Adaptive Support Ventilation and Lung-Protective Ventilation in ARDS

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BACKGROUND: Adaptive support ventilation (ASV) is a partially closed-loop ventilation mode that adjusts tidal volume (V_T) and breathing frequency (f) to minimize mechanical work and driving pressure. ASV is routinely used but has not been widely studied in ARDS. METHODS: The study was a crossover study with randomization to intervention comparing a pressure-regulated, volume-targeted ventilation mode (adaptive pressure ventilation [APV], standard of care at Beth Israel Deaconess Medical Center) set to V_T 6 mL/kg in comparison with ASV mode where V_T adjustment is automated. Subjects received standard of care (APV) or ASV and then crossed over to the alternate mode, maintaining consistent minute ventilation with 1–2 h in each mode. The primary outcome was V_T corrected for ideal body weight (IBW) before and after crossover. Secondary outcomes included driving pressure, mechanics, gas exchange, mechanical power, and other parameters measured after crossover and longitudinally. RESULTS: Twenty subjects with ARDS were consented, with 17 randomized and completing the study (median P_{aO_2}/F_{IO_2} 146.6 [128.3–204.8] mm Hg) and were mostly passive without spontaneous breathing. ASV mode produced marginally larger V_T corrected for IBW (6.3 [5.9–7.0] mL/kg IBW vs 6.04 [6.0–6.1] mL/kg IBW, $P = .035$). Frequency was lower with patients in ASV mode (25 [22–26] breaths/min vs 27 [22–30)] breaths/min, $P = .01$). In ASV, lower respiratory-system compliance correlated with smaller delivered V_T/IBW ($R^2 = 0.4936$, $P = .002$). Plateau (24.7 [22.6–27.6] cm H_2O vs 25.3 [23.5–26.8] cm H_2O, $P = .14$) and driving pressures (12.8 [9.0–15.8] cm H_2O vs 11.7 [10.7–15.1] cm H_2O, $P = .29$) were comparable between conventional ventilation and ASV. No adverse events were noted in either ASV or conventional group related to mode of ventilation. CONCLUSIONS: ASV targeted similar settings as standard of care consistent with lung-protective ventilation strategies in mostly passive subjects with ARDS. ASV delivered V_T based upon respiratory mechanics, with lower V_T and mechanical power in subjects with stiffer lungs. *Key words: ASV; ARDS; mechanical ventilation; driving pressure; transpulmonary pressure; esophageal balloon; lung-protective ventilation.* [Respir Care 2022;67(12):1542–1550. © 2022 Daedalus Enterprises]

Introduction

Adaptive support ventilation (ASV) is a partially closed-loop mode of mechanical ventilation that continuously performs breath-by-breath evaluation of respiratory mechanics and patient effort to target a set minute ventilation by adjusting the breathing frequency (f) and tidal volume (V_T).[1,2] ASV determines the f-V_T combination aiming to minimize mechanical work of breathing and the applied force with each breath (using a proprietary interpretation and application of Otis and Mead equations) and the total peak pressures that can be directly limited by the clinician.[3] The ASV algorithm provides individual adjustment to the patient's specific pathophysiology secondary to variability in compliance, resistance, and expiratory time constant (RCexp) between different disease states, resulting in patients with high compliance and resistance receiving lower f and larger V_T, whereas patients with low compliance receive lower V_T and higher f.[4]

Treatment of ARDS is defined by lung-protective ventilation,[5] minimizing V_T and plateau pressures,[6] with a goal to reduce ventilation-induced lung injury[7] and improve mortality.[8] Additionally, retrospective analysis suggests that lower driving pressure (ΔP)[9,10] and mechanical power[11-13] are associated with improved outcomes. Whereas ASV has been extensively investigated during weaning and has demonstrated potential improved speed of extubation and shorter ICU length of stay,[2]

many of the potential benefits remain speculative including pilot data suggesting that ASV reduces applied mechanical power.[14] Despite lack of existing evidence, the underlying mechanism in ASV employing mechanical work, ΔP, and peak pressure limitation, which lowers V_T and limits applied pressures in response to low-compliance states, provides motivation to consider this mode during lung-protective ventilation in patients with ARDS. Preliminary data suggest that ASV may be safely applied in ARDS.[15] However, this requires further investigation and larger studies.

In this pilot investigation of subjects with ARDS, we aimed to compare the automated ASV settings with standard-of-care lung-protective ventilation strategy at Beth Israel Deaconess Medical Center (BIDMC) in Boston, Massachusetts, comparing V_T and other ventilator and mechanics parameters in a randomized open-label crossover study.

QUICK LOOK

Current knowledge

Adaptive support ventilation (ASV) is an automated partially closed-loop ventilation mode that adjusts breathing frequency and tidal volume (V_T) to maintain a set minute ventilation. Lung-protective ventilation settings are required in ARDS to prevent ventilator-induced lung injury, with limitation of V_T representing the highest-quality evidence for reduction of mortality.

