Assisted Ventilation in the ICU: When and to Whom?

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Mechanical ventilation is a life-saving therapy for most critically ill patients [1]. We can distinguish between:

Controlled mechanical ventilation: during controlled mechanical ventilation, the patient has no role in the gas delivery process. Spontaneous respiratory muscle activity needs to be abolished.

Assisted mechanical ventilation: assisted mechanical ventilation involves a deep interaction between the patient and the ventilator machine. During this process, the patient's spontaneous respiratory effort is recognized by the ventilator and assisted with positive pressure applied at the airway open. In this way, the work of breathing (WOB) is shared between the patient and the ventilator. Ventilator's assistance needs to be synchronized with the patient's inspiratory effort. Breathing pattern should ideally remain totally under the patient control. Respiratory rate (RR), tidal volume (VT), inspiratory time and inspiratory time/expiratory time ratio (I:E ratio) should be variable on a breath by breath basis.

7.1 When Do We Use Controlled Mechanical Ventilation in the Intensive Care Unit (ICU)?

During controlled mechanical ventilation, patient's spontaneous respiratory effort should be absent due to pathological conditions or pharmacologically abolished for clinical reasons. Controlled ventilation is often used to rest the exhausted

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respiratory muscles immediately after the institution of invasive mechanical ventilation in dyspnoeic patients. It is mandatory in pathological conditions deeply affecting the chain of respiratory impulse transmission from the respiratory centres to the respiratory muscles. The need to use deep sedation and eventually paralysis (such as in brain-injured patients) is another classical indication for controlled mechanical ventilation.

The duration of the controlled mechanical ventilation period should be ideally to be as short as possible since it is hampered by several side effects:

- *Ventilator-induced diaphragm disfunction*: according to Levine and co-workers, diaphragm atrophy may occur after only 18–69 h of controlled mechanical ventilation. The resulting diaphragm dysfunction is one of the commonest causes of weaning failure [2–4].
- *Reduced aereation of lung tissue*: diaphragmatic inactivity affects alveolar aeration by generating actelectasis in the dependent lung regions. Abnormally high intra-abdominal pressures worsen this scenario [5].
- *Haemodynamic impact*: in general, positive pressure mechanical ventilation has a double haemodynamic impact [6], the "preload" and the "afterload" effect. The first one is due to the reduction of venous return (RV). During spontaneous inspiration the right atrial pressure falls, following the negative pleural pressure. The resulting pressure gradient favours the RV. On the contrary, during positive pressure mechanical ventilation, the continuous positive intrathoracic pressure increases the right atrial pressure, negatively affecting the RV. On the other hand, mechanical ventilation has the potential to increase pulmonary vascular resistance by compressing the alveolar vessels. Pulmonary vascular resistances are the main determinant of the right ventricle afterload (afterload effect). Finally, positive intrathoracic pressure causes a decrease in the transmural aortic pressure and therefore in left ventricle afterload. The interplay between the preload and the afterload effect with specific pathological conditions such as hypovolemia, ARDS, the use of high PEEP or VT levels, the effects of drugs acting on the cardiovascular system or pre-existing cardiac or pulmonary diseases, determines the overall impact of mechanical ventilation on cardiovascular function. The controlled mechanical ventilation mode specifically amplifies the "preload effect" because it implies the absence of diaphragm contraction.

By definition, since assisted ventilation preserves and promotes diaphragmatic contraction, as compared to controlled ventilation, it should improve aeration in the dependent regions, attenuate the haemodynamic impact and, obviously, decrease the risk of ventilator-induced diaphragm atrophy. This is true if one thinks to the myriad of physiological studies on the assisted ventilator modes [1, 7, 8]. However, we lack randomized controlled trials to demonstrate the impact of assisted ventilation on clinically meaningful outcome parameters. Nevertheless, assisted ventilation is extensively used in clinical practice to reduce mechanical ventilation duration, ICU length of stay, ventilator acquired pneumonia, improve patients comfort and decrease the need of sedation.

7.2 How Does Assisted Ventilation Work?

Pressure support ventilation (PSV) is the prototype mode of assisted mechanical ventilation [9]. The two newer assisted modes, neurally adjusted ventilator assist (NAVA) and proportional assist ventilation (PAV), that have been recently introduced in clinical practice are called "proportional modes". They deliver a support that is proportional, on a breath-by-breath basis, to the patient's inspiratory effort [10–12].

7.3 Pressure Support Ventilation (PSV)

During PSV, every breath is patient-started and patient-terminated. The support level (i.e. the amount of positive pressure that the ventilator will apply at the airway opening to assist the spontaneous inspiratory effort) is fixed. All the breathing pattern parameters (VT, RR, inspiratory and expiratory time) depend on patient's spontaneous respiratory activity.

Pressure support assistance is delivered throughout three different phases (see Figs. 7.1 and 7.2):

1. Recognition of the start of patient's spontaneous inspiration (inspiratory trigger): during this phase, the ventilator shifts from the expiratory to the inspiratory phase.

