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Noninvasive ventilation through a helmet in postextubation hypoxemic patients: physiologic comparison between neurally adjusted ventilatory assist and pressure support ventilation

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Abstract *Purpose:* Neurally adjusted ventilatory assist (NAVA) has been shown to improve patient–ventilator interaction and reduce asynchronies in intubated patients, as opposed to pressure support ventilation (PSV). This is a short-term head-to-head physiologic comparison between PSV and NAVA in delivering noninvasive ventilation through a helmet (h-NIV), in patients with postextubation hypoxemic acute respiratory failure. *Methods:* Ten patients underwent three 20-min trials of h-NIV in PSV, NAVA, and PSV again. Arterial blood gases (ABGs) were assessed at the end of each trial. Diaphragm electrical activity (EAdi) and airway pressure (P_{aw}) were recorded to derive neural and mechanical respiratory rate and timing, inspiratory ($delay_{TR\text{-}insp}$) and expiratory trigger delays ($delay_{TR\text{-}exp}$), time of synchrony between diaphragm contraction and ventilator assistance ($time_{synch}$), and the asynchrony index (AI). *Results:* ABGs, peak EAdi, peak P_{aw}, respiratory rate, either neural or mechanical, neural timing, and $delay_{TR\text{-}exp}$ were not different between trials. Compared with PSV, with NAVA the mechanical expiratory time was significantly shorter, while the inspiratory time and duty cycle were greater. $Time_{synch}$ was 0.79 ± 0.35 s in NAVA versus 0.60 ± 0.30 s and 0.55 ± 0.29 s during the PSV trials ($p < 0.01$ for both). AI exceeded 10% during both PSV trials, while not in NAVA ($p < 0.001$). *Conclusions:* Compared with PSV, NAVA improves patient–ventilator interaction and synchrony, with no difference in gas exchange, respiratory rate, and neural drive and timing.

Keywords Noninvasive ventilation · Helmet · Patient–ventilator interaction · Patient–ventilator asynchrony · Neurally adjusted ventilatory assist (NAVA) · Pressure support ventilation (PSV)

Introduction

Noninvasive ventilation (NIV) is an effective technique in patients with acute respiratory failure (ARF) [1]. Tolerance is a crucial determinant of NIV success [2, 3] and depends on both the interface [4] and the interaction between a patient's spontaneous breathing and ventilator assistance [5].

The helmet is a relatively new interface that has been shown to be more tolerated than the face mask over time, requiring fewer discontinuations and allowing longer time of continuous application [6, 7]. Compared with the conventional application using a mask, however, NIV delivery by helmet (h-NIV) has a more problematic patient–ventilator interaction. This regards primarily the synchrony between spontaneous breathing and ventilator cycling, consequent on specific characteristics of this interface, such as the soft compliant wall, the elevated internal compressible volume, and, most importantly, the upward displacement of the helmet due to the movement of the soft collar throughout insufflation [8]. Neurally adjusted ventilatory assist (NAVA) is a form of partial ventilator assistance in which the machine delivers assistance in proportion to the electrical activity of the diaphragm (EAdi), as assessed by means of transesophageal electromyography, which is the closest available signal to the brainstem respiratory centers [9, 10].

Compared with pressure support ventilation (PSV), NAVA has been shown to improve patient–ventilator interaction in intubated patients with ARF and healthy volunteers undergoing h-NIV [11]. Accordingly, we hypothesized that, compared with PSV, NAVA should also enhance patient–ventilator interaction and synchrony in patients with ARF during h-NIV. This study was therefore designed to evaluate the short-term physiologic effects of NAVA in delivering h-NIV, by performing a head-to-head comparison with PSV.

Methods

The study was performed in the intensive care units (ICUs) of the University Hospital "Maggiore della Carità" (Novara, Italy) and Policlinico "A. Gemelli" (Roma, Italy) between October 2008 and June 2009. The ethics committees of both institutions approved the protocol and informed consent was obtained from each patient (expanded methods in the electronic supplementary material, ESM).

