Noninvasive Ventilation Automated Technologies: A Bench Evaluation of Device Responses to Sleep-Related Respiratory Events

Mathieu Delorme, Karl Leroux, Antoine Leotard, Ghilas Boussaid, Helene Prigent, Bruno Louis, and Frederic Lofaso

BACKGROUND: Noninvasive ventilation (NIV) is the reference standard treatment for most situations of chronic respiratory failure. NIV settings must be titrated to both preserve upper-airway patency and control hypoventilation. Automatic adjustment of pressure support (PS) and expiratory positive airway pressure (EPAP) may facilitate the initiation and follow-up of domiciliary NIV. However, whether the automatic-adjustment algorithms embedded into current devices accurately detect, respond to, and score common sleep-related respiratory events remains unclear. METHODS: A bench was set up to simulate central hypopnea (CH), central apnea (CA), obstructive hypopnea (OH), and obstructive apnea (OA). Four home ventilators were evaluated, with their dedicated modes for automatic PS and EPAP adjustment. RESULTS: All 4 devices increased PS during CH, CA, and OH. However, PS adjustment varied widely in magnitude, with tidal volumes within 100 ± 20% of the target being provided by only 3 devices for CH, one for CA, and one for OH. Two devices increased EPAP for OH and 3 for OA, including one that also increased EPAP for CA. Only 2 devices scored residual hypopnea after simulated CA, and only one scored a residual event after OH. One device scored no event. CONCLUSIONS: Current NIV devices differed markedly in their responses to, and reporting of, standardized sleep-related respiratory events. Further improvements in embedded NIV algorithms are needed to allow more widespread out-of-laboratory initiation and follow-up of NIV. *Key words: automated algorithms; bench study; chronic respiratory failure; noninvasive ventilation; sleep-related respiratory events.* [Respir Care 2023;68(1):18–30. © 2023 Daedalus Enterprises]

Introduction

Noninvasive ventilation (NIV) has been shown to improve outcomes of patients with most types of chronic respiratory failure[1-6] and is currently the standard of care for chronic alveolar hypoventilation.[7-12] Sleep-related respiratory events such as central and/or obstructive apnea and hypopnea affect the efficiency of NIV.[13] NIV settings should, therefore, be individualized to both control nocturnal hypoventilation and prevent or treat such respiratory events.[14,15]

Polysomnography (PSG) is the recommended method for identifying optimal NIV pressure settings.[16,17] However, patients face long waiting lists for PSG, which is also costly.[18] In addition, the inspiratory and expiratory pressures must strike a compromise between minimizing pressure-related adverse effects on the one hand and preventing upper-airway obstruction and/or treating central events during sleep on the other. Needs may change within a given night and from night to night depending on body position, sleep stage, nasal patency, inspiratory muscle efficiency, and other factors, such as the ingestion of alcohol or hypnotic agents that may be used at home.[15]

To replace PSG titration in sleep laboratories, simpler tools allowing remote monitoring of home NIV parameters and residual respiratory events, as well as adjustments of settings, would considerably facilitate the initiation and follow-up of long-term home NIV.[19-22] Manufacturers have developed sophisticated algorithms embedded within NIV devices. These algorithms can automatically adjust basic settings such as expiratory positive airway pressure (EPAP) and pressure support (PS) in response to changes in upper-airway mechanics and air flow.[15,18] However, these algorithms vary widely across manufacturers, who do not always provide detailed descriptions of them or their updates.[23] For example, some devices adapt their parameters cycle by cycle after identifying an event, whereas others seek to avoid events throughout the NIV session by

continuously adjusting the settings even when no events occur. These embedded algorithms will improve care only if they provide good-quality monitoring and setting adjustment.[18,24,25] More data on this point are needed.

We, therefore, designed a bench study to qualitatively evaluate the appropriateness of automatic setting adjustments by several NIV devices in response to common sleep-related respiratory events. We also assessed the accuracy of device detection and scoring of these events.

QUICK LOOK

Current knowledge

Automatic adjustment of pressure support and expiratory positive airway pressure may facilitate the initiation and follow-up of home noninvasive ventilation (NIV). Devices have a wide array of algorithms for detection of sleep-related events and responses which may have varied effectiveness.

What this paper contributes to our knowledge

Current NIV devices varied substantially in their responses and reports of standardized sleep-related respiratory events. Further improvements in embedded NIV algorithms are needed to allow broader out-of-laboratory initiation and follow-up of home NIV.

Methods

Bench Model

We used a 2-chamber Michigan test lung (MII Vent Aid TTL; Michigan Instruments, Grand Rapids, Michigan). The driving chamber was connected to, and ventilated by, a dedicated ventilator (Elisée 150, ResMed, Bella Vista, New South Wales, Australia), and the experimental chamber was connected to the tested NIV device (Fig. 1).

Both chambers were physically connected to each other by a small metal component that allowed the driving chamber to lift the experimental chamber, thereby simulating the spontaneous inspiratory effort, as described previously.[25] The generation of positive pressure in the driving chamber decreased the pressure in the experimental chamber, triggering a pressure supported breath. The driving ventilator was in pressure controlled mode with the following settings: inspiratory pressure 10 cm H_2O, PEEP 5 cm H_2O (total inspiratory pressure 15 cm H_2O), breathing frequency 16 breaths/min, and inspiratory time 1.2 s (inspiration:expiration 1:2).

Between the experimental chamber and the tested NIV device, the following were connected in sequence: a parabolic resistor (5 cm H_2O/L/s) (PneuFlo Rp5, Michigan Instruments), a flow sensor, a collapsible chamber acting as a Starling resistor to allow on-demand partial circuit obstruction,[26,27] a shut-off valve allowing on-demand complete circuit closure, and a pressure sensor (Fig. 1). Compliance of the experimental chamber was set at 60 mL/cm H_2O. The tested NIV devices were connected to the system through a 15-mm circuit and a standard 4-mm diameter intentional leak port. Additional information is provided in the supplementary material (see related supplementary materials at http://www.rcjournal.com).

Devices and Ventilatory Modes

We evaluated 4 ventilators: Vivo 45 (v. 3.1.4–3.1.4, Breas Medical, Mölnlycke, Sweden), Prisma VENT40 (v. 3.7.00.14, Löwenstein Medical Technology, Hamburg, Germany), BiPAP A40 Pro (v. 1.1.3, Philips Respironics, Murrysville, Pennsylvania,), and Stellar 150 (v. SX483-0252, ResMed). All devices were set with their dedicated modes for automatic adjustment of PS based on a prespecified target tidal volume (V_T) and of EPAP based on upper-airway patency. Automatic calibration of the devices and circuit was performed according to manufacturer recommendations before study data acquisition.

