



Literature List APRV

2017

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Categories

CLIN = Clinical Study

REV = Review

CASE = Case study

ANM = Animal Study

CLIN	Li JQ. et al.	Clinical research about airway pressure release ventilation for moderate to severe acute respiratory distress syndrome.	<i>Eur Rev Med Pharmacol Sci. 2016 Jun;20(12):2634-41</i>
<p>Rationale and Objectives: To evaluate clinical effects of airway pressure release ventilation (APRV) in patients suffering from moderate to severe acute respiratory distress syndrome (ARDS).</p> <p>Methods and Measurements: From August 2012 to August 2014, fifty-two cases with moderate to severe ARDS were randomly divided into two groups. In the first group (APRV) the airway pressure release ventilation was used; the second group (SIMV) was ventilated using synchronized intermittent mandatory ventilation mode and positive end expiratory pressure (PEEP). Changes in oxygenation index, respiratory mechanics, extravascular lung water, functional residual capacity change and hemodynamics were recorded in both groups after mechanical ventilation. TNF-α and IL-10 levels in alveolar lavage were also measured. Acute physiology and chronic health evaluation (APACHE) II and Murray scores were evaluated. Pneumothorax and mediastinal emphysema during ventilation were also recorded. The probability of survival, the duration of ICU stay, days without organ failure and days without sedation were compared.</p> <p>Main Results: Conditions in APRV were improved significantly. Oxygenation index was increased, airway peak pressure (Ppeak) was reduced, the lung dynamic compliance improved, extravascular lung water was relieved, functional residual capacity increased and Murray score was improved. In APRV group ventilation central venous pressure (CVP) and systemic circulation resistance index (SVRI) were reduced, but cardiac index (CI) increased, and at the same time lac and oxygen saturation of central venous blood (ScvO₂) were improved. Free sedatives days were significantly reduced in APRV group while days without mechanical ventilation were increased and days in ICU were shortened significantly. TNF-α and IL-10 concentrations in the alveolar lavage, probability of survival and days without organ failure were similar in both groups.</p>			
<p>Conclusion: In patients suffering from moderate to severe ARDS, application of APRV improved lung function and hemodynamics. It also reduced the need for sedatives and the duration of mechanical ventilation as well as days in ICU.</p>			

CASE	Morimoto et al	Successful management using airway pressure release ventilation for severe postoperative pulmonary oedema	<i>Int J Surg Case Rep. 2016 Aug 28;27:93-95</i>
<p>Introduction: Postoperative pulmonary oedema is a fatal adverse event after a cardiac surgery. We here report successful management using airway pressure release ventilation (APRV) for severe hypoxia with pulmonary oedema after a cardiac surgery.</p> <p>Presentation of Case: A 58-year-old man underwent an uneventful mitral valve repair. Immediately afterwards, the patient became agitated and made vigorous inspiratory efforts. His oxygen saturation dropped to 90%. Coarse inspiratory rhonchi were heard on auscultation, and copious, pink, frothy sputum was obtained with suctioning. Initial chest radiograph showed right-sided patchy opacities and interstitial infiltrates. A transthoracic echocardiogram demonstrated normal cardiac function. With worsening respiratory failure on mechanical ventilation, APRV was attempted. His condition and blood gas was subsequently improved. Over the following 3days, the patient experienced an uneventful postoperative course and was discharged to home on postoperative day 14.</p> <p>Discussion: Extra corporal membrane oxygenation (ECMO) is the most effective for severe hypoxia with pulmonary oedema; however, ECMO is associated with hemorrhage and infectious complications. Alternatively, APRV was required for the successful management for severe hypoxia with pulmonary oedema.</p>			
<p>Conclusions: APRV could be effective for severe hypoxia with pulmonary oedema after a cardiac surgery.</p>			

CLIN	Lim et al	Characteristics and outcomes of patients treated with airway pressure release ventilation for acute respiratory distress syndrome: A retrospective observational study.	<i>J Crit Care. 2016 Aug;34:154-9. doi: 10.1016/j.jcrc.2016.03.002. Epub 2016 Mar 9</i>
<p>Background: The optimal mode of ventilation in acute respiratory distress syndrome (ARDS) remains uncertain. Airway pressure release ventilation (APRV) is a recognized treatment for mechanically-ventilated patients with severe hypoxaemia. However, contemporary data on its role as a rescue modality in ARDS is lacking. The goal of this study was to describe the clinical and physiological effects of APRV in patients with established ARDS.</p>			
<p>Methods: This retrospective observational study was performed in a 23-bed adult intensive care unit in a tertiary extracorporeal membrane oxygenation (ECMO) referral centre. Patients with ARDS based on Berlin criteria were included through a prospectively-collected APRV database. Patients receiving APRV for less than six hours were excluded.</p>			
<p>Measurements and Results: Fifty patients fulfilled the eligibility criteria. Prior to APRV initiation, median Murray Lung Injury Score was 3.5 (interquartile range (IQR) 2.5-3.9) and PaO₂/FiO₂ was 99mmHg (IQR 73-137). PaO₂/FiO₂ significantly improved within twenty-four hours post-APRV initiation (ANOVA F(1, 27)=24.34, P<.005). Two patients (4%) required intercostal catheter insertion for barotrauma. Only one patient (2%) required ECMO after APRV initiation, despite a majority (68%) fulfilling previously established criteria for ECMO at baseline. Hospital mortality rate was 38%.</p>			
<p>Conclusions: In patients with ARDS-related refractory hypoxaemia treated with APRV, an early and sustained improvement in oxygenation, low incidence of clinically significant barotrauma and progression to ECMO was observed. The safety and efficacy of APRV requires further consideration.</p>			

