https://doi.org/10.5664/jcsm.9546

JCSM | Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Sleep increases leaks and asynchronies during home noninvasive ventilation: a polysomnographic study

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Study Objectives: In patients treated with noninvasive ventilation, sleep-related breathing changes can modify patient-ventilator interactions, which could reduce its effectiveness. The aim of this prospective observational study was to determine the impact of sleep/wake state on leaks, upper airway obstructive events, and asynchronies in patients treated by long-term noninvasive ventilation.

Methods: Stable patients adapted to noninvasive ventilation were considered for nocturnal polysomnography. Unintentional leaks, upper airway obstructive events, and asynchronies were compared between sleep and awake periods.

Results: Twenty-eight patients were enrolled. Underlying diagnoses were neuromuscular disease (n = 11), chest wall disease (n = 8), and obesity-hypoventilation (n = 9). Leaks were more frequent in sleep than in awake periods, with a median of 10% (interquartile range [IQR], 0%–75%) vs 1% (IQR, 0%–9%) of time ($P < .001$), respectively. During sleep, asynchronies with and without associated leak affected 27% of breaths (IQR, 16%–39%) compared with non–leak-related asynchronies that were recorded in 8% (IQR, 3%–25%) of breaths ($P < .001$). Asynchronies affecting more than 10% of total breaths were more frequent in sleep (25 patients, 89%) than in awake time (8 patients, 29%; $P = .25$). Eleven patients (39%) presented with 5 or more upper airway obstructive events without reduction in ventilatory drive per hour of sleep.

Conclusions: In patients adapted to home noninvasive ventilation, leaks, asynchronies, and upper airway obstructive events are frequent during the night and are concentrated in sleep periods. Asynchronies are often associated with leaks. These findings may have clinical implications considering that in patients with low sleep efficiency respiratory events could be underestimated if sleep is not evaluated.

Keywords: noninvasive ventilation, patient-ventilator asynchrony, polysomnography, sleep, unintentional leak

Citation: Martí S, Ferré A, Sampol G, et al. Sleep increases leaks and asynchronies during home noninvasive ventilation: a polysomnographic study. *J Clin Sleep Med*. 2022;18(1):225–233.

BRIEF SUMMARY

Current Knowledge/Study Rationale: In patients treated by home noninvasive ventilation, sleep-related breathing changes can modify patient-ventilator interactions, which could reduce its effectiveness. However, studies that address sleep objectively in this population are lacking.

Study Impact: In patients with low sleep efficiency, respiratory events such as leaks and asynchronies could be underestimated if sleep is not addressed. Nocturnal polysomnography can be useful for evaluating home noninvasive ventilation in a subgroup of patients who present with problems after evaluation with more simple tools.

INTRODUCTION

Noninvasive ventilation (NIV) has proved to be an effective treatment for chronic hypercapnic respiratory failure, with an increasing number of indications.[1–3] It is predominantly applied at night, when sleep-related changes in ventilatory patterns, respiratory drive, and respiratory muscle activity occur. These changes may modify the interactions between the patient and the ventilator, thus inducing leaks, upper airway events, and patient-ventilator asynchronies (PVAs). These events have been associated with clinically relevant consequences, such as decreased adherence to treatment, impaired nocturnal gas exchange and poor sleep quality,[4–8] and mortality.[9] As a result, there is a need to assess whether the ventilation is being delivered effectively during sleep.[10]

Simple tools, defined as oximetry, transcutaneous capnometry, and built-in ventilator software, can provide important information when monitoring NIV. However, it has been shown that this monitoring may not adequately explore certain aspects of the therapy, which may have a negative effect on its efficacy. First, even though marked differences have been observed between events recorded during the day and those recorded at night,[6] usually studies have not considered whether the patient is asleep or awake during the nighttime monitoring.[6,11] Low sleep efficiency has been found in patients treated with home NIV,[5,7,8] and differences in sleep efficiency may lead to discordant results when simple tools are used. Second, the built-in software in home ventilators supplies valuable data on patient treatment, such as adherence, leaks, and residual apnea and hypopnea indexes. Nonetheless, it has been suggested that the

validity of several parameters that are estimated, not directly measured, by the NIV devices should be validated further by independent clinical and/or bench test studies.[12–14] Therefore, although simple tools are recommended as first-line monitoring, polysomnography (PSG) remains the gold standard for monitoring NIV during sleep and, in some cases, plays an important role in optimizing NIV settings.[12,15–17]

In recent years, it has been pointed out that the nomenclature defining abnormal nocturnal respiratory events during sleep in spontaneous breathing is not applicable for describing respiratory events occurring under NIV, and a standardized classification of polygraphic recordings for evaluating NIV during sleep has been proposed.[10,18] However, studies evaluating sleep objectively and following this standardized methodology are lacking.

Based on these considerations, the objective of the present study was to determine the impact of sleep/wake state on the prevalence of respiratory events in a group of patients who are well adapted to home NIV. Additionally, we assessed the repercussions of these events on nocturnal gas exchange, sleep quality, and quality of life.

