A Randomized Prospective Trial of Airway Pressure Release Ventilation and Low Tidal Volume Ventilation in Adult Trauma Patients With Acute Respiratory Failure

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Background: Airway pressure release ventilation (APRV) is a mode of mechanical ventilation, which has demonstrated potential benefits in trauma patients. We therefore sought to compare relevant pulmonary data and safety outcomes of this modality to the recommendations of the Adult Respiratory Distress Syndrome Network.

Methods: Patients admitted after traumatic injury requiring mechanical ventilation were randomized under a 72-hour waiver of consent to a respiratory protocol for APRV or low tidal volume ventilation (LOVT). Data were collected regarding demographics, Injury Severity Score, oxygenation, ventilation, airway pressure, failure of modality, tracheostomy, ventilator-associated pneumonia, ventilator days, length of stay (LOS), pneumothorax, and mortality.

Results: Sixty-three patients were enrolled during a 21-month period ending in February 2006. Thirty-one patients were assigned to APRV and 32 to LOVT. Patients were well matched for demographic variables with no differences between groups. Mean Acute Physiology and Chronic Health Evaluation II score was higher for APRV than LOVT (20.5 ± 5.35 vs. 16.9 ± 7.17) with a p value = 0.027. Outcome variables showed no differences between APRV and LOVT for ventilator days (10.49 days ± 7.23 days vs. 8.00 days ± 4.01 days), ICU LOS (16.47 days ± 12.83 days vs. 14.18 days ± 13.26 days), pneumothorax (0% vs. 3.1%), ventilator-associated pneumonia per patient (1.00 ± 0.86 vs. 0.56 ± 0.67), percent receiving tracheostomy (61.3% vs. 65.6%), percent failure of modality (12.9% vs. 15.6%), or percent mortality (6.45% vs. 6.25%).

Conclusions: For patients sustaining significant trauma requiring mechanical ventilation for greater than 72 hours, APRV seems to have a similar safety profile as the LOVT. Trends for APRV patients to have increased ventilator days, ICU LOS, and ventilator-associated pneumonia may be explained by initial worse physiologic derangement demonstrated by higher Acute Physiology and Chronic Health Evaluation II scores.

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In 2000 the Adult Respiratory Distress Syndrome (ARDS) Network demonstrated that low tidal volume ventilation improved outcomes in patients with acute lung injury (ALI) and ARDS.[1] Interleukin-6 levels were lower in the group treated with 6 mL/kg tidal volumes, suggesting that lower tidal volumes reduced ventilator-induced lung injury and blunted the inflammatory cascade.[2,3] Organ failure, ventilator-free days, and mortality rates were significantly better in patients treated with reduced tidal volumes.

The results of this study established a standard of care for the treatment of hypoxic respiratory failure with reduced tidal volumes.[1] However, the study population was heterogeneous, and the majority of the patients had underlying medical disorders such as pneumonia, sepsis, and aspiration. Only 13% in the treatment group sustained trauma, thereby potentially limiting the strength of any conclusions in this subgroup.

The etiology of respiratory failure after multisystem trauma is multifactorial involving direct lung and chest wall injury, fluid sequestration within the lung after shock, resuscitation and reperfusion, and the elaboration of numerous inflammatory mediators from soft tissue and gastrointestinal sources.[4,5] Decreased lung compliance can be severe and elevated airway pressures may be necessary to prevent life-threatening hypoxia. Using low tidal volume ventilation (LOVT) may lead to derecruitment, repetitive shear forces, low volume lung injury, and further respiratory deterioration.[6,7]

Airway pressure release ventilation (APRV) has shown promise as a mode of mechanical ventilation in critically ill patients with ALI and ARDS.[8–12] In this pressure-limited, time-cycled mode of ventilation, alveolar recruitment occurs over extended periods of inspiration. A unique feature of APRV is a double-valve flow system that permits spontaneous respiration independent of the prescribed ventilator settings. Spontaneous ventilation may improve patient tolerance, aid in recruitment in dependent lung areas, and improve cardiovascular performance.[6,13–15] New generations of ventilators capable of using APRV make this modality readily available in the critical care setting.

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No prospective trials have compared the use of APRV directly with the lung protective ventilation. The present study is a randomized prospective trial comparing the outcomes between APRV and LOVT in critically ill patients with respiratory failure after multisystem trauma.

PATIENTS AND METHODS

Patients

Trauma patients admitted to the Surgical or Trauma ICU of our level I trauma center were eligible for enrollment if they required intubation and positive pressure ventilation for greater than 72 hours. Exclusion criteria were pregnancy, age younger than 18 years, legal incarceration, presence of a bronchopleural fistula, an immunocompromising disorder such as AIDS, Childs-Pugh Class B or C cirrhosis, terminal cancer, patients extubated before 72 hours or patients not immediately enrolled in the study after developing respiratory failure. Enrollment was permitted at any point during the hospitalization if respiratory failure was not present on admission. A 72-hour Institutional Review Board waiver of consent allowed early enrollment and time to locate appropriate family or surrogates for informed consent. Patients for whom informed consent was not obtained within 72 hours were excluded from the study protocol. Assignment to APRV or LOVT was determined by a randomization table that was generated for each of the two ICUs. On arrival to the ICU, patients were initiated into the study by the respiratory therapist after discussion with the on call trauma attending. Patients were transported throughout the hospital and to the operating room on their assigned ventilator mode obviating potential variances from the study protocol.

ALI was defined as partial pressure of arterial oxygen to fraction of inspired oxygen ratio (PaO_2/FiO_2) $\leq$ 300 and ARDS was defined as $PaO_2/FiO_2 \leq 200$ in the presence of bilateral pulmonary infiltrates without signs of congestive heart failure or left atrial enlargement. Pneumonia was defined by bronchoalveolar lavage with greater than 100,000 colony forming units growth of pathogenic bacteria in the face of leukocytosis and/or fever in patients with purulent sputum and/or a new or evolving infiltrate on chest radiograph. Timing of tracheostomy was determined at the discretion of the attending of record when it became evident that mechanical ventilation would be required for greater than 5 days to 7 days.

