. Between points **a** and **b**, the P-V relationship is linear.

The straight line corresponding to the linear section of the curve also allows the identification of the upper inflection zone, that represents over distension. The point of start of over distension, identified in Fig. 7-3 as point b, corresponds to a pressure of 26 cmH_2O and a volume of only 500 ml above FRC. This means that, in this patient, during tidal ventilation, over distension should occur when a static end-inspiratory pressure higher than 26 cmH_2O is applied. In practice, during CMV, over distension can be avoided by checking that the ventilator setting results in a maximal value of end-inspiratory pause pressure equal to the pressure of point b. During PCV, protection against over distension will be much easier: over distension will be excluded by avoiding any setting, for the absolute inspiratory pressure delivered by the ventilator, higher than the pressure of point b.

The problem of over distension can be considered also from the standpoint of tidal volume. Should we use in this patient a PEEPe level of 11 cmH_2O (i.e., equal to the best PEEP), we can predict that over distension is avoided only when the tidal volume is maintained within a maximum value of 370 ml, that is, the difference between the volume of point b and the volume corresponding to the best PEEP. Evidently, in this patient only a strategy of tidal volume reduction could simultaneously achieve the targets of maximal recruitment and protection against over distension.

The slope of the straight line corresponding to the linear section of the curve represents the best compliance of the respiratory system. This parameter can be calculated from two couples of points on the straight line, for instance, from the extremities of the linear segment of the curve, point a and point b. In the example of Fig. 7-3, a best compliance of (500 - 370) / (27 - 11) = 24.7 ml/cmH_2O can be calculated. This value should correspond to the static compliance of the respiratory system during tidal ventilation with optimal settings, i.e., with a PEEPe equal to the best PEEP and with a tidal volume low enough to avoid over distension. The best compliance measurement provides information on the amount of normally aerated lung tissue after maximal alveolar recruitment has been accomplished.

A different measurement of compliance is known as starting compliance (Cstart), and corresponds to the ratio between volume and pressure at 100 ml above FRC, i.e., at the start of the static P-V curve. In the example of Fig. 7-3, we can calculate a value for Cstart of 100 / 9 = 11.1 ml/cmH_2O. Cstart describes the elasticity of the respiratory system at the FRC, and is correlated with the amount of normally aerated lung tissue at the beginning of inflation. The ratio between best compliance and Cstart provides information about the alveolar recruitment that we can possibly achieve by application of the best PEEP. In our example, this ratio equals 2.2, which means that a PEEPe of 11 cmH_2O can increase by more than double the respiratory system compliance, and hence the amount of normally aerated tissue.

A third kind of measurement of compliance on the static P-V curve is represented by the ratio between volume and pressure taken at a point that corresponds to a standard volume, e.g., 8 ml/Kg of body weight. The patient of Fig. 7-3 had a body weight of 70 Kg, and hence a standard compliance of 560 / 32 = 17.5 ml/cmH_2O. In the ARDS patients, the static compliance referenced to a standard volume typically exhibits a value lower than the best compliance, since it includes the effect of the lower inflection zone, and frequently also the effect of the upper inflection zone. This kind of measurement cannot provide any useful information for the optimal setting of mechanical ventilation, but can be useful for the comparison different patients.

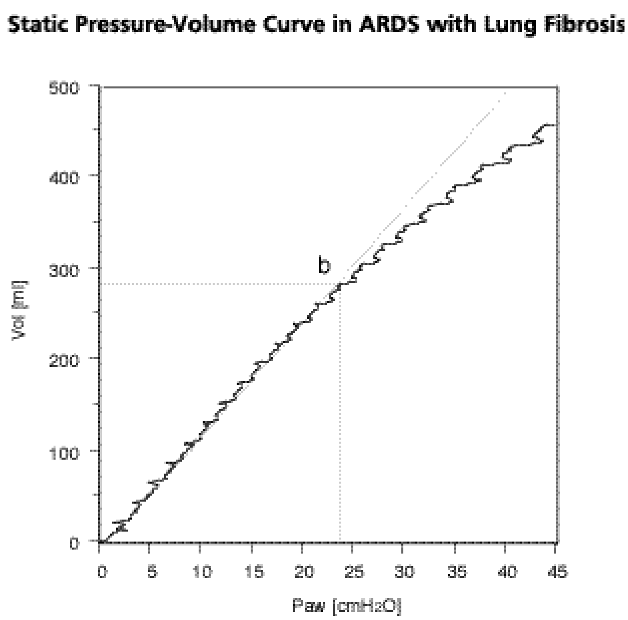

Fig. 7-4
Typical static pressure-volume curve of an advanced-stage ARDS patient, with lung fibrosis. The curve has no lower inflection zone. Point **b** corresponds to the start of the upper inflection zone. The pressure-volume relationship is linear from FRC (zero Volume), up to point **b.**

The P-V curve of Fig. 7-4 was recorded on the same ARDS patient of Fig. 7-3, one month before. At that time the P-V relationship was even worse, as we can notice from the differences in the scales of both axes, and also from the different shape of the curve. The curve of Fig. 7-4 is directly linear from the start (i.e., from FRC), with no lower inflection, while the upper inflection zone starts at the very low volume of 285 ml above FRC, corresponding to 24 cmH_2O (point b). In this example, the slope of the linear section of the curve equals to 11.9 ml/ cmH_2O, corresponding to both the Cstart and the best compliance. The standard compliance at 8 ml/Kg cannot be calculated, since a volume of 8 ml/Kg could not be reached, for safety reasons. This example is typical of advanced-stage ARDS, with lung fibrosis. The ratio between best compliance and Cstart equals 1, and apparently predicts that, at this stage, the patient has no recruitable alveoli. Nonetheless, it is common practice to use a PEEPe of at least 5 cmH_2O in these cases. For a PEEPe level of 5 cmH_2O, corresponding on the curve to 50 ml above FRC, we can calculate that over distension can be avoided by limiting the tidal volume to just 235 ml. In this particular case, we were compelled to moderately exceed this safety tidal volume, in order to maintain hypercapnia at acceptable levels.

7.4. Conclusions

The study of the static P-V curve has a great interest in those patients whose respiratory system has a marked non-linear elastic behavior. In the ARDS patients, the static P-V curve provides useful information for the setting of PEEPe. In all patients, useful information is provided for the choice of a ventilator setting that avoids over distension of the lungs.

A practical, simple approach limits the study to the inflation curve. By means of the low constant flow method, the P-V curve can be obtained even without highly specialized equipment. For practical reason, however, it is advisable that the measurement of the static P-V curve be implemented using the special functions provided by modern mechanical ventilators.

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Section C

RESPIRATORY MECHANICS IN THE ACTIVELY BREATHING PATIENT

8. MECHANICAL MEASUREMENTS OF THE ENERGETICS OF BREATHING

8.1. Mechanical measurements of energetics

The energy expenditure of ventilation can by assessed by means of mechanical measurements. During full spontaneous breathing, these measurements concern only the mechanical output of the respiratory muscles. In the more complex context of mechanical ventilation, we should consider also the mechanical output of the ventilator, that is, either the partner of the respiratory muscles during par-tial ventilatory support, or the sole promoter of ventilation during total ventilatory support. In any case, the major interest remains in those measurements that reflect the activity of the respiratory muscles.

The energy expenditure of ventilation can be assessed by measurements of work of breathing, or by measurements of pressure-time product.

8.1.1. Work of breathing

In general, external work is performed when a force moves its point of application through a distance. When the direction of the force corresponds with that of the displacement, work is the product of force and distance. In the particular case of a fluid system, work is performed when a pressure changes the volume of the system, and work corresponds to the product of pressure and volume change.

During passive mechanical ventilation, the tidal changes in volume are due to the action of the pressure changes applied at the airway opening. During partial ventilatory support, the tidal changes in volume are due to the combined action of the changes in Paw and of the changes in the pressure applied by the respiratory muscles to the passive components of the respiratory system.

Hence, we must distinguish between work of breathing performed by the ventilator (Wvent) and work performed by the patient (Wpat). Wvent can be assessed from measurements taken from the signals of Paw and Vol, but for Wpat, it is necessary to obtain a measurement of the pressure changes generated by the whole complex of the respiratory muscles. As discussed in § 2.5.1., the Pes signal contains such information (although it is influenced also by the passive mechanical features of the chest wall). Hence, Wpat can be calculated from measurements taken on the signals of Pes and Vol. Without an esophageal balloon catheter in place, a direct measurement of Wpat is impossible. The sum of Wvent and Wpat gives the total work performed by the system made of the mechanical ventilator and of the respiratory muscles.

The work of breathing must also be distinguished between the work performed during the inspiratory phase of the cycle (Winsp) and the work performed during the expiratory phase (Wexp), with the cycle phases defined by the instance of flow reversal. Both Winsp and Wexp can be positive or negative. Positive work means that a given volume change is promoted by the pressure change that is taken into consideration, while negative work means that the volume change takes place against the pressure change that is taken into consideration. A typical example of negative work is represented during the initial phase of an assisted breath. In this phase, while the patient starts to contract his inspiratory muscles and before the machine responds, no ventilator is able to maintain a perfectly stable airway pressure. This means that the initial volume change of a breath is entirely due to the patient, and opposed by the ventilator. In this phase, hence, the ventilator performs a negative Winsp, while the patient Winsp is positive.

The measurements of work of breathing during mechanical ventilation have a great interest during assisted breathing, and during full spontaneous breathing through the ventilator circuit. The inspiratory work performed by the patient (Winsp,pat) is the parameter of major interest, reflecting the output of the patient's inspiratory muscles. Moreover, the simultaneous assessment of the inspiratory work performed by the ventilator (Winsp,vent) can be interesting. The latter parameter should be divided into the positive Winsp,vent, i.e., the ventilator work synergistic with the patient inspiratory muscles, and the negative Winsp,vent, that represents the opposition made by the ventilator against the inspiratory muscles.

