What Is the Evidence Base for the Newer Ventilation Modes?

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New ventilation modes are introduced as answers to current clinical conundrums but also as marketing tools. Rarely is a mode introduced with sound evidence from bench, animal, and patient testing. The industry cannot support the extensive testing required to demonstrate the superiority of a new mode or technique. Instead, clinicians often rely on their own experience and the results of small observational trials that show positive effects on surrogate variables such as oxygenation and work of breathing or less tangible variables such as patient comfort. This report reviews the newer ventilation modes and attempts to find the evidence among the claims and confusion. *Key words: mechanical ventilation, work of breathing, evidence-based medicine.*
[Respir Care 2004;49(7):742–760.

Introduction

The advent of microprocessor control of mechanical ventilators has added complexity to operation and comprehension previously unimagined. Maintaining pace with the updates and advances in ventilator technology is a substantial challenge for clinicians. Not all updates in ventilator technology are necessarily advances. Many changes to ventilator operation and function have been accomplished with a paucity of evidence to guide safe and effective implementation to clinical practice. This report reviews the evidence regarding the newer ventilation modes. Technical descriptions and operational details of newer ventilation modes are in other publications.[1–5]

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Richard D Branson MSc RRT FAARC presented a version of this report at the 19th Annual New Horizons Symposium at the 49th International Respiratory Congress, held December 8–11, 2003, in Las Vegas, Nevada.

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The Question

The question "What is the evidence base for the newer ventilation modes?" is broad and difficult to answer. We could ask, "What is the evidence that the newer modes improve outcomes?" but that would bring this article to an abrupt end, because the answer is, "There is none." We could instead ask for the evidence that the newer modes reduce time on the ventilator, which again would result in a short answer and review. On the opposite extreme we could ask, "Do new ventilation modes perform as intended?" The answer might be more encouraging and this report more extensive, but the impact on practice and outcomes would be negligible. This leaves us with the unenviable task of using surrogate outcomes, such as blood gas values, airway pressures, and patient comfort. We review the available literature regarding new modes and attempt to frame the question around the available surrogate outcomes. Case reports and reviews will not be considered. Table 1 shows the evidence categorization system we use in the present analysis.

Table 1. Evidence Categorization System Used in the Present Report

Evidence Level	Type of Study or Evidence	Evidence Grade
I	Randomized controlled trial with a statistically significant result	A
II	Randomized controlled trial (questions of validity or bias)	A
III	Observational study	B
IV	Studies with historical controls	B
V	Bench study, animal study, case report	C
(not applicable)	Expert opinion	D

Dual-Control Modes

"Dual-control" refers to a ventilation mode that allows the clinician to set a volume target and the ventilator delivers pressure-controlled breaths.[6,7] In "dual-control within-a-breath" mode the ventilator switches from pressure-control to volume-control during the breath. This technique is known as volume-assured pressure-support (VAPS) or pressure augmentation.[6–10] Dual-control breath-to-breath is simpler because the ventilator operates in either the pressure-support or pressure-control mode.[6,7] The only difference is that the pressure limit increases or decreases to maintain a clinician-selected tidal volume (V_T). Dual-control breath-to-breath is analogous to having a respiratory therapist at the bedside increasing or decreasing the pressure limit of each breath based on the delivered V_T of the previous breath.

Dual-Control Within-a-Breath: VAPS and Pressure Augmentation

The proposed advantage of dual-control within-a-breath ventilation is lower work of breathing (WOB) while maintaining constant minute volume ($\dot{V}_E$) and V_T. Examples of this mode include VAPS (on the Bird 8400Sti, TBird, and Avea ventilators [Viasys, Palm Springs, California]) and pressure augmentation (on the Bear 1000 ventilator [Viasys, Palm Springs, California]). Conceptually, VAPS and pressure augmentation are meant to combine the high initial flow of a pressure-limited breath with the constant volume delivery of a volume-limited breath.

Amato et al described the VAPS technique as an alternative to volume-controlled ventilation (VCV). They reported a WOB reduction of nearly 50% with VAPS, as well as improved dynamic compliance, airway resistance, and intrinsic positive end-expiratory pressure (PEEPi).[8] This was attributed to the higher inspiratory flow during VAPS. They also suggested that VAPS improved patient-ventilator synchrony by matching ventilator output to patient demand. One criticism of that study[6,7] was the relatively low peak flow during VCV (46 L/min) and the significantly larger V_T during VAPS (0.72 L vs 0.59 L). That V_T difference may explain the lower WOB. It could be argued that no differences would have been reported if V_T and inspiratory flow during VCV were equivalent to that during VAPS.

Haas et al evaluated VAPS with the Bird 8400STi and attempted to replicate the findings of Amato et al, while optimizing V_T and inspiratory flow during VCV[9] by setting the VAPS pressure limit to produce a V_T equivalent to VCV and by setting inspiratory flow to closely approximate patient demand during VCV prior to initiating VAPS. Patient effort, respiratory drive, and esophageal pressure changes were significantly less with VAPS than with VCV. Despite attempts to maintain constant V_T over the course of the 40-min study period, it rose slightly during VAPS. That is an important observation in that, because patients' demands differ, the ability to increase V_T may play an important role in the sensation of breathlessness.

MacIntyre et al evaluated the pressure augmentation function of the Bear 1000 in a lung model at various degrees of simulated patient demand. Pressure augmentation matched ventilator output to simulated patient demand more effectively than did traditional volume ventilation.[10]

The evidence regarding dual-control within-a-breath techniques is based on 2 patient trials (which included a total of 25 patients) and a lung model study (Table 2). The evidence suggests that dual-control within-a-breath improves patient comfort and patient-ventilator synchrony in short-term observations. Long-term studies have not been done, so this mode's influence on outcomes (eg, duration

Table 2. Studies of Dual-Control Within-a-Breath Ventilation

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Amato[8] (1992)	Observational, cross-over trial. Patients were their own controls. 40 min in each mode. (n = 8)	Ventilatory work load and mechanics: pressure-time product, WOB, PEEPi, compliance, $P_{0.1}$, V_T, blood gases	Higher V_T and inspiratory flow. Improved compliance. Lower WOB, pressure-time product, and $P_{0.1}$	III: Short-term observational study with a small number of patients	B
Haas[9] (1995)	Observational, cross-over trial. Conventional ventilation followed by VAPS and then a second period of conventional ventilation. Patients were their own controls. 40 min in each mode. (n = 17)	Ventilatory work load and mechanics: pressure-time product, WOB, PEEPi, compliance, $P_{0.1}$, V_T, maximum negative esophageal pressure, blood gases, hemodynamics	Higher V_T and inspiratory flow. Reduced pressure-time product, $P_{0.1}$, and lower maximum negative esophageal pressure	III: Short-term observational study with a small number of patients	B
MacIntyre[10] (1994)	Bench study with a lung model	Simulated WOB	Reduced simulated WOB	V: Short-term bench study	C

WOB = work of breathing
PEEPi = intrinsic positive end-expiratory pressure
$P_{0.1}$ = airway occlusion pressure 0.1 s after the onset of inspiratory effort
V_T = tidal volume
VAPS = volume-assured pressure support

of ventilation or survival) are not known. To my knowledge dual-control within-a-breath has not gained widespread acceptance or use. The last published evaluation is a decade old and no improvements or modifications have been made.

Dual-Control Breath-to-Breath, Pressure-Limited, Flow-Cycled Ventilation

Breath-to-breath dual-control is available as volume-support ventilation (VSV) (on the Siemens 300 ventilator, Siemens Medical Systems, Danvers, Massachusetts) and variable-pressure-support (on the Venturi, Cardiopulmonary Corporation, New Haven, Connecticut). Its proposed advantages are to provide the positive attributes of pressure-support ventilation (PSV) with constant $\dot{V}_E$ and V_T and automatic weaning of pressure limit as patient compliance improves and patient effort increases.