METHODS

This was a prospective observational study conducted at the Respiratory Department of a tertiary university hospital. The study was approved by the Institutional Review Board (PR[AG] 143/12) at the Hospital Universitari Vall d'Hebron, and written informed consent was obtained from all patients.

Patients

Patients treated with long-term (≥ 3 months) home nocturnal bilevel NIV between January 2015 and December 2017, in stable clinical condition, were considered for inclusion in the study if they had an arterial carbon dioxide level ($PaCO_2$) ≤ 45 mm Hg in arterial blood gas measurements on room air while awake. NIV had been initiated in an acute care hospital setting by experienced respiratory physicians in patients experiencing chronic hypercapnic respiratory failure.[19] Exclusion criteria were as follows: (1) age < 18 years, (2) history of acute respiratory failure within the past 3 months, (3) nonadherence to treatment (< 4 hours average daily use), (4) rapidly progressive neuromuscular disease (eg, amyotrophic lateral sclerosis), (5) chronic obstructive pulmonary disease as the cause of respiratory failure, and (6) oxygen added to NIV.

Patient-reported outcomes

Immediately prior to nocturnal monitoring, the following variables were assessed in all participants. Sleep quality was measured by the Pittsburgh Sleep Quality Index,[20] which assesses a wide variety of factors over the previous month; higher scores indicate worse sleep quality. Somnolence was evaluated with the Epworth Sleepiness Scale.[21] The Fatigue Severity Scale[22] rated the severity of fatigue symptoms during the previous week, and higher scores were related with more fatigue. And health-related quality of life was measured by a disease-specific tool, the Severe Respiratory Insufficiency questionnaire, designed for patients treated with home NIV;[23,24] scores on 7 subscales are added together to form 1 summary scale, with higher scores indicating better health-related quality of life.

Nocturnal monitoring

Nocturnal PSG recordings were performed at the Sleep Unit during a single night, under NIV with the patient's home ventilator, with their usual settings and mask. The intervention of the sleep technicians was kept to a minimum throughout the study and limited to reattaching sensors. In addition to standard recorded parameters, other measures included the following: mask pressure, flow signal recorded with an external pneumotachograph (PT2 Dual; Braebon, Kanata, Canada) inserted between the interface (a mask with an integrated intentional leak) and a single-limb circuit, surface diaphragm electromyography, and transcutaneous capnometry (TOSCA 500; Radiometer, Copenhagen, Denmark). The recording time comprised the start of ventilation (lights-off, beginning of the PSG) until the ventilator was switched off (lights on, end of the PSG). PSG data were collected and stored using an E-Series digital system (Compumedics, Abbotsford, Australia). Sleep and arousals were scored according to the American Academy of Sleep Medicine criteria.[25]

All tracings were scored by manual analysis performed by an experienced sleep physician. Respiratory parameters were assessed blinded to the patient's identity and to the signals indicating whether the patient was asleep or awake. The following respiratory events were identified in accordance with prior definitions:[10,11,26]

Unintentional leaks were identified by: (1) an increase in flow amplitude and reduction in thoracic and abdominal belt signals (these findings may be accompanied by a loss of the basal line in the airflow signal leading to an upward displacement of the trace); (2) loss of inspiratory flow decrease, with the inspiratory flow curve showing a characteristic double slope with an initial rapid increase followed by a slower increase until cycling; (3) a fall in positive pressure (inspiratory and expiratory) could be seen in case of major leaks. The presence of leaks detected from previous points can favor the nondetection of the patient's inspiratory efforts by the ventilator and switch to back-up respiratory frequency.

Upper airway obstruction (UAO) with reduction of ventilatory drive was identified by: (1) progressive and smooth reduction in flow amplitude while the amplitude of pressure signal remains unchanged; (2) simultaneous reduction in or disappearance of thoracic and abdominal belt signal; (3) switch of ventilator to back-up respiratory rate without thoracic or abdominal movements; (4) no effort in diaphragm electromyography (EMG) channel; (5) synchronous resumption of flow and thoracoabdominal movements without fighting movements.

UAO without reduction in ventilatory drive was considered according to the following criteria: (1) sudden reduction in flow amplitude during insufflation while inspiratory positive pressure is maintained; (2) phase opposition in thoracic and abdominal belts can be observed; (3) increased effort in diaphragm EMG channel; (4) increase in respiratory rate at the end of the event due to increase in patient's efforts to open the airways; (5) poor detection of the patient's inspiratory efforts associated with a switch to back-up respiratory rate can be observed.

