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Performance of noninvasive ventilation algorithms on ICU ventilators during pressure support: a clinical study

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Abstract *Objective:* To evaluate the impact of noninvasive ventilation (NIV) algorithms available on intensive care unit ventilators on the incidence of patient-ventilator asynchrony in patients receiving NIV for acute respiratory failure.
Design: Prospective multicenter randomized cross-over study.
Setting: Intensive care units in three university hospitals.
Methods: Patients consecutively admitted to the ICU and treated by NIV with an ICU ventilator were included. Airway pressure, flow and surface diaphragmatic electromyography were recorded continuously during two 30-min periods, with the NIV (NIV+) or without the NIV algorithm (NIV0). Asynchrony events, the asynchrony index (AI) and a specific asynchrony index influenced by leaks (AIleaks) were determined from tracing analysis.
Results: Sixty-five patients were included. With and without the NIV algorithm, respectively, auto-triggering was present in 14 (22%) and 10 (15%) patients, ineffective breaths in 15 (23%) and 5 (8%) ($p = 0.004$), late cycling in 11 (17%) and 5 (8%) ($p = 0.003$), premature cycling in 22 (34%) and 21 (32%), and double triggering in 3 (5%) and 6 (9%). The mean number of asynchronies influenced by leaks was significantly reduced by the NIV algorithm ($p < 0.05$). A significant correlation was found between the magnitude of leaks and AIleaks when the NIV algorithm was not activated ($p = 0.03$). The global AI remained unchanged, mainly because on some ventilators with the NIV algorithm premature cycling occurs.
Conclusion: In acute respiratory failure, NIV algorithms provided by ICU ventilators can reduce the incidence of asynchronies because of leaks, thus confirming bench test results, but some of these algorithms can generate premature cycling.

Keywords Noninvasive ventilation · Mechanical ventilation · Patient-ventilator interaction · Asynchrony

Introduction

Non-invasive ventilation (NIV) has become a standard of care in patients with acute respiratory failure [1–3]. Although practices may vary, intensive care unit (ICU) ventilators are often preferred by ICU practitioners to perform NIV during acute respiratory failure [4]. However, a recent study showed that severe patient-ventilator asynchrony is present in 43% of these patients, mainly as a result of leaks at the patient-mask interface [5]. This latter finding is not surprising, as leaks are known to interfere with several key aspects of ventilator function [6–10]. The problem with ICU ventilators is that they were originally designed to function with a leak-free closed circuit, conditions that are very different from the leak-prone conditions of NIV [11]. To address this issue, manufacturers have developed NIV algorithms, so-called "NIV modes" on their machines, whose main function is to alleviate the impact of leaks on ICU ventilator performance [10]. A recent bench model study showed that NIV algorithms could indeed correct this problem, albeit with variations between machines [10]. However, to date no study has shown whether the same results could be achieved in the clinical setting.

The purpose of this study was to evaluate the impact of NIV algorithms on the incidence, nature and severity of patient-ventilator asynchrony in patients receiving NIV for acute respiratory failure.

Materials and methods

This was a prospective, randomized, cross-over study, conducted at three university hospital ICUs, one medical (Creteil), and two medical-surgical (Brussels, Geneva). The protocol was approved by the ethics committee of each participating center. All patients in the ICU receiving NIV for an acute respiratory failure were eligible. Informed consent was obtained from the patients. Patients were included as soon as possible after initiation of NIV. All patients were ventilated with ICU ventilators routinely used in the units and in which bench model tests had shown the efficacy of the NIV algorithm in correcting various asynchrony parameters [10]: Evita 4 and XL (Draeger, Lübeck, Germany), Servo I (Maquet, Solma, Sweeden), G5 (Hamilton Medical, Rhäzuns Switzerland) and Engström Carestation (GE Healthcare, Fairfield, CT). NIV algorithms are based on technology varying from one manufacturer to another [10]. Their goal is to attenuate the impact of leaks on ICU ventilator function by measuring and compensating for leaks while adapting alarms. They are usually referred to as "NIV modes," although they are not ventilatory modes. On our bench test they partly corrected the negative effects of leaks on trigger delay, auto-triggering, pressurization and late cycling [10]. We observed on the bench test that with the correction of late cycling, we had no more ineffective efforts in obstructive respiratory mechanics conditions. Without leaks, the NIV algorithm performs generally as well as pressure support when the NIV algorithm is not activated, except on the Servoi, in which trigger delay is increased by 18% in normal respiratory mechanics from 110 to 130 ms (unpublished data).

