



Patient-ventilator asynchrony

Gaston Murias^a, Umberto Lucangelo^b, and Lluís Blanch^{c,d,e}

Purpose of review

The purpose of the review is to alert clinicians to the prevalent and frequently underrecognized problem of asynchrony in mechanically ventilated patients. To provide a mechanistic model of patient-ventilator asynchrony to help personnel understand how different asynchronies develop. To provide practical advice on how to recognize and solve different asynchronies in different contexts.

Recent findings

Patient-ventilator asynchrony is a serious problem that is associated with prolonged mechanical ventilation, prolonged ICU and hospital stays, and increased mortality. Asynchronies can occur in all modes of invasive and noninvasive ventilation in all care contexts.

Summary

The review provides insights into the causes of patient-ventilator asynchrony and mechanisms involved in the development of specific types of asynchrony. It explores the effects of sedation on the development of asynchrony and the impact of new ventilator modes. It also discusses the prevalence of asynchrony and its effects on outcome.

Keywords

mechanical ventilation, patient-ventilator asynchrony, respiratory mechanics

INTRODUCTION

Mechanical ventilation is a supportive treatment for improving oxygenation, unloading the respiratory muscles, and gaining time until the patient's condition improves. Harmonious patient-ventilator interaction is advisable to avoid excessive sedation, discomfort, fighting with the ventilator, potential cognitive alterations, prolonged mechanical ventilation, and additional risk of lung or respiratory muscle injury [1]. Moreover, asynchronies hinder recognition of breathing patterns and cyclical changes in intrathoracic pressure, thus affecting hemodynamic measurements [2] and respiratory mechanics [3].

UNDERSTANDING ASYNCHRONIES

To analyze patient-ventilator asynchrony during partial ventilatory support, this review considers a model of the respiratory system [4] in which two communicating compartments are placed in series. The central compartment represents the airways and the peripheral compartment represents the alveoli. The two compartments are separated by the airway resistance. Pressure in the central compartment (P_{CC}) can be calculated as volume in the central compartment (V_{CC}) multiplied by the elastance of the central compartment (E_{CC}):

($P_{CC} = V_{CC} \times E_{CC}$). Similarly, pressure in the peripheral compartment (P_{PC}) can be calculated as volume in the peripheral compartment (V_{PC}) multiplied by the elastance of the peripheral compartment (E_{PC}): ($P_{PC} = V_{PC} \times E_{PC}$) (Fig. 1). P_{PC} can be modified by a change in V_{PC} or a change in E_{PC} ; however, since airway elastance is considered constant, P_{CC} can only be modified by a change in V_{CC} . Thus, P_{CC} traces changes in V_{CC} : when V_{CC} decreases, P_{CC} falls (negative slope in pressure-time scalars), and when V_{CC} increases, P_{CC} rises (positive slope in pressure-time scalars).

During inspiration, P_{CC} is higher than P_{PC} and gas flows from the central compartment to the peripheral compartment according to the equation: $F = \Delta P / R$, where F represents flow, ΔP represents the

^aClinica Bazterrica y Clínica Santa Isabel, Buenos Aires, Argentina,

^bDepartment of Perioperative Medicine, Intensive Care and Emergency, Cattinara Hospital, Trieste University, Trieste, Italy, ^cCritical Care Center, Hospital de Sabadell, Corporació Sanitària Universitària Parc Taulí, Universitat Autònoma de Barcelona, Sabadell, ^dCIBER Enfermedades Respiratorias, ISCIII, Madrid and ^eInstitut de Investigació i Innovació Parc Taulí, I3PT, Sabadell, Spain

Correspondence to Gaston Murias, Clínica Bazterrica y Clínica Santa Isabel, 517 bis #1096 entre 5bis y 7, (1901) Ringuet (La Plata), Buenos Aires, Argentina. Tel: +54 9 11 4474 2329; e-mail: gmurias@gmail.com