CLIN	Bellani et al	Epidemiology, Patterns of Care, and Mortality for Patients With Acute Respiratory Distress Syndrome in Intensive Care Units in 50 Countries	JAMA. 2016 Feb 23;315(8):788-800. doi: 10.1001/jama.2016.0291
<p>Rationale and Objectives: To evaluate intensive care unit (ICU) incidence and outcome of ARDS and to assess clinician recognition, ventilation management, and use of adjuncts-for example prone positioning-in routine clinical practice for patients fulfilling the ARDS Berlin Definition.</p> <p>Design, Settings, and Participants: The Large Observational Study to Understand the Global Impact of Severe Acute Respiratory Failure (LUNG SAFE) was an international, multicentre, prospective cohort study of patients undergoing invasive or non-invasive ventilation, conducted during 4 consecutive weeks in the winter of 2014 in a convenience sample of 459 ICUs from 50 countries across 5 continents.</p> <p>Main Outcomes and Measures: The primary outcome was ICU incidence of ARDS. Secondary outcomes included assessment of clinician recognition of ARDS, the application of ventilatory management, the use of adjunctive interventions in routine clinical practice, and clinical outcomes from ARDS.</p>			
<p>Conclusions and Relevance: Among ICUs in 50 countries, the period prevalence of ARDS was 10.4% of ICU admissions. This syndrome appeared to be under recognized and undertreated and associated with a high mortality rate. These findings indicate the potential for improvement in the management of patients with ARDS.</p>			

REV	Sumeet et al	<p>The 30-year evolution of airway pressure release ventilation (APRV)</p>	<p><i>Intensive Care Med Exp. 2016, 4:11. Published online 2016 May 20. doi: 10.1186/s40635-016-0085-2</i></p>
<p>Abstract: Airway pressure release ventilation (APRV) was first described in 1987 and defined as continuous positive airway pressure (CPAP) with a brief release while allowing the patient to spontaneously breathe throughout the respiratory cycle. The current understanding of the optimal strategy to minimize ventilator-induced lung injury is to “open the lung and keep it open”. APRV should be ideal for this strategy with the prolonged CPAP duration recruiting the lung and the minimal release duration preventing lung collapse. However, APRV is inconsistently defined with significant variation in the settings used in experimental studies and in clinical practice. The goal of this review was to analyze the published literature and determine APRV efficacy as a lung-protective strategy. We reviewed all original articles in which the authors stated that APRV was used. The primary analysis was to correlate APRV settings with physiologic and clinical outcomes. Results showed that there was tremendous variation in settings that were all defined as APRV, particularly CPAP and release phase duration and the parameters used to guide these settings. Thus, it was impossible to assess efficacy of a single strategy since almost none of the APRV settings were identical. Therefore, we divided all APRV studies divided into two basic categories: (1) fixed-setting APRV (F-APRV) in which the release phase is set and left constant; and (2) personalized-APRV (P-APRV) in which the release phase is set based on changes in lung mechanics using the slope of the expiratory flow curve. Results showed that in no study was there a statistically significant worse outcome with APRV, regardless of the settings (F-APRV or P-APRV). Multiple studies demonstrated that P-APRV stabilizes alveoli and reduces the incidence of acute respiratory distress syndrome (ARDS) in clinically relevant animal models and in trauma patients. In conclusion, over the 30 years since the mode’s inception there have been no strict criteria in defining a mechanical breath as being APRV. P-APRV has shown great promise as a highly lung-protective ventilation strategy.</p>			
<p>Conclusions: P-APRV allows for a personalized control of lung stability on a breath-to-breath basis that is not possible with other modes of ventilation. P-APRV is an adaptive, flow directed, duration dependent ventilation strategy that adapts the setting to each patient regardless of their lung pathophysiology. This personalized, adaptive mechanical breath may prove more efficacious at treating and preventing ARDS than the current standard of care.</p>			

REV	Sadowitz et al	Preemptive mechanical ventilation can block progressive acute lung injury.	World J Crit Care Med. 2016 Feb 4;5(1):74-82. doi:10.5492/wjccm.v5.i1.74. eCollection 2016
<p>Abstract: Mortality from acute respiratory distress syndrome (ARDS) remains unacceptable, approaching 45% in certain high-risk patient populations. Treating fulminant ARDS is currently relegated to supportive care measures only. Thus, the best treatment for ARDS may lie with preventing this syndrome from ever occurring. Clinical studies were examined to determine why ARDS has remained resistant to treatment over the past several decades. In addition, both basic science and clinical studies were examined to determine the impact that early, protective mechanical ventilation may have on preventing the development of ARDS in at-risk patients. Fulminant ARDS is highly resistant to both pharmacologic treatment and methods of mechanical ventilation. However, ARDS is a progressive disease with an early treatment window that can be exploited. In particular, protective mechanical ventilation initiated before the onset of lung injury can prevent the progression to ARDS.</p> <p>Airway pressure release ventilation (APRV) is a novel mechanical ventilation strategy for delivering a protective breath that has been shown to block progressive acute lung injury (ALI) and prevent ALI from progressing to ARDS. ARDS mortality currently remains as high as 45% in some studies. As ARDS is a progressive disease, the key to treatment lies with preventing the disease from ever occurring while it remains subclinical.</p> <p>Early protective mechanical ventilation with APRV appears to offer substantial benefit in this regard and may be the prophylactic treatment of choice for preventing ARDS.</p>			
<p>Conclusions: ARDS remains a troubling clinical entity with an unacceptably high mortality. Treating fulminant ARDS has proven futile for decades; there are currently no effective pharmacologic or mechanical ventilation strategies for curing ARDS, and treatment is relegated to aggressive supportive care measures. Thus, the key to treating this highly morbid disease lies with preventing the disease from ever occurring. Indeed protective mechanical ventilation strategies are being employed in the operating room and in the intensive care unit before the development of lung injury.</p> <p>Moreover, data from both our laboratory and the clinical realm indicate that appropriately setting APRV generates a protective MBP that may be the most viable and accessible method of preventing lung injury and the subsequent progression to ARDS.</p>			