The dimension of work is pressure times volume, and the unit is the joule. One joule is equal to 1 l·kPa, i.e., 1 l x 10.2 cmH_2O. The measurements of work of breathing calculated as work per breath do not reflect well the energy expenditure of the respiratory muscle. For example, let us consider two different breaths, one of 0.5 liter and the second one of 1 liter, both generated by the same pressure of 10.2 cmH_2O. Evidently in the latter case the impedance of the respiratory system is much less than in the former case. For the 1-liter breath, the work of breathing calculated per breath, as the product of pressure by volume, will be equal to 1 J, i.e., the double of the value corresponding to the 0.5-liter breath. A better estimate of the energy expenditure can be obtained by indexing the work of a breath on the tidal volume, as work per liter. In this case the unit is the J/l.

8.1.2. Pressure-time product

The measurements of work of breathing may not adequately reflect the energy expenditure of the respiratory muscles, even when indexed on the tidal volume as work per liter. An extreme example is represented by an isometric muscle contraction, as it may happen during an occlusion maneuver. In this case, since the airway opening is occluded and there is no volume change, work is always zero, whatever are the forces applied by the respiratory muscles.

This limit of the measurements of work of breathing gave rise to the interest for the alternative approach represented by the pressure-time product (PTP). The PTP concept is very simple. The parameter just takes into consideration the pressure that is applied and the duration of the application. Let us suppose that the inspiratory muscles generate a pressure drop of 6 cmH_2O, maintained for 1 second: the PTP will be equal to 6 x 1 = 6 $cmH_2O \cdot s$. Should the same effort be maintained for 1.5 seconds, the corresponding PTP would be 6 x 1.5 = 9 $cmH_2O \cdot s$. Thus, we can obtain a measurement of the mechanical output of the respiratory muscles that, on one hand, is independent from the volume change generated, and on the other hand, takes into account the duration of the effort.

In a similar way to the measurements of work, we can distinguish different kinds of measurement of PTP. The parameter of major interest is the PTP that reflects the exertion of the respiratory muscles for inspiration (PTPinsp,pat). PTPinsp,pat can be calculated from the Pes signal, in the time interval between the inspiratory effort start and the end of the inspiratory phase of a cycle. From the Paw signal, we can also calculate the PTP that reflects the inspiratory action of the ventilator during the entire inspiratory phase (PTPinsp,vent). In particular, it may be interesting to distinguish the negative component of PTPinsp,vent. This latter parameter has a meaning similar to the negative Winsp,vent, reflecting the opposition made by the ventilator against the inspiratory muscles, and hence the amount of inspiratory effort the patient must perform because of the mechanical ventilator.

The PTP can be calculated as PTP per breath, with $cmH_2O \cdot s$ as the unit. The PTP per breath can also be multiplied by the respiratory rate, thus giving a PTP per minute, with $cmH_2O \cdot s/min$ as the unit.

8.2. Measurements of work of breathing

8.2.1. Preliminary measurements

The work performed in any given phase of a breath, as the product of pressure and volume, corresponds to area enclosed under the dynamic pressure-volume curve for that phase. Typically, during any given phase of a breath, the pressures that promote the volume change are not constant. Rather, the dynamic relationships between Paw and Vol, and between Pes and Vol, follow complex shapes. This makes impossible the calculation of work by simple multiplication of a single value of pressure by a single value of volume. The areas corresponding to work must be calculated by integration of the pressure-flow product over the time of the considered phase.

Although in practice, work of breathing is calculated by numerical integration, a graphic approach allows an easier understanding of the procedures and of the meaning of the results.

Fig. 8-1 represents the real-time curves of V'aw, Vol, Paw, and Pes in an actively breathing patient, assisted by PSV. The inspiratory synchronization of the ventilator was based on a flow-trigger. Both the V'aw curve and the Pes curve denote dynamic pulmonary hyperinflation (see § 3.2.2. and 3.4.2). The time of start of the mechanical support is delayed, relative to the start of the patient inspiratory effort. This delay is due partly to dynamic hyperinflation (some time is required for the inspiratory muscles to brake and stop the exhalation of the previous cycle), and partly to the mechanical ventilator (some time is required for the trigger threshold to be reached, and the ventilator to react).

The first step in the measurement of work of breathing is represented by the identification of a respiratory cycle, and by the distinction between inspiration and expiration. The phases of a cycle are identified on the V'aw signal, by the points of flow reversal. The curves of Fig. 8-1 include a full respiratory cycle, with the cycle start and the cycle end marked by two vertical dotted lines. Inspiration and exhalation are separated by a vertical grey line. The points of cycle start and end have been used also for the identification of the baseline of Paw (i.e., the PEEPe), marked as an horizontal dotted line on the Paw curve. On the Pes curve, an horizontal dotted line corresponds to the level of start of the inspiratory effort, identified according to the principles outlined at § 3.2.2. and 3.4.2.

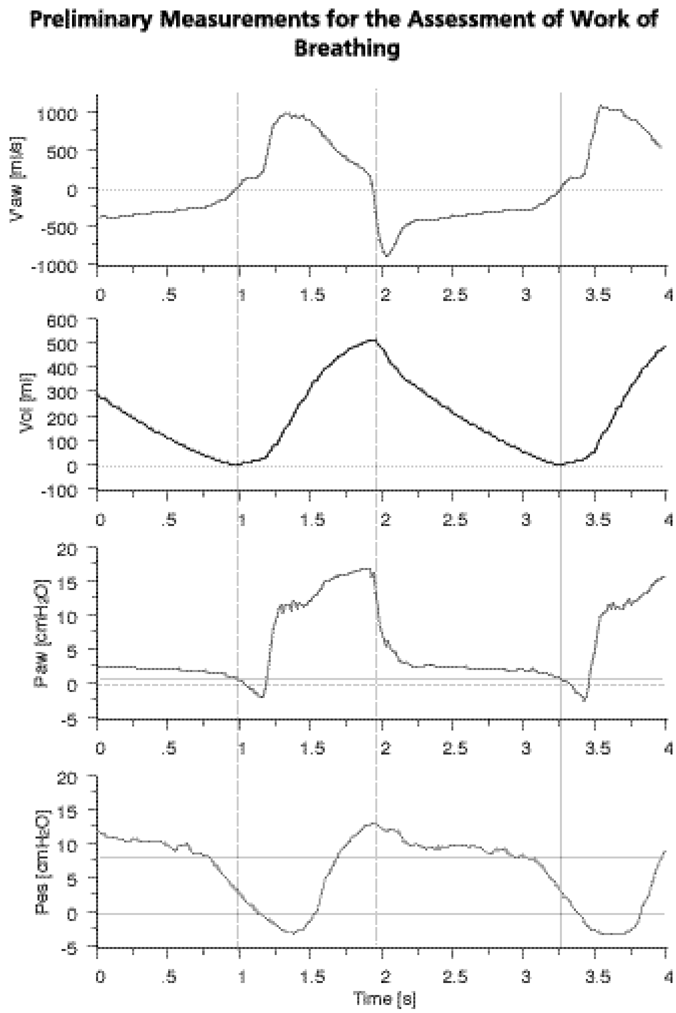

Fig. 8-1
Real-time plot of V'aw, Vol, Paw, and Pes in a dynamically hyperinflated patient, actively breathing, in PSV. The vertical dotted lines delimit a respiratory cycle, while the vertical grey line delimits inspiration from exhalation. The horizontal line on the Paw curve is the Paw baseline, while the horizontal line on the Pes curve corresponds to the Pes level of inspiratory effort start.
The same cycle is analyzed in Figs. 3-8, 3-9, 6-3, 8-1, 8-2, 8-3, 8-5

8.2.2. Dynamic inspiratory airway pressure vs. volume curve

In order to measure Winsp,vent and its components, we can plot the dynamic airway pressure vs. volume curve for inspiration, as shown in Fig. 8-2 for the cycle identified in Fig. 8-1.

The curve starts from the bottom, at the baseline volume of zero, with a Paw of 1 cmH_2O. This level of pressure, that corresponds to the PEEPe of the previous cycle, represents the baseline of Paw, and has been identified in Fig. 8-2 by drawing a vertical line through the point of cycle start. Whenever Paw is higher than its baseline, it means that the ventilator is promoting inspiration, and thus reducing the workload for the patient. Whenever Paw is below its baseline, it means that the ventilator is opposing inspiration, and thus creating an additional workload for the patient. When Paw is equal to the baseline, the ventilator is neutral, exactly as though ar atmosphere during normal breathing with a PEEPe of zero.

Inspiration starts with a leftward deflection of the Paw-Vol curve, below the Paw baseline. The area enclosed between this part of the curve and the Paw baseline, marked by a minus sign and accounting for a work of -0.07 J, corresponds to the negative Winsp,vent. After only 30 ml of increase in volume, the curve crosses the Paw baseline and continues rightwards, up to the end of inspiration. The area enclosed between this part of the curve and the Paw baseline, marked with a plus sign, accounts for a work of 0.55 J and corresponds to the positive Winsp,vent. The algebraic sum of the two areas is the total Winsp,vent, equal to 0.55 - 0.07 = 0.48 J. This parameter reflects the net action of the ventilator in promoting inspiration.

As already mentioned, the negative Winsp,vent reflects the imperfect pressurization performed by the ventilator in the period preceding the start of mechanical inflation. In modern ventilators, the negative Winsp,vent always has very low values, unless the sensitivity of the inspiratory trigger has been set incorrectly. The positive Winsp,vent reflects the setting of the ventilator for what concerns the support of inspiration. In PSV, for instance, the positive Winsp,vent is strictly connected with the pressure support setting. During CPAP ventilation, with no inspiratory support, the Paw-Vol curve of an ideal system corresponds to a vertical line coincident with the Paw baseline. Hence, for an ideal CPAP system, both the negative and the positive Winsp,vent should be equal to zero.