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The devices studied were supplied by ASV Santé, a home care provider involved in the conducting of the current study.

Drs Lofaso and Louis are co-senior authors.

Supplementary material related to this paper is available at http://www.rcjournal.com.

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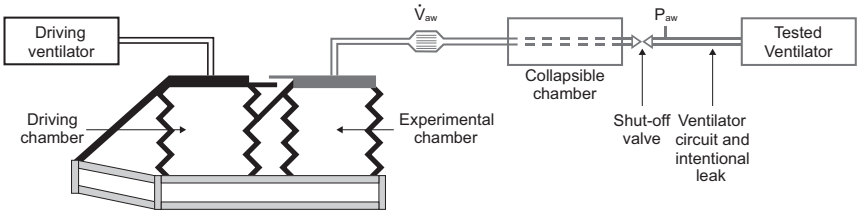

Fig. 1. Experimental setup. $\dot{V}_{aw}$ = respiratory flow; P_{aw} airway pressure.

Table 1. Settings for Each of the 4 Tested Devices

Device	Vivo 45	Prisma VENT40	BiPAP A40 Pro	Stellar 150
Mode	PSV (TgV) - AE	AutoST +V	AVAPS-AE	iVAPS-AE
Target V_T,* mL	320	240	290	260
PS (min–max), cm H_2O	2–14	2–14	2–14	2–14
EPAP (min–max), cm H_2O	4–14	4–14	4–14	4–14
Breathing frequency, breaths/min	12	12	12	16‡
T_I (timed), s	1.2	1.2	1.2	
T_I (min–max), s	0.9–1.9	0.9–1.9		0.9–1.9
Rise time†	4	2	2	200
Trigger	4	4	4 L/min	Medium
Cycling	7	25%	25%	Medium

* The baseline tidal volume (V_T) monitored by the tested devices during the baseline run (with pressure support and target V_T set at the minimum values available on the tested devices) was 360, 270, 320, and 290 mL for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively. The target V_T for the experiments was 90% of the baseline V_T.
† Rise time was set to provide similar duration between beginning of inspiratory effort and peak inspiratory flow for each device.
‡ The target breathing frequency in iVAPS mode was set at 16 breaths/min to be in line with the spontaneous breathing frequency of the model. With this setting, the backup breathing frequency threshold (below which controlled cycles are generated) is comparable to that of other tested devices (ie, approximately 12 breaths/min).
PSV(TgV) = pressure-support ventilation with target V_T
AutoST +V = automatic spontaneous timed mode with target V_T
iVAPS = intelligent volume-assured pressure support
AE = auto-EPAP
AVAPS = average volume assured pressure support
EPAP = expiratory positive airway pressure
V_T = tidal volume
PS = pressure support
T_I = inspiratory time
Specific settings:
Vivo 45: EPAP step: 2.0 cm H_2O.
Prisma VENT 40: AutoF: off; trigger type: manual; target V_T speed: III; ΔP: 12 cm H_2O; expiratory fall time: 2.
BiPAP A40 Pro: AVAPS speed: 5.0 cm H_2O/min; trigger type: flow.
Stellar 150: height: 175 cm; target V_T: 2.3 L/min; expiratory fall time: 200 ms.

Standardization of Settings Across Devices

The purpose of this study was to assess the response of each device to standardized respiratory events rather than the accuracy of delivered V_T. When using ventilatory modes with a set target V_T, PS is adjusted based on V_T recorded by the device, as opposed to actual V_T. However, in several studies, the accuracy of V_T monitoring differed across devices.[28-32] To overcome this potential source of bias, we standardized the target V_T settings as follows.

Before each experiment, a baseline run was performed with the target V_T and PS set to the minimum values available on the devices (300, 100, 200, and 160 mL; and 2, 0, 2, and 0 cm H_2O, for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively). During this run, ventilation of the experimental chamber was, therefore, mainly related to the spontaneous respiratory effort generated by the driving ventilator. The V_T value recorded by the tested device during this run was defined as the baseline V_T. For all experimental conditions, the target V_T was then set at 90% of the baseline V_T, rounded to the nearest 10.

During the baseline runs, V_T recorded by the device was 360, 270, 320, and 290 mL for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively. Accordingly, during the experiments, target V_T was 320, 240, 290, and 260 mL for these devices, respectively. Device-recorded V_T values were used only for this standardization procedure: all V_T data recorded for the experiments

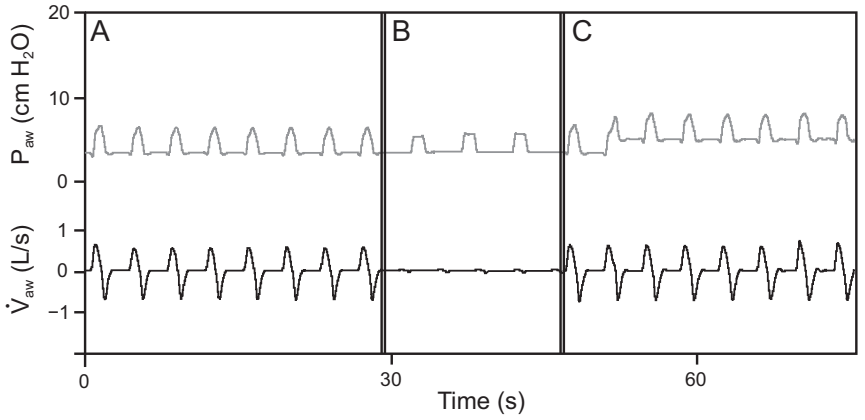

Fig. 2. Data acquisition and periods of interest. Example of data recorded during a simulated episode of obstructive apnea. The periods of interest were the 30 s preceding the event (A: *pre-event* period), 15–20 s of event duration (B: *event* period), and 30 s following the event (C: *post-event* period). $\dot{V}_{aw}$ = respiratory flow; P_{aw} = airway pressure.

were derived from respiratory flow ($\dot{V}_{aw}$) measured by the pneumotachograph.

For all experimental conditions and for each device, the minimum and maximum PS values were 2 and 14 cm H_2O, respectively; and the minimum and maximum EPAP values were 4 and 14 cm H_2O, respectively. Table 1 reports the device settings.