Ventilator Setup

The ventilators used in the study were Draeger EvitaXL and Draeger Evita 2dura (Draeger Medical Inc., Telford, PA). After enrollment, predicted body weight was determined and initial tidal volume was set at 6 cc/kg while on synchronized intermittent mandatory ventilation (SIMV).[1,16,17]

APRV

For patients entering the APRV study arm, the initial high pressure setting (P_H) was adjusted to equal the plateau pressure from the original SIMV settings. The low pressure setting was set at zero by convention. Time spent at P_H (T_H) was set based on spontaneous respiratory rate. Duration of the low pressure setting was adjusted, so pressure release terminated at 25% to 75% of peak expiratory flow. FiO_2 was initially set at 100%.

For hypoxic conditions (PaO_2 <65 mm Hg and/or arterial oxygen saturation [SaO_2] <92%), P_H was increased by 2 cm H_2O, followed by an increase in T_H by 0.5 seconds and then an increase in FiO_2 by 10%. This cycle was repeated as necessary to restore arterial oxygen levels.

Carbon dioxide retention was treated only in the setting of concomitant respiratory acidosis. If CO_2 was >50 mm Hg and arterial pH <7.35, then P_H was increased and T_H was subsequently decreased.

Weaning in APRV was initiated when PaO_2 >70 mm Hg, SaO_2 >92%, and pH >7.32 and was conducted on a time based protocol. The primary method used to wean APRV was an alternate decrease in P_H by 2 cm H_2O followed by an increase in T_H of 0.5 seconds to 1.0 seconds. This "drop and stretch" method was used to achieve a P_H of 12 cm H_2O on 40% FiO_2, at which time patients were evaluated for extubation or converted to low level continuous positive airway pressure (CPAP) if a tracheostomy was present. Figure 1, A displays a flow diagram for the APRV ventilator protocol.

Low Tidal Volume Ventilation

After initial ventilator setup, patients in the LOVT study arm remained on SIMV with pressure support. Initial minute ventilation was set at 6,000 mL and the ventilator rate was determined by dividing this amount by the set tidal volume. Positive end expiratory pressure and pressure support were set at 10 cm H_2O. FiO_2 was initially set at 100%. If spontaneous respirations were >26 breaths per minute, the ventilator rate, and/or pressure support were adjusted.

For hypoxic conditions, positive end expiratory pressure was increased in 2 cm H_2O increments, repeated twice as necessary, followed by an increase in FiO_2 of 10%. This cycle was repeated as necessary until $PaO_2 \geq 65$ mm Hg or $SaO_2 \geq 92\%$.

Respiratory acidosis was treated by increasing the ventilator rate by two breaths per minute as indicated. Pressure support settings could also be increased at the respiratory therapist's discretion to keep spontaneous respiratory rate <28 to 30 breaths per minute.

Weaning LOVT was conducted on a time-based protocol similarly to the APRV arm. The set ventilator rate was weaned as long as spontaneous respirations were <30 breaths per minute. When weaned off SIMV, patients were placed on CPAP and pressure support. Pressure support and CPAP were alternately weaned in increments of 2 cm H_2O to keep the spontaneous respiratory rate <30 breaths per minute and SaO_2 >92%. When CPAP was reduced to 5 cm H_2O and pressure support was 8 cm H_2O, patients were evaluated for extubation or placed on low level CPAP if a tracheostomy was present. Figure 1, B displays a flow diagram for the LOVT ventilator protocol.

Failure of Modality

APRV or LOVT failure was defined as the inability to maintain a $PaO_2 \geq 60$ mm Hg or a $PaCO_2$ <60 mm Hg and a pH $\geq$7.18. Patients who failed a modality were switched to the alternate study modality or any other modality that allowed successful treatment of the patient's respiratory failure.

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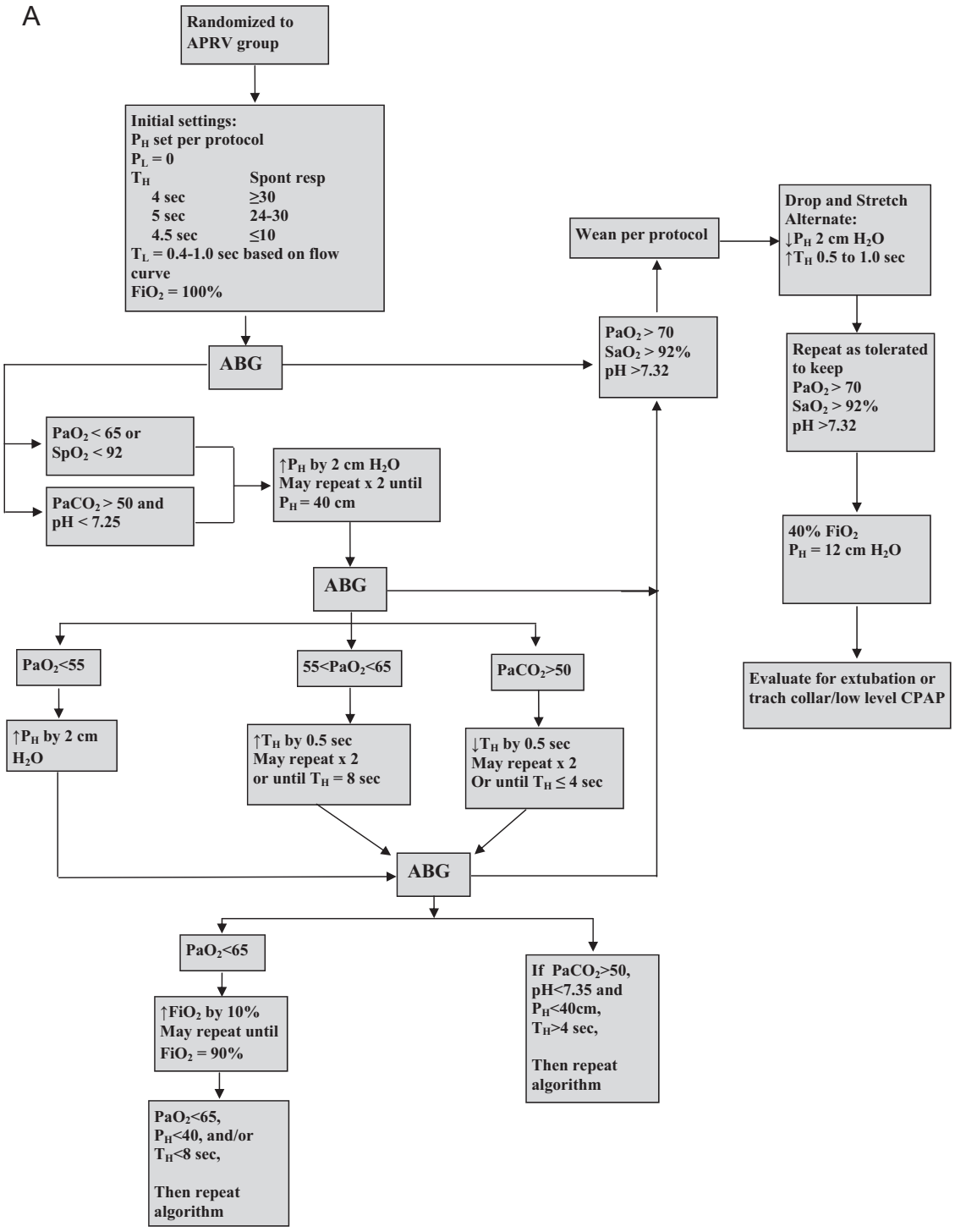