Subjects and study protocol

We considered eligible all patients presenting, after extubation following at least 48 h of invasive ventilation for ARF, respiratory rate (RR) greater than 30 breaths/min, dyspnea, and arterial oxygen tension to inspiratory oxygen fraction (PaO_2/FiO_2) less than 300 breathing through a Venturi mask at a nominal FiO_2 of at least 40%. The exclusion criteria are provided in the ESM.

After enrolment, a catheter designed for EAdi detection (Maquet Critical Care, Sölna, Sweden) was inserted and correct positioning was ensured [12]. A transparent helmet (Castar, Starmed, Mirandola) was placed, secured, and connected to the ventilator, as previously described.

Each patient underwent three 20-min NIV trials delivered by a Servo-I ventilator (Maquet Critical Care, Sölna, Sweden). The following trials were applied in sequence: (1) first application of PSV (PSV_1), (2) NAVA, (3) PSV again (PSV_2). Positive end-expiratory pressure (PEEP) was always set at 10 cmH_2O. Both PSV trials were delivered with a preset inspiratory pressure of 12 cmH_2O, using the NIV software compensating for air leaks. NAVA was set to achieve a peak inspiratory airway pressure ($P_{aw\ peak}$) equivalent to the preset PSV, as previously described [12]. Dedicated software to deliver NAVA in NIV mode was not available at the time of the study. The airway pressure limit was set at 30 cmH_2O throughout the study period. The fastest rate of pressurization and an expiratory trigger threshold (ET_{TH}) of 50% of peak inspiratory flow were set for PSV. NAVA has a fixed I/E cycling set at 70% of peak EAdi ($EAdi_{peak}$). FiO_2 was set to obtain a peripheral oxygen saturation (SpO_2) value of at least 94% before starting the first trial and was then maintained unmodified throughout the study period. Patients did not receive sedatives throughout the period of the study protocol and in the previous 6 h. Detailed criteria for protocol discontinuation are provided in the ESM.

Data acquisition and analysis

Arterial blood was sampled at the end of each trial for gas analysis from a catheter placed in the radial artery. Airflow, airway pressure (P_{aw}), and EAdi were acquired from the ventilator through a RS232 interface at a sampling rate of 100 Hz, recorded by means of dedicated software (NAVA Tracker V. 2.0, Maquet Critical Care, Sölna, Sweden). The last 5 min of each trial was recorded, stored on a personal computer, and manually analyzed off-line using customized software based on Microsoft Excel, as previously described [12]. Ventilator inspiratory time (TI_{mec}), expiratory time (TE_{mec}), and rate of ventilator cycling (RR_{mec}) were determined on the flow tracing. Patient's neural respiratory rate (RR_{neu}), neural inspiratory time (TI_{neu}), and neural expiratory time (TE_{neu}) were determined on the EAdi tracing; TI_{neu} was measured as the time interval between onset of EAdi swing and $EAdi_{peak}$. Neural ($TI/TTOT_{neu}$) and mechanical ($TI/TTOT_{mec}$) inspiratory duty cycle were computed as the ratio between TI_{neu} and total neural respiratory time ($TTOT_{Neu}$) and as the ratio between TI_{mec} and total mechanical respiratory time ($TTOT_{mec}$), respectively. The amount of ventilator assistance was evaluated as the integral of P_{aw} over TI_{mec}, either per breath (PTP_{aw}/br) or per minute (PTP_{aw}/min) [13].

Table 1 Patient characteristics at enrolment

Patient	Gender	Age (years)	Weight (kg)	BMI (kg/m^2)	Admission pathology	Days of MV	FiO_2
1	M	79	60	19.6	Bowel necrosis, abdominal surgery	3	0.40
2	M	77	60	25.3	Pneumonia	3	0.40
3	F	75	80	29.4	Gall bladder empyema, abdominal surgery	22	0.40
4	M	47	70	24.2	Peritonitis, abdominal surgery	12	0.40
5	M	60	85	26.2	Pancreatitis	37	0.40
6	M	48	110	33.9	Pneumonia	16	0.40
7	M	45	80	24.7	Polytrauma	4	0.40
8	M	56	60	22.0	Polytrauma	5	0.40
9	F	76	70	26.0	Pancreatitis	10	0.40
10	M	48	70	24.0	Peritonitis, abdominal surgery	8	0.40
Mean (SD)		61(14)	74 (15)	25.5 (3.9)		12 (11)	0.40 (0)

