

Ventilators for Noninvasive Ventilation to Treat Acute Respiratory Failure

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Summary

The application of noninvasive ventilation (NIV) to treat acute respiratory failure has increased tremendously both inside and outside the intensive care unit. The choice of ventilator is crucial for success of NIV in the acute setting, because poor tolerance and excessive air leaks are significantly correlated with NIV failure. Patient-ventilator asynchrony and discomfort can occur if the physician or respiratory therapist fails to adequately set NIV to respond to the patient's ventilatory demand, so clinicians need to fully understand the ventilator's technical peculiarities (eg, efficiency of trigger and cycle systems, speed of pressurization, air-leak compensation, CO₂ rebreathing, reliability of fraction of inspired oxygen reading, monitoring accuracy). A wide range of ventilators of different complexity have been introduced into clinical practice to noninvasively support patients

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in acute respiratory failure, but the numerous commercially available ventilators (bi-level, intermediate, and intensive care unit ventilators) have substantial differences that can influence patient comfort, patient-ventilator interaction, and, thus, the chance of NIV clinical success. This report examines the most relevant aspects of the historical evolution, the equipment, and the acute-respiratory-failure clinical application of NIV ventilators. *Key words: acute respiratory failure, ventilator, mechanical ventilation, bi-level, intensive care unit, noninvasive ventilation, pressure-support ventilation.* [Respir Care 2008;53(8):1054–1080. © 2008 Daedalus Enterprises]

Introduction

Since its first introduction in the early 1990s, noninvasive ventilation (NIV) has been increasingly used in the care of patients suffering from acute respiratory failure (ARF) of various etiologies. A high level of scientific evidence clearly shows that in severe exacerbations of chronic obstructive pulmonary disease (COPD) NIV reduces the need for endotracheal intubation, shortens hospital and intensive care unit (ICU) stay, lowers mortality, and avoids complications associated with invasive mechanical ventilation (eg, nosocomial pneumonia).^{1–7} NIV has also been successfully applied to selected cases of hypoxemic ARF and acute cardiogenic pulmonary edema refractory to medical therapy. NIV can facilitate ventilator weaning in patients with COPD, and it prevents post-extubation respiratory failure in some patients.^{1–7} NIV has gained great popularity in the ICU and other settings, such as the respiratory high dependency unit, emergency department, and ordinary wards.^{8–14}

The choice of a ventilator may be crucial for the success of NIV in the acute setting, because intolerance and excessive air leaks are significantly correlated with NIV failure.^{14,15} Patient-ventilator asynchrony and discomfort can occur if the physician or respiratory therapist fails to adequately set NIV to respond to the patient's ventilatory demand, so clinicians need to fully understand the ventilator's technical peculiarities (eg, efficiency of trigger and cycle systems, speed of pressurization, air-leak compensation, CO₂ rebreathing, reliability of fraction of inspired oxygen [F_{IO_2}] reading, and monitoring accuracy). With the growing use of NIV, a wide range of ventilators has been produced to provide NIV to patients in ARF, both in randomized controlled trials and in everyday clinical practice.^{4,11,13,16–21}

This review examines the most relevant aspects of the historical evolution, the equipment, and the clinical ARF applications of NIV ventilators commonly used in the “real world” ICU and other clinical environments.

History and Evolution of NIV Ventilators

After the “iron lung” era in the 1950s, the first portable volume-controlled home ventilators were specifically de-

signed for long-term invasive support of ventilator-dependent patients with chronic respiratory failure.^{17,18} When NIV gained popularity, volume-controlled home ventilators were the first machines used to deliver noninvasive support, mostly in domiciliary care. These ventilators could also deliver synchronized intermittent mandatory ventilation, and some could deliver pressure-controlled modes. However, even if well equipped with alarms, monitoring systems, and internal battery, portable volume-controlled home ventilators have some important limitations, especially for NIV, including poor air-leak compensation, lack of positive end-expiratory pressure (PEEP) (or PEEP applicable only with an external valve, which can interfere with trigger sensitivity), and high cost.^{16–18,22,23} Their application is today limited to home NIV in selected cases of neuromuscular disorders and ventilator-dependent tracheostomized patients.²⁴ Surprisingly, even the most reliable aspect of a volume-controlled home ventilator (the guarantee of a preset tidal volume [V_T], whatever the respiratory load), has been recently put up for discussion.^{25,26}

To overcome the limitations of volume-controlled home ventilators in delivering NIV, in the 1980s the first bi-level ventilator was built, with the objective of compensating for air leaks.²⁷ The phrase “bi-level” refers to the capability of supporting spontaneous breathing with 2 different pressures: an inspiratory positive airway pressure (IPAP) and a (lower) expiratory positive airway pressure (EPAP) or PEEP. The prototype (Respironics BiPAP) was designed as the natural evolution of continuous-positive-airway-pressure (CPAP) devices, to improve tolerance in patients with obstructive sleep apnea.²⁸ The first generation of bi-level ventilators lacked alarms or monitoring systems but featured easy handling, transportability, and low cost, so they met the needs of patients who required nocturnal NIV but who also had relatively high ventilatory autonomy.^{16–19,27,29} The original Respironics BiPAP ventilator consisted of a simple CPAP blower modified with a magnetic valve that provided IPAP and EPAP through a single-limb-circuit with a leak port (ie, Respironics Whisper Swivel). It initially functioned only in “T” mode, which was time-triggered, time-cycled, and pressure-limited, with a fixed respiratory rate and fixed duty cycle (ratio of inspiratory time to total-breathing-cycle time). Soon thereafter, a sensitive trigger was added, which enabled the new

device (Respironics BiPAP S/T) to deliver 2 other NIV modes, “S” and “S/T,” which provided pressure-support ventilation (PSV) without and with a back-up respiratory rate, respectively.^{17,19} However, most of these first-generation bi-level ventilators had important technical limitations, including limited pressure-generation ability; poor performance if respiratory-system load increased; risk of CO₂ rebreathing; and lack of ventilatory monitoring, alarms, or battery.¹⁶⁻¹⁸ Later, more sophisticated bi-level ventilators were designed to deliver NIV for acute conditions and higher levels of care, as well as for home ventilation in tracheotomised patients.¹⁶⁻¹⁹

Conventional ICU ventilators were designed exclusively for invasive ventilation via cuffed endotracheal tube or tracheal cannula in the ICU or surgery setting. Once NIV was introduced in the ICU, the clinicians realized the limitations of those ventilators in compensating for air leaks during noninvasive PSV. Then a newer-generation of ICU ventilators was developed to efficiently assist acutely ill patients with NIV, thanks to the addition of the air-leak compensation function, which provides the “NIV modes”.³⁰⁻³²

More recently some companies produced a third category of “intermediate” ventilators that combine some features of bi-level, home, volume-controlled ventilators and some features of ICU ventilators (dual-limb circuit, sophisticated alarm and monitoring systems, internal battery, volume-controlled ventilation, pressure-controlled ventilation, PSV modes, wide range of inspiratory and expiratory parameters).¹⁶⁻¹⁸ These intermediate ventilators are designed for home use, hospital-care, and patient transport, including of critically ill patients.

Current NIV Equipment, Settings, and Modes

In this section we will discuss key points about NIV equipment, settings, and modes that are likely to influence the performance of the various ventilators in NIV in the clinical setting (Table 1).

Types of Ventilators

There is substantial overlap among the 3 ventilator categories (bi-level, intermediate, and ICU), and to date there is no consensus in the literature on a classification system to assign a ventilator to one of the categories. However, we believe that, despite the limitations of the 3-category classification we are using here and used in another review article,¹⁸ this schematic definition of these 3 ventilator types may help the reader to easily assign a similar complexity of technical features and a similar spectrum of clinical application to a specific ventilator (Tables 2, 3, and 4).

Because of the huge gap between the increasing number of newer commercially available ventilators and their care-

Table 1. Key Performance Points of Ventilators for Noninvasive Ventilation

Gas source
Compressed gas from a cylinder
Compressor or electrically supplied turbine pump
Oxygen supply
High-pressure source with a blender
Low-pressure sources with connection at the ventilator, circuit, or mask
Circuit
Single-limb circuit with non-rebreathing valve, plateau exhalation valve, or Whisper Swivel
Double-limb circuit
Inspiratory trigger with/without adjustable sensitivity
Flow, pressure, volume, mixture of flow, pressure, and/or volume
Expiratory cycle
Flow-dependent (with/without adjustable threshold), time-dependent, auto-function
Inspiratory flow
May be adjustable
Backup respiratory rate
Air-leak compensation
Humidification
Heated humidifier, heat-and-moisture exchanger
Battery
Internal, additional external
Alarms
Lack or minimal
Sophisticated
Monitoring systems
Only some inspiratory parameters
Inspiratory and expiratory parameters
Flow, volume, pressure curves
Ventilation mode
Only spontaneous modes without a guaranteed V _T (pressure-support ventilation, proportional-assist ventilation) or with a guaranteed V _T (volume-assured pressure-support)
Both spontaneous modes (pressure-support ventilation, proportional-assist ventilation) and mandatory modes (volume-controlled or pressure-controlled modes)
Interface
Nasal mask, full-face mask, total-face mask, helmet, mouth-piece

(Adapted from Referenced 9).

ful physiologic and clinical evaluation, unfortunately there is still no published data about several sophisticated ventilators routinely used in clinical practice. Some of the most crucial and sometimes controversial general aspects of the performance of the various NIV ventilators are discussed below.

First, the performance of bi-level ventilators differs in delivered V_T, inspiratory trigger, expiratory cycle criterion, response to high inspiratory demand, rebreathing, air-leak compensation, response to simulated efforts, and patient-ventilator synchrony.^{22,23,33-41} The difference in de-

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Table 2. Characteristics of Bi-Level Ventilators for Noninvasive Ventilation

Bi-Level Ventilator	Available Modes	IPAP (cm H ₂ O)	EPAP (cm H ₂ O)	Circuit	Backup Respiratory Rate (breaths/min)	Adjustable Rise Time	Adjustable Maximum/Minimum T _I	Adjustable Inspiratory/Expiratory Trigger	Display monitor	Alarms	Battery	Weight (kg)
BiPAP Harmony Respironics	Spontaneous/timed	4–30	4–15	Single limb with Whisper Swivel or plateau exhalation valve	4–30	No	No/No	No/No	Yes	Patient disconnect, low P _{aw}	No	2.6
BiPAP Synchrony Respironics	CPAP, spontaneous, spontaneous/timed, timed, PCV	4–30	4–20	Single limb with Whisper Swivel or plateau exhalation valve	4–30	Yes	No/No	No/No	Yes	Patient disconnect, high/low P _{aw} , low V _E , apnea, power failure	External	2.7
BiPAP S/T D30 Respironics	CPAP, spontaneous, spontaneous/timed, timed	4–30	4–20	Single limb with Whisper Swivel or plateau exhalation valve	4–30	No	No/No	No/No	Yes	High/low P _{aw}	No	4.3
BiPAP M Series (Plus or Auto) with Bi-Flex Respironics	CPAP, spontaneous	4–25	4–25	Single limb with Whisper Swivel or plateau exhalation valve	No	Yes	No/No	No/No	No	Patient disconnect	External	1.0
BiPAP Vision Respironics	CPAP, spontaneous/timed, (proportional-assist ventilation)†	4–40	4–20	Single limb with Whisper Swivel or plateau exhalation valve	4–40	Yes	No/No	No/No	Yes‡	Patient disconnect, high/low P _{aw} and f, low V _E , apnea, power failure, O ₂ disconnect	No	15.4
BiPAP Focus Respironics	CPAP, spontaneous/timed	4–30	4–20	Single limb with Whisper Swivel or plateau exhalation valve	1–30	Yes	Yes/No	No/No	Yes	Patient disconnect, high/low P _{aw} , apnea, power failure	Internal	4.5
Knightstar 320 Mallinckrodt	CPAP, spontaneous, spontaneous/timed	3–20	3–20	Single limb with Whisper Swivel	No	No	No/No	No/No	No	No	No	3.9
Knightstar 330 Mallinckrodt	CPAP, spontaneous, spontaneous/timed, timed	3–30	3–20	Single limb with Whisper Swivel	3–30	Yes	No/No	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} , power failure, leak	Internal/external	1.0
Knightstar 335 Mallinckrodt	CPAP, spontaneous, spontaneous/timed	3–35	3–20	Single limb with Whisper Swivel	3–30	No	No/No	Yes/Yes	Yes	Patient disconnect, high/low P _{aw}	No	8.6
Smartair S Airox	CPAP, spontaneous	6–30 mbar	4–20 mbar	Single limb with Whisper Swivel	No	Yes	No/No	Yes/Yes	Yes	Low P _{aw}	No	2.7
VPAP II Resmed	CPAP, spontaneous	2–25	2–25	Single limb with Whisper Swivel or plateau exhalation valve	No	Yes	Yes/Yes	No/No	Yes	Patient disconnect, high/low P _{aw} , power failure	External	3.5
VPAP II ST-A Resmed	CPAP, spontaneous, spontaneous/timed, timed	2–25	2–25	Single limb with Whisper Swivel or plateau exhalation valve	3–30	Yes	Yes/Yes	No/No	Yes	Patient disconnect, high/low P _{aw} , power failure, leak	External	3.5
VPAP III Resmed	CPAP, spontaneous	3–25	3–25	Single limb with Whisper Swivel or plateau exhalation	No	Yes	Yes/Yes	Yes/Yes	Yes	Patient disconnect	External	2.3
VPAP III ST-A Resmed	CPAP, spontaneous, spontaneous/timed, timed	3–30	3–25	Single limb with Whisper Swivel or plateau exhalation valve	5–30	Yes	Yes/yes	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} , low V _E , power failure	External	2.3
PV 102+ Breas	Spontaneous/timed	4–30	No	Single limb with non-rebreathing valve	6–40	Yes	No/No	Yes/Yes	Yes	Power failure, leak	External	3.2
PV 401 Breas	Spontaneous/timed	6–40	No	Single limb with non-rebreathing valve	4–40	Yes	No/No	Yes/Yes	Yes	Low P _{aw} , power failure	External/ Internal/external	5.3
Respicare N Dräger	CPAP, spontaneous	5–30 mbar	3–20 mbar	Single limb with Whisper Swivel	6–60	Yes	No/No	Yes/Yes	No	Patient disconnect, high P _{aw}	No	4.2
Respicare S Dräger	CPAP, spontaneous, spontaneous/timed	5–30 mbar	3–20 mbar	Single limb with Whisper Swivel	6–60	Yes	Yes/No	Yes/Yes	No	Patient disconnect, high P _{aw}	No	4.2
Respicare SC Dräger	CPAP, spontaneous, spontaneous/timed, timed, PCV	5–30 mbar	3–20 mbar	Single limb with Whisper Swivel	6–60	Yes	Yes/No	Yes/Yes	Yes	Patient disconnect, high P _{aw}	No	4.2
VS Serena Saime	CPAP, spontaneous, spontaneous/timed	4–30 hPa	4–20 hPa	Single limb with Whisper Swivel	5–50	Yes	Yes/Yes	No/No	Yes	Patient disconnect, power failure	External	2.5
PV 403 Breas	Spontaneous/timed, timed, PCV, VCV	6–50	No	Single limb with non-rebreathing valve	6–40	Yes	No/No	Yes/Yes	Yes	Low V _T and P _{aw} , power failure, leak	External/ Internal/external	5.5
Smartair ST Airox	CPAP, spontaneous, spontaneous/timed, timed, PCV	6–30 mbar	4–20 mbar	Single limb with Whisper Swivel	4–40	Yes	No/No	Yes/Yes	Yes	Low P _{aw}	No	2.7