Patient-ventilator asynchronies (PVAs): (1) Ineffective effort: the patient exhibits an inspiratory effort demanding a breath that is not followed by a ventilator-delivered pressurization. We scored ineffective effort when an increase in inspiratory flow was not followed by an assisted cycle in the pressure channel. During the inspiratory flow increase an effort is also recorded in thoracic and abdominal belts and diaphragm EMG. (2) Double triggering is an asynchronous event in which a patient demands a single breath but 2 breaths are delivered by the ventilator. The first cycle must be patient-triggered, the second cycle is not. (3) Auto-triggering: the patient makes a single continuous demand for a breath that triggers multiple ventilator-delivered breaths. This was recorded when at least 3 rapid successions of pressurization occurred. (4) Premature cycling: the patient's inspiratory effort continues as the ventilator cycles into expiration. This was recorded when the ventilator cycles to expiration, which is defined as a reduction in the pressure signal toward the baseline, while the maximum inspiratory effort in thoraco-abdominal belts and/or diaphragm EMG continues. (5) Delayed cycling: the patient inspiratory effort ceases but the ventilator continues to deliver a breath. This was recorded when the pressure wave is maintained or increased as the patient attempts to breathe out, and maximum inspiratory effort in thoraco-abdominal belts and/or diaphragm EMG ceases before expiratory ventilator cycling.

PVAs were defined as triggering or cycling asynchronies. Triggering asynchronies included ineffective efforts, double triggering, and auto-triggering; cycling asynchronies included premature and delayed cycling. Asynchronies were not scored if a UAO event was present. In an attempt to evaluate leak-related events a second reading was performed, in which in the presence of leaks no other concomitant events were considered. Leaks were quantified as percentages of recording time, and major leaks were considered when a 50% or greater increase in airflow was observed. UAO events were scored as number of events per hour. Frequency of PVAs was calculated as the number of asynchronous breaths divided by the total number of breaths multiplied by 100. All of these measures were performed separately for sleep and wake periods.

Statistical analysis

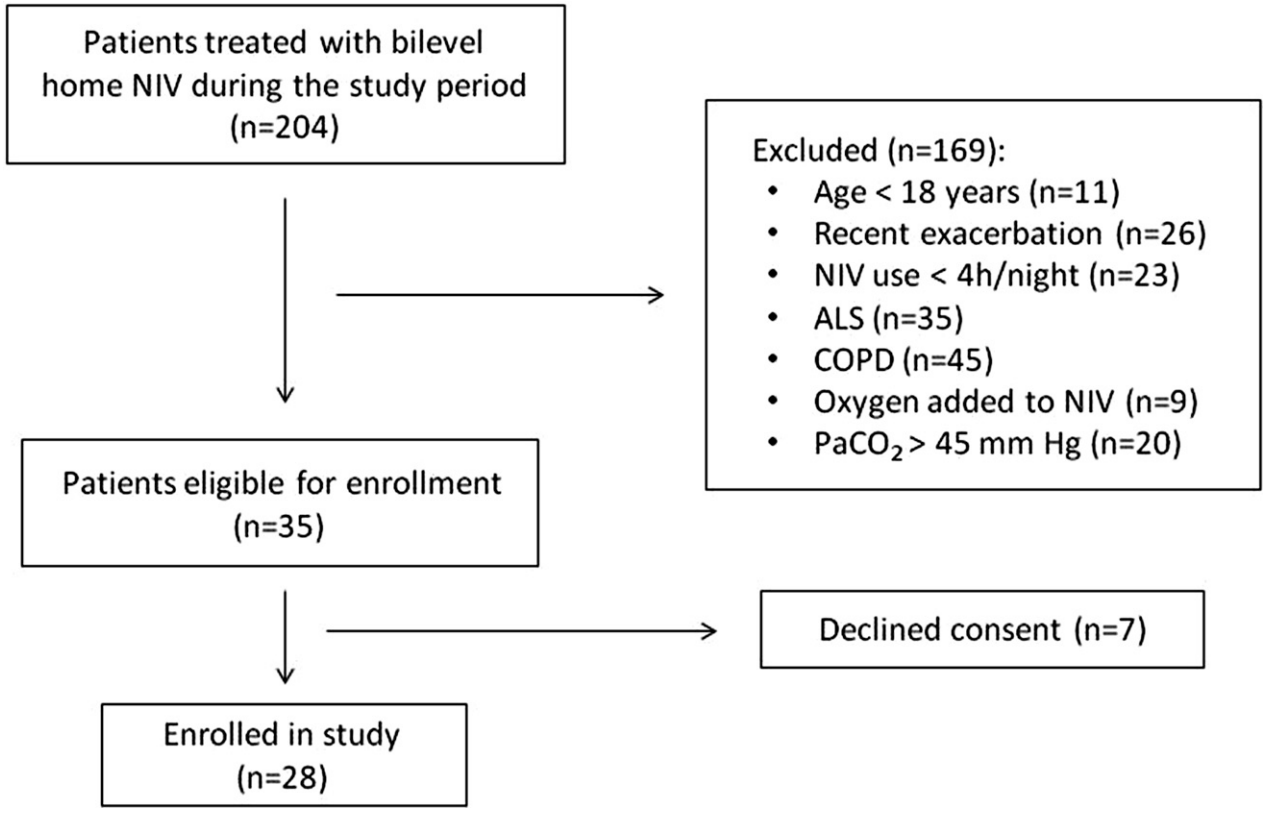
Descriptive data are presented as percentages and medians (interquartile range [IQR]). Comparisons between groups were performed with the Mann-Whitney *U* test or the Kruskal-Wallis test, as appropriate. Analyses were conducted using Stata IC 14 (StataCorp LP, College Station, TX).