BMI body mass index, *MV* mechanical ventilation, *FiO_2* inspiratory oxygen fraction, *SD* standard deviation

Leaks were computed as the difference between the volume insufflated into the helmet by the ventilator ($h\text{-}VT_{insp}$) and the volume exhaled from the helmet back to the ventilator ($h\text{-}VT_{exp}$) multiplied by RR_{mec}; leaks are expressed as both absolute value (l/min) and rate of the exhaled volume over 1 min [5].

The inspiratory trigger delay ($delay_{TR\text{-}insp}$) was calculated as the time lag between onset of EAdi swing and commencement of ventilator support, while the expiratory trigger delay ($delay_{TR\text{-}exp}$) was calculated as the time lag between the point at which EAdi started to fall toward baseline and the end of ventilator support. The time of synchrony between neural effort and ventilator support ($time_{synch}$) was calculated as the period of time in the course of inspiration during which the diaphragm was active and the ventilator was concurrently delivering support [8]. To estimate the extent of asynchrony we used the asynchrony index (AI) which expresses in percentage the number of asynchronous events (ineffective efforts, auto-triggering, and double triggering) divided by the sum of ventilator cycles and ineffective efforts [14].

Statistical analysis

Normal data distribution was confirmed by the Kolmogorov–Smirnov test ($p > 0.1$). All data were analyzed with the one-way analysis of variance (ANOVA) for repeated measures; when a significant difference was found, the Student–Newman–Keuls post hoc test was applied. Differences in the proportion of patients with AI greater than 10% between trials were ascertained with the Fisher exact test. *P* values no greater than 0.05 were considered significant.

Results

All patients completed the study protocol. Anthropometric and clinical characteristics of the patients at enrolment are provided in Table 1. Information about eligible patients and reasons for exclusion is provided in detail in the ESM.

Table 2 Inspiratory and expiratory (helmet) tidal volume and leak

	PSV_1	NAVA	PSV_2
$h\text{-}VT_{insp}$ (l)	1.01 ± 0.21	1.15 ± 0.26	0.93 ± 0.18
$h\text{-}VT_{exp}$ (l)	0.97 ± 0.20	0.84 ± 0.18	0.89 ± 0.14
Leak			
(l/min)	1.04 ± 1.03	8.11 ± 10.08*	1.09 ± 1.65†
(%)	4.8 ± 3.9	42.9 ± 54.2*	4.9 ± 5.8†

$h\text{-}VT_{insp}$ volume insufflated by the ventilator in the helmet during inspiration, *$h\text{-}VT_{exp}$* volume exhaled from the helmet to the ventilator throughout expiration

* $p < 0.05$ NAVA versus PSV_1

† $p < 0.05$ PSV_2 versus NAVA

As described in Table 2, air leaks, either in absolute value (l/min) or percent, were significantly larger with NAVA than with PSV ($p < 0.05$ NAVA vs. PSV_1 and PSV_2). The effects of the two modes on gas exchange, breathing pattern, and patient–ventilator interaction are shown in Table 3. Arterial gases were not different between PSV_1, NAVA, and PSV_2. Both RR_{neu} and RR_{mec} did not show significant differences between the three trials. The neural timing, i.e., TI_{neu}, TE_{neu}, $TI/TTOT_{neu}$, was also not significantly different between trials. The mechanical timing, in contrast, differed between trials: TI_{mec} was significantly longer in NAVA (1.09 ± 0.35 s), compared with both PSV_1 (0.67 ± 0.12 s) ($p < 0.001$) and PSV_2 (0.65 ± 0.11 s) ($p < 0.001$); TE_{mec} was shorter in NAVA (1.72 ± 0.60 s), in comparison with PSV_1 (2.23 ± 0.99 s) ($p < 0.05$) only, while it was not significantly different from PSV_2 (2.00 ± 0.59); $TI/TTOT_{mec}$ was greater in NAVA (0.39 ± 0.04), as compared with both PSV_1 (0.25 ± 0.05) and PSV_2 (0.25 ± 0.05) ($p < 0.001$).