ANM	Arrindell et al	Lung volume recruitment in a preterm pig model of lung immaturity.	Am J Physiol Lung Cell Mol Physiol . 2015 Nov 15;309(10):L1088-92. doi: 10.1152/ajplung.00292.2015. Epub 2015 Sep 25.
<p>Abstract: A translational preterm pig model analogous to infants born at 28 wk of gestation revealed that continuous positive airway pressure results in limited lung recruitment but does not prevent respiratory distress syndrome, whereas assist-control + volume guarantee (AC+VG) ventilation improves recruitment but can cause injury, highlighting the need for improved ventilation strategies.</p> <p>We determined whether airway pressure release ventilation (APRV) can be used to recruit the immature lungs of preterm pigs without injury. Spontaneously breathing pigs delivered at 89% of term (model for 28-wk infants) were randomized to 24 h of APRV (n = 9) vs. AC+VG with a tidal volume of 5 ml/kg (n = 10). Control pigs (n = 36) were provided with supplemental oxygen by an open mask. Nutrition and fluid support was provided throughout the 24-h period. All pigs supported with APRV and AC+VG survived 24 h, compared with 62% of control pigs. APRV resulted in improved lung volume recruitment compared with AC+VG based on radiographs, lower Pco₂ levels (44 ± 2.9 vs. 53 ± 2.7 mmHg, P = 0.009) and lower inspired oxygen fraction requirements (36 ± 6 vs. 44 ± 11%, P < 0.001), and higher oxygenation index (5.1 ± 1.5 vs. 2.9 ± 1.1, P = 0.001). There were no differences between APRV and AC+VG pigs for heart rate, ratio of wet to dry lung mass, pro-inflammatory cytokines, or histopathological markers of lung injury.</p> <p>Lung protective ventilation with APRV improved recruitment of alveoli of preterm lungs, enhanced development and maintenance of functional residual capacity without injury, and improved clinical outcomes relative to AC+VG. Long-term consequences of lung volume recruitment by using APRV should be evaluated.</p>			

REV	Nieman et al	Reducing acute respiratory distress syndrome occurrence using mechanical ventilation	<i>World J Respirol 2015 November 28; 5(3): 188-198 ISSN 2218-6255 (online)</i>
<p>Abstract: The standard treatment for acute respiratory distress syndrome (ARDS) is supportive in the form of low tidal volume ventilation applied after significant lung injury has already developed. Nevertheless, ARDS mortality remains unacceptably high (> 40%). Indeed, once ARDS is established it becomes refractory to treatment, and therefore avoidance is key. However, preventive techniques and therapeutics to reduce the incidence of ARDS in patients at high-risk have not been validated clinically. This review discusses the current data suggesting that preemptive application of the properly adjusted mechanical breath can block progressive acute lung injury and significantly reduce the occurrence of ARDS.</p>			
<p>Conclusions: To our knowledge we are the only group that is conducting experiments investigating the optimal mechanical breath necessary to reduce the incidence of ARDS in animal models of secondary ARDS (i.e., hemorrhagic shock and sepsis). Our work clearly shows that preemptive APRV using the settings developed by our group will reduce ARDS incidence in a rat trauma/hemorrhagic shock model and in a high fidelity, clinically applicable porcine ARDS model [27,35]. Because our animal model so closely represents the clinical progression from injury (i.e., hemorrhagic shock and sepsis) to established-ARDS, it is considered “good evidence” that any treatment shown efficacious in this model will be successful in a clinical trial [57]. In addition, we have shown that part of the protective mechanism of preemptive APRV is minimizing μ-strain in the alveolus and alveolar ducts, highlighting the importance of understanding the impact of any given PTI on the microenvironment [16,17]. The meta-analysis on severely injured trauma patients showed an order of magnitude reduction in ARDS incidence and mortality with preemptive application of APRV strongly suggesting that a prospective clinical trial is warranted. In conclusion, the optimal method of protecting a patient’s lung with established-ARDS, as described by Dr. Lachmann [60] in 1992, is to “Open the Lung and Keep it Open” and likewise, the goal of preemptive mechanical ventilation to reduce ARDS incidence is to “Never let the Lung Collapse”.</p>			