What this paper contributes to our knowledge

This crossover study randomizing to order of ventilation mode compared standard-of-care lung-protective ventilation with V_T manually set to 6 mL/kg ideal body weight with ASV where V_T adjustment was automated. ASV targeted similar although marginally larger V_T compared with standard-of-care mode as well as similar driving pressures, plateau pressures, mechanics, and gas exchange. Notably, ASV targeted lower V_T than standard-of-care mode in subjects with low respiratory-system compliance as well as lower mechanical power. ASV settings were similar overall to the standard of care, as were individual adjustments based on subject physiology. Larger studies are needed to determine if this individual titration has clinical benefits.

Methods

Study Design and Population

This was a crossover study with randomization to order of intervention that was conducted between February 2018–November 2020 in ICUs of BIDMC, Boston, Massachusetts. The study was approved by the local institutional review board and registered in ClinicalTrials.gov under identifier NCT03715751. The study protocol is available in the supplementary material (Appendix 1 and 2, see related supplementary materials at http://www.rcjournal.com).

Subjects were eligible when undergoing mechanical ventilation, who were 18 y or older, and if they met the Berlin criteria for ARDS.[5] Although passive breathing was not a specific inclusion criteria, none of the subjects were triggering spontaneous breaths at the time of enrollment, with one demonstrating spontaneous breathing during data collection on day 1. Clinical team refusal, esophageal injury, or contraindication precluding placement of the esophageal balloon were the main exclusion criteria. Informed consent for enrollment was obtained from the legally authorized representative for each subject.

Study Interventions and Protocol

An esophageal balloon was inserted, if not already being used for clinical care, and positioning confirmed using depth, cardiac oscillations, and manual thoracic compressions to assure optimal placement.[16,17] Esophageal pressures (P_{es}) were used to estimate transpulmonary pressures (P_L = airway opening pressure [P_{ao}] − P_{es}), whereas flow and volume were recorded simultaneously.

Baseline measurements were obtained prior to randomization. Before initial randomization to a study group, all subjects were clinically optimized per standard-of-care lung-protective ventilation settings. This included adjustment of

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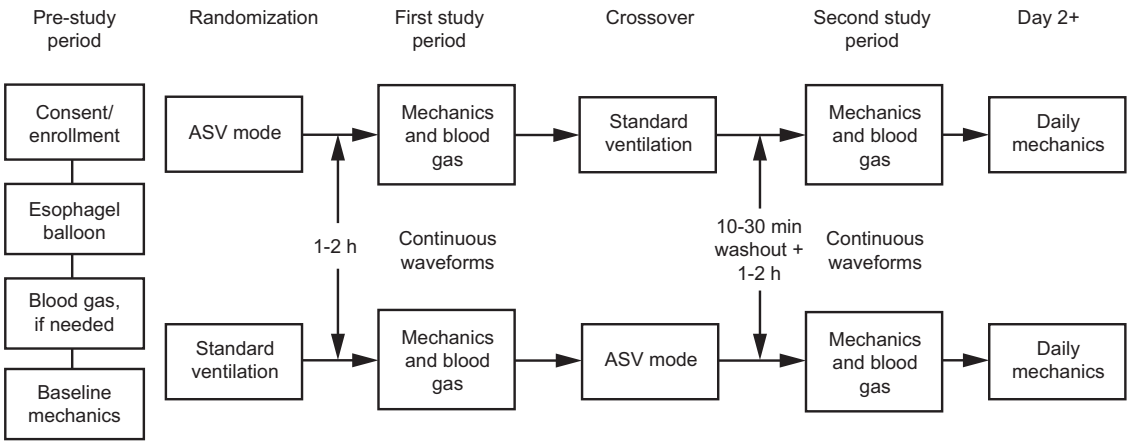

Fig. 1. Study schema. ASV = adaptive support ventilation.

PEEP using the esophageal balloon data, targeting an end-expiratory P_L 0 cm H_2O as per standard practice at BIDMC. Further adjustments were allowed if clinically indicated by the treating team; however, PEEP was required to be kept the same before and after crossover. As per standard of care at BIDMC, the V_T was changed to 6 mL/kg ideal body weight (IBW) if not already set. If the V_T was changed to target a different V_T, f was changed to target consistent minute ventilation. Lastly, F_{IO_2} was adjusted to achieve S_{pO_2} 95% to reduce need for further adjustment during the pre- and post-crossover data collection.

After baseline optimization, subjects were randomized with a nonsequential 1:1 utilizing a computer-generated randomization list to order of intervention, receiving either ASV mode or standard of care followed by crossover to the alternate mode. The randomization was performed by study team within a REDCap database. Standard-of-care ventilation mode at BIDMC was a pressure-regulated, volume-targeted mode called adaptive pressure ventilation (APV), a mode similar to pressure-regulated volume control modes. The randomization list was created by an independent statistician. Research and clinical teams were unblinded to the result of randomization. Of note, sedation and analgesic medications were maintained at the same levels before and after crossover. After randomization, a strict protocol was followed (with the schema in Fig. 1) (further detail in Appendix 1 and 2, see related supplementary materials at http://www.rcjournal.com).

After randomization to order of intervention, stable minute ventilation was maintained before and after crossover while in APV or ASV. Subjects were studied for 1–2 h in the initial mode and then switched to the alternate regimen for an additional 1–2 h. When in ASV, the V_T and f were determined by the automated mode. When returned to or continued on standard of care (APV), the V_T was set to 6 mL/kg and f adjusted to maintain consistent minute ventilation to prior. Mechanics, V_T, and blood gases were recorded at the end of each study period, which lasted up to 2 h. Blood gas measurements were provided to the clinical team for safety, with plans to restart data collection and crossover if the clinical team needed to make any changes to assure consistency before and after crossover.