RESULTS

Patients and NIV characteristics

Figure 1 shows the flowchart of patient recruitment. Twenty-eight patients were studied (16 males). Eleven patients had neuromuscular disease, 8 had chest wall disease, and 9 had obesity

Figure 1—Flow chart of patient recruitment.



ALS = amyotrophic lateral sclerosis, COPD = chronic obstructive pulmonary disease, NIV = noninvasive ventilation, $PaCO_2$ = arterial carbon dioxide.

Table 1—Characteristics of included patients.

	All (n = 28)	NMD[a] (n = 11)	CWD[b] (n = 8)	OHS (n = 9)	*P* Value
Age, y	66 (55–74)	57 (26–70)	70 (63–74)	72 (58–77)	.26
Sex (female/male), n/n	12/16	3/8	6/2	3/6	.13
BMI, kg/m^2	31 (24–38)	29 (23–33)	24 (22–29)	38 (37–45)	.001
FVC, % predicted	47 (38–54)	47 (46–54)	32 (25–46)	48 (46–69)	.03
FEV_1, % predicted	47 (37–60)	50 (46–58)	32 (24–43)	60 (47–82)	.004
FEV_1/FVC, %	76 (68–81)	80 (72–81)	66 (63–74)	77 (69–81)	.03
PaO_2, mm Hg	76 (69–82)	81 (68–86)	79 (74–81)	75 (67–76)	.25
$PaCO_2$, mm Hg	41 (37–43)	41 (37–44)	41 (38–43)	43 (38–43)	.88
Bicarbonate, mmol/L	26 (23–28)	24 (22–28)	26 (23–28)	26 (25–27)	.63

Data are shown as median (interquartile range) or ratio. [a]Patients with NMD included those with diaphragm paralysis (n = 5) and 1 patient each with one of the following diagnoses: Lambert-Eaton myasthenic syndrome, Duchenne muscular dystrophy, myotonic dystrophy, inclusion body myopathy, and congenital myopathy. [b]Patients with CWD included those with kyphoscoliosis (n = 5) and with tuberculosis sequelae (n = 3). BMI = body mass index, CWD = chest wall disease, FEV_1 = forced expiratory volume in 1 second, FVC = forced vital capacity, NMD = neuromuscular disease, OHS = obesity hypoventilation syndrome, $PaCO_2$ = arterial carbon dioxide level, PaO_2 = arterial oxygen level.

hypoventilation syndrome. Patients' clinical characteristics are shown in **Table 1**. Ventilator settings are summarized in **Table 2**. NIV was provided through an oronasal (n = 18) or a nasal (n = 10) mask.

Sleep, gas exchange, and respiratory events

Nocturnal PSG with NIV showed a sleep efficiency of 71% (IQR, 48%–77%) in the patient group as a whole (**Table 3**). Wake after sleep onset (WASO) was 126 minutes (IQR, 92–215 minutes). There were no significant differences in sleep architecture parameters between diagnostic groups. The periods of sleep showed a poorer gas exchange than wake periods (**Table 4**).

In our population, total leaks, major leaks, UAO events with or without reduction in ventilatory drive, and PVAs were recorded more frequently during sleep than during wake periods (**Table 5**). Seventy-four percent (IQR, 65%–83%) of total detected leaks were major leaks. Leaks (**Figure 2**) were present during more than 25% of the time in 12 patients (43%) in sleep periods and in 6 patients (21%) in wake periods ($P = .02$). During sleep, leaks were greater with nasal masks (52% total sleep time [TST]; IQR, 4%–79%) than with oronasal masks (5% TST; IQR, 0%–67%; $P = .18$). Asynchronies affected > 10% of the total breaths in 25 patients (89%) in sleep periods and in 8 patients (29%) in wake periods ($P = .25$). Triggering asynchronies were the more frequent type, and ineffective effort was the most commonly isolated asynchrony, affecting 12% (IQR, 3%–20%) of breaths during sleep. Asynchronies were often associated with leaks, both in wake and sleep periods (**Figure 3**). During sleep, PVAs with and without associated leak affected 27% (IQR, 16%–39%) of breaths, compared with non–leak-related PVAs that were recorded in 8% (IQR, 3%–25%) of breaths ($P < .001$). In 15 patients with leaks during more than 5% of total register time (median leak time 43%;

Table 2—Noninvasive ventilation characteristics.

