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Know Your Ventilator to Beat the Leak

One of the significant advances in respiratory critical care over the past 20 years has been the emergence of noninvasive ventilation (NIV). Evidence supporting the use of NIV is strongest for COPD exacerbation and acute cardiogenic pulmonary edema. For these conditions, the use of NIV decreases the need for endotracheal intubation and affords a survival benefit.[1]

Although the use of NIV has increased, it remains underused.[2-4] Moreover, a significant number of patients fail on NIV and go on to intubation.[5] Factors that contribute to NIV failure include poor patient selection, progression of the underlying disease process, clinician inexperience, and lack of appropriate equipment.[6] Several surveys have identified lack of appropriate equipment as an impediment to the implementation of NIV.[3,4] Inappropriate equipment can refer to the choice of interface or the choice of ventilator.

The interface distinguishes NIV from invasive ventilation. A variety of interfaces are available, and these have improved in variety and quality in recent years. Unlike invasive ventilation where the airway is sealed, leaks of variable degree occur with NIV. Leaks during NIV can be a significant contributor to patient-ventilator asynchrony. Large leaks can also compromise inspiratory and expiratory pressures and tidal volume delivery.[7] The most common asynchrony during invasive ventilation is missed trigger. However, the most common asynchrony during NIV is auto-triggering caused by leaks and the inability of the ventilator to distinguish the patient's trigger signal within the noise of the leak.

Three categories of ventilators can be used for NIV: bilevel ventilators, critical care ventilators, and intermediate ventilators.[8] Bilevel ventilators use a single-limb circuit with a passive exhalation port. Critical care ventilators have separate inspiratory and expiratory limbs with an active exhalation valve. Intermediate ventilators are typically used for patient transport or home ventilation; they may have a passive exhalation port or an active exhalation valve. Ventilators that use an active exhalation valve have traditionally been leak intolerant. However, the newer generation of critical care ventilators feature NIV modes to compensate for leaks. With bilevel ventilators, leaks comprise an intentional leak through the passive exhalation port as well as unintentional leaks that may be present in the circuit or at the interface.

Several recent studies evaluated the ability of critical care ventilators to compensate for leaks. In a bench study, Vignaux et al[9] found that leaks interfere with the function of ICU ventilators and that NIV modes can correct this problem but with wide variations between ventilators. In a follow-up clinical study, Vignaux et al[10] reported that NIV modes on ICU ventilators decreased the incidence of asynchronies typically associated with leaks. However, there was no change in overall asynchrony perhaps because the correction of one asynchrony leads to an increase in another. In a bench study, Ferreira et al[11] found that in the presence of leaks, most ICU ventilators required adjustments to maintain synchrony with a lung model.

With this background, what can we say about the article by Carteaux et al[12] in this issue of *CHEST* (see page 367)? First, confirmation of the laboratory findings in a clinical study is unique and gives the results clinical meaning. The laboratory study uses a clinically relevant simulation of breathing patterns and leaks but is limited by using only a single set of lung mechanics, only one breathing pattern, and only one inspiratory and expiratory leak. Even here, the authors should be congratulated for modeling a system in which the inspiratory leak is greater than the expiratory leak, which is more indicative of the clinical situation than the fixed leak used in other studies. Moreover, any limits of the bench trial can be overlooked because of the clinical study, which enrolled subjects with a variety of respiratory mechanics, breathing patterns, and leaks. A criticism of the clinical study is the use of the BiPAP Vision ventilator (Philips Respironics), which is no longer commercially available and has been replaced with the V60 ventilator. However, evidence from the bench study suggests that the performance of the V60 is at least as good, if not better, than the Vision. In the clinical study, Carteaux et al[12] used an oronasal mask, so the results may not be transferrable to other interfaces where mouth leak is likely to occur.

The results reported by Carteaux et al[12] have clinical consequence. As a group, the bilevel ventilators promoted better patient-ventilator synchronization than critical care and transport ventilators, even when the NIV mode was used. Most of the bilevel ventilators studied demonstrated synchronization in the presence of leaks equivalent to that of the critical care ventilators in the absence of leaks. The response of critical care ventilators and transport ventilators to the presence of leaks was not consistent; thus, the use of each of these ventilators for NIV should be considered individually. Generally, the NIV modes of critical care and transport ventilators improve synchrony in the presence of leaks, but these modifications typically fall short of matching performance of the bilevel devices.

Patient-ventilator asynchrony during NIV is related to the underlying disease process and the presence of leaks.[7] The following two approaches to dealing with leaks during NIV are important: (1) minimizing the leak and (2) compensating for the leak. Minimizing the leak relates to choosing an appropriate interface and appropriate fitting of the interface. Regarding leak compensation, the results of Carteaux et al[12] suggest that as a group, bilevel ventilators outperform critical care ventilators. However, the NIV modes on some critical care ventilators improve synchrony in the presence of leaks. The NIV operation of most critical care ventilators includes an automated leak compensation algorithm and disabling of nuisance alarms. Some critical care ventilators also allow clinicians to make adjustments to improve synchrony. These embellishments include an adjustable trigger type and sensitivity, adjustable flow cycle criteria with pressure support ventilation, and a maximum inspiratory time during pressure support ventilation.

We can speculate about the mechanism whereby bilevel ventilators compensate better for leaks than many critical care ventilators. This might relate to the intentional leak incorporated into the design of bilevel ventilators. We wonder whether it might be easier to design leak compensation algorithms when the starting point is a circuit with a leak rather than a gas delivery system originally designed to function leak free. However, engineers have been able to design NIV modes into some critical care ventilators that compensate well for leaks.[11,12]

Whether the use of a ventilator with good leak compensation improves the success of NIV is not known. To test this hypothesis would be arduous. A sample size of >500 subjects would be required to demonstrate a clinically important 10% reduction in failure rate. Moreover, given that patient-ventilator synchrony is widely accepted as good,[13,14] the ethics of such a study is questionable. A ventilator should be selected with good leak compensation when applying NIV. Other ventilator performance factors may also be considered when choosing a ventilator for NIV in acute care, including accurate inspired oxygen delivery, accurate volume monitoring, and graphics display. Given the available evidence, the best choice for maximizing patient-ventilator synchrony usually will be a bilevel ventilator but could be one of the few critical care ventilators with an NIV mode that offers good leak compensation.