After completion of day 1 measurements, the clinical team dictated all further care but subjects could be left on ASV if desired. Subjects on APV were titrated to support ventilation as deemed ready by treating team. For subjects on ASV after crossover, the treating team was encouraged to continue on ASV when weaning to support mode and to allow the algorithm to automatically make this transition. Subjects were followed with serial P_{ao}, P_L, P_{es}, flow, volume, and mechanics.

Outcomes

The primary end point was V_T (corrected for IBW) compared between standard-of-care lung-protective ventilation (APV set to 6 mL/kg) and ASV mode before and after crossover on day 1. At the termination of each 1–2 h recording before and after crossover, expiratory V_T was recorded in each mode as the average obtained from 10 sequential breaths.

The secondary end points comparing day 1 before and after crossover data included driving pressure, end-inspiratory and end-expiratory pressures of respiratory system, chest wall and transpulmonary systems, f, oxygenation, P_{aCO_2}, pH, P_{aO_2}, P_{aO_2}/F_{IO_2}, and P_{aCO_2} after 1–2 h in each mode before and after crossover. Additionally, inspiratory work of breathing was calculated from continuous recordings for each single breath from the area under the inspiratory limb of the airway pressure/volume curves. Averaged inspiratory work of breathing was then multiplied with f to calculate mechanical power in joules per minute as previously described[18] (Appendix 3, see related supplementary materials at http://www.rcjournal.com). Subjects were

monitored after day 1 with collection of mechanics and V_T, but these were not included as part of the primary analysis due to the small numbers and lack of crossover.

Adverse events were assessed by monitoring for events related to study procedures or ventilation mode, which included death, any life-threatening events believed to be related to study procedures, persistent disability greater than expected, esophageal injury, hemodynamic compromise, barotrauma, and any other complication related to the placement of the esophageal balloon (see Appendix 1 for full list of adverse events reporting, see related supplementary materials at http://www.rcjournal.com). Lastly, time to extubation, ICU length of stay, and in-hospital mortality as ascertained by medical record review were compared between subjects continuing on ASV and subjects receiving standard of care (APV) after the initial crossover period.

Statistical Analysis

The target sample size was determined utilizing previous data indicating mean V_T 6.2 mL/kg IBW (SD 0.9)[17] in standard volume control modes as well as preliminary data using ASV that reported mean V_T 6.4 mL/kg (SD 1.1). With an estimated correlation 0.30 between measurements pre- and post-crossover, alpha 0.05, and 80% power, and allowing for a margin up to 1 mL/kg in ASV to be considered equivalent, we calculated a need to recruit a total of 16 subjects with complete day 1 measurements. Assuming loss of roughly 4 subjects, we planned to enroll 20 for this pilot study. Sample size estimation was performed using SAS software (SAS Institute, Cary, North Carolina) by an independent statistician.

Baseline demographics as well as pre- and post-crossover measurements were displayed as median with interquartile range (IQR). Normality was assessed using Wilks-Shapiro test. Paired variables before and after crossover were compared with paired *t* test and Wilcoxon signed-rank test as indicated. Linear regression was used for comparison of continuous variables. Data from one subject were removed from linear regression comparing V_T with compliance and RCexp as V_T limitation occurred secondary to total pressure limits and was not secondary to usual ASV algorithm utilizing RCexp. Hierarchical mixed models were used for comparison of variables on subsequent study days (after day 1) with subject ID and day of measurement clustered with random effects. Estimated marginal means with 95% CI were used to display difference between study arms after day 1. Analysis was performed using Stata 14.2 (StataCorp, College Station, Texas).

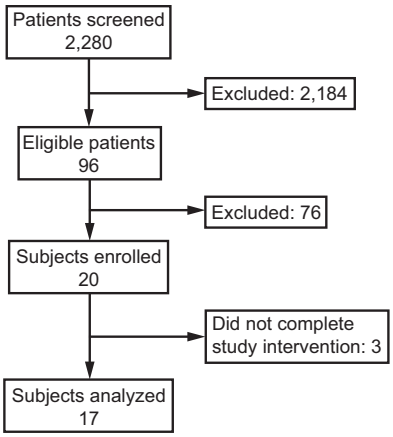

Fig. 2. Consort diagram with screened, eligible, and enrolled subjects.

Results

Study Population

A total of 20 subjects were consented; 17 were enrolled and underwent randomization and completed the study protocol with crossover comparison (Fig. 2). The 3 subjects who were consented but did not initiate the study and were not randomized were excluded because they were weaned off lung-protective ventilation to pressure support before study procedures were able to be initiated, and it was not clinically appropriate to re-sedate them for inclusion. Overall, subjects presented with moderate-severe ARDS (median P_{aO_2}/F_{IO_2} 146.6 [IQR 128.3–204.8]) and showed high morbidity with baseline Acute Physiology and Chronic Health Evaluation (APACHE) II 27 (21–32) and Sequential Organ Failure Assessment 12 (11–13). Baseline mechanics, driving pressure, and cause of ARDS are shown in Table 1.