Keenan and Martin reported a retrospective case series in which VSV was used with infants and children.[11] Peak inspiratory pressure (PIP) and set V_T were lowered when children were switched to VSV, and PIP and V_T further decreased over the course of VSV. They also observed a failure rate of nearly 50% with VSV, much of which was attributed to clinician unfamiliarity with this mode. That retrospective study was partially intended to identify the role of VSV in weaning, and 12 of 20 patients were successfully extubated from VSV.

Sottiaux reported 3 selected cases that demonstrated asynchrony and V_T instability during VSV.[12] That case series describes the combined effects of patient-ventilator asynchrony, PEEPi, and missed triggers, which defeat the VSV algorithm and cause excessive V_T. Higher V_T in that case worsened the asynchrony and exacerbated PEEPi, causing a greater number of missed triggers. The description of 3 selected cases of VSV complications should be viewed similarly to selected cases of VSV success. Observational, selected case series are useful for helping to select or exclude patients for given techniques.

The literature regarding VSV is scant: only 2 case series (a total of 23 patients). The evidence for VSV is Level V evidence, with a grade of C. Table 3 summarizes trials of dual-control, breath-to-breath PSV.

Dual-Control Breath-to-Breath, Pressure-Limited, Time-Cycled Ventilation

This approach is available as pressure-regulated volume-control (PRVC) (on the Siemens 300 ventilator), adaptive pressure ventilation (on the Galileo, Hamilton Medical, Reno, Nevada), auto-flow (on the Evita 4, Dräger, Telford, Pennsylvania), volume-control+ (on the 840, Puritan Bennett, Carlsbad, California), or variable-pressure-control (Venturi, Cardiopulmonary Corporation, New Haven, Connecticut). Proposed advantages of this approach are the positive attributes of pressure-controlled ventilation (PCV) with constant $\dot{V}_E$ and V_T and automatic wean-

Table 3. Studies of Dual-Control Breath-to-Breath, Pressure-Support Ventilation

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Keenan[11] (1997)	Retrospective case review ($n = 20$)	V_T, airway pressure, weaning success	Lower V_T and peak inspiratory pressure. No measurable effect on weaning	V	C
Sottiaux[12] (2001)	Prospective, selected case series ($n = 3$)	Patient comfort, missed triggers, patient-ventilator synchrony	Worsening patient ventilator interaction	V	C

V_T = tidal volume

ing of pressure limit as patient compliance improves and/or patient effort increases.

Piotrowski et al compared PRVC to volume-controlled intermittent mandatory ventilation (IMV) in a randomized, prospective study that included 60 neonates suffering respiratory distress syndrome.[13] Thirty patients received IMV and 27 received PRVC. All the patients suffered from either respiratory distress syndrome or congenital pneumonia and weighed < 2,500 g. The primary outcome variables were duration of mechanical ventilation and incidence of bronchopulmonary dysplasia. The secondary outcomes were complications, including the incidence of air leaks, intraventricular hemorrhage, and hemodynamic instability. They found no differences in the main outcome variables, but the SIMV group had a greater incidence of grade II or higher intraventricular hemorrhage. Patients who had bronchopulmonary dysplasia had shorter duration of ventilation and lower incidence of being 1,000 g ($n = 10$) and a lower incidence of hypotension, but that post hoc analysis included only 10 patients in each group.

Table 4 summarizes the trials of dual-control breath-to-breath PCV. Alvarez et al compared PRVC, VCV, and pressure-limited, time-cycled ventilation, with 10 adult patients suffering acute respiratory failure. PRVC had lower peak airway pressure and slightly better carbon dioxide clearance.[14] Patients received 1 h of each of PRVC, PCV, and VCV with a constant inspiratory flow waveform. Not surprisingly, PIP was highest with the constant-flow waveform and there were no differences between PCV and PRVC.

Kesecioglu et al compared VCV and PRVC (using an inverse inspiratory-expiratory ratio) with a pig model of acute respiratory distress syndrome, and reported in a series of publications.[15–17] The studies used short-term observational periods following saline-lavage-induced acute respiratory distress syndrome. PRVC had lower airway pressures and slightly better gas exchange than VCV with a constant inspiratory flow.

In a prospective, open, cross-over trial with 44 patients suffering acute respiratory failure Guldager et al compared PRVC to VCV with a constant flow.[18] Patients were evaluated during an 8-h stabilization period and then randomized to one mode or the other. After 2 h of measurements the patient was switched to the other mode for 2 h, at the end of which measurements were obtained; then the patient was returned to the initial ventilation mode for the duration of ventilatory support. During the short-term observations, blood gases, airway pressure, and mean arterial pressure were recorded. Long-term outcomes included duration of mechanical ventilation, days with PIP > 50 cm H_2O, and survival. During ventilation with either mode, V_T was set at 5–8 mL/kg and inspiratory-expiratory ratio of 1:3. PIP was significantly lower with PRVC (24 vs 20 cm H_2O) but plateau pressure was not recorded. All other short-term observational variables were not clinically or statistically different. Survival and duration of ventilation were similar. Two patients in the VCV group (vs no patients in the PRVC group) had a PIP > 50 cm H_2O. That difference was not statistically significant nor is it surprising, since pressure can be limited during PRVC.

Kocis et al compared PRVC to VCV with infants after surgery for congenital heart disease.[19] Nine patients were studied after repair of either tetralogy of Fallot or atrioventricular septal defects. Patients were initially stabilized using VCV for 30 min. At the end of that period blood gases, hemodynamics, and ventilation variables were measured. Patients then received PRVC for 30 min and those variables were measured again. This was followed by a second period of VCV. The only statistically significant difference in any of the measured variables was a PIP decrease of 19% during PRVC (decrease from 31 to 25 cm H_2O). As in other studies, plateau pressures were not recorded.

The studies of dual-control pressure-control confirm that it provides lower PIP than does VCV with a constant-flow waveform. The studies have failed to show any advantage such as shorter duration of ventilation, fewer complications, improved survival, or better patient-ventilator synchrony. The total number of patients studied is small (123), with half being neonates and a quarter without lung dis-

Table 4. Studies of Dual-Control Breath-to-Breath, Pressure-Control Ventilation

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Piotrowski[13] (1997)	Prospective, randomized trial. PRVC vs volume-controlled SIMV. Neonates < 2,500 g. (n = 60)	Duration of ventilation, incidence of BPD, hypotension, intraventricular hemorrhage	No difference in duration of ventilation or incidence of BPD. SIMV group had greater incidence of grade II or higher intraventricular hemorrhage. Patients <1000 grams (n = 10) had shorter duration of ventilation and lower incidence of BPD.	II: Prospective, randomized trial with a small number of patients. The only significant differences occurred in subgroup, post hoc analysis.	B
Alvarez[14] (1998)	Prospective, cross-over trial. Patients were their own controls. (n = 10)	Airway pressure, blood gases, respiratory mechanics	Peak inspiratory pressure was less with PCV and PRVC than with VCV. P_{aCO_2} was statistically lower (2 mm Hg)	III: Short-term observational study with a small number of patients	C
Kesecioglu[15–17] (1994 and 1996)	Prospective, cross-over trial. Adult pigs with surfactant-depleted respiratory failure. 1 h in each mode. (n = 15)	Gas exchange, airway pressure, hemodynamics, distribution of ventilation, lung compliance	Better gas exchange and lower peak inspiratory pressure with PRVC	V: Animal study with short-term observation	C
Guldager[18] (1997)	Prospective, randomized, open, cross-over trial. Patients in ARF. 2 × 2 design. (n = 44)	Gas exchange, airway pressure, hemodynamics, duration of ventilation, survival, incidence of PIP > 50 cm H_2O	No difference in duration of ventilation or survival. PIP was lower with PRVC (20 vs 24 cm H_2O). No differences in outcomes	II: Prospective, randomized trial	B
Kocis[19] (2001)	Prospective, cross-over trial. Infants after repair of congenital heart disease. (n = 9)	Airway pressure, blood gases, respiratory mechanics	No change in any hemodynamic or gas-exchange variables. Lower PIP with PRVC (25 vs 31 cm H_2O)	III: Short-term observational study with a small number of patients	C

PRVC = pressure-regulated volume control ventilation
SIMV = synchronized intermittent mandatory ventilation
BPD = bronchopulmonary dysplasia
PCV = pressure-controlled ventilation
VCV = volume-controlled ventilation
ARF = acute respiratory failure
PIP = peak inspiratory pressure

ease. That PRVC offers lower PIP than VCV with a constant-flow waveform is easily explained and predictable. Dual-control modes are quite popular for several reasons, but similar effects can be accomplished with traditional PCV or VCV with a decelerating-flow waveform.[20] The evidence indicating advantage with dual-control PCV is limited to Level III, for reducing PIP—hardly a mandate for adopting this method.