The neural drive to breathe, as indicated by $EAdi_{peak}$, was not significantly different between PSV_1, NAVA, and PSV_2. $P_{aw\ peak}$ also did not significantly differ between trials. PTP_{aw}/br and PTP_{aw}/min, however, were greater in

Table 3 Arterial blood gases, breathing pattern, and patient–ventilator interaction

	PSV_1	NAVA	PSV_2
ABGs			
pH	7.45 ± 0.06	7.43 ± 0.71	7.44 ± 0.07
PaO_2/FiO_2 (mmHg)	289 ± 86	303 ± 81	286 ± 91
$PaCO_2$ (mmHg)	40.8 ± 4.1	42.3 ± 5.4	42.0 ± 5.5
Breathing pattern			
RR_{neu} (breath/min)	25.2 ± 9.4	23.4 ± 7.6	26.3 ± 7.0
RR_{mec} (breath/min)	22.7 ± 6.4	23.5 ± 7.7	24.0 ± 6.2
TI_{neu} (s)	0.84 ± 0.25	0.92 ± 0.32	0.85 ± 0.28
TI_{mec} (s)	0.67 ± 0.12	1.09 ± 0.35***	0.65 ± 0.11†††
TE_{neu} (s)	1.92 ± 1.09	1.89 ± 0.66	1.60 ± 0.48
TE_{mec} (s)	2.23 ± 0.99	1.72 ± 0.60*	2.00 ± 0.59
$TI/TTOT_{neu}$	0.32 ± 0.07	0.33 ± 0.05	0.35 ± 0.05
$TI/TTOT_{mec}$	0.25 ± 0.05	0.39 ± 0.04***	0.25 ± 0.05†††
Patient–ventilator interaction			
$P_{aw\ peak}$ (cm/H_2O)	21.0 ± 3.5	22.6 ± 6.6	21.0 ± 3.5
PTP_{aw}/br (cmH_2O s)	3.6 ± 0.8	5.9 ± 2.9**	3.2 ± 0.9††
PTP_{aw}/min (cmH_2O s min^{-1})	78 ± 19	123 ± 42**	76 ± 21††
$EAdi_{peak}$ (μV)	18.7 ± 13.6	20.8 ± 13.5	21.3 ± 14.5
$Delay_{TR\text{-}insp}$ (s)	0.31 ± 0.13	0.14 ± 0.06***	0.36 ± 0.13†††
$Delay_{TR\text{-}exp}$ (s)	0.19 ± 0.10	0.21 ± 0.06	0.22 ± 0.11
$Time_{synch}$ (s)	0.60 ± 0.30	0.79 ± 0.35**	0.55 ± 0.29††

ABGs arterial blood gases, PaO_2/FiO_2 arterial oxygen tension to inspiratory oxygen fraction, $PaCO_2$, arterial carbon dioxide tension, RR_{neu} patient's own (neural) respiratory rate, RR_{mec} rate of ventilator cycling, TI_{neu} neural (patient) inspiratory time, TI_{mec} mechanical (ventilator) inspiratory time, TE_{neu} neural expiratory time, TE_{mec} mechanical expiratory time, $TI/TTOT_{neu}$ neural inspiratory duty cycle, $TI/TTOT_{mec}$ mechanical inspiratory duty cycle, $P_{aw\ peak}$ peak inspiratory airway pressure, PTP_{aw}/br integral of P_{aw} over TI_{mec} per breath, PTP_{aw}/min integral of P_{aw} over TI_{mec} per minute, $Eadi_{peak}$ peak diaphragm electrical activity, $delay_{TR\text{-}insp}$ inspiratory trigger delay, $delay_{TR\text{-}exp}$ expiratory trigger delay, $time_{synch}$ time of synchrony (between neural effort and ventilator support)