Criteria for initiating NIV followed the usual practice guidelines of each center, which are based on previous published studies on hypercapnic [12] and non-hypercapnic respiratory failure [2] (see ESM).

Patients presenting any contraindication to NIV were excluded [13].

NIV was applied via a standard oro-nasal mask, in Pressure Support mode. NIV settings were those made by the clinician in charge of the patient, according to usual standard procedure of each center. No adjustments were made by the investigators, except the activation and deactivation of the NIV algorithm. Two consecutive NIV sessions in random order were applied, one with the NIV algorithm (NIV+), the other without the NIV algorithm (NIV0). The duration of each session was 30 min. When the NIV algorithm was not activated, alarms were silenced when necessary and patients surveyed as usual.

The respiratory parameters [respiratory rate, expired tidal volume (VTE), minute volume, leaks at the mask, inspiratory times of the patient (ti_p) and of the ventilator (ti_v)] were assessed by analysis of the flow, pressure and surface diaphragmatic electromyographic activity (EMGdi) as described in a previous study [5]. Asynchrony events (ineffective triggering, double-triggering, auto-triggering, premature cycling and delayed cycling) were detected by visual inspection of the recordings (Figs. 1, 2). The assessment of respiratory parameters and asynchrony events is detailed in the ESM.

A global asynchrony index (AI) was computed as previously published [5, 14]. An AI > 10% was considered as severe [5, 14]. As a new concept, we defined a specific asynchrony index, which takes into account only asynchronies influenced by leaks (AIleaks). Detailed definitions are provided in the ESM.

Statistics

Statistics were performed with SigmaStat 2.0–SPSS Science (Systat, San Jose, CA) and Stata version IC10 (STATA Corp., College Station, TX).

Continuous data are expressed as median (25th–75th percentile) or mean (SD) depending on the parametric or non-parametric nature of data distribution.

Inter-group comparison of continuous variables was made with a paired Student's *t* test or a Wilcoxon test, depending on the parametric or non-parametric nature of data distribution. Inter-group comparison of continuous variables for more than two groups were made by a one-way ANOVA test or an ANOVA on ranks depending on the parametric or non-parametric nature of data distribution. To isolate the group or groups that differ from the others, a multiple comparison procedure was used: an AI Pairwise Multiple Comparison Procedure (Dunn's Method). Comparison of the number of patients presenting each type of asynchrony between the two groups was made by a McNemar test.

The relationship between leaks and delta of each type of event described above was explored through linear regression.

To determine which parameters were associated with AIleaks, with or without the NIV algorithm, a generalized estimation equations model (a linear regression model using an exchangeable correlation matrix) and ANCOVA (covariance analysis) were used. Variables that in univariate analysis presented a significance level of 0.10 or less were included in the model. The effect of leaks on AIleaks was then analyzed on the two samples (NIV0 and NIV+).

All p values <0.05 were considered significant.

