

Preliminary Experience with Airway Pressure Release Ventilation in a Trauma/Surgical Intensive Care Unit

Benjamin W. Dart IV, MD, Robert A. Maxwell, MD, FACS, Charles M. Richart, MD, FACS, Donald K. Brooks, RRT, David L. Ciraulo, DO, FACS, Donald E. Barker, MD, FACS, and R. Phillip Burns, MD, FACS

Background: Airway pressure-release ventilation (APRV) is a pressure-limited, time-cycled mode of mechanical ventilation. The purpose of this study was to evaluate our initial experience with the use of APRV in acutely injured, ventilated patients.

Methods: Since March 2003, APRV has been used selectively in adult trauma patients with or at risk for acute lung injury/acute respiratory distress syndrome. Data were obtained before and during the 72 hours after switching to

APRV. A retrospective analysis of these data was then performed.

Results: Complete data were available on 46 of 60 patients (77%) for the first 72 hours of APRV. Before APRV, the average P_{aO_2}/F_{iO_2} ratio was 243 and the average peak airway pressure was 28 cm H_2O . Peak airway pressure decreased 19% ($p = 0.001$), P_{aO_2}/F_{iO_2} improved by 23% ($p = 0.017$) and release tidal volumes improved by 13% ($p = 0.020$) over the course of the analysis.

Conclusion: APRV significantly im-

proved oxygenation by alveolar recruitment and allowed for a reduction in peak airway pressures. This relatively new modality had favorable results and appears to be an effective alternative for lung recruitment in traumatically injured patients at risk for acute lung injury/acute respiratory distress syndrome.

Key Words: Airway pressure-release ventilation, Acute lung injury, Acute respiratory distress syndrome, Recruitment maneuvers.

J Trauma. 2005;59:71-76.

Multisystem trauma is a well-recognized risk factor for the development of acute lung injury (ALI).^{1,2} Despite welcomed new strategies designed to treat pulmonary dysfunction, ALI and acute respiratory distress syndrome (ARDS) remain major sources of morbidity. The cause of respiratory failure after trauma is a complex process involving lung and chest wall injuries and elaboration of inflammatory mediators from multiple sources. Sedation, neuromuscular paralysis, and supine positioning are often necessary in these patients and contribute to additional ventilation-perfusion mismatching and hypoxia.³⁻⁵ Frequent transfusions, sepsis, and ventilator-associated lung injury can lead to further derangements, placing the trauma population at high risk for major respiratory embarrassment. The progression of ALI to ARDS indicates a spiraling process that may frequently herald the onset of multiple organ failure.^{6,7}

Numerous strategies have been attempted to prevent or treat ARDS. Recently, studies focused on limiting ventilator-induced lung damage offer promising results. Currently, the

use of positive-pressure ventilation with limited peak airway pressures (P_{aw}) and low tidal volumes has been recommended.^{8,9} However, ventilation with lower tidal volumes may lead to decreased oxygenation, necessitating implementation of recruitment maneuvers to transiently improve gas exchange.¹⁰

One mode of ventilation that may offer the ability to achieve recruitment and improve oxygenation while maintaining acceptable peak P_{aw} is airway pressure-release ventilation (APRV). Originally described by Downs and Stock in 1987, APRV is a pressure-limited, time-cycled mode of mechanical ventilation that permits spontaneous breathing throughout the ventilatory cycle.^{11,12} The modality consists of a high-pressure setting (P_H) and a low-pressure setting (P_L). Recruitment and oxygenation occur during P_H at a set time interval (T_H), whereas ventilation occurs by brief controlled releases to P_L at a corresponding time interval (T_L). We hypothesized that APRV is an easily implemented, well-tolerated mode of mechanical ventilation in a trauma/surgical intensive care that may provide improved oxygenation at lower peak airway pressures than conventional ventilator modalities.