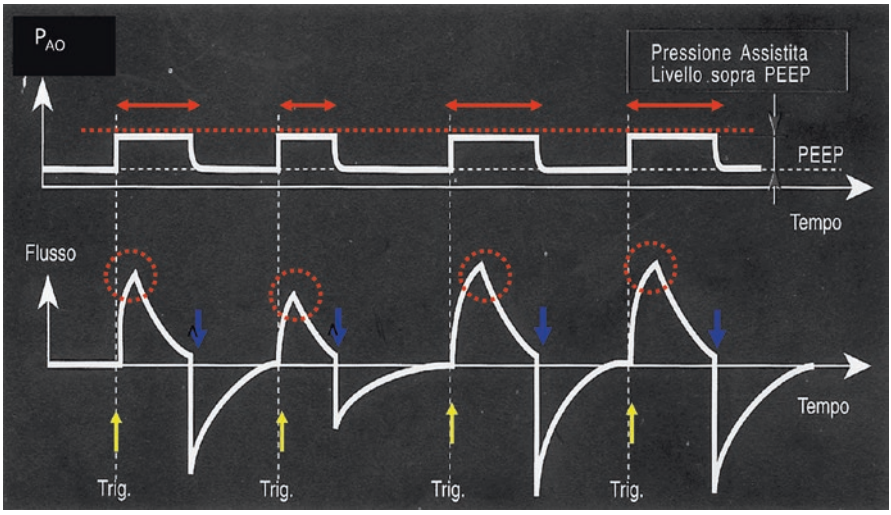

Fig. 7.1 Pressure support ventilation (PSV) algorithm: each patient's effore troggers the ventilator (*yellow arrows*). The ventilator assists the spontaneous inspiratory effort with a pre-set constant level of pressure (*dotted red line*). The interplay between the ventilator assistance and the spontaneous effort generates an ispiratory flow peak (*dotted red circles*) that ts different on a breth by breath basis. Once the inspiratory flow decays below a prefixed threshold (*expiratory trigger*, *blue arrows*) the ventilator cycles off into the expiratory phase

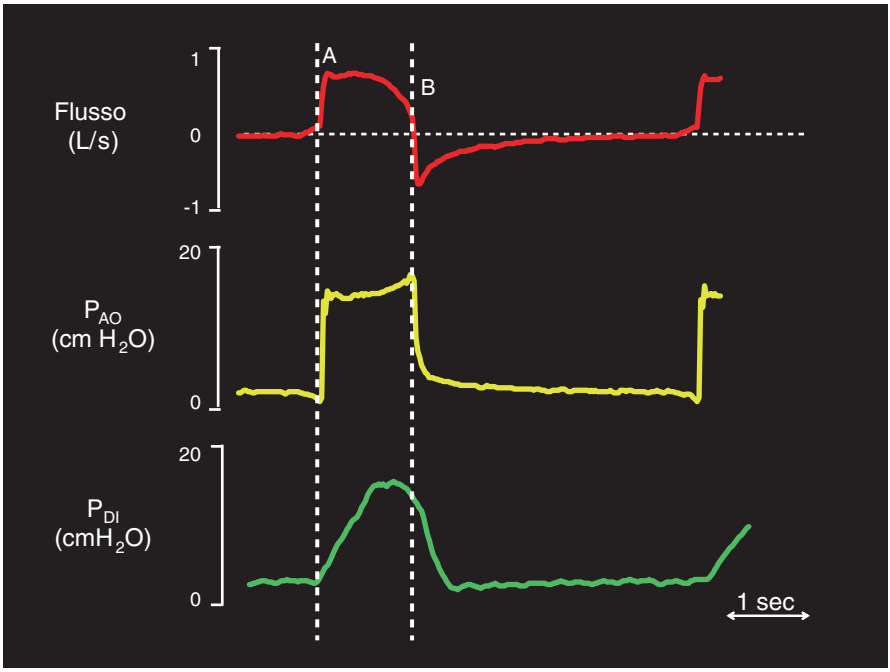

Fig. 7.2 Flow (*red trace*), airway opening pressure (P_{AO}- *yellow trace*) and transdiaphragmatic pressure (P_{DI}- *green trace*) during PSV. The dotted white line A indicates the inspiratory trigger phase. The dotted white line B indicates the expiratory trigger phase

2. Pressurization: during this phase, the ventilator maintains the preset level of positive pressure at the airway opening.
3. Recognition of the end of the inspiratory phase and start of the expiratory phase (expiratory trigger).

Generally, during PSV, the breaths are flow triggered but the pressure trigger mode can be used too.

With the pressure trigger, the ventilator starts to deliver the assistance when the patient's spontaneous respiratory effort generates a negative pressure inside the ventilator circuit. Instead, if the flow trigger is used, the assistance starts when the patient subtracts a predefined portion of a continuous gas flow ("bias" flow) that circulates in the circuit at end expiration. Any delay in the delivery of the assistance is named "inspiratory trigger delay". The amount of delay is greatly influenced by the technical features of the single ventilator but depends also on several clinical parameters, mainly patient's breathing pattern and the presence of dynamic hyperinflation [13].

The positive pressure applied by the ventilator to assist the spontaneous inspiratory effort is constant throughout the whole pressurization phase. During this phase, the ventilator maintains the preset level of positive pressure at the airway opening

by replacing (virtually in real time) moment by moment the volume delivered to the patient. In most ventilators it is possible to adjust the pressurization rate (the time needed to reach the pressure support level, i.e. the slope of pressurization). In the common practice, the pressurization slope is set at 0.1–0.2 s. A peak and a subsequent approximately exponential decay characterize the inspiratory flow profile. The peak flow is greatly influenced by the slope of pressurization and by the early inspiratory effort. The subsequent flow rate decay depends on the interplay between the inspiratory efforts, the mechanical properties of the respiratory system and the amount of volume delivered to the patient. Ideally, until the inspiratory effort is active, after the inspiratory flow peak there will be a sustained, slowly decaying flow. When the inspiratory effort comes to an end, the inspiratory flow sharply decreases. The expiratory trigger is generally activated when the inspiratory flow decays below a given threshold, suggesting that the patient is no longer active in generating the inspiratory effort. Usually the expiratory trigger threshold is not fixed but is a percentage of the previous flow peak. For example, if the threshold is 30% of the inspiratory flow peak rate, the cycle will occur at 0.3 L/min if the peak flow is 1 L/min. In most ventilators, the expiratory trigger threshold is adjustable from 70 to 10% of the flow peak.

Figure 7.1 shows a typical ventilator screen during PSV. We can see pressure (PAO) and flow curves. The yellow arrows indicate the inspiratory trigger activation. The red dotted line represents the pressure support level. Note that the inspiratory time changes breath by breath (red arrows). The flow peak is also variable as indicated by red dotted cycles. The blue arrows indicate the expiratory trigger activation.