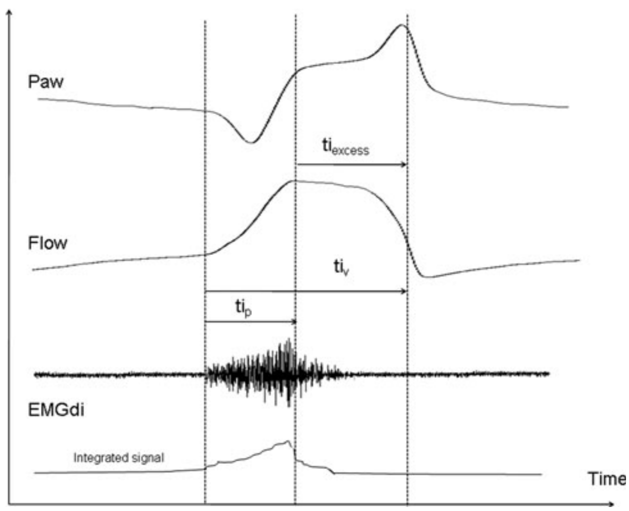
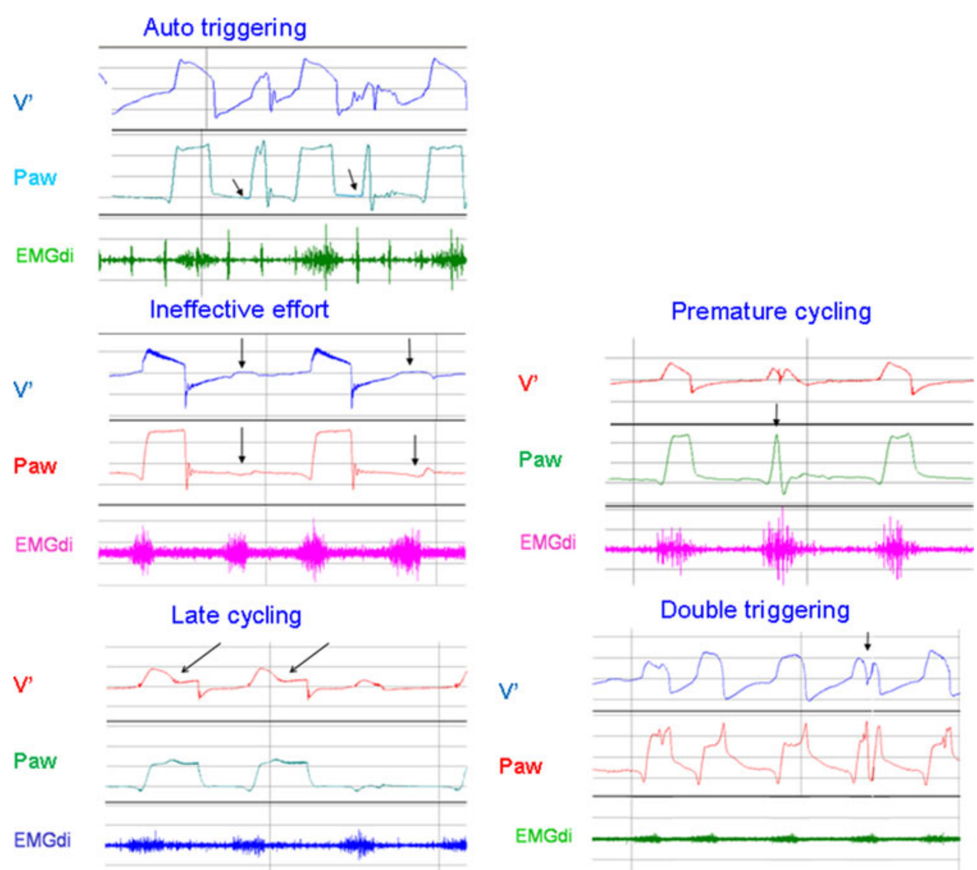


Fig. 1 Pressure-time, flow-time and diaphragmatic EMG-time tracings, allowing determination of patient inspiratory time (ti_p), ventilator inspiratory time (ti_v) and inspiratory time in excess (ti_{excess})

Results

Seventy-five consecutive patients were screened, five of whom refused to participate; 70 patients were therefore

Fig. 2 Representative tracings of the five types of asynchrony. *EMGdi* diaphragmatic electromyography tracing; *Paw* airway pressure; *V′* instantaneous flow. *Downward pointing arrows* indicate relevant events



included. Five were excluded after recording because their electromyography curves were not analyzable. The final study population was therefore 65 patients, whose main clinical characteristics are outlined in Tables 1 and 2. All received NIV via a classical face mask (i.e., oronasal, Vygon, Ecouen, France). Inclusion was made 1 ± 0.3 days after initiation of NIV. Thirty-three patients (51%) were hypercapnic ($PaCO_2 > 42$ mm Hg or 5.6 kPa). Causes of ARF were consistent with those reported in the literature: 23 patients (35%) had an acute episode of their chronic pulmonary disease, 18 (28%) received NIV after extubation, 17 (26%) had a community acquired pneumonia, 14 (22%) were post-operative, 2 (3%) had an acute pulmonary edema and 1 (2%) a thoracic traumatism.

Ventilators used were 28 Evita 4 (43%), 19 Evita XL (29%), 14 Servoi (22%), 3 Engström Carestation (5%) and 1 G5 (2%). Ventilator settings and main respiratory parameters are presented in Table 3. Among these respiratory parameters, the only significant difference between NIV0 and NIV+ was the ti_{excess}, with a median of 28% (16–37) and 19% (9–27), respectively.