PATIENTS AND METHODS

Approval for a retrospective data analysis was obtained from our institutional review board. Patients were identified through a prospectively collected log of patients ventilated during the first 6 months of APRV use. Charts were reviewed and demographic information and data points were compiled. Patients were excluded if data were unavailable or the course

Submitted for publication June 21, 2004.

Accepted for publication April 20, 2005.

Copyright © 2005 by Lippincott Williams & Wilkins, Inc.

From the Department of Surgery, Division of Surgical Critical Care, University of Tennessee College of Medicine, Chattanooga Unit (B.W.D., C.M.R., R.A.M., D.L.C., D.E.B., R.P.B.), and the Department of Adult Respiratory Care, Erlanger Medical Center (D.K.B.), Chattanooga, Tennessee.

Address for reprints: Robert A. Maxwell, MD, Department of Surgery, University of Tennessee College of Medicine, Chattanooga Unit, 979 East Third Street, Suite B-401, Chattanooga, TN 37403; E-mail: maxwelra@erlangers.com

of APRV did not exceed 48 hours. Statistical analysis was conducted using SPSS Version 11.5 (SPSS, Inc., Chicago, IL). Continuous data are reported as mean \pm SD. Categorical data are shown with frequency distribution. Repeated measures analysis of variance and test of within-subjects contrasts were performed with statistical significance set at $p \leq 0.05$.

Before the study period, trauma patients admitted to the trauma/surgical intensive care units at our regional Level I trauma center were mechanically ventilated using any of the various conventional ventilator modalities depending on individualized pulmonary mechanics and degree of respiratory failure. Frequently used modalities included synchronized intermittent mandatory ventilation (SIMV), continuous positive airway pressure (CPAP) augmented with pressure support (PS), assist control, pressure-controlled ventilation, and inverse ratio pressure-controlled ventilation.

In February 2003, the respiratory therapy department, trauma nurses, surgical housestaff and trauma attendings underwent an inservicing process for familiarization with APRV. The course consisted of didactic lectures, live telemedicine presentations, and on-site demonstrations by respiratory therapists experienced with the modality.

Beginning in March 2003, randomly selected trauma patients with risk factors for ARDS or established ALI/ARDS were switched to APRV after an initial period of conventional positive-pressure mechanical ventilation with SIMV or CPAP/PS. Risk factor assessment was determined subjectively by the attending trauma surgeon and based on age, presence of pulmonary contusions, injury severity, transfusion requirements, infectious complications, or declining P_{aO_2}/F_{iO_2} ratio despite increasing ventilatory support. Established ALI and ARDS were defined by the criteria set forth by the American-European Consensus Conference with respect to P_{aO_2}/F_{iO_2} values and radiographically demonstrated bilateral infiltrates.¹³ All patients were ventilated using a Dräger Evita 2 dura ventilator (Dräger, Lübeck, Germany).

Before conversion to APRV, ventilator settings on conventional modes including level of positive end-expiratory pressure, F_{iO_2} , and tidal volume (Vt) were recorded. Conventional ventilator settings were optimized using an existing protocol for mechanically ventilated trauma patients based on maintaining plateau pressures less than 35 cm H₂O and achieving a normal acid-base balance. Arterial blood gasses (ABGs), mean P_{aw} , and peak P_{aw} were also noted. P_{aO_2}/F_{iO_2} ratios were calculated for each patient. The ventilator mode was then changed to APRV. P_H was set to allow a slight increase in the mean P_{aw} above that seen in conventional mode ventilation. T_H was initially determined empirically on the basis of the patient's respiratory drive. In the absence of spontaneous respirations, T_H was set at 3 to 4 seconds to allow for 15 to 20 releases of pressure per minute. Adjustments to T_H were made on the basis of ABG interpretations. Permissive hypercapnia was allowed provided the pH was maintained in the normal range. By convention, P_L was always set at 0. T_L was determined by examining the expiratory