Figure 7.2 illustrates an ideal PSV breath. The diaphragmatic electrical activity (EAdi) trace (green line) is also visible. In this ideal situation, the diaphragm contraction activates the inspiratory trigger and the pressurization phase starts (PAO-yellow trace). Letter A indicates the flow peak. At the end of diaphragmatic contraction, the flow reduces and, at last, it decays to the expiratory trigger threshold.

In clinical practice, the level of support is titrated to obtain a VT between 5 and 8 ml/predicted body weight (PBW) and a RR between 15 and 30 breaths/min [9, 14]. That's why, according to physiological studies, a VT higher than 8 ml/PBW and a RR lower than 15 bpm are generally signs of over-assistance while, on the contrary, a VT lower than 5 ml/PBW and a RR higher than 30 bpm are signs of under-assistance [15].

Several physiological studies demonstrated the PSV ability, as compared with controlled mechanical ventilation, to reduce the adverse effects of prolonged sedation and ventilator-induced diaphragm dysfunction [5, 7, 9, 15]. Despite these positive reports, however, poor patient-ventilator interactions frequently occur during PSV. To understand why this occurs, it is convenient to introduce the "neuro-ventilatory coupling" concept [10] (Fig. 7.3). In healthy subjects, small changes in the respiratory effort determine high variations of flow and VT, and the physiological effort is about the 20–30% of the maximum inspiratory capacity (green line, Fig. 7.3) [16]. Whenever the neuro-ventilatory coupling is impaired, the slope and the variability of the neural output/VT or neural output/inspiratory flow relationship

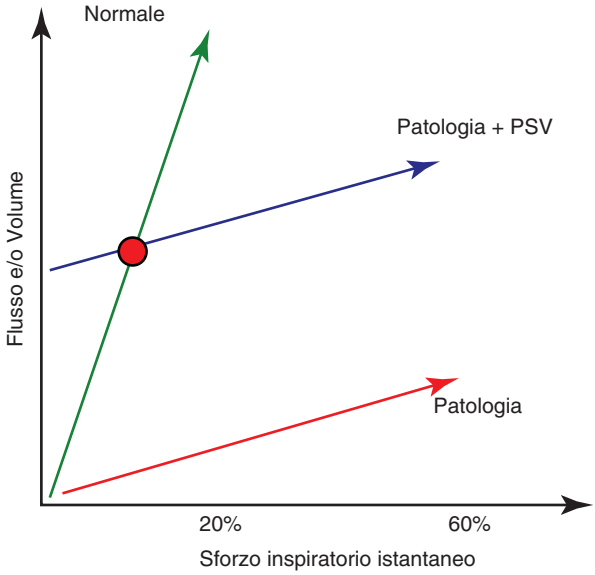

Fig. 7.3 Neuro-ventilatory coupling. Neuro-ventilatory coupling relationship in healty subjects (*green line*), pathological subjects (*red line*), pathological subjects during PSV (*blue line*). The red point figures out the only one point in which physiological neuro-ventilatory coupling, during PSV, is preserved

decrease (red line, Fig. 7.3). Considering a patient with an impaired neuro-ventilatory coupling ventilated in PSV, the slope of the neuro-ventilatory coupling remains a pathological one, but the inspiratory assistance provides a bust that translates each point of the line toward a higher VT and inspiratory flow. Accordingly there will be only one point (red point, Fig. 7.3), where the neuro-ventilatory coupling is "normal". This may explain why the over-assistance phenomenon frequently occurs during PSV. Over-assistance may reduce assisted mechanical ventilation advantages and side effects, generally associated with controlled mechanical ventilation, may prevail.

Over-assistance may frequently occur during PSV. Since the level of assistance is fixed and doesn't change with the patient's spontaneous effort, if the patient effort is weak and ceases very early, the ventilator inflates the passive patient up to the expiratory trigger threshold. Accordingly, the combination of high levels of PSV, weak and short inspiratory effort and low expiratory trigger threshold easily generates over-assistance during PSV. If the patient just triggers the ventilator and immediately ceases the inspiratory effort, the assistance delivery will be independent by the patient effort, and VT depends entirely on the level of assistance and the mechanical properties of the respiratory system. During over-assistance, the inspiratory mechanical time (Ti_{mech}) is longer than the neural inspiratory time (Ti_{neur}).

In most cases, as said above, when a patient is over-assisted, the VT is higher than 8–10 ml/Kg predicted body weight (PBW), and/or the RR is lower than 15 breaths/min. However, recent studies point out that, interestingly, over-assistance may occur even if RR and VT are in the suggested clinical range. Figure 7.5, adapted from ref. [17], shows the VT, RR and diaphragmatic WOB trend in 12 patients ventilated in PSV for 48 h [17]. Note that the diaphragmatic WOB was

constantly under its physiological range throughout the period despite the PSV settings were in line with the clinical best practice, i.e. the PSV level was titrated to obtain a VT between 5 and 8 ml/PBW and RR between 15 and 30 breaths/min. Our group recently recorded the diaphragmatic electrical activity (EAdi) during prolonged PSV (12 h), in 17 patients (unpublished data). The EAdi represents the neural ventilator output and is strictly related with diaphragmatic WOB; we predefined four EAdi categories:

- NO EAdi: EAdi absent (the patient starts the breath with the accessory muscles and is subsequently over-assisted by the ventilator)
- LOW EAdi: EAdi under 5 μV
- NORMAL or MEDIUM: EAdi in the normal range of 5–15 μV
- HIGH: EAdi above 15 μV

The results are shown in Fig. 7.4. The NO EAdi condition occurred the 20.9% of the total recorded patients' breaths. The LOW EAdi condition occurred in the 52.8% of the total breaths and, finally the NORMAL and the HIGH EAdi conditions occurred in the 20.7 and the 5.6%, respectively.

Figure 7.5 illustrates PAO, flow and EAdi traces in one representative patient. Note that the EAdi decreased during the 12 h, whereas the flow and the PAO curves didn't change significantly.

Over-assistance is one of the most important causes of patient-ventilator asynchrony [18]. Several clinical trials have demonstrated that a high incidence of patient-ventilator asynchronies is correlated with a longer ICU length of stay and mechanical ventilation duration, a higher incidence of tracheostomy and, at last, a higher mortality [19–21].