Comparison of different types of events, with and without the NIV algorithm, is illustrated in Table 4.

Table 1 Demographic and clinical characteristics of the patients ($n = 65$)

Demographics and main respiratory parameters	Mean ± standard deviation
Age (years)	69 ± 12
Men:women (*n*)	41:24
BMI (kg/m^2)	25 ± 5
SAPS II	44 ± 14
BR (*n*/min)	28 ± 8
PaO_2/FiO_2	225 ± 72
$PaCO_2$ (mmHg)	47 ± 15

Values are expressed as mean ± standard deviation
Main respiratory parameters were recorded at study inclusion
BMI body mass index; *SAPS II* simplified acute physiology score II [38, 39]; *BR* breath rate; FiO_2 inspired fraction of oxygen

Table 2 Chronic conditions

Condition	*n* (%)
Chronic obstructive pulmonary disease	25 (38)
Cardiac insufficiency	9 (14)
Obesity (BMI > 30)	7 (10)
Bronchial carcinoma	2 (3)
Mixed obstructive/restrictive disease	1 (2)
Pulmonary hypertension	1 (2)
Neuromuscular disease	1 (2)

Several chronic conditions can co-exist in a given patient
Values are expressed as number (%)
BMI body mass index

Auto triggering

The number of auto triggerings was significantly lower if the NIV algorithm was activated ($p = 0.01$). If patients are separated into two groups, one with "low" assistance (≤14 cm H_2O) and another with "high" assistance (≥15 cm H_2O), one can observe that the NIV algorithm

Table 3 ventilator settings and main respiratory parameters

Ventilator settings	Mean (SD) or median (25th–75th)	
PSL (cmH_2O)	13 (3)	
PEEP (cmH_2O)	5 (5–7)	
Slope (ms)	200 (100–200)	
Inspiratory trigger		
Flow (l/min) ($n = 64$)	1 (0.3–2)	
Pressure (cm H_2O) ($n = 1$)	−1	
ETS (%PIF)	25	
FiO_2	0.37 (0.1)	
Respiratory parameters during NIV	**NIV0**	**NIV+**
Breath rate (patient)	26 (8)	26 (7)
ti_p (ms)	830 (260)	840 (240)
ti_{excess} (%)	28 (16–37)	19 (9–27)*
VTE		
ml	570 (220)	560 (210)
ml/kg	9 (3)	9 (3)
MV (l/min)	13.4 (5)	13.4 (5)
Leaks		
l/min	4 (1–7)	3.5 (1–7)
% MV	28 (10–56)	23 (9–52)

All values are expressed in mean (standard deviation) or median (25th–75th percentile), according to the parametric or non-parametric nature of their distribution
PSL pressure support level, *PEEP* positive end expiratory pressure; *ETS* expiratory trigger setting; expressed in percentage of peak inspiratory flow (*PIF*); *NIV0 and NIV+* without and with NIV mode respectively; *RRp* respiratory rate of the patient; t_{ip}. inspiratory time of the patient; ti_{excess} inspiratory time of the ventilator in excess reported to the ti_p; *VTE* expired tidal volume, expressed in absolute value and in ml/kg of ideal body weight (IBW). Leaks are expressed in absolute value and in percentage of minute ventilation (MV)
* $p < 0.05$ vs. NIV0

Table 4 number of asynchronies with and without NIV mode

	NIV0 Mean ± SD	NIV+ Mean ± SD	NIV0 *n* (%)	NIV+ *n* (%)
Auto triggering	1.2 ± 2.8	0.5 ± 0.8*	14 (22)	10 (15)
Ineffective efforts	1.4 ± 3.1	0.5 ± 1.1*	15 (23)	5 (8)*
Late cycling	0.6 ± 1.6	0.2 ± 0.6*	11 (17)	5 (8)*
Premature cycling	2.1 ± 5	3.3 ± 7	22 (34)	21 (32)
Double triggering	0.2 ± 0.5	0.3 ± 0.8	3 (5)	6 (9)
Asynchrony index (AI)	18 ± 20	19 ± 27	30 (46)	25 (38)
AIleaks	9 ± 12	5 ± 7*	18 (28)	8 (12)*

n Number of patients presenting each type of asynchrony (>1/min) or an AI > 10%
* $p < 0.05$ vs. NIV0

efficiency is higher in the “high” assistance group [delta auto triggering = −0.01 (−0.3; 0.1) and −0.2 (−0.5; 0) auto triggering/min for “low” and “high” assistance, respectively $p = 0.05$)] even if the level of leaks and the incidence of auto triggering is comparable at NIV0 in the two groups.