	All (n = 28)	NMD (n = 11)	CWD (n = 8)	OHS (n = 9)	*P* Value
IPAP, cm H_2O	16 (15–19)	16 (14–18)	16 (15–19)	18 (18–22)	.02
EPAP, cm H_2O	6 (4–7)	6 (4–6)	4 (4–5)	8 (6–8)	.13
Backup rate, breaths/min	15 (14–15)	15 (12–15)	15 (14–15)	15 (14–15)	.46
Ventilatory mode, PSV/PCV	21/7	9/2	5/3	7/2	.75
Mask, nasal/oronasal	10/18	4/7	4/4	2/7	.47
Time on NIV, mo	48 (26–68.5)	48 (30–72)	48 (35.5–70.5)	36 (12–67)	.66
Objective adherence, h/night	7 (6–9)	7 (6–9)	8.6 (7–9.5)	6.4 (5–8)	.29

Data are shown as median (interquartile range) or ratio. Bilevel pressure-cycled ventilators used were: VPAP IV ST (n = 4) and Stellar 150 (n = 2) (ResMed, Bella Vista NSW, Australia) and Vivo 30 (n = 6) and Vivo 40 (n = 16) (Breas Medical, Mölnlycke, Sweden). CWD = chest wall disease, EPAP = expiratory positive airway pressure, IPAP = inspiratory positive airway pressure, NIV = noninvasive ventilation, NMD = neuromuscular disease, OHS = obesity hypoventilation syndrome, PCV = pressure-control ventilation, PSV = pressure-support ventilation.

Table 3—Sleep data during nocturnal polysomnography with noninvasive ventilation.

Variable	Values
TST, min	343 (247–423)
Sleep efficiency, %	71 (48–77)
Sleep latency, min	25 (12–39)
WASO, min	126 (92–215)
REM sleep, % TST	13 (8–19)
Non-REM sleep stage N3, % TST	18 (13–23)
Arousal index, events/h	22 (15–36)

Data are shown as median (interquartile range); n = 28. REM = rapid eye movement, TST = total sleep time, WASO = wake after sleep onset.

IQR, 18%–52%), 82% (IQR, 49%–87%) of total PVAs were observed during the leak periods. An index of 1.8 (IQR, 0.5–10.3) UAO events without reduction in ventilatory drive occurred during sleep, with 11 patients (39%) presenting 5 or more events per hour.

Association of sleep events with sleep architecture and gas exchange

We compared the frequency of sleep respiratory events with sleep gas exchange (average oxygen saturation from pulse oximetry [SpO_2]), time with SpO_2 < 90%, desaturation index 3%, average partial pressure of transcutaneous carbon dioxide ($PtcCO_2$), time with $PtcCO_2$ > 50 mm Hg, and PSG data (sleep efficiency, arousal index, WASO, rapid eye movement [REM] sleep, and non-REM sleep stage N3) (see **Table S1** in the supplemental material). An above-median presence of leaks (≥ 10% TST) was associated with higher oxygen desaturation index, percentage of time with SpO_2 < 90% and WASO, and with lower sleep efficiency. However, leaks were not associated with $PtcCO_2$. Above-median PVAs (≥ 27% of breaths) were associated with a greater percentage of REM sleep. Finally, a score of 5 or more UAO events per hour without reduction in ventilatory drive was associated with higher oxygen desaturation index and lower percentage of slow-wave sleep.

Patient-reported outcomes

Results of patient-reported sleep quality (Pittsburgh Sleep Quality Index), somnolence (Epworth Sleepiness Scale),

Table 4—Gas exchange data during nocturnal polysomnography with noninvasive ventilation, awake, and sleep.

	Awake	Sleep	*P* Value
Average $PtcCO_2$, mm Hg	44 (40–46)	47 (42–49)	<.001
Time spent with $PtcCO_2$ > 50 mm Hg, %	0 (0–7)	2 (0–40)	.002
Average SpO_2	94 (93–96)	93 (91–95)	<.001
Time spent with SpO_2 < 90%, %	0 (0–5)	1 (0–27)	.001
ODI 3%, events/h	0 (0–0)	11 (5–25)	<.001