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CHEST

Original Research

CRITICAL CARE

Patient-Ventilator Asynchrony During Noninvasive Ventilation

A Bench and Clinical Study

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Background: **Different kinds of ventilators are available to perform noninvasive ventilation (NIV) in ICUs. Which type allows the best patient-ventilator synchrony is unknown. The objective was to compare patient-ventilator synchrony during NIV between ICU, transport—both with and without the NIV algorithm engaged—and dedicated NIV ventilators.**

Methods: **First, a bench model simulating spontaneous breathing efforts was used to assess the respective impact of inspiratory and expiratory leaks on cycling and triggering functions in 19 ventilators. Second, a clinical study evaluated the incidence of patient-ventilator asynchronies in 15 patients during three randomized, consecutive, 20-min periods of NIV using an ICU ventilator with and without its NIV algorithm engaged and a dedicated NIV ventilator. Patient-ventilator asynchrony was assessed using flow, airway pressure, and respiratory muscles surface electromyogram recordings.**

Results: **On the bench, frequent auto-triggering and delayed cycling occurred in the presence of leaks using ICU and transport ventilators. NIV algorithms unevenly minimized these asynchronies, whereas no asynchrony was observed with the dedicated NIV ventilators in all except one. These results were reproduced during the clinical study: The asynchrony index was significantly lower with a dedicated NIV ventilator than with ICU ventilators without or with their NIV algorithm engaged (0.5% [0.4%-1.2%] vs 3.7% [1.4%-10.3%] and 2.0% [1.5%-6.6%], *P* < .01), especially because of less auto-triggering.**

Conclusions: **Dedicated NIV ventilators allow better patient-ventilator synchrony than ICU and transport ventilators, even with their NIV algorithm. However, the NIV algorithm improves, at least slightly and with a wide variation among ventilators, triggering and/or cycling off synchronization.**

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Abbreviations: AI = asynchrony index; ICUniv− = ICU ventilator with the noninvasive ventilation algorithm turned off; ICUniv+ = ICU ventilator with the noninvasive ventilation algorithm turned on; NIV = noninvasive ventilation; NIVv = dedicated noninvasive ventilation ventilator; PEEP = positive end-expiratory pressure; TD = triggering delay; Tiexcess = insufflation time in excess; Tisim = simulated active inspiration time; Tivent = time between the beginning of a simulated inspiratory effort and the end of the ventilator's insufflation

Noninvasive ventilation (NIV) has become a standard of care for the management of many causes of acute respiratory failure.[1-3] During NIV, the unavoidable presence of leaks around the mask[4] can interfere with the ventilator performance. Expiratory leaks can mimic an inspiratory effort for the ventilator, leading to auto-triggering[5]; and inspiratory leaks can mimic a sustained inspiration, leading to delayed cycling.[6] Not surprisingly, patient-ventilator asynchronies have, therefore, been reported to occur with a high incidence during NIV in critically ill patients.[7]

Different ventilators are now used to conduct NIV in ICU: ICU ventilators,[2] dedicated NIV ventilators,[8] and also transport ventilators when needed.[9-11] Most ICU ventilators were initially built to work without any leak, at least in adults, and are prone to be disrupted

For editorial comment see page 274

by the presence of leaks during NIV.[12] To address this issue, manufacturers have implemented NIV algorithms (so called "NIV modes") on the latest generation of ICU ventilators to compensate and better manage the leaks. Both bench[12,13] and clinical[14] studies assessing the performance of NIV algorithms on ICU ventilators have shown mixed results, partly due to large variations among the ventilators, making it difficult to draw an overall conclusion. Dedicated NIV ventilators stem from bilevel home ventilator technology, which has been particularly oriented toward leakage management and comfort. Some bench studies suggested that a dedicated NIV ventilator could produce better performance and synchronization than ICU ventilators in the presence of leaks.[13,15] However, no bench model concerning ventilator synchronization during NIV has been clinically validated, raising the question of their clinical relevance in critically ill patients. Consequently, the kind of ventilator that allows the best synchronization during NIV in the ICU is still unknown. In some areas, NIV is mainly delivered with dedicated NIV ventilators,[8] whereas in other countries ICU ventilators are almost exclusively preferred,[2] and this distribution reflects local habits rather than an evidence-based approach.

The purpose of this study was to compare patient-ventilator synchronization during NIV using ICU and transport ventilators with or without their NIV algorithm, and finally dedicated NIV ventilators. We designed a bench model to assess ventilator synchronization with a simulated inspiratory effort in different leak conditions, simulating the different challenges to be faced by the ventilator. Furthermore, we conducted a clinical study in critically ill patients to compare the incidence of patient-ventilator asynchrony between ICU ventilators with and without their NIV algorithm engaged, and a dedicated NIV ventilator.

Materials and Methods

This study involved a bench part and a clinical part. An extensive description of both the bench and clinical protocols is provided in e-Appendix 1.

Bench Study

All 19 ventilators tested are reported in Table 1 and included eight ICU ventilators, five transport ventilators, and six dedicated NIV ventilators. The test lung, an Active Servo Lung 5000 (ASL 5000; IngMar Medical, Ltd), was used to simulate a moderate inspiratory effort in the presence of an 80 mL/cm H_2O respiratory system compliance and 10 cm H_2O/L/s resistance to mimic a mild obstructive condition. The simulated respiratory rate was 15 breaths/min and the inspiratory time 0.8 s. Three leak conditions were generated (Fig 1A): absence of leak, continuous leak (to reveal triggering asynchronies during expiratory leak), and inspiratory leak (to reveal cycling-off asynchronies). For this last experiment, the leak started at a pressure corresponding to a water column of 7 cm H_2O, as detailed in e-Appendix 1. The inspiratory leak was characterized by a nonlinear pressure-flow relationship with a flow varying from 0 to 22 L/min for a pressure from 7 to 15 cm H_2O. The continuous (expiratory) leak was characterized by a flow of 16 L/min at 5 cm H_2O pressure.