Ineffective efforts

There were fewer ineffective efforts with the NIV algorithm ($p < 0.001$). Improvement was proportional to the magnitude of ineffective efforts with NIV0 ($r = 0.9$; $p < 0.001$). Fifteen patients (23%) had more than one ineffective effort per minute with NIV0, and six (8%) with the NIV algorithm ($p = 0.007$). NIV algorithm efficiency was higher in the “high” assistance group [delta ineffective effort = −0.02 (−0.3; 0.08) and −0.2 (−1.5; −0.03) ineffective efforts/min for “low” and “high” assistance, respectively $p = 0.03$) even though the incidence of ineffective effort was comparable at NIV0 in the two groups, $p = 0.1$)].

Late cycling

When the NIV algorithm was activated, late cycling decreased significantly ($p = 0.003$). This improvement was correlated with the magnitude of late cycling with NIV0 ($r = 0.9$; $p < 0.001$). Without the NIV algorithm, this type of event was considered as present ($n > 1$) for 11 (17%) patients, and for 5 (8%) with the NIV algorithm ($p = 0.05$). Late cycling was more prevalent in the “high” assistance group [0.03 (0; 0.3) and 0.3(0.04; 1.1) late cycling/min for “low” and “high” assistance, respectively, $p = 0.02$]. When the NIV mode was activated, there was no difference between the two groups.

Premature cycling

The NIV algorithm led to a non-significant trend towards an increase in PC. Twenty-two patients (34%) had PC with NIV0, 21 (32%) with NIV+ ($p = 0.8$).

Double triggering

No difference was observed whether the NIV algorithm was activated or not.

Ti_{excess}

It was significantly lowered when the NIV algorithm was used. The delta ti_{excess} was −14.2% (−20; −5) for Servoi, −4.4% (−9; −2) for Evita 4, and −0.5 (−12; 2) for Evita XL ($p = 0.01$). The correction capacity was higher for the Servoi, versus Evita 4 or Evita XL ($p < 0.05$). Conversely, premature cycling was increased by the NIV algorithm of the Servoi [+1.3 (−0.04; 17)] compared to Evita XL and Evita 4 (0, $p = 0.04$).

Asynchrony index (AI)

No difference was noted in the AI whether or not the NIV algorithm was activated ($p = 0.69$). At NIV0, 30 patients (46%) presented with a severe AI and 25 patients (38%) with NIV+, a non-significant difference.

AIleaks

The AIleaks was significantly associated with the NIV algorithm: when the NIV algorithm was activated, AIleaks was lower [regression coefficient = −4.22; confidence interval (−7; −1.5); $p = 0.002$)] independently of the sequence (NIV+ then NIV0 or NIV0 then NIV+), VTE, respiratory rate or level of leaks. Improvement was correlated to the magnitude of AIleaks with NIV0 ($r = 0.9$; $p < 0.001$).

AIleaks was significantly and independently associated with the pressure support level [regression coefficient = +0.76 by cmH2O of pressure support added; confidence interval (0.2; −1.3); $p = 0.009$]. The NIV algorithm had a higher efficiency in the “high” assistance group [Delta AIleaks = −0.6 (−2.5; 1) and −2.2 (−12; −1.3) % for “low” and “high” assistance, respectively, $p = 0.007$].

Covariance analysis performed on patients with and without the NIV algorithm showed that the level of leaks, expressed in percentage of minute ventilation, was positively and significantly associated with AIleaks in patients in NIV0 conditions [regression coefficient = +0.069 by percent of leaks, confidence interval (0.007–0.13); $p = 0.03$].

However, this correlation did not persist for the same level of leaks with the NIV algorithm activated.

AIleaks, with and without the NIV algorithm, and delta AIleaks were not associated with presence of chronic obstructive pulmonary disease, hypercapnia or type of ventilator.

Discussion

This study is the first to evaluate the clinical effects of ICU ventilator NIV algorithms on patient-ventilator interaction. The main results with the NIV algorithm turned on are the following:

1. The number of patients presenting each type of asynchrony decreased by an average of 50%.
2. Although the specific AIleaks was decreased by 45%, on average, the AI, which reflects overall asynchrony, remained unchanged by NIV algorithms.
3. Some NIV algorithms tend to over-correct ti_{excess}, leading to an increase in the incidence of premature cycling.