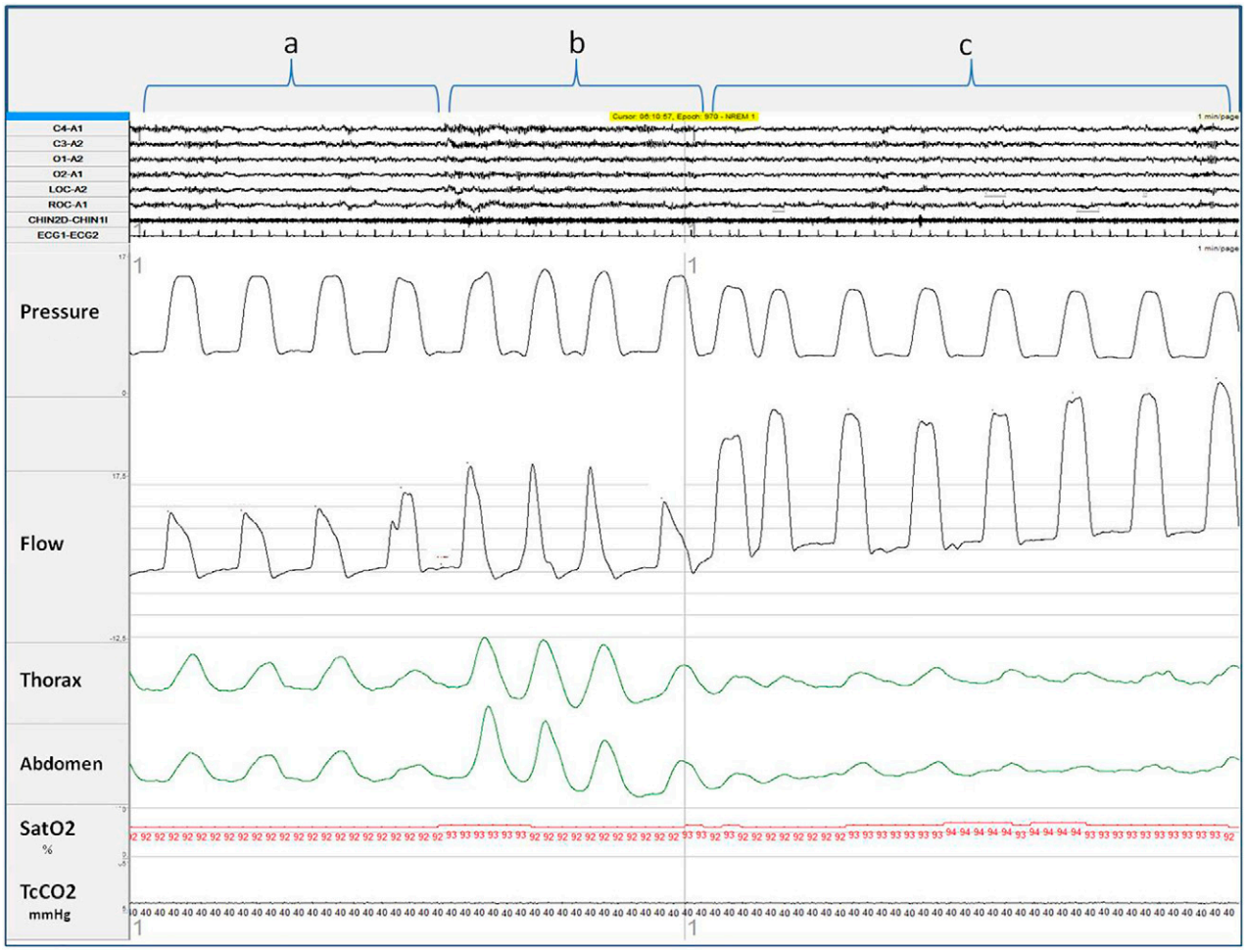
Data are shown as median (interquartile range); n = 28. ODI = oxygen desaturation index, $PtcCO_2$ = partial pressure of transcutaneous carbon dioxide, SpO_2 = oxygen saturation from pulse oximetry.

Table 5—Respiratory events during nocturnal polysomnography with noninvasive ventilation: awake vs sleep comparison.

	Awake	Sleep	*P* Value
Leaks, time (%)	1 (0–9)	10 (0–75)	<.001
Major leaks, time (%)	1 (0–6)	10 (0–52)	<.001
Upper airway obstruction, events/h			
Without reduction of ventilatory drive	—	1.8 (0.5–10.3)	
With reduction of ventilatory drive	—	0.1 (0–1.1)	
Asynchronies, % breaths			
Ineffective effort	1 (0–3)	12 (3–20)	<.001
Auto-triggering	0.1 (0–1)	1 (0–4)	<.001
Double triggering	1 (0–2)	4 (1–7)	<.001
Premature cycling	0.1 (0–1)	0.1 (0–1)	.71
Delayed cycling	0.2 (0–2)	0.4 (0–6)	.18
All asynchronies (triggering + cycling)	6 (2–14)	27 (16–39)	<.001

Data are shown as median (interquartile range).

Figure 2—Unintentional leaks.



Initially a period of synchronic breathing without leak is registered **(a)**. After a spontaneous arousal associated with an increase in breathing effort **(b)**, a period of leak **(c)** is observed, characterized by an increase in the flow signal that is accompanied by a loss of the basal line, a decrease in the inspiratory pressure in the pressure channel, and a decrease in the amplitude of the thoracic-abdominal belt signals. Tracing duration, 1 minute. $SatO_2$ = oxygen saturation from pulse oximetry, $TcCO_2$ = partial pressure of transcutaneous carbon dioxide.