Figure 7.6 shows the relationship between mechanical respiratory rate (RR_{mech}) and spontaneous "neural" respiratory rate (RR_{neur}) in 20 patients ventilated in PSV for 8 h (unpublished data). In a group of patients, that were mainly patients with moderate-severe COPD, the figure shows a severe discrepancy between RR_{mech} and RR_{neural}. Figure 7.7 shows the flow, the volume, the PAO and the oesophageal pressure (Pes) traces in one representative patient ventilated in PSV for 8 h. Each panel represents 30 s taken at the beginning of each hour of the study. In this patient,

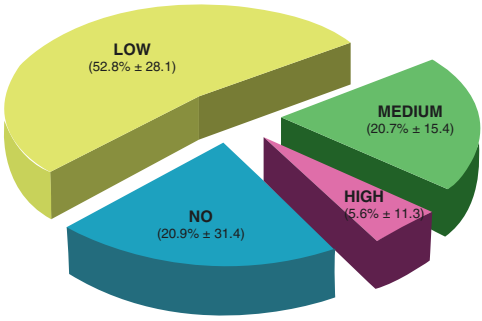

Fig. 7.4 Percentage of Eadi cathegories in 17 patients during prolonged PSV (12 hours). Please note the prevalence of NO-EAdi and LOW-Eadi conditions

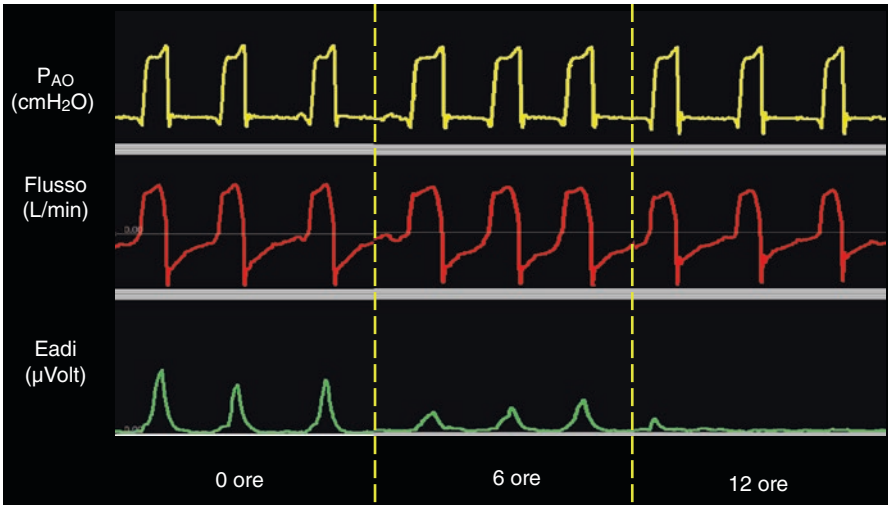

Fig. 7.5 P_{AO} (*yellow trace*), Flow (*red trace*) and Eadi (*green trace*) in one representive patient during the 12 hours of PSV. Eadi significantly decreased throughout the hours whether P_{AO} and flow traces remained unchanged

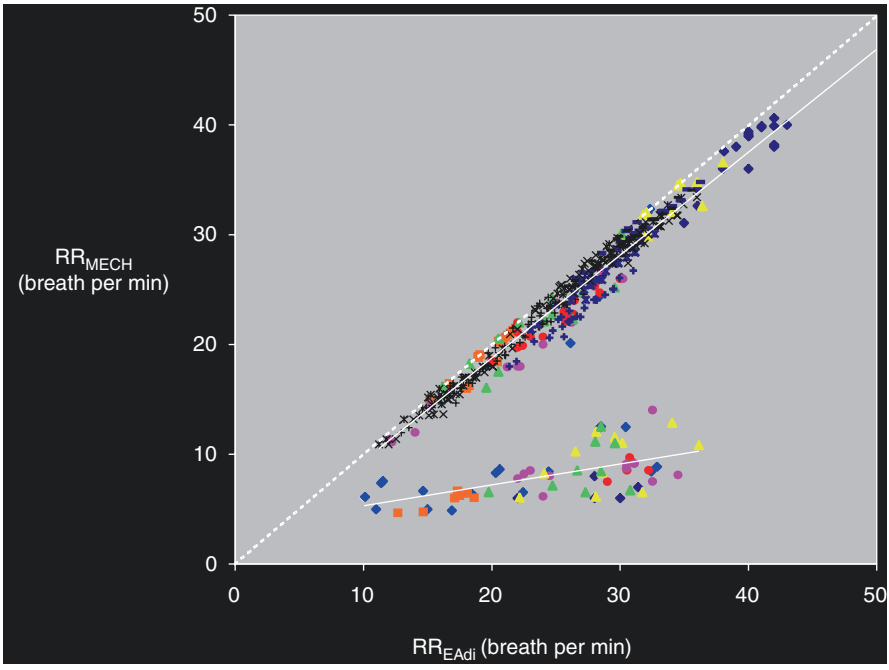

Fig. 7.6 Relationship between mechanical respiratory rate (RR_{mech}) and spontaneous "neural" respiratory rate (RR_{neural}) in 20 patients ventilated in PSV mode for 8 hours. The figure illustrates the discrepancy between RR_{mech} and RR_{neural} in some of the studied patients