Experimental Conditions

For each device, after a 3-min stabilization period with stable ventilation, 4 respiratory events were simulated in the following order: central hypopnea (CH), central apnea (CA), obstructive hypopnea (OH), and obstructive apnea (OA). Each event lasted 5 breaths (about 15−20 s), and events were separated by 1 min of simulated spontaneous ventilation.

CH was simulated by halving the PS of the driving ventilator and CA by switching the driving ventilator to CPAP mode. For OH, increasing the pressure about the collapsible chamber allowed precise control of its degree of opening with variation of the Starling resistance, thereby simulating upper-airway collapse independently from EPAP, to achieve a 50–60% V_T decrease from the *pre-event* period of stable ventilation to the first respiratory cycle of the OH event. OA was simulated by closing the shut-off valve located between the intentional leak port and the experimental chamber.

Finally, we performed additional experiments to evaluate whether the duration of the simulated events affected devices responses. We performed CA and OA experiments in which each event lasted 1 min instead of 15–20 s. For these experiments, the tested devices were switched on and off between the events to ensure that the starting PS and EPAP were similar for CA and OA.

Data Acquisition

$\dot{V}_{aw}$ was measured close to the experimental chamber using a pneumotachograph (Fleish no. 2; Fleish, Lausanne, Switzerland) connected to a differential pressure transducer (Validyne DP45 ± 2.25 cm H_2O; Validyne, Northridge, California). Airway pressure (P_{aw}) was measured using another pressure transducer (Validyne DP45 ± 56 cm H_2O) positioned between the shut-off valve and the circuit. The sensors were calibrated according to the manufacturers' recommendations before the experiments. The signals were digitized at 200 Hz using an analog/digital system (MP100, Biopac Systems, Goleta, California) and recorded on a microcomputer for further analysis. The raw data from the devices were downloaded and analyzed via the manufacturers' dedicated software to identify whether the simulated events were detected and scored.

Data Analysis

For each simulated event, 3 periods of interest were defined: 30 s before the event (*pre-event* period), 15–20 s during the event (*event* period), and 30 s after the event (*post-event* period) (Fig. 2). All respiratory cycles during these 3 periods were included in the analysis. For each respiratory cycle, we determined inspiratory positive airway pressure (IPAP) defined as the maximum P_{aw} during the inspiratory plateau, EPAP as the mean P_{aw} during the last 500 ms of expiration, PS as IPAP(n) – EPAP(n-1), V_T as the integral of flow over time, total cycle time (T_{tot}) as the time between 2 insufflations from the tested device, and breathing frequency as $60/T_{tot}$. V_T overshoot was defined as a $> 20\%$ difference from the mean *pre-event* V_T.

Detection of an event by the device was defined as the occurrence of an automatic setting adjustment between the

pre-event and *post-event* periods and/or a scored residual event in the software report. According to current recommendations,[16,33] an appropriate device response to an event was defined as the following changes from the *pre-event* to *post-event* periods: for CH, a PS increase; for CA, a PS increase combined with backup breathing frequency activation; for OH, an EPAP increase combined, when the actual V_T was below target, with a PS increase; and for OA, an EPAP increase. When necessary, the manufacturers were contacted to obtain additional information on the device algorithms that might help us understand our findings.

Statistical Analysis

The data are described as mean ± SD. Most of the results presented are for descriptive purposes only. For instance, the description of the V_T decrease induced by the simulation of an event (relative to mean *pre-event* V_T), or the V_T reached during the simulation of an event (relative to target V_T), did not necessitate using statistical analyses. However, to highlight the adjustment of settings that occurred between the *pre-event* and *post-event* periods, comparisons of variable values during these 2 periods were performed with the paired-sampled *t* test. Analyses were performed using Jamovi (version 1.6.15) and R (version 4.0, R Foundation for Statistical Computing, Vienna, Austria). Two-sided *P values* < .05 were considered statistically significant.

Results

Consistency of Experimental Conditions Across Devices

Before simulation of the first event, that is, during the first *pre-event* period for CH, V_T was above target for all 4 devices (Table 2). Despite this, none of the 4 devices delivered the set minimum PS. All 4 devices provided similar PS levels: 2.5 ± 0, 2.6 ± 0.1, 2.7 ± 0, and 2.8 ± 0.1 cm H_2O for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively, (Table 2). The mean first *pre-event* V_T calculated from the pneumotachograph data were 360 mL (± 5%) for all tested devices (Table 2).

Compared with the mean *pre-event* V_T, V_T during the first cycle of the simulated CH was lower by 39, 38, 42, and 40% for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively. Corresponding decreases were 65, 70, 70, and 67%, respectively, for CA; 53, 51, 48, and 48%, respectively, for OH; and 100% with all devices for OA.

Device Responses to the Simulated Events

Table 2 reports the responses of each device to the simulated events, and Figures 3 and 4 show the pressure and flow variations recorded for central and obstructive events, respectively. Figure 5 diagrams the dynamic behavior of the devices from the first to the last cycle of each period of interest.

All 4 devices increased PS during CH, CA, and OH. However, the magnitude of the PS increase varied considerably across devices (Table 2 and Fig. 5). For CH, all devices except the BiPAP A40 Pro reached 100 ± 20% of the target V_T at the last cycle of the event (Fig. 5). V_T overshoot occurred during the first *post-event* cycle with the Vivo 45 (Fig. 5A). For CA, only the Prisma VENT40 reached 100 ± 20% of the target V_T at the last cycle of the event. The Vivo 45 and BiPAP A40 Pro did not increase PS sufficiently to reach the target V_T during the event (Figs. 5A through 5C). Conversely, the PS increase by the Stellar 150 in response to CA resulted in a V_T of 148% of the target at the last event cycle and in a V_T overshoot at the first *post-event* cycle (Fig. 5D). For OH, only the Prisma VENT40 increased PS sufficiently to reach 100 ± 20% of the target V_T during the event (Fig. 5). Both the Prisma VENT40 and Stellar 150 induced V_T overshoot after the event (Figs. 5B and 5D). For OA, the BiPAP A40 Pro and Prisma VENT40 did not significantly modify PS (Table 2), whereas Vivo 45 and Stellar 150 increased PS during the event, with the latter inducing V_T overshoot at the first *post-event* cycle (Fig. 5D).

All devices activated the backup breathing frequency for CA and OA (Figs. 5A through 5D). The Stellar 150 increased breathing frequency during CA and OA, achieving the target breathing frequency (Fig. 5D). The Vivo 45 also activated backup breathing frequency for OH, inducing asynchronies during the event (Fig. 4A).