Primary Outcome

V_T adjusted for IBW was higher in subjects receiving ASV (6.29 [5.87–6.99] mL/kg IBW vs 6.04 [6.01–6.06] mL/kg IBW, $P = .035$), with no statistical difference in uncorrected V_T (440.5 [393.4–497.4] mL vs 417.7 [392.7–440.8] mL, $P = .058$) (Table 2 and Fig. 3). During the period on ASV, there was a wider variability in V_T than in subjects receiving standard-of-care ventilation (APV) (Fig. 3A–B). Variability in V_T was primarily explained by range in compliance and RCexp between subjects (except in one subject where V_T was limited by ASV peak pressure limits). In the remaining subjects, RCexp and compliance demonstrated correlation with V_T ($R^2 = 0.52$, $P = .002$; and $R^2 = 0.34$, $P = .02$, respectively) and with V_T/IBW ($R^2 = 0.33$, $P = .02$; and $R^2 = 0.49$, $P = .002$, respectively) (Fig. 4), demonstrating that V_T was

Table 1. Characteristics of Study Subjects (N = 17)

Male	13 (76)
Age, y	57 (45–70)
White	13 (76)
Hispanic	2 (12)
Weight, kg	86.3 (73.5–92.1)
Predicted body weight, kg	68.0 (63.5–75.3)
APACHE II score	27 (21–32)
SOFA score	12 (11–13)
P_{aO_2}/F_{IO_2}, mm Hg	146.6 (128–205)
Glasgow coma scale	3 (3–8)
RASS score	−4 (−5 to −1)
ARDS risk factors	
Pneumonia	12 (70)
Sepsis	11 (65)
Surgery	1 (6)
Pancreatitis	5 (29)
Aspiration	3 (18)
Other	8 (47)
Arterial blood gas	
pH	7.34 (7.31–7.39)
P_{aCO_2}, mm Hg	42 (36–46)
P_{aO_2}, mm Hg	86 (71–102)
Baseline ventilator settings	
Adaptive pressure ventilation(pressure-regulated, volume-targeted mode)	17 (100)
F_{IO_2}	0.5 (0.4–0.6)
PEEP, cm H_2O	12 (10–16)
Breathing frequency, breaths/min	24 (22–30)
Set V_T, mL	420 (390–440)
Set V_T, mL/kg IBW	6.7 (6.0–7.5)
Minute ventilation, L/min	10.5 (8.8–11.7)
Baseline mechanics, cm H_2O or mL/cm H_2O	
Plateau pressure	24.4 (23.8–26.0)
Total PEEP	12.6 (10.4–16.2)
End inspiratory P_L	9.3 (7.5–11.3)
End expiratory P_L	0.2 (−1.1 to 1.3)
End inspiratory P_{es}	15.2 (13.8–18.7)
End expiratory P_{es}	12.7 (10.7–15.9)
Respiratory-system driving pressure	11.8 (9.8–14.1)
Transpulmonary driving pressure	8.9 (6.3–12.7)
Chest wall driving pressure	2.7 (2.1–3.8)
Respiratory-system compliance	34.0 (27.3–42.6)
Transpulmonary compliance	44.1 (36.8–62.3)
Chest wall compliance	134.6 (91.9–207.4)
Expiratory time constant, s	0.44 (0.39–0.54)
Subject outcomes	
Duration of mechanical ventilation, d	9 (6–20)
ICU LOS, d	12.5 (8.0–21.0)
Hospital LOS, d	25.8 (12.0–32.0)
Hospital mortality	8 (47)

Data are presented as n (%) or median (IQR).
APACHE II = Acute Physiology and Chronic Health Evaluation II
SOFA = Sequential Organ Failure Assessment
RASS = Richmond Agitation Sedation Scale
V_T = tidal volume
IBW = ideal body weight
P_{es} = esophageal pressure
P_L = transpulmonary pressure
LOS = length of stay

smaller in subjects with low compliance and larger in subjects with higher compliance.

Secondary Outcomes

Respiratory-system driving pressure (12.8 [9.0–15.8] cm H_2O APV vs 11.7 [10.7–15.1] cm H_2O ASV, $P = .29$) and plateau pressures (24.7 [22.6–27.6] APV vs 25.3 [23.5–26.8] ASV, $P = .14$) were similar (Table 2, Fig. 3C–D). Frequency was marginally lower in ASV (27 [22–30] breaths/min APV vs 25 [22–26] breaths/min ASV, $P = .01$). Lung and respiratory system mechanics including transpulmonary driving pressure, lung and respiratory-system compliance, plateau pressure, elastance, and RCexp were similar, as was gas exchange with P_{aCO_2}, P_{aO_2}, and P_{aO_2}/F_{IO_2} before and after crossover (Table 2). Calculated mechanical power was also similar before and after crossover (Table 2). However, in subjects with lower compliance, ASV decreased the applied mechanical power (Fig. 5A) particularly in the subset of subjects where V_T was reduced while in ASV (Fig. 5B).