REV	Andrews et al	<p>Early application of airway pressure release ventilation may reduce mortality in high-risk trauma patients: a systematic review of observational trauma ARDS literature.</p>	<p><i>J Trauma Acute Care Surg.</i> 2013 Oct;75(4):635-41. doi: 10.1097/TA.0b013e31829d3504</p>
<p>Background: Adult respiratory distress syndrome is often refractory to treatment and develops after entering the health care system. This suggests an opportunity to prevent this syndrome before it develops. The objective of this study was to demonstrate that early application of airway pressure release ventilation in high-risk trauma patients reduces hospital mortality as compared with similarly injured patients on conventional ventilation.</p>			
<p>Methods: Systematic review of observational data in patients who received conventional ventilation in other trauma centres were compared with patients treated with early airway pressure release ventilation in our trauma centre. Relevant studies were identified in a PubMed and MEDLINE search from 1995 to 2012 and included prospective and retrospective observational and cohort studies enrolling 100 or more adult trauma patients with reported adult respiratory distress syndrome incidence and mortality data.</p>			
<p>Measurements and Main Results: Early airway pressure release ventilation as compared with the other trauma centres represented lower mean adult respiratory distress syndrome incidence (14.0% vs. 1.3%) and in-hospital mortality (14.1% vs. 3.9%).</p>			
<p>Conclusions: These data suggest that early airway pressure release ventilation may prevent progression of acute lung injury in high-risk trauma patients, reducing trauma-related adult respiratory distress syndrome mortality.</p>			

REV	Shreyas et al	Early Airway Pressure Release Ventilation prevents ARDS – A novel preventive approach to lung injury	<i>SHOCK, Vol. 39, No. 1, pp. 28Y38, 2013</i>
<p>Abstract: Acute respiratory distress syndrome (ARDS) afflicts 200,000 patients annually with a mortality rate of 30% to 60% despite wide use of low tidal volume (LTV) ventilation, the present standard of care. High-permeability alveolar oedema and instability occur early in the development of ARDS, before clinical signs of lung injury, and represent potential targets for therapy. We hypothesize that early application of a protective ventilation strategy (airway pressure release ventilation [APRV]) will stabilize alveoli and reduce alveolar oedema, preventing the development of ARDS. Yorkshire pigs (30Y40 kg) were anesthetized and subjected to two-hit injury: (a) intestinal ischemia-reperfusion, (b) peritoneal sepsis, or sham surgery. Following surgery, pigs were randomized into APRV (n = 4), according to current published guidelines for APRV; LTV ventilation (n = 3), using the current published ARDS Network guidelines (6 mL/kg); or sham (n = 5). The clinical care of all pigs was administered per the Surviving Sepsis Campaign guidelines. Animals were killed, and necropsy performed at 48 h. Arterial blood gases were measured to assess for the development of clinical lung injury. Lung tissue epithelial cadherin (E-cadherin) was measured to assess alveolar permeability. Broncho alveolar lavage fluid (BALF) surfactant protein A was measured to assess alveolar stability. Lung oedema content and histopathology were analysed at 48 h. Airway pressure release ventilation pigs did not develop ARDS. In contrast, pigs in the LTV ventilation met ARDS criteria (PaO₂/FIO₂ ratio) (APRV: baseline = 471 T 16; 48 h = 392 T 8; vs. LTV ventilation: baseline = 551 T 28; 48 h = 138 T 88; P G 0.001). Airway pressure release ventilation preserved alveolar epithelial integrity demonstrated by higher levels of E-cadherin in lung tissue as compared with LTV ventilation (P G 0.05). Surfactant protein A levels were higher in BALF from the APRV group, suggesting APRV preserved alveolar stability. Quantitative histologic scoring showed improvements in all stigmata of ARDS in the APRV group versus the LTV ventilation (P G 0.05). Airway pressure release ventilation had significantly lower lung oedema (wet-dry weight) than LTV ventilation (P G 0.05). Protective ventilation with APRV immediately following injury prevents development of ARDS. Reduction in lung oedema, preservation of lung E-cadherin and surfactant protein A abundance in BALF suggest that APRV attenuates lung permeability, oedema, and surfactant degradation. Protective ventilation could change the clinical paradigm from supportive care for ARDS with LTV ventilation to preventing development of ARDS with APRV.</p>			
<p>Conclusions: The current study demonstrates that systemic inflammatory response syndrome Y induced ARDS can be prevented with high airway P/TP when APRV is used early in the course of mechanical ventilation in a clinically relevant translational porcine model of lung injury. Airway pressure release ventilation prevented clinical and histologic lung injury by preserving alveolar epithelial integrity, reducing lung oedema, preserving surfactant, and maintaining alveolar stability. In summary, these data suggest that ARDS development involves a close interplay of both systemic inflammation as well as mechanical ventilation with low P/TP. Future studies are needed to elucidate the mechanical ventilation strategies that will offer the appropriate P/TP for prevention of ARDS.</p>			