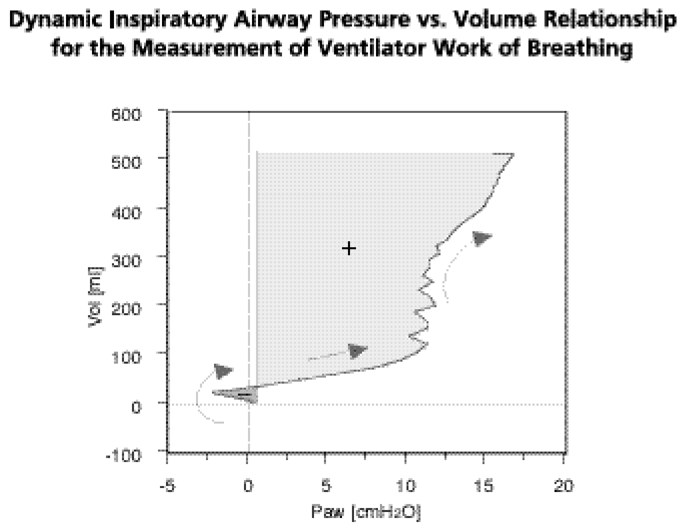

Fig. 8-2
Dynamic inspiratory airway pressure vs. volume curve of the respiratory cycle identified in Fig. 8-1. The vertical dotted line is the Paw baseline. The area to the left (marked by a – sign) is the negative inspiratory work performed by the ventilator (Winsp, vent), while the area to the right (marked by a + sign) is the positive Winsp, vent.
The same cycle is analyzed in Figs. 3-8, 3-9, 6-3, 8-1, 8-2, 8-3, 8-5

8.2.3. Dynamic esophageal pressure vs. volume loop, and Campbell diagram

In order to measure Winsp,pat, we can plot the entire dynamic Pes-Vol loop of a breath, as shown in the upper panel of Fig. 8-3, again based on the cycle previously identified in Fig. 8-1.

In the upper panel of Fig. 8-3, we can see that the cycle starts from the bottom, at the volume baseline of zero, with a Pes of 3 cmH_2O. Inspiration is performed along a curve that firstly goes to the left, and then returns to the right and overcomes the Pes level of cycle start. Exhalation runs along a curve that, although irregular due to noise mainly of cardiac origin, tends to a straight line directed downwards and leftwards, before ending with an evident leftward inflection. The straight part of the exhalation curve reflects a condition of relaxation, while the final leftward inflection is due to the inspiratory effort that starts for the next breath. The point of junction between the linear decrease of Pes with Vol and the sharp leftward inflection represents the point of start of the inspiratory effort, and is also the last relaxed point of exhalation. This point is very important for the measurements of Wpat.

The main problem for the measurement of Winsp,pat is in the identification of the baseline of Pes. The Pes baseline is the value of Pes that corresponds, at any volume, to the full relaxation of the respiratory muscles. The relaxed Pes does not have a constant value for the entire cycle. Rather, it increases with volume, according to the chest wall compliance (Cw). For a linear single-compartment model, the relaxed Pes-Vol relationship runs along a straight line, with a slope corresponding to Cw. Since at least one relaxed point has already been identified in the dynamic Pes-Vol loop (i.e., the last relaxed point of exhalation), the relaxation Pes-Vol line can be drawn through this point, with a slope equal to Cw. This kind of plot, simultaneously including the dynamic Pes-Vol loop and the calculated relaxed Pes-Vol relationship, is known as Campbell diagram.

The lower panel of Fig. 8-3 represents the Campbell diagram of the cycle under examination, with a relaxed Pes-Vol relationship calculated according to a Cw value, previously measured, of 90 ml/cmH_2O. The area of Winsp,pat has been filled, corresponding to the entire area enclosed between the inspiratory curve and the relaxation line. This area of total Winsp,pat corresponds to 0.5 J, and can be divided into three different areas. The left area (a), limited on the right side by the actual Pes of cycle start (3 cmH_2O), corresponds to the Winsp,pat performed to move the lungs. The right area (c), limited on the left side by the relaxed Pes of cycle start (7.5 cmH_2O), corresponds to the Winsp,pat performed to move the elastic components of the chest wall. The middle area (b) corresponds to the Winsp,pat performed against the elastic load due to dynamic hyperinflation. When dynamic hyperinflation is absent, the actual Pes of cycle start is coincident with the relaxed Pes of cycle start, and hence the middle area (b) is absent.

The lower panel of Fig. 8-3 represents just one of the possible Campbell-diagram shapes that can be observed. This shape, represented by panel b) of Fig. 8-4, is typical of a pressure-supported breath with substantial participation of both patient and ventilator to the process of inspiration. Towards the end of inspiration, the participation of the patient becomes very low, and at end-inspiration the actual Pes is coincident with the relaxed Pes-Vol relationship. In a patient breathing through a CPAP system with no pressure support, the Campbell-diagram shape will be different. Typically, as shown in panel a) of Fig. 8-4, the point of end-inspiration will be somewhere to the left of the relaxed Pes-Vol relationship. Some inspiratory muscle contraction will continue during the first part of exhalation, and this will cause the first part of the dynamic expiratory Pes-Vol curve to lay to the left of the relaxed Pes-Vol line. The opposite condition is represented by a patient who just triggers the ventilator, and then prematurely relaxes

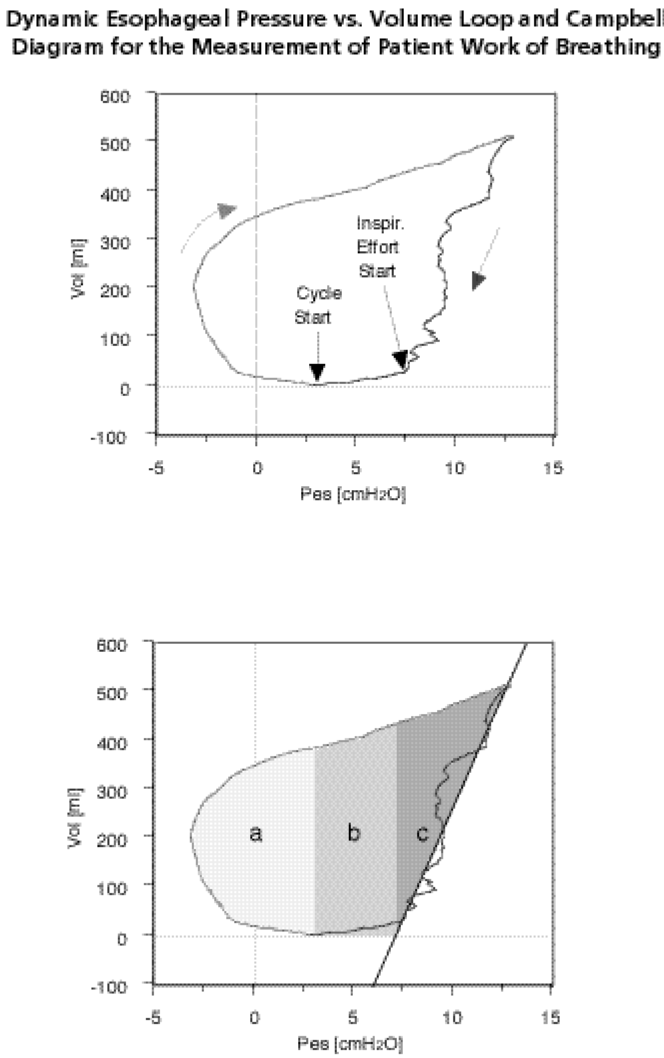

Fig. 8-3
Upper panel: Dynamic esophageal pressure vs. volume loop of the respiratory cycle identified in Fig. 8-1. Lower panel: Campbell diagram. The straight line corresponds to the calculated relaxed Pes-Vol relationship for a Cw of 90 ml/cmH_2O. The filled area is the inspiratory work performed by the patient (Winsp,pat).
The same cycle is analyzed in Figs. 3-8, 3-9, 6-3, 8-1, 8-2, 8-3, 8-5

his inspiratory muscles, like in panel c) of Fig. 8-4. In this case, the dynamic inspiratory Pes-Vol curve will prematurely join the relaxed Pes-Vol line, and inspiration will continue on this line as long as the ventilator maintains inspiration.

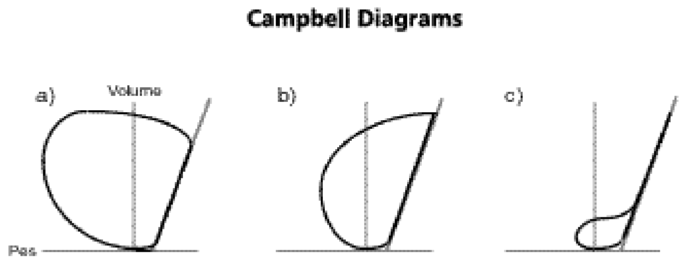

Fig. 8-4
Schematic Campbell diagrams of: a) a fully spontaneous breath, with inspiratory muscle exertion extended to all inspiration and also to the start of exhalation; b) a partially supported breath, with inspiratory muscle exertion extended to all inspiration, and with relaxed exhalation; c) a partially supported breath, with inspiratory muscle exertion limited to the start of inspiration, and with relaxed exhalation. Tidal volume and Cw are the same in a), b), and c)

8.3. Measurements of pressure-time product

8.3.1. Pressure-time product for airway pressure

The PTP calculated on the Paw signal expresses the action of the ventilator. The most interesting parameter is represented by the negative PTP expressed by the ventilator during inspiration (negative PTPinsp,vent). Contrarily to the negative Winsp,vent, the negative PTPinsp,vent is able to quantify the additional load imposed by the ventilator also in a condition of isometric contraction of the inspiratory muscles, as typically happens when the ventilator makes use of a pressure-trigger, with no flow-by.