Table 1 Patient Demographics

| | |
|--------------------------------|-------------------|
| Number of patients, n | 46 |
| Age, years | 41 \pm 20 |
| Gender M (%) / F (%) | 33 (72) / 13 (28) |
| Mechanism of Injury | |
| Motor Vehicle Collision, n (%) | 29 (63) |
| Gunshot wound, n (%) | 5 (11) |
| Fall, n (%) | 3 (7) |
| Other, n (%) | 9 (19) |
| ISS | 27.6 \pm 9.9 |
| ICU length of stay, days | 17 \pm 7 |
| Hospital length of stay, days | 25 \pm 9 |
| Mortality, n (%) | 4 (9) |

ISS, injury severity score; ICU, intensive care unit.

flow curve such that the release of pressure terminated at approximately 40% to 50% of the peak expiratory flow. Settings (P_H , P_L , T_H , T_L , and F_{iO_2}), ABGs, mean P_{aw} , release Vt, and calculated P_{aO_2}/F_{iO_2} were recorded initially and in the morning of each of the first three consecutive 24-hour periods after conversion to APRV. It is standard practice at our institution to record ventilator settings at the time of ABG collection and interpretation. Because APRV was a relatively new modality, it was routine to obtain these data within several hours after conversion to APRV from another ventilator mode. Also, standard practice dictates that ABG collection be performed every morning at approximately 6 AM, provided that a patient remains mechanically ventilated. F_{iO_2} was weaned to keep oxygen saturation above 93% according to our standard protocol.

RESULTS

Our initial 6-month experience included 60 patients ventilated with APRV for a total of 9,332 ventilator hours. Six (10%) patients were ventilated using APRV for less than 48 hours and were excluded from the analysis. Five (8%) patients did not have specified data points available for analysis and were also excluded. Three (5%) patients did not tolerate conversion to APRV, were switched back to conventional mechanical ventilation, and were likewise not included. Forty-six (77%) of these patients had complete data sets for the first 72 hours using APRV after an initial course of conventional ventilation and constitute the study population.

Demographic data (Table 1) were reflective of our typical trauma population in the intensive care unit at our Level I regional trauma center. Age ranged from 16 to 86 years, with a mean of 41 \pm 20 years. Seventy-two percent of the patients were male patients. The majority of patients (63%) were injured in motor vehicle collisions. The degree of injury is reflected by the mean Injury Severity Score (ISS) of 27.6 \pm 9.9. Intensive care unit length of stay and hospital length of stay were 17 \pm 7 and 25 \pm 9 days, respectively. Four patients died during their hospitalization, for an overall mortality of 9%.

Table 2 Mechanical Ventilation Data

| | |
|---|------------|
| Conventional Ventilation time prior to APRV, days | 1.8 ± 2.0 |
| APRV time, days | 7.3 ± 4.0 |
| Total ventilator days | 13.0 ± 8.9 |

APRV, Airway pressure release ventilation.

The study population varied in the degree of pulmonary dysfunction. Twenty patients were identified with ARDS. Ten patients had ALI. Sixteen patients were placed on APRV because of identified risk factors for ALI/ARDS. Most of these 16 patients had multiple risk factors identified, including 10 patients with pulmonary contusions, 10 patients with ISS > 25, 5 patients with ventilator-associated pneumonia, and 4 patients with transfusion requirements that exceeded 10 units of packed red blood cells in a 24-hour period.

Ventilatory time data were obtained (Table 2). Intubated patients spent an average of 1.8 ± 2.0 days on conventional mechanical ventilation before initiation of APRV. Conventional modalities used included SIMV in 30 patients, CPAP/PS in 14 patients, and AC in 2 patients. The mean time spent on APRV was 7.3 ± 4.0 days. Patients were then converted back to CPAP before extubation, and the total mean time spent on a ventilator was 13.0 ± 8.9 days.