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, NAVA versus PSV_1

† $p < 0.05$, $^{\dagger\dagger}p < 0.01$, $^{\dagger\dagger\dagger}p < 0.001$, PSV_2 versus NAVA

NAVA (5.9 ± 2.9 cmH_2O s and 123 ± 42 cmH_2O s min^{-1}, respectively) than in PSV_1 (3.6 ± 0.8 cmH_2O s and 78 ± 19 cmH_2O s min^{-1}, respectively) ($p < 0.01$ for both) and PSV_2 (3.2 ± 0.9 cmH_2O s and 76 ± 21.5 cmH_2O s min^{-1}, respectively) ($p < 0.01$ for both).

Patient–ventilator synchrony was affected by the mode of ventilation. In fact, $delay_{TR\text{-}insp}$ was shorter in NAVA (0.14 ± 0.06 s) than in PSV_1 (0.31 ± 0.13 s) and PSV_2 (0.36 ± 0.13 s) ($p < 0.001$ for both), while $delay_{TR\text{-}exp}$ did not significantly differ between trials. $Time_{synch}$ was longer with NAVA (0.79 ± 0.35 s) than in PSV_1 (0.60 ± 0.30 s) and PSV_2 (0.55 ± 0.29 s) ($p < 0.01$ for both).

Figure 1 shows an experimental record from one patient. The ineffective efforts occurring during PSV, as indicated by the mismatch between P_{aw} and EAdi, disappeared with NAVA; it is noteworthy, however, that consequent above all on the upward displacement of the helmet, the initial part of the inspiration remained unassisted. As depicted in Fig. 2, AI exceeded 10% in 70% and 80% of patients in PSV_1 and PSV_2, respectively, while no patient reached that threshold with NAVA ($p < 0.001$ NAVA vs. PSV_1 and PSV_2). Figure 3 depicts the relative incidence of ineffective efforts, auto-triggered and double-triggered breaths on the overall number of asynchronies. Ineffective efforts were the highest represented form of asynchrony during PSV. No asynchrony was observed with NAVA.

Discussion

This is, to our knowledge, the first study evaluating NAVA in a head-to-head comparison with PSV. We found in patients receiving h-NIV for postextubation hypoxemic ARF that, compared with PSV, NAVA improved patient–ventilator interaction and overall resulted in a better synchrony, with no significant difference in gas exchange, respiratory rate, and neural drive and timing.

Before discussing these results, some limitations of our study must be addressed. First of all, the inspiratory pressure support was arbitrarily set for all patients at 12 cmH_2O, a value already used by previous investigators to provide NIV in ICU patients. Very recently, Vargas et al. [15] showed that to achieve with h-NIV the same effects of NIV delivered through a facial mask, both PEEP and PSV should be increased by 50%; unfortunately this information was not available at the time our