Curr Opin Crit Care 2016, 22:000–000

DOI:10.1097/MCC.0000000000000270

KEY POINTS

- To understand how different patient-ventilator asynchronies develop, it is useful to view the respiratory system as two communicating compartments placed in series.
- Ineffective inspiratory efforts are a major problem in patient-ventilator interaction, and they are the most common asynchrony phenomenon.
- Asynchrony is underrecognized but prevalent throughout mechanical ventilation, in all modes of invasive and noninvasive ventilation, and in all care contexts.
- If adjusting ventilator setting does not correct asynchronies, proportional ventilation modes should be considered.
- Patient-ventilator asynchrony is associated with worse outcomes (prolonged mechanical ventilation, prolonged ICU and hospital stays, and increased mortality).

difference Δ in pressure between the two compartments, and R represents airway resistance. During expiration, inspiratory muscles stop contracting, allowing the elastic recoil of the respiratory system to increase P_{PC} and inverting the pressure gradient between compartments and thereby reversing flow (also explained by this equation).

In the two-compartment model, pressure is generated entirely by elastic forces (no pressure can be explained by resistance, even though

resistance explains a pressure gradient between compartments when flow is present).

VENTILATOR TRIGGERING AND INEFFECTIVE INSPIRATORY EFFORTS

The ventilator is triggered when a given drop in airway pressure (or a given diversion of airway flow) is achieved. Because the patient cannot directly modify the behavior of the central compartment, this change in airway pressure (or flow) has to be produced by a change in the peripheral compartment.

At the end of a calm expiration, the respiratory system achieves its functional residual capacity and the pressures are the same throughout the system. The contraction of inspiratory muscles increases the size of the peripheral compartment (which reduces the E_{PC}) and produces a drop in P_{PC} , resulting in a pressure gradient between compartments. This pressure gradient drives gas flow from the central to the peripheral compartment across airway resistance. The reduction in the amount of gas located in the central compartment produces a fall in P_{CC} that triggers the ventilator (Fig. 2). If the inspiratory effort starts before functional residual capacity has been achieved [i.e., gas remains in the alveoli, auto-positive end-expiratory pressure (autoPEEP)], the first part of the inspiratory effort has to equalize pressures, increasing ventilatory load. Moreover, if the effort is insufficient to overcome auto-PEEP (and trigger threshold), an ineffective inspiratory effort

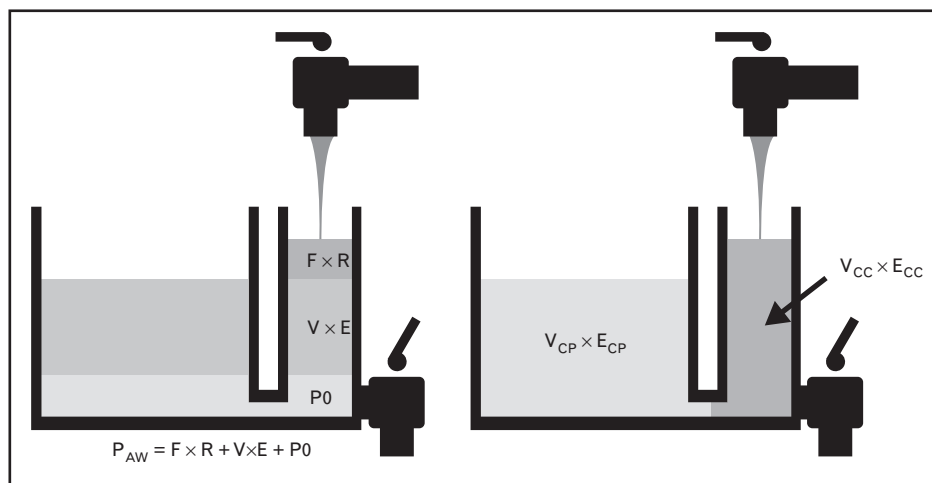


FIGURE 1. Two-compartment model of the respiratory system. In the diagram on the left, the equation of motion is used to show the determinants of airway pressure (P_{AW}): the 'elastic' pressures are shown in gray (lighter gray for total PEEP and middle gray for tidal volume) and the 'resistive' pressure is shown in dark gray. Airway pressure is regarded as the alveolar pressure ($V \times E + P_0$) plus the pressure difference between compartments ($F \times R$). In the diagram on the right, volumes in each compartment have been unified and, although they communicate with each other, each compartment is pictured as an entity (see text for details).