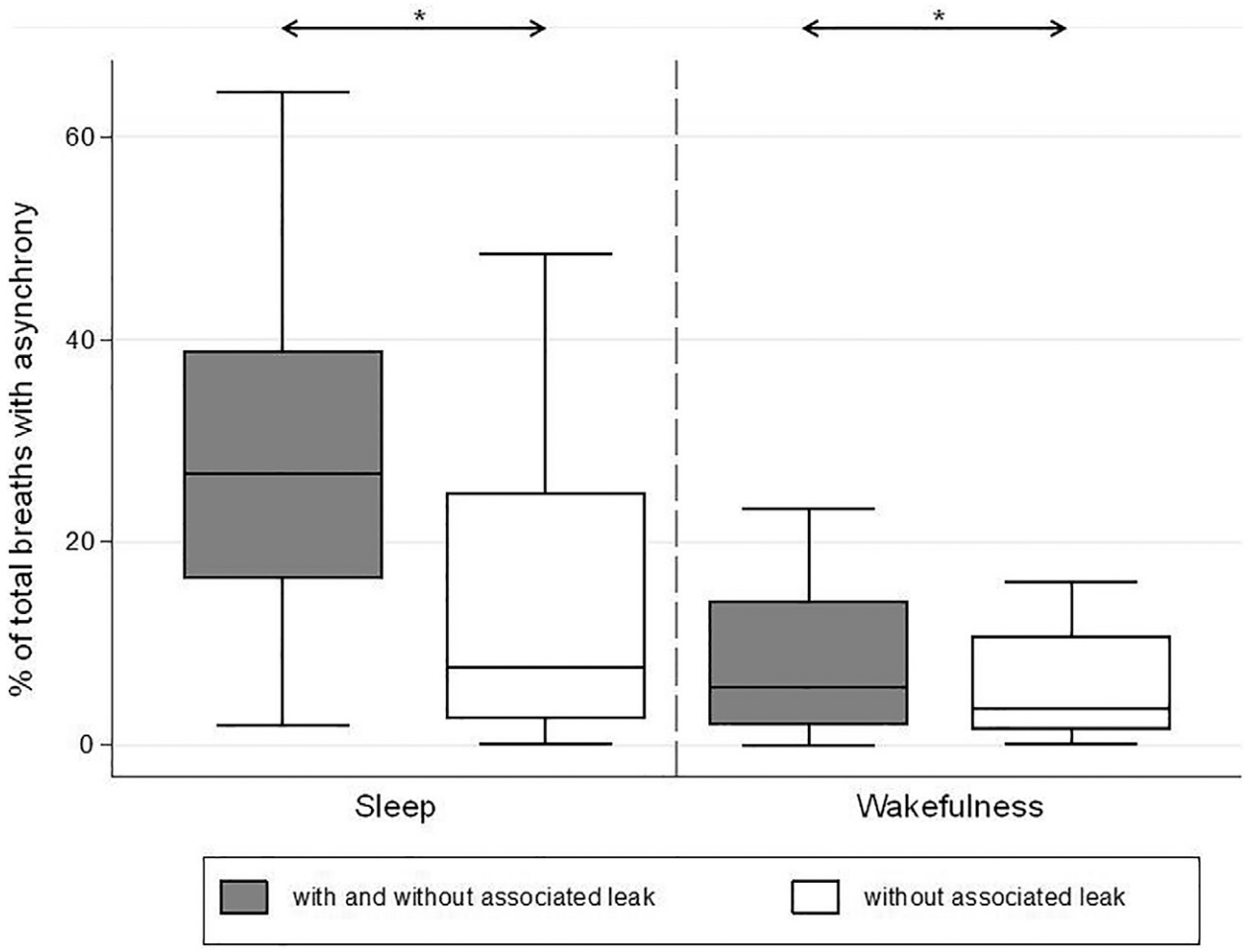
fatigue (Fatigue Severity Scale), and disease-specific health-related quality of life (Severe Respiratory Insufficiency) questionnaires are shown in **Table S1** and **Table S2** in the supplemental material. Only UAO events without reduction in ventilatory drive (≥ 5 events/hour) were associated with higher Epworth Sleepiness Scale values.

DISCUSSION

In the present study, we found that in stable patients adapted to long-term NIV, the presence of leaks, asynchronies, and upper airway events was frequent during the night and was concentrated in the periods of sleep. Asynchronies were often associated with unintentional leaks. With regard to the consequences of respiratory events, we found an association between them and poorer sleep structure, and between leaks and hypoxemia.

To our knowledge, this is the first study to evaluate the influence of the state of sleep or wakefulness on the patient-ventilator interactions in home NIV. The higher presence of respiratory events at night than during the day was previously noted by Fanfulla et al.[6] However, they restricted their observations to a single type of PVA (ineffective effort) and they did not evaluate the association of their findings with the patient's nocturnal sleep/wake state. Using full nocturnal PSG and a standardized methodology,[10] we found that more nocturnal respiratory events associated with long-term NIV occurred in sleep periods than in wake periods. Sleep efficiency has been previously reported to be low in patients treated with home NIV,[5,7,8] as we found in our patients, and it may be even lower in exacerbated patients or in patients poorly adapted to NIV. Therefore, we believe that our findings may be clinically relevant. They showed that respiratory events during sleep could be markedly underestimated if quantified using ventilator software alone, or through simplified systems that do not assess the patient's sleep/wake status.

Figure 3—Patient-ventilator asynchronies depending on the state of sleep or wakefulness, and on the association with leaks.



*$P < .05$.

Leaks were frequent in our study, being recorded in 10% of TST. They were associated with a high number of other events: in fact, more than two-thirds of all PVAs occurred during leak periods. In accordance with our findings, bench[27,28] and clinical[7,26,29] studies have shown that unintentional leaks create optimal conditions for PVAs. It has also been suggested that, in the monitoring of nocturnal NIV, leaks and/or obstructive events should be eliminated before the presence of PVA is evaluated.[12] However, the real impact of leaks on other respiratory events in a long-term ventilated clinical population had not been previously studied using full PSG. In the present study we found that the presence of leaks depends clearly on sleep/wake status, with a notable predominance of leaks during sleep. Additionally, our 2-step scoring protocol showed a marked decrease in PVA frequency during periods without leak, supporting a causal relationship.