Ventilator settings, pressure measurements, and ABG analysis during four separate time periods (TP¹⁻⁴) from the start of APRV to the time of data collection were then compared with corresponding conventional ventilatory data (Table 3). TP¹ was 1:48 ± 1:46 (hours:minutes). TP²⁻⁴ were 15:20 ± 7:13, 39:20 ± 6:53, and 63:03 ± 7:02. The maximum P_{aw} decreased from 28.2 ± 9.2 cm H₂O to 24.5 ± 6.4 cm H₂O at TP¹ (*p* = 0.005) and then to 22.9 ± 5.5 cm H₂O by TP⁴ (*p* = 0.001). The average mean P_{aw} increased from 15.5 ± 5.8 in conventional ventilatory modes to 20.1 to 21.0 (*p* < 0.001) in APRV. Release Vt progressively increased during APRV to 840 ± 198 mL at TP⁴ (*p* = 0.02). In contrast, FiO₂ progressively decreased throughout the APRV period to a minimal value of 39 ± 11% (*p* < 0.001) at TP⁴.

pH was slightly higher during APRV but remained in the established normal range (7.35–7.45). There were no statistically significant changes in P_{aco}₂ during the analysis. P_{ao}₂ did decrease significantly to 113 ± 32 mm Hg (*p* = 0.020) by TP² and remained so throughout APRV. However, there was a marked improvement in P_{ao}₂/F_iO₂ by TP³ to 294 ± 103 (*p* = 0.017).

DISCUSSION

The ability to safely and adequately ventilate acutely injured trauma patients can be challenging using lung protective strategies promoted by the ARDS Network.⁹ Low tidal volumes can lead to decreases in P_{ao}₂/F_iO₂, increase in shunt, and a decrease in lung compliance.¹⁰ Relative hypoxia may become problematic, reflecting alveolar collapse. Thus, various recruitment maneuvers have been proposed to offset difficulties with oxygenation, but the ideal recruitment technique remains desired.^{14,15}

APRV appears to be an ideal modality that can innately incorporate recruitment techniques into a simplistic form of ventilation. Maintenance of an acceptable level of prolonged, continuous pressure at P_H facilitates alveolar recruitment. Keeping the T_L small prevents collapse of these alveoli during the release. This is accomplished clinically by monitoring the expiratory flow of gas waveform to ensure that T_L terminates at approximately 40% to 50% of the peak expiratory flow (Fig. 1). Therefore, the actual P_L never reaches zero. This situation is analogous to auto-positive end-expiratory pressure. The number of releases to P_L is minimized to limit shear forces secondary to repeated opening and closing of alveoli.

On analysis of pressure-volume curves, airway pressures during APRV are maintained between traditional upper and lower inflection points, with the majority of the time spent near the upper inflection point (Fig. 2). Because the majority of the controlled ventilator cycle is spent near the upper inflection point in APRV, maintenance of an adequate P_{aw} to promote alveolar recruitment can be easily accomplished.

Table 3 Conventional ventilation versus APRV

| | Conventional Ventilation | APRV time (hours:min) | | | |
|--|--------------------------|--------------------------------|---------------------------------|---------------------------------|---------------------------------|
| | | TP ¹ 1:48 ± 1:46 | TP ² 15:20 ± 7:13 | TP ³ 39:20 ± 6:53 | TP ⁴ 63:03 ± 7:02 |
| Peak P _{aw} or P _H (cm H ₂ O) | 28.2 ± 9.2 | 24.5 ± 6.0* | 24.8 ± 6.0* | 24.3 ± 5.3* | 22.9 ± 5.5* |
| Mean P _{aw} (cm H ₂ O) | 15.5 ± 5.8 | 20.4 ± 5.3* | 21.0 ± 5.1* | 20.9 ± 4.4* | 20.1 ± 5.0* |
| Set Vt (ml) | 688 ± 170 | N/A | N/A | N/A | N/A |
| Release Vt (ml) | N/A | 743 ± 195 | 789 ± 220 | 788 ± 188 | 840 ± 198† |
| Set FiO ₂ (%) | 68 ± 27 | 55 ± 22* | 46 ± 17* | 41 ± 14* | 39 ± 11* |
| pH | 7.35 ± 0.1 | 7.38 ± 0.08 | 7.40 ± 0.07* | 7.42 ± 0.06* | 7.40 ± 0.05* |
| PaCO ₂ , mm Hg | 42 ± 7 | 41 ± 9 | 40 ± 11 | 39 ± 7 | 43 ± 8 |
| PaO ₂ , mm Hg | 155 ± 111 | 137 ± 64 | 113 ± 32* | 111 ± 30* | 110 ± 26* |
| PaO ₂ /F _i O ₂ | 243 ± 141 | 269 ± 116 | 270 ± 102 | 294 ± 103* | 299 ± 88* |