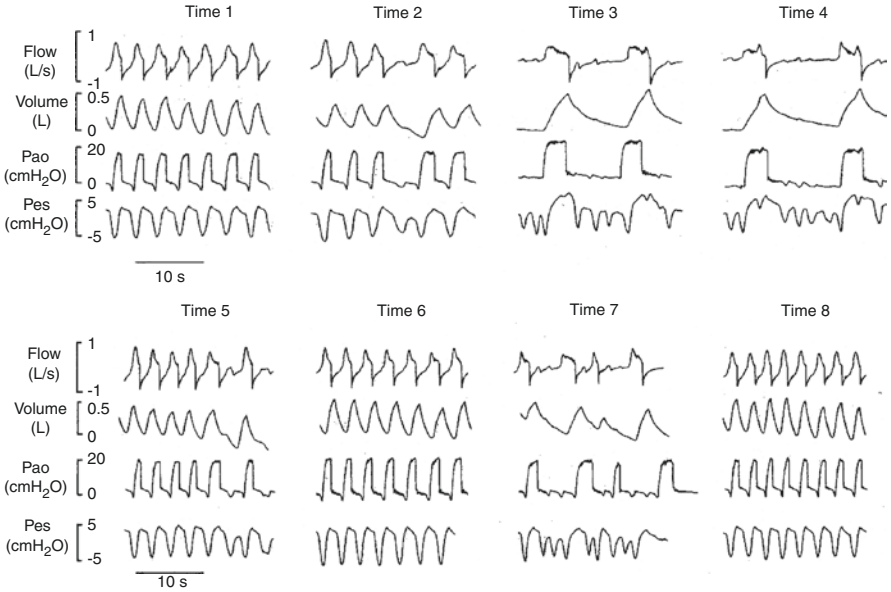

Fig. 7.7 Flow, volume, P_{AO} and esophageal pressure (P_{es}) in one representive patient during the 8 hours of PSV. We can see the changes in terms of patient-ventilator interactions throughout the study. Please note the high percentage of asynchronies at 3, 4, and 7 hours

patient-ventilator interactions remarkably varied throughout the study period. Asynchronies were evident at 3, 4 and 7 h.

Prolonging mechanical insufflation into neural expiration has been shown to worsen dynamic hyperinflation and cause ineffective inspiratory efforts. This may happen principally in COPD patients who need a higher respiratory effort to overcome the intrinsic PEEP ($PEEP_i$) [22].

A mean to improve the patient-ventilator interactions during PSV is to titrate the slope of pressurization, the level of assistance and the expiratory trigger threshold in order to optimize patient-ventilator interactions, assure the optimal diaphragmatic workload and minimize the asynchronies [20]. Generally speaking, the peak inspiratory flow increases with the slope of pressurization and vice versa, and, thus, the higher is the peak inspiratory flow the higher will be the mechanical inspiratory time (because the expiratory trigger threshold is a percentage of the peak inspiratory flow). On the other hand, the expiratory trigger threshold has a deep influence on the inspiratory time (the lower the threshold, the higher the mechanical inspiratory time). Titrating the assistance level could serve to circumvent over- and under-assistance. However, the PSV critically depends from the single clinicians' expertise, and one could consider it more an art than a science. The fact that during PSV the over-assistance may occur even if RR and VT are in the "optimal" range (see above) makes it difficult to trust solely on the flow and PAO traces to titrate the PSV level, the slope of pressurization and the expiratory trigger threshold. Experts are concordant in suggesting bedside monitoring of respiratory muscle activity to easily

detect asynchronies and to avoid over- or under-assistance, but on the other hand, reliable indexes of diaphragmatic and intercostal muscle activity to be used at the bedside are scanty. The recent introduction in clinical practice of the EAdi monitoring (see below) and of diaphragmatic electromyography could represent a turning point to monitor diaphragm activity bedside on a breath-by-breath basis [23, 24].

7.3.1 EAdi and NAVA

During NAVA, the ventilator assistance is proportional to the patient's spontaneous diaphragmatic activity (EAdi). The diaphragmatic electromyography strictly correlated with phrenic nerve discharge [12, 25] and hence to the neuro-ventilatory drive. From a technical point of view, the EAdi is measured through an array of eight electrodes mounted within a nasogastric tube (NAVA catheter) (Fig. 7.8). The EAdi signal is obtained from the crural portion of the diaphragm, amplified and filtered from cardiac artefacts and other electrical contaminations.

Fig. 7.8 Eadi signal acquisition during NAVA. Eadi is measured through a naso-gastric tube equipped with 8 electrodes (NAVA catheter) and is processed and visualized on the ventilator screen

Besides monitoring the neuro-ventilatory drive, the EAdi signal can be used to evaluate the diaphragmatic efficiency in terms of neuromechanical and neuro-ventilatory efficiency (NME and NVE, respectively) [23, 26]. The NME is calculated as the ratio between the negative pressure developed by the diaphragm and the EAdi peak during an end-expiratory occlusion and is expressed in $cmH_2O/\ \mu V$. The neuro-ventilatory efficiency, expressed in ml/ μV, is calculated as the ratio between VT and the correspondent EAdi peak. Figure 7.9 shows how to calculate these two parameters. Bellani and co-workers validated a technique to continuously calculate the diaphragmatic WOB from NME and the EAdi signal [27]. Recently Liu and coll [26] demonstrated that the NME and NVE evaluation was useful to predict extubation readiness.

In the neurally adjusted ventilator assist mode (NAVA), the EAdi signal is used to drive the ventilator's assistance [25]. Briefly, during NAVA the EAdi triggers on and cycles off the ventilator, and, most important, the assistance delivery is proportional to EAdi according to the following formula:

$$\mathrm{PAO}\left(\mathrm{cmH_2O}\right) = \mathrm{NAVA\ level} \times \mathrm{EAdi}\left(\mu\mathrm{V}\right).$$

The NAVA level must be set by the clinician. As an example, if the NAVA level is 1, the ventilator applies a positive pressure of 1 cmH_2O for each μV (Fig. 7.10).