Fig. 8-5 represents the PTP analysis on the same real-time curves already analyzed for work of breathing at § 8.2. The cycle start, marked by the second vertical dotted line from the left, corresponds to a Paw baseline of 1 cmH_2O. We can see that the cycle start is immediately followed by a negative Paw deflection below the baseline. Then, as soon as the trigger threshold is reached and the ventilator reacts, Paw rises and crosses the baseline. The negative PTPinsp,vent corresponds to the area enclosed between the Paw signal and the Paw baseline, from the point of cycle start to the point where Paw, after its initial negative deflection, crosses the baseline. This area has been filled in Fig. 8-5, and accounts for a PTPinsp,vent of -0.38 $cmH_2O \cdot s$.

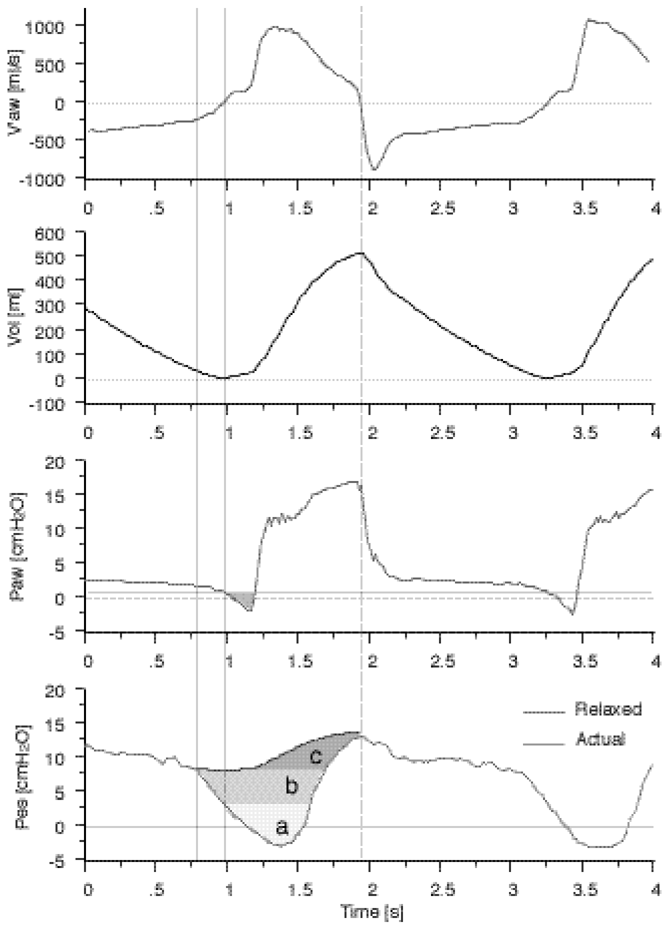

Fig. 8-5
Real-time plot of V'aw, Vol, Paw, and actual Pes in a dynamically hyperinflated patient, actively breathing, in PSV. The first vertical dotted line corresponds to the inspiratory effort start, the second vertical dotted line is the inspiratory phase start, and the third vertical dotted line is the inspiratory phase end. Relaxed Pes has been calculated for a Cw of 90 ml/cmH_2O, from effort start to end-inspiration. The area filled in the Paw plot is the negative ventilator inspiratory PTP (PTPinsp,vent), while the area filled in the Pes plot is the patient inspiratory PTP (PTPinsp, pat).
The same cycle is analyzed in Figs. 3-8, 3-9, 6-3, 8-1, 8-2, 8-3, 8-5

8.3.2. Pressure-time product for esophageal pressure

The PTP calculated on the Pes signal expresses the action of the respiratory muscles of the patient. Usually, we calculate the PTP that expresses the exertion of the inspiratory muscles for inspiration (PTPinsp,pat).

In Fig. 8-5 the first vertical dotted line indicates the start of the inspiratory effort. This point has been identified according to the principles outlined at § 3.2.2. and 3.4.2. In this patient, who presents dynamic pulmonary hyperinflation, the inspiratory effort starts during an exhalation, and is anticipated as to the cycle start, marked by the second vertical dotted line. The inspiratory effort is represented by a negative deflection of Pes. In this example, the inspiratory muscle contraction reaches its maximum approximately at half inspiration, then is progressively released during the second half of inspiration.

The measurement of PTPinsp,pat requires firstly the identification of the Pes baseline during inspiration. The Pes baseline is the Pes that corresponds, at any instant of inspiration, to the full relaxation of the respiratory muscles. As we have seen when considering the measurements of work of breathing, during tidal breathing the Pes baseline moves with the volume change, according to the value of Cw. The instantaneous Pes baseline, or relaxed Pes (Pes,rel), can be calculated as the Pes of effort start (Pes,0), plus the ratio between all subsequent volume changes and Cw:

$$\text{Pel,rel(t)} = \text{Pes,0} + \frac{\text{Vol(t)}}{\text{Cw}}$$

In Fig. 8-5, a curve for the relaxed Pes has been calculated from the time of inspiratory effort start to the time of end-inspiration, on the basis of a Cw value, previously measured, of 90 ml/cmH_2O. An actual Pes lower or higher than the relaxed Pes indicates an activity of the inspiratory or of the expiratory muscles, respectively.

In the example of Fig. 8-5, the actual Pes curve reaches the relaxed Pes curve exactly at end-inspiration. As we have already considered, this patient maintains some inspiratory effort up to the end of inspiration, and no longer, like in panel c) of Fig. 8-6. However, in different cases it may happen that the relaxed Pes curve is reached before the end of the inspiratory phase. In these cases the patient fully relaxes his inspiratory muscles when he is still in the inspiratory phase of the cycle, while inspiration is continued by the ventilator, like in panel b) of Fig. 8-6. On the contrary, it may happen that a substantial inspiratory acti-

Esophageal Pressure during Relaxation or Active Breathing

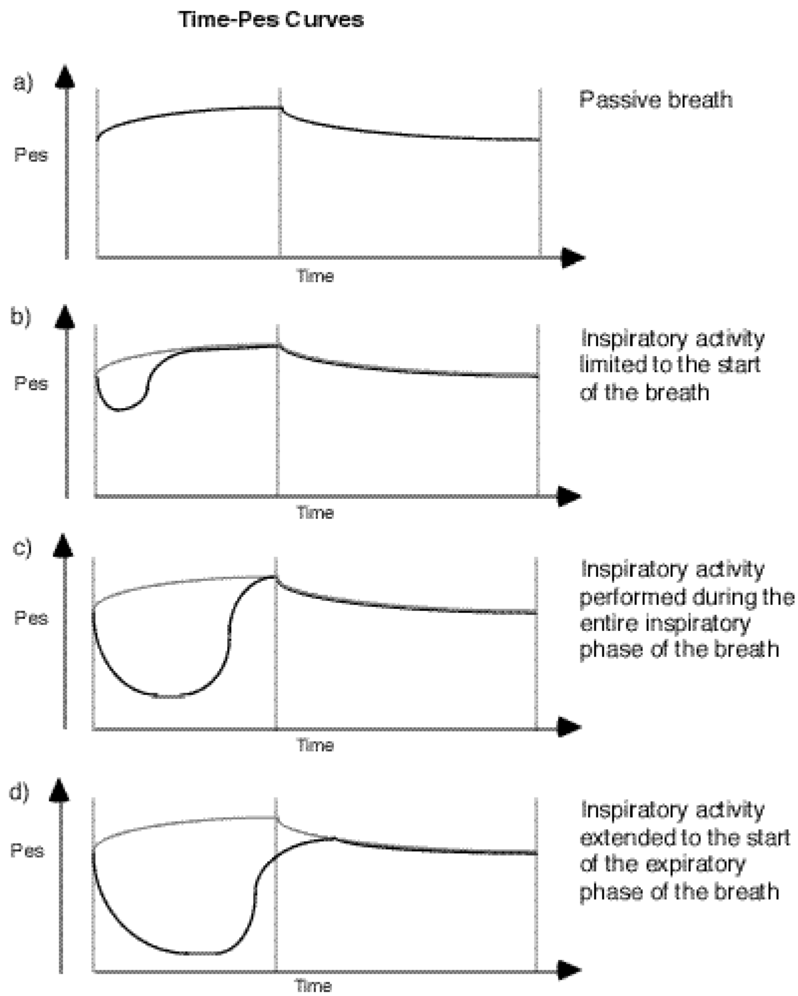

Fig. 8-6
Schematic diagrams of real-time Pes (continuous curves) in different conditions. In the conditions of active breathing b), c), and d), the corresponding relaxed Pes is plotted (dotted curves). Spirogram and Cw (and hence relaxed Pes) are the same in a), b), c), and d).

vity is still maintained at the end of the inspiratory phase, and continued during the first part of exhalation, like in panel d) of Fig. 8-6. As already mentioned, usually the calculation of PTPinsp,pat goes from the time of effort start to the end of the inspiratory phase of a cycle, as maximum time. Thus, usually, a post-inspiratory activity of the inspiratory muscles is not included in the calculation.

PTPinsp,pat corresponds to the area enclosed between the relaxed Pes curve and the actual Pes curve, from the inspiratory effort start, either to the end of inspiration, or to the interception of the actual Pes with the Pes baseline, whichever comes first. The calculation of PTPinsp,pat has been graphically represented, in Fig. 8-5, by filling the area enclosed between the relaxed Pes and the actual Pes, in the interval from effort start to end-inspiration. This area corresponds to a PTPinsp,pat of 8.1 $cmH_2O \cdot s$.

The total area of PTPinsp,pat corresponds to the sum of different areas, denoted in Fig. 8-5 as a, b, and c. The area (a), below the Pes level of cycle start, expresses the inspiratory activity performed just for the inflation of the lungs. The area (c), above the Pes level of effort start, expresses the inspiratory activity performed for moving the elastic components of the chest wall. As we have seen at § 3.4.2., the difference in the Pes level between effort start and cycle start corresponds to the dynamic PEEPi. Hence, the area (b), enclosed between these two Pes levels, corresponds to the inspiratory activity performed because of dynamic pulmonary hyperinflation. In patients with no dynamic hyperinflation, the effort start will be coincident with the cycle start, and hence the area (b) will be absent.