P_{aw}, airway pressure; Vt, tidal volume; TP, time period; N/A, not applicable; * *p* < 0.05 compared to conventional data; † *p* < 0.05 compared to TP¹.

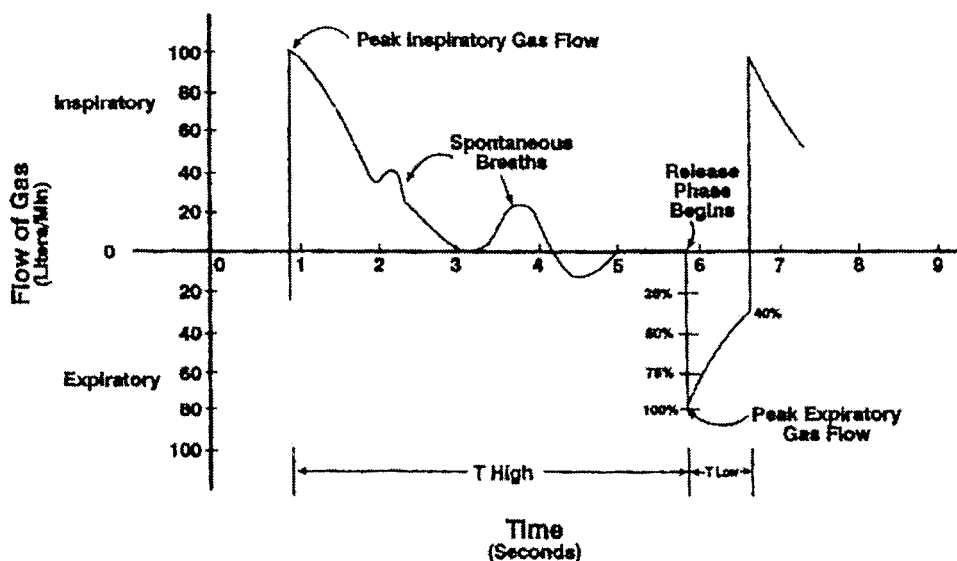


Fig. 1. T_L terminates at 40% of peak expiratory gas flow to prevent collapse of alveoli during release of pressure. (Reprinted from Frawley PM, Habashi NM. Airway pressure release ventilation: theory and practice. AACN Clin Issues. 2001;12:234–246. Used with permission.)

Our interest in APRV was sparked after acquiring a ventilator fleet capable of this modality and successful application in a patient with multisystem trauma refractory to conventional modes of ventilation. Subsequently, an additional 59 patients were ventilated with APRV during a 6-month period. Data obtained from our experience adds support to the proposal that APRV may offer advantages over conventional ventilation by promoting alveolar recruitment and improving oxygenation at lower peak P_{aw} .

In this study, the mean ISS was 27.6, indicating a fairly severely injured population. The P_{aO_2}/F_{iO_2} ratio before starting APRV was 243 without using strict low tidal volume ventilation settings. This reflects the overall severity of injury

and the baseline degree of pulmonary dysfunction in our study population. Attempts to follow an ARDS Network protocol with an initial mean F_{iO_2} requirement of 68% would have likely led to increased oxygen requirements and further worsening of the P_{aO_2}/F_{iO_2} ratio.

Alveolar recruitment is reflected by a 13% improvement in release V_t ($p = 0.020$) during APRV and a 23% improvement in the P_{aO_2}/F_{iO_2} ratio ($p = 0.017$) over the course of the analysis (Fig. 3). Within the same time period, peak P_{aw} decreased by 19% ($p = 0.001$) (Fig. 4).