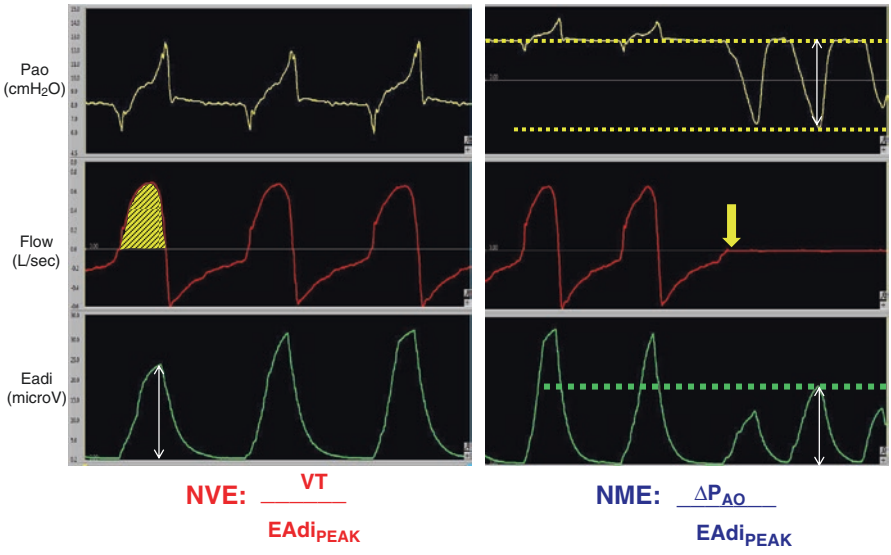

Fig. 7.9 Neuro-ventilatory efficiency (*NVE, panel on the left*) and neuro-mechanical efficiency (*NME, panel on the right*) calculation. The NVE is the ratio between tidal volume (*VT, yellow area under the flow trace, red trace*) and the Eadi peak (*white arrow under the green trace*). The NME is the ratio between negative pressure during an end-expriratory occlusion (*yellow trace*) and Eadi peak (*green trace*). During the expriratory occlusion the flow is zero (*red trace*)

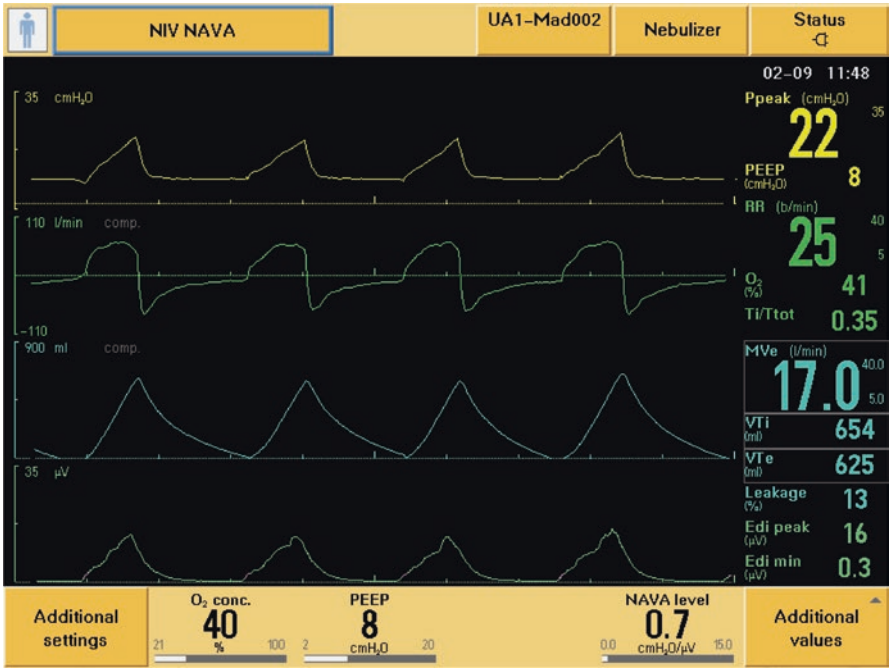

Fig. 7.10 Ventilator screen during NAVA. NAVA level, PEEP and O_2 concentration must be set by the clinician

Several physiological studies have shown the NAVA ability, as compared with PSV, to improve neuro-ventilatory coupling and patient-ventilator synchrony [12, 18]. Di Mussi and co-workers [17] compared NAVA vs PSV during a prolonged ventilation period (48 h) to test the impact of the two techniques on NVE and NME. Both NME and NVE significantly improved in patients randomized to NAVA whereas both were not affected by PSV. During the 48 h, the diaphragmatic WOB was constantly in the physiological range during NAVA and almost constantly under the physiological range during PSV, suggesting over-assistance. Patient-ventilator asynchronies were significantly less during NAVA than during PSV [17]. However in 20–30% of the patients included in the study, NAVA failed because of EAdi signal instability or difficult reading. Further studies are needed to evaluate the real percentage of NAVA failures in the clinical scenario.

7.3.2 Proportional Assist Ventilation (PAV)

PAV was first described in 1992 by Magdy Younes [10]. During PAV, the positive pressure applied to each breath is proportional to the spontaneous patient's inspiratory airflow, which is used as a surrogate of respiratory muscles effort [28]. The

clinician can adjust the PAV gain, i.e. the percentage of total WOB to be performed from the ventilator.

To understand PAV one must preliminarily consider that, according to the "equation of motion" applied to mechanical ventilation, WOB is the result of (a) a resistive component to overcome airway resistance (R), proportional to the airway flow (resistive WOB = flow × R); (b) an elastic component that is needed to overcome the respiratory system elastance (E), proportional to the delivered gas volume (elastic WOB = volume × E); and a component needed to overcome positive intrinsic end-expiratory pressure (PEEPi). Provided that the ventilator software knows R, E and PEEPi, based on the "equation of motion" it can calculate the instantaneous patient's spontaneous inspiratory effort by measuring the spontaneous inspiratory flow and volume. Based on the instantaneous patient's WOB determination, the ventilator in the PAV mode applies positive pressure in proportion to the spontaneous WOB. Figure 7.11 shows the principles of the PAV algorithm. The ventilator is represented as a freely mobile piston inserted in a cylinder. The patient respiratory system is represented by a single alveolus (the airway resistances are represented by two orange triangles and the respiratory system elastance is represented by a single light blue triangle). The patient effort is represented by a yellow triangle. When the patient starts its spontaneous effort, the piston moves toward the patient: the velocity of the movement represents the instantaneous inspiratory flow, and the piston displacement represents the instantaneous inspired volume. The ventilator software is therefore able to calculate the instantaneous patient's WOB in terms of the elastic and resistive pressure generated by the respiratory muscles. The PAV assistance is applied by a motor that supports a predefined portion of the instantaneous piston movement toward the patient.