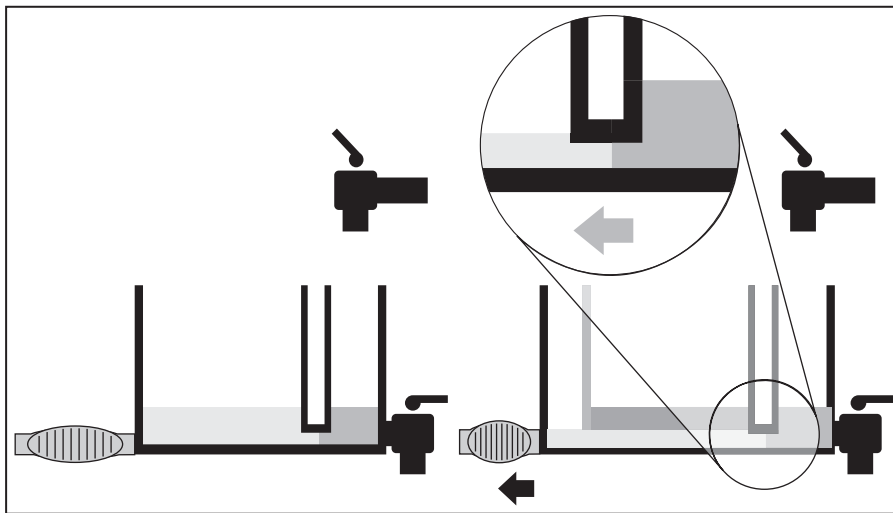


FIGURE 2. Ventilator triggering. The diagram on the left shows the two-compartment model at functional residual capacity. In the diagram on the right, the contraction of inspiratory muscles reduces E_{PC} and P_{PC} falls (black arrow), generating a pressure gradient between compartments. As a consequence, gas flow from the central compartment to the peripheral compartment (gray arrow) reduces V_{CC} and P_{CC} . If deep enough to overcome the trigger threshold, the fall in P_{CC} triggers the ventilator.

(IIE) occurs. The IIE does not result in a change in the volume of the central compartment, so no changes in P_{CC} can be expected. However, because P_{PC} falls (and the pressure gradient between compartments drops), a sudden reduction in expiratory flow can be observed (Fig. 3).

IIEs are the most common type of asynchrony. However, because IIEs result in the stacking of two expirations (without an inspiration in between), they reset end-expiratory volume to a lower level, limiting auto-PEEP.

PHASE ASYNCHRONY

In phase asynchrony there is a mismatch between the start (initial asynchrony) or the end (terminal asynchrony) of the patient's (TI_P) and the ventilator's inspiratory time (TI_V). During initial asynchrony, there is a delay between the start of patient's effort and the start of machine's inspiration. Usually, this is caused by auto-PEEP (patient effort has to overcome auto-PEEP before triggering the ventilator). During terminal asynchrony, TI_P might be shorter or longer than TI_V . If $TI_P < TI_V$, the patient starts to exhale when the airway is still pressurized from ventilator inflow; on pressure-time scalars, P_{CC} shows a sudden increase when the patient activates the expiratory muscles (Fig. 4). If $TI_P > TI_V$, the patient's inspiratory muscles are still active when the ventilator starts expiration, impeding elastic recoil from increasing P_{PC} , and the peak expiratory flow is aborted. If the patient's inspiratory effort is strong enough to invert the pressure gradient between compartments, it could produce a fall in

P_{CC} that will trigger the ventilator (double-triggering) (Fig. 5). In volume-controlled ventilation (VCV) and pressure-controlled ventilation, where TI_V is fixed, double-triggering doubles inspiratory time.