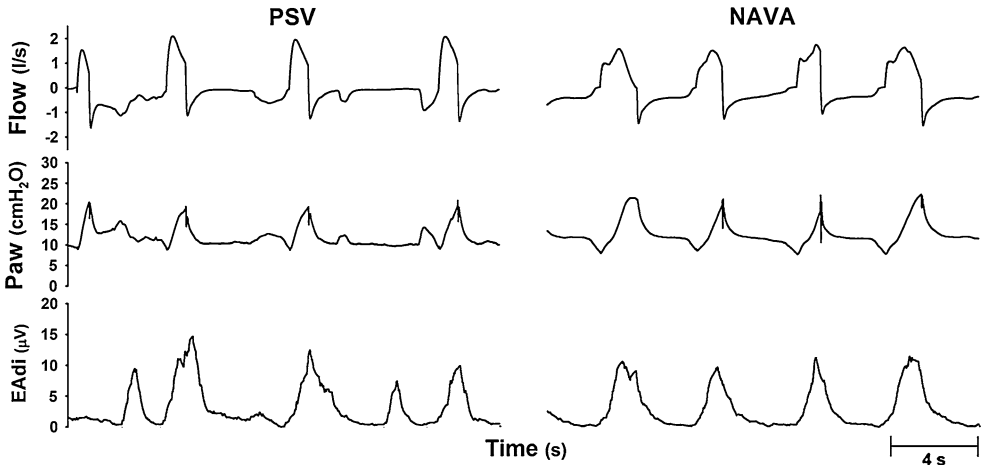

Fig. 1 Examples of tracings from one representative patient undergoing h-NIV in PSV (*left panel*) and NAVA (*right panel*) are displayed. Flow, P_{aw}, and EAdi tracings are shown from *top* to *bottom*, for PSV (*left panel*) and NAVA (*right panel*). The ineffective efforts occurring during PSV, as indicated by the mismatch between P_{aw} and EAdi, disappear with NAVA. *h-NIV* noninvasive ventilation through helmet, P_{aw} airway pressure, *EAdi* diaphragm electrical activity, *PSV* pressure support ventilation, *NAVA* neurally adjusted ventilator assist

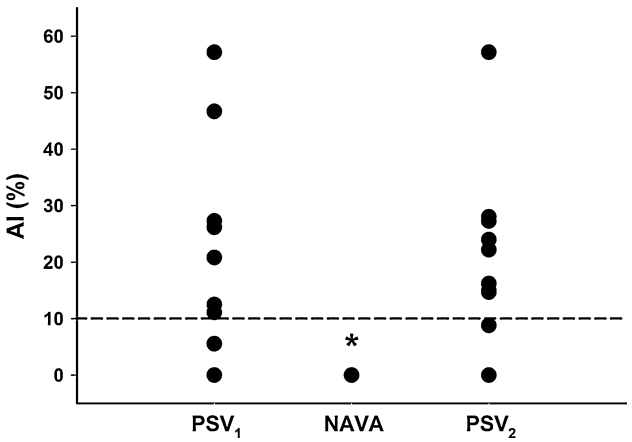

Fig. 2 Values of AI at least 10% are shown for all patients at each trial. *Filled circles* indicate individual data points of patients with AI at least 10%. AI exceeded 10% in seven patients during PSV_1, no patient in NAVA, and eight patients during PSV_2. (*$p < 0.001$). *AI* asynchrony index, *PSV_1* pressure support ventilation (first trial), *NAVA* neurally adjusted ventilatory assist, *PSV_2* pressure support ventilation (second trial)

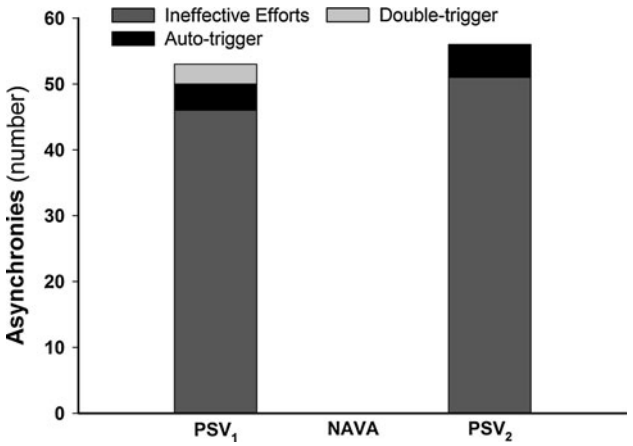

Fig. 3 Relative incidence of ineffective efforts, auto-triggered and double-triggered breaths on the overall number of asynchronies is shown. Ineffective efforts were the highest represented form of asynchrony during PSV_1 (87%) and PSV_2 (91%). Auto-triggered breaths accounted for 7.5 and 9% of all asynchronies during PSV_1 and PSV_2, respectively; double triggering was 5.5% of the asynchronies during PSV_1, while it did not occur during PSV_2. No asynchrony was observed with NAVA. *PSV_1* pressure support ventilation (first trial), *PSV_2* pressure support ventilation (second trial), *NAVA* neurally adjusted ventilatory assist