No device adjusted EPAP for central events, with the exception of the Vivo 45, which increased EPAP in response to CA (Table 2 and Fig. 5). Only the Vivo 45 and the Stellar 150 increased EPAP in response to OH (Table 2). All devices except the BiPAP A40 Pro increased EPAP in response to OA. Consistent with its algorithm, BiPAP A40 Pro adjusted EPAP independently of the occurrence of any simulated event (Supplementary Fig. 1, see related supplementary materials at http://www.rcjournal.com).

Detection and Scoring of the Simulated Events

Table 3 reports event detection and the appropriateness of device responses. Central events induced PS increases with all 4 devices and were, therefore, considered detected. For CH, none of the tested devices scored residual events. Although the mean V_T drop during CA compared with the mean *pre-event* V_T was 56, 54, 62, and 16% for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively, (Fig. 3B) only the BiPAP A40 Pro and Stellar 150 scored residual hypopnea in their software reports (Table 3).

Table 2. Automated Adjustment of Settings and Tidal Volume Variations From the Pre-Event to the Post-Event Period for Each of the 4 Tested Devices

	CH		CA		OH		OA	
	Pre-event	Post-event	Pre-event	Post-event	Pre-event	Post-event	Pre-event	Post-event
Vivo 45								
PS, cm H_2O								
Mean ± SD	2.5 ± 0	3.3 ± 0.9*	2.4 ± 0	3.0 ± 0.2*	2.4 ± 0	2.8 ± 0.5†	2.4 ± 0	2.7 ± 0.4
First cycle–last cycle	2.5–2.5	4.7–2.5	2.4–2.4	3.3–2.9	2.5–2.5	3.8–2.5	2.4–2.4	3.4–2.4
EPAP, cm H_2O								
Mean ± SD	3.4 ± 0	3.3 ± 0	3.3 ± 0	4.2 ± 0*	4.2 ± 0	5.1 ± 0*	5.1 ± 0	5.8 ± 0.3*
First cycle–last cycle	3.4–3.4	3.4–3.3	3.4–3.4	4.2–4.2	4.2–4.2	5.1–5.1	5.1–5.1	5.1–6.0
V_T, mL								
Mean ± SD	371 ± 6	387 ± 43	346 ± 5	401 ± 40*	343 ± 1	351 ± 20	335 ± 2	341 ± 17
First cycle–last cycle	375–361	454–348	335–353	370–460	342–343	388–339	338–333	382–336
Prisma VENT40								
PS, cm H_2O								
Mean ± SD	2.6 ± 0.1	2.8 ± 0.4†	2.7 ± 0	2.8 ± 0.3†	2.7 ± 0	4.7 ± 0.8*	2.7 ± 0	2.7 ± 0.1
First cycle–last cycle	2.6–2.5	3.7–2.6	2.7–2.7	3.6–2.6	2.6–2.7	6.0–3.6	2.7–2.8	2.9–2.7
EPAP, cm H_2O								
Mean ± SD	3.4 ± 0	3.3 ± 0*	3.3 ± 0	3.3 ± 0	3.3 ± 0	3.3 ± 0	3.3 ± 0	4.7 ± 0*
First cycle–last cycle	3.4–3.4	3.3–3.3	3.3–3.3	3.3–3.3	3.3–3.3	3.3–3.3	3.3–3.3	4.6–4.6
V_T, mL								
Mean ± SD	352 ± 4	360 ± 23	347 ± 3	360 ± 9*	341 ± 6	430 ± 32*	353 ± 3	339 ± 12*
First cycle–last cycle	351–354	414–343	341–348	379–353	329–347	482–386	354–347	310–340
BiPAP A40 Pro								
PS, cm H_2O								
Mean ± SD	2.7 ± 0	3.2 ± 0.3*	2.6 ± 0	3.6 ± 0.1*	2.6 ± 0	3.8 ± 0.3*	2.8 ± 0.1	2.7 ± 0
First cycle–last cycle	2.7–2.6	3.7–2.9	2.6–2.7	3.8–3.5	2.7–2.6	4.2–3.5	2.7–2.8	2.7–2.8
EPAP, cm H_2O								
Mean ± SD	3.9 ± 0	3.9 ± 0	3.9 ± 0	3.9 ± 0	5.9 ± 0	5.9 ± 0	8.0 ± 0	8.0 ± 0
First cycle–last cycle	3.9–3.9	3.9–3.9	3.9–3.9	3.9–3.9	5.9–6.0	5.9–6.0	8.0–8.0	8.0–8.0
V_T, mL								
Mean ± SD	358 ± 11	364 ± 15*	344 ± 8	345 ± 25	336 ± 3	368 ± 13*	345 ± 5	347 ± 2
First cycle–last cycle	372–344	392–353	336–355	368–333	332–334	386–345	356–341	346–346
Stellar 150								
PS, cm H_2O								
Mean ± SD	2.8 ± 0.1	3.2 ± 0.6†	2.8 ± 0.1	3.7 ± 1.7†	2.8 ± 0.1	4.2 ± 2.1†	2.7 ± 0.1	8.0 ± 5.4*
First cycle–last cycle	2.8–2.8	4.1–2.8	2.8–2.9	7.1–2.8	2.7–2.7	7.9–2.7	2.8–2.7	14.5–3.1
EPAP, cm H_2O								
Mean ± SD	3.9 ± 0	3.9 ± 0	3.9 ± 0	3.9 ± 0	3.9 ± 0	4.4 ± 0*	4.4 ± 0	5.8 ± 1.2*
First cycle–last cycle	3.9–3.9	3.9–3.9	3.9–3.9	3.9–3.9	3.9–3.9	4.4–4.4	4.4–4.4	4.4–7.2
V_T, mL								
Mean ± SD	344 ± 2	358 ± 22	346 ± 11	369 ± 55	305 ± 10	388 ± 73*	339 ± 7	466 ± 247
First cycle–last cycle	344–342	393–345	343–373	482–338	294–320	520–343	350–331	765–310

* $P < .05$ compared to the *pre-event* value.

† Although the statistical analysis did not demonstrate a significant difference between *pre-event* and *post-event* values, the response of the device during the event was appropriate.