Figure 1. (*A*) Flow diagram for APRV ventilator protocol. (*B*) Flow diagram for LOVT ventilator protocol. PL, low pressure setting; TL, time spent at low pressure setting; VT, tidal volume; RR, respiratory rate; PEEP, positive end expiratory pressure; PS, pressure support; Ppk, peak airway pressure; PC, pressure control.

Sedation

Patients were sedated with an intravenous infusion of fentanyl and supplemented with lorazepam intravenous bolus or infusion according to a preexisting ICU protocol. Supplemental sedation was obtained with propofol if adequate control was not obtained with fentanyl and lorazepam. Sedation levels were measured by the Motor Activity Assessment Scale and maintained in the 2 to 3 range.[18] Values of these two agents were totaled at the end

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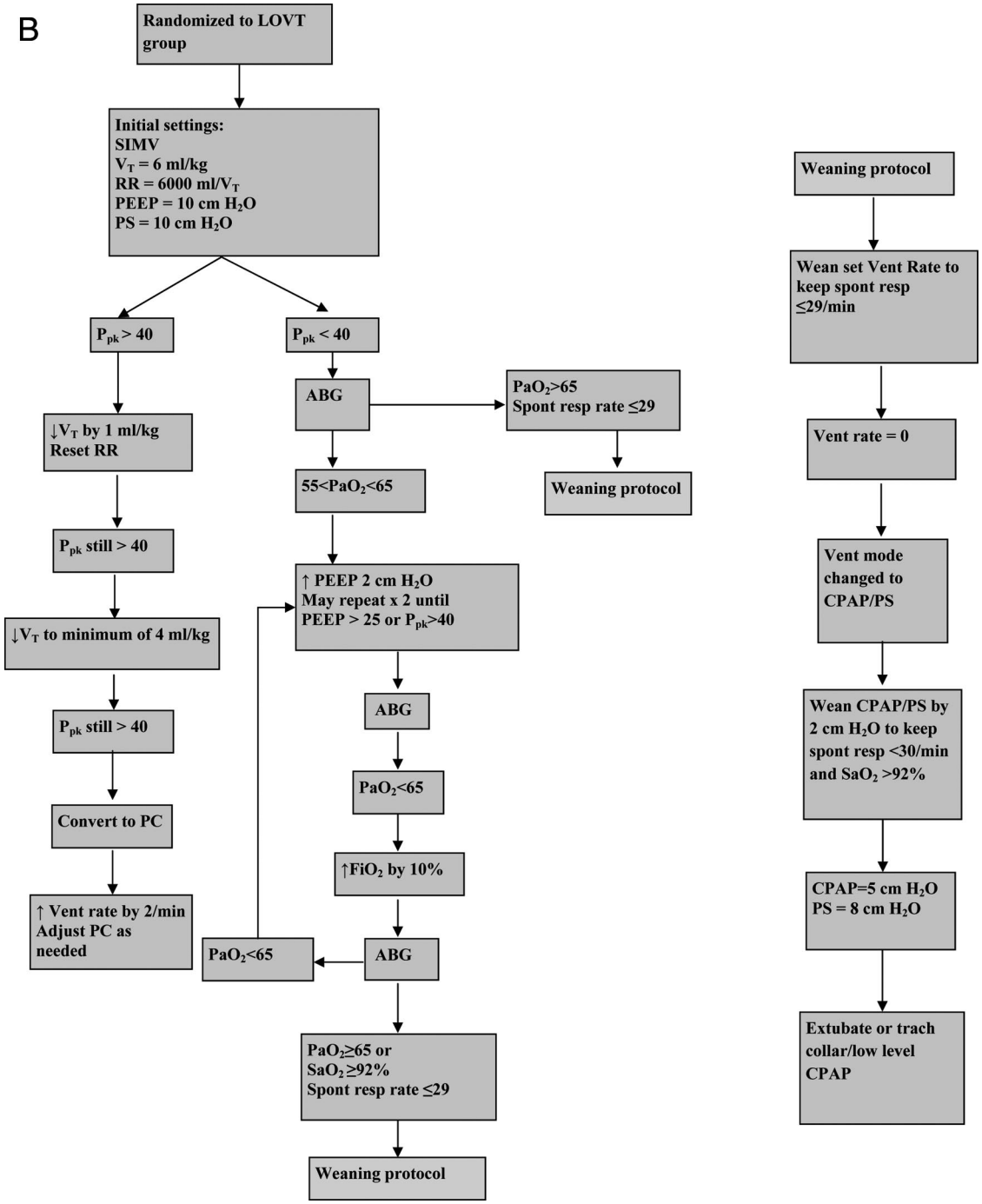

Figure 1. (*Continued*).

of each shift by nursing personnel. Additional agents used for severe agitation or withdrawal were not assessed.