Before discussing these results, some limitations of this study should be underlined. First, EMG tracings analysis may be prone to observer interpretation variability. To alleviate this problem, two different investigators, blinded to patient characteristics and whether tracings were acquired during NIV0 or NIV+, performed the analysis. Furthermore, a strict methodology, used in a previous trial, was followed [5]. No inter-observer difference was noted. Moreover, sternocleidomastoid electromyography was used besides diaphragmatic electromyography as a backup in cases where the diaphragmatic signal proved difficult to interpret.

Second, the level of leaks found in our study might not reflect that found in other centers, as the three participating ICUs have a great deal of experience with NIV. Of note, the same three centers performed a recent observational study on asynchrony during NIV [5], and the patient populations were comparable, as were the levels of leaks and severity of asynchronies. Third, five different ventilators were used for this study, which could have influenced results because of their different NIV algorithm performances. Bench test results of these machines showed that their NIV algorithms corrected part or all of leak-associated asynchronies, but with variable efficacy [10]. In this study, one of the ventilators' NIV algorithm (Servoi) had a different behavior with inspiratory time in excess and premature cycling. This ventilator was more efficient to correct ti_{excess}, but induced more premature cycling. Finally, only 65 patients were included, which does not allow a precise sub-group analysis by respiratory mechanics category. As each patient is his own control, this could have influenced results.

Studies have shown that during NIV, auto-triggering, ineffective efforts and late cycling were associated with leaks [6, 7]. The same observation was made in the present study, confirming the findings of our previous observational study [5].

Because only these asynchronies are associated with leaks, and partially corrected by NIV algorithms, the specific AIleaks could be used when one is interested in asynchronies favored by leaks. Assessment of global asynchrony still requires the use of the AI.

The main finding of this study was that activating the NIV algorithm has a clear and significant effect on the number and severity of asynchrony events resulting from leaks. These results are consistent with the findings of a recent bench model study in which NIV algorithms were shown to correct such events, albeit with large variation between machines [10]. Moreover, the number of AIleaks was higher and the NIV algorithm more efficient in the group with "high" assistance. In the studies by Thille et al. [14, 15], the level of pressure support was correlated with the asynchrony index, but was independent of the level of leaks. Patient-ventilator asynchrony was found to be correctible by reducing the level of pressure support and shortening ventilator insufflation time [15]. This approach is also valid during NIV. However, the additional problem of leaks needs to be addressed. Therefore, NIV algorithms could provide an added benefit for optimizing patient-ventilator interaction, and this study suggests their efficacy in pursuing that goal. However, the approach is different from one ventilator to another. Some ventilators (the Servoi in this study) tend to over-correct ti_{excess}, leading to an increase in the incidence of premature cycling. This may explain why the NIV algorithm can partially correct the AIleaks while the global AI remains unchanged. This difference between ventilators was not apparent in our previous bench testing [10], suggesting that even if the trend is the same, a ventilator can have a different behavior in bench testing and in the clinical setting.

In invasive ventilation, asynchronies are a risk factor for an increase in the duration of mechanical ventilation [14]. An adverse impact of asynchronies on patient outcome has not been demonstrated with NIV [5]. Nonetheless, since patient intolerance to the technique has been shown to be a risk factor for NIV failure [11, 16], one can at least hypothesize that decreasing asynchronies during NIV could be a part of a strategy to maximize the chances of its success. While clearly representing a step in the right direction, NIV algorithms probably need some more fine-tuning so that all machines can provide optimal patient–ventilator synchrony in such leak-prone conditions. Technologies derived from those of home ventilators might be part of the solution, as these machines have a long history of dealing with major leaks [10].

Conclusion

Activating the NIV algorithm on ICU ventilators during the application of NIV for ARF decreases the incidence of those asynchronies typically associated with leaks, while not necessarily changing the overall asynchrony situation. Part of this mixed message comes from the varying technological solutions in different machines, the correction of one asynchrony leading to the increase of another. Therefore, future studies should explore whether a more homogenous approach among manufacturers or resorting to solutions used in home ventilators could help make further progress in harmonizing patient-ventilator synchrony during NIV.

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