Ventilators were set in pressure support ventilation, with a pressure support level at 15 cm H_2O and a positive end-expiratory pressure (PEEP) at 5 cm H_2O. ICU and transport ventilators were tested with and without their NIV algorithm engaged, except the Elisee 250, whose NIV algorithm cannot be turned off. Data were acquired at 512 Hz from ASL 5000 and stored in a laptop computer for subsequent analysis (Acqknowledge 3.7.3; BIOPAC Systems, Inc). Inspiratory triggering synchronization was assessed using the triggering delay, the triggering pressure-time product, and the incidence of auto-triggering, expressed as a percentage and calculated as follows: auto-triggering incidence (%) = (auto-triggered cycles/total ventilator cycles) × 100. The pressurization was assessed using the pressure-time product at 300 milliseconds. Cycling synchronization was assessed by determining ventilator insufflation time in excess (TIexcess), expressed as a percentage and calculated as follows: $TIexcess = [(TIvent - TIsim)/TIsim] \times 100$, where TIvent is the time between the beginning of the simulated inspiratory effort and the end of the ventilator's insufflation, and TIsim the simulated active inspiration time. Delayed cycling was defined by a $TIvent \geq 2\ TIsim$ and premature cycling by a $TIvent \leq 2/3\ TIsim$.

Clinical Study

A prospective, randomized, crossover study was conducted in two university hospital ICUs. The protocol was approved by the ethics committee CPP-Ile-de-France IX (number: 08-021), and informed consent was obtained from all patients. We included 15 patients in the ICU receiving NIV in pressure support ventilation mode with PEEP via a standard oronasal mask. The ventilator settings chosen by the clinician in charge of the patient were kept identical for the study. Three consecutive NIV sessions were applied in a random order, using the same oronasal mask: (1) use of an ICU ventilator whose NIV algorithm has been turned off

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Table 1—*Bench Study: Characteristics of the ICU, Transport, and NIV Ventilators Tested in the Bench Study*

Ventilator	Supplier	Use	Gas Source	Circuit	NIV Mode	ET Range	IT Range
Avea	CareFusion	ICU	Pressurized	Double	Manual	5%-45%	0.1-20 L/min
Engstrom	GE Healthcare	ICU	Pressurized	Double	Manual	5%-50%	1-9 L/min; −1 to −10 cm H_2O
Evita XL	Dräger	ICU	Pressurized	Double	Automatic	Automatic	0.3-15 L/min
G5	Hamilton Co	ICU	Pressurized	Double	Manual	5%-70%	0.5-15 L/min
PB840[a]	Covidien	ICU	Pressurized	Double	Manual	1%-80%	0.2-20 L/min
Servo-i	MAQUET GmbH & Co KG	ICU	Pressurized	Double	Manual	1%-40%	0%-100%; −20 to 0 cm H_2O
V500	Dräger	ICU	Pressurized	Double	Automatic/manual	Automatic; 5%-70%	Automatic; 0.2-15 L/min
Vela	CareFusion	ICU	Turbine	Double	Manual	5%-40%	1-8 L/min
Elisee 250	ResMed	Transport	Turbine	Double	Automatic/manual	Automatic; 1%-6%	Automatic
Medumat	Weinmann Medical Technology	Transport	Pneumatic	Single	Automatic	5%-50%	1-15 L/min
Oxylog 3000	Dräger	Transport	Pneumatic	Single	Automatic	Automatic	Automatic
Supportair	Covidien	Transport	Turbine	Single	Manual	5%-95%	01-05
T1	Hamilton Co	Transport	Turbine	Double	Manual	5%-80%	1-20 L/min
BiPAP Vision	Philips Respironics	NIV	Turbine	Single	Automatic	Automatic	Automatic
Carina	Dräger	NIV	Turbine	Single	Automatic	Automatic	Analogical (sensible/normal)
Trilogy 100	Philips Respironics	NIV	Turbine	Single	Automatic	Automatic	Automatic
V60	Philips Respironics	NIV	Turbine	Single	Automatic	Automatic	Automatic
Vivo 40	Breas	NIV	Turbine	Single	Automatic	Automatic	Automatic
VPAP 4	ResMed	NIV	Turbine	Single	Automatic	Automatic	Automatic

ET = expiratory trigger, expressed as a percentage of peak inspiratory flow; IT = inspiratory trigger; NIV = noninvasive ventilation.
[a]Version comprising both an NIV mode and leak compensation.

(ICUniv−), (2) use of an ICU ventilator whose NIV algorithm has been turned on (ICUniv+), and (3) use of a dedicated NIV ventilator (NIVv). Each session was 20 min long. ICU ventilators used in the clinical study were: Evita XL or EVITA 4 (Dräger) (n = 12) and Engstrom Carestation (GE Healthcare) (n = 3). The dedicated NIVv was the BiPAP Vision (Philips Respironics). We selected this ventilator because it is widely used in ICUs using NIV ventilators and also because it has been used in many clinical and physiologic studies concerning NIV. Flow, airway pressure, and diaphragmatic and inspiratory neck muscles surface electromyograms were continuously recorded throughout the three NIV sessions and stored in a laptop for subsequent analysis, as described in e-Appendix 1. All tracings were analyzed by one investigator (G. C.). The methodology used was previously described without noticing any interobserver difference,[7,14] and allowed the quantification of major asynchrony events (ineffective triggering, double-triggering, auto-triggering, premature cycling, and delayed cycling) (Fig 1B). A global asynchrony index (AI), expressed as a percentage, was computed as follows[16]: AI (%) = (number of asynchronies/[ineffective breaths + ventilator cycles]) × 100.

Statistics

Statistical analyses were performed with Statistical Package for the Social Sciences (version 16.0, SPSS). Continuous data are expressed as the median (25th-75th percentile). In both the bench and clinical study, the variables did not display a normal distribution, so only nonparametric tests, detailed in e-Appendix 1, were used. A *P* value of < 0.05 was considered statistically significant.