8.4. Automatic measurements of work of breathing and pressure-time product

It is evident that, unlike other measurements of respiratory mechanics, the calculations of work of breathing and PTP cannot be performed unless powerful instrumentation is available. The minimal option is based on digital recording of the signals of V'aw, Vol, Paw, and Pes, and off-line computer-assisted processing. The measurements can be performed by means of a generic software for graphical representation and mathematical processing, but the operations are complex and time-consuming.

Presently, some respiratory monitors include the measurements of work of breathing and PTP between the results of automatic breath analysis. For instance, the monitoring system of the ventilator Hamilton Medical Galileo normally provides breath-by-breath measurements of negative Winsp,pat and negative PTPinsp,pat. When an esophageal balloon catheter is connected, the monitoring system of Galileo can be switched to the analysis of Pes, thus providing automatic breath-by-breath measurements of Winsp,pat and PTPinsp,pat.

Winsp,vent, with its negative and positive components, can be easily calculated by a breath analyzer, after an automatic identification of the Paw baseline. Total Winsp,vent is calculated by numerical integration of the Paw-V'aw product over the entire time of inspiration, after subtraction of the Paw baseline from the actual Paw signal. The negative Winsp,vent is calculated by limiting the integration to the time interval from cycle start to the point of return of Paw to the baseline, after its initial negative deflection. In a similar way, the negative PTPinsp,vent is calculated by numerical integration of Paw subtracted for the Paw baseline, over the same time interval.

Winsp,pat can be automatically calculated by numerical integration of the pressure-flow product over inspiration, with pressure corresponding to the instan-taneous difference between the Pes baseline and the actual Pes signal. In turn, PTPinsp,pat is calculated by numerical integration of the difference between the Pes baseline and the actual Pes, over the time interval between the effort start and either the end of the inspiratory phase (defined by flow reversal) or the interception of the Pes baseline by the actual Pes, whichever comes first.

The only difficulty for the automatic calculation of Winsp,pat and PTPinsp,pat lies in the identification of the Pes baseline. As we have seen, in order to calculate the Pes baseline, the last relaxed point of exhalation must be identified, and the value of Cw must be known.

The identification of the last relaxed point of exhalation can be automatically performed, for instance by studying the derivative of Pes around the period of transition between one cycle and the next one. For what concerns the value of Cw, there are different options:

- The calculation can be made without entering a value for Cw. In this case, the calculated value of Winsp,pat and PTPinsp,pat will not include the inspiratory activity performed by the patient for moving the elastic components of the chest wall (areas c of Figs. 8-3 and 8-5), but will express all the entire inspiratory activity performed for moving the lungs and for compensating dynamic hyperinflation. With this approach, a calculated value of zero for Winsp,pat and/or PTPinsp,pat does not necessarily mean that inspiration is entirely passive: should the patient perform some inspiratory activity in the field of the chest wall, this will not be detected.

- The calculation can be made on the basis of a predicted value of Cw, entered by the user. Cw can be predicted from the sex, height, and age of the patient. However, in many cases the actual value of Cw is much lower than the predicted one. In our example, the actual Cw was 90 ml/cmH_2O, against a predicted value of 170 ml/cmH_2O.
- The calculation can be made on the basis of the real value of Cw, entered by the user as previously measured during controlled ventilation and full relaxation. The value for Cw can be obtained with the classic method (§ 4.4.) or with the least square fit method (§ 5.4.).

All the three approaches are acceptable. It is only important to know the limits of the method that is being used. A common approach that is used also by the monitoring system of the ventilator Galileo is to skip the entry of the value of Cw. It is very important, however, that any automatic breath analyzer base the calculations on the point of start of the inspiratory effort, and not simply on the point of cycle start. Should the point of effort start be arbitrarily identified with the point of cycle start, a major underestimate of both Winsp,pat and PTPinsp,pat would result in all dynamically hyperinflated patients.

8.5. Conclusions

The energetics of ventilation can be assessed by measurements of work of breathing and/or of PTP. The measurement of PTP may be more significant than the one of work, especially for what concerns the case of an isometric contraction of the respiratory muscles.

A full picture requires the invasive measurement of Pes, specialized equipment, and complex processing of signals. However, the measurements of work of breathing and PTP are presently managed by some respiratory monitors in a fully automatic way. The most common parameters include the negative Winsp,vent, the negative PTPinsp,vent, as well as Winsp,pat and PTPinsp,pat.

When considering the measurements of negative Winsp,vent and PTPinsp,vent, based on the analysis of Paw, it must be clearly understood that these parameters provide information only about the performance of the ventilator, and about the setting of the sensitivity of the inspiratory trigger. The finding of low values for these parameters means good ventilator performance and appropriate trigger setting. On the contrary, the measurements of the negative Winsp,vent and of the negative PTPinsp,vent provide no information about the total inspiratory activity of the patient.

The parameters Winsp,pat and PTPinsp,pat provide a direct measurement of the mechanical output of the inspiratory muscles of the patient, but are necessarily based on the invasive measurement of Pes.

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9. MEASUREMENT OF THE MAXIMAL INSPIRATORY PRESSURE

9.1. Maximal inspiratory pressure

The strength of the whole complex of the inspiratory muscles can be assessed by means of the measurement of the maximal inspiratory pressure (MIP). This parameter corresponds to the negative pressure generated by the inspiratory muscles during a maximal inspiratory effort, performed during temporary occlusion of the airway opening. This parameter is also denoted as PIMax, or as NIP (from negative inspiratory pressure), and is generally expressed as a positive number, in cmH_2O.

In order to obtain comparable results, a standardization of the lung volume at which the effort is undertaken is very important, since the ability to generate a negative pressure is expected to vary with the lung volume. The performance of the inspiratory muscles is optimized at low volumes. For this reason, the occlusion maneuver for the measurement of MIP is to be performed either at the end-expiratory volume, after removal of any PEEPe applied by the ventilator, or below the end-expiratory volume.

The energetic balance of the inspiratory muscles depends on the maximal force that can be developed, and on the current force demanded at any breath. During normal breathing, a subject exploits only a minimal part of his maximal force, and a wide reserve is left for facing an increase in the requirement of ventilation and/or in the impedance to ventilation. A critical energetic imbalance, due to an increase in the current force demand and/or to a decrease in the maximal force, leads to muscle fatigue and exhaustion, which means that an external mechanical ventilatory support is needed.

The MIP explores the capability of the inspiratory muscles, i.e., the first term of the energetic balance. The second term, i.e., the demand, can be assessed by measurements of minute ventilation, of the mechanical workload of inspiration, or of $P_{0.1}$. Hence MIP is an important parameter for the assessment of the need of mechanical support of a patient, but should normally be interpreted together with other parameters.

In particular, the sole finding of extremely low values of MIP allows a reliable prediction of respiratory muscle fatigue and exhaustion, should the patient be left without ventilatory support. On the contrary, the finding of less pathological values of MIP simply means that the inspiratory muscles are weaker than normal, while a prediction about ventilator dependency necessary requires combined information about the performance currently demanded at any breath.

9.2. Measurements of maximal inspiratory pressure

9.2.1. Maximal stimulation of respiration by prolonged airway occlusion

The key point in the measurement of MIP is the achievement of an inspiratory effort that really corresponds to the maximal performance of the inspiratory muscles. Ventilated patients in the ICU are frequently obtunded and uncooperative. However, it has been shown that even when cooperation cannot be secured, a prolonged airway occlusion maneuver creates the condition for a maximal stimulation of respiration. Air hunger forces the patient to progressively increase his inspiratory efforts, and a maximal effort is generally achieved after 20 seconds of occlusion, or after 10 occluded efforts, and in any case within 25 seconds from the start of the occlusion maneuver.

The maneuver of prolonged airway occlusion for the MIP measurement has been criticized because of poor repeatability of the results. In our experience, the repeatability is good, provided that the operator check the following points:

- The patient should not be hyperventilated previous to the start of the maneuver. Should a patient present a low $PaCO_2$, it is very unlikely that a 25-second occlusion maneuver can stimulate a maximal inspiratory effort.
- The patient must be actively breathing before the start of the maneuver, either in a fully spontaneous mode, or in a partial ventilatory support mode. Attention should be paid that the ventilator is not self-cycling.
- The patient respiratory muscles should be already adequately loaded previous to the start of the maneuver. During partial ventilatory support, according to ventilator setting, the respiratory muscles may be nearly totally unloaded by the mechanical ventilator, which depresses the patient respiratory drive. In this case, a few minutes before the start of the maneuver, the mechanical support should be decreased.
- The respiratory muscles should not be fatigued before the start of the maneuver. Obviously, respiratory muscle fatigue is difficult to demonstrate. In turn, an experienced clinician can easily understand when a given respiratory load cannot be tolerated any longer by the patient.

In practice, in order to obtain reliable results, the operator must check for, or create, a condition in which the patient has a fair, but not excessive, respiratory activity, previous to the start of the prolonged occlusion maneuver. This requires some training and experience on the part of the operator.

It has been suggested that multiple MIP trials be performed and the highest of the observed values be retaired. However, the prolonged occlusion maneuver may represent an important stress for the patient. Since we believe that an accurate patient preparation can considerably reduce the variability of the results, we suggest the measurement be repeated no more than twice. Should the patient present any deleterious side effect before the completion of the 25-second occlusion maneuver, the latter should be immediately interrupted.

9.2.2. Measurement of MIP at the end-expiratory lung volume (method I)

A first method for the measurement of MIP is based on a total occlusion of the airway opening, performed at the end of the exhalation phase of a cycle. This kind of measurement, known as the Marini's method-I MIP, explores the performance of the inspiratory muscles at the end-expiratory volume.