There were no study-related adverse events noted in any subjects. One subject was taken off ASV at discretion of clinical team when switched into prone position to target ultralow V_T; however, this was not considered an adverse event, and the switch was performed after crossover measurements were obtained without impacting the primary and most of the secondary end points. Hemodynamics appeared to be similar in ASV and APV.

Three subjects completed the study with only day 1 measurements obtained (one due to prone positioning as above, one due to early extubation, and one due to being made comfort measures only with subsequent terminal extubation) and were included in the analysis of the primary end point. Eight of the remaining subjects who had been randomized were kept on ASV and were automatically transitioned within ASV mode from fully ventilator-controlled breathing to supported breaths at median 6 d (IQR 3–8). Subjects were followed for median 4 d (IQR 2–7), and there was no difference in V_T between ASV and control arms of study over the course of subsequent follow-up (Appendix 4, Supplemental Table, see related supplementary materials at http://www.rcjournal.com).

Discussion

In our cohort of mechanically ventilated subjects with ARDS, ASV provided a minor but statistically significant increase in V_T/IBW when compared to standard of care at BIDMC (APV). This difference was small in terms of absolute difference (~0.25 mL/kg), and the authors consider this difference to not be clinically relevant. Importantly, V_T during ASV ventilation were all within what is generally considered lung-protective ventilation range, <8 mL/kg.[6] Indeed, in a subset of subjects with lower compliance and

Table 2. Comparison Between Ventilator Modes Before and After Crossover on Day 1

Ventilation Mode ($N = 17$)	APV(Standard of Care)	ASV	P
V_T, mL	417.7 (392.7–440.8)	440.5 (393.4–497.4)	.058
V_T IBW, mL/kg	6.04 (6.01–6.06)	6.29 (5.87–6.99)	.035*
Breathing frequency, breaths/min	27 (22–30)	25 (22–26)	.01
Minute ventilation, L/min	10.4 (8.6–12.1)	10.5 (9.1–12.2)	.33
Plateau pressure, cm H_2O	24.7 (22.6–27.6)	25.3 (23.5–26.8)	.14
Total PEEP, cm H_2O	12.8 (10.4–15.1)	12.8 (10.6–15.5)	.44
End expiratory P_L, cm H_2O	0 (−1.7 to 1.8)	0.2 (−1.1 to 1.3)	.62
End inspiratory P_L, cm H_2O	8.7 (6.6–11.8)	8.6 (7.2–11.9)	.46
End expiratory P_{es}, cm H_2O	13.2 (12.1–15.3)	12.4 (11.0–16.3)	.72
End Inspiratory P_{es}, cm H_2O	15.5 (13.8–18.3)	15.2 (11.9–19.6)	.89
Respiratory-system driving pressure, cm H_2O	12.8 (9.0–15.8)	11.7 (10.7–15.1)	.29
Transpulmonary driving pressure, cm H_2O	7.8 (7.0–10.7)	8.3 (7.3–12.8)	.68
Chest wall driving pressure, cm H_2O	3.0 (1.6–3.9)	2.6 (2.3–4.3)	.95
Respiratory system compliance, mL/cm H_2O	33.2 (24.7–40.9)	35.3 (25.3–43.8)	.74
Transpulmonary compliance, mL/cm H_2O	44.6 (34.0–58.0)	49.5 (35.0–67.0)	.36
Chest wall compliance, mL/cm H_2O	139.0 (113.0–268.3)	119.3 (90.4–178.6)	.061
Expiratory time constant, s	0.42 (0.39–0.53)	0.47 (0.41–0.55)	.13
pH	7.40 (7.31–7.45)	7.40 (7.31–7.44)	.10
P_{CO_2}	42 (37–45)	39 (36–49)	.10
P_{aO_2}/F_{IO_2}	200 (150–235)	168.0 (146.0–207.5)	.22
Mechanical power, J/min	26.9 (23.8–37.9)	28.2 (22.2–36.4)	.84

Data are presented as median (IQR).
All comparisons made with paired t test except where indicated by *, which is indicative of nonparametric distribution and use of Wilcoxon paired signed-rank test.
APV = adaptive pressure ventilation
ASV = adaptive support ventilation
V_T = tidal volume
IBW = ideal body weight
P_L = transpulmonary pressure
P_{es} = esophageal pressure

short RCexp, ASV targeted *lower* V_T, demonstrating individual titration inherent to the ASV mode, tailoring lower V_T in subjects with stiffer lungs. Of note, in subjects who received a higher V_T in ASV, compliance was also higher with resulting driving pressures that remained at similar levels with control.[10,19] Other markers for ventilation parameters including respiratory-system and transpulmonary driving pressures, plateau pressures, and mechanics in each mode were similar, while achieving similar effectiveness in gas exchange, further reiterating similar ventilation that ASV provides in addition to the individualized parameters unique to subject's physiology and ventilation needs.