AutoMode

AutoMode is available on the Siemens 300A ventilator. Its proposed advantages are automatic weaning from pressure-control to pressure-support, and automated escalation of support as the patient's condition worsens or effort diminishes. AutoMode combines VSV and PRVC in a single mode. If the patient is paralyzed, the ventilator will provide PRVC. All breaths are mandatory breaths that are time-triggered, pressure-limited, and time-cycled. The pressure limit increases or decreases to maintain the clinician-set V_T. If the patient breathes spontaneously for 2 consecutive breaths, the ventilator switches to VSV. In that case all breaths are patient-triggered, pressure-limited, and flow-cycled. If the patient becomes apneic (for 12 s in the adult setting, 8 s in the pediatric setting, or 5 s in the neonatal setting), the ventilator switches back to the PRVC mode. The change from PRVC to VSV is accomplished at equivalent peak pressures. This mode is the combination of 2 existing modes, using the conditional

Table 5. Studies of AutoMode Ventilation

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Roth[21] (2001)	Prospective, randomized trial. AutoMode vs SIMV. Patients with normal lungs after neurosurgery. (n = 40)	Weaning time, number of ventilator manipulations required, airway pressure, blood gases, respiratory mechanics	No difference in airway pressure, blood gases, respiratory mechanics, or weaning time. Fewer manipulations with AutoMode (0.5 vs 5) and less variability in P_{aCO_2} during the late phase of weaning (39.5 ± 3 vs 38.3 ± 7 mm Hg). No important outcome differences	II: Prospective, randomized trial	B
Holt[22] (2001)	Prospective, observational trial. AutoMode performance during spontaneous breathing and neuromuscular blockade. Piglets. (n = 6)	Ventilatory drive, triggering effectiveness, WOB, algorithm success	AutoMode algorithm performed according to specifications Confirmed algorithm performance	V: Short-term observational study with animals	C

SIMV = synchronized intermittent mandatory ventilation
WOB = work of breathing

variable of patient effort to decide if the next breath will be time-cycled or flow-cycled.

Roth et al used an open, randomized design to compare AutoMode to synchronized intermittent mandatory ventilation (SIMV) with 40 patients who did not have lung disease, following surgery for brain tumors.[21] The primary outcome variables were duration of ventilation (weaning time) and number of ventilator manipulations required. At 5 predetermined time points, gas exchange, and hemodynamic and ventilatory variables were measured. Duration of ventilation was 136 ± 46 min with AutoMode and 169 ± 68 min with SIMV—approximately a half-hour difference, which was not statistically different. The number of ventilator manipulations by the staff was 5 with SIMV versus 0.5 with AutoMode. None of the physiologic variables were different. During the late phase of the weaning protocol P_{aCO_2} was more tightly controlled with AutoMode than with SIMV (39.5 ± 3.1 vs 38.3 ± 7.3 mm Hg). The authors concluded that AutoMode was useful in weaning patients who have normal lungs.

Holt et al designed an animal experiment to verify the AutoMode algorithm by allowing spontaneous breathing and then abolishing breathing with succinylcholine.[22] Using 6 piglets, they found that the algorithm operated according to specifications.

AutoMode promises automatic weaning, but the current literature regarding liberation from mechanical ventilation questions the need for traditional slow, methodical withdrawal of support. Current weaning methods rely on daily spontaneous breathing trials (SBTs), not the gradual reduction of PSV. The evidence base for AutoMode (Table 5) consists of 40 patients without lung disease ventilated for a mean time of 2 h. AutoMode appears to operate according to specifications, but little else about AutoMode is supported by the literature.

Proportional-Assist Ventilation

Proportional-assist ventilation (PAV) was designed to increase or decrease airway pressure in proportion to patient effort by amplifying airway pressure proportional to inspiratory flow and volume. Unlike other modes, which deliver a preset volume or pressure, PAV determines the amount of support relative to patient effort, assisting ventilation with a uniform proportionality between the ventilator and the patient. The advantage of proportional (as opposed to fixed) ventilatory support lies in its ability to track changes in ventilatory effort, which can rapidly occur in patients suffering respiratory failure. To the extent that inspiratory effort is a reflection of ventilatory demand, PAV may provide a more physiologic breathing pattern. Patient effort determines the ventilating pressure, which is determined by central drive and respiratory mechanics.[23,24]

PAV was met with great fanfare and considerable scientific investigation (Table 6).[23–50] Many of those studies simply evaluated patient response to PAV, whereas others compared PAV to PSV. In several cases PAV was compared to PSV in normal volunteers or normal volunteers with external thoracic binding to simulate increased im-

pedance. About half the studies have been with noninvasive ventilation[29–31,36,38,39,41–47,49] and the other half included intubated patients.[25–27,32–35,37,40,48,50] Two studies evaluated PAV with infants.[35,40]

The present report concentrates on the evidence, so randomized trials comparing PAV to PSV will be discussed here.

Gay et al compared noninvasive ventilation with PAV to PSV in a randomized, prospective trial with 44 patients.[41] Twenty-three patients were ventilated with PSV with a Puritan Bennett 7200 ventilator and 21 received PAV from a Vision ventilator (Respironics, Murrysville, Pennsylvania). PAV was associated with greater patient comfort than was PSV during noninvasive ventilation, but there were no differences in intubation rate or mortality. Patients in the PAV group had fewer complications and were less likely to give up on noninvasive ventilation. Conventional wisdom would suggest that if PAV reduced complications, improved comfort, and facilitated patient acceptance of noninvasive ventilation, some advantage would also be seen in intubation rate, but that was not the case.

Fernandez-Vivas et al conducted the largest trial to date of noninvasive pressure-support compared to PAV, with patients suffering acute respiratory failure.[48] They evaluated the hypothesis that better comfort with PAV might correlate to better outcomes. They randomized 117 consecutive patients suffering acute respiratory failure to either PSV or noninvasive PAV. Surprisingly, approximately 40% of each group suffered from COPD, but 40% also suffered from hypoxemic respiratory failure—a group perhaps less likely to be treated successfully with noninvasive ventilation. The study again demonstrated the feasibility of PAV but found no difference in the frequency of intubation (37 vs 34%), mortality (29 vs 28%), or duration of hospital stay (8.6 vs 8.9 d). In a similar study of noninvasive PAV versus PSV, Porta et al found no differences in V_T, ventilatory timing, or pressure-time product.[44] Interestingly, they found that initial set-up of PAV required on average a little over 10 min, whereas initial set-up of PSV required on average only 4 min. That may relate to the apparent difficulty in understanding the best methods to choose the PAV settings.

One common finding in the observational studies is that PAV allows a greater V_T variability than does PSV.[33,36,37,43,44] Other common findings include more missed triggers with intubated patients as the PSV level is increased, which does not occur with PAV,[26,31,32,49] and better comfort with PAV, owing to the proportional increase in output with increasing patient effort.[40,41,43,48,50]

Despite the flurry of excitement regarding PAV, it has failed to demonstrate superiority in any of the randomized controlled trials to date.[41,48] Though admittedly those studies have had limited numbers of participants, the only advantages demonstrated so far are better patient tolerance and comfort; the trials have not identified any outcome benefits from PAV. PAV has helped us understand PSV more completely and appreciate the nuances of patient-ventilator interaction, but PAV is currently unavailable in the United States.