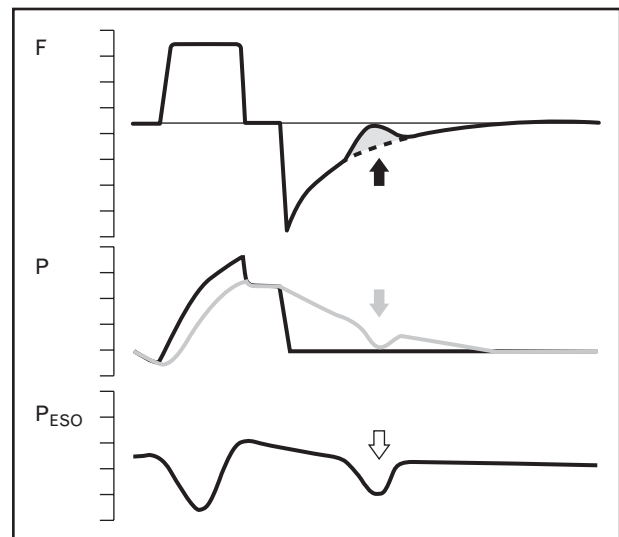


FIGURE 3. Ineffective inspiratory efforts. Flow (upper), P_{CC} (middle; black), P_{PC} (middle; gray), and esophageal pressure (lower)/time scalars during an IIE. The activation of inspiratory muscles reduces P_{ESO} (white arrow) and P_{PC} (gray arrow), but is insufficient to invert the pressure gradient between compartments or to reduce P_{CC} enough to trigger the ventilator. However, the reduction in driving pressure for expiration produces a sudden reduction in expiratory flow (black arrow) that causes the F scalar to deviate from the expected (dotted line). P_{CC} , pressure in the central compartment; P_{ESO} , esophageal pressure.

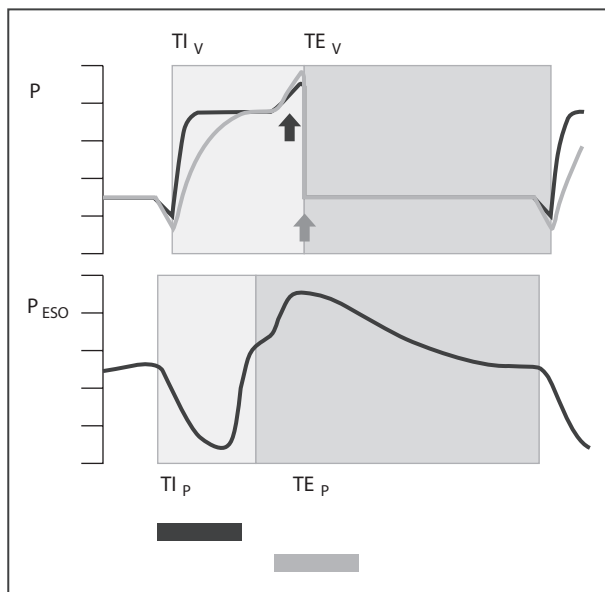


FIGURE 4. Phase asynchrony ($TI_p < TI_v$). When patients arrive at end-inspiration, they expect the airway to be free of resistance and ready to allow expiration. However, if the ventilator's inspiratory time (TI_v) is longer than the patient's inspiratory time (TI_p), the airway is still being pressurized. If the delay in the ending of TI_v is long enough (or is systematic and the patient can anticipate it), the patient activates expiratory muscles, increasing esophageal pressure (P_{ESO}) (down) and the pressure of the peripheral compartment (up; gray). When P_{PC} becomes higher than the pressure of the central compartment (up; black), the patient 'blows' and adds volume to the central compartment, increasing P_{CC} (black arrow) to the point where the ventilator's expiratory valve opens (gray arrow). The bars at the bottom schematize inspiratory muscle (black) and expiratory muscle (gray) activity.

In VCV, it also doubles tidal volume; however, in pressure-controlled ventilation, when inspiratory muscles relax, P_{PC} increases and flow stops, which usually results in a tidal volume that is less than double.

REVERSE TRIGGERING

Originally described 30 years ago [5,6], reverse triggering is a frequently underrecognized form of patient-ventilator dyssynchrony in which the patient's respiratory center is activated in response to a passive insufflation of the lungs [7]. During reverse triggering, the patient's inspiratory effort starts some time after the start of TI_v . These efforts often continue after the end of TI_v , resulting in the amputation of peak expiratory flow or double-triggering (see phase asynchrony above).