study was designed. It should be noted, however, that to minimize the negative effect on synchrony related to the helmet compliance [8], we applied 10 cmH_2O of PEEP, a value definitely higher compared with the average 5 cmH_2O used by Vargas et al. [15]. The preset inspiratory support in our study was 12 cmH_2O, which is 20% higher than the average 10 cmH_2O used by Vargas et al. [15] and, as a matter of fact, was effective in maintaining $PaCO_2$ and pH within the range of normal physiologic values. Second, we used the "NAVA preview" function to estimate the NAVA level necessary to achieve a level of assistance similar to that provided with PSV, as previously described [12, 16, 17]. Consequent on the elevated breath-to-breath variability in EAdi and P_{aw} observed with NAVA [12, 18, 19], this approach could be unsuccessful. As shown in Table 3, however, the average values of $P_{aw\ peak}$ during NAVA were similar to those applied in the two PSV trials. Furthermore, as $PaCO_2$ and $EAdi_{peak}$ were not different between trials, it is quite

reasonable to assume that comparable amounts of assistance were provided with NAVA and PSV. Third, as previously done [8, 20–22], we considered the point in time corresponding to $EAdi_{peak}$ as the termination of TI_{neu}, while, during NAVA, cycling from inspiration to expiration (I/E) occurs when EAdi falls to 70% of $EAdi_{peak}$, which introduces an inherent delay between the end of neural inspiration and the end of mechanical inspiration that explains why, during NAVA, TI_{mec} exceeds TI_{neu}. Fourth, we included patients who developed hypoxemia and respiratory distress following extubation. As postextubation ARF is a somewhat specific type of respiratory failure, it is uncertain whether our results can be extended to other forms of ARF. Finally, we did not assess patient tolerance to h-NIV throughout trials. As NAVA improved $delay_{TR\text{-}insp}$, an improvement in patient comfort could be expected. It should be noted, however, that patient tolerance, while being significantly affected in clinical studies covering a long-term period (i.e., days) [6, 7], did not vary in previous short-term studies (i.e., minutes) [4, 8, 15, 23]. In particular, Vargas et al. [15] did not find significant changes in patient comfort, as assessed by a comfort score, when varying PEEP and inspiratory assistance, in spite of significant changes in $delay_{TR\text{-}insp}$ and inspiratory effort. Also, Costa et al. [23] who evaluated different PSV settings in healthy subjects undergoing h-NIV, did not find significant variations in patient comfort, as assessed by visual analog scale, despite significant changes in breathing pattern and inspiratory effort.

The most valuable difference between NAVA and PSV we observed regarded patient–ventilator synchrony, which improved in NAVA, as opposed to PSV. The clinical benefit of a better patient–ventilator synchrony during NIV has not been fully established yet. Asynchronies have been found to be related to increased gastric distension [24] and patient discomfort [25]. Very recently, Vignaux et al. [5] demonstrated that patients with AI greater than 10% during NIV have a lower comfort, as opposed to those with AI less than 10%, suggesting that a better synchrony improves patient tolerance to NIV.

$Delay_{TR\text{-}insp}$ was halved with NAVA, as compared with PSV, a difference that could have been amplified by the characteristics of the helmet, since, compared with the facial mask, this interface worsens the performance of the pneumatic trigger during PSV [8]. Although the rate of improvement in $delay_{TR\text{-}insp}$ we observed with NAVA, as opposed to PSV, is quite similar to those reported by other studies performed in intubated patients [21, 22], further studies are necessary to ascertain whether this improvement in $delay_{TR\text{-}insp}$ would be observed with different NIV interfaces.