Results

Bench Study

Triggering Delay: The ICU and transport ventilators with their NIV algorithm turned off in the absence of leaks exhibited a total triggering delay (TD) of 117 milliseconds (99-131 milliseconds) and 143 milliseconds (114-174 milliseconds), respectively (*P* = .37) (Fig 2).The addition of inspiratory leaks did not significantly modify these values except for the Engstrom, G5, and T1, which had an increased TD, and the Medumat, which showed a reduced TD. Turning on the NIV algorithm while maintaining inspiratory leaks led to different behaviors among ICU and transport ventilators: TD significantly increased for five ventilators (Medumat, Evita XL, Servo-i, V500, Supportair), decreased for three (Engstrom, PB840, T1), and was not modified for the others. In this last condition, the TD of ICU, transport, and dedicated NIV ventilators were 107 (83-120), 126 (112-190), and 125 (102-145) milliseconds, respectively (*P* > .05 for every intergroup comparison). When NIV algorithms were used in the presence of inspiratory leaks, six ICU ventilators (Avea, Engstrom, PB840, Servo-i, V500, Vela), two transport ventilators (Elisee 250, Supportair), and two NIV ventilators (BiPAP Vision, V60) exhibited a TD < 117 milliseconds (ie, the median TD of ICU ventilators with the NIV algorithm turned off in absence of leaks). The additional assessment of the triggering pressure-time product is reported in e-Appendix 1 and e-Figure 1.

Auto-Triggering: Occurrence of auto-triggering was assessed during the presence of continuous leaks (Fig 3). Expiratory leaks induced an incidence of auto-triggering between 0% and 100% among ICU and transport ventilators when their NIV algorithm was

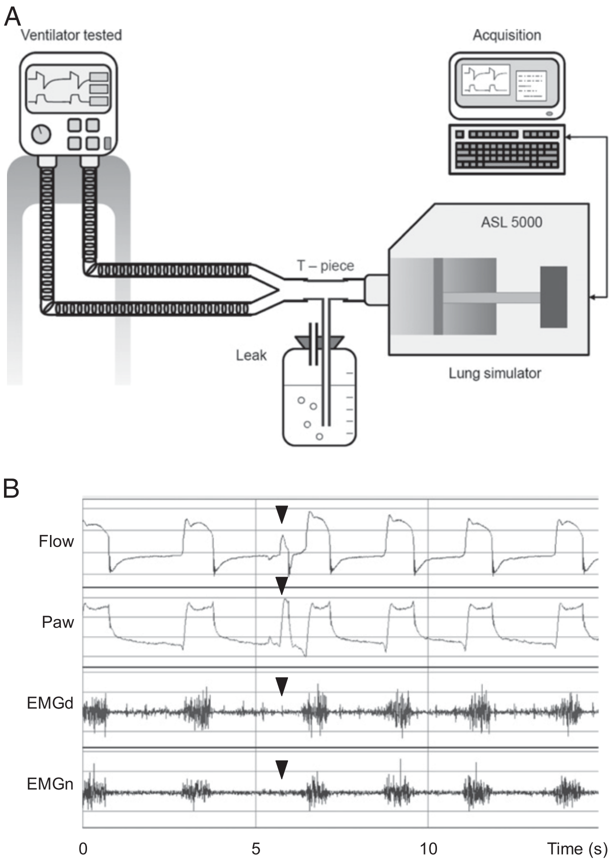

FIGURE 1. Experimental protocols. A, Bench study experimental design. To experimentally reproduce noninvasive ventilation (NIV) conditions with calibrated leaks, we placed a T-piece between the ASL5000 (lung simulator) and the ventilator circuit. Three situations were generated: no leak, in which the free extremity of the T-piece was closed; inspiratory leak, in which the free extremity of the T-piece was connected to a tube immersed in a 7 cm H_2O column, allowing leaks to occur during insufflation only when the pressure in the circuit was higher than the height of the water column; and continuous leak using the same experimental assembly without water in the receptacle, allowing leaks to occur during the whole respiratory cycle. B, Clinical study representative record of an auto-triggered cycle. EMGd = diaphragmatic electromyogram; EMGn = neck muscles electromyogram; Paw = airway pressure.

turned off. The activation of the NIV algorithm led to a heterogeneous response among these ventilators: the incidence of auto-triggering fell to or remained at 0% for three ICU ventilators (PB840, Servo-i, V500) and three transport ventilators (Elisee 250, Supportair, T1), was not modified for one ICU ventilator (Avea), and decreased slightly for the other ICU and transport ventilators. By contrast, no auto-triggering occurred with any NIV ventilator.

Cycling and Insufflation Time: ICU and transport ventilators without their NIV algorithm in the absence of leaks exhibited a Tɪexcess of 32% (30%-34%) and 49% (24%-75%), respectively ($P = .93$) (Fig 4). Inspiratory leaks led to a significant increase in insufflation time for six ICU ventilators (Avea, Engstrom, G5, PB840, Servo-i, Vela) and all four transport ventilators whose NIV algorithm can be turned off. The NIV algorithms generally minimized the insufflation time, which remained significantly higher than without leaks for only two ICU ventilators (Avea, G5) and three transport ventilators (Oxylog 3000, Supportair, T1). With NIV algorithm and inspiratory leaks, ICU, transport, and dedicated NIV ventilators exhibited a Tɪexcess of 34% (29%-43%), 37% (25%-43%), and 37% (18%-49%), respectively. In this condition, the Tɪexcess was < 32% for four ICU ventilators (Engstrom, Evita XL, Servo-i, V500), two transport ventilators (Medumat, Supportair), and three dedicated NIV ventilators (BiPAP Vision, Trilogy 100, V60).

During inspiratory leaks when NIV algorithms were turned off, delayed cycling occurred with four ICU ventilators (Avea, G5, PB840, Vela) and three transport ventilators (Medumat, Oxylog 3000, T1). The activation of the NIV algorithm eliminated delayed cycling for all of these ventilators but one (G5). However, the NIV algorithm of the Servo-i overcorrected the Tɪexcess (−4%). Concerning dedicated NIV ventilators subjected to inspiratory leaks, one of them (VIVO 40) exhibited delayed cycling.

We also assessed the ability of the ventilators to pressurize the airway in the first 300 milliseconds with or without leaks. For the sake of simplicity, these data are only shown in e-Appendix 1 and e-Figure 2.