FLOW STARVATION

To reduce ventilatory load, ventilators have to provide positive pressure during inspiration. To do that, they have to increase the amount of gas in the central compartment, generating a flow that must be greater than patient inspiratory flow. In VCV, where flow is fixed, if the patient's inspiratory flow is high, it can prevent the ventilator from increasing P_{CC} or even produce a fall in P_{CC} . The slope in the airway pressure scalar reflects the ratio between the flow the ventilator is providing and the flow the patient is demanding. If P_{CC} during inspiration is lower than during expiration, the ventilator actually increases ventilatory load (Fig. 6). In other modes in which flow is allowed to increase in response to the patient's demand, flow starvation is not possible.

PREVALENCE OF ASYNCHRONIES

Studies have found that patient-ventilator asynchrony is common in patients with acute exacerbations of chronic airflow obstruction [8], in general ICU patients [9,10], and during all modes [11]; however, the evaluation periods in all these studies were short. Recently, Blanch *et al.* [12^{**},13] used dedicated software to study the prevalence and time course of five types of asynchronies: IIE, double-triggering, aborted inspirations, and short and long-ventilatory cycling. The median asynchrony index per patient during the entire course of mechanical ventilation was 3.41%. Asynchronies occurred throughout the entire period of mechanical ventilation, around the clock, even in machine-triggered breaths, and were associated with mortality. As in previous studies, IIE was the most common asynchrony in all modes. Identifying asynchronies by using esophageal balloons [3], dedicated software [12^{**},13,14], or electromyography of respiratory muscles [15,16] might help obtain a more accurate picture of the prevalence of asynchronies.

ASYNCHRONIES AND MODES OF VENTILATION

Proper adjustments of flow rate, avoiding double-triggering, avoiding excessive levels of assistance, and promptly switching from assist-control modes to pressure support ventilation (PSV) or proportional modes seem to be related with better patient-ventilator interaction and a reduced risk of ventilator-induced injury to respiratory muscles or lungs [3,7,17,18^{**}].

Vignaux *et al.* [19] studied the prevalence of asynchrony events during invasive-assisted mechanical ventilation in PSV mode and in neurally

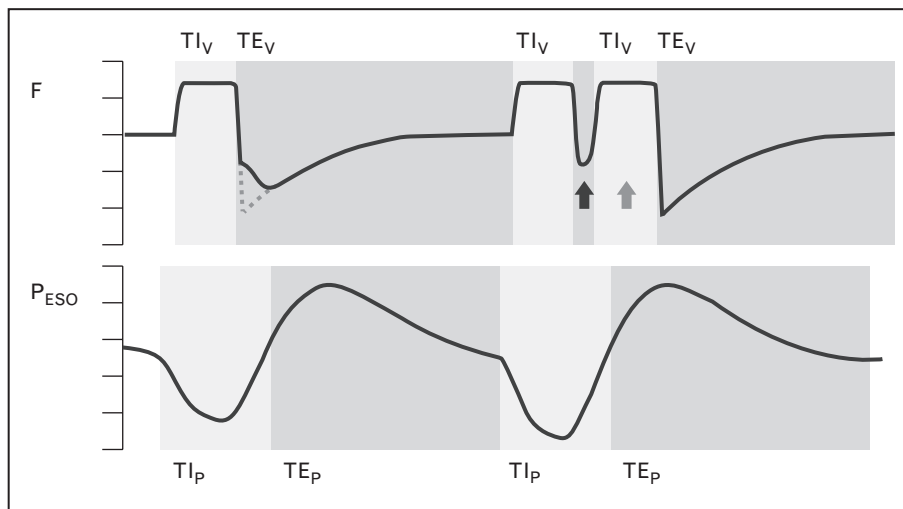


FIGURE 5. Phase asynchrony ($T_{I_p} > T_{I_v}$). If the patient's inspiratory time (T_{I_p}) is longer than the ventilator's inspiratory time (T_{I_v}) ($T_{I_p} > T_{I_v}$), two different consequences can be expected. In the first schematized breath, the persistence of inspiratory muscle activation prevents the increase in the pressure of the peripheral component (P_{PC}) produced by the elastic recoil of the respiratory system, limiting peak expiratory flow and causing the flow trace to deviate from the expected (dotted line). In the second schematized breath, the persistence of the effort inverts the pressure gradient between compartments, drags volume from the central compartment, and can trigger the ventilator a second time without allowing expiration (double-triggering). Qualitatively, the two events are the same; the difference is merely quantitative, depending on the magnitude and duration of the patient's inspiratory effort (in fact, they are often seen together in the same traces).