REV	Habashi et al	Ventilator strategies for posttraumatic acute respiratory distress syndrome: airway pressure release ventilation and the role of spontaneous breathing in critically ill patients	<i>Current Opinion in Critical Care</i> <i>2004, 10:549–557</i>
<p>Purpose of review : Patients who experience severe trauma are at increased risk for the development of acute lung injury and acute respiratory distress syndrome. The management strategies used to treat respiratory failure in this patient population should be comprehensive. Current trends in the management of acute lung injury and acute respiratory distress syndrome consist of maintaining acceptable gas exchange while limiting ventilator-associated lung injury.</p> <p>Recent findings: Currently, two distinct forms of ventilator-associated lung injury are recognized to produce alveolar stress failure and have been termed low-volume lung injury (intra-tidal alveolar recruitment and de-recruitment) and high-volume lung injury (alveolar stretch and overdistension). Pathologically, alveolar stress failure from low- and high-volume ventilation can produce lung injury in animal models and is termed ventilator-induced lung injury. The management goal in acute lung injury and acute respiratory distress syndrome challenges clinicians to achieve the optimal balance that both limits the forms of alveolar stress failure and maintains effective gas exchange. The integration of new ventilator modes that include the augmentation of spontaneous breathing during mechanical ventilation may be beneficial and may improve the ability to attain these goals.</p> <p>Main Results: Airway pressure release ventilation is a mode of mechanical ventilation that maintains lung volume to limit intra-tidal recruitment /de-recruitment and improves gas exchange while limiting over distension. Clinical and experimental data demonstrate improvements in arterial oxygenation, ventilation-perfusion matching (less shunt and dead space ventilation), cardiac output, oxygen delivery, and lower airway pressures during airway pressure release ventilation. Mechanical ventilation with airway pressure release ventilation permits spontaneous breathing throughout the entire respiratory cycle, improves patient comfort, reduces the use of sedation, and may reduce ventilator days.</p>			

REV	Nieman et al	Lung stress, strain, and energy load: engineering concepts to understand the mechanism of ventilator-induced lung injury (VILI)	<i>Intensive Care Medicine Experimental 2016 Dec: 4:16</i>
<p>Abstract:</p> <p>It was recently shown that acute respiratory distress syndrome (ARDS) mortality has not been reduced in over 15 years and remains ~40 %, even with protective low tidal volume (LVt) ventilation. Thus, there is a critical need to develop novel ventilation strategies that will protect the lung and reduce ARDS mortality. Protti et al. have begun to analyse the impact of mechanical ventilation on lung tissue using engineering methods in normal pigs ventilated for 54 h. They used these methods to assess the impact of a mechanical breath on dynamic and static global lung strain and energy load. Strain is the change in lung volume in response to an applied stress (i.e., Tidal Volume-Vt). This study has yielded a number of exciting new concepts including the following: (1) Individual mechanical breath parameters (e.g., Vt or Plateau Pressure) are not directly correlated with VILI but rather any combination of parameters that subject the lung to excessive dynamic strain and energy/power load will cause VILI; (2) all strain is not equal; dynamic strain resulting in a dynamic energy load (i.e., kinetic energy) is more damaging to lung tissue than static strain and energy load (i.e., potential energy); and (3) a critical consideration is not just the size of the Vt but the size of the lung that is being ventilated by this Vt. This key concept merits attention since our current protective ventilation strategies are fixated on the priority of keeping the Vt low. If the lung is fully inflated, a large Vt is not necessarily injurious. In conclusion, using engineering concepts to analyse the impact of the mechanical breath on the lung is a novel new approach to investigate VILI mechanisms and to help design the optimally protective breath. Data generated using these methods have challenged some of the current dogma surrounding the mechanisms of VILI and of the components in the mechanical breath necessary for lung protection.</p>			
<p>Conclusions: ...high tidal volume or plateau pressures are safe as long as dynamic strain and energy/power load are maintained in the safe range [10, 11]. ...</p>			

ANM	Kollisch-Singule et al	<p>The effects of airway pressure release ventilation on respiratory mechanics in extra pulmonary lung injury</p>	<p><i>Intensive Care Medicine Experimental (2015) 3:35</i></p>
<p>Abstract:</p> <p>BACKGROUND: Lung injury is often studied without consideration for pathologic changes in the chest wall. In order to reduce the incidence of lung injury using preemptive mechanical ventilation, it is important to recognize the influence of altered chest wall mechanics on disease pathogenesis. In this study, we hypothesize that airway pressure release ventilation (APRV) may be able to reduce the chest wall elastance associated with an extrapulmonary lung injury model as compared with low tidal volume (LVt) ventilation.</p> <p>METHODS: Female Yorkshire pigs were anesthetized and instrumented. Fecal peritonitis was established, and the superior mesenteric artery was clamped for 30 min to induce an ischemia/reperfusion injury. Immediately following injury, pigs were randomized into (1) LVt (n = 3), positive end-expiratory pressure (PEEP) 5 cmH₂O, V t 6 cc kg⁻¹, FiO₂ 21 %, and guided by the ARDSnet protocol or (2) APRV (n = 3), P High 16-22 cmH₂O, P Low 0 cmH₂O, T High 4.5 s, T Low set to terminate the peak expiratory flow at 75 %, and FiO₂ 21 %. Pigs were monitored continuously for 48 h. Lung samples and bronchoalveolar lavage fluid were collected at necropsy.</p> <p>RESULTS: LVt resulted in mild acute respiratory distress syndrome (ARDS) (PaO₂/FiO₂ = 226.2 ± 17.1 mmHg) whereas APRV prevented ARDS (PaO₂/FiO₂ = 465.7 ± 66.5 mmHg; p < 0.05). LVt had a reduced surfactant protein A concentration and increased histologic injury as compared with APRV. The plateau pressure in APRV (34.3 ± 0.9 cmH₂O) was significantly greater than LVt (22.2 ± 2.0 cmH₂O; p < 0.05) yet transpulmonary pressure between groups was similar (p > 0.05). This was because the pleural pressure was significantly lower in LVt (7.6 ± 0.5 cmH₂O) as compared with APRV (17.4 ± 3.5 cmH₂O; p < 0.05). Finally, the elastance of the lung, chest wall, and respiratory system were all significantly greater in LVt as compared with APRV (all p < 0.05).</p>			
<p>Conclusions:</p> <p>APRV preserved surfactant and lung architecture and maintenance of oxygenation. Despite the greater plateau pressure and tidal volumes in the APRV group, the transpulmonary pressure was similar to that of LVt. Thus, the majority of the plateau pressure in the APRV group was distributed as pleural pressure in this extrapulmonary lung injury model. APRV maintained a normal lung elastance and an open, homogeneously ventilated lung without increasing lung stress.</p>			