To assess the clinical consequences of respiratory events in our patients, we examined their impact on gas exchange and sleep structure. We found an association between leaks and hypoxemia during sleep, but not with carbon dioxide levels. Moreover, we have found no association of PVA and nocturnal gas exchange. Previously, Fanfulla et al[5] found a relationship between PVA and nocturnal oxygen and carbon dioxide levels in a group of patients with neuromuscular diseases. However, those authors used a spontaneous ventilatory mode with no back-up respiratory rate. On the contrary, as in the present study, using a mandatory back-up rate, Ramsay et al[11] did not find a correlation between PVAs and nocturnal blood gases. This mode of ventilation, jointly with the fact of selecting patients without hypercapnia while awake, might have limited the impact of respiratory events on nocturnal blood gases in our study.

In agreement with previous studies,[5,7,8] we found a relationship between respiratory events and poor sleep quality. In our patients the presence of leaks was related with lower sleep efficiency and increased WASO. Interestingly, we found an association between PVAs and higher percentage of REM sleep. We hypothesize that this association may be related to the unstable ventilatory control that characterizes REM sleep.[30]

UAOs without reduction in ventilatory drive were more common than those with reduction in ventilatory drive. These findings are in accordance with previous work in patients undergoing long-term NIV.[31] Conversely, UAO with reduction

in ventilatory drive has been described more frequently at the beginning of home NIV,[32] and may be related to ventilator-induced hyperventilation.[33]

Nasal masks were associated with a higher number of unintentional leaks during sleep than oronasal masks. This finding was not statistically significant, but it may be clinically relevant. Previous work has demonstrated the presence of leaks when using nasal masks and the improvement in the effectiveness of NIV when they are corrected.[4] Thus, when nasal masks are used, our results stress the need to check for possible nocturnal leaks.

This study has several limitations. First, we studied a clinically stable and well-adapted population treated with long-term home NIV, without awake hypercapnia. These characteristics and the small sample size probably limited the impact of respiratory events on some of the evaluated outcomes, such as self-reported quality of sleep. The impact of sleep on NIV and the associated clinical consequences could be greater in patients with persistent hypercapnia or during the adaptation phase to nocturnal ventilator support. Second, we have excluded patients with chronic obstructive pulmonary disease although they represent a high proportion of home NIV cases.[34,35] However, these patients have characteristics such as poor sleep efficiency and frequent nocturnal clinical symptoms that could have interfered in our study objectives. Additionally, a high-intensity ventilation approach, with high pressure and high respiratory back-up rate, has been described in patients with chronic obstructive pulmonary disease treated successfully with home NIV.[36,37] Therefore, we believe that evaluation of sleep-related events during NIV in this population deserves to be specifically addressed. Third, our approach to the measurement of respiratory effort could have underestimated some PVAs.[38] However, the use of an esophageal catheter to record diaphragm electromyogram and esophageal pressure, which has been described as the gold standard for measuring respiratory effort,[39] is an invasive method that would have altered sleep and would probably have caused leaks. In order to analyze the patient-ventilator interaction, we used pressure and flow tracings from an external pneumotachograph, combined with thoracic and abdominal belts, as proposed elsewhere.[10] In addition, supporting our results, a recent study comparing pressure and flow signals with esophageal pressure measurement found a good correlation for detecting ineffective effort,[36,40] the most frequent PVA registered in our study. Fourth, we have not recorded the estimated leak provided by the ventilator software and we could not compare it with our polysomnographic registers, although it is known that the reliability and accuracy of the leak estimation by the built-in software could be highly variable from one device to another.[13] Finally, although our patients used their usual ventilator and settings, the "first-night effect" may have impacted our findings. Nevertheless, our patients presented an acceptable sleep efficiency of 71% in the group as a whole, similar to that previously reported in patients with NIV.[5,7,8]

In conclusion, in clinically stable patients adapted to long-term NIV, leaks, UAO events, and asynchronies were more frequent during sleep than during waking periods. Our findings suggest that, in patients with low sleep efficiency, respiratory events may be underestimated if the sleep/wake status is not evaluated. Patient-ventilator asynchronies were often associated with periods of leaks during sleep. These findings support the usefulness of nocturnal PSG for evaluating NIV in a subgroup of patients who present problems after evaluation with more simple tools. Further research addressing sleep evaluation in patients with NIV and new ventilators able to respond to leaks without inducing asynchronies are needed.

ABBREVIATIONS

EMG, electromyography
IQR, interquartile range
NIV, noninvasive ventilation
PSG, polysomnography
$PtcCO_2$, partial pressure of transcutaneous carbon dioxide
PVA, patient-ventilator asynchrony
REM, rapid eye movement
SpO_2, oxygen saturation from pulse oximetry
TST, total sleep time
UAO, upper airway obstruction
WASO, wake after sleep onset

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SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication October 22, 2020
Submitted in final revised form July 6, 2021
Accepted for publication July 6, 2021
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DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. The authors report no conflicts of interest.