Our initial aim was to allow slight elevations in mean airway pressures so that closing forces in the lung could be overcome and recruitment of previously nonaerated, dependent lung units could be accomplished. This is reflected by our data, which indeed show that mean P_{aw} was elevated by

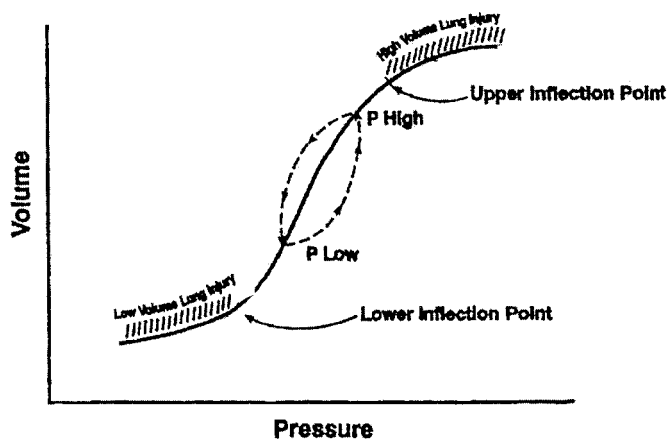


Fig. 2. Pressure-volume curve with airway pressures maintained between upper and lower inflection points. (Reprinted from Frawley PM, Habashi NM. Airway pressure release ventilation: theory and practice. AACN Clin Issues. 2001;12:234–246. Used with permission.)

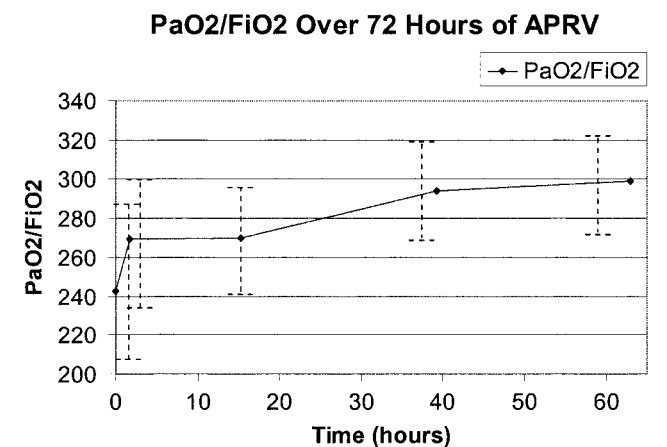


Fig. 3. P_{aO_2}/F_{iO_2} ratio over 72 hours of APRV. Box and whisker bars represent mean \pm 2 SEM. Time zero represents change of ventilatory mode from conventional ventilation to APRV mode.

Peak Airway Pressure Over 72 Hours of APRV

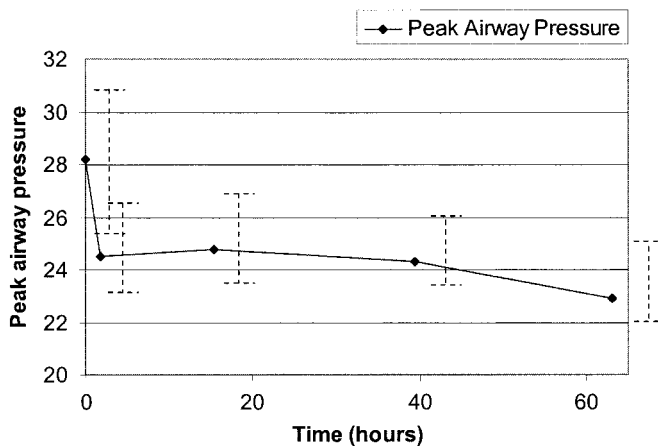


Fig. 4. Peak airway pressure over 72 hours of APRV. Box and whisker bars represent mean \pm 2 SEM. Time zero represents change of ventilatory mode from conventional ventilation to APRV mode.