Differently from previous studies comparing these two modes during either invasive ventilation [21, 22] or NIV [11], the difference in $delay_{TR\text{-}exp}$ between NAVA and PSV is here quite small and not significant. Type of interface [8, 26], mechanical properties of the respiratory system of the subjects investigated [27, 28], and expiratory trigger threshold settings [28] are all factors potentially contributing to explain this discrepancy. Costa et al. [26] showed that $delay_{TR\text{-}exp}$ is reduced with the helmet, as opposed to the endotracheal tube, when setting ET_{TH} between 25 and 50% of the peak inspiratory flow; they also found that reducing ET_{TH} down to 5% of the peak inspiratory flow remarkably increases $delay_{TR\text{-}exp}$, irrespective of the interface. Delayed ventilator cycling has been observed in the presence of obstructive airway disease, which is significantly affected by ET_{TH}, i.e., the lower ET_{TH}, the higher $delay_{TR\text{-}exp}$ [28]. We studied patients with hypoxemic ARF and set ET_{TH} in PSV mode at 50% of the peak inspiratory flow. Different results would be expected when evaluating COPD patients and adopting lower ET_{TH} in PSV. In our study, $delay_{TR\text{-}exp}$ during PSV is lower than reported by Piquilloud et al. [21] who studied intubated patients, 33% of whom had COPD. $Delay_{TR\text{-}exp}$ in PSV was even higher in another study also performed in intubated patients, 78% of whom had COPD [22]; in addition, these authors utilized a fixed ET_{TH} corresponding to 5% of peak inspiratory flow [22]. Moerer et al. [11] compared in normal volunteers h-NIV delivered in PSV mode, either pneumatically or neurally triggered. Compared with our data, they found longer $delay_{TR\text{-}exp}$ when pneumatically cycling, and shorter $delay_{TR\text{-}exp}$ when cycling was neurally determined. The longer $delay_{TR\text{-}exp}$ when pneumatically cycling is consequent on the different ET_{TH}, i.e., 5% in the Moerer study, as opposed to 50% in ours. The shorter $delay_{TR\text{-}exp}$ they observed when I/E was neurally determined is explained by the different type of analysis performed: in our study cycling-off in NAVA occurred when EAdi fell to 70% of $EAdi_{peak}$, while we considered the end of TI_{neu} as the point in time corresponding to $EAdi_{peak}$; in contrast, in the study by Moerer et al. [11] I/E occurred when EAdi fell to 60% of $EAdi_{peak}$ and the end of TI_{neu} also corresponded to the point at which EAdi fell to 60% of $EAdi_{peak}$, thereby eliminating the aforementioned inherent delay.

Overall, patient–ventilator interaction and synchrony improved with NAVA, compared with PSV, as indicated by the significantly longer $time_{synch}$ and lower AI. It is noteworthy that $time_{synch}$ accounted for 86% of TI_{neu} in NAVA, and 71% and 65% of TI_{neu} during PSV_1 and PSV_2, respectively. This better matching resulted in an improved ventilator assistance, i.e., an increased PTP_{aw}/br and PTP_{aw}/min, in NAVA, as opposed to PSV. It is worth mentioning that although several studies performed in patients undergoing invasive ventilation showed that, compared with PSV, NAVA significantly decreases the occurrence of asynchronies, this is, to our knowledge, the first study showing that asynchronies are also significantly reduced in NIV. Interestingly, this was achieved despite a significantly larger amount of air leaks observed with

NAVA, as opposed to both PSV trials. It is important to remark that, in contrast to NAVA, PSV was delivered using a dedicated NIV software.

In keeping with the results of previous studies comparing the helmet and oronasal mask in delivering NIV, we found that, despite the improvement in patient–ventilator interaction observed with NAVA, there was no significant difference in ABGs between the two modes [8, 15]. Vignaux et al. [5], who determined the prevalence of asynchronies in 60 patients receiving NIV for treatment of ARF, did not report differences in gas exchange between patients with AI above and below the 10% threshold.

EAdi was also not significantly different between NAVA and the PSV trials. On the one hand, PSV delivered through a helmet was proved to be effective in reducing inspiratory effort in healthy subjects [23], stable COPD [8], and patients at risk of developing postextubation respiratory distress [15]. On the other hand, previous studies performed in intubated patients showed that, compared with PSV, NAVA improves patient–ventilator synchrony without determining a more pronounced decrease in neural effort [12, 16, 22].

In conclusion, the results of this study show that, compared to PSV, delivering h-NIV with NAVA is equally effective in maintaining an adequate gas exchange and has similar effects on neural effort, while improving patient–ventilator interaction and decreasing asynchronies. It is worth remarking, however, that this is just a short-term physiologic study performed on a limited number of patients and that further studies are clearly necessary to ascertain whether or not the advantage suggested by our data translates to a better NIV outcome.

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