The prolonged occlusion maneuver for the method-I measurement can be easily performed by the end-expiratory occlusion function provided by several mechanical ventilators, after removal of any PEEPe for the last few cycles before the start. However, the relevant negative pressures that may be observed during the MIP measurement may be out of the Paw scale of many ventilators. In this case, an external manometer should be connected to the external circuit of the ventilator, for the purpose of the MIP measurement. Particular attention should be paid to those ventilators, like the Hamilton Medical Amadeus, that are provided with a safety valve that opens whenever a negative pressure lower than -10 cmH_2O is generated in the circuit. This kind of valve prevents the use of the ventilator for the measurement of MIP.

Fig. 9-1 shows the maneuver for the MIP measurement obtained with the end-expiratory occlusion function of a ventilator. The patient was assisted by PSV, with a PEEPe of zero. The occlusion maneuver starts at the zero time. The first efforts against the occluded airway already correspond to a fair negative deflec-

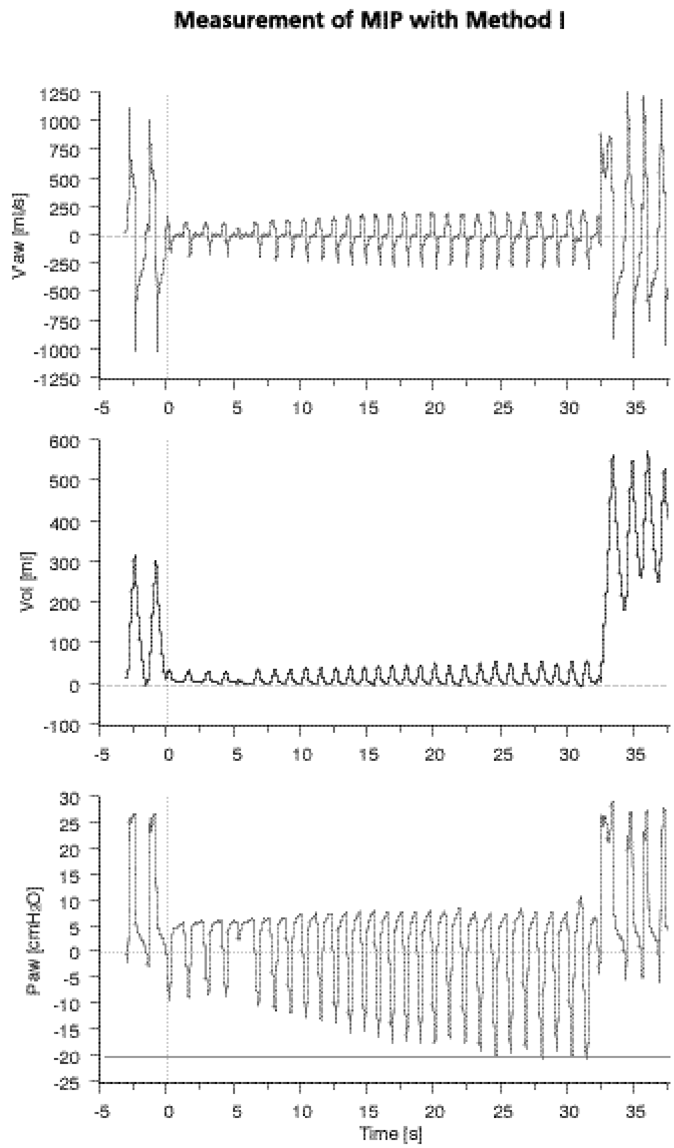

Fig. 9-1
Real-time plot of V'aw, Vol and Paw during a prolonged occlusion maneuver for the measurement of MIP with method I.

tion of Paw (10 cmH_2O), and indicate that the patient respiratory muscles are already well loaded at the start of the maneuver. After the first four efforts, the negative pressure generated progressively increases, and reaches a maximum value of 20 cmH_2O at 25 seconds from the start. The further prolongation of the occlusion maneuver demonstrates that the patient is unable to further increase the negative pressure generated by his inspiratory muscles.

During the maneuver, the V'aw signal of Fig. 9-1 exhibits some oscillations around the baseline, due to minor movements of gas, pulled and pushed by the respiratory efforts of the patient, to and from the external circuit of the ventilator. These gas movements correspond in this example to tiny tidal volumes of 35 ml maximum, and are made possible by the location of the occluded valves, that are inside the ventilator, and not at the airway opening. This phenomenon is not relevant for the validity of the maneuver. The baseline of the spirogram remains stable at the level of start of the occlusion maneuver, i.e., the end-expiratory volume, as required by the method-I measurement of MIP.

9.2.3. Measurement of MIP at low lung volume (method II)

A second method for the measurement of MIP, known as the Marini's method II, performs the measurement below FRC. Since at low lung volume the performance of the inspiratory muscles is better, method II typically provides results higher by one third than method I. With method II, the airway opening occlusion is limited to inspiration, while the patient is free to exhale through a one-way valve.

The MIP measurement with method II requires very simple equipment, but up to now is not allowed by mechanical ventilators. Method II requires a T-piece with three wide ports for ventilation and an additional pressure port. One port of the T-piece must be connected directly to the endotracheal tube, the second one is open to the ambient for ventilation, and the third one is connected to a one-way valve that allows exhalation while impeding inhalation. The pressure port must be connected to a manometer able to read negative pressures. When disconnected from the ventilator and connected to the special T-piece, the patient can breathe ambient air through the ambient port. The maneuver is initiated by occluding the ambient port with a hand, at any time during the respiratory cycle.

Fig. 9-2 shows the real-time plots of V'aw, Vol, and Paw during a MIP measurement performed with method II. The measurement has been obtained in

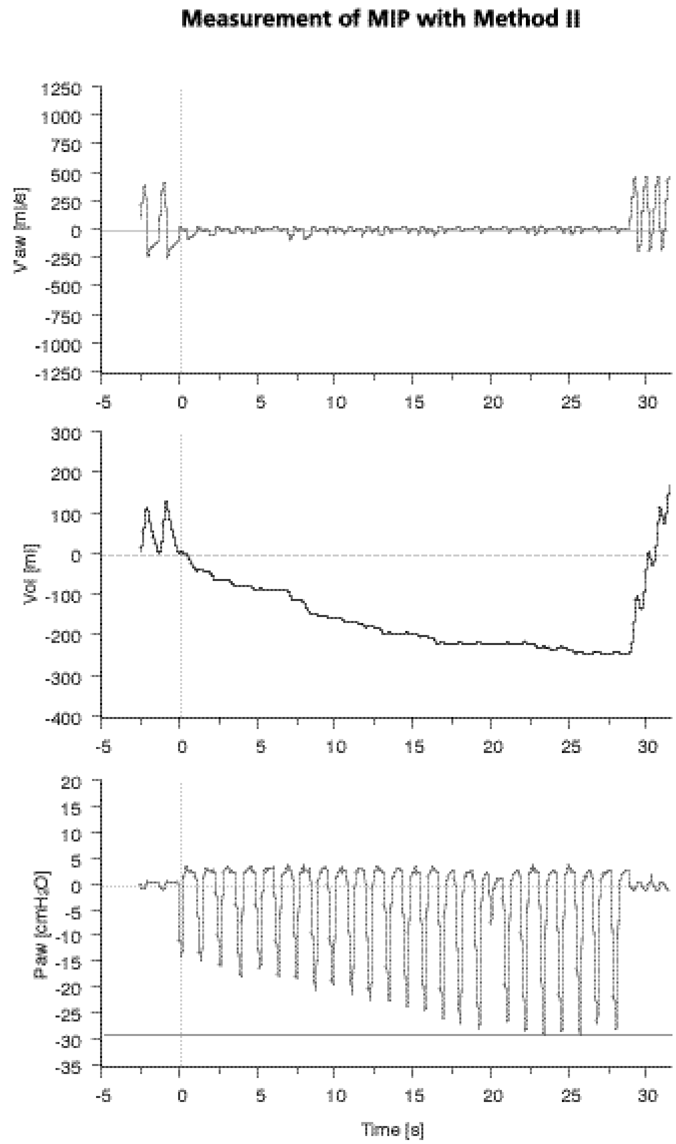

Fig. 9-2
Real-time plot of V'aw, Vol, and Paw during a prolonged occlusion maneuver for the measurement of MIP with method II.

the same patient of Fig. 9-1. At the start of the recording, the patient was already connected to the device for the measurement of MIP. The recording starts with two spontaneous breaths through the ambient port. The zero time of the plots corresponds to the manual occlusion of the ambient port. After this time, the patient performs a series of inspiratory efforts against the occluded airway. In the intervals between the inspiratory efforts, the patient remains free to passively or actively exhale through the one-way valve.

The V'aw plot confirms that inspiration is completely impeded. In this example, representing a patient with dynamic pulmonary hyperinflation, for a few cycles exhalation is passive and due to the elastic recoil pressure of the dynamically hyperinflated respiratory system. Later, once the FRC is reached, exhalation continues due to the activation of the expiratory muscles. The result can be observed on the spirogram plot: first the FRC is reached, then the lung volume further decreases due to active exhalation, probably approaching to the residual volume.

On the Paw plot, we can see that the negative deflections become deeper and deeper, and within 25 seconds reach a plateau indicating a MIP of 29 cmH_2O. A few minutes before, the method I provided a MIP of 20 cmH_2O on the same patient.

9.3. Conclusions

The measurement of MIP provides information about the strength of the inspiratory muscles. This measurement can be used for the assessment of the patient need for ventilatory support, especially when combined with information about the performance currently demanded of the inspiratory muscles.

The measurement of MIP is based on a prolonged airway opening occlusion maneuver (25 seconds), that allows a maximal inspiratory effort to be obtained, even without patient cooperation.