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Table 2. Characteristics of Bi-Level Ventilators for Noninvasive Ventilation (Continued)

Bi-Level Ventilator	Available Modes	IPAP (cm H ₂ O)	EPAP (cm H ₂ O)	Circuit	Backup Respiratory Rate (breaths/min)	Adjustable Rise Time	Adjustable Maximum/Minimum T _I	Adjustable Inspiratory/Expiratory Trigger	Display monitor	Alarms	Battery	Weight (kg)
Smartair Plus Airox	CPAP, spontaneous, spontaneous/timed, timed, PCV, volume-assured pressure-support	5–30 mbar	4–20 mbar	Single limb with non-rebreathing valve or Whisper Swivel	4–40	Yes	Yes/Yes	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} and V _T , high f, power failure, apnea	Internal	3.5
Twinair Airox	Spontaneous/timed, timed, PCV, VCV, volume-assured pressure-support	5–40 mbar	0–20 mbar	Single limb with non-rebreathing valve, or dual limb	6–40	Yes	No/No	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} , f, and V _T , power failure, leak	Internal	9.5
Onyx plus Mallinckrodt	Spontaneous, spontaneous/timed, PCV, volume-assured pressure-support, VCV	3–40*	0–15	Single limb with non-rebreathing valve	4–40	Yes	No/No	Yes/Yes	Yes	Patient disconnect, high/low V _T , power failure	External	9.7
Ventil+ Mallinckrodt	CPAP, spontaneous, spontaneous/timed, VCV	4–30	4–20	Single limb with Whisper Swivel	4–30	No	No/No	Yes/Yes	No	Patient disconnect, power failure	No	7.0
Helia 2 Saime	Spontaneous/timed, timed, PCV, volume-assured pressure-support, VCV	5–60 hPa*	0–12 hPa	Single limb with non-rebreathing valve or double limb	5–60	Yes	Yes/No	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} and V _T , high f, power failure, leak	Internal	10.0
VS Integra Saime	Spontaneous, spontaneous/timed, timed, PCV	5–50 hPa	0–20 hPa	Single limb with non-rebreathing valve or Whisper Swivel	5–50	Yes	Yes/Yes	Yes/Yes	Yes	Patient disconnect, high f, high/low V _T , power failure	Internal/external	3.5
VS Ultra Saime	Spontaneous, spontaneous/timed, timed, PCV, volume-assured pressure-support, VCV	5–50 hPa*	0–20 hPa	Single limb with non-rebreathing valve or Whisper Swivel, or dual limb	5–60	Yes	Yes/Yes	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} and V _T , high f, power failure	Internal/external	3.5

*Pressure-support level implemented with an algorithm over expiratory positive airway pressure (EPAP) (ie, pressure support = IPAP + EPAP)

†O₂ blender

‡Sophisticated graphics display (flow, P_{aw}, V_T curves)

IPAP = inspiratory positive airway pressure

EPAP = expiratory positive airway pressure

f = respiratory rate

V_T = tidal volume

T_I = inspiratory time

CPAP = continuous positive airway pressure

Spontaneous = pressure-support ventilation without a backup respiratory rate

Spontaneous/timed = pressure-support ventilation with a backup respiratory rate

Timed = machine triggered, pressure targeted, machine cycled breaths

PCV = pressure-controlled ventilation

VCV = volume-controlled ventilation

V_E = minute ventilation

P_{aw} = airway pressure

(Adapted from Referenced 9).

livered V_T between some bi-level ventilators is probably due to a discrepancy between the delivered versus the set IPAP and EPAP, and the different pressure and flow wave-forms.^{22,23,36} Surprisingly, the variable behavior of some bi-level ventilators in response to different simulated efforts and air-leaks is unpredictable from the operating principles reported in the manufacturers' descriptions. However, 2 bi-level ventilators were similarly effective in improving overnight gas exchange and sleep during NIV in stable patients with chronic respiratory failure,³⁹ despite the fact that the 2 ventilators had different performances in the laboratory.²³ In a short-term study with awake patients

with chronic respiratory failure receiving NIV, Vitacca et al⁴⁰ found no differences among the 5 tested bi-level ventilators, except for patient comfort.

Second, even if supported by limited bench-study data, some intermediate ventilators show heterogeneous performance because of variable efficiency of their inspiratory trigger and the expiratory-cycle functions.⁴² Compared to 3 other intermediate ventilators working in PSV,⁴² the Pulmonetics LTV1000 had the worst performance, probably because its exhalation valve is attached to an incomplete expiratory limb of the circuit. The prototype of the Respironics Esprit had intractable auto-triggering at higher in-

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Table 3. Characteristics of Intermediate Ventilators for Noninvasive Ventilation

Intermediate Ventilator	Available Modes	IPAP (cm H ₂ O)	EPAP (cm H ₂ O)	Circuit	Backup Respiratory Rate (breaths/min)	Adjustable Rise Time	Adjustable Maximum/Minimum T _I	Adjustable Inspiratory/Expiratory Trigger	Display monitor	Alarms	Battery	Weight (kg)
Legendair Airox	Spontaneous/timed, timed, PCV, VCV, volume-assured pressure-support, SIMV	5–40 mbar	0–20 mbar	Single limb with non-rebreathing valve or double limb	6–60	Yes	No/No	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} , f, and V _T , power failure, leak	Internal	4.5
Support-air Airox	Spontaneous/timed, timed, PCV, VCV, volume-assured pressure-support, SIMV†	5–40 mbar	0–20 mbar	Single limb with non-rebreathing valve or double limb	6–60	Yes	No/No	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} , f, and V _T , power failure, leak	Internal	4.5
Achieva Mallinckrodt	CPAP, spontaneous/timed, PCV, VCV, SIMV, apnea ventilation†	1–50*	0–20	Single limb with non-rebreathing valve	1–80	Yes	Yes/Yes	Yes/No	Yes	Patient disconnect, high/low P _{aw} , apnea, power failure, O ₂ disconnect	Internal/external	14.5
I-Vent 201 Versamed	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–60*	5–20	Incomplete double-tube circuit	1–50	Yes	Yes/Yes	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} , f, and V _T , apnea, power failure, leak, O ₂ disconnect	Internal/external	8.5
Legacy T-Bird Viasys Healthcare	CPAP, spontaneous/timed, VCV, SIMV, apnea ventilation†	1–60*	0–30	Double limb	2–80	Yes	Yes/Yes	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} , f, and V _T , apnea, power failure, O ₂ disconnect	Internal/external	20
LTV1000 Pulmonetics	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–60*	0–20	Incomplete double-tube circuit	1–80	Yes	Yes/Yes	Yes/Yes	Yes	Patient disconnect, high/low P _{aw} , low V _E , apnea, power failure, O ₂ disconnect	Internal/external	5.7
LTV1200 Pulmonetics	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–99*	0–20	Incomplete double-tube circuit	1–80	Yes	Yes/Yes	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} and EPAP, low V _E , high f, apnea, power failure, O ₂ disconnect	Internal/external	6.5
Esprit Respironics	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–100*	0–35	Double limb	1–80	Yes	Yes/Yes	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} , f, and V _T , low V _E , apnea, power failure, O ₂ disconnect	Internal/external	35
Dräger Carina	CPAP; Spontaneous/timed, PCV, volume assured pressure support, VCV, SIMV, apnea ventilation†	5–50 mbar	1–20 mbar	Single-limb with Whisper Swivel or non-rebreathing valve	5–50	Yes	Yes/Yes	Yes/No	Yes‡	Patient disconnect, high/low P _{aw} , f and V _E , apnea, power failure	Internal/External	5.5

*Pressure-support level implemented with an algorithm over expiratory positive airway pressure (EPAP) (ie, pressure support = IPAP + EPAP)

†O₂ blender

‡Sophisticated graphics display (flow, P_{aw}, V_T curves)

IPAP = inspiratory positive airway pressure

EPAP = expiratory positive airway pressure

f = respiratory rate

V_T = tidal volume

T_I = inspiratory time

CPAP = continuous positive airway pressure

Spontaneous = pressure-support ventilation without a backup respiratory rate

Spontaneous/timed = pressure-support ventilation with a backup respiratory rate

Timed = machine triggered, pressure targeted, machine cycled breaths

PCV = pressure-controlled ventilation

VCV = volume-controlled ventilation

SIMV = synchronized intermittent mandatory ventilation

V_E = minute ventilation

P_{aw} = airway pressure

(Adapted from Referenced 9).

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Table 4. Characteristics of Intensive Care Ventilators for Noninvasive Ventilation

Intensive Care Ventilator	Available Modes	IPAP (cm H ₂ O)	EPAP (cm H ₂ O)	Circuit	Backup Respiratory Rate (breaths/min)	Adjustable Rise Time	Adjustable Maximum/Minimum T _I	Adjustable Inspiratory/Expiratory Trigger	Display monitor	Alarms	Battery	Weight (kg)
Vela Viasys Healthcare	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–60*	0–35	Double limb	2–80	Yes	Yes/Yes	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} , f, and V _T , low V _E , apnea, power failure, O ₂ disconnect	Internal/external	17.2
7200 Puritan Bennett	CPAP, spontaneous/timed, PCV, VCV, SIMV, proportional-assist ventilation†	1–70*	0–45	Double limb	1–100	Yes	Yes/Yes	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} , high f, low V _E , apnea, power failure, O ₂ disconnect	Internal	50.8
8400 Puritan Bennett	CPAP, spontaneous/timed, PCV, VCV, SIMV, proportional-assist ventilation†	1–70*	0–45	Double limb	1–100	Yes	Yes/Yes	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} , and V _E , apnea, high f, power failure, O ₂ disconnect	Internal	71
Servo 900C Siemens	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–120*	0–50*	Double limb	5–120	Yes	Yes/No	Yes/No	Yes	Patient disconnect high P _{aw} , low V _E , apnea, power failure, O ₂ disconnect	Internal	19
Servo 300 Siemens	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–100*	0–100*	Double limb	1–40	Yes	Yes/No	Yes/No	Yes‡	Patient disconnect, high/low V _E , high P _{aw} , power failure, O ₂ disconnect	Internal	24
Evita 2 Dura Dräger	CPAP, spontaneous/timed, PCV, VCV, SIMV†	1–80 mbar*	0–35 mbar	Double limb	1–100	Yes	Yes/Yes	Yes/Yes	Yes‡	Patient disconnect, high/low P _{aw} , and V _E , apnea, high f, power failure, O ₂ disconnect	Internal	27

*Pressure-support level implemented with an algorithm over expiratory positive airway pressure (EPAP) (ie, pressure support = IPAP + EPAP)

†O₂ blender

‡Sophisticated graphics display (flow, P_{aw}, V_T curves)

IPAP = inspiratory positive airway pressure

EPAP = expiratory positive airway pressure

f = respiratory rate

V_T = tidal volume

T_I = inspiratory time

CPAP = continuous positive airway pressure

Spontaneous = pressure support ventilation without a backup respiratory rate

Spontaneous/timed = pressure support ventilation with a backup respiratory rate

Timed = machine triggered, pressure targeted, machine cycled breaths

PCV = pressure-controlled ventilation

VCV = volume-controlled ventilation

SIMV = synchronized intermittent mandatory ventilation

V_E = minute ventilation

P_{aw} = airways pressure

(Adapted from Reference 9)

spiratory flows, but this technical problem may have been solved in the new version of the Esprit, which is designed for the clinical market.⁴²

Third, according to several studies,^{33,34,43–47} despite a quite wide range of variability, some bi-level and intermediate ventilators had at least the same performance as some conventional ICU ventilators in inspiratory triggering, pressurization rate, inspiratory ventilator work, expiratory cycling, circuit-induced expiratory work, and response to different ventilatory demands. In an experimental study⁴⁶ of 5 single-limb-circuit bi-level ventilators versus one ICU ventilator,⁴⁸ the Mallinckrodt Onyx had flow delivery similar to or better than that of the ICU device with

consequent potential clinical advantages in lower work of breathing (WOB) and better patient comfort during COPD exacerbation.⁴⁹ In another lung-model investigation, Bunburaphong et al³⁴ found that all except 2 (Taema DP90 and ResMed VPAP) of the 9 studied single-limb-circuit bi-level ventilators outperformed one traditional ICU ventilator (Nelcor Puritan Bennett 7200ae) in all the inspiratory and expiratory variables measured at various levels of lung compliance, pressure support, and ventilatory demand (Fig. 1). In a subsequent experimental study,⁴³ one bi-level ventilator (ResMed VPAP II) worked as well as one ICU ventilator (Hamilton Galileo) but less well than other 2 ICU ventilators (Dräger Evita 4 and Siemens Servo 300).