CH = central hypopnea

CA = central apnea

OH = obstructive hypopnea

OA = obstructive apnea

PS = pressure support

EPAP = expiratory positive airway pressure

V_T = tidal volume

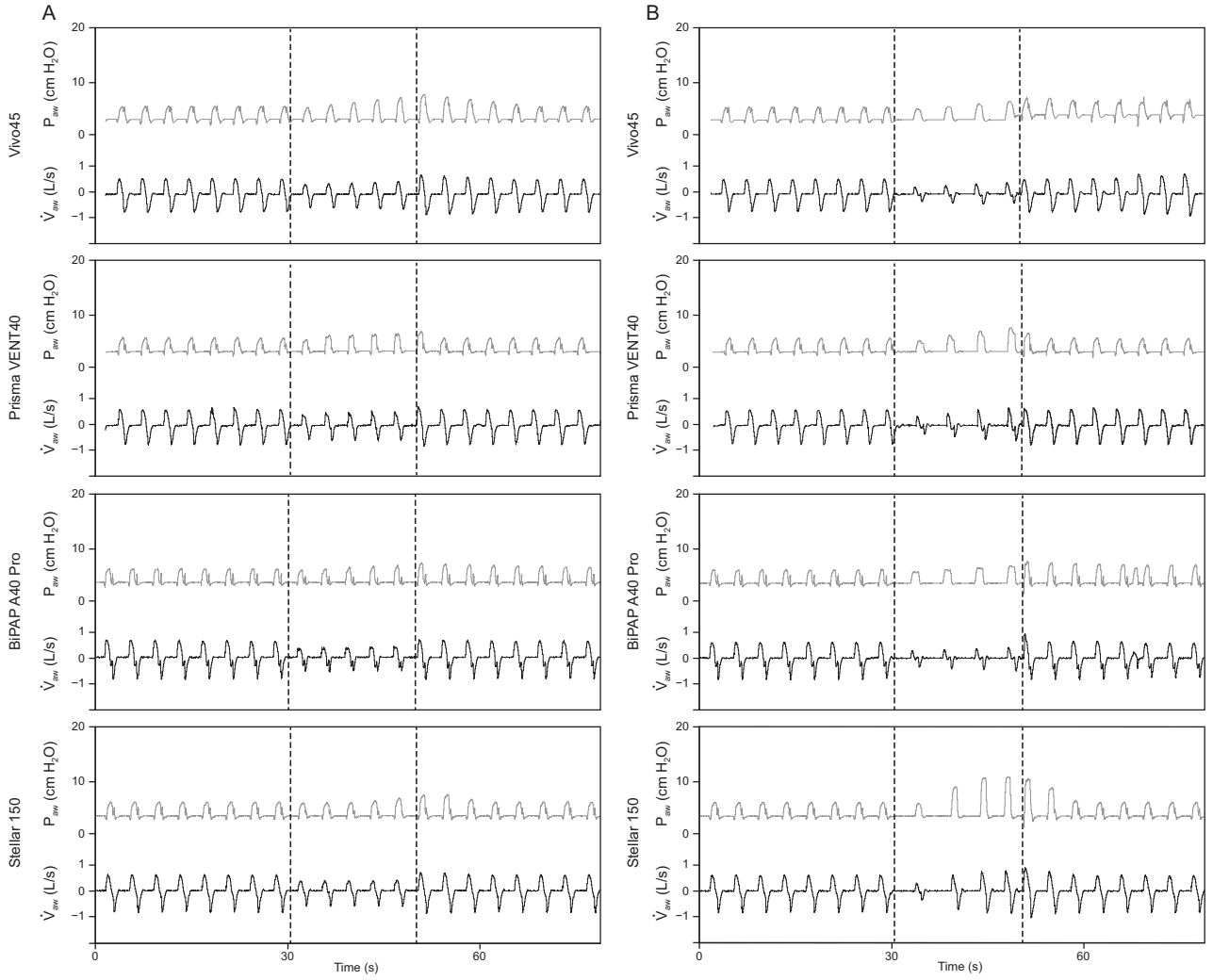

Fig. 3. Device responses to central hypopnea and apnea. 3A: Central hypopnea. 3B: Central apnea. The dashed vertical lines show the beginning and end of the event period. $\dot{V}_{aw}$ = respiratory flow; P_{aw} = airway pressure.

OH induced automatic setting adjustments by all 4 devices and were, therefore, considered detected. The mean V_T drop during OH was 62, 46, 56, and 48% for Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar 150, respectively. Only the Stellar 150 scored residual hypopnea in its report (Table 3).

For OA, all devices were considered to have detected the event based on the occurrence of setting adjustments (Vivo 45, Prisma VENT40, Stellar 150) and/or on appropriate scoring in the device software (Prisma VENT40, BiPAP A40 Pro, Stellar 150).

Effects of Event Duration and Pre-Event Pressure

During the 1-min CA, all 4 devices increased PS, providing 95, 127, 100, and 103% of the target V_T at the end of the event for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively. The target V_T was reached after 18, 5, 11, and 2 cycles for these 4 devices, respectively. V_T overshoot at the first *post-event* cycle occurred with all 4 devices (Supplementary Fig. 2A through 2D, see related supplementary materials at http://www.rcjournal.com). During the 1-min OA, the BiPAP A40 Pro and Prisma VENT40 did not significantly modify PS, whereas the Vivo 45 and Stellar 150 increased PS over the course of the event, with the latter overshooting the V_T target at the first *post-event* cycle (Supplementary Fig. 2D).

All 4 devices activated backup breathing frequency for the 1-min CA and OA (Supplementary Fig. 2A through 2D). The Stellar 150 increased breathing frequency during both events, achieving the target breathing frequency (Supplementary Fig. 2D).