Adaptive Support Ventilation

Adaptive support ventilation (ASV) is available on the Galileo ventilator. Its proposed advantages are automated escalation or withdrawal of support, based on changes in patient effort and lung mechanics, and automated selection of initial ventilation parameters.

ASV is based on the minimal-WOB concept developed by Otis et al,[51] which suggests that the patient will breathe at a V_T and respiratory frequency (f) that minimizes the elastic and resistive loads while maintaining oxygenation and acid-base balance. The ASV algorithm uses that formula, along with patient weight (which determines dead space), to adjust several ventilation variables. The clinician enters the patient's ideal body weight; sets the high-pressure limit, PEEP, and fraction of inspired oxygen (F_{IO_2}); and adjusts the rise time and flow cycle variable for pressure-support breaths from 10–40% of initial peak flow. The ventilator attempts to deliver a $\dot{V}_E$ of 100 mL/kg/min to an adult or 200 mL/kg/min to a child. This can be adjusted by a setting known as the "percentage $\dot{V}_E$" control, which can be set from 20 to 200%. In the latter case (200%) a $\dot{V}_E$ of 200 mL/kg/min would be delivered to an adult patient. The percentage $\dot{V}_E$ setting allows the clinician to provide full ventilatory support or encourage spontaneous breathing and facilitate weaning. Campbell et al reviewed the technical aspects of ASV.[52]

Weiler et al reported that the ASV algorithm provided adequate ventilation in 5 patients undergoing major abdominal surgery.[53] No instances of PEEPi were identified, and delivered and target V_T were different by only 28 mL. Laubscher et al compared the ASV algorithm's selection of initial ventilation variables to clinician settings, with 25 adult and 17 pediatric patients, using a version of ASV that incorporated carbon dioxide monitoring.[54] The ASV algorithm provided gas exchange equivalent to that obtained with clinician-set variables. The algorithm consistently chose smaller V_T and higher f than did the clinicians. Linton et al applied adaptive lung ventilation during weaning of 30 post-surgery patients who had normal lungs, 30 COPD patients, and 30 patients with parenchymal lung disease.[55] The adaptive lung ventilation algorithm appropriately chose V_T and f commensurate with patient respiratory mechanics. Linton et al were among the first to note that adaptive lung ventilation could increase ventilatory support when required. However, that trial was observational and did not attempt to evaluate outcomes.

Table 6. Studies of Proportional Assist Ventilation (Continued on next 2 pages)

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Ranieri[25] (1996)	PSV vs PAV. Patients weaning from mechanical ventilation during addition of mechanical dead space. (n = 12)	WOB, V_T, f, $\dot{V}_E$, blood gases, PTP, discomfort	$\dot{V}_E$ increase required to meet hypercapnic challenge results in greater WOB and more discomfort with PSV than with PAV	III: Short-term observational trial	B
Navalesi[26] (1996)	Effects of varying flow- and volume-assist on breathing pattern. Intubated patients in ARF. PAV vs spontaneous breathing through the ETT. (n = 8)	WOB, V_T, f, $\dot{V}_E$, inspiratory effort, PTP	PAV had lower WOB and more normal breathing pattern than spontaneous breathing through ETT	III: Short-term observational trial	C
Ranieri[27] (1997)	PAV with and without flow- and volume-assist-plus-PEEP vs CPAP and spontaneous breathing. Intubated patients with COPD in ARF. (n = 8)	V_T, f, $\dot{V}_E$, inspiratory effort, PTP, inspiratory time, asynchrony, dyspnea	PAV with the flow-assist portion active plus PEEP gave better comfort and lower PTP than the other methods. Adding volume-assist worsened comfort by increasing PEEPi. Demonstrated negative aspects of PAV	III: Short-term observational trial	C
Bigatello[28] (1997)	Lung model. PAV vs PSV	Simulated WOB, V_T	PAV had lower WOB than PSV. PAV provided uniform unloading of the work	V: Bench study with a lung model	C
Ambrosino[29] (1997)	Spontaneous breathing in stable patients compared to 60 min of nasal PAV at 80% flow- and volume-assist. Stable patients with chronic hypercapnia. 30 patients with COPD and 12 patients with chest-wall restriction. (n = 42)	Blood gases, dyspnea measured with a visual analog scale	PAV significantly improved P_{aO_2}, P_{aCO_2}, and dyspnea	III: Prospective, short-term (60 min) observational study	C
Bianchi[30] (1998)	PAV vs CPAP-plus-PSV via nasal mask. Hypercapnic patients with COPD during cycle ergometry (n = 15)	Breathing pattern, S_{pO_2}, end-tidal CO_2, heart rate, dyspnea (measured with Borg scale), endurance time	All ventilation techniques improved endurance time. PAV gave greatest improvement	III: Prospective, short-term observation during exercise	C
Appendini[31] (1999)	PAV vs CPAP vs CPAP-plus-PAV, in random sequence. Difficult-to-wean patients. 20 min with each ventilation technique (n = 8)	PTP, $P_{0.1}$, breathing pattern, f, missed triggers, PEEPi	PAV plus CPAP gave lower PTP, $P_{0.1}$, and f than did PAV or CPAP alone, without increasing missed triggers	III: Prospective, short-term observational trial	B
Giannouli[32] (1999)	PAV vs PSV. Mechanically ventilated patients (n = 14)	V_T, f, $\dot{V}_E$, blood gases, missed triggers	No difference in blood gases. Fewer missed triggers with PAV	III: Prospective, short-term observational trial	B
Wrigge[33] (1999)	PAV vs PSV. Mechanically ventilated patients with COPD (n = 13)	WOB, $P_{0.1}$, breathing pattern, f, missed triggers, PEEPi	PAV and PSV reduced WOB and $P_{0.1}$ equally. PAV had lower f and $\dot{V}_E$. V_T variability was greater with PAV, indicating patient's ability to control V_T	III: Prospective, short-term observational trial	B
Schulze[34] (1999)	PAV vs IMV vs AC. Very-low-birthweight infants. (n = 36)	Airway pressure, oxygenation, apnea episodes, periods of arterial oxygen desaturation	PAV provided similar oxygenation at lower transpulmonary pressure. No difference in apnea episodes or desaturations	III: Prospective, short-term observational trial	B

Table 6. Studies of Proportional Assist Ventilation (Continued from previous page)

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Grasso[35] (2000)	PSV vs PAV. Intubated patients with COPD-exacerbation ($n = 7$)	Blood gases, breathing pattern, inspiratory effort, V_T, f, $\dot{V}_E$	PAV increased V_T and $\dot{V}_E$. PAV improved P_{aO_2} (65 ± 15 vs 97 ± 36 mm Hg) and P_{aCO_2} (80 ± 11 vs 76 ± 13 mm Hg). PAV significantly reduced PTP	III: Prospective, short-term observational trial	B
Vitacca[36] (2000)	PAV vs PSV. Patients weaning from mechanical ventilation, with chest and abdominal binding to increase respiratory impedance. ($n = 10$)	V_T, f, $\dot{V}_E$, PTP	PAV gave lower PTP. $\dot{V}_E$ was preserved by increasing f as V_T decreased from increased impedance. The increase in f was 14% less with PAV than with PSV	III: Prospective, short-term observational trial	B
Mols[37] (2000)	PAV vs PSV. Healthy volunteers breathing through a mouthpiece, before and after thoracic binding. ($n = 15$)	Respiratory comfort (measured with a visual analog scale), V_T, f, $\dot{V}_E$, airway pressure	PAV was associated with better respiratory comfort and greater V_T variability	III: Prospective, double-blind short-term trial	C
Polese[38] (2000)	PAV vs spontaneous breathing via nasal mask. Hypercapnic patients with COPD ($n = 15$)	V_T, f, $\dot{V}_E$, blood gases, PTP, electrical activity of the diaphragm	PAV reduced PTP, increased V_T and $\dot{V}_E$. P_{aCO_2} was reduced with PAV (76 to 72 mm Hg)	III: Prospective, short-term observational trial	B
Musante[39] (2001)	PAV vs CPAP. Preterm infants suffering thoracoabdominal dyssynchrony ($n = 10$)	V_T, airway pressure, esophageal pressure, total compartmental displacement ratio	PAV reduced thoracoabdominal dyssynchrony. PAV had higher V_T	III: Prospective, short-term observational trial	C
Hernandez[40] (2001)	PAV vs spontaneous breathing during exercise testing. Patients with COPD ($n = 8$)	Exercise duration, blood gases, breathing pattern	PAV increased exercise duration, improved oxygenation, and reduced dyspnea.	III: Prospective, short-term observational trial	C
Gay[41] (2001)	PAV vs PSV during noninvasive ventilation. Patients with COPD exacerbation ($n = 44$)	Comfort, survival, refusal of noninvasive ventilation, f, intubation rate, complications	PAV had a lower refusal rate, more rapid reduction in f, and fewer complications. No difference in mortality or intubation rate	II: Prospective, randomized trial	B
Serra[42] (2002)	PAV vs PSV via noninvasive ventilation. Stable hypercapnic cystic fibrosis patients ($n = 12$)	V_T, $\dot{V}_E$, f, comfort, P_{tcCO_2}, diaphragmatic electromyography	No difference in V_T, P_{tcCO_2}, or diaphragmatic activity	III: Prospective, short-term observational trial	C
Wysocki[43] (2002)	PAV vs PSV via noninvasive ventilation. Patients with COPD admitted for hypercapnic respiratory failure ($n = 12$)	V_T, f, $\dot{V}_E$, blood gases, esophageal pressure, PTP, breathing comfort measured with a visual analog scale	No differences except in breathing comfort and V_T variability	III: Prospective, randomized, cross-over trial with short-term observation	C