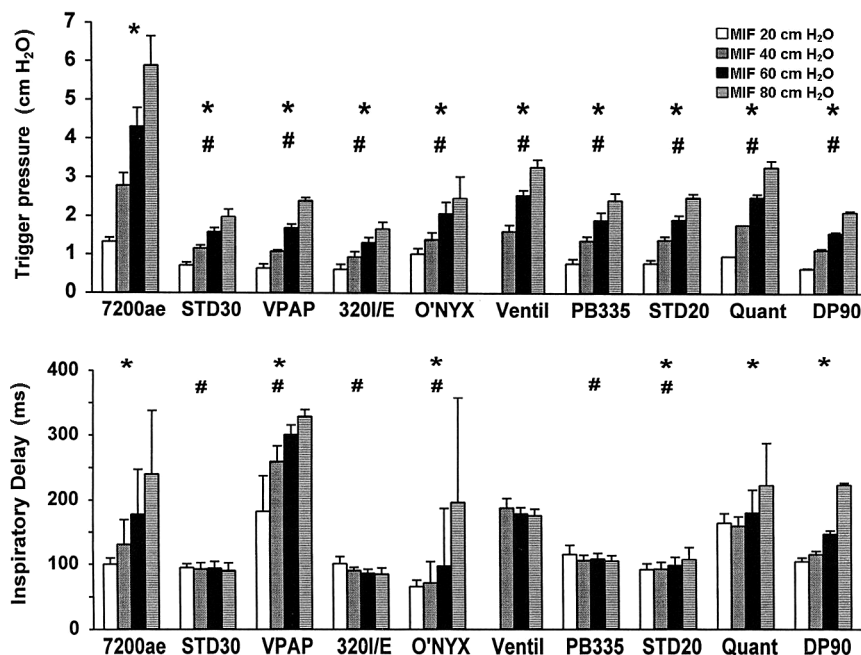


Fig. 1. Lung-model differences in inspiratory trigger sensitivity (upper graph) and inspiratory time delay (lower graph) between an intensive-care ventilator (Puritan Bennett 7200ae) and 9 bi-level home ventilators, at maximum inspiratory flows of 20, 40, 60, and 80 L/min. All the bi-level home ventilators had a significantly higher trigger sensitivity than the 7200ae at all inspiratory flows. For inspiratory trigger sensitivity: * $P < .05$ compared to the other bi-level ventilators. # $P < .05$ compared to the 7200ae. The STD30, 320I/E, O'nyx, PB335, and STD20 had significantly shorter delay times than the 7200ae at flows > 20 L/min. For inspiratory delay time: * $P < .05$ compared to the other bi-level ventilators; # $P < .05$ compared to the 7200ae. (Adapted from Reference 34.)

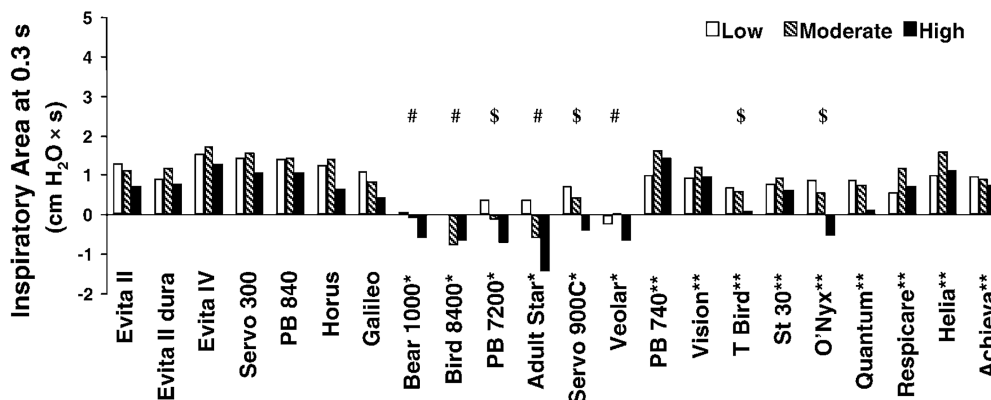


Fig. 2. Pressurization rate, as measured by the inspiratory area in the first 0.3 s of inspiration, during the early phase of inspiration, in a lung model, at pressure support (PS) of 5, 10, and 15 cm H₂O, and at 3 simulated inspiratory-efforts (low, moderate, high) with 22 ventilators. From left to right: 7 newer-generation intensive-care ventilators, 6 older-generation intensive-care ventilators (marked with one asterisk), and 9 piston-driven or turbine-driven home ventilators (marked with 2 asterisks). All the newer-generation intensive-care ventilators, and most of the home ventilators, outperformed the older-generation intensive-care ventilators. # $P < .05$ versus all the newer-generation intensive-care ventilators. \$ $P < .05$ versus at least one of the newer-generation intensive-care ventilators. (Adapted from Reference 44.)

Richard et al⁴⁴ found that some piston-driven and-turbine-driven home ventilators had better trigger sensitivity and pressurization speed than most of the older-generation ICU ventilators, especially at high inspiratory demand (Fig. 2). In another bench study,⁴² the performance of 4 intermediate ventilators (Nellcor Puritan Bennett 740, Respironics Esprit, Viasys Healthcare T-Bird Legacy, and Pulmonetics

LTV1000) was comparable to that of the Nellcor Puritan Bennett 7200, and had a shorter inspiratory-rise time and expiratory-pressure-decrease time.

Recently, in a lung-model study, Miyoshi et al⁴⁵ found that, in the presence of increasing degrees of air leak, the trigger function of 2 bi-level ventilators that had unchangeable trigger sensitivity (Respironics BiPAP Vision and

BiPAP S/T-D) outperformed that of 2 conventional ICU ventilators with adjustable trigger sensitivity (Nellcor Puritan Bennett 7200ae and Puritan Bennett 840).

However, according to bench and clinical data, because of their exhalation air systems, single-limb-circuit first-generation bi-level ventilators may have several technical limitations (CO_2 rebreathing, impaired inspiratory trigger function, and greater expiratory resistance) and physiological limitations (greater inspiratory load and higher intrinsic PEEP, worse gas exchange, and less patient-ventilator interaction) compared to dual-limb circuit ventilators.¹⁶⁻¹⁹

In a clinical study with 7 patients weaning from invasive mechanical ventilation, Lofaso et al⁴⁶ found that the Respironics BiPAP with the Whisper Swivel was associated with significantly greater \dot{V}_T , minute ventilation (\dot{V}_E), and WOB than the Respironics BiPAP equipped with a non-rebreathing valve, or two conventional ICU ventilators, possibly due to the hyperventilatory response that is supposed to compensate the substantial CO_2 rebreathing. Conversely, in a subsequent study with 27 intubated patients in the weaning process, Patel and Petrini⁴⁷ found no differences in WOB, respiratory rate, $P_{a\text{CO}_2}$, or \dot{V}_E between the Respironics BiPAP equipped with the Whisper Swivel and one conventional ICU ventilator (Siemens Servo 900C). That different finding was probably because Patel and Petrini used a higher level of pressure support and PEEP than did Lofaso et al⁴⁶ (15/5 cm H_2O and 5/2 cm H_2O , respectively), which may have prevented the rebreathing and the consequent increase in WOB.

In another clinical investigation with 7 patients during weaning from invasive ventilation,³³ the Respironics BiPAP with a non-rebreathing valve had higher WOB, compared to one older ICU ventilator, presumably because of the Respironics BiPAP's lesser inspiratory trigger sensitivity, slower pressurization speed, and higher expiratory work.

Fourth, another crucial point is whether the performance of the newer ICU ventilators equipped with "NIV modes" is better than that of the conventional ICU ventilators. Older-generation ICU ventilators were originally designed to provide invasive ventilation to critically acutely ill intubated patients, with minimal or no air leaks. Conversely, newer-generation ICU ventilators have "NIV modes" that aim to minimize the impact of leaks on key ventilator functions and to optimize patient interaction with all phases of PSV.^{30-32,43,44} Though there have been few clinical and physiological *in vivo* studies of the ICU ventilators, lung-model investigations have clearly shown that certain newer ventilators (Nellcor Puritan Bennett 840, Siemens Servo 300, Dräger Evita II and Evita IV) outperformed certain earlier ventilators (Bear 1000, Nellcor Puritan Bennett 7200) in trigger time delay and pressurization slope.⁴⁴ Some newer ICU ventilators have monitors showing colored pressure, flow, and volume waveforms and have touch-

screen technology, which might allow quicker and/or easier interpretation of the patient's ventilatory status breath by breath.

Two recent lung-model studies showed significant differences in the performance of several newer-generation ICU ventilators in all the inspiratory and expiratory variables tested, and in the pressure-time and flow-time waveforms.^{30,31} The Nellcor Puritan Bennett 840 and Siemens Servo 300A had better inspiratory trigger function, whereas the Hamilton Galileo and TBird AVS had worse expiratory function.³⁰ Similar to bi-level ventilators,³⁴ the response of most of the new ICU ventilators diminished as the lung-model peak flow was increased, whereas increasing the pressure setting caused those ventilators to perform near to their ideal functioning.³⁰ That finding may have clinical implications for some ventilators, such as the likelihood of failure to adequately support acutely ill patients who have high ventilatory demand.

With new ICU ventilators (eg, Nellcor Puritan Bennett 840 or Dräger Evita series), when the setting is changed from conventional to "NIV modes," first, the ventilator becomes able to compensate for large leaks (30 L/min) with the goal of maintaining a stable inspiratory pressure and an adequate trigger sensitivity. Then, unnecessary alarms are eliminated and their limits may be reset according to the patient's needs, to minimize noise-discomfort. Finally, the criterion for expiratory cycling may be more finely adjusted by setting a maximum inspiratory time (T_I) to optimize patient-ventilator synchrony, even with a large leak.

Recently, Vignaux et al³² reported a bench study of the performance of 8 new ICU ventilators working in PSV mode, with and without the implementation of "NIV modes," and with and without simulated air leaks. With most of the ventilators in conventional PSV mode, their performance was sensibly impaired by leaks, because of auto-triggering, delay in inspiratory triggering, delay in expiratory cycling, increase in work load, and decrease in the pressurization rate. The "NIV modes" with PSV partially or totally corrected those interferences with the majority of the tested ventilators, though there were large differences between the machines. Paradoxically, with some ventilators the "NIV modes" worsened the leak-induced dysfunctions, for reasons unexplained. Moreover, with some ventilators the correction of the delayed trigger time by switching on "NIV modes" may be achieved at the price of a higher work load, probably due to a slower pressurization.³² Though the "NIV modes" may correct the delayed cycling in normal and obstructive respiratory mechanics with some ventilators, they have no effect or worsen the problem in restrictive conditions, and cause premature cycling at the default setting.³²

Limitations of In Vitro Studies

Because there have been very few *in vivo* investigations, the majority of data about the performance of the available ventilators is from *in vitro* lung-model studies, so some doubts remain about the real clinical importance of the technical differences observed in the bench studies. Consequently, extrapolating experimental data to the clinical setting must be done cautiously, because no lung model can simulate the ventilatory variability of patients, especially acutely ill patients on NIV. In contrast to the lung-model tests, where the simulated respiratory mechanics and the degree of air leak are fixed, the impedance of the respiratory system and the amount of unintentional mask leak can change very quickly breath-by-breath in unstable critically ill patients on NIV, and this dynamic variability can affect ventilator performance, especially inspiratory triggering and expiratory cycling. Up to now it is impossible to fully reproduce that complexity in bench experiments.¹⁶⁻¹⁹

Gas Source

Unlike ICU ventilators, which use high-pressure gas sources, bi-level ventilators and several intermediate ventilators use either a compressor or an electronic turbine pump to pressurize the room air, and those systems may not assure stable pressures.^{16,17}

Oxygen Supply

Most patients with ARF receiving NIV need supplemental O₂ to keep an adequate arterial oxygen saturation. Unlike all ICU ventilators and some intermediate ventilators, which use high-pressure O₂, bi-level ventilators generally do not have a blender where the O₂ and room air are mixed and the F_{IO₂} is controlled.⁵⁰ In a bi-level ventilator that does not have a blender, O₂ is delivered from a low-pressure source and the F_{IO₂} during NIV is not easily predictable because it is affected by the site of the O₂ enrichment, type of exhalation port, ventilator settings, O₂ flow, breathing pattern, and amount of leak.^{4,16-19}

In an experimental setting, Waugh and De Kler⁵¹ found that, with a bi-level ventilator and the leak port inside the mask, the F_{IO₂} was higher with lower IPAP and EPAP settings, and when O₂ was added at the ventilator outlet instead of the mask inlet. In a study with 3 volunteers and the Respirationics BiPAP STD30 ventilator with a leak port in the circuit, Thys et al⁵² evaluated 3 O₂ insertion sites. The F_{IO₂} was higher with lower IPAP and when O₂ was added at the mask inlet than when added at the ventilator outlet. Interestingly, the greatest oxygen concentration was when O₂ was added at the mid-point in the circuit. However, O₂ supplementation at that site is not practical be-

cause it requires cutting the circuit. Thys et al also found that, although the F_{IO₂} increased with the O₂ flow, it was difficult to obtain an F_{IO₂} > 0.30 without a very high O₂ flow (4 L/min and IPAP > 12 cm H₂O).