approximately 5 cm H₂O on conversion to APRV, with a subsequent statistically significant reduction in peak P_{aw} from the start of APRV to the end of the study period. The concept of monitoring mean P_{aw} is not unique to APRV but is important because mean P_{aw} has been noted to most closely approximate true alveolar pressure.¹⁶

After the original description of APRV, a clinical trial monitored 14 patients ventilated with APRV after coronary revascularization. The study demonstrated the efficacy of this mode in supplying oxygen at lower peak P_{aw} than conventional positive-pressure ventilation.¹⁷ Since that time, several comparative clinical studies have confirmed that APRV was superior to more conventional modes of ventilation in reducing peak P_{aw} without compromising oxygenation.^{18–23}

Spontaneous breathing that occurs with APRV has been observed in other studies to improve ventilation-perfusion matching and arterial oxygenation in trauma patients with severe ARDS²⁴ when compared with controlled mechanical ventilation or APRV alone (without spontaneous breathing). Furthermore, less sedation,^{23,25} improved cardiopulmonary function,^{23,25} and decreased duration of ventilatory support²⁵ have been demonstrated during APRV with spontaneous breathing.

In our experience, APRV was very well tolerated. Of the three patients who required early termination of APRV, each was unique and warrants further discussion. One patient had a large bronchopleural fistula, and attempts to ventilate the patient using APRV resulted in excessive loss of volume while at P_H. It is probable that measured mean P_{aw} underestimated true alveolar pressure and P_H was set too high to compensate for this discrepancy. Another patient had a severe closed head injury requiring intracranial pressure monitoring. APRV led to unacceptably high intracranial pressure. It is unclear whether this was caused by transmitted intrathoracic pressure or transient hypercapnia. Several other patients in-

cluded in this analysis had similar injuries and were successfully ventilated using APRV without any elevation in their intracranial pressure measurements. This issue has not been adequately addressed in the literature and awaits further investigation. Finally, APRV was discontinued in one patient with late-stage ARDS attributable to tachypnea and patient discomfort. The exact cause of this is unknown but may have been related to extremely poor pulmonary compliance, premature conversion back to conventional ventilation, and insufficient time spent in APRV to allow for alveolar recruitment.

Because this was a retrospective investigation of our initial experience with APRV, there are several limitations. First, there is a learning curve associated with implementation of any new treatment modality, and it is possible that our current understanding of APRV would lead to different results. However, ongoing analysis continues to demonstrate favorable findings. Second, the retrospective nature of this report prevents direct comparisons between APRV and conventional ventilator modalities or previously described recruitment maneuvers. Third, some patients were randomly selected for APRV on the basis of risk factors for ARDS alone, introducing potential selection bias. Finally, we were unable to assess the effects that APRV had on hemodynamics and sedation requirements.

In conclusion, APRV has a number of unique features that lend themselves to lung recruitment in trauma/surgical intensive care unit patients at risk or who have ALI or ARDS. It is a relatively simple modality that we implemented easily in a wide variety of conditions that resulted in pulmonary dysfunction. Peak P_{aw} can be reduced while achieving improved Pao₂/Fio₂ ratios during APRV. Prospective studies need to be performed to validate these findings. Currently, we are enrolling patients in a prospective, randomized trial to validate these findings.

REFERENCES

- Hudson LD, Milberg JA, Anardi D, Maunder RJ. Clinical risks for development of the acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 1995;151:293–301.
- Garber BG, Herbert PC, Yelle JD, Hodder RV, McGowan J. Adult respiratory distress syndrome: a systemic overview of incidence and risk factors. *Crit Care Med.* 1996;24:687–695.
- Helman DL Jr, Sherner JH, Fitzpatrick TM, Callender ME, Shorr AF. Effect of standardized orders and provider education on head-of-bed positioning in mechanically ventilated patients. *Crit Care Med.* 2003;31:2285–2290.
- Drakulovic MB, Torres A, Bauer TT, Nicolas JM, Nogue S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomized trial. *Lancet.* 1999;354:1851–1858.
- Wheeler AP. Sedation, analgesia and paralysis in the intensive care unit. *Chest.* 1993;104:566–577.
- Faist E, Baue AE, Dittmer H, Heberer G. Multiple organ failure in polytrauma patients. *J Trauma.* 1983;23:775–787.
- Regel G, Grotz M, Weltner T, et al. Pattern of organ failure following severe trauma. *World J Surg.* 1996;20:422–429.