Table 6. Studies of Proportional Assist Ventilation (Continued from previous page)

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Porta[44] (2002)	PAV vs PSV via mask. Patients with COPD and chest wall disease (n = 18)	Breathing pattern, V_T, f, $\dot{V}_E$, lung mechanics, patient-ventilator interaction, esophageal pressure	PAV and PSV both increased V_T and $\dot{V}_E$, with no change in f. V_T variability was greater with PAV	III: Prospective, randomized, cross-over trial with short-term observation	C
Hawkins[45] (2002)	Exercise ergometry Program. Patients with severe COPD randomized to receive PAV or not over 6 wk (n = 19)	Peak work rate, constant work rate, $\dot{V}_E$, heart rate, lactate	PAV allowed higher-intensity exercise and improved maximum exercise capacity	II: Randomized, prospective trial	B
Hart[46] (2002)	PAV vs PSV. Stable patients with neuromuscular and chest wall deformity (n = 15)	S_{pO_2}, P_{tcCO_2}, $\dot{V}_E$, V_T, f, diaphragmatic electromyography, comfort measured with a visual analog scale	PSV had greater diaphragm unloading	III: Prospective, randomized, cross-over trial with short-term observation	C
Delaere[47] (2003)	PAV vs PSV. Intubated patients (no COPD) weaning from mechanical ventilation (n = 20)	Arterial blood gases, breathing pattern, respiratory effort, PTP, WOB	No difference in WOB. PTP was higher during PAV	III: Prospective, randomized, cross-over trial with short-term observation	C
Fernandez-Vivas[48] (2003)	PAV vs PSV during noninvasive ventilation for ARF (n = 117)	Intubation frequency, mortality, duration of stay, comfort, intolerance of noninvasive ventilation	No difference in intubation rate (37 vs 34%), mortality (29 vs 28%), or duration of stay. PAV had better comfort and less intolerance	I: Prospective, randomized, controlled trial	A
Passam[49] (2003)	PAV vs PSV. Hypercapnic patients with COPD (n = 9)	Blood gases, V_T, airway pressure, esophageal pressure, f, missed triggers, PTP	No difference in blood gases or ventilation variables. Increasing PSV increased the number of missed triggers. PAV suffered from "runaway"	III: Prospective, randomized, cross-over trial with short-term observation	C
Wysocki[50] (2004)	PAV vs PSV via noninvasive ventilation. Volunteers with external chest wall restriction (n = 7)	Airway pressure, volume, flow, V_T, esophageal pressure	No difference in V_T or f. Inspiratory muscle effort was lower with PAV	III: Prospective, randomized, cross-over trial with short-term observation	C

PSV = pressure support ventilation
PAV = proportional assist ventilation
WOB = work of breathing
V_T = tidal volume
f = respiratory rate
$\dot{V}_E$ = minute volume
PTP = pressure-time product
ARF = acute respiratory failure
ETT = endotracheal tube
PEEP = positive end-expiratory pressure
CPAP = continuous positive airway pressure
COPD = chronic obstructive pulmonary disease
PEEPi = intrinsic positive end-expiratory pressure
$P_{0.1}$ = airway occlusion pressure 0.1 s after the onset of inspiratory effort
IMV = intermittent mandatory ventilation
AC = assist control
P_{tcCO_2} = transcutaneously measured arterial partial pressure of carbon dioxide

In a follow-up study with 30 patients (weight range 15–100 kg) Laubscher et al compared initial ventilation settings chosen by adaptive lung ventilation to house-rules settings chosen by physicians. The ASV algorithm chose a slightly lower V_T, slightly higher f, and slightly lower peak pressure than did the clinicians. Blood gas values were not different between the ventilation-setting methods.[56] The test period was approximately 20 min and no outcomes were measured. They concluded that ASV could safely initiate mechanical ventilation by automated selection of ventilation variables.

Weiler et al compared ASV to conventional ventilation during surgery as patients were placed in the extreme lateral decubitus position.[57] They found that during extreme position changes the ASV algorithm adapted to provide more appropriate ventilator settings in response to position-induced changes in lung mechanics. In a more drastic example Weiler et al evaluated the ASV response upon switching from 2-lung to 1-lung ventilation during thoracic surgery.[58] The ASV algorithm maintained a safe V_T and preserved $\dot{V}_E$ as lung volume and compliance were altered. These studies demonstrate the feasibility of allowing the ventilator to automatically select ventilation variables and to make changes in response to patient effort and lung mechanics, but they do not evidence that ASV is superior to other ventilation modes.

A group of more recent trials[59–62] evaluated ASV during ventilator weaning. Three of those trials used ASV during weaning after cardiac surgery and found that ASV was safe and effective.[59,61,62] However, only one of those studies compared ASV to conventional weaning and that trial showed no difference in time to extubation.[62] The major findings of that study were that ASV selected a lower PIP and required fewer ventilator manipulations. Interestingly, those studies also found that there were fewer high-pressure alarms during ASV than during SIMV, perhaps because ASV uses pressure-control, whereas SIMV uses volume-control.

ASV and its precursor adaptive lung ventilation have been studied extensively over the past decade (Table 7). Both techniques appear to be safe and effective, compared to traditional manual approaches, but none of the studies has provided evidence that ASV is superior to conventional ventilation. To use a term from the Food and Drug Administration, ASV appears to be "substantially equivalent" to conventional clinician-set ventilation approaches.

Automatic Tube Compensation

Automatic tube compensation (ATC) compensates for endotracheal tube (ETT) resistance via closed-loop control of *calculated* tracheal pressure.[63,64] The proposed advantages of ATC are (1) to overcome the WOB imposed by the artificial airway, (2) to improve patient-ventilator synchrony by varying inspiratory flow commensurate with demand (similar to PAV), and (3) to reduce air-trapping by compensating for imposed expiratory resistance. ATC uses the known resistive coefficients of the ETT (or tracheostomy tube) and measurement of instantaneous flow to apply pressure proportional to resistance throughout the total respiratory cycle. The equation for calculating tracheal pressure is:

$$\text{tracheal pressure} = \text{proximal airway pressure} - (\text{tube coefficient} \times \text{flow}^2)$$

Most of the interest in ATC revolves around eliminating the imposed WOB during inspiration. However, during expiration there is also a flow-dependent pressure drop across the ETT. ATC compensates for that flow resistance and may reduce expiratory resistance and unintentional hyperinflation. ATC may also improve patient-ventilator interaction by reducing hyperinflation that can occur during PSV. During expiration the calculated tracheal pressure is greater than airway pressure and under those conditions a negative airway pressure could reduce expiratory resistance. But since that is not always desirable or possible, ATC can reduce PEEP to no less than 0 cm H_2O during exhalation, to compensate for expiratory resistance imposed by the ETT. Because in vivo ETT resistance tends to be greater than in vitro resistance, ETT compensation can be incomplete. Additionally, kinks, bends, or secretions in the ETT change its airflow resistance, which can cause incomplete compensation.