In a laboratory study, Schwartz et al⁵³ evaluated the O₂ delivery concentration with a bi-level ventilator and 3 types of exhalation system: leak port inside the mask, leak port within the circuit, and plateau exhalation valve. In contrast to the above-described previous papers,^{51,52} Schwartz et al⁵³ also studied the effect of O₂ injection directly into the mask. The O₂ concentration was significantly lower with the leak port into the mask than with the other 2 ports, with higher IPAP and EPAP settings and with lower O₂ flow. With the mask leak port, the O₂ concentration was greater when O₂ was added into the circuit than into the mask, presumably because in the latter much of the O₂ was exhausted out the exhalation port because of the close proximity of the O₂ entrainment site to the port. Conversely, with the plateau exhalation valve, the O₂ concentration was not different with the 2 oxygen injection sites. The absolute highest O₂ concentration was achieved with the leak port in the circuit and O₂ added into the mask by using lower IPAP and EPAP values (Fig. 3). The impact of the "unintended leaks" (mouth leaks with nasal ventilation and/or leaks at the mask-face interface) on the F_{IO₂} has not been evaluated.

Circuit

The Respirationics BiPAP, like most of the first generation bi-level ventilators, has a single-limb circuit, and the exhaled air passes through the Whisper Swivel, which is a fixed-resistance, variable-flow leak port situated in the circuit, near the interface.^{16,17} In a clinical study of nasal BiPAP in 6 patients with hypercapnic chronic respiratory failure and 4 normal volunteers, Ferguson and Gilmartin⁵⁴ observed that when the Whisper Swivel was used at lower EPAP settings, there was significant CO₂ rebreathing and increased dead-space ventilation, and P_{aCO₂} did not fall. The degree of CO₂ rebreathing decreased with increasing EPAP, and CO₂ rebreathing was fully eliminated with an EPAP of 8 cm H₂O (Fig. 4). When the expiratory flow rate overcomes the leak rate of the Whisper Swivel at a low EPAP (< 4 cm H₂O), the exhaled air flows back into the ventilator, a portion of which may be inhaled during the following breath, causing CO₂ rebreathing. When EPAP is raised, the leak rate out of the Whisper Swivel increases and the volume of gas exhaled back into the ventilator decreases, and at an EPAP of 8 cm H₂O the rebreathing is fully eliminated.

The inverse correlation between rebreathing and PEEP with the Whisper Swivel was confirmed in another bench study.³³ However, higher PEEP is rarely tolerated by patients during NIV and may increase the risk of excessive

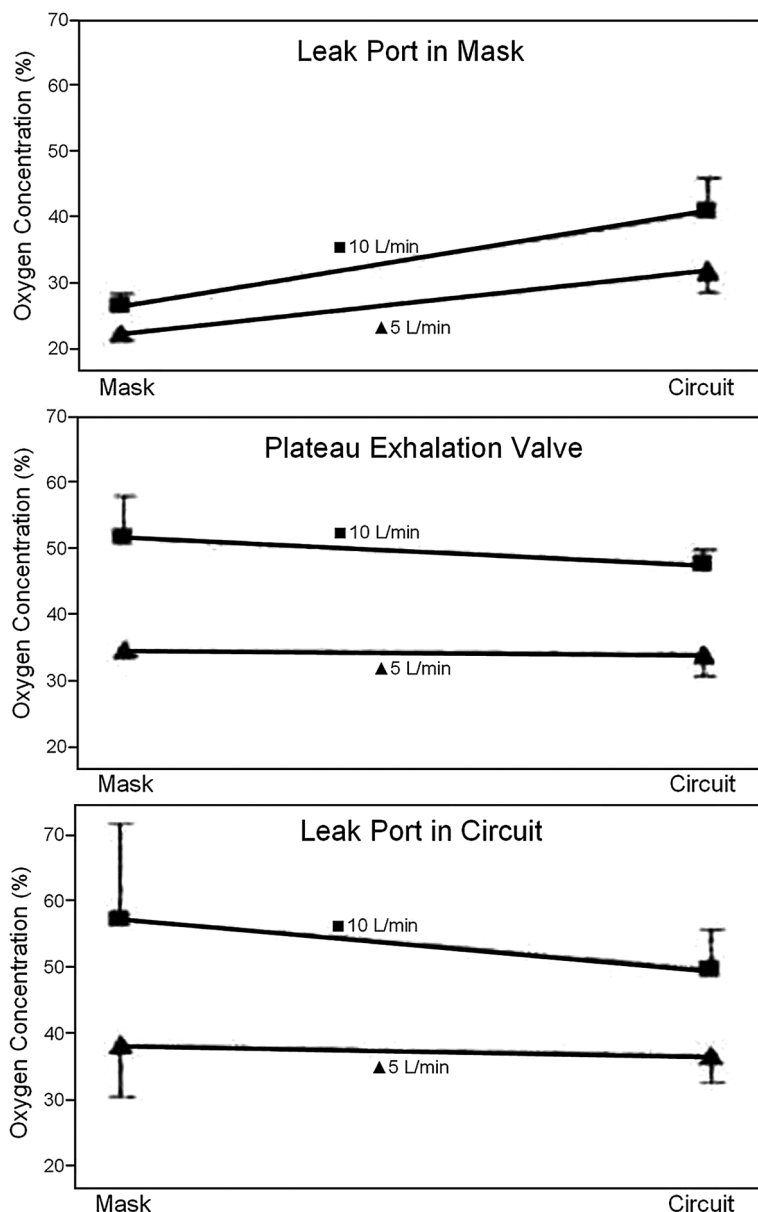


Fig. 3. Effect of the location and type of leak port (Whisper Swivel in the mask, plateau exhalation valve, or Whisper Swivel in the circuit), the site of O_2 injection (inside the mask or into the circuit), and the oxygen flow (5 or 10 L/min) on the measured oxygen concentration during noninvasive ventilation delivered via bi-level positive airway pressure in a lung model. The oxygen concentration was lower with the leak port in the mask than with the other 2 exhalation ports. (Adapted from Reference 53.)

air leak, gastro-distention, and lung hyperinflation in patients with COPD and intrinsic PEEP lower than the external PEEP.^{2,4} As a matter of fact, in newer single-limb-circuit bi-level ventilators (eg, BiPAP Vision) a minimum EPAP is set by default (usually 4 cm H_2O), which greatly reduces or fully abolishes rebreathing. Moreover, the degree of rebreathing with the Whisper Swivel is inversely correlated with the expiratory time: the longer the expiratory time, the greater the chance of ensuring a full CO_2 wash-out.^{16,17} As described above, CO_2 rebreathing negatively influences WOB.⁴⁶ Ferguson and Gilmartin⁵⁴ found

that when patients were ventilated with either a non-rebreathing valve or the plateau exhalation valve, CO_2 rebreathing was minimal or absent, even at a low EPAP. The plateau exhalation valve has a diaphragm that limits air leaks during inspiration and allows unidirectional flow during expiration. The greater leak rate at any EPAP level through the plateau exhalation valve significantly reduces the amount of CO_2 exhaled back into the tubing to a lower level, which is therefore washed out at the start of the following inspiration. Because of its CO_2 -removal mechanism, the term “valve” is inappropriate for the plateau

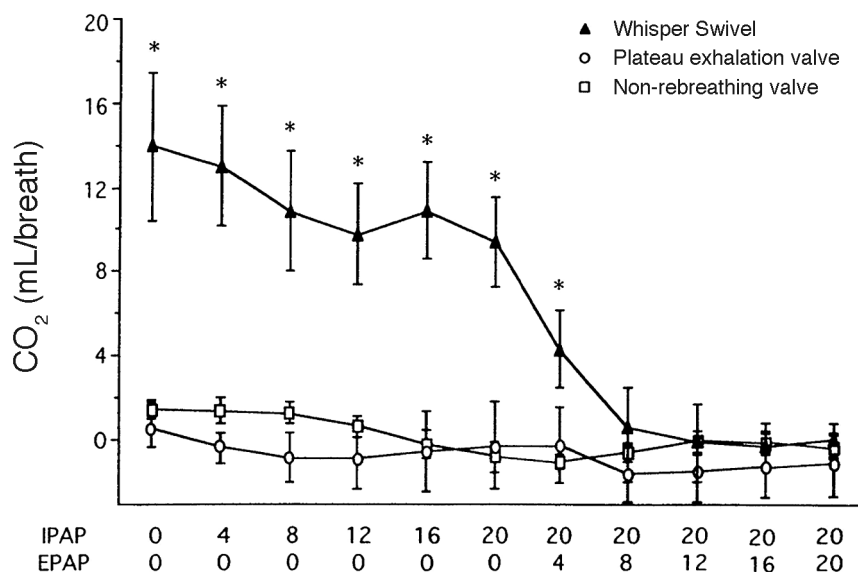


Fig. 4. Amount of rebreathing, measured as volume of CO₂ inhaled, with a bi-level-positive-airway-pressure (BiPAP) ventilator with a single-limb-circuit, at various inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) settings, with 3 different exhalation valves. Substantial rebreathing occurred only with the Whisper Swivel at lower EPAP. The plateau exhalation valve and the non-rebreathing valve prevented rebreathing with all ventilator settings. * $P < .05$ compared to the other exhalation devices at similar BiPAP settings. (Adapted from Reference 54.)

exhalation valve, because it works as a larger leak port. However, in a recent crossover study with 7 patients receiving long-term nocturnal nasal BiPAP,⁵⁵ the plateau exhalation valve did not improve daytime or nocturnal gas exchange or symptoms, compared to the Whisper Swivel. Thus, the plateau exhalation valve has been successfully applied only with BiPAP; the extension of its use to other bi-level ventilators has not been proved.^{16,17} Another option to prevent CO₂-rebreathing with single-limb bi-level ventilators is to apply a non-rebreathing valve (“mushroom,” “diaphragm,” or “balloon” valve) in the circuit, near the interface. A non-rebreathing valve works as a “true valve” because during inspiration the diaphragm or its balloon is inflated with a full occlusion of the expiratory circuit limb; during the expiration, as the valve is deflated, the air is allowed to be exhaled through it.

Lofaso et al⁴⁶ found that the substantial rebreathing observed with the Whisper Swivel was fully abolished with a non-rebreathing valve, even at a low EPAP setting. However, by prolonging the constant time required to reach the equilibrium of the system, the additional expiratory load induced by the valve increased the intrinsic PEEP and therefore impaired the inspiratory trigger sensitivity, which decreased the V_T .^{33,34} There were significant differences in resistance and expiratory work among the 5 non-rebreathing valves used with a bi-level ventilator in an in vitro study; specifically, the least resistive valve (Bennett) was associated with lower WOB than the most resistive valve (Peters) in 10 patients receiving invasive PSV.⁵⁶

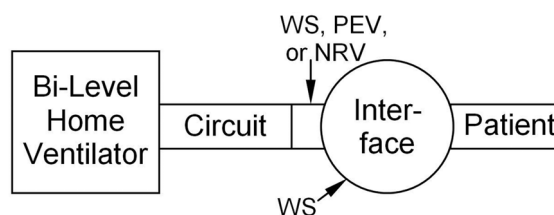


Fig. 5. Schematic representation of a bi-level home ventilator with a single-limb circuit and different types of exhalation systems situated either at the level of the distal portion of the tube or at the interface side. WS = Whisper Swivel. PEV = plateau exhalation valve. NRV = non-rebreathing valve.

The CO₂ rebreathing is also influenced by the site of the exhalation port. In a double-chamber lung-model study, Schettino et al⁵⁷ recently found that during CPAP and PSV with a single-limb-circuit ventilator in a simulated state of COPD and hypercapnic ARF, the CO₂ rebreathing was significantly lower with a face mask with the exhalation port in the mask than in the circuit or with a total face mask with the exhalation port in the mask. Figure 5 shows the various exhalation-system options with a single-limb-circuit bi-level ventilator. Note that the different single-limb-circuits combined with the dedicated exhalation system (leak port, plateau exhalation valve, or “true valve”) are not interchangeable among the ventilators. In other words, bi-level NIV ventilators should be used only with the dedicated circuits and interfaces for which they are approved.

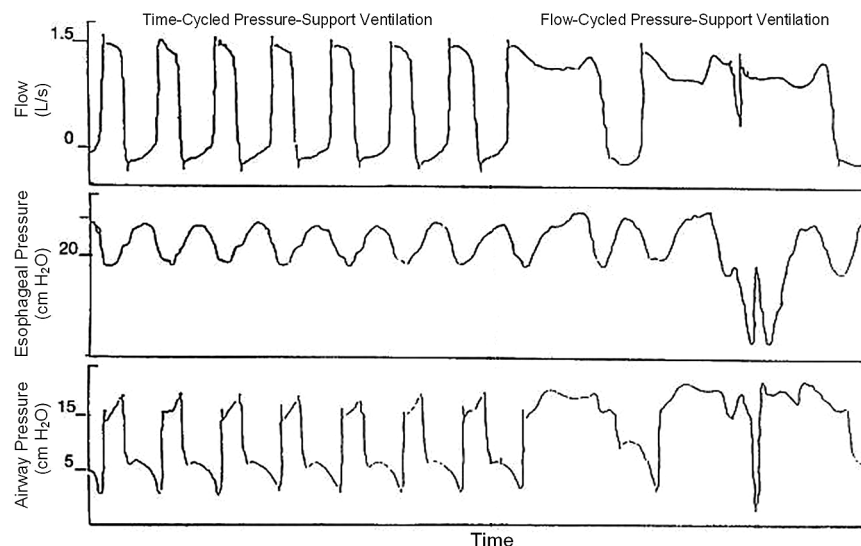


Fig. 6. Flow, esophageal pressure, and airway pressure waveforms from a patient during noninvasive ventilation with substantial air leaks due to incomplete face-mask seal. Note the regularity of the breaths during time-cycled ventilation. During conventional flow-cycled ventilation there is patient-ventilator asynchrony from wasted inspiratory efforts, because of a persistently high compensatory inspiratory flow. (Adapted from Reference 62.)