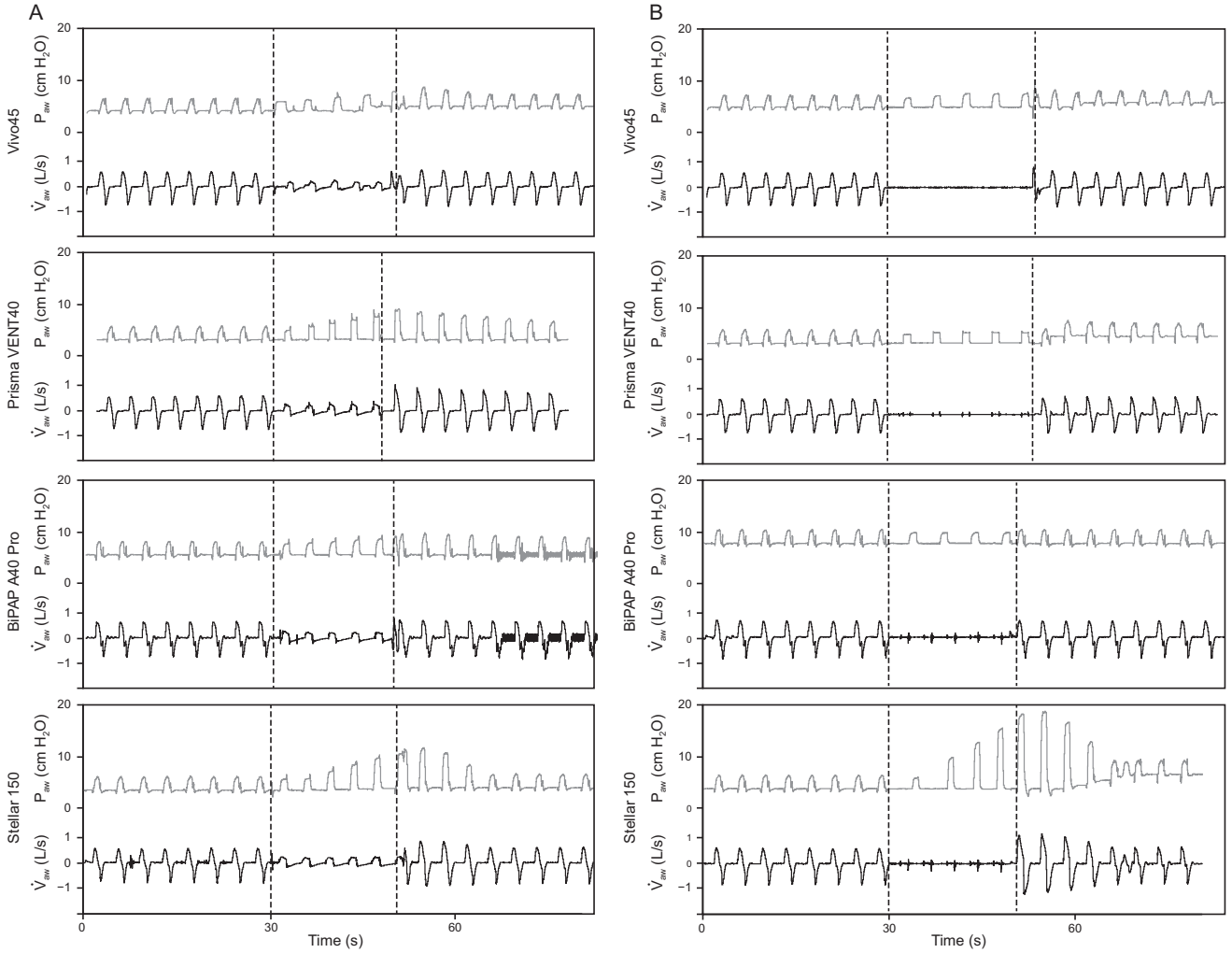

Fig. 4. Device responses to obstructive hypopnea and apnea. 4A: Obstructive hypopnea. 4B: Obstructive apnea. The dashed vertical lines show the beginning and end of the event period. $\dot{V}_{aw}$ = respiratory flow; P_{aw} = airway pressure.

Again, the only device that adjusted EPAP for central events was Vivo 45, which increased EPAP in response to CA (Supplementary Fig. 2A). The mean EPAP before the 1-min OA was 3.3 ± 0, 3.4 ± 0, 3.4 ± 0, and 3.4 ± 0 cm H_2O for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively. All devices except the BiPAP A40 Pro increased EPAP in response to OA. The EPAP increase from the mean *pre-event* period to the last *post-event* cycle was 1.7, 1.2, 0, and 5.4 cm H_2O for the Vivo 45, Prisma VENT40, BiPAP A40 Pro, and Stellar150, respectively, (compared to 0.9, 1.4, 0, and 2.8 cm H_2O for the 15–20 s OA simulation, respectively).

Despite the longer duration of the events and the comparable *pre-event* EPAP values across devices and between CA and OA, the pattern of EPAP adjustment during the 1-min events was similar to that of the 15–20 s events (Supplementary Figs. 2A through 2D). The scoring of these events by the device software was also the same as for the 15–20 s events.

Discussion

This bench study demonstrated that automatic responses to simulated sleep-related respiratory events varied considerably across 4 NIV devices. Moreover, variability also occurred in the device software reports of events. For all 4 devices, the responses to the simulated events raise concerns about the appropriateness of automatic adjustments in clinical practice. This finding is somewhat surprising given the existence of clear recommendations about setting adjustments in response to sleep-related apneas and hypopneas due to central or obstructive mechanisms.[16,33]

We evaluated whether the automatic responses of the devices to events responsible for a V_T decrease, namely CH, CA, and OH, were appropriate. To correct a V_T decrease, PS must be increased. All devices increased PS in these situations, and as such, their responses were appropriate. Although quantitative assessment of the accuracy of

delivered V_T, which has already been evaluated in dedicated bench studies,[28-32] was beyond the scope of the present work, it is worth noting that differences between the delivered V_T and the target V_T were marked and common. V_T fell below the set target in some cases and, in others, was maintained only at the cost of an overshoot after event termination. These V_T variations may adversely affect patients, for instance, by altering sleep architecture. Achieving the complex balance between efficacy and clinical tolerance is, therefore, a continuing challenge to manufacturers.