Investigations by Fabry et al[65] and Guttmann et al[66] found better patient comfort with ATC than with PSV, much of which was attributed to ATC's prevention of hyperinflation. Fabry et al also showed that with changing patient demand ATC consistently eliminated imposed WOB, whereas PSV was unable to compensate for changes in patient demand. That ability to maintain the normal "noisy" pattern of ventilation may also be an advantage of ATC.

Haberthur et al compared ATC to 3 levels of PSV and to continuous positive airway pressure (CPAP), in a study with 10 tracheostomized patients[67] and measured total WOB and added WOB. They found that ATC eliminated added WOB without increasing V_T, whereas PSV did increase V_T. The idea that ATC eliminates overcompensation and thus increases alveolar ventilation is important in understanding the potential of ATC. In COPD patients the added volume supplied by PSV may worsen air trapping. Mols et al compared ATC to PSV with normal subjects breathing through a mouthpiece and through an ETT.[68] The subjects indicated that ATC was more comfortable than PSV.

Table 7. Studies of Adaptive Support Ventilation

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Weiler[53] (1994)	Prospective evaluation of patients undergoing major abdominal surgery to determine safety of ASV-selected respiratory pattern. (n = 5)	Airway flow, pressure, end-tidal CO_2, ventilator settings, blood gases, compliance, resistance	ALV-selected ventilator settings were adapted to lung mechanics and provided safe and acceptable ventilation	III: Prospective observational trial with short-term observation	C
Laubscher[54] (1994)	Prospective study. Initial ventilator settings selected by ASV vs settings selected by physicians. Patients were their own controls (n = 42; 25 adults, 17 children)	Airway flow, pressure, end-tidal CO_2, ventilator settings	Ventilator settings selected by the ALV algorithm were not statistically different from those chosen by house rules (physician protocol)	III: Prospective, cross-over trial with short-term observation	B
Linton[55] (1994)	2 h of ALV during weaning of normals, patients with COPD, and patients with parenchymal lung disease. (n = 27)	Airway flow and pressure, end-tidal CO_2, ventilator settings, blood gases, compliance, resistance, hemodynamic variables, $P_{0.1}$	ALV provided safe and efficient ventilation during weaning and responded to inadequate ventilation by increasing support	III: Short-term observational trial	C
Laubscher[56] (1996)	Cross-over study. Physician-selected ventilator settings vs ALV-selected settings. 20-min observation times. (n = 30; 20 adults, 10 children)	Airway flow, pressure, end-tidal CO_2, ventilator settings, blood gases, compliance, resistance, hemodynamic variables, dead space, time constant, f, V_T, $\dot{V}_E$, PIP, mean airway pressure	ALV settings provided similar gas exchange and patient comfort at lower peak and mean airway pressure	III: Prospective, randomized, cross-over study	B
Weiler[57] (1996)	Conventional ventilation vs ALV. Patients undergoing surgery in the extreme lateral decubitus position. (n = 20)	Airway flow, pressure, end-tidal CO_2, ventilator settings, blood gases, compliance, resistance, hemodynamic variables, dead space, time constant, f, V_T, $\dot{V}_E$, PIP, mean airway pressure	Position change reduced compliance, which caused the ALV algorithm to decrease V_T and PIP while increasing f	III: Prospective, randomized, cross-over study	B
Weiler[58] (1998)	Conventional ventilation vs ALV. Patients undergoing thoracic surgery and 1-lung ventilation (n = 9)	Airway flow, pressure, end-tidal CO_2, ventilator settings, blood gases, compliance, resistance, hemodynamic variables, dead space, time constant, f, V_T, $\dot{V}_E$, PIP, mean airway pressure	With 1-lung ventilation the ALV algorithm reduced PIP and V_T while increasing f to maintain $\dot{V}_E$, whereas conventional ventilation increased PIP and required operator intervention	III: Prospective, randomized, cross-over trial	B
Sulzer[59] (2001)	Prospective, randomized study. ASV weaning vs conventional weaning, after cardiac surgery (n = 36; 20 conventional weaning, 16 ASV)	Duration of intubation, sedation requirement, number of blood gas analyses	ASV patients had fewer blood gas analyses (3 vs 4), shorter time until extubation (3.2 vs 4.1 h), and fewer ventilator manipulations	II: Prospective, randomized controlled trial	B
Tassaux[60] (2002)	Prospective, cross-over study. ASV vs SIMV plus pressure-support, during weaning (n = 10)	Respiratory mechanics, $P_{0.1}$, sternocleidomastoid electromyography, blood gases, hemodynamics	ASV resulted in higher V_T and lower f. Sternocleidomastoid activity was significantly less with ASV. No difference in $\dot{V}_E$	III: Prospective, cross-over trial with short-term observation	B
Cassina[61] (2003)	Prospective study. ASV during weaning from mechanical ventilation after cardiac surgery (n = 155)	Airway pressure, volume, and flow, time to extubation, ease of use	All patients except 1 weaned in <6 h. Average time to extubation was 3.6 h	III: Prospective, observational study	C
Petter[62] (2003)	Prospective, randomized study. ASV weaning vs conventional SIMV weaning, after cardiac surgery (n = 34)	Duration of intubation, ICU stay, ventilator variables, number of ventilator manipulations	ASV patients had lower PIP (17.5 vs 22 cm H_2O), fewer ventilator manipulations (2.4 vs 4 per patient), and fewer high-pressure-alarm conditions (0.7 vs 2.9). No difference in duration of intubation or ICU stay	II: Prospective, randomized controlled trial	B

ASV = adaptive support ventilation
ALV = adaptive lung ventilation (ASV with the addition of end-tidal CO_2)
COPD = chronic obstructive pulmonary disease
$P_{0.1}$ = airway occlusion pressure 0.1 s after the onset of inspiratory effort
f = respiratory frequency
V_T = tidal volume
$\dot{V}_E$ = minute volume
PIP = peak inspiratory pressure
SIMV = synchronized intermittent mandatory ventilation
ICU = intensive care unit

Wrigge et al studied patients breathing spontaneously during airway pressure-release ventilation (APRV) with and without ATC.[69] ATC significantly reduced WOB and increased $\dot{V}_E$ without any hemodynamic interference. Haberthur et al compared ATC, T-piece, and PSV as techniques applied during SBT, with 90 patients.[70] There were no differences in extubation success between the 3 techniques. The patients who failed SBT with T-piece or PSV were all extubated following a trial of ATC, but the importance of that finding is unclear. The only defensible conclusion from this study appears to be that ATC is an alternative SBT method, but it is not superior to other SBT methods.

Oczenski et al compared ATC, PSV, and CPAP during SBT after cardiac surgery, measuring oxygen consumption, breathing pattern, blood gases, and hemodynamic differences.[71] They found no difference in any of the measured variables. Cohen et al performed a similar trial, comparing ATC to PSV during SBT, and they also found no differences between the 2 techniques.[72]

Fujino et al used a lung model to evaluate ATC with the Puritan Bennett 840. They found that as ETT diameter was decreased, the ability of ATC to completely account for the imposed WOB decreased as well.[73] Kuhlen et al[74] and Sasaki[75] each compared ATC to PSV during weaning and found no advantage with either technique.

ATC is currently available on the Evita 4 and Puritan Bennett 840 ventilators. The role of ATC remains to be determined. The evidence identified for the present review does not suggest any superiority of ATC over PSV or other methods during weaning (Table 8). In isolated cases ATC appears to match patient ventilatory timing better than PSV, preventing overdistention, PEEPi, and patient-ventilator asynchrony. However, the evidence for that effect is strictly anecdotal. Clearly, ATC will remain an option, but its future will depend on our understanding of how and when to use it.