Similar to the ICU ventilators, new-generation bi-level ventilators have dual-limb circuits that eliminate the risk of rebreathing and mechanical interference. There are also 2 intermediate ventilators (VersaMed I-Vent201 and Pulmonetics LTV1000) that have an incomplete dual-limb circuit; the expiratory limb is only a short tube with a PEEP valve. Note that that setup has potential negative effects on triggering and cycling.^{16,17,42}

Inspiratory Trigger and Expiratory Cycle

Optimization of patient-ventilator interaction during NIV is essentially based on the technological efficiency of the ventilator in detecting the patient's inspiratory effort (the inspiratory trigger) as quickly as possible, and in ending the inspiration as close as possible to the beginning of the patient's expiration (expiratory cycling) independently from the respiratory-system impedance or the air leak.^{16,17} Ideally the inspiratory trigger should be set at the highest sensitivity capable of reducing the inspiratory effort needed to trigger the ventilator.⁵⁸ With NIV ventilators, flow triggers are associated with a lower WOB and shorter triggering delay than are pressure triggers.^{35,59} However, during NIV a too-sensitive trigger, especially a flow trigger, may cause auto-triggering if there is substantial air leak, which compromises patient-ventilator synchrony and causes wasted inspiratory efforts.^{17,18}

Bench studies have indicated that inspiratory trigger function may significantly differ among bi-level, ICU, and intermediate ventilators, and among ventilators in a given

category.^{22,23,30-37,42-45} Design aspects of the circuits of certain first-generation bi-level ventilators, (single-limb circuit with high resistance)^{33,34,56,57} and of some intermediate ventilators (eg, Pulmonetics LTV1000 with an "incomplete dual-limb circuit" and a PEEP valve in the short expiratory limb)^{16,17,42} may negatively influence trigger efficiency. Other potential mechanisms underlying the variability in trigger function include the heterogeneity in pressure-time and flow-time waveforms,³¹ trigger response to the inspiratory flow,^{30,34-37} and leak-induced auto-triggering during flow-triggered NIV.^{32,36,45}

During PSV, cycling is flow-dependent and occurs at a threshold, the point at which flow decreases to a default percentage, an adjustable percentage, or an absolute flow.^{16,17} In NIV, patient-ventilator asynchrony with expiratory muscle activation⁶⁰ and wasted efforts due to incomplete lung emptying⁶¹ can occur with large air leaks, which delays or prevents the inspiratory flow from reaching the threshold ("inspiratory hang-up"). Strategies to prevent "inspiratory hang-up" include: set a suitable threshold and/or a maximum T_I , use a special algorithm, and/or switch to a pressure-controlled mode in which expiratory cycling is time-dependent (Fig. 6).⁶² The option to set the expiratory cycling in the "auto function" on some ventilators optimizes the end of the inspiration breath-by-breath with a special algorithm designed to minimize air-leak-induced asynchrony.^{16,17} This is the case with the AutoTrack system in the Respiration BiPAP Vision, which aims to optimize patient-ventilator synchrony breath-by-breath, independently of the presence of air leaks (Table 5).

Table 5. Algorithm of the Auto-Track System in the BiPAP Vision Ventilator

“Enhanced leak estimation” identifies the leak by comparing the original baseline flow to the new baseline flow, and uses complex digital signal processing to recognize the differences as leaks and to quickly adjust.
“Volume trigger” feature triggers IPAP during spontaneous breathing in the spontaneous/timed mode. When patient effort generates inspiratory flow and causes 6 mL of volume to accumulate above the baseline leak, IPAP is triggered.
“Flow reversal”, “shape trigger”, and “spontaneous expiratory threshold” recognize an abnormal increase in flow due to a leak during the latter part of inspiration with an immediate return to EPAP, keeping a good synchronization with the patient’s breathing effort.

IPAP = inspiratory positive airway pressure
EPAP = expiratory positive airway pressure

On some newer bi-level, intermediate, and ICU ventilators it is possible to set the expiratory cycling threshold and to view the respiratory-mechanics waveforms, which may help the clinician optimize patient-ventilator synchrony and comfort, and possibly achieve NIV success. However, the cycling thresholds may be different and are not always comparable among the different ventilators.^{29,63} As with inspiratory triggering, the cycling behavior of different ventilators differs in a lung model, and there is marked heterogeneity with a given ventilator in response to various conditions of respiratory mechanics and air leak.^{30-35,37,41,42}

Figure 7 shows the differences between 2 new ICU ventilators.³¹ Generally speaking, most of the bi-level ventilators cycle at a higher fraction of inspiratory flow than do most of the ICU ventilators, to avoid deleterious mask-leak-induced prolongation of T_I . As a matter of a fact, newer bi-level ventilators tend to prematurely cycle to expiration if the respiratory mechanics are normal, and this tendency is increased by restrictive conditions. Conversely, in obstructive conditions most of the bi-level ventilators are less likely to have a delayed cycling, which may be facilitated by air leaks. Consequently, at the default setting, bi-level ventilators seem to be better adapted to supporting patients with obstructed respiratory mechanics.³⁷ Unlike bi-level ventilators, in the absence of leak and at the default setting, newer ICU ventilators have some delay in cycling to expiration, which is worsened by obstructive conditions, whereas restrictive mechanics lead to premature cycling.³² The addition of leak increases the cycling delay in normal and obstructive conditions and partially corrects premature cycling in restrictive conditions. Expiratory cycling dyssynchrony can be prevented by using “NIV modes” in normal or obstructive mechanics.

Inspiratory Flow

Severely dyspneic patients with COPD cope better with higher inspiratory flow, whereas patients with neuromuscular diseases do better with lower inspiratory flow (pressure-rise times of 0.05–0.1 s and 0.3–0.4 s, respectively).^{17,18} In most of the bi-level ventilators the rise time is unchangeable, whereas in more advanced bi-level ventilators and most intermediate and ICU ventilators the rise time can be set, which may profoundly affect inspiratory triggering.³¹ A recent physiological study⁶⁴ of rise time (range 30–200 cm H₂O/s) in 15 patients with COPD recovering from episodes of hypercapnic ARF that required NIV found that the highest pressurization rate was associated with greater air leak and poorer NIV tolerance, even though the diaphragmatic effort was more reduced than with lower pressurization speeds, without significant differences in blood gas values or breathing pattern. Patient comfort was not different at the lower pressurization speed, so Prinianakis et al suggested that the individual titration should aim for good tolerance and minimal air leaks, keeping a relatively high pressurization rate.⁶⁴

Backup Respiratory Rate

Some bi-level ventilators do not have the option of setting a back-up respiratory rate, which therefore lowers the costs.¹⁷ Conversely, most newer bi-level ventilators and all intermediate and ICU ventilators have an adjustable back-up respiratory rate, which is particularly advantageous in sicker patients who have respiratory-drive instability, because the back-up rate prevents apneas and periodic breathing (ie, Cheyne-Stokes respiration) in chronic heart failure. The back-up respiratory rate may also be useful when a cautious sedation is administered to improve patient compliance with NIV.⁶⁵

Air-Leak Compensation

Because of the used interface, air leak is almost constant during NIV, especially in acutely ill patients, and leak may decrease patient comfort, patient-ventilator synchrony, and the likelihood of success.¹⁵⁻¹⁷ “Unintended” leaks may occur though the mouth during nasal ventilation and/or between the skin and the mask, but the attempt to tightly fit the mask to try to reduce leak is not recommended, because discomfort from the tight mask might reduce the patient’s tolerance and lead to skin damage. Because some leak is unavoidable, it’s important to use a ventilator that can adequately compensate for the leaks. Air-leak compensation is better with bi-level than with volume-targeted home ventilators; the V_T decrease can be $> 50\%$ with volume-targeted home ventilators (Fig. 8).²² Conversely, with bi-level ventilators leaks decrease $V_T < 10\%$, and

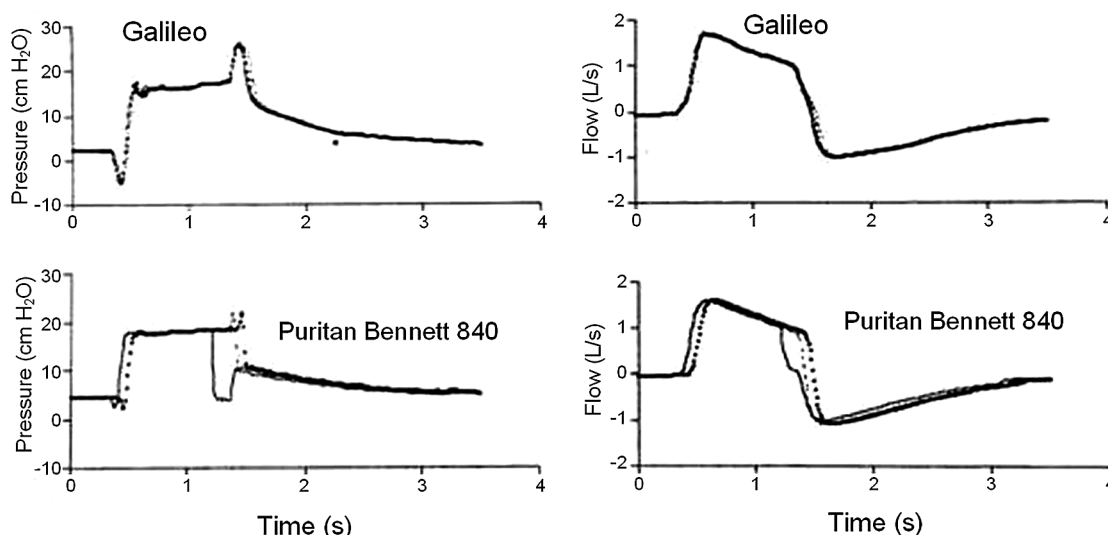


Fig. 7. Pressure-time (left column) and flow-time (right column) waveforms from the Hamilton Galileo and Nellcor Puritan Bennett 840 ventilators with the minimum (solid line), medium (dotted line) and maximum (dashed line) inspiration-termination (cycle threshold) criteria. (From Reference 31.)

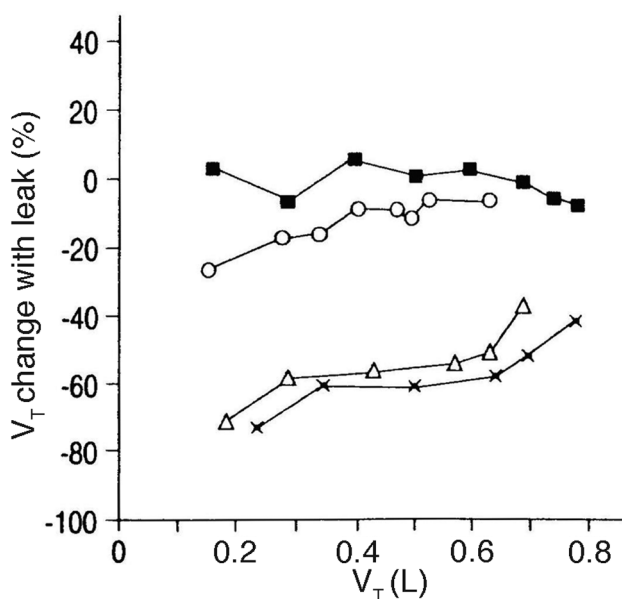


Fig. 8. Effect of an additional leak on the tidal volume (V_T) delivered by 4 home ventilators tested with a lung model. The relationship between the percentage changes in V_T with leak opened and the V_T delivered in absence of leak showed that pressure-targeted home ventilators (BiPAP [■], Nippy [○]) adequately compensated for leak, whereas volume-targeted home ventilators (Monnal D [△], Companion 2801 [X]) did not. (Adapted from Reference 22.)