This individualization is of particular interest considering recent focus moving beyond V_T alone to identify improved markers of lung stress. ASV uses an underlying proprietary algorithm that determines best combination of V_T and f to limit degree of driving pressure applied to the lungs as well as to limit the applied mechanical work. Driving pressure initially gained interest in a large retrospective study demonstrating a strong link between driving pressure and mortality.[19] A recent paper furthered this concept in a retrospective data set including subjects randomized to high versus low V_T strategies, which suggested that limitation of V_T to target lower driving pressures only provides benefit in subjects with stiffer lungs.[20] Strict limitation of V_T in all subjects may not provide benefits we hope to achieve and may indeed result in increased sedation requirements to allow tolerance of these settings. A dynamic approach that tolerates larger V_T in some patients with higher compliance, with highly protective V_T in other patients with stiffer lungs, may be the future of personalized ventilation management. Extrapolation of our findings from this pilot study, the growing understanding of driving pressure as a clinical target, and the underlying algorithm of ASV, together illustrate the potential for individualized partially closed-loop modes such as ASV.

The concept of mechanical power has recently gained attention as a possible cause of lung injury as it incorporates not only the energy required to inflate the lung during a single breath but also the effect of total applied energy to the respiratory system over time.[12,21,22] Power is calculated by inte gration of pressure over volume change during a breath, multiplied by f, and can be directly calculated via waveforms or through a simple formula. Mechanical power is independently associated with higher in-hospital mortality, hospital length of stay, and fewer ventilator-free days even in subjects receiving low V_T,[12] and limitation of applied power has been postulated

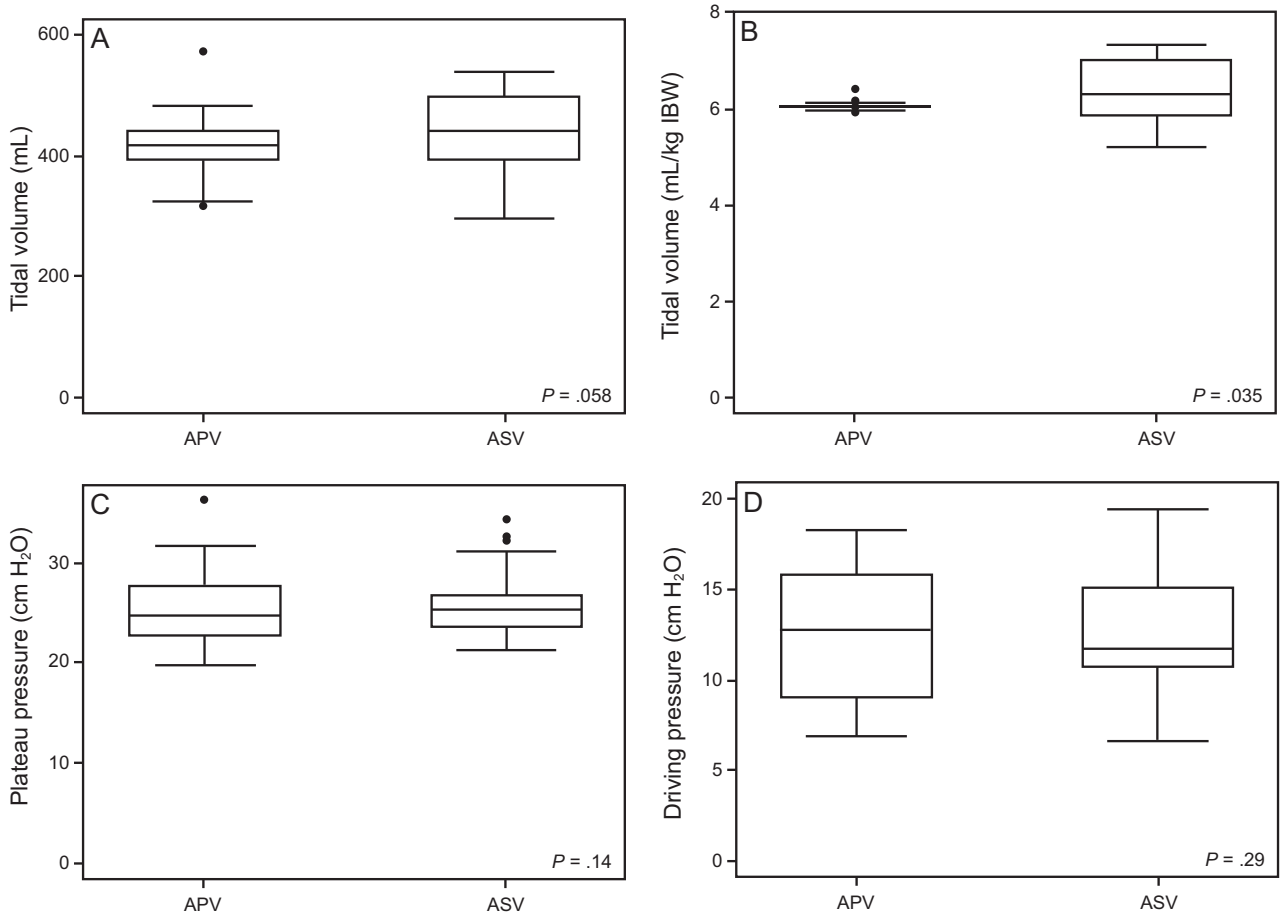

Fig. 3. Distribution box plots comparing the crossover between standard of care at Beth Israel Deaconess Medical Center, a pressure-regulated volume-targeted mode called adaptive pressure ventilation (APV), and adaptive support ventilation (ASV) mode. A: Tidal volume (V_T) (mL) comparison. $P = .058$. B: V_T/ideal body weight (IBW) (mL/kg). $P = .035$. C: Plateau pressure (cm H_2O). $P = .14$. D: Driving pressure (cm H_2O). $P = .29$. $N = 17$ subjects with crossover measurements. Statistical comparison performed via paired *t* test (A, C, and D) and Wilcoxon paired signed-rank test (B) due to nonparametric distribution. Star indicates statistical significance.