Airway Pressure-Release Ventilation

APRV produces alveolar ventilation as an adjunct to CPAP. Airway pressure is transiently released to a lower level, after which it is quickly restored to reinflate the lungs. For a patient who has no spontaneous breathing efforts, APRV is similar to pressure-controlled inverse-ratio ventilation, but unlike pressure-controlled inverse-ratio ventilation, APRV allows spontaneous breathing at any time during the respiratory cycle. The distinguishing feature of APRV is the maintenance of spontaneous breathing. All the proposed advantages of APRV (improved gas exchange, reduced dead space, decreased requirement for sedation and analgesia, and improved hemodynamics) owe to the preservation of spontaneous breathing. Since PIP during APRV does not exceed the CPAP level, the hazards associated with high airway pressure (eg, alveolar overdistention, hemodynamic compromise) may be minimized. V_T for the APRV breath depends on lung compliance, airways resistance, the magnitude and duration of the pressure release, and the magnitude of the patient's spontaneous breathing efforts. Of concern is the potential for alveolar derecruitment during the pressure release.

Biphasic intermittent positive airway pressure (BIPAP) is a modification of APRV. Unlike APRV the inspiratory-expiratory ratio used with BIPAP is normal. BIPAP is also partially synchronized to the patient's inspiratory efforts, allowing the inspiratory and expiratory times to be reduced by as much as 25%, based on the patient's respiratory efforts. Without spontaneous breathing, BIPAP is similar to PCV. Stock et al were first to describe APRV and are credited with its introduction.[76]

Stock et al found that with canines APRV was associated with lower PIP and better oxygenation than was continuous mandatory ventilation.[76] Garner et al performed the first patient trial, with 14 adults, and confirmed the animal-study findings.[77] Rasanen et al (from the same research group) studied APRV with canines and found that APRV resulted in less circulatory interference than did continuous mandatory ventilation.[78] Martin et al used a neonatal lamb model of oleic-acid injury and found that APRV provided similar gas exchange at lower PIP.[79] A multi-institution trial of APRV, which included 50 patients, showed that APRV successfully controlled P_{aCO_2} in 47 patients.[80] As in previous trials APRV was associated with significantly lower PIP (55%) than was conventional ventilation. Additional trials with patients in acute respiratory failure,[81] after cardiac surgery,[82] and in postoperative respiratory failure[83] again confirmed that APRV provided similar gas exchange and lower PIP than conventional ventilation.

Putensen et al conducted an animal study in which they used the multiple inert-gas elimination technique (MIGET) and found that APRV provided better ventilation/perfusion ($\dot{V}/\dot{Q}$) matching than PSV.[84] That report confirmed the contention that the role of APRV is to establish lung volume and allow spontaneous breathing. The $\dot{V}/\dot{Q}$ differences were all associated with the presence of spontaneous breathing.

Sydow et al compared APRV to volume-controlled inverse-ratio ventilation, with 18 patients in acute respiratory failure.[85] Each mode was provided in random sequence for 24 h. APRV provided better gas exchange and lower PIP.

Calzia et al introduced the term "biphasic CPAP" in a study with 19 patients after coronary bypass surgery.[86] They compared biphasic CPAP to PSV and found that PTP and WOB were both greater during biphasic CPAP. Rathgeber et al performed the largest trial of any reviewed in the present report; they compared continuous manda-

Table 8. Studies of Automatic Tube Compensation

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Fabry[65] (1997)	ATC vs PSV. 10 subjects with normal lungs, 6 with lung injury (n = 16)	V_T, f, $\dot{V}_E$, WOB	Lung injury patients had better comfort and lower WOB with ATC. ATC adapted to the patients' breathing patterns	III: Prospective, cross-over trial	C
Guttmann[66] (1997)	ATC during inspiration only vs ATC during inspiration and expiration. Healthy volunteers breathing through an ETT with PSV (n = 10)	Subjective volunteer assessment of comfort, V_T, $\dot{V}_E$, f, flow	ATC was perceived as more comfortable than PSV. Discomfort during PSV was thought to be due to overinflation.	III: Prospective, single blind, cross-over study	C
Haberthur[67] (2000)	CPAP vs PSV 5, 10, and 15 cm H_2O vs ATC. Tracheostomized patients (n = 10)	Total WOB and WOB due to the airway	ATC eliminated ETT WOB without causing higher V_T than PSV	III: Prospective, cross-over trial	B
Mols[68] (2000)	PSV vs ATC. Normal volunteers breathing through an ETT or mouthpiece (n = 10)	V_T, f, $\dot{V}_E$, maximum inspiratory and expiratory pressure, inspiratory and expiratory comfort, flow, respiratory pattern	ATC was perceived as more comfortable. PSV had large V_T, causing discomfort. Timing was better with ATC	III: Observational, cross-over trial	C
Wrigge[69] (2001)	APRV with vs without ATC (n = 14)	Airway pressure, transdiaphragmatic pressure, tracheal pressure, $\dot{V}_E$, V_T, f, blood gases, end-expiratory pressure, hemodynamics	Adding ATC to APRV increased $\dot{V}_E$ and reduced WOB without adversely affecting hemodynamics	III: Randomized, prospective, cross-over trial with short-term observations	B
Haberthur[70] (2002)	Compare 3 SBT methods. Randomized block design of ATC, PSV (5 cm H_2O), and T-piece for 2-h SBT (n = 90)	Tolerance of SBT, f, V_T, f/V_T, S_{pO_2}, heart rate, reintubation	No difference in extubation success/failure rate. Half of patients who failed SBT with T-piece or CPAP were successfully weaned with ATC	III: Randomized controlled trial	B
Oczenski[71] (2002)	CPAP vs ATC vs PSV (5 cm H_2O). Patients after cardiac surgery. 30-min observation periods (n = 21)	Oxygen consumption, breathing pattern, blood gases, hemodynamics	No difference in any measured variables	III: Prospective, randomized trial	B
Cohen[72] (2002)	ATC vs CPAP (n = 43)	f/V_T, $\dot{V}_E$, successful extubation, peak pressure, $P_{0.1}$	f/V_T measured at the end of the SBT was the best predictor of successful extubation	III: Prospective cohort study	B
Fujino[73] (2003)	ATC vs PSV. Lung model.	Simulated WOB, PTP	ATC with the PB840 was equivalent to 4 cm H_2O PSV	V: Bench study	C
Kuhlen[74] (2003)	ATC vs T-piece vs PSV (7 cm H_2O). 30-min SBTs during weaning (n = 12)	Breathing pattern, work load, PTP, WOB	PSV reduced WOB and PTP. WOB and PTP were similar during ATC and T-piece SBTs	III: Prospective, cross-over trial	B
Sasaki[75] (2003)	ATC vs PSV (5 cm H_2O) vs ATC-plus-PSV (5 cm H_2O). Post-esophagectomy patients (n = 10)	V_T, f, $\dot{V}_E$, duty cycle, f/V_T	PSV was equivalent to ATC with these patients, who had normal respiratory mechanics. During PSV V_T was higher and f was lower.	III: Prospective, cross-over trial	C

AC = assist control
ATC = automatic tube compensation
CPAP = continuous positive airway pressure
f = respiratory frequency
$P_{0.1}$ = airway occlusion pressure 0.1 s after the onset of inspiratory effort
PB840 = Puritan Bennett 840 ventilator
PEEPi = intrinsic PEEP
PTP = pressure-time product
S_{pO_2} = arterial oxygen saturation measured via pulse oximetry
V_T = tidal volume
ARF = acute respiratory failure
COPD = chronic obstructive pulmonary disease
ETT = endotracheal tube
IMV = intermittent mandatory ventilation
PAV = proportional assist ventilation
PEEP = positive end-expiratory pressure
PSV = pressure support ventilation
SBT = spontaneous breathing trial
$\dot{V}_E$ = minute volume
WOB = work of breathing