In the first PAV version, the clinician had to measure E, R and PEEPi to feed the ventilator algorithm. Considering the difficulties related to the assessment of respiratory mechanic in actively breathing patients, the quality of E and R estimation was strictly related to the clinicians' expertise. This was a major concern of the technique, since the quality of the quality of assistance was strictly dependent on the accuracy of E and R measurements. If E and R were underestimated, patients were

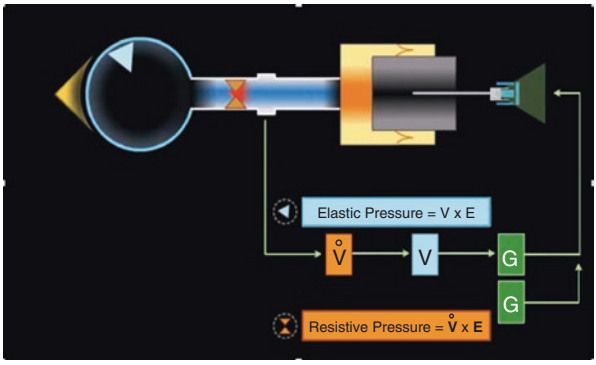

Fig. 7.11 Principles of PAV + algorythm. Freely mobile piston in the cilinder = ventilator; alveolous = patient's respiratory system; orange triangles = airway resistance; light blue triangle = respiratory system elastance; yellow triangle = patient's respiratory effort

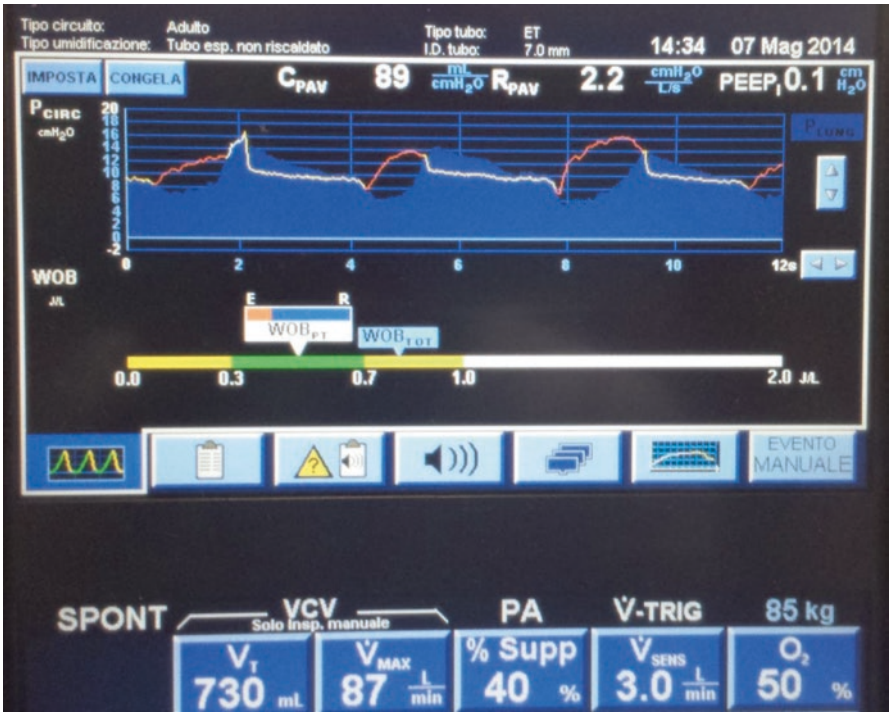

Fig. 7.12 Ventilator screen during PAV+ . Yellow dotted circles = respiratory mechanics values; Red circle = total work of breathing (WOB_{total} = $WOB_{patient}$ + $WOB_{ventilator}$). Optimal WOB should be in the green part of the scale

over-assisted whereas, on other side, if E and R were overestimated, patients were under-assisted. In the last and definitive PAV version, the PAV plus (PAV +), E, R and PEEPi are automatically calculated by the ventilator through an end-inspiratory occlusion of 200 ms automatically performed every 10–15 breaths [29–31].

During PAV +, the ventilator screen continuously shows the WOB performed by the patient and by the ventilator, respectively. Accordingly, it is possible for the clinician to adjust the PAV + gain to keep the patient's spontaneous WOB in a physiological range. Figure 7.12 illustrates the ventilator screen during PAV +. The yellow dotted circles indicate the respiratory mechanics values. The red circle evidences the total WOB. The total WOB is composed by the WOB performed by the patient and the WOB performed by the ventilator (WOB_{total} = $WOB_{patient}$ + $WOB_{ventilator}$). The patient's WOB is divided in the elastic and resistive components. The optimal WOB should be in the green part of the scale.

Figure 7.13 illustrates the impact of PAV + on the slope of the neuro-ventilatory coupling relationship [31]. In the lower panel, the depressed neuro-ventilatory coupling of a spontaneously breathing patient is compared with the physiological neuro-ventilatory coupling (blue-dotted line). In the middle panel, PAV + with a gain of 30% improves the physiological coupling improving its slope from 1.5 to 8. Finally, in the higher panel, a PAV gain of 80% further improves the slope [27].