to decrease the risk for developing lung injury. The application of the Otis formula in ASV has serendipitously gained interest due to the formula solving for f that minimizes the work of breathing in spontaneously breathing patients. Whereas this is clearly a different work of breathing measurement than energy applied from the ventilator (the newer concept), this has raised interest in examining ASV for its ability to provide limitations in applied mechanical power.[14] In our study, although mechanical power was overall similar between modes, lower compliance correlated with decrease in mechanical power while in ASV. This decrease in power seemed to be primarily driven by decrease in V_T. Targeted limitation of mechanical power and ventilation strategies that facilitate this warrant further large-scale investigation.

Notably, the secondary outcomes including driving pressure, end-inspiratory and expiratory respiratory system, chest wall and P_L, V_T, f, oxygenation, and CO_2 clearance were similar before and after crossover, making the argument again that ASV seems to be generally equivalent to the standard of care within this population of ARDS during passive mechanical ventilation.

Whereas safety was not specifically tested for in this study, there were no adverse events during use of ASV. Additionally, the similar overall settings compared with standard of care (APV) were suggestive that ASV could be applied as a reasonable alternative in subjects with ARDS with parameters within clinically acceptable goal ranges. Of note, the mode was less commonly applied in the very sickest subjects (with only 2 subjects with $P_{aO_2}/F_{IO_2} < 100$ mm Hg), although this was not intentional by study team. Additionally, study did not look at use during prone positioning, although there is no reason to suspect that the mode would not perform as expected. Nonetheless, eliminating clinician control of specific V_T was felt by some providers as a barrier for its use. The authors believe this is more an issue of education and experience with the mode rather than a weakness specific to the mode itself.

There are several important limitations to this study that bear mentioning. The total number of subjects who were

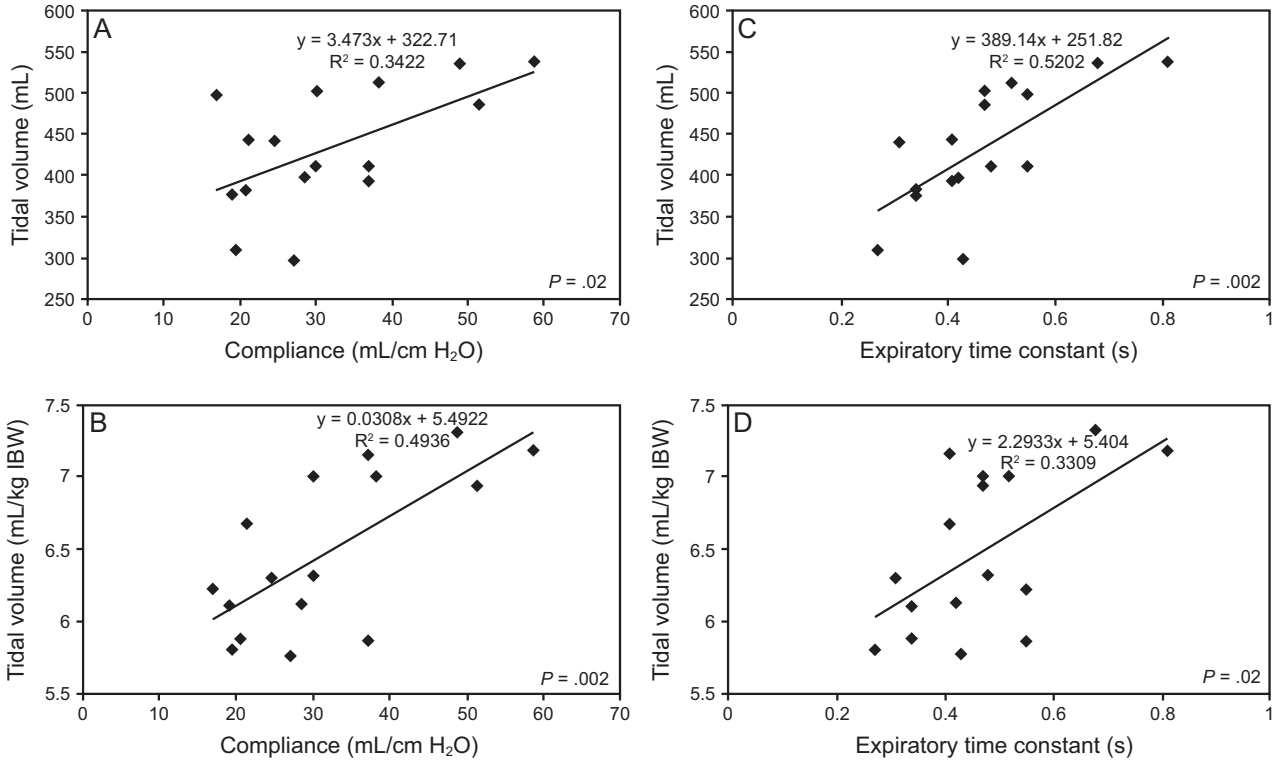

Fig. 4. Adaptive support ventilation (ASV) adjusts tidal volume (V_T) and breathing frequency (f) on a breath-to-breath basis based upon expiratory time constant (RCexp), which is product of resistance and compliance. Figures include $n = 16$ subjects, with one patient not included due to V_T being set by ASV pressure limits. A and B: V_T and V_T/IBW have strong linear correlation to respiratory-system compliance. C and D: Similarly, V_T and V_T/IBW also have strong linear correlation with RCexp. Correlations were performed using linear regression.