Clinical Study

Fifteen patients of median age 68 years old (61-76 years) were included, 13 men and two women, with a median BMI of 24 kg/m² (20-27 kg/m²). At inclusion, Simplified Acute Physiology Score II was 47 (32-62) and arterial blood gas levels were as follows: pH = 7.36 (7.29-7.42), Pa_{CO_2} = 48 mm Hg

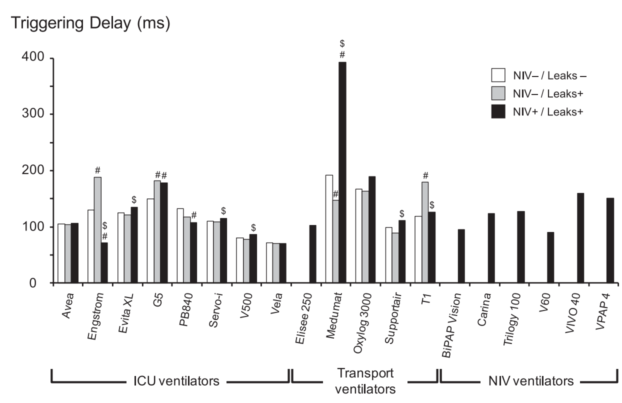

FIGURE 2. Bench study triggering delay. Representation of the triggering delay for ICU and transport ventilators with their NIV algorithm turned off in the absence of any leak (NIV−/Leaks−, white bars), then in the presence of inspiratory leaks (NIV−/Leaks+, gray bars); and for ICU and transport ventilators with their NIV algorithm turned on as well as for NIV ventilators in the presence of inspiratory leaks (NIV+/Leaks+, black bars). # $P < .05$ vs NIV−/Leaks−. \$ $P < .05$ vs NIV−/Leaks+. See Figure 1 legend for expansion of abbreviation.

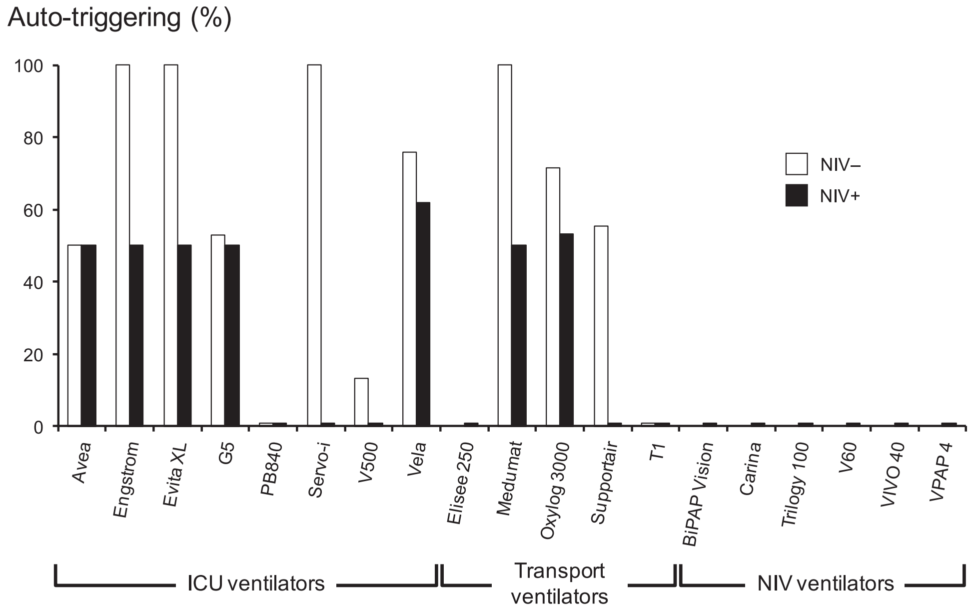

FIGURE 3. Bench study incidence of auto-triggering during continuous leaks. Incidence of auto-triggering is represented as a percentage of the total ventilator cycles ([Auto-triggered cycles]/[total ventilator cycles] × 100) during continuous leaks with ICU and transport ventilators without NIV algorithm (NIV−, white bar) and with the same ventilators with the NIV algorithm turned on, and with NIV ventilators (NIV+, black bar). The activation of the NIV algorithm on ICU and transport ventilators unequally led to an improvement in inspiratory triggering synchronization, whereas no auto-triggering occurred with any NIV ventilator. See Figure 1 legend for expansion of abbreviation.

(41-63 mm Hg), $PaO_2/FIO_2 = 206$ mm Hg (183-252 mm Hg). Patients had spent one median day (0.3-1.0 days) under NIV before inclusion. Indications for NIV were the following: to avert respiratory failure after extubation (n = 5), exacerbation of COPD (n = 4), cardiogenic pulmonary edema (n = 3), community-acquired pneumonia (n = 2), and post thoracic surgery (n = 1). Eight patients (53%) had COPD. Ventilator settings were pressure support level = 10 cm H_2O (8-11 cm H_2O), PEEP = 4 cm H_2O (4-5 cm H_2O), inspiratory trigger = 1 L/min (1-2 L/min), pressurization slope = 100 milliseconds (100-100 milliseconds), and $FIO_2 = 40\%$ (30%-50%). There was no significant difference between the three NIV sessions regarding ventilator settings, respiratory parameters, and the measured level of leaks (Table 2). ICU ventilators used in the clinical study had a similar response to leaks as during the bench study in terms of asynchrony: a propensity to auto-triggering with expiratory leaks, partially corrected by the NIV algorithm, but no delayed cycling with the NIV algorithm and inspiratory leaks (Figs 3, 4).

Patient-Ventilator Synchrony: The asynchrony index (AI) did not significantly differ when using ICU ventilators without (ICUniv−) or with (ICUniv+) their NIV algorithm engaged, 3.7% (1.4%-10.3%) vs 2.0% (1.5%-6.6%), respectively, $P = .118$. By contrast, AI was significantly lower with NIVv (0.5% [0.4%-1.2%]) than with both ICUniv− and ICUniv+ ($P = .001$ for both comparisons) (Fig 5). The incidence of each asynchrony during the three NIV sessions is represented in Figure 6. Auto-triggering had the highest incidence. The incidence of auto-triggering, however, was significantly lower with NIVv than with ICUniv− and ICUniv+, 0.1/min (0.1-0.1/min) vs 0.5/min (0.1-1.1/min) and 0.3/min (0.1-1.2/min), $P < .001$, and the proportion of patients who exhibited a high incidence of auto-triggering (> 1/min) was significantly lower with NIVv than with ICUniv− and ICUniv+ (Table 3). Four patients (27%) had an AI > 10% with ICUniv−, two (13%) with ICUniv+, and none with NIVv ($P = .091$). The level of leaks throughout the clinical study was noticeably high in these two last patients (14 and 16 L/min, respectively). The proportion of patients who exhibited at least one asynchrony with a high incidence (> 1/min) was significantly higher with ICUniv− and ICUniv+ than with NIVv (Table 3).