Data Analysis

Data on demographics, mechanism of injury, Glasgow Coma Scale (GCS), Injury Severity Score (ISS), Acute Physiology and Chronic Health Evaluation II score (APACHE II), length of ventilation, airway pressures, arterial blood gas analysis, sedation use, ventilator complications, modality failure, ventilator-associated pneumonia (VAP), and mortality were collected. Data were analyzed with SPSS version 15.0 software. Mean values are expressed ± SD. Repeated measures of analysis of variance were used to compare serial arterial blood gas values and ventilator measurements. Analysis of covariance was used to compare dependent variables and group means were compared controlling for ISS, APACHE II, degree of lung injury, and GCS. Two-way χ^2 analysis was used to compare nonparametric variables.

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RESULTS

The study was conducted over a 21-month period ending in February of 2006. A total of 63 patients successfully completed the protocol, 31 in the APRV group and 32 in LOVT. Three patients completed the study and were later excluded from analysis due to violations of the ventilator protocol.

There were no differences in baseline demographics or physiologic parameters between APRV and LOVT groups except for APACHE II that was significantly worse for APRV than LOVT patients (20.5 ± 5.3 vs. 16.9 ± 7.2), $p = 0.027$. There was a trend for GCS score to be worse in APRV than LOVT patients (5.3 ± 4.1 vs. 7.2 ± 5.0, $p = 0.089$), but this difference did not reach significance. ARDS was present in eight APRV and nine LOVT patients and ALI was present in six APRV and two LOVT patients at the time of enrollment. Demographic and baseline physiology data are displayed in Table 1.

TABLE 1. Patient Demographics and Baseline Physiology Parameters

Parameter	APRV	LOVT
Age (yr)	40.5 ± 14.1	42.4 ± 16.0
Gender, n (%)		
Male	24/31 (77.4)	22/32 (68.8)
Female	7/31 (22.6)	10/32 (31.2)
Mechanism, n (%)		
Blunt	31/31 (100)	31/32 (96.9)
Penetrating	0	1/32 (3.1)
Smoking, n (%)		
Yes	19/30 (63.3)	17/32 (53.1)
No	11/30 (36.7)	15/32 (46.9)
ISS	30.3 ± 9.8	28.6 ± 6.4
GCS score	5.3 ± 4.1	7.2 ± 5.0
APACHE II	20.5 ± 5.3	16.9 ± 7.2
ARDS, n (%)	8/31 (25.8)	9/32 (28.1)
ALI, n (%)	6/31 (19.3)	2/32 (6.25)
Total ARDS/ALI, n (%)	14/31 (45.2)	11/32 (34.3)

The mean tidal volume per body weight for the LOVT patients at study outset was 6.4 mL/kg ± 1.2 mL/kg, indicating a reasonable compliance with ARDS Network criteria. At 72 hours, all but two SIMV patients were weaned to CPAP and pressure support per protocol. For those remaining on SIMV at 72 hours, the mean tidal volume per body weight was 7.11 mL/kg ± 0.98 mL/kg.

Arterial blood gas values and ventilator measurements were compared for the first 5 days of ventilation. Partial pressure of arterial oxygen to fraction of inspired oxygen (PaO_2/FiO_2) ratios were similar between groups throughout the analysis reflecting no measurable difference in oxygenation. Results are displayed in Figure 2. Minute ventilation was greater in LOVT patients with a significant group effect by repeated measures analysis of variance, $p = 0.004$. Surprisingly, $PaCO_2$ was also greater in LOVT patients during this same period, $p < 0.039$ (Fig. 3, A and B). Arterial pH remained similar between groups despite differences in minute ventilation and $PaCO_2$ (Fig. 3. C).

Peak inspiratory pressure and mean airway pressure are displayed in Figure 4, A and B. Although these values trended downward as patients were weaned from the ventilator, APRV patients had significantly higher mean airway pressure throughout the observation period, $p < 0.001$.

Mean ventilator days (10.49 days ± 7.23 days, 8.00 days ± 4.01 days) and ICU length of stay (16.47 days ± 12.83 days vs. 14.18 days ± 13.26 days) were not different between APRV and LOVT patients, respectively. Similarly, the incidence of tracheostomy (61.3% vs. 65.6%) and pneumothorax (0% vs. 3.1%) did not differ between APRV and LOVT. Mean number of VAPs per patient (1.00 ± 0.0.86 vs. 0.56 ± 0.67) did not differ for APRV or LOVT either. Failure of ventilator modality (12.9% vs. 15.6%) and mortality

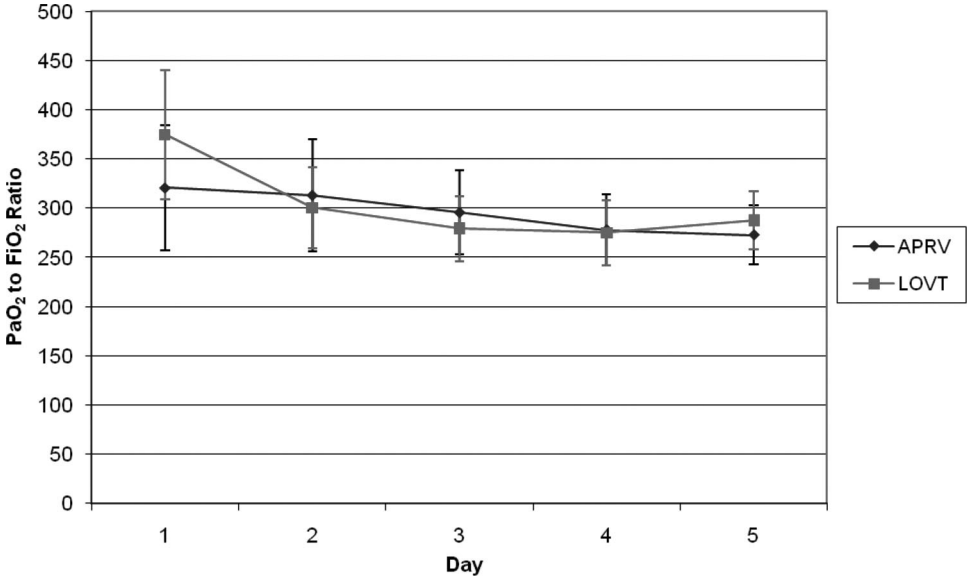

Figure 2. PaO_2 to FiO_2 ratios did not differ between groups throughout the period of observation.