Table 9. Studies of Airway Pressure-Release Ventilation and Biphasic Ventilation

First Author	Study Design	Measurements	Findings	Evidence Level	Grade
Stock[76] (1987)	APRV vs IPPV. Dogs with ALI. (n = 10)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$	Hemodynamics were not different at equivalent $\dot{V}_E$. With APRV PIP and physiologic dead space were lower, mean airway pressure was higher, and oxygenation was better.	V: Animal study, small n, and short-term observations	C
Garner[77] (1988)	APRV vs conventional ventilation, Patients after cardiac surgery. (n = 14)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$	Similar oxygenation and ventilation at lower peak airway pressure	III: Observational, cross-over trial	C
Rasanen[78] (1988)	APRV vs conventional ventilation vs CPAP. Anesthetized dogs. (n = 10)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$	APRV had similar effects on blood gases but with significantly fewer adverse hemodynamic effects	V: Animal studies, small n, and short-term observations	C
Martin[79] (1991)	APRV vs CPAP vs conventional ventilation vs spontaneous breathing. Neonatal sheep with oleic-acid lung injury. (n = 7)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$	APRV increased $\dot{V}_E$ more than CPAP. APRV provided similar gas exchange to conventional ventilation, but with fewer adverse hemodynamic effects	V: Animal studies, small n, and short-term observations	C
Davis[83] (1993)	APRV vs SIMV. Surgery patients with ALI. (n = 15)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$	APRV provided similar gas exchange with lower PIP, but no hemodynamic advantage was identified	III: Prospective, cross-over trial with short-term observations	C
Putensen[84] (1994)	APRV (with and without spontaneous breathing) vs PSV. Anesthetized dogs. (n = 10)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$, ventilation/perfusion determined by multiple-inert-gas-elimination technique	PSV had highest $\dot{V}_E$. APRV had higher cardiac output, P_{aO_2}, and oxygen delivery. APRV had better $\dot{V}/\dot{Q}$ and less dead space	V: Animal studies, small n, and short-term observations	C
Sydow[85] (1994)	APRV vs volume-controlled inverse-ratio ventilation. Patients with ALI. 24-h observation periods. (n = 18)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$	APRV provided 30% lower PIP, less venous admixture (14 vs 21%), and better oxygenation. No difference in hemodynamics	III: Prospective, randomized, cross-over trial	B
Calzia[86] (1994)	BiPAP vs CPAP. Patients after bypass surgery. (n = 19)	WOB and PTP	No difference	III: Prospective, cross-over trial	B
Rathgeber[87] (1997)	BiPAP vs conventional ventilation vs SIMV. Patients after cardiac surgery. (n = 596)	Duration of intubation, sedation requirement, analgesia requirement	APRV had shorter duration of intubation (10 h) than SIMV (15 h) or conventional ventilation (13 h). Conventional ventilation was associated with greater doses of midazolam. APRV was associated with less need for analgesia.	II: Prospective, randomized, controlled, open trial over 18 months, uneven randomization	B
Kazmaier[89] (2000)	BiPAP vs SIMV vs PSV. Patients after coronary artery bypass. (n = 24)	Blood gases, hemodynamics, lung volume, airway pressure, f, V_T, $\dot{V}_E$	No differences in blood gases or hemodynamics	III: Prospective, cross-over trial with short-term observations	B
Putensen[93] (2001)	APRV vs pressure-controlled conventional ventilation. Patients with ALI after trauma. (n = 30)	Gas exchange, hemodynamics, sedation requirement, hemodynamic support, duration of ventilation, ICU stay	APRV was associated with fewer ICU days, fewer ventilator days, better gas exchange, better hemodynamic performance, better lung compliance, and less need for sedation and vasopressors	II: Randomized controlled, prospective trial, small n. The conventional ventilation group received paralysis for the first 3 days, potentially confounding results	C

APRV = airway pressure-release ventilation
IPPV = intermittent positive-pressure ventilation
ALI = acute lung injury
f = respiratory frequency
$\dot{V}_E$ = minute volume
V_T = tidal volume
PIP = peak inspiratory pressure
CPAP = continuous positive airway pressure
PSV = pressure support ventilation
V/Q = ventilation/perfusion ratio
BiPAP = bilevel positive airway pressure
SIMV = synchronized intermittent mandatory ventilation
WOB = work of breathing
PTP = pressure-time product
ICU = intensive care unit

tory ventilation, IMV, and biphasic CPAP, with 596 post-cardiac-surgery patients.[87] Patients were randomized to the 3 groups, but the continuous mandatory ventilation group contained 123 patients, the IMV group 431 patients, and the biphasic CPAP group only 42 patients. Patients in the biphasic CPAP group had about 3–4 h shorter duration of intubation. Patients in the continuous mandatory ventilation group required greater sedation and analgesia than those in the IMV or biphasic CPAP group. Rathgeber et al concluded that the maintenance of spontaneous breathing during biphasic CPAP improves patient comfort and thus reduces pain and anxiety.

Staudinger et al compared the oxygen cost of breathing during BIPAP and PSV with 20 patients receiving long-term ventilation in a medical intensive care unit.[88] They found no difference in any of the measured variables. They concluded that both BIPAP and PSV are acceptable for partial ventilatory support of those patients.

Kazmaier et compared BIPAP, SIMV, and PSV with 24 patients after cardiac surgery, and found no difference in gas exchange or hemodynamic variables.[89] PIP was lower with BIPAP than with SIMV or PSV.

In an animal study of oleic-acid lung injury, Neumann and Hedenstierna found that APRV provided better oxygenation than did CPAP, owing to the higher mean airway pressure.[90]

In a comparison of APRV and PSV at equal airway pressures Putensen et al found that APRV provided better $\dot{V}/\dot{Q}$ matching with patients who had acute lung injury.[91] That study evaluated APRV with and without patient spontaneous breathing and again highlighted the importance of spontaneous breathing for $\dot{V}/\dot{Q}$ matching.

Kaplan et al studied 12 acute-lung-injury patients and compared APRV to pressure-controlled inverse-ratio ventilation.[92] APRV provided lower airway pressure, better cardiac performance, and was associated with less vasopressor use. That may have been due to the positive effects of spontaneous breathing or the lower PEEPi with APRV.

Perhaps the most-often-cited study of APRV versus continuous mandatory ventilation is the study by Putensen et al, which included 30 trauma patients suffering acute respiratory distress syndrome.[93] They randomized patients (15 in each group) to receive APRV or pressure-controlled continuous mandatory ventilation. The APRV group had better gas exchange, hemodynamic performance, and lung compliance, and required less sedation and fewer vasopressors. The APRV group had shorter duration of ventilation (15 vs 21 d) and shorter intensive care unit stay (23 vs 30 d). But these results are tempered by the fact that patients in the continuous mandatory ventilation group were paralyzed and sedated for the first 3 days, to eliminate spontaneous breathing. That seemingly important intervention, required to determine the importance of spontaneous breathing, may have resulted in additional disadvantage in the continuous mandatory ventilation group. The authors of that trial are experienced, skilled clinical trialists, but in an effort to ensure scientific integrity, they may have introduced a flaw into the design.

APRV can hardly be considered a new mode at this point. The evidence is strong that APRV provides lower PIP than does continuous mandatory ventilation (Table 9). However, the evidence that APRV is associated with better hemodynamic performance and less need for sedation and vasopressors is not as strong (evidence level III).

Summary

Ventilator technology advances at an alarming rate. Evidence is lacking that any ventilation mode provides better outcomes, though there are potential advantages suggested by surrogate physiologic variables. Principles of ventilation are probably more important than the mode used to honor those principles. As an example, lung-protective ventilation can be accomplished with APRV, dual-control pressure-control, or ASV. SBTs can be accomplished with CPAP or ATC. The key to ventilator application is the bedside caregiver's understanding of the ventilation mode's functioning. Clinicians must strive to be good consumers, to evaluate the technology based on evidence-proven merit, and implement only the modes and approaches that benefit patient care.

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