IPAP < 8%, because bi-level ventilators adequately increase the inspiratory flow and T_I .²³ Volume-targeted ventilation modes are less able to compensate for leaks, because inspiratory flow and T_I either could not be increased or could only be slightly increased. Setting a larger V_T

does not significantly improve V_T , especially with a large leak.⁴³

However, the effects of air leak during NIV are more complex than simply a decrease in IPAP and V_T , because of other variables such as T_I , expiratory cycling, and inspiratory trigger sensitivity, as shown by Mehta et al³⁶ in their bench study. Even though all the studied bi-level ventilators were able to compensate for air leaks, their performance was not uniform. The Respironics BiPAP in “S/T” mode, which does not allow setting the duty cycle, had the greatest proportional drop in the delivered V_T due to leak-induced delayed expiratory cycling. Conversely, bi-level ventilators with adjustable T_I compensated better for small and large leaks. Mehta et al³⁶ also found that leak compensation, especially with a large leak, was impaired by a too-sensitive trigger, with all bi-level ventilators except one (Puritan Bennett 335) because of the auto-triggering-induced decrease in the delivered V_T . Finally, an increase in respiratory-system impedance negatively affected the leak compensation with all bi-level ventilators.³⁶

Mathematical models of the complex interaction between air leaks and PSV in obstructive conditions and their potential clinical implications^{41,64} suggested that the leak-compensation capabilities of most of the intermediate and newer ICU ventilators with “NIV modes” are good at improving patient-ventilator synchrony with a large mask leak.^{32,42}

Battery

With an acutely ill patient who has a high level of dependence on NIV, a battery power source is mandatory,

in case of electricity-supply failure or the need to transport the patient.¹⁷ Lack of an internal battery makes most of the older bi-level ventilators unsuitable and unsafe for transporting critically ill patients. If a patient with ARF who starts NIV in the emergency department needs to be transported for imaging or to another environment (eg, ICU, respiratory high-dependence unit, ward),^{42,66,67} an internal battery is an advantage. However, be aware that battery duration differs greatly among portable ventilators and may be shorter than that reported in the operator's manual. Moreover, portable ventilator battery duration is affected by the setting, the lung impedance characteristics, and the ventilator features. This was clearly shown in a recent study⁶⁸ of the effects of ventilation mode (pressure-controlled vs volume-controlled), PEEP, and F_{IO_2} on battery duration in 8 intermediate ventilators. The pneumatically driven ventilators had a longer duration than the electrically driven ventilators. The battery duration of the pneumatically driven ventilators was minimally affected by the ventilator settings, but with the electrically driven ventilators the duration was shortened by pressure-controlled ventilation, higher PEEP, and higher F_{IO_2} . Fortunately, in that study the low-battery alarms functioned properly with all the studied ventilators.

An external battery is an alternative (or addition) to an internal battery to guarantee longer ventilator autonomy in case of institutional electricity failure. However, an external battery may make the ventilator too heavy for transport.¹⁶⁻¹⁸

Alarm and Monitoring System

The need for sophisticated alarms and monitoring system during NIV is essentially based on clinical practice, because, to our knowledge there is no scientific evidence of their clinical utility. The prototype of the Respironics BiPAP did not have alarms or monitoring features,²⁷ which gave it an advantage in cost and transportability. In the acute-care setting, the availability of sophisticated alarms (eg, low and high pressure, V_T , respiratory rate, F_{IO_2} , leak) and monitoring (flow, V_T , and pressure curves) in the newer bi-level, intermediate, and ICU ventilators may improve safety and patient-ventilator interaction.^{16,17} In a recent Spanish multicenter quality-control study²⁶ with 300 home mechanically ventilated patients, the alarms for power-off, disconnection, and obstruction did not work when subjected to an effective test in 0.9%, 18.6%, and 5.1% of the tested ventilators, respectively. On the other hand, too-elaborate alarms may be counterproductive in clinical practice because they frequently indicate very minor leaks that are common during NIV.

The key variable to monitor is the expiratory V_T , because excessive air leak may cause a significant discrepancy between the inspiratory and expiratory V_T .¹⁶⁻¹⁸ Sin-

gle-limb-circuit bi-level ventilators allow monitoring of only the inspiratory V_T , which corresponds to the sum of the patient's V_T and the air leaks. The inspiratory V_T increases from leak compensation, so it doesn't directly reflect the patient's \dot{V}_E . Moreover, the expiratory V_T estimated by some bi-level ventilators has not been validated.^{16,17} Dual-limb-circuit bi-level ventilators (and most of the intermediate and all the ICU ventilators) allow close monitoring of the expiratory V_T , the measurement of which is more reliable at the expiratory branch of the Y-piece than at the inlet of the expiratory tube into the ventilator.^{9,17}

Ventilation Mode

Although NIV has been successfully applied in volume-controlled, pressure-controlled, and PSV modes, PSV has been used most commonly in randomized controlled trials. With bi-level ventilators, again, PSV has been most commonly used.^{1-4,69} Conversely, there is a lack of evidence about synchronized intermittent mandatory ventilation or volume-assured pressure-support modes⁷⁰ during NIV. In a clinical study of hypercapnic ARF due to COPD exacerbation, Vitacca et al⁷¹ found no outcome differences between NIV in a volume-controlled mode versus NIV in PSV, though the PSV was better tolerated. In a subsequent study with 12 patients with COPD in acute decompensation, Meecham-Jones et al⁷² found no significant difference in P_{aO_2} improvement if NIV was delivered with volume-controlled ventilation versus PSV. Girault et al⁷³ randomized 15 patients with COPD exacerbation to nasal NIV in volume-controlled ventilation or PSV. Both modes markedly improved WOB, breathing pattern, and gas exchange (compared to unsupported spontaneous breathing); WOB was kept lower, but at the cost of higher patient discomfort and less ability to compensate for mask leaks in volume-controlled ventilation than in PSV.

With bi-level ventilators, PEEP is an important option during NIV in ARF. If adequately set, PEEP counterbalances the intrinsic PEEP in COPD exacerbation, which reduces WOB, compared to only PSV.¹⁶⁻¹⁹ Applied PEEP also reduces CO_2 rebreathing with single-limb circuits, prevents upper-airway collapse in obstructive sleep apnea, and recruits poorly ventilated and nonventilated lung units in hypoxemia.^{1,2,16,17} With applied PEEP the bi-level ventilator settings depend on whether the ventilator works with an algorithm over or under PEEP: with the former it is possible to set the pressure support without taking into account the PEEP level; in the latter the clinician has to set the inspiratory pressure at a value that is the sum of the chosen pressure support plus the PEEP.^{17,18}

Some newer bi-level ventilators (eg, Respironics BiPAP Vision) offer the option of proportional-assist ventilation, which aims to enhance patient-ventilator synchrony.⁷⁴ Un-

like PSV, which uses a preset inspiratory pressure, proportional-assist ventilation provides inspiratory flow and pressure in proportion to the patient's instantaneous breathing effort. Cycling to expiration is not flow-dependent in the same fashion as PSV; rather, proportional-assist ventilation terminates the assistance with the cessation of patient effort. Short-term application of NIV proportional-assist ventilation improved \dot{V}_E and blood gas values, unloaded respiratory muscles, and was well-tolerated in patients with COPD and hypercapnic ARF.⁷⁵ In a randomized crossover study, Wysocki et al⁷⁶ found that, despite a similar improvement in WOB and blood gases, the comfort and the V_T variability were significantly greater with the Respironics BiPAP Vision with proportional-assist ventilation than with PSV in 12 patients with COPD and hypercapnic ARF. Concerning clinical outcomes, Patrick et al⁷⁷ reported that NIV proportional-assist ventilation avoided intubation in 8 of 11 patients with de novo ARF. Subsequently, Gay et al⁷⁸ randomized 44 patients in ARF of various etiologies to receive NIV with either proportional-assist ventilation from the Respironics BiPAP Vision or PSV from the Nellcor Puritan Bennett 7200. The mortality and intubation rates were similar, but proportional-assist ventilation had a lower refusal rate, a faster respiratory-rate reduction, and fewer complications.

Interface

The NIV interfaces currently available are nasal mask, oronasal mask (which covers only the nose and mouth), total-face mask (which covers the entire face), nasal pillows, mouth-piece, and helmet. The impact of the interface on the performance of the ventilator depends on several factors, including air leak, rebreathing, dynamic total dead space, and comfort. Nasal and oronasal masks have been successfully applied to deliver NIV from bi-level and ICU ventilators.¹⁻⁷ In a randomized controlled trial by Kwok et al⁷⁹ with 70 patients in ARF, the nasal and oronasal masks they studied performed similarly in improving gas exchange and avoiding intubation, though the oronasal mask was better tolerated. Nasal masks allow large mouth air leaks and encounter greater resistive load, which may limit their efficacy, compared to oronasal masks, especially if the ventilator is poorly able to compensate for leaks or to respond to high ventilatory demand.^{80,81} However, in acutely ill patients, NIV failure with oronasal mask has been reported because of discomfort and large air leaks.^{2-4,14}

A new kind of interface, the total-face mask, is supposed to increase adherence to NIV in patients who have poor adherence to nasal or oronasal mask.^{82,83} Although it covers the entire face, the feeling of claustrophobia is lessened, probably because of an unobstructed field of vision, the ability to verbally communicate, and the sen-

sation of air flowing over the entire face. Clinical findings in patients in ARF^{79,83} suggest that the greater dead space with the total-face mask (vs the oronasal mask) and with the oronasal mask (vs the nasal mask)^{57,82} is not a disadvantage.

This unexpected finding might be explained by a recent elegant lung-model study, in which Saatci et al⁸⁴ evaluated the influence of different mask designs (18 oronasal and one total-face mask) and different NIV modes delivered by 5 single-limb-circuit bi-level ventilators on the total dynamic dead space, defined as the sum of physiologic dead space plus apparatus dead space. Surprisingly, Saatci et al found a poor relationship between the static volume within the masks and their respective dead space (Fig. 9A), probably because of the streaming effect of gas through the mask. When using ventilators, the differences between the face masks were accentuated and the dynamic dead space decreased in all of them, depending on the ventilation mode and the interface. Bilevel and CPAP modes were more effective in decreasing the dynamic dead space than was PSV or pressure-controlled ventilation without PEEP, because positive pressure was applied throughout the expiratory phase in bilevel and CPAP modes (see Fig. 9B). There was no important difference in dead space between bi-level and CPAP modes or among the different bi-level ventilators. Concerning the interfaces, face masks that had the expiratory port over the nasal bridge showed beneficial flow characteristics within the face mask and nasal cavity, resulting in lower dead space, but only if used in combination with NIV modes that employed positive pressure throughout the expiratory phase (see Fig. 9C).⁸⁴ This may have clinical implications, because of the amount of CO₂ rebreathing and the WOB reduction with the application of single-limb-circuit bi-level ventilators with different interfaces and different NIV modes.

A relatively new NIV interface, the helmet, has potential advantages, including wider patient-environment interaction, no risk of facial skin damage from the mask, and applicability regardless of the patient's facial contours,⁴ particularly in hypoxemic patients⁸⁵ in whom NIV complications (skin necrosis, gastric distention, eye irritation) are less common than with the oronasal mask, despite a similar rate of success, hospital stay, and oxygenation improvement. However, one of the major concerns about the helmet is the risk of rebreathing, because of its large inner volume, compared to the face mask, as was recently demonstrated in exacerbations of hypercapnic COPD.⁸⁶ This may be more evident with single-limb-circuit bi-level ventilators, which do not have efficient exhalation systems. Moreover, the helmet may also interfere with inspiratory triggering, expiratory cycling, and patient-ventilator interaction, because of the compressible volume within the circuit.⁸⁷⁻⁹⁰ The helmet requires careful clinical monitoring and setting by an expert team, who should use an

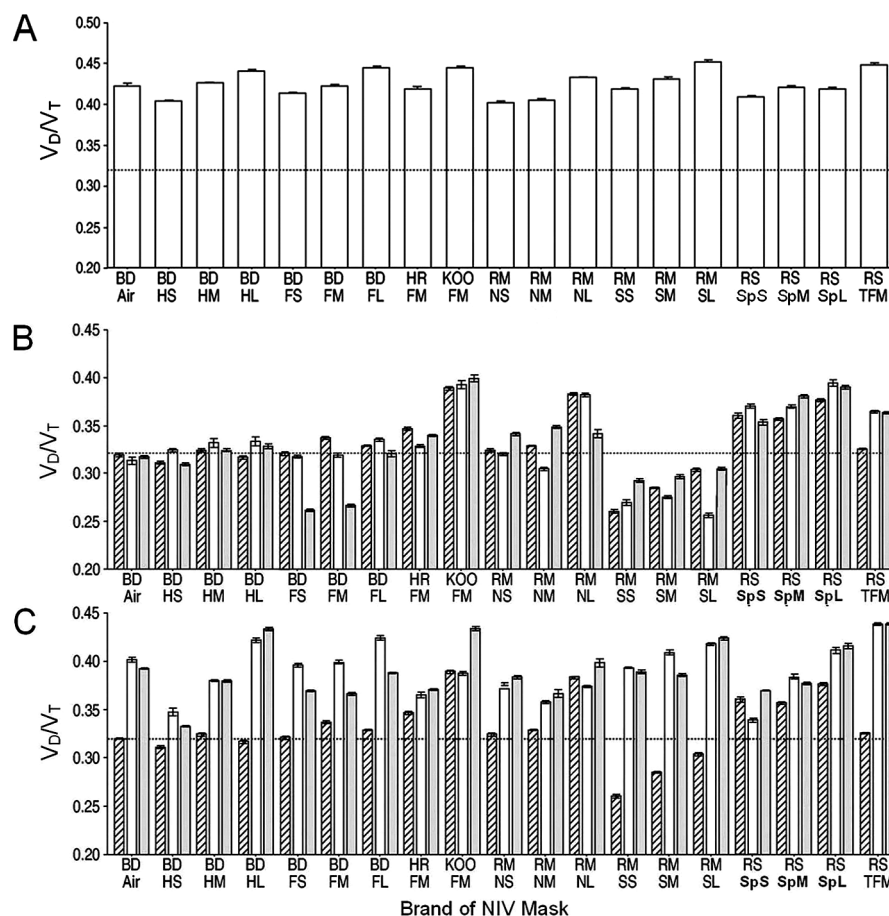


Fig. 9. **A:** Total dynamic dead space (ratio of dead space [V_D] to tidal volume [V_T]) of various face masks during spontaneous breathing. **B:** Total dynamic dead space with various face mask and 3 types of noninvasive ventilation: bi-level ventilation from the Respironics BiPAP S/T (striped bars), pressure-support ventilation from the Breathe 401 (white bars), and pressure-controlled ventilation from the Nippy 1 (light gray bars). **C:** Total dynamic dead space of various face masks during bi-level ventilation with the Respironics BiPAP S/T (striped bars), the Puritan Bennett Knightstar 335 Bilevel (white bars), and the ResMed Sullivan VPAP S/T (light gray bars).