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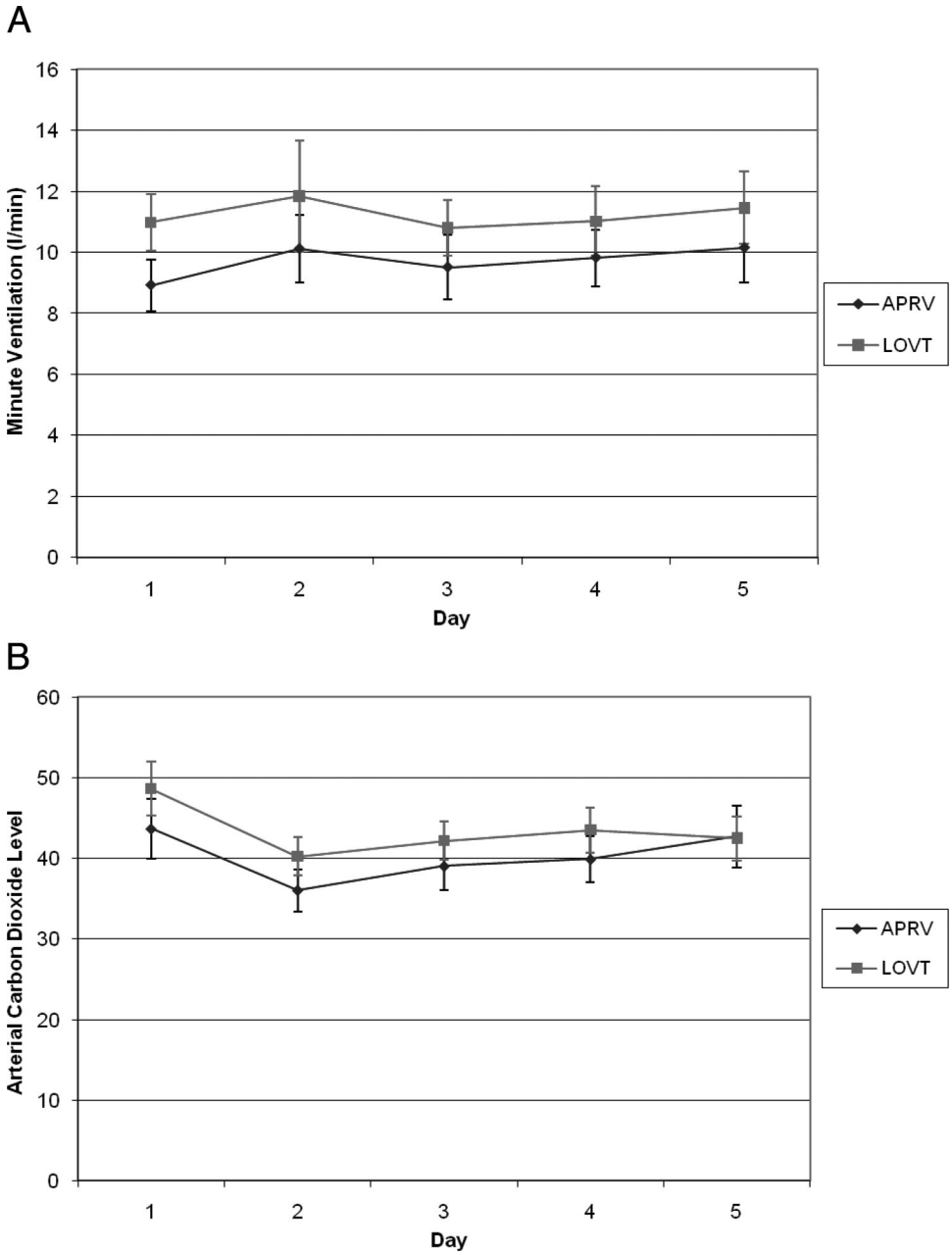

Figure 3. (*A*) Minute ventilation values for LOVT are greater than APRV throughout the period of observation and follow a tightly matched parallel course. Repeated measures analysis of variance showed a significant group effect during this period, $F_{1,54} = 8.886$; $p < 0.01$. (*B*) $PaCO_2$ values are greater for LOVT patients throughout the first 4 days of observation until they converge on day 5. Repeated measures analysis of variance showed significant group effect over the period of observation, $F_{1,54} = 4.478$; $p < 0.05$. (*C*), Arterial pH was similar between groups during the period of observation.

(6.45% vs. 6.25%) were also similar between APRV and LOVT. These outcome data are displayed in Table 2.

Fentanyl and lorazepam amounts were totaled for each 24-hour period and are displayed in Figure 5 for the first 5 days of the study period. There was no difference between fentanyl or lorazepam use between groups. There was no difference in the need for supplemental sedation with propofol with three APRV and two LOVT patients requiring this agent.

DISCUSSION

Our previous experience with APRV was favorable, demonstrating improved oxygenation with decreased peak airway pressures in a relatively ill population of trauma patients with a mean ISS of 27.6.[4] This preliminary work reflected other positive reports of APRV in mixed medical, cardiac, surgical, and trauma populations.[8,10,11,19–22] One other prospective random-

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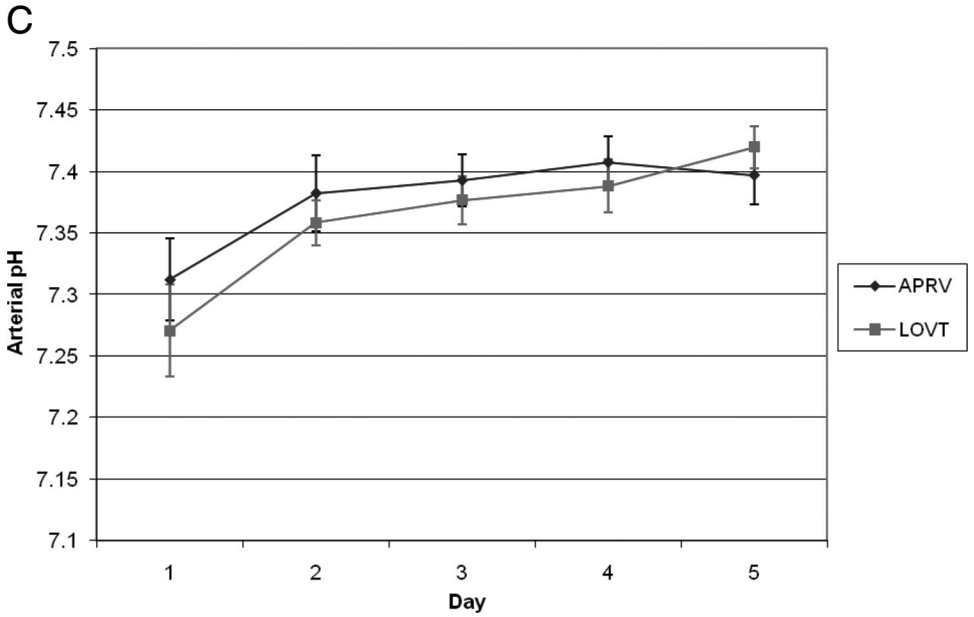