8. Amato MBP, Barbas CSV, Medeiros DM, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. *N Engl J Med.* 1998;338:347–354.
9. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome: the Acute Respiratory Distress Syndrome Network. *N Engl J Med.* 2000;342:1301–1308.
10. Johannigman JA, Miller SL, Davis BR, Davis KD Jr, Campbell RS, Branson RD. Influence of low tidal volumes on gas exchange in acute respiratory distress syndrome and the role of recruitment maneuvers. *J Trauma.* 2003;54:320–325.
11. Downs JB, Stock MC. Airway pressure release ventilation: a new concept in ventilatory support. *Crit Care Med.* 1987;15:459–461.
12. Stock MC, Downs JB, Frolicher DA. Airway pressure release ventilation. *Crit Care Med.* 1987;15:462–466.
13. Bernard GR, Artigas A, Brigham KL, et al. The American-European Consensus Conference on ARDS: definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med.* 1994;149(3 pt 1):818–824.
14. Dries DJ, Marini JJ. A rationale for lung recruitment in acute respiratory distress syndrome. *J Trauma.* 2003;54:326–328.
15. Barbas CSV. Lung recruitment maneuvers in acute respiratory distress syndrome and facilitating resolution. *Crit Care Med.* 2003;31(suppl 4):S265–S271.
16. Marini JJ, Ravenscraft SA. Mean airway pressure: physiologic determinants and clinical importance—part 2: clinical implications. *Crit Care Med.* 1992;20:1604–1616.
17. Garner W, Downs JB, Stock MC, Rasanen J. Airway pressure release ventilation: a human trial. *Chest.* 1988;94:779–781.
18. Cane RD, Peruzzi WT, Shapiro BA. Airway pressure release ventilation in severe acute respiratory failure. *Chest.* 1991;100:460–463.
19. Rasanen J, Cane RD, Downs JB, et al. Airway pressure release ventilation during acute lung injury: a prospective multicenter trial. *Crit Care Med.* 1991;19:1234–1241.
20. Sydow M, Burchardi H, Ephraim E, Zielmann S, Crozier TA. Long-term effect of two different ventilator modes on oxygenation in acute lung injury: comparison of airway pressure release ventilation and volume-controlled inverse ratio ventilation. *Am J Respir Crit Care Med.* 1994;149:1550–1556.
21. Davis K, Johnson DJ, Branson RD, Campbell RS, Johannigman JA, Porembka D. Airway pressure release ventilation. *Arch Surg.* 1993;128:1348–1352.
22. Valentine DD, Hammond MD, Downs JB, Sears NJ, Sims WR. Distribution of ventilation and perfusion with different modes of mechanical ventilation. *Am Rev Respir Dis.* 1991;143:1262–1266.
23. Kaplan LJ, Bailey H, Formosa V. Airway pressure release ventilation increases cardiac performance in patients with acute lung injury/adult respiratory distress syndrome. *Crit Care.* 2001;5:221–226.
24. Putensen C, Mutz NJ, Putensen-Himmer G, Zinserling J. Spontaneous breathing during ventilatory support improves ventilation-perfusion distributions in patients with acute respiratory distress syndrome. *Am J Respir Crit Care Med.* 1999;159:1241–1248.
25. Putensen C, Zech S, Wrigge H, et al. Long term effects of spontaneous breathing during ventilatory support in patients with acute lung injury. *Am J Respir Crit Care Med.* 2001;164:43–49.