adjusted ventilator assist (NAVA) in 19 children during 14 h. The most common asynchronies were autotriggering, IIE, and short cycling. Interestingly, these asynchronies were markedly reduced by the

best expiratory trigger setting and further reduced using NAVA. Given that severe asynchrony is associated with longer duration of mechanical ventilation, longer ICU stay, higher tracheostomy rate,

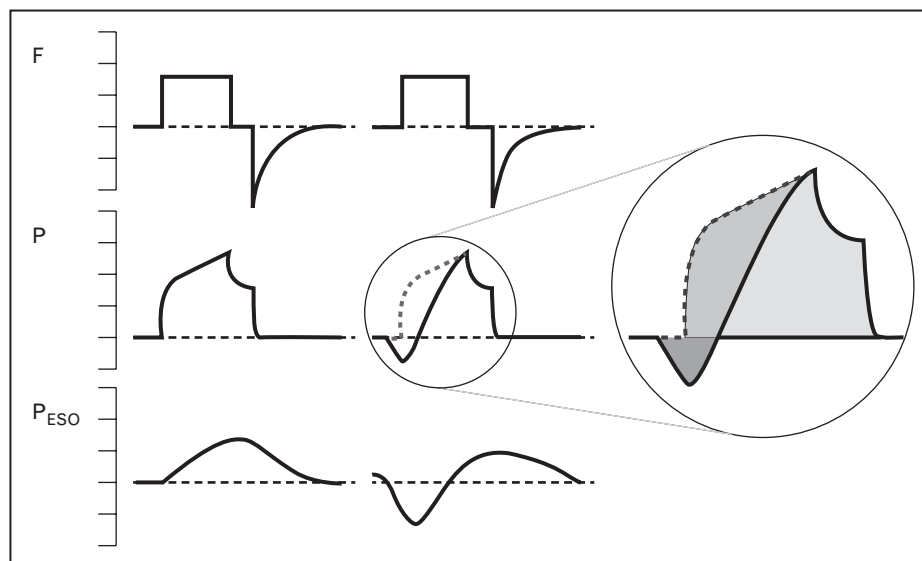


FIGURE 6. Flow starvation and ventilatory load. Volume-controlled ventilation traces during controlled (left) and assisted (right) ventilation. The occurrence of the patient's inspiratory effort results in a deviation of the traces of the P_{CC} from the expected (dotted line). The expanded view of the pressure trace details the work of breathing: the area below the actual P_{CC} trace represents the work provided by the machine (light gray), and the area in between the actual and the expected P_{CC} represents the work done by the patient (middle gray). The dark gray sector in which the inspiratory P_{CC} is lower than the expiratory P_{CC} represents work generated by the ventilator that the patient has to overcome. P_{CC} , pressure of the central component.

and higher mortality, large-scale randomized multicenter trials focused on the impact of asynchronies on morbidity and mortality are warranted in both pediatric and adult patients.

Patient-ventilator asynchronies can occur in all ventilation modes and during both invasive [19] and noninvasive ventilation [20] in anesthesia settings as well as in the ICU [21]. Asynchronies should be corrected by adjusting the ventilator settings; for instance, reducing PSV or inspiratory duration can decrease the incidence of IIE without inducing excessive work of breathing or modifying the patient's respiratory rate [8,22,23]. If asynchronies persist after adjustments, proportional ventilation modes [proportional assisted ventilation (PAV) or NAVA] should be considered [1]. Yonis *et al.* [24] found the asynchrony index in difficult-to-wean patients was lower in NAVA than in PSV. However, another study found that NAVA produced more double-triggering than PSV, probably because of the biphasic appearance of electrical activity of diaphragm signals [24,25]. Schmidt *et al.* [26] found that PSV was less able to prevent hyperinflation because of overassistance and produced more asynchrony than NAVA or PAV. NAVA also improved asynchronies during noninvasive ventilation in children admitted to pediatric intensive care [26].