Discussion

To our knowledge, this study is the first to compare patient-ventilator synchronization during NIV between ICU, transport, and dedicated NIV ventilators, with both a bench and a clinical evaluation. The observations made with these two approaches were consistent, offering a strong validation of the bench model, a logical explanation for the clinical data, and

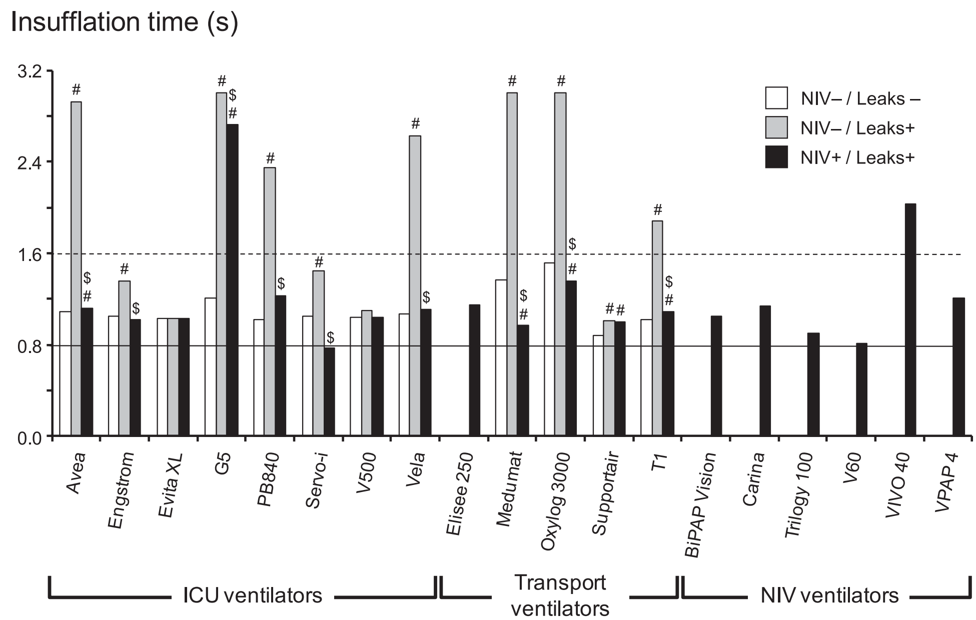

FIGURE 4. Bench study on the effect of inspiratory leaks on insufflation time. Representation of the insufflation time for ICU and transport ventilators without their NIV algorithm in the absence of leak (NIV−/Leaks−, white bars), then in the presence of inspiratory leaks (NIV−/Leaks+, gray bars); and for ICU and transport ventilators with their NIV algorithm turned on as well as for dedicated NIV ventilators in the presence of inspiratory leaks (NIV+/Leaks+, black bars). The simulated inspiratory time was 0.8 s (solid line). When insufflation time reached 1.6 s (dotted line) it corresponded to delayed cycling. For ICU and transport ventilators, the introduction of inspiratory leaks led to an increase in insufflation time when the NIV algorithm was turned off. This prolongation of insufflation due to leaks was partly and unequally minimized by the NIV algorithm. #$P < .05$ vs NIV−/Leaks−. \$$P < .05$ vs NIV−/Leaks+. See Figure 1 legend for expansion of abbreviation.

lending strength to the main results of this study, which are:

- In NIV conditions, most dedicated NIV ventilators allowed better patient-ventilator synchronization than ICU and transport ventilators, even when the NIV algorithm was engaged, especially regarding the risk of auto-triggering.
- Most of the dedicated NIV ventilators exhibited a synchronization performance in the presence of leaks equivalent to that of the ICU ventilators in absence of leaks.
- Synchronization performance in the presence of leaks remains heterogeneous among ICU as well as transport ventilators, and each machine should be considered individually.
- The NIV algorithm usually improved, at least slightly, the triggering and/or cycling synchronization of ICU and transport ventilators in the presence of leaks.

Table 2—*Clinical Study: Main Respiratory Parameters*

Respiratory Parameters	ICUniv−	ICUniv+	NIVv	*P* Value
RRp, per min	29 (22-31)	27 (22-31)	26 (24-30)	.982
TIp, ms	780 (599-914)	674 (558-957)	749 (629-923)	.057
TIexcess, %	14 (4-24)	12 (6-23)	13 (11-21)	.344
VTE, mL	467 (269-633)	465 (322-548)	487 (278-539)	.931
VTE, mL/kg	6.5 (4.3-9.4)	6.9 (4.6-8.3)	7.0 (4.6-9.0)	.797
V̇E, L/min	11.5 (8.7-15.5)	10.3 (9.2-16.7)	10.6 (8.6-14.0)	.683
Leaks, L/min	6.3 (4.3-10.8)	6.2 (2.6-12.1)	7.3 (3.0-11.7)	.947
Leaks, % V̇E	55 (39-101)	47 (26-113)	81 (16-121)	.612

Main respiratory parameters recorded throughout the three NIV sessions during the clinical study. ICUniv− = NIV session using an ICU ventilator whose NIV algorithm has been turned off; ICUniv+ = NIV session using an ICU ventilator whose NIV algorithm has been turned on; NIVv = NIV session using a dedicated NIV ventilator; RRp = patient's respiratory rate measured with the use of the electromyogram signal; TIexcess = percentage of insufflation time that exceeds the neural inspiratory time; TIp = patient's neural inspiratory time; V̇E = minute ventilation; VTE = expired tidal volume. See Table 1 legend for expansion of other abbreviation.