ANM	Shreyas et al	Early stabilizing alveolar ventilation prevents acute respiratory distress syndrome: A novel timing-based ventilatory intervention to avert lung injury	<i>J Trauma Acute Care Surg</i> <i>Volume 73, Number 2</i>
<p>Abstract:</p> <p>BACKGROUND: Established acute respiratory distress syndrome (ARDS) is often refractory to treatment. Clinical trials have demonstrated modest treatment effects, and mortality remains high. Ventilator strategies must be developed to prevent ARDS.</p> <p>HYPOTHESIS: Early ventilatory intervention will block progression to ARDS if the ventilator mode (1) maintains alveolar stability and (2) reduces pulmonary edema formation.</p> <p>METHODS: Yorkshire pigs (38Y45 kg) were anesthetized and subjected to a “two-hit” ischemia-reperfusion and peritoneal sepsis. After injury, animals were randomized into two groups: early preventative ventilation (airway pressure release ventilation [APRV]) versus nonpreventative ventilation (NPV) and followed for 48 hours. All animals received anaesthesia, antibiotics, and fluid or vasopressor therapy as per the Surviving Sepsis Campaign. Titrated for optimal alveolar stability were the following ventilation parameters: (1) NPV group Vtidal volume, 10 mL/kg + positive end-expiratory pressure/5 cm/H2O volume-cycled mode; (2) APRV group Vtidal volume, 10 to 15 mL/kg; high pressure, low pressure, time duration of inspiration (Thigh), and time duration of release phase (Tlow). Physiological data and plasma were collected throughout the 48-hour study period, followed by BAL and necropsy.</p> <p>RESULTS: APRV prevented the development of ARDS (p G 0.001 vs. NPV) by PaO2/FIO2 ratio. Quantitative histological scoring showed that APRV prevented lung tissue injury (p G 0.001 vs. NPV). Bronchoalveolar lavage fluid showed that APRV lowered total protein and interleukin 6 while preserving surfactant proteins A and B (p G 0.05 vs. NPV). APRV significantly lowered lung water (p G 0.001 vs. NPV). Plasma interleukin 6 concentrations were similar between groups.</p>			
<p>Conclusions:</p> <p>Early preventative mechanical ventilation with APRV blocked ARDS development, preserved surfactant proteins, and reduced pulmonary inflammation and oedema despite systemic inflammation similar to NPV. These data suggest that early preventative ventilation strategies stabilizing alveoli and reducing pulmonary oedema can attenuate ARDS after ischemia-reperfusion and sepsis.</p>			

ANM	Shreyas et al	<p>Preemptive application of Airway Pressure Release Ventilation prevents development of ARDS in a rat traumatic hemorrhagic shock model</p>	<p><i>Shock. 2013 Sep;40(3):210-6.</i> doi: 10.1097/SHK.0b013e31829efb06</p>
<p>Abstract:</p> <p>Background: Once established, the acute respiratory distress syndrome (ARDS) is highly resistant to treatment and retains a high mortality. We hypothesized that preemptive application of airway pressure release ventilation (APRV) in a rat model of trauma/hemorrhagic shock (T/HS) would prevent ARDS.</p> <p>Methods: Rats were anesthetized, instrumented for hemodynamic monitoring, subjected to T/HS, and randomized into two groups: (a) volume cycled ventilation (VC) (n = 5, tidal volume 10 mL/kg; positive end-expiratory pressure 0.5 cmH₂O) or (b) APRV (n = 4, P_{high} = 15Y20 cmH₂O; T_{high} = 1.3Y1.5 s to achieve 90% of the total cycle time; T_{low} = 0.11Y0.14 s, which was set to 75% of the peak expiratory flow rate; P_{low} = 0 cmH₂O). Study duration was 6 h.</p> <p>Results: Airway pressure release ventilation prevented lung injury as measured by PaO₂/FIO₂ (VC 143.3 T 42.4 vs. APRV 426.8 T 26.9, P G 0.05), which correlated with a significant decrease in histopathology as compared with the VC group. In addition, APRV resulted in a significant decrease in bronchoalveolar lavage fluid total protein, increased surfactant protein B concentration, and an increase in epithelial cadherin tissue expression. In vivo microscopy demonstrated that APRV significantly improved alveolar patency and stability as compared with the VC group.</p>			
<p>Conclusions:</p> <p>Our findings demonstrate that preemptive mechanical ventilation with APRV attenuates the clinical and histologic lung injury associated with T/HS. The mechanism of injury prevention is related to preservation of alveolar epithelial and endothelial integrity. These data support our hypothesis that preemptive APRV, applied using published guidelines, can prevent the development of ARDS.</p>			