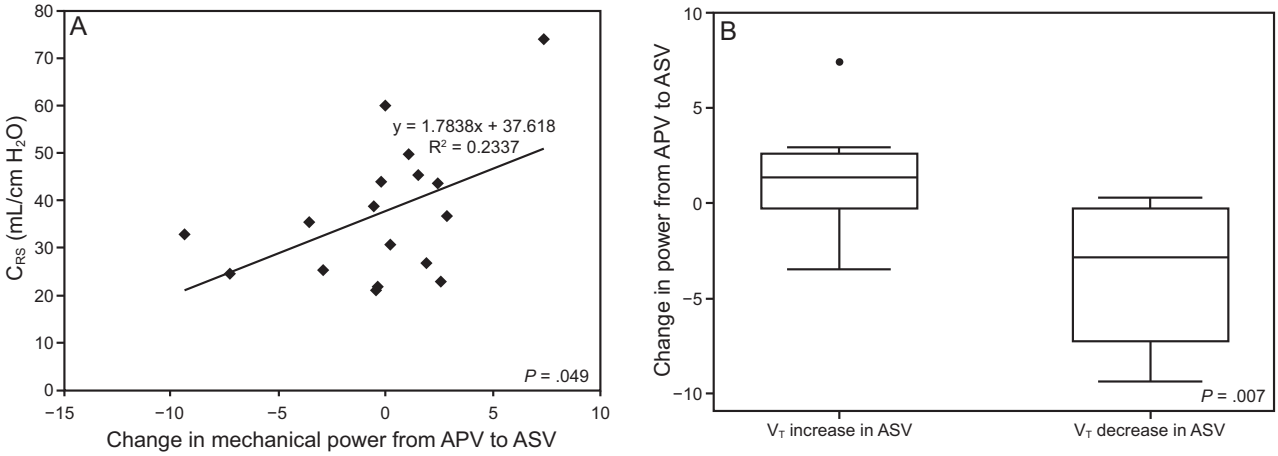

Fig. 5. Inspiratory work of breathing was calculated from continuous recordings for each single breath from area under inspiratory limb of airway pressure/volume curves. Averaged inspiratory work of breathing was then multiplied with breathing frequency to calculate mechanical power in joules per minute. A: Comparison of respiratory-system compliance with change in mechanical power from adaptive pressure ventilation (APV) (pressure-regulated, volume-targeted standard of care used at Beth Israel Deaconess Medical Center) to adaptive support ventilation (ASV) demonstrates linear correlation ($R^2 = 0.2337$, $P = .049$). This correlation shows that in subjects with stiffer lungs ASV lowers delivered mechanical power. B: Bar graph comparing subjects with increased V_T ($n = 12$) and subjects with decreased V_T ($n = 5$) when transitioned to ASV mode, showing a significant decrease in applied mechanical power in this subgroup of subjects.

enrolled was small; however, the crossover allowed for improved ability to directly compare modes and address the primary end point. Although there were no adverse events with the mode, as mentioned the duration of each crossover period and enrolled numbers preclude any true comparison of safety. Additionally, use in sickest subjects with very low P_{aO_2}/F_{IO_2} and prone positioning was not validated in this study, although there is no reason to suspect that the mode would perform differently under these circumstances. This was a single-center study, potentially limiting its generalizability; however, ASV was not commonly used at start of study, suggesting ease of implementation over time. There was minimal spontaneous activity during day 1 measurements before and after crossover, so parameters during spontaneous breathing were not tested for in primary and secondary end points. This study was not powered to detect differences in V_T beyond the initial study day, nor was it powered to detect differences in other parameters including outcomes as this was not the purpose of this pilot study. Extrapolations based upon mechanical power and driving pressure remain speculative but important to discuss.

Conclusions

ASV is a partially closed-loop mechanical ventilation mode that applies patient-specific tailored ventilation that continuously evolves with the patient's mechanics. In this cohort of subjects with ARDS, ASV was found to provide marginally larger V_T but otherwise similar ventilation parameters to what is considered standard of care at BIDMC. These preliminary pilot data suggest that this mode could be used in many patients with ARDS interchangeably with the current standard of care. Automated modes of ventilation may represent an important future direction of mechanical ventilation; demonstrating application of these modes in ARDS is important. ASV appeared to provide similar overall care to standard lung-protective ventilation in passive subjects, while also providing individually titrated care. These pilot data provide rationale for larger studies focusing on automated modes in subjects with ARDS.

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