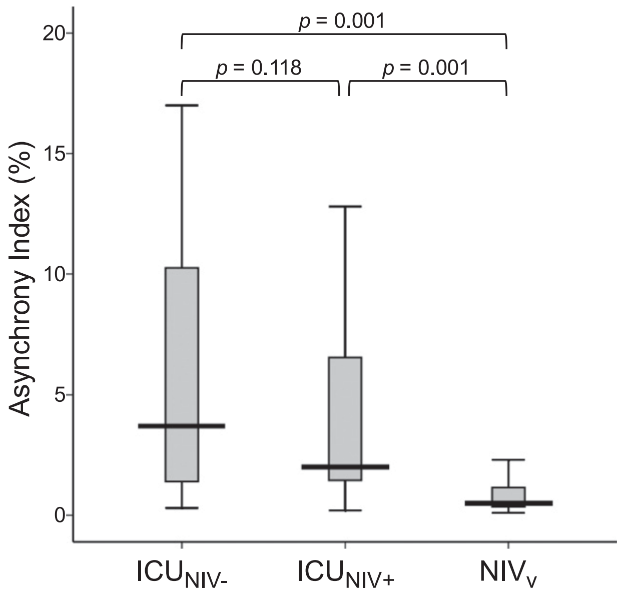

FIGURE 5. Clinical study asynchrony index during the three NIV sessions. The box plots represent the asynchrony index (thick horizontal bar: median; extremities of the boxes: 25th and 75th percentiles; thin horizontal bars: fifth and 95th percentiles) during each 20-min NIV session: ICU_{NIV-}, ICU_{NIV+}, and NIV_V. The asynchrony index was significantly lower with NIV_V than with ICU_{NIV-} and ICU_{NIV+}. ICU_{NIV-} = ICU ventilator with NIV algorithm turned off; ICU_{NIV+} = ICU ventilator with NIV algorithm turned on; NIV_V = dedicated NIV ventilator. See Figure 1 legend for expansion of abbreviation.

Patient-Ventilator Interactions During NIV

Patient-ventilator asynchrony is frequent during both invasive[16,17] and noninvasive[7,14] mechanical ventilation. However, the respective proportion of each type of major asynchrony markedly differs between these two techniques. During invasive mechanical ventilation, ineffective effort represents the most prevalent asynchrony.[16,18] Its occurrence is largely favored by overassistance and can frequently be avoided by reducing the amount of support both in terms of tidal volume and inspiratory time.[19,20] By contrast, during NIV, additional asynchronies, especially auto-triggering and delayed cycling, are induced by the presence of leaks around the mask[4,7] and reflect more the ventilator's ability to manage leaks than the settings chosen by the clinician. Our bench study showed a wide variation in this ability among ICU ventilators and their NIV algorithms, which is consistent with previous bench studies.[12,13] More interestingly, our bench results were also well reproduced during our clinical study. In fact, auto-triggering represented the most frequent asynchrony with ICU ventilators used in the clinical study, as predicted during their bench evaluation. Furthermore, there was a trend toward less asynchrony with the NIV algorithm, which usually minimized asynchronies during the bench study. Vignaux et al[14] assessed the impact of the NIV algorithm on the incidence of patient-ventilator asynchronies during NIV in a clinical study involving 65 patients and five ICU ventilators. Without the NIV algorithm engaged, 46% of the patients had an AI > 10%. The NIV algorithm permitted a decrease in the incidence of asynchronies due to leaks but without a decrease in the overall incidence of patient-ventilator asynchronies (38% vs 46%, $P = .69$), due to a high incidence of asynchronies not directly related to leaks. We report a lower proportion of patients exhibiting an AI > 10% due to a lower incidence of some major asynchronies. Several reasons explain this discrepancy. First, the level of assistance in our study was lower than the one observed in the study by Vignaux et al,[14] leading to a lower tidal volume, which might explain our low incidence of ineffective efforts.[20] Second, we have modified the definition of premature cycling, considering that the previous one was too sensitive in terms of clinical relevance and what can be considered as a "major" patient-ventilator asynchrony. This definition modification has automatically led to less recorded premature cycling, so to a lower AI. Third, the ICU ventilators used in our clinical assessment had the same behavior during our bench evaluation: a propensity to auto-triggering with expiratory leaks, but no delayed cycling in the presence of inspiratory leaks. Although the strength of our bench model was to assess separately the impact of expiratory and inspiratory leaks on triggering and cycling synchronizations, respectively, the originality of our clinical study was to use ICU ventilators that had the same behavior during their bench evaluation. This led to intelligible results and gave a mutual validation to the two assessments. In the meantime, as a part of this behavior was to avoid delayed cycling, this logically led to a decrease in the overall AI during the clinical study as compared with previous studies conducted with other ventilators. Finally, an AI > 10% in our clinical study was mainly related to a high incidence of auto-triggering, which reflects the ventilator's ability to manage leaks rather than the relevance of the settings chosen by the clinician.

As with ICU ventilators, our bench evaluation also showed very uneven performances of transport ventilators and their NIV algorithms in the presence of leaks. Such heterogeneity has also been previously reported with transport ventilators assessed in invasive conditions.[21,22]

On the whole, our results suggest that rather than being considered as belonging to a group of ventilators, each ICU and transport ventilator should be examined individually regarding its ability to manage NIV conditions. By contrast, dedicated NIV ventilators exhibited more homogeneous behavior during our bench evaluation, with an ability to avoid auto-triggering or delayed cycling while keeping a short