Figure 3. (*Continued*).

ized trial specifically evaluated APRV in a pure trauma population reporting the potential benefits of spontaneous breathing during APRV versus pressure control ventilation.[23] We conducted a randomized prospective control trial in a pure trauma population comparing APRV with similar lung protective strategy put forth by the ARDS Network.

Although data were collected throughout the entire study period, a 5-day period of observation was chosen for ventilator and blood gas values. We used this window of observation because repeated measures analysis of variance methodology eliminates all data from the data set for a patient once they are extubated. Longer periods of observation significantly reduce the statistical power of this technique.

A waiver of consent was obtained, allowing patients to be enrolled early in the treatment course of their respiratory failure when different lung recruitment strategies may play a pivotal role in the prevention of ARDS.[22] However, our results showed no differences in PaO_2 (data not shown), overall PaO_2/FiO_2 ratio, ventilator days, incidence of pneumonia, ICU length of stay, mortality, or any other outcome measure analyzed. These findings simply may mean that when applied to a cohort of trauma patients at risk for ARDS, APRV and low tidal volume strategy have similar efficacy.

Several limitations to that conclusion deserve consideration. First, despite having equivalent baseline demographic and physiology parameters in all other ways, a randomization error may have occurred because APRV patients had worse APACHE II scores (20.5 ± 5.3 vs. 16.9 ± 7.2, $p = 0.027$) and a trend for worse head injury (GCS score 5.3 ± 4.1 vs. 7.2 ± 5.0, $p = 0.089$), which could have affected their susceptibility to pneumonia and increased the duration of ventilator therapy. Indeed, the average number of VAP episodes per patient was 1.00 ± 0.86 in the APRV group versus 0.56 ± 0.67 in the LOVT though this difference was not significant. Such factors could have had a disproportionate negative effect on our outcome measures for APRV patients when APRV may actually have had unappreciated beneficial results. Subgroup analysis of the individual components of the APACHE II score did not further explain why these scores differed between the two groups.

Second, after the initial period of stabilization, most patients rapidly weaned off SIMV and were adequately ventilated with CPAP and pressure support. In fact, 72 hours after enrollment, only two patients still remained on SIMV. Based on the initial intention-to-treat for patients at risk for ARDS, requiring mechanical ventilation for greater than 72 hours, APRV seems to have no benefit over LOVT or CPAP and pressure support. At study outset, only 45.2% of APRV and 34.3% of LOVT patients had ARDS or ALI. Clearly, in future studies, a sicker population with ALI and ARDS defined by international criteria should only be enrolled with equal numbers of patients included in each experimental group. A multicenter trial will almost certainly be necessary for adequate patient accrual.

In the ARDS Network low tidal volume trial, patients were initially placed on the volume-assist control mode in both arms of the study. The control patients in the present study were initially placed on SIMV with pressure support and rapidly weaned to CPAP and pressure support as their clinical condition warranted. It is unclear, however, how long patients in the ARDS Network study were on volume-assist control before being switched to another mode like SIMV or CPAP and pressure support. In summary, the present study design does not directly reflect the ARDS Network protocol for LOVT but uses a common, clinically relevant application of low tidal volume strategy in the control group.

Finally, we did not consider spontaneous breathing trials via a T-piece in our experimental design. T-piece trials may have facilitated weaning and extubation and may be considered for future studies.[24] SIMV weaning without pressure support has also been shown to be inferior to pressure

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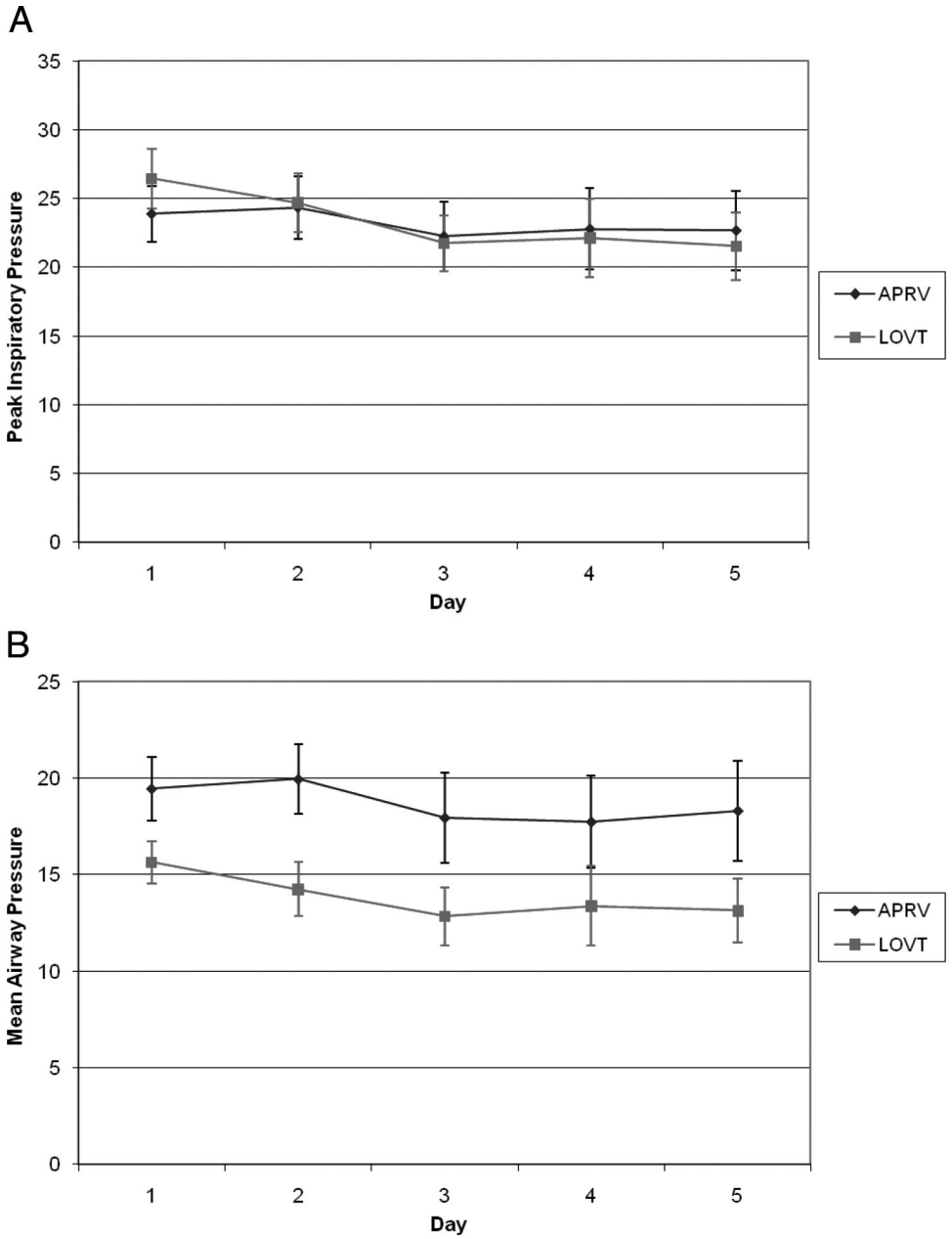