ANM	Kollisch-Singule et al	Mechanical Breath Profile of Airway Pressure Release Ventilation The Effect on Alveolar Recruitment and Microstrain in Acute Lung Injury	<i>JAMA Surg.</i> <i>doi:10.1001/jamasurg.2014.1829</i>
<p>Abstract:</p> <p>OBJECTIVE To examine whether the mechanical breath profile of airway pressure release ventilation (APRV), consisting of a prolonged pressure-time profile and brief expiratory release phase, reduces microstrain.</p> <p>DESIGN, SETTING, AND PARTICIPANTS In a randomized, non-blinded laboratory animal study, rats were randomized into a controlled mandatory ventilation group (n = 3) and an APRV group (n = 3). Lung injury was induced by polysorbate lavage. A thoracotomy was performed and an in vivo microscope was placed on the lungs to measure alveolar mechanics.</p> <p>MAIN OUTCOMES AND MEASURES In the controlled mandatory ventilation group, multiple levels of positive end-expiratory pressure (PEEP; 5, 10, 16, 20, and 24 cm H₂O) were tested. In the APRV group, decreasing durations of expiratory release (time at low pressure [Tlow]) were tested. The Tlow was set to achieve ratios of termination of peak expiratory flow rate (T-PEFR) to peak expiratory flow rate (PEFR) of 10%, 25%, 50%, and 75%(the smaller this ratio is [ie, 10%], the more time the lung is exposed to low pressure during the release phase, which decreases end-expiratory lung volume and potentiates derecruitment). Alveolar perimeters were measured at peak inspiration and end expiration using digital image analysis, and strain was calculated by normalizing the change in alveolar perimeter length to the original length. Macrostrain was measured by volume displacement.</p> <p>RESULTS Higher PEEP (16-24 cm H₂O) and a brief Tlow (APRV T-PEFR to PEFR ratio of 75%) reduced microstrain. Microstrain was minimized with an APRV T-PEFR to PEFR ratio of 75% (mean [SEM], 0.05 [0.03]) and PEEP of 16 cm H₂O (mean [SEM], 0.09 [0.08]), but an APRV T-PEFR to PEFR ratio of 75%also promoted alveolar recruitment compared with PEEP of 16 cm H₂O (mean [SEM] total inspiratory area, 52.0% [2.9%] vs 29.4%[4.3%], respectively; <i>P</i> < .05). Whole-lung strain was correlated with alveolar microstrain in tested settings (<i>P</i> < .05) except PEEP of 16 cm H₂O (<i>P</i> > .05).</p>			
<p>Conclusions:</p> <p>Increased positive-end expiratory pressure and reduced time at low pressure (decreased Tlow) reduced alveolar microstrain. Reduced microstrain and improved alveolar recruitment using an APRV T-PEFR to PEFR ratio of 75% may be the mechanism of lung protection seen in previous clinical and animal studies.</p>			

ANM	Kollisch-Singule et al	Airway Pressure Release Ventilation Reduces Conducting Airway Micro-Strain in Lung Injury	<i>J Am Coll Surg</i> 2014;219:968e976
<p>Abstract:</p> <p>BACKGROUND: Improper mechanical ventilation can exacerbate acute lung damage, causing a secondary ventilator-induced lung injury (VILI). We hypothesized that VILI can be reduced by modifying specific components of the ventilation waveform (mechanical breath), and we studied the impact of airway pressure release ventilation (APRV) and controlled mandatory ventilation (CMV) on the lung micro-anatomy (alveoli and conducting airways). The distribution of gas during inspiration and expiration and the strain generated during mechanical ventilation in the micro-anatomy (micro-strain) were calculated.</p> <p>STUDY DESIGN: Rats were anesthetized, surgically prepared, and randomized into 1 uninjured control group (n ¼ 2) and 4 groups with lung injury: APRV 75% (n ¼ 2), time at expiration (T_{Low}) set to terminate appropriately at 75% of peak expiratory flow rate (PEFR); APRV 10% (n ¼ 2), T_{Low} set to terminate inappropriately at 10% of PEFR; CMV with PEEP 5 cm H₂O (PEEP 5; n ¼ 2); or PEEP 16 cm H₂O (PEEP 16; n ¼ 2). Lung injury was induced in the experimental groups by Tween lavage and ventilated with their respective settings. Lungs were fixed at peak inspiration and end expiration for standard histology. Conducting airway and alveolar air space areas were quantified and conducting airway micro-strain was calculated.</p> <p>RESULTS: All lung injury groups redistributed inspired gas away from alveoli into the conducting airways. The APRV 75% minimized gas redistribution and micro-strain in the conducting airways and provided the alveolar air space occupancy most similar to control at both inspiration and expiration.</p>			
<p>Conclusions:</p> <p>In an injured lung, APRV 75% maintained micro-anatomic gas distribution similar to that of the normal lung. The lung protection demonstrated in previous studies using APRV 75% may be due to a more homogeneous distribution of gas at the micro-anatomic level as well as a reduction in conducting airway micro-strain.</p>			

REV	Nieman et al	Mechanical Ventilation as a Therapeutic Tool to Reduce ARDS Incidence	<i>CHEST 2015; 148 (6): 1396 - 1404</i>
<p>Abstract:</p> <p>Trauma, hemorrhagic shock, or sepsis can incite systemic inflammatory response syndrome, which can result in early acute lung injury (EALI). As EALI advances, improperly set mechanical ventilation (MV) can amplify early injury into a secondary ventilator-induced lung injury that invariably develops into overt ARDS. Once established, ARDS is refractory to most therapeutic strategies, which have not been able to lower ARDS mortality below the current unacceptably high 40%. Low tidal volume ventilation is one of the few treatments shown to have a moderate positive impact on ARDS survival, presumably by reducing ventilator-induced lung injury. Thus, there is a compelling case to be made that the focus of ARDS management should switch from treatment once this syndrome has become established to the application of preventative measures while patients are still in the EALI stage. Indeed, studies have shown that ARDS incidence is markedly reduced when conventional MV is applied preemptively using a combination of low tidal volume and positive end-expiratory pressure in both patients in the ICU and in surgical patients at high risk for developing ARDS. Furthermore, there is evidence from animal models and high-risk trauma patients that superior prevention of ARDS can be achieved using preemptive airway pressure release ventilation with a very brief duration of pressure release.</p>			
<p>Conclusions:</p> <p>Preventing rather than treating ARDS may be the way forward in dealing with this recalcitrant condition and would represent a paradigm shift in the way that MV is currently practiced.</p>			