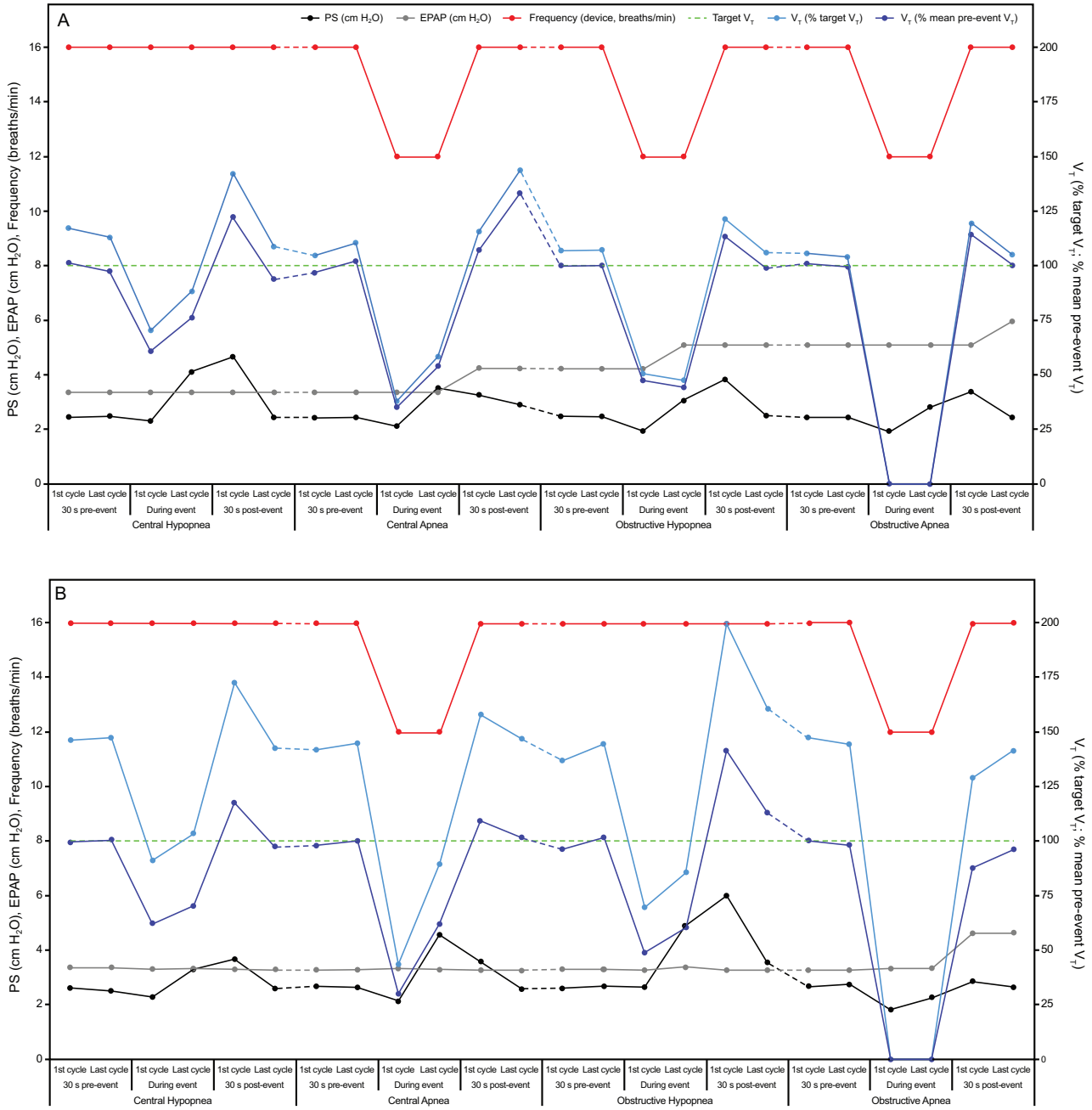

Fig. 5. Diagram of dynamic device behavior from the first to the last cycle of each period of interest. The tidal volume (V_T) values presented are derived from the pneumotachograph and presented as a percentage of the target V_T (set on the tested NIV device) or of the mean *pre-event* V_T (measured by the pneumotachograph). A: Vivo45, B: Prisma VENT40, and C: BiPAP A40 Pro. *Note that the greater expiratory positive airway pressure level at the beginning of the obstructive hypopnea and obstructive apnea simulations was not induced by the events but was related to the algorithm of the device as described in supplementary Figure 1. D: Stellar 150. *V_T = 294% of target V_T; 226% of mean *pre-event* V_T; PS = pressure support; EPAP = expiratory positive airway pressure.

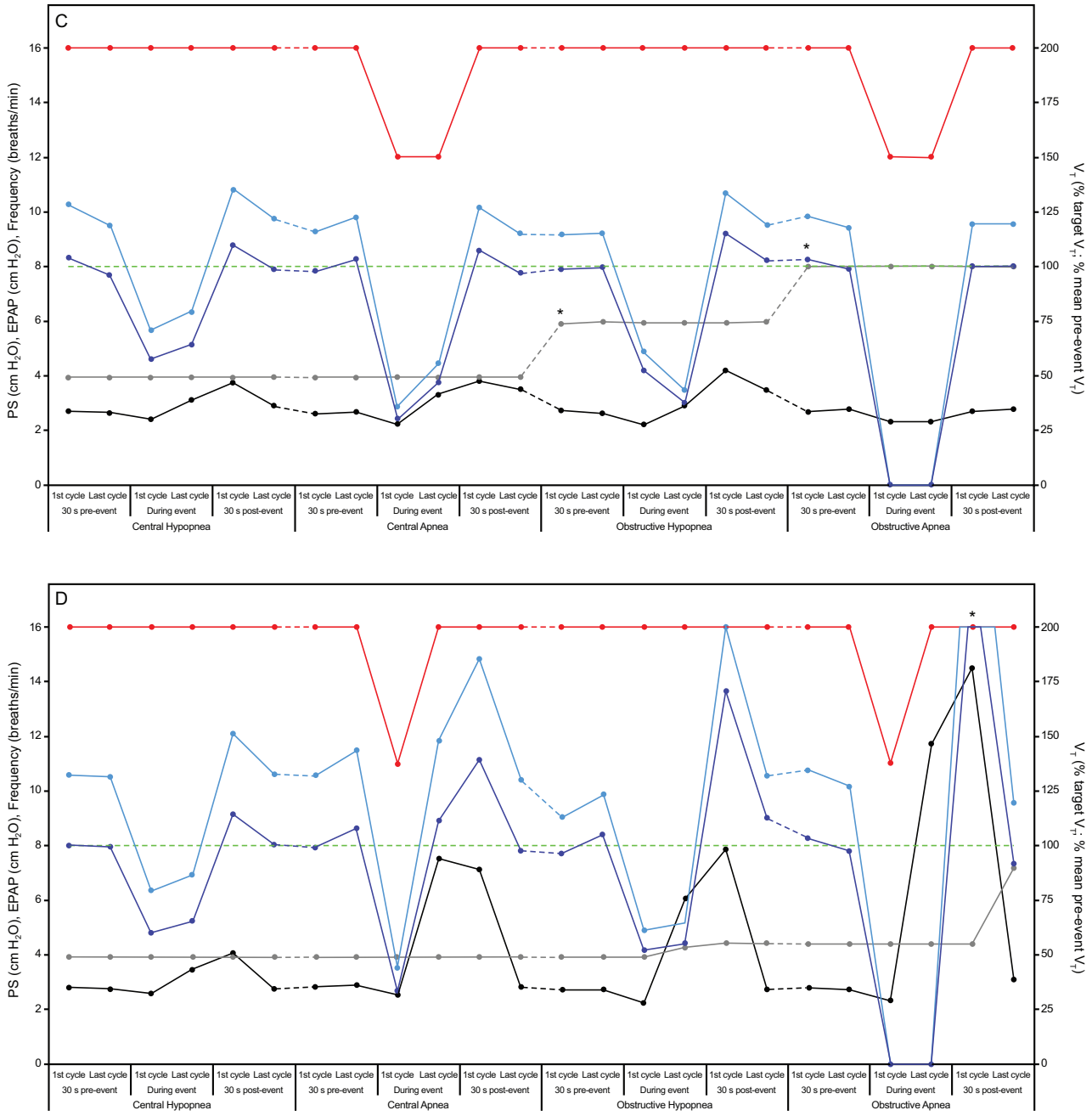

Fig. 5. *Continued*.