SEDATION AND ASYNCHRONY GENERATION

Different sedative drugs might affect respiratory patterns and drive, as well as decrease inspiratory muscle effort during mechanical ventilation. Decreased respiratory drive associated with deeper sedation may result in IIE [27,28]. Vaschetto *et al.* [29] found that deep (but not light) propofol sedation increased asynchronies in adults undergoing PSV, but this effect disappeared after ventilation was switched to NAVA. Deeply sedated patients with IIE often do not appear to be asynchronous unless the clinician carefully examines the patient and ventilator waveforms [19]. A failure to appreciate IIE will lead to false conclusions about a patient's respiratory rate. Similarly, Chanques *et al.* [17] found that adapting the ventilator to patient breathing effort (switching to PSV or increasing inspiratory time in assisted VCV) was much more effective in reducing delayed triggering than adjusting the sedation dose.

Asynchronies could be present in deeply sedated patients even when the patient is not triggering the ventilator. Akoumianaki *et al.* [7] found that a VCV or PCV breath can initiate a breathing effort in deeply sedated seemingly apneic patients (reverse

triggering), and reverse triggering was associated with different patterns of respiratory entrainment. Reverse triggering can lead to pliometric contractions of the diaphragm and cytokine release, increased muscle work, and cardiovascular instability. The prevalence of reverse triggering is unknown.

Mechanically ventilated patients can experience two main types of dyspnea: 'air hunger' and 'excessive work of breathing' [29]. In dyspneic patients, the first two actions to consider are optimizing the flow rate and adjusting the dose of ventilation; however, the relationship between dyspnea and asynchronies is poorly understood. In intubated adult patients, Schmidt *et al.* [15] found that dyspnea was less intense under the highest levels of assistance, even though those high levels increased IIE and dynamic hyperinflation. Accordingly, decreasing ventilatory support decreased the prevalence of IIE dramatically, but increased the intensity of dyspnea and use of extra-diaphragmatic inspiratory muscles [30]. Therefore, reducing the level of assistance to correct asynchronies might induce dyspnea, which causes discomfort and may also be associated with negative clinical outcomes [15,30].

ASYNCHRONIES AND OUTCOME

Some studies on asynchronies found that patients with IIE or an asynchrony index higher than 10% had longer duration of mechanical ventilation, had longer ICU and hospital stays, and were less likely to be discharged home [9,10]. Blanch *et al.* [12] examined the effects of asynchronies on outcomes in a pilot study in 50 mechanically ventilated patients. Using software that continuously records airflow, airway pressure, and tidal volume from admission until liberation from the ventilator or death, these authors grouped patients according to whether their asynchrony index was lower or higher than 10%. They found similar reintubation and tracheostomy rates between the two groups, but those with an asynchrony index higher than 10% had significantly higher rates of both ICU and hospital mortality, as well as a trend toward longer duration of mechanical ventilation. Whether asynchronies increase mortality or are just a biomarker of illness severity remains to be determined; regardless, it seems reasonable to make diagnosing and correcting asynchronies a priority throughout the course of mechanical ventilation.

CONCLUSION

Asynchronies are common but underrecognized. Assessing patient-ventilator interaction and detecting asynchronies requires both careful examination

of the patient at bedside and thorough observation of waveforms on the ventilator screen. Asynchronies can occur during all phases of the respiratory cycle, including breath initiation, flow and pressure delivery, the transition from inspiration to expiration, and throughout expiration.

Understanding how asynchronies develop can help physicians deal with this common problem.

Patients on mechanical ventilation need to be able to breathe comfortably, without fighting with the ventilator to avoid excessive work of breathing and avoiding dyspnea.

Acknowledgements

None.

Financial support and sponsorship

ISCIII PI09/91074, PI13/02204, CIBER Enfermedades Respiratorias, Fundación Mapfre, Fundació Parc Taulí, Plan Avanza TSI-020302-2008-38, MCYIN and MITYC (Spain).

Conflicts of interest

L.B. and G.M. are inventors of one Corporació Sanitària Parc Taulí owned US patent: 'Method and system for managed related patient parameters provided by a monitoring device,' US Patent No. 12/538,940. L.B., G.M., and U.L. own stock options of BetterCare S.L., which is a research and development spin off of Corporació Sanitària Parc Taulí (Spain).

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