Mask manufacturers: BD Air: B&D Electromedical, Aircraft (size medium). BD HS, HM and HL: B&D Electromedical, Hebden (size small, medium and large). BD FS, FM and FL: B&D Electromedical, Fleximask (size small, medium and large). HR FM: Hans Rudolph, Full face mask. KOO FM: Koo, Full face mask system. RM NS, NM and NL: ResMed, Mirage NV full face mask (size small, medium and large). RM SS, SM and SL: ResMed Full, face series 2 (size small, medium and large). RS SpS, SpM and SpL: Respironics, Spectrum (size small, medium and large). RS TFM: Respironics, Total face mask. (Adapted from Reference 84.)

advanced bi-level or ICU ventilator that provides fine-tuning of the inspiratory trigger and expiratory cycling, and monitoring of flow and pressure waves. The helmet is not approved in some countries, including the United States.

Another NIV interface is the mouth-piece, which is less popular, especially in ARF, because it is less well tolerated than face mask.⁹¹

Clinical Applications of NIV Ventilators in Acute Respiratory Failure

NIV has been successfully applied outside the ICU to treat ARF, mostly due to cardiogenic pulmonary edema and COPD exacerbation. The impact of the wide hetero-

geneous performance of the different categories of ventilators for NIV on the clinical outcomes of acutely ill patients is largely unknown. In delivering NIV, most of the newer-generation bi-level and ICU ventilators seem to have important technological advantages over older-generation ventilators. Because of their potential advantages (Table 6), bi-level ventilators are at least as reliable as ICU ventilators in delivering NIV in different acute settings.^{33,34,43-47} Accordingly, in most of the randomized controlled trials^{13,92-107} and in one “real world” investigation¹⁰⁸ performed outside the ICU, bi-level ventilators have successfully applied NIV. Since their performance substantially differs among the wide range of categories, the choice of ventilator and equipment (interface, circuit, expiratory

Table 6. Advantages of Bi-Level Home Ventilators for Noninvasive Ventilation Outside the Intensive Care Unit

Easy handling
Easy transportable
Light and not cumbersome
Good air-leak compensation
Internal battery
Low-pressure oxygen source
High technical performance
Less expensive

valve, humidification, and mode) should be tailored to the etiology, the severity, and the pathophysiology of the acute disorder.

Concerning the type of air supply, in a turbine-driven bi-level ventilator the lack of a high-pressure gas source may mean there is no guarantee of stable pressurization, particularly at a higher level of the ventilator's performance, though the clinical importance of this is not clear.^{16,17} When O₂ enrichment is needed during NIV with a bi-level ventilator that does not have a blender, the O₂ concentration is unstable and depends on a complex interaction of several factors: a high O₂ flow into the mask and a leak port in the circuit are the best option to achieve higher F_{IO₂}.⁵¹⁻⁵³ In these circumstances we strongly suggest the use of pulse oximetry to continuously monitor oxygenation and to titrate the O₂ flow.^{4,16-19} If the patient is severely hypoxemic, we highly recommend a ventilator that has an O₂ blender (ie, an ICU or newer bi-level ventilator).^{4,16-19}

When using a bi-level ventilator with a single-limb-circuit on a hypercapnic patient in ARF, a low-resistance valve and adequate PEEP lower the risk of CO₂ rebreathing.^{46,54,56} A dual-limb circuit prevents rebreathing and maximizes the chance of reversing severe acute hypercapnia.¹⁶⁻¹⁹ Moreover, in this clinical scenario the oronasal mask should be preferred to the helmet, because the oronasal mask has greater efficiency in lowering the P_{aCO₂}.⁵⁷

Clinicians should be aware of how the various interfaces, exhalation systems, pressure settings, and humidification devices interfere with the performance of the different categories of ventilators. With the latest generation of ventilators, the ability to set various parameters (inspiratory trigger sensitivity, expiratory cycling, rise time, T_I, NIV modes) and observe the flow, volume, and pressure waveforms and numeric monitoring display may help lower WOB and improve synchrony, comfort, and outcomes. The leak-compensation capabilities of modern bi-level ventilators are surely clinically preferred to volume-targeted home ventilators.^{22,23,43} Moreover, newer intermediate and ICU ventilators working in "NIV modes" show good performance in compensating for large air leaks.^{32,42} Again, in case of substantial leaks, the ability to

adjust trigger sensitivity, inspiratory flow, T_I, and expiratory cycling may help support unstable patients in ARF by optimizing leak compensation and patient-ventilator synchrony.^{36,41,64}

The clinician should use special care if the patient needs humidification during NIV. Heated humidifiers have great clinical and physiological advantages, compared to heat-and-moisture exchangers (HMEs), even though a heated humidifier is more time-consuming.^{109,110} When using a heated humidifier with a single-limb-circuit, the clinician should consider the risk of ventilator malfunction from the possibility of a water recoil into the circuit and into the expiratory valve.^{16,17}

We do not have clear scientific evidence of clinical advantage for specific NIV modes in ARF, even though bi-level-positive pressure modes are better-tolerated.⁶⁹ Despite the positive physiologic effects of proportional-assist ventilation, its wide "acute" use in NIV clinical practice is still prevented by the need of great expertise to correctly set the support level. The choice of interface may affect ventilator performance and the clinical outcome of NIV, so special attention should be given to the potential effects of the interface on rebreathing, unintended leaks, triggering, and patient comfort.⁸⁴

Crucial is the problem of transporting highly ventilator-dependent critically ill patients; we strongly recommend a bi-level or intermediate ventilator that has an internal or external battery power source.

In selected cases, patient comfort during NIV, patient-ventilator synchrony, and, consequently, the chance of NIV success may be improved by sedation when managed by teams with great expertise. Although sedation can play an important role in NIV, the risk of oversedation and causing the need for intubation has prevented the widespread use of sedation in clinical practice, as shown in a recent multicenter survey.⁶⁵

In the absence of strong evidence of advantage with a specific ventilator, the choice of ventilator in ARF should also take into account the costs and the team's experience with the ventilator.^{1-4,16,17} Bear in mind that the more sophisticated the ventilator, the longer the operator training required. Because of the tremendous and continuing growth and complexity of the home ventilator market, a recent study¹¹¹ found that 11 new home ventilators were not user-friendly, even for trained ICU physicians and respiratory therapists without practical experience in home mechanical ventilation. ICU clinicians were slower than the technicians to unlock the ventilator and change the ventilation mode; some of the physicians completely failed the tests. Mistakes occurred in close to 50% of the tests of implementing the ventilation mode and recognizing the settings. The mean time for the most rapid of the clinicians in all the tests was almost 4-fold greater than that of the technician.

In light of that study, we suspect that the smaller the variety of NIV ventilators (and related devices) in everyday practice, the greater the likelihood that all the team members will get enough experience to rapidly set up and adjust NIV, which could lower costs and work load. We recommend continuous and accurate training with newer devices and interfaces to optimize clinician knowledge about the technological aspects of NIV. In an Italian respiratory ICU, increased experience with NIV applied to treat ARF significantly improved outcomes and allowed the team to manage more severely ill patients with the same rate of clinical success as that obtained previously.¹¹²

Humidification and Aerosol Delivery With NIV Ventilators

Humidification during NIV for ARF is still controversial. Unlike in invasive mechanical ventilation, the upper airway is not bypassed with NIV. With a bi-level ventilator much of the delivered gas (except the O₂) comes from the ambient air and thus has the same humidity that the patient would receive breathing without NIV.^{4,17} Although pharyngeal and nasal dryness and thickness of secretions are common during NIV, only one case of life-threatening inspissated secretions has been reported.¹¹³ Richards et al⁸¹ found that mouth leaks with nasal CPAP caused a large increase in nasal resistance, which was mostly prevented by humidifying the inspired air. Martins de Araújo et al¹¹⁴ reported that a heated humidifier significantly reduced inhaled air dryness during CPAP. We suspect the findings would be similar with NIV.

The 2 options for humidification during NIV are heated humidifier and HME. In a randomized, crossover study, Lellouche et al¹⁰⁹ compared heated humidifier to HME in 9 patients on NIV for ARF. Despite a similar P_{aCO₂}, HME was associated with significantly higher \dot{V}_E and WOB. In a similar crossover study with 24 patients in ARF, Jaber et al¹¹⁰ found that \dot{V}_E and P_{aCO₂} were significantly greater with HME than with heated humidifier, because the HME added dead space, which interfered with patient-ventilator synchrony.

During mechanical ventilation in intubated patients with COPD, inhaled bronchodilator can unload respiratory muscle by reducing airway resistance and intrinsic PEEP.^{115,116} Inhaled β_2 agonists and anticholinergics can be administered during mechanical ventilation via nebulizer or metered-dose inhaler (MDI) with spacer, placed in-line between the circuit and the interface. In an intubated mechanically ventilated patient, synchronizing the nebulization with the inspiration more effectively delivers the drug to the lower airways than does nebulization performed throughout the respiratory cycle.¹¹⁵ Similarly, synchronizing MDI actuation with the patient's inspiration greatly increases lower-airway deposition during invasive venti-

lation.^{115,116} Both MDIs and nebulizers can deliver similar doses of drug and produce similar therapeutic benefits during different modes of invasive mechanical ventilation. However, nebulizers are more problematic because of the risk of bacterial contamination, the need to adjust the V_T and inspiratory flow, and efficiency differences among the various devices. Conversely, MDI/spacer aerosol administration to an intubated patient is easier, less time-consuming, and less costly than nebulization, and MDI/spacer does not require adjusting ventilator settings for a set $V_T \geq 400$ mL.

Heated humidification is needed during invasive ventilation to prevent drying of airway mucus, but circuit humidification decreases lower-respiratory-tract aerosol delivery (from MDI or nebulizer) by $\geq 40\%$, compared to aerosol delivery through a non-humidified circuit.^{117,118} Circuit humidity enlarges nebulizer aerosol droplets. With MDI aerosol droplets humidity may interfere with propellant evaporation, so the aerosol droplets remain larger, which increases aerosol-loss from impaction on the walls of the spacer and airways.¹¹⁸ Moreover, the density of the inhaled gas influences lung deposition: an 80% helium 20% oxygen mixture (80/20 heliox) increased albuterol delivery 50% during invasive mechanical ventilation, compared to the conventional air-oxygen mixture.¹¹⁷

The evidence about aerosol delivery during invasive ventilation has been described in some detail, but this is not the case for NIV.¹¹⁵⁻¹¹⁷ Several issues are still not resolved. The characteristics of the ventilator seem to have a crucial influence on the effects of aerosol therapy during NIV. If NIV is delivered with a dual-limb circuit, the nebulizer or MDI is placed in the inspiratory limb, as with intubated patients. One might think that the findings on aerosol delivered to invasively ventilated patients would apply to NIV provided with a dual-limb circuit, but though that expectation seems reasonable, it has not been systematically demonstrated.

Most of the few available in vitro and in vivo studies on NIV aerosol delivery were performed with single-limb-circuit ventilators. In a bench study, Chatmongkolchart et al¹¹⁹ found that nebulized albuterol during NIV with the Respironics BiPAP ST-D30 ranged from 5.2% to 24.5% of the nominal dose and was significantly affected by the position of the nebulizer, respiratory rate, and BiPAP settings, but not by the nebulizer flow. Albuterol delivery was greater with the nebulizer at the distal position (between the leak port of the circuit and the interface) than at the proximal position (ventilator outlet), at a higher respiratory rate (20 breaths/min vs 10 breaths/min) and at higher IPAP and lower EPAP (Fig. 10).

More recently, in a similar experimental setting, Bracconnier and Hess¹²⁰ evaluated whether albuterol delivery during NIV with the Respironics BiPAP ST30 was affected by the use of a nebulizer or an MDI/spacer, and by

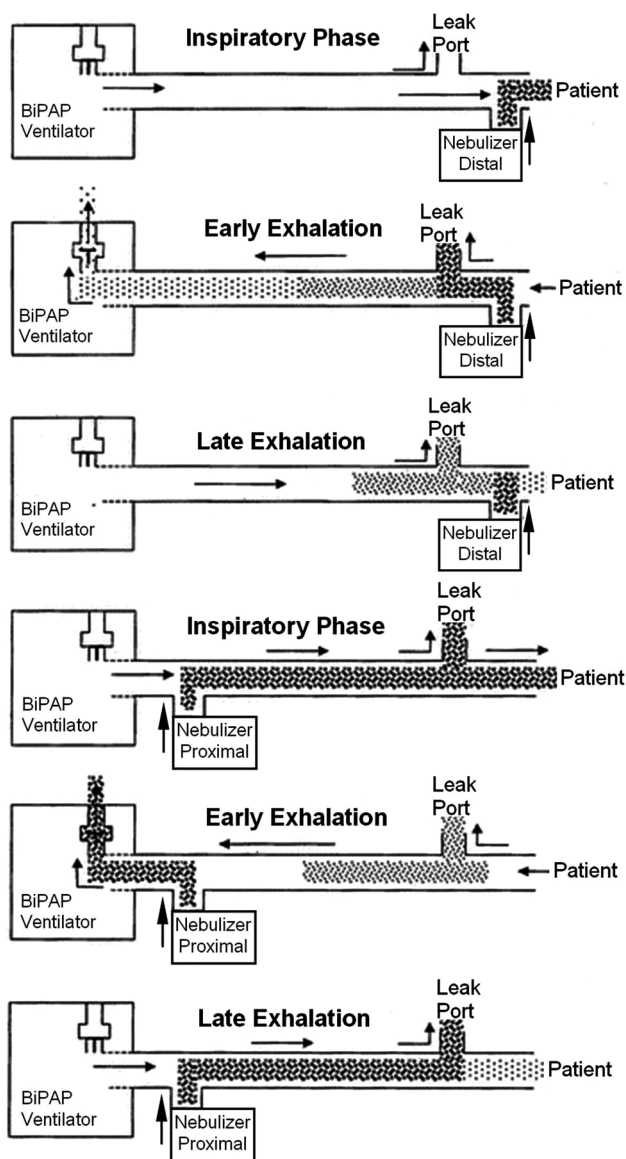


Fig. 10. Effect of nebulizer location in a single-limb bi-level circuit ventilator. When the nebulizer is located distal (nearest the patient): during inspiration the aerosol travels through less circuit than when the nebulizer is located proximal (closer to the ventilator); during early exhalation aerosol is lost primarily through the leak port, but some aerosol is blown retrograde into the circuit; and during late exhalation some aerosol is blown toward the patient by the ventilator. With the nebulizer proximal to the ventilator: during the inspiratory phase some aerosol is lost through the leak port; during early exhalation the expiratory flow dilutes the aerosol in the circuit and blows some aerosol toward the ventilator; and during late exhalation aerosol is delivered into the circuit and is lost through the leak port. (Adapted from Reference 119.)