The measurement can be performed either at the end-expiratory lung volume (method I), or at low lung volume, between the FRC and the residual volume (method II). In the former case, the measurement can be performed by means of the end-expiratory occlusion function of mechanical ventilators. In the latter case, a very simple equipment is required, expressly designed for the maneuver.

In both cases, the measurement is based on the analysis of Paw, and can be based just on the observation of a simple manometer. On average, the results provided by method II are higher by one third than those provided by method I.

The prolonged occlusion maneuver may represent an important stress for the patient. Adequate patient preparation for the maneuver is critical for the achievement of reliable results, and prevents the need for a series of repeated measurements.

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10. MEASUREMENT OF AIRWAY OCCLUSION PRESSURE AT 0.1 SECOND ($P_{0.1}$)

10.1. Occlusion pressure at 0.1 second ($P_{0.1}$)

$P_{0.1}$ is a parameter mainly known as a mechanical index of respiratory drive. $P_{0.1}$ corresponds to the drop in Paw, or in Pes, observed during the first 100 ms of an inspiratory effort performed against the occluded airway opening, with the occlusion performed at the end of exhalation. Generally the measurement is performed on the Paw signal, which is easier to measure and less affected by noise than the Pes signal.

An inspiratory effort performed against the occluded airway results in a drop in Paw denoted as the occlusion pressure wave. This wave directly expresses the force applied by the inspiratory muscles. Since, during occlusion, gas flow is zero and there is no volume change, the occlusion pressures are independent from the passive mechanical characteristics of the respiratory system, namely from resistance and compliance. Obviously, a conscious subject is greatly disturbed by an occlusion maneuver. However it has been shown that, even for conscious subjects, no relevant reaction to an unexpected occlusion ever takes place before 200 ms from the start of the inspiratory effort. This means that the initial part of an occlusion pressure wave represents a free window that shows how that inspiration has been programmed by the respiratory centers, without relevant interference from unconscious or conscious reactions. $P_{0.1}$ explores the initial part of the occlusion pressure wave, namely the first 100 ms. Since in this part the occlusion pressure wave generally corresponds to a linear pressure drop, the analysis can be very simple. $P_{0.1}$ measures the difference in Paw between the point of occlusion start and the point that comes 100 ms later. $P_{0.1}$ is generally expressed as a positive number, in cmH_2O.

$P_{0.1}$ is primarily a mechanical measurement of the output of the whole complex of the inspiratory muscles. Interestingly, in patients assisted by partial ventilatory support, it has been shown that $P_{0.1}$ correlates well with the measurements of the patient workload of inspiration (the work of breathing and the pressure-time product). When the spinal cord, the respiratory nerves, the neuromuscular junctions, and the inspiratory muscles are not damaged, $P_{0.1}$ can also be used as an index of the motor output of the respiratory centers.

In practice, we can say that the finding of high levels of $P_{0.1}$ is a clear indication of high patient workload and high central respiratory drive. On the contrary, the finding of low levels of $P_{0.1}$ is more difficult to interpret. For sure, low $P_{0.1}$ is associated with a low level of muscular inspiratory activity. In a normal subject, the inspiratory activity is low when the ventilation requirement and the respiratory system impedance are normal, like in normal resting breathing. However, in respiratory disease, low $P_{0.1}$ and low inspiratory activity may be due to respiratory center depression, or to a damage in any element of the long chain that goes from central nervous system to the respiratory muscles. Only the comparison between $P_{0.1}$ and other parameters, like alveolar ventilation and blood gases, allows us to interpret whether a low value of $P_{0.1}$ means that everything goes well, or it expresses a dysfunction. In particular, low $P_{0.1}$ should normally be associated with a normal alveolar ventilation and normal blood gases, while the combination of low $P_{0.1}$, low alveolar ventilation, high $PaCO_2$, and low pH is pathological and means that either the respiratory centers are depressed, or the motor output of the respiratory centers cannot be translated into an effective respiratory activity.

As any other measurement of the mechanical output of the inspiratory muscles, the occlusion pressure is also affected by the lung volume, the muscle performance being better at low volumes, where the muscles are more stretched. For this reason, it is important to standardize the volume at which we perform the occlusion for the measurement of $P_{0.1}$. The measurement of $P_{0.1}$ must be performed by occluding the airway opening at the end of the expiratory phase of a normal breath. Also, it should be remembered that $P_{0.1}$ exhibits a fair breath-by-breath variability. For this reason, several measurements should be performed, and the average value should be retained.

$P_{0.1}$ has been proposed as a predictive index of successful weaning in COPD patients, the persistence of high values of $P_{0.1}$ indicating that the patient still needs a mechanical support. Probably a more reliable index of weaning is represented by the ratio between MIP and $P_{0.1}$, that expresses the energetic balance of the inspiratory muscles, i.e., the ratio between the maximal performance and the current demand (see § 9.).

In general, $P_{0.1}$, as a simple index of the inspiratory effort performed by the patient, provides interesting information for decision making about the setting of the external mechanical support. The finding of high $P_{0.1}$ levels means that the ventilator is not adequately supporting the patient, while very low values of $P_{0.1}$ may denote excessive mechanical support. It must be clearly stated that a measurement of $P_{0.1}$ is just a snapshot of the inspiratory activity of a patient, that may change very rapidly due to changes in ventilation requirement, gas exchange, respiratory system impedance, and external mechanical support. Interestingly, it has been shown that during PSV, patients respond rapidly to a given change in the pressure support level with an opposite change in $P_{0.1}$. Hence, a given value of $P_{0.1}$ must be interpreted in strict connection with the state in which the measurement has been taken.

10.2. Measurement of $P_{0.1}$

10.2.1. Single-breath measurement of $P_{0.1}$

As originally described, the measurement of $P_{0.1}$ was based on an occlusion maneuver directly performed at the airway opening, and required specialized equipment. However, it has been also shown that the use of the internal valves of ventilators can result in an occlusion maneuver valid for the measurement of $P_{0.1}$. Thus, with several mechanical ventilators, the measurement of $P_{0.1}$ can be easily performed by means of the end-expiratory occlusion function of the machine. The measurement requires that a pressure-trigger is being used and that the ventilator provides no flow-by. In these conditions, once the end-expiratory occlusion function is activated, as soon as the patient starts his inspiratory effort and drops the expiratory flow to zero, an occlusion is generated. Since $P_{0.1}$ will be read in the very first part of the occlusion period, the maneuver can be rapidly released.

Fig. 10-1 represents an end-expiratory occlusion maneuver performed by means of a ventilator, for the purpose of the measurement of $P_{0.1}$. The patient was assisted by PSV, and the machine was working with a pressure-trigger, and without flow-by. The vertical shaded area indicates the first 100 ms of the occluded inspiratory effort, while the horizontal shaded area indicates the corresponding pressure drop. The instant of start of the occlusion is identified on the V'aw signal, where V'aw crosses the baseline. At this point we can read a first value of Paw of 1 cmH_2O. A second reading of Paw must be taken 100 ms later, corresponding in the example to -2 cmH_2O. $P_{0.1}$ is given by the algebraic difference between the first and the second Paw reading, and hence corresponds to 3 cmH_2O.

Fig. 10-1 shows that an occlusion maneuver performed by the ventilator valves is necessarily imperfect. During the occluded effort, some flow can be measured at the airway opening, and a minor volume change can be observed. These minor

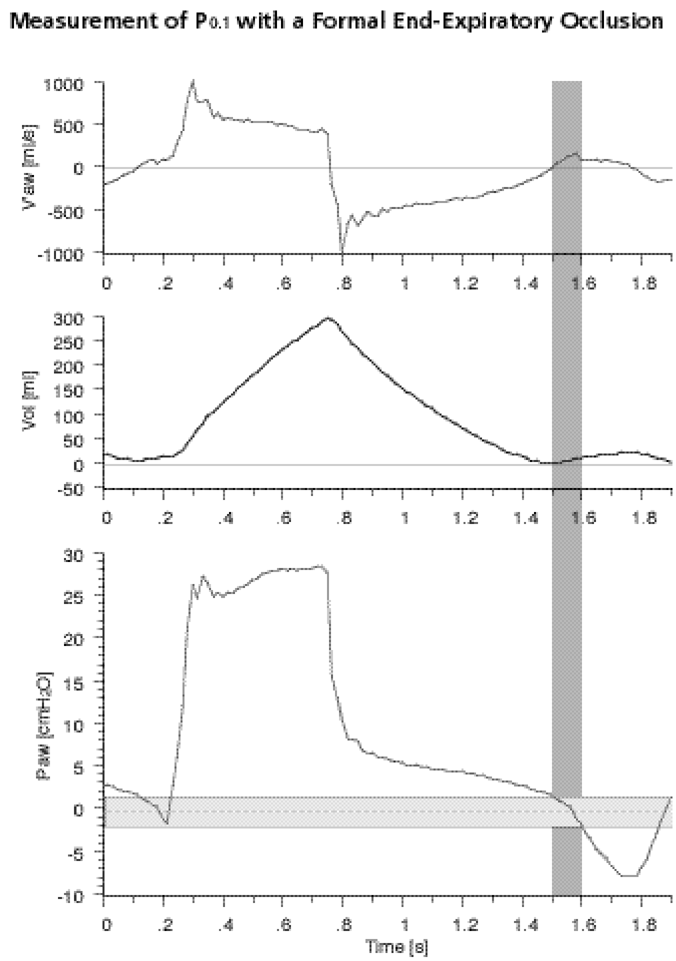

Fig. 10-1
Real-time curves of V'aw, Vol, and Paw during PSV, with an end-expiratory occlusion performed for a single-breath measurement of $P_{0.1}$. The vertical shaded area corresponds to 0.1 s, while the horizontal shaded area corresponds to $P_{0.1}$.

movements of gas are made possible by the location of the occlusion valves far from the airway opening. Even when the ventilator valves are closed, the forces applied by the patient can move some gas by decompression and compression of the volume of the external circuit of the ventilator. This phenomenon does not affect significantly the measurement of $P_{0.1}$.