Moreover, we did not combine the respiratory events with unintentional leaks, which might have further impaired the ability of the devices to maintain sufficient V_T.[31,32]

The mean V_T reduction during simulated CA ranged from 16–62%, with only half the devices scoring a residual hypopnea after CA simulation. After OH, a single device scored a residual event based on a $\dot{V}_{aw}$ decrease > 50% for > 10 s. These discrepancies across devices are understandable because no formal recommendations exist for scoring hypopneas during NIV.[16,34] In the absence of pulse oximetry and/or arousal detection systems, automatic hypopnea scoring by the device can rely only on flow and pressure variations, resulting in limited sensitivity of hypopnea detection and in variable scoring quality.

Furthermore, NIV is effective only if the upper airway is patent.[16] Three devices appropriately increased EPAP in

Table 3. Event Detection and Appropriateness of Device Responses to Simulated Respiratory Events

	Vivo 45	Prisma VENT40	BiPAP A40 Pro	Stellar 150
		Central Hypopnea		
Detected	Yes	Yes	Yes	Yes
Automatic adjustment	Yes	Yes	Yes	Yes
Scoring	No	No	No	No
Appropriateness of response	Acceptable	Appropriate	Acceptable	Appropriate
Concerns	V_T overshoot at first post-event cycle	None	Last event cycle: V_T = 79% of target V_T	None
		Central Apnea		
Detected	Yes	Yes	Yes	Yes
Automatic adjustment	Yes	Yes	Yes	Yes
Scoring	No	No	Yes (H)	Yes (H)
Appropriateness of response	Not appropriate	Appropriate	Acceptable	Acceptable
Concerns	Last event cycle: V_T = 58% of target V_T ↑ EPAP post-event V_T overshoot at last post-event cycle	None	Last event cycle: V_T = 56% of target V_T	V_T overshoot at first post-event cycle
		Obstructive Hypopnea		
Detected	Yes	Yes	Yes	Yes
Automatic adjustment	Yes	Yes	Yes	Yes
Scoring	No	No	No	Yes (H)
Appropriateness of response	Acceptable	Not appropriate	Not appropriate	Acceptable
Concerns	Last event cycle: V_T = 48% of target V_T Asynchronies with backup breathing frequency activation	No EPAP modification V_T overshoot at first post-event cycle	No EPAP modification Last event cycle: V_T = 43% of target V_T	Last event cycle: V_T = 65% of target V_T V_T overshoot at first post-event cycle
		Obstructive Apnea		
Detected	Yes	Yes	Yes	Yes
Automatic adjustment	Yes	Yes	No	Yes
Scoring	No	Yes (OA)	Yes (OA)	Yes (OA)
Appropriateness of response	Acceptable	Appropriate	Not appropriate	Acceptable
Concerns	↑ PS during the event	None	No EPAP modification	↑ PS during the event V_T overshoot at first post-event cycle

V_T = tidal volume
H = hypopnea
EPAP = expiratory positive airway pressure
OA = obstructive apnea
PS = pressure support
Criteria for an appropriate or acceptable response were as follows: central hypopnea (CH): pressure support (PS) increase during the event; central apnea (CA): PS increase and backup breathing frequency activation during the event; obstructive hypopnea (OH): expiratory positive airway pressure (EPAP) increase, combined with PS increase if tidal volume (V_T) was below target during the event or between the *pre-event* and *post-event* periods; and obstructive apnea (OA): EPAP increase between the *pre-event* and *post-event* periods. An acceptable response was defined as an appropriate response with a device behavior that raised concerns. For PS adjustment, concerns were defined as failure to maintain V_T within 80–120% of the target during the last cycle of CH, CA, or OH or as failure to reach 80–120% of the mean *pre-event* value after the event for all 4 event types or as V_T overshoot to more than 20% > the mean *pre-event* value.

response to OA, although one also increased EPAP during CA. In contrast to OH, OA cannot be terminated by an EPAP increase, as the intraluminal pressure required to open the completely closed upper airway is substantially higher than that required to prevent complete upper-airway closure and is greater than the inspiratory pressure plateau.[35,36] Therefore, automatic adjustment seeks to generate an EPAP just above the upper-airway closure pressure once OA is detected then to maintain this level to prevent further occlusion.[14,15] For OH, only 2 devices provided an appropriate EPAP response.

This finding is of particular concern given that OH accounts for the vast majority of sleep-related events during NIV in patients with chronic hypoventilation.[13]

An important limitation of this study is that sleep-related respiratory events were simulated for short-term periods. The behavior of the devices may be different over a full night. During the simulated events, low or high velocity of PS changes resulted in undercompensation or overcompensation of V_T, respectively. The optimal rate of PS adjustment remains unclear but may be related to the time course of the event responsible for the V_T decrease.[25] Conceivably, faster adjustment may be required during short-term events, whereas slower adjustment might be more appropriate when compliance decreases due to body position. Furthermore, the BiPAP A40 Pro algorithm is not designed to respond to single events, such as those simulated for our study, but instead continuously assesses airway resistance using the intermittent forced oscillation technique[37] and adjusts EPAP to prevent events over the full night. In a randomized controlled study, NIV using this algorithm provided similar benefits to standard PS ventilation in subjects with obesity hypoventilation syndrome, without altering sleep quality or gas exchange.[38] This finding suggests that our bench study may have underestimated the effectiveness of this device. Nevertheless, our results underline that clinical trial results have external validity only for the tested device given the possibility of major differences across devices.[38,39]

Conclusions

Current NIV devices differed substantially in their responses to standardized simulated sleep-related respiratory events. Moreover, event recording in software reports also varied considerably. Clinical guidelines for the management of OA include CPAP titration using automated devices at home.[40] The ability to do the same in patients who require NIV is impatiently awaited. However, to meet this expectation, our results suggest a need for further improvements in algorithms embedded in NIV devices.

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