Figure 4. (*A*) Peak inspiratory pressure was similar between groups and trended downward throughout the period of observation. (*B*) Although both groups trended downward as weaning occurred, mean airway pressure was consistently higher in APRV than LOVT patients throughout the period of observation. Repeated measures analysis of variance showed significant group effect over the period of observation, $F_{1,54} = 20.404$; $p < 0.001$.

TABLE 2. Outcome Data

Dependent Measure	APRV	LOVT
Ventilator days	10.49 ± 7.23	8.00 ± 4.01
ICU length of stay (d)	16.47 ± 12.83	14.18 ± 13.26
Pneumothorax	0	3.1%
VAP per patient	1.00 ± 0.86	0.56 ± 0.67
Tracheostomy (%)	61.3	65.6
Failure of modality (%)	12.9	15.6
Mortality (%)	6.45	6.25

support weaning and T-piece trials.[25] We are unaware of any studies using a mixed SIMV/pressure support wean used in this study. However, patients were generally weaned from SIMV plus pressure support to pressure support alone rapidly when their underlying physiologic status permitted, and then weaned from pressure support in this study.

The present data demonstrate that when P_H is set at the plateau pressure during LOVT, APRV increases mean airway pressure while peak pressures remain unchanged. This strategy seems to be a safe starting point for initiating APRV as

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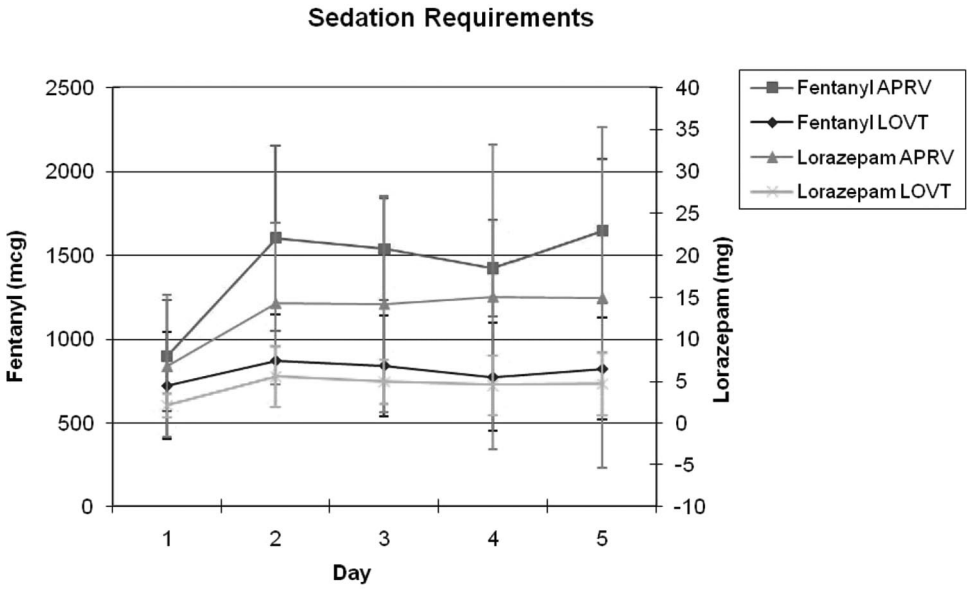

Figure 5. Sedation requirements for fentanyl and lorazepam are displayed for the first 5 days of observation. APRV patients have a trend to require more of both agents but large standard errors abrogate any significance.

it will likely obviate any immediate risk of ventilator-induced lung injury secondary to high airway pressures and may improve alveolar recruitment.

In our original work, we showed both decreased peak inspiratory pressure and increased mean airway pressure in APRV patients compared with control.[4] In this original study, P_H was set "slightly" above the mean airway pressure while in the conventional mode of ventilation. Only one-third of these patients had ARDS by definition and therefore two-thirds of these patients were not ventilated by lung protective strategy, likely explaining why mean airway pressure increased and peak pressure decreased. Sydow et al. also reported significantly decreased peak inspiratory pressures and increased mean airway pressures in 1994, well before the advent of lung protective strategy. These patients were ventilated with 8 mL/kg to 12 mL/kg tidal volumes in conventional SIMV. P_H was set according to release volume in APRV. The findings of these two studies show that when patients are converted from conventional SIMV ventilator settings to APRV, mean airway pressure seems to increase while peak inspiratory pressure decreases without detrimental effect.

Stock et al.[12] and Varpula et al.[12,22] both have shown that, while controlling for mean airway pressure or plateau pressure, peak inspiratory pressure will decrease when converting to APRV from other modes of ventilation. Kaplan et al.[21] showed that both peak inspiratory pressure and mean airway pressure were reduced when patients were converted from pressure control ventilation to APRV when P_H was set at 75% of the peak pressure.