Should a ventilator make use of a flow-trigger and of a flow-by, the matter is completely different. With this combination, effective occlusion is delayed and takes place only after an interval of free inspiration, made possible by the flow-by. Therefore, the occlusion maneuver, delayed and starting at a volume higher than the end-expiratory one, cannot be used for the measurement of $P_{0.1}$.

In practice, a manual measurement of $P_{0.1}$ requires a high-speed recording of the real-time curves of Paw and V'aw. The measurement can be performed either on a printout, or even directly on the screen, when the monitor is provided with facilities for reading the instantaneous values of selected points. Presently, the single-breath measurement of $P_{0.1}$ can even be found included between the special monitoring functions of ventilators. Upon call, the ventilator will operate a short occlusion maneuver and automatically perform the analysis for $P_{0.1}$.

10.2.2. Breath-by-breath measurement of $P_{0.1}$

When a ventilator works with a pressure-trigger and no flow-by, the delay in opening the inspiratory valve necessarily generates a short end-expiratory occlusion maneuver at the start of any patient-initiated breath. This mini-occlusion can be exploited for a breath-by-breath measurement of $P_{0.1}$, without any additional maneuver.

In several machines of the past generation, the delay in opening the inspiratory valve was much longer than 100 ms, and hence the conditions for the measurement of $P_{0.1}$ were perfectly met. However, this long delay caused an additional load for the inspiratory muscles, and represented a waste of time for inspiration. For this reason, the performance of the new-generation ventilators has been greatly improved, and presently the overall time necessary for the trigger threshold to be reached, and the ventilator to react, may be even less 100 ms. Nonetheless, the mini-occlusions contain information concerning $P_{0.1}$, and an equivalent of $P_{0.1}$ can be calculated even for occlusions shorter than 100 ms.

Fig. 10-2 is a real-time recording of V'aw, Vol, Paw, and Pes in a patient assisted by PSV, with a ventilator synchronized by means of a pressure-trigger. The first vertical dashed line represents the point of start of the inspiratory effort, while the second vertical dotted line is the point of start of the mini-occlusion. The breath-by-breath measurement of $P_{0.1}$ is based on the identification of the straight line that best fits on Paw drop in the interval of the mini-occlusion. In Fig. 10-2 we can see that this straight line has the same slope as the simultaneous drop in Pes. Once the slope of the Paw drop is identified, an equivalent of $P_{0.1}$ can be easily extrapolated also for those cases in which the mini-occlusion is shorter than 100 ms.

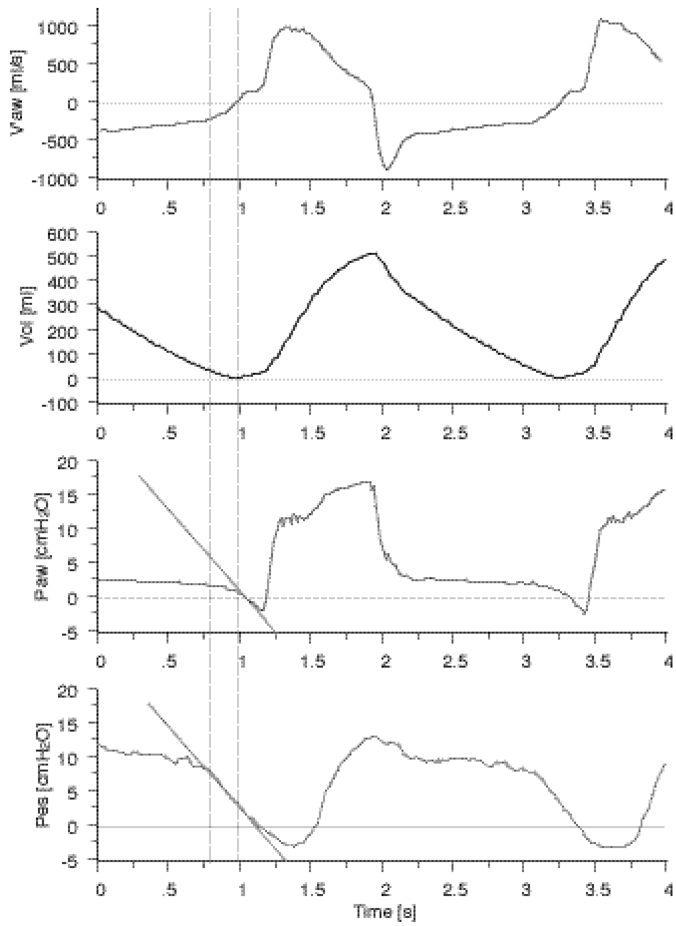

Fig. 10-2
Real-time curves of V'aw, Vol, and Paw during PSV. The mini-occlusion imposed by the pressure-trigger with no flow-by can be analyzed for a breath-by-breath measurement of $P_{0.1}$ on either Paw or Pes. The same recording is analyzed in Figs. 10-2, 10-3

The breath-by-breath measurement of $P_{0.1}$ has been implemented in the monitoring system of the ventilator Hamilton Medical Galileo. This monitoring system samples the mechanical signals of respiration at a frequency of 60 Hz, and hence collects a point for each signal at every interval of 16.7 ms. Starting backwards from the point of minimum Paw of every cycle, i.e., from the point of end of the

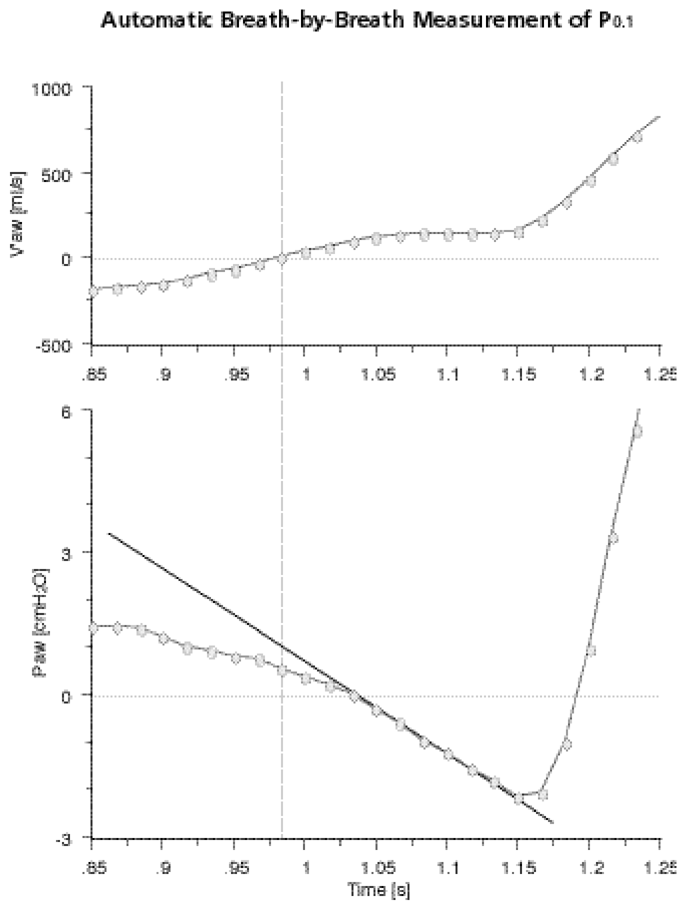

Fig. 10-3
Zoom of Fig. 10-1 for V'aw and Paw, corresponding to the mini-occlusion imposed by the pressure-trigger with no flow-by. Each point is a sample taken by the monitoring system. The straight line corresponds to the maximum slope of the Paw drop during the mini-occlusion, and can be used for the calculation of an equivalent of $P_{0.1}$.
The same recording is analyzed in Figs. 10-2, 10-3

mini-occlusion, the monitoring system performs an analysis of the slope of the Paw signal vs. time. In order to counteract noise, groups of four successive points are analyzed, by using a first-in, first-out technique. This analysis allows a reliable identification of the maximum slope of the Paw drop during the mini-occlusion. An equivalent of $P_{0.1}$ is then calculated from the maximum slope. Fig. 10-3 shows a zoom of Fig. 10-2, for the signals of V'aw and Paw during the mini-occlusion.

The vertical dotted line represents the start of the mini-occlusion. Each point represents one sample taken by the monitor. The continuous straight line corresponds to the maximum slope of the Paw drop, as identified by the monitor. The method is designed for working with mini-occlusions as short as 67 ms. It is primarily conceived for working on the Paw signal, but can also be used on the Pes signal.

The above described method has been proven to provide results very close to the formal occlusion method, provided that flow-trigger and flow-by are not in use. The advantage of breath-by-breath monitoring of $P_{0.1}$ is promising. On one side, the observation of a trend curve for $P_{0.1}$ allows us to overcome the problem of the intrinsic breath-by-breath variability of the parameter. On the other side, continuous monitoring of $P_{0.1}$ is a simple way for monitoring the inspiratory activity of the patient, without need for complex and invasive methods like the measurements of work of breathing and PTP.

10.3. Conclusions

The measurement of $P_{0.1}$ provides synthetic information about the activity of the complex of the inspiratory muscles. When the physiological chain that starts from the respiratory centers and ends with the inspiratory muscles is assumed to be intact, $P_{0.1}$ also provides information about the central neural respiratory drive. The parameter has been used for the prediction of weaning from mechanical ventilation, and can be used for the manual, and even the automatic tuning of the setting of the ventilator.

$P_{0.1}$ can be measured on single breaths with a simple analysis of an end-expiratory occlusion maneuver performed by the ventilator. Continuous monitoring of $P_{0.1}$ is made possible by an automatic analysis of the mini-occlusion necessarily generated when a ventilator works with a pressure-trigger and no flow-by. The use of flow-trigger with flow-by strongly disturbs both the manual and the automatic measurements of $P_{0.1}$.

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