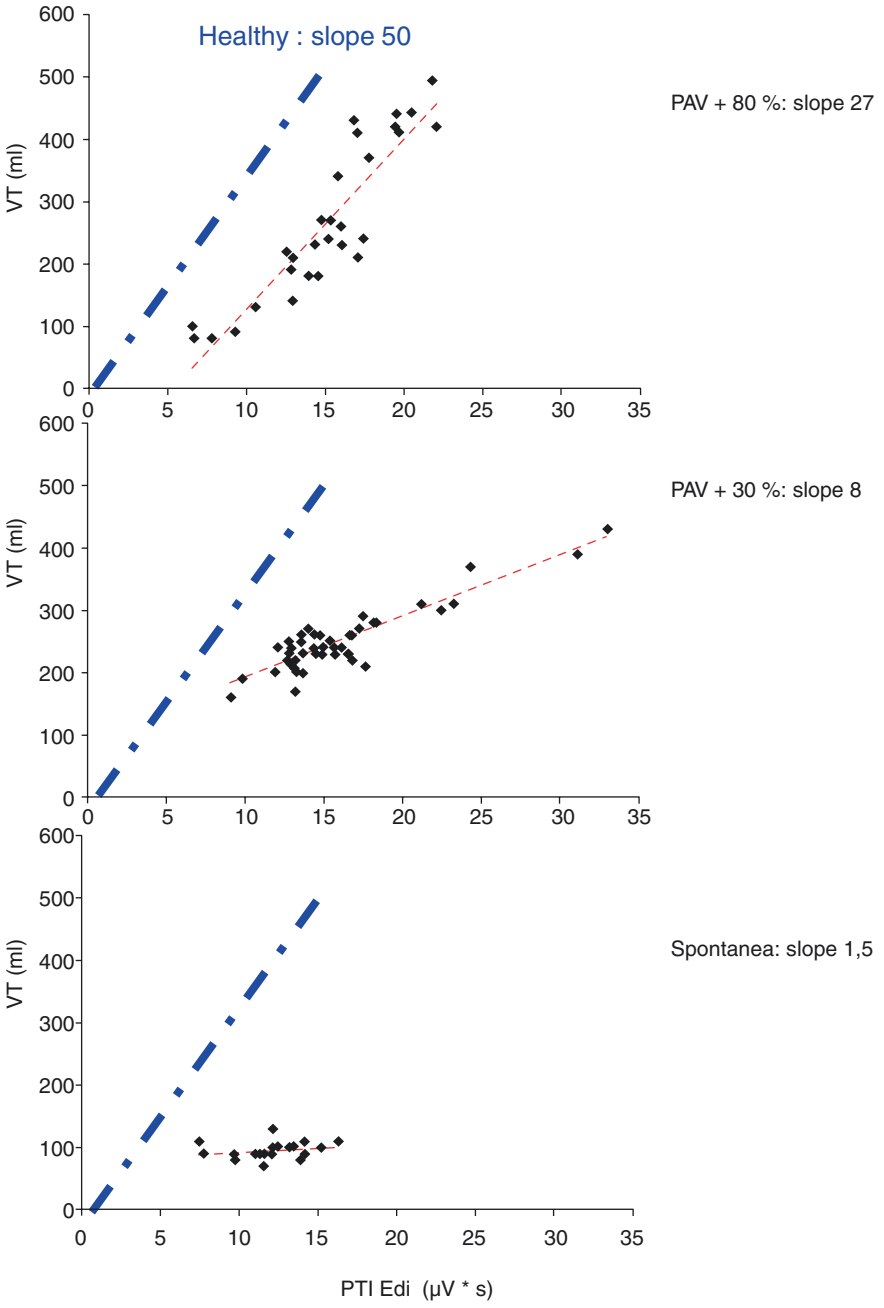

Fig. 7.13 Lower panel = physiological neuro-ventilatory coupling (blue dotted line) vs depressed neuroventilatory coupling in a spontaneously breathing patient (*red dotted line*). Middle panel= physiological neuro ventilatory coupling (*blue dotted line*) vs neuro-ventilatory coupling during PAV+ with the 30% of assistance (*red dotted line*). Upper panel: physiological neuro-ventilatory coupling (*blue dotted line*) vs neuro-ventilatory coupling during PAV+ with the 80% of assistance. The slope of the neuro-ventilatory coupling relationship increases at the same time as the % of assistance

From 1992 on, several physiological studies have clearly shown that, as compared with PSV, during PAV+ the breathing pattern is more variable (and hence more physiological), the number of patient-ventilator asynchronies, especially missed efforts, is decreased and the discrepancy between mechanical and neural inspiratory times significantly decreases [29, 32, 33]. PAV+ has been shown to unload respiratory muscles and prevent patient-ventilator asynchronies even in patients with severe chronic obstructive pulmonary disease (COPD) [34].

7.4 Indications and Contraindications to Assisted Ventilation

Assisted ventilation should be applied to patients able to trigger the ventilator and to subsequently sustain a spontaneous inspiratory effort [1, 8, 35]. The prerequisite for any assisted technique should be the integrity of the neuro-ventilatory drive. In critically ill patients, sedative drugs are often used. For this reason, in order to be confident that an excess of sedation could not excessively depress the neuro-ventilatory drive, it's important to quantify the sedation level. Considering that the level of sedation is strictly related to the quality and the concentration of sedative drugs [36–38], breathing pattern parameters and patient-ventilator interactions should be thoughtfully monitored in sedated patients. For example, with the Richmond agitation and sedation scale [39], only patients with a score between 0 (patient calm, alert, with open eyes that responds to simple orders) and −2 (patient with the eyes closed but briefly awakens—eye opening/eye contact—to voice) are suitable for assisted ventilation [36].

On the other hand, an excessively high respiratory drive during assisted ventilation may cause dynamic hyperinflation and haemodynamic derangement because of the increase of intrathoracic pressure and favour ventilation-induced lung injury (VILI) [40, 41]. In some instances the high respiratory drive results from the discrepancy between high respiratory load and the ability of the respiratory muscle to handle it. In these cases an attempt to decrease the inspiratory workload with assisted ventilation is warranted. However in some instances (ARDS, sepsis, fever, metabolic acidosis, some neurological conditions) the increased respiratory drive is independent from the mechanical load. In these instances assisted ventilation is not indicated. Several studies have shown the worsening of lung injury caused by assisted ventilation in patients with ARDS and an inappropriately high respiratory drive [42]. In these cases, sedation and eventually paralysis associated with controlled mechanical ventilation is the best choice, waiting for the normalization of the respiratory drive.

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