Putensen et al.[23] showed multiple beneficial cardiopulmonary and pharmacological effects of APRV compared with patients given neuromuscular blockade and ventilated with the same basic pressure settings as the APRV group. All of the beneficial effects were ameliorated when paralysis was withdrawn. Another group ventilated with pressure control allowing for spontaneous breathing may have been useful in this comparison. However, the findings of this study do indicate that patients ventilated with APRV will likely do better than patients being chemically paralyzed while on pressure control ventilation.

Increasing mean airway pressure while preventing excessive peak inspiratory pressure has certain theoretic beneficial effects. Increased mean airway pressure, particularly by increasing time spent at P_H, can recruit collapsed areas of atelectatic lung without increasing peak pressure. Recruiting and holding collapsed lung units open at lower airway pressures reduces low volume lung injury caused by repeated opening and closing of the diseased alveolus. Lower airway pressures also prevent excessive stretch and over distension of relatively normal lung segments.[7,26,27] Keeping diseased lung units open without excessive stretch in normal lung is the basic theory behind open lung ventilation.[6,7,27,28] These key features illustrate why APRV has such attractive properties for alveolar recruitment. Additionally, APRV allows spontaneous breathing to occur independently from the set ventilator cycle, which may allow recruitment of dependent lung areas adjacent to the heart and diaphragm.[6,23]

Marini and Ravenscraft[29] have shown that mean airway pressure is the closest clinical correlate to mean alveolar pressure but that mean airway pressure does not always adequately reflect mean alveolar pressure. In conditions of poor lung compliance, mean alveolar and transmural pressure may significantly increase above mean airway pressure during spontaneous breathing potentially leading to barotrauma. Because our results are not necessarily what we expected based on the theoretical benefits of APRV as a recruitment strategy, comparing alveolar pressure to airway pressure would facilitate a greater understanding of the mechanics of APRV and should be considered in future investigations.

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Perhaps, the most interesting finding of this study is that despite having significantly higher minute ventilation, LOVT patients had higher $PaCO_2$ values. We did not measure work of breathing or functional residual capacity (FRC), but the observed differences in gas exchange may reflect greater FRC in the APRV patients.[30] In other words, increased mean airway pressure may in fact improve recruitment, which in turn would increase FRC and gas exchange. $PaCO_2$ is therefore reduced at lower levels of minute ventilation. Future studies of APRV should address this potential phenomenon.

Protocol-based sedation requirements were not different between groups although they seem to trend higher for APRV patients. Large SD abrogated any statistical significance in this trend. It is unclear why such variability of the mean daily sedation requirement occurred. Varpula et al.[22] reported no difference in propofol or fentanyl requirements between APRV and SIMV groups. Putensen et al.[23] showed decreased sufentanil and midazolam use in APRV compared with pressure control ventilation patients for the first 72 hours of the study. After neuromuscular blockade was withdrawn in the pressure control group, these differences were no longer evident. The current body of knowledge regarding sedation use in APRV compared with other modes of ventilation suggests that there are no differences in sedation requirements when chemical paralysis is not used.

CONCLUSION

This study is the largest reported randomized trial of APRV to date. Trauma patients at risk for ARDS ventilated with APRV had similar outcomes as those treated with LOVT despite worse baseline physiologic derangement and head injury. APRV seems to be a safe alternative ventilator modality that provides increased mean airway pressure as a potential recruitment mechanism. Sedation requirements seem to be similar to SIMV. Additional trials in patients with documented ARDS will be necessary for further clarification of its ultimate utility.

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EDITORIAL COMMENT

Airway pressure release ventilation (APRV) is a mode designed to allow spontaneous breathing in patients who are receiving high airway pressure with intermittent pressure release. High airway pressure maintains alveolar recruitment. Oxygenation is determined by high airway pressure and FiO_2. The timing and duration of the pressure release (low airway pressure) and spontaneous breathing on the part of the patient determine alveolar ventilation. Ventilator-determined tidal volume depends on lung compliance, airway resistance, and timing of the pressure release maneuver.[1,2]

Spontaneous respiration is permitted by an active exhalation valve. Thus, spontaneous breathing can occur throughout the respiratory cycle. Diaphragmatic activity associated with spontaneous breaths during APRV may open dependent juxtadiaphragmatic alveoli and reduce shunt to improve oxygenation. Because the ability of the patient to breathe spontaneously is preserved, APRV allows for prolonged inspiratory (high) pressure without the need for heavy sedation or administration of muscle relaxants. To sustain alveolar recruitment, the greater part of the total duty cycle (80–95%) occurs at high airway pressure.[1–3]

The theoretical advantages of APRV described above make the work of Maxwell et al. important.[4] The approach to APRV, with prolonged periods of high pressure frequently, is not a familiar modality for one schooled in traditional modes of mechanical ventilation. These workers provide an algorithm for the use of APRV and a rationale for the approach taken.

Unfortunately, I also have several concerns about this work. The authors describe comparison with the ARDSNet Study of low tidal volume ventilation in patients with acute respiratory distress syndrome (ARDS). Unfortunately, many of these patients do not have ARDS and, with administration of positive end-expiratory pressure, may not qualify as patients with acute lung injury. Thus, we do not have a good test group for the value of APRV. In addition, volume-assist control ventilation was used in both experimental arms of the ARDSNet Low Tidal Volume Trial. These investigators compare APRV with synchronized intermittent mandatory ventilation where the use of pressure support for spontaneous breaths is not controlled.

Although spontaneous breathing offers significant potential advantages, tidal volumes of approximately 1 L and large pleural pressure swings have been reported with APRV.[1,3] This type of ventilation may not be effective in ARDS or acute lung injury treatment. In fact, patients with severe hypoxemic respiratory failure may not be good candidates for spontaneous breathing during acute respiratory management. If a component of increased airway resistance is present, auto-positive end-expiratory pressure may occur to augment pressure swings associated with APRV. This uncontrolled breath stacking could also be deleterious.[1]

In summary, the potential benefits of improved oxygenation and reduced sedation make APRV an attractive mode for further study. Maxwell et al. suggest a way to use this means of ventilator support. However, the data provided demonstrate little more than safety.

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