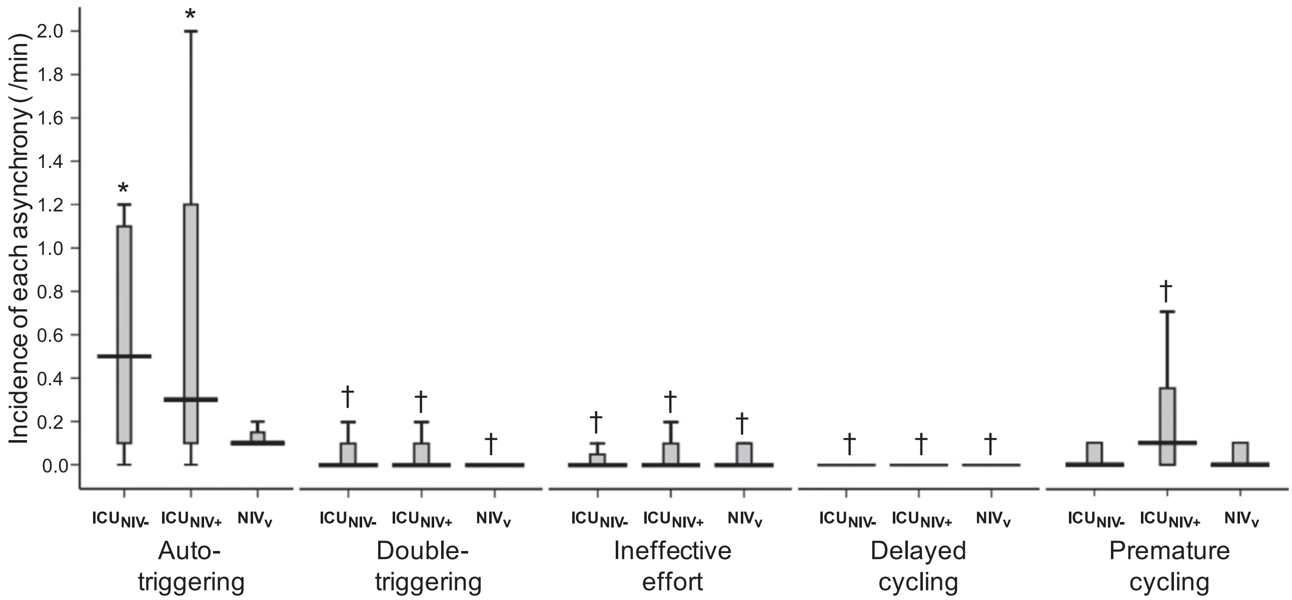

Figure 6. Clinical study incidence of each patient-ventilator asynchrony during the three NIV sessions. Each patient-ventilator asynchrony is represented as box plots (thick horizontal bar: median; extremities of the boxes: 25th and 75th percentiles; thin horizontal bars: fifth and 95th percentiles) for each 20-min NIV session: ICU_{NIV-}, ICU_{NIV+}, and NIV_V. *$P < .05$ vs NIV_V, †$P < .05$ vs auto-triggering. See Figure 1 and 5 legends for expansion of abbreviations.

triggering delay despite the presence of leaks. This is consistent with two previous bench studies that showed a better synchronization ability of a dedicated NIV ventilator as compared with several ICU ventilators without[15] or with[13] their NIV algorithm engaged. Our clinical study is the first to our knowledge to confirm that the use of a NIV ventilator to perform NIV in critically ill patients led to a significant decrease in the incidence of patient-ventilator asynchrony.

Limitations

Several limitations of this study should be underlined. First, during the bench study, only mild obstructive respiratory mechanics were simulated, as respiratory mechanics are known to affect the cycling delay. Our aim was to uncover delayed cycling in the presence of inspiratory leaks, which could be minimized in the case of restrictive respiratory mechanics.[12] In addition, COPD represents the most recognized indication for NIV in ICU.[23] Second, only one level of both inspiratory and expiratory leaks was designed. These experimental conditions may not reproduce what happens in clinical conditions. However, our clinical study showed that our bench model succeeded in capturing the kind of asynchronies that may occur in the presence of leaks with each ventilator in the clinical setting.

Clinical Relevance

It is currently unknown if patient-ventilator asynchronies, especially those due to leaks, can affect the clinical outcome of NIV and therefore influence ventilator choice by clinicians. However, several arguments favor the best possible synchronization during NIV. First, it seems reasonable to assume that auto-triggering and delayed cycling will reduce the tolerance of the procedure, an important key to NIV success.[24,25] Second, the occurrence of delayed cycling

Table 3—*Clinical Study Patients Presenting Each Type of Asynchrony With a High Incidence (> 1/min) or an Asynchrony Index > 10%*

Type of Asynchrony	ICUniv−	ICUniv+	NIVv	*P* Value
Auto-triggering	5 (33)	5 (33)	0	.016
Double-triggering	0	1 (7)	0	…
Ineffective effort	0	0	0	…
Delayed cycling	0	0	0	…
Premature cycling	3 (20)	1 (7)	0	.097
At least one asynchrony	6 (40)	5 (33)	0	.012
Asynchrony index > 10%	4 (27)	2 (13)	0	.091

Data are presented as No. (%). See Table 1 and 2 legends for expansion of abbreviations.

can lead to dynamic hyperinflation and contribute to the development of ineffective efforts,[6,19] which are associated with a prolongation of the ventilation during invasive mechanical ventilation.[26] Given the benefits of NIV when avoiding intubation,[23,25,27,28] each factor potentially involved in its success should logically be promoted. However, if no patient exhibited a high incidence of asynchrony with the NIV ventilator in our study, just a few had an AI > 10% with ICU ventilators. We cannot know to what extent this difference may be clinically relevant and further clinical studies addressing the impact of different devices on the outcome of different groups of patients under NIV are needed to formulate some recommendations.

Conclusion

In conclusion, our study shows that dedicated NIV ventilators allow a better patient-ventilator synchrony in the presence of leaks than ICU and transport ventilators, even if their NIV algorithm is engaged, especially for what concerns auto-triggering. When using an ICU or transport ventilator to perform NIV, the NIV algorithm usually improves, at least slightly and with variations among ventilators, triggering and/or cycling synchronization.

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Dr Carteaux: contributed to the study design, patient enrollment, data collection, data analysis, data interpretation, and manuscript preparation, and read and approved the final manuscript.
Dr Lyazidi: contributed to the study design, patient enrollment, data collection, data analysis, data interpretation, and manuscript preparation, and read and approved the final manuscript.
Dr Cordoba-Izquierdo: contributed to the study design, patient enrollment, data collection, data analysis, data interpretation, and manuscript preparation, and read and approved the final manuscript.
Ms Vignaux: contributed to the study design, patient enrollment, and data collection, and read and approved the final manuscript.
Dr Jolliet: contributed to the study design and patient enrollment, and read and approved the final manuscript.
Dr Thille: contributed to the study design, data analysis, data interpretation, and manuscript preparation, and read and approved the final manuscript.
Dr Richard: contributed to reading and approving the final manuscript.
Dr Brochard: contributed to the study design, data analysis, data interpretation, and manuscript preparation, and read and approved the final manuscript.
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Additional information: The e-Appendix and e-Figures can be found in the "Supplemental Materials" area of the online article.

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