REV	Nieman et al	Impact of mechanical ventilation on the pathophysiology of progressive acute lung injury	<i>J Appl Physiol</i> 119: 1245–1261, 2015.
<p>Abstract:</p> <p>The earliest description of what is now known as the acute respiratory distress syndrome (ARDS) was a highly lethal double pneumonia. Ashbaugh and colleagues (Ashbaugh DG, Bigelow DB, Petty TL, Levine BE <i>Lancet</i> 2: 319-323, 1967) correctly identified the disease as ARDS in 1967. Their initial study showing the positive effect of mechanical ventilation with positive end-expiratory pressure (PEEP) on ARDS mortality was dampened when it was discovered that improperly used mechanical ventilation can cause a secondary ventilator-induced lung injury (VILI), thereby greatly exacerbating ARDS mortality. This Synthesis Report will review the pathophysiology of ARDS and VILI from a mechanical stress-strain perspective. Although inflammation is also an important component of VILI pathology, it is secondary to the mechanical damage caused by excessive strain. The mechanical breath will be deconstructed to show that multiple parameters that comprise the breath—airway pressure, flows, volumes, and the duration during which they are applied to each breath—are critical to lung injury and protection. Specifically, the mechanisms by which a properly set mechanical breath can reduce the development of excessive fluid flux and pulmonary oedema, which are a hallmark of ARDS pathology, are reviewed.</p>			
<p>Conclusions:</p> <p>Using our knowledge of how multiple parameters in the mechanical breath affect lung physiology, the optimal combination of pressures, volumes, flows, and durations that should offer maximum lung protection are postulated.</p>			

ANM	Sumeet et al	The role of high airway pressure and dynamic strain on ventilator-induced lung injury in a heterogeneous acute lung injury model	<i>Intensive Care Medicine Experimental (2017) 5:25</i>
<p>Abstract:</p> <p>Background: Acute respiratory distress syndrome causes a heterogeneous lung injury with normal and acutely injured lung tissue in the same lung. Improperly adjusted mechanical ventilation can exacerbate ARDS causing a secondary ventilator induced lung injury (VILI). We hypothesized that a peak airway pressure of 40 cmH₂O (static strain) alone would not cause additional injury in either the normal or acutely injured lung tissue unless combined with high tidal volume (dynamic strain).</p> <p>Methods: Pigs were anesthetized, and heterogeneous acute lung injury (ALI) was created by Tween instillation via a bronchoscope to both diaphragmatic lung lobes. Tissue in all other lobes was normal. Airway pressure release ventilation was used to precisely regulate time and pressure at both inspiration and expiration. Animals were separated into two groups: (1) over-distension + high dynamic strain (OD + HDS, n = 6) and (2) over-distension + low dynamic strain (OD + LDS, n = 6). OD was caused by setting the inspiratory pressure at 40 cmH₂O and dynamic strain was modified by changing the expiratory duration, which varied the tidal volume. Animals were ventilated for 6 h recording hemodynamics, lung function, and inflammatory mediators followed by an extensive necropsy.</p> <p>Results: In normal tissue (NT), OD + LDS caused minimal histologic damage and a significant reduction in BALF total protein (p < 0.05) and MMP-9 activity (p < 0.05), as compared with OD + HDS. In acutely injured tissue (ALIT), OD + LDS resulted in reduced histologic injury and pulmonary oedema (p < 0.05), as compared with OD +HDS.</p>			
<p>Conclusions:</p> <p>Both NT and ALIT are resistant to VILI caused by OD alone, but when combined with a HDS, significant tissue injury develops.</p>			

REV	Habashi	Other approaches to open-lung ventilation: Airway pressure release ventilation	Crit Care Med 2005 Vol. 33, No. 3 (Suppl.)
<p>Abstract: Objective: To review the use of airway pressure release ventilation (APRV) in the treatment of acute lung injury/acute respiratory distress syndrome. Data Source: Published animal studies, human studies, and review articles of APRV. Data Summary: APRV has been successfully used in neonatal, paediatric, and adult forms of respiratory failure. Experimental and clinical use of APRV has been shown to facilitate spontaneous breathing and is associated with decreased peak airway pressures and improved oxygenation/ventilation when compared with conventional ventilation. Additionally, improvements in hemodynamic parameters, splanchnic perfusion, and reduced sedation/ neuromuscular blocker requirements have been reported.</p>			
<p>Conclusions: APRV may offer potential clinical advantages for ventilator management of acute lung injury/acute respiratory distress syndrome and may be considered as an alternative “open lung approach” to mechanical ventilation. Whether APRV reduces mortality or increases ventilator-free days compared with a conventional volume-cycled “lung protective” strategy will require future randomized, controlled trials.</p>			