the location of the leak port. With the nebulizer a significantly greater amount of albuterol was delivered to the lung model when the leak port was in the circuit than in the mask (Spectrum vs Mirage mask, respectively) and when the nebulizer was used in place of MDI, with both

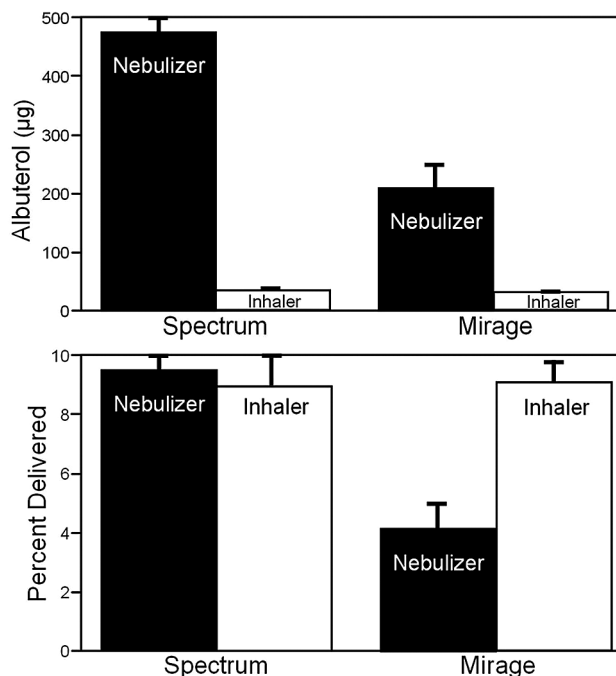


Fig. 11. Albuterol delivered via nebulizer versus metered-dose inhaler, via the Spectrum mask and Mirage mask. With the Spectrum mask the leak port is in the circuit, whereas Mirage has the leak port in the mask. (Adapted from Reference 120.)

masks (Fig. 11). However, the efficiency of albuterol delivery was similar with nebulizer and MDI with the leak port in the circuit, even if it was greater with MDI when the leak port was within the mask. These findings may be explained by the fact that MDI delivers aerosol only during inhalation, whereas the nebulizer delivers aerosol throughout the respiratory cycle, which allows loss of albuterol through the leak port during exhalation.

There are very limited data on aerosol delivery in clinical investigations. Pollack et al¹²¹ conducted a short-term randomized controlled trial in an emergency department to determine whether inhaled albuterol was more effective in treating acute bronchospasm during nasal or oronasal NIV (with the Respironics BiPAP). The aerosol was from a nebulizer placed between the interface and the leak port ($n = 60$), compared to spontaneous breathing through a small-volume nebulizer ($n = 40$). The 2 treatment groups experienced similar changes in blood oxygen saturation (measured via pulse oximetry), heart rate, and respiratory rate after each treatment of 20 min at 2 doses of inhaled albuterol, whereas the NIV patients had a significantly greater increase in peak expiratory flow than the spontaneously breathing patients.

Fauroux et al¹²² evaluated radioaerosol deposition with NIV PSV delivered with a bi-level ventilator (Mallinckrodt Onyx) to the lungs of 18 children with stable cystic fibrosis. Aerosol deposition quantity and efficacy were

significantly greater after the NIV session than after the control session, without any differences in the regional deposition pattern or homogeneity of uptake.

In a randomized controlled trial with 18 patients with stable severe COPD, Nava et al¹²³ found that, compared to placebo, albuterol significantly improved forced expiratory volume in the first second, whether delivered via MDI during oronasal NIV in volume-assured pressure-support mode or via MDI/spacer during spontaneous breathing. França et al¹²⁴ compared the pulmonary radioaerosol deposition with jet nebulization in 13 healthy volunteers during spontaneous breathing versus oronasal NIV with the Respironics BiPAP. The position of the nebulizer in relation to the leak port was not specified. Radioaerosol lung deposition was almost 50% lower with nebulization during NIV than during spontaneous breathing. The clinical impact of the findings of that study are unclear, given that the subjects were young and had normal lung function and were therefore unlikely to need NIV. A potential message from that negative study may be that the dose has to be increased when administering aerosol during NIV.

There is presently no commercial system designed specifically for aerosol delivery during NIV with a bi-level ventilator. The peculiarities of bi-level ventilators may greatly influence the efficiency of aerosol delivery during NIV. The continuous flow through the single-limb-circuit of less sophisticated bi-level ventilators may cause a substantial loss of aerosol through the leak port, which is increased by mask leak-induced higher inspiratory flow. Aerosol loss may also occur through the mask leak itself.¹¹⁷ Flow through the circuit is also increased, and so does aerosol loss during NIV with bi-level ventilators set at higher IPAP and EPAP levels, as well as when the O₂ is titrated into the circuit. Ideally, to enhance the aerosol delivery during NIV, the MDI or nebulizer should be placed between the leak port of the circuit and the mask, and the aerosol administration should be synchronized with the inspiration.

Masks used for NIV are not likely to achieve efficient lung penetration of the nominal dose, because much of the aerosol may impact the face, or worse, the eyes. Cases of anisocoria have been reported in patients on NIV who received nebulized albuterol and ipratropium via a poorly fitting oronasal mask.¹²⁵ For this reason the total-face mask and the helmet should not be used for aerosol delivery, although this disadvantage has yet to be clearly demonstrated. With an oronasal mask, breathing through the nose reduces the penetration of aerosol to the lungs because a great deal of the aerosol is lost to the nasal cavities, so a nose clip may improve aerosol delivery with oronasal mask. The literature on aerosol delivery during NIV is limited to β_2 agonists; to our knowledge, other inhaled drugs have not been tested.

Heliox With NIV Ventilators

Heliox (70–80% helium and 20–30% oxygen) has a lower density than air or oxygen, so it has lower gas turbulence during flow, which improves flow through narrowed airways (as in COPD) during spontaneous breathing or mechanical ventilation.^{126,127} However, 2 recent meta-analyses^{128,129} concluded that there is no definitive evidence of benefit from heliox in spontaneously breathing patients with severe COPD, so heliox is not recommended for everyday practice. In intubated and mechanically ventilated patients with COPD, heliox significantly decreases WOB (mainly by reducing intrinsic PEEP and resistive load) and enhances ventilator-patient synchrony by reducing wasted inspiratory efforts, though there is some inter-case variability.^{130–133} Similarly, in severe exacerbations of COPD, heliox via NIV significantly unloads the respiratory muscles and improves P_{aCO₂}, though heliox does not seem to provide a clear advantage in intubation rate or ICU stay, compared to ventilation without heliox.^{134–136}

Despite the promising findings about heliox during NIV in severe COPD exacerbations, the use of heliox is hampered by lack of wide availability of an approved heliox-delivery system.¹²⁶ The commonly used ventilators are calibrated to operate with gas mixtures that contain only air and oxygen, and some investigations with ICU ventilators found that helium's lower density and higher thermal conductivity can adversely affect ventilator performance and monitoring.^{137–139} Tassaux et al¹³⁷ used a lung model to evaluate 7 ICU ventilators with heliox, to develop correction factors for the safe use of heliox. They found some discrepancy between the set and the delivered F_{IO₂} with heliox, which varied both between the ventilators and as a function of the set F_{IO₂}. In a volume-controlled mode there was a significant difference between the delivered V_T and both the set V_T and the measured exhaled V_T, and wide variability among the tested ventilators. The delivered V_T was higher than the set V_T with 4 ventilators (Veolar FT, Hamilton Galileo, Dräger Evita 2, and Siemens Servo 900C), and the magnitude of the discrepancy was linearly, inversely related to F_{IO₂} and directly related to the helium concentration. Compared to the delivered V_T, the measured exhaled V_T was underestimated by some ventilators (Veolar FT, Hamilton Galileo, Siemens Servo 900C, and Servo 300) and overestimated by others (Dräger Evita 2, Dräger Evita4, Nellcor Puritan Bennett 7200) and the discrepancy was a function of F_{IO₂}. The results for the delivered F_{IO₂} and V_T were predicted by theoretical models based on gas density and on ventilator design with all the ventilators except the Siemens Servo 300 and the Nellcor Puritan Bennett 7200. These

findings were mostly confirmed by a further bench study¹³⁸ of 5 ICU ventilators. With the Nellcor Puritan Bennett 7200 the delivered V_T was lower and the delivered F_{IO_2} higher than the set values. With the other 4 ventilators the delivered F_{IO_2} was lower than the set F_{IO_2} . With the Siemens Servo 300 and 900C this difference could be explained by the lack of 21% oxygen when helium was connected to the air-supply port. The V_T delivered by the Siemens Servo 300 was independent of helium concentration, probably because the flow-regulating valve has a compensatory mechanism for a gas with a different density. Conversely, with the other 3 ventilators the delivered V_T was greater than the set V_T , depending on helium concentration.

More recently, in a lung-model study, Brown et al¹³⁹ found that heliox significantly affected both the measured exhaled and delivered V_T of 2 new ICU ventilators (eVent Medical Inspiration and Maquet Critical Care Servo-i). With the eVent Medical Inspiration the delivered V_T was higher than both the set and the measured exhaled V_T , because of the faster flow with helium and the underestimation of heliox flow. Conversely, with the Maquet Critical Care Servo-i the delivered V_T was lower than the set V_T but remained within the manufacturer's specifications, presumably because this ventilator is equipped with separate modules for air and oxygen. The overestimation of exhaled V_T , compared to set V_T , with the Maquet Critical Care Servo-I is caused by heliox's interference with the ultrasonic flow transducer. However, in most cases, the actual delivered V_T with the 2 tested ICU ventilators can be reliably calculated if the F_{IO_2} and the set or the exhaled V_T are known.

The only ventilator that is approved in the United States for heliox delivery during both invasive and noninvasive ventilation is the Viasys Avea,¹²⁶ thanks to its "smart" technology. Changing the connector on the back panel identifies the gas input and automatically adjusts all volumes by compensating for the presence of heliox. In a lung-model study there were no significant differences between exhaled measured and delivered V_T with the Viasys Avea when using various helium/oxygen mixtures in various ventilation modes.

There are very few data on heliox with bi-level ventilators. In the only lung-model study,¹⁴⁰ which was performed with 5 single-limb-circuit bi-level ventilators and 80/20 heliox, the helium concentration was dependent on the heliox flow, NIV settings, site of heliox infusion, and the type of ventilator. A new heliox-delivery system for NIV recently became available, the GE Healthcare Apataér,¹²⁶ which uses a premixed blend of heliox from a gas cylinder and delivers it to the patient through a sealed face mask.

Summary

The application of NIV to treat ARF is increasing tremendously both inside and outside ICU. The choice of ventilator is crucial for NIV success in the acute setting, because poor tolerance and excessive air leaks are significantly correlated with NIV failure. Patient-ventilator asynchrony and discomfort may occur if the clinician fails to adequately set NIV to respond to the patient's ventilatory demand, so the clinician must understand the technical peculiarities of the ventilator (efficiency of the triggering system, speed of pressurization, air-leak compensation, CO_2 rebreathing, reliability of F_{IO_2} reading, and monitoring accuracy).

A wide range of ventilators, of diverse complexity, have been introduced for NIV for acutely ill patients. Newer bi-level, intermediate, and ICU ventilators equipped with "NIV modes" have several technological advantages for supporting critically ill patients, which may increase the likelihood of achieving the best comfort and patient-ventilator interaction and, thus, NIV success. Technical aspects, such as circuit, interface, O_2 supplementation, battery, humidification, monitoring and alarm complexity, sophistication of settings, and ventilation modes, may impact ventilator performance.

Most of the physiologic data have come from lung-model investigations, and translating those findings into clinical practice must be done with caution. We need further and larger clinical studies with different categories of ventilator, matched with various interfaces and ventilation modes, in patients with ARF of various etiologies. As we await clearer details about ventilators applied in the "real world," we recommend to clinicians who administer NIV in the acute setting that they familiarize themselves as much as possible with a limited number of NIV devices and strive to match the NIV device and setting selection to the patient's needs, based on the etiology of the respiratory failure.

Although it seems that, during NIV, inhaled drugs (eg, bronchodilators) could be efficiently delivered via either nebulizer or MDI/spacer, there is not enough consistent evidence about the ventilator features (eg, category, settings, circuit, interface) specifically designed and approved for this application in everyday practice. Finally, the promising introduction of heliox NIV into clinical practice is quite limited by the lack of wide availability of an approved dedicated heliox-delivery system and by the fact that it is still unclear which patients will benefit from heliox.

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