Should Recruitment Maneuvers Be Used in the Management of ALI and ARDS?

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Lung recruitment maneuvers are being used in the management of acute lung injury and acute respiratory distress syndrome, but recruitment maneuvers are controversial. The proponents argue that when properly applied to appropriately selected patients, they are effective and can be safely applied. The expectation is that the recruitment maneuver will change the course of ARDS and improve outcomes. Those opposed to recruitment maneuvers argue that no data indicate better outcomes with recruitment maneuvers and that they are potentially unsafe. Outcome data are clearly needed before recruitment maneuvers can be fully incorporated into clinical practice. If a recruitment maneuver is conducted, a decremental positive end-expiratory pressure (PEEP) trial must be done to determine the minimum PEEP that sustains the benefits of the recruitment maneuver. We explore both sides of the lung recruitment controversy. *Key words: acute lung injury, acute respiratory distress syndrome, lung recruitment, positive end-expiratory pressure, fraction of inspired oxygen, ALI, ARDS.* [Respir Care 2007;52(5):622–631.

Introduction

Over the last 15 to 20 years, large gains in our knowledge of acute lung injury (ALI) and its management have been made. It has been clearly established that mechanical ventilation can induce lung injury by causing overdisten-

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tion and repetitive opening and closing of unstable lung units.[1] Data from a number of randomized controlled trials indicate that small tidal volume (V_T) along with low plateau pressure reduces mortality in ALI and acute respiratory distress syndrome (ARDS), compared to large V_T and high plateau pressure.[2–4] Controversy, however, still exists over the use of high versus low positive end-expiratory pressure (PEEP),[3–5] the method of setting PEEP,[3–5] and the use of lung recruitment maneuvers in the management of ALI/ARDS.[6,7] A lung recruitment maneuver (Fig. 1) requires briefly increasing the alveolar pressure to a level above that recommended during ongoing management of ALI/ARDS, to open lung units with high opening pressure.[8]

For a recruitment maneuver to be successful, the appropriate PEEP must be selected following the maneuver.[9] That is, the lowest PEEP setting that maintains the recruited lung open should be determined.[9] Because of the hysteresis between the inflation and deflation limbs of the pressure-volume curves of the lung (see Fig. 1), any given PEEP level applied after lung recruitment maintains a larger lung volume than before, if lung was recruited by the maneuver.[9]

In this paper we present the controversy surrounding lung recruitment maneuvers. Since no randomized controlled trials clearly establish benefit from recruitment maneuvers, opinions differ on whether lung recruitment should be used in the routine management of ALI/ARDS.

Pro: Lung Recruitment Should Be Used Routinely

The use of lung recruitment in the management of ALI/ARDS should be routine, because:

1. Regardless of the V_T, there is the potential that unstable lung units will open and close with inspiration and increase the lung injury.
2. Mortality in ARDS is still very high, and strategies in addition to small V_T are necessary to decrease mortality.
3. Sustained improvement in lung function occurs following lung recruitment if PEEP is properly set.
4. Minimal risks have been associated with properly timed and performed recruitment maneuvers.

Theoretical Considerations

Repetitive opening and closing of unstable lung units induces severe lung injury. Mead and colleagues[10] in 1970 calculated the shear stress experienced by an open lung unit positioned adjacent to a collapsed unit that opened and closed with each breath. They determined that when a peak transalveolar pressure of 30 cm H_2O was applied to these units, the stress on the wall between the 2 units is approximately 140 cm H_2O. This stress injures the healthy lung unit adjacent to the collapsed unit. As discussed by Arnold,[11] in ALI/ARDS, 3 types of lung units exist: (1) collapsed, atelectatic, or consolidated lungs units, mostly in a dependent position; (2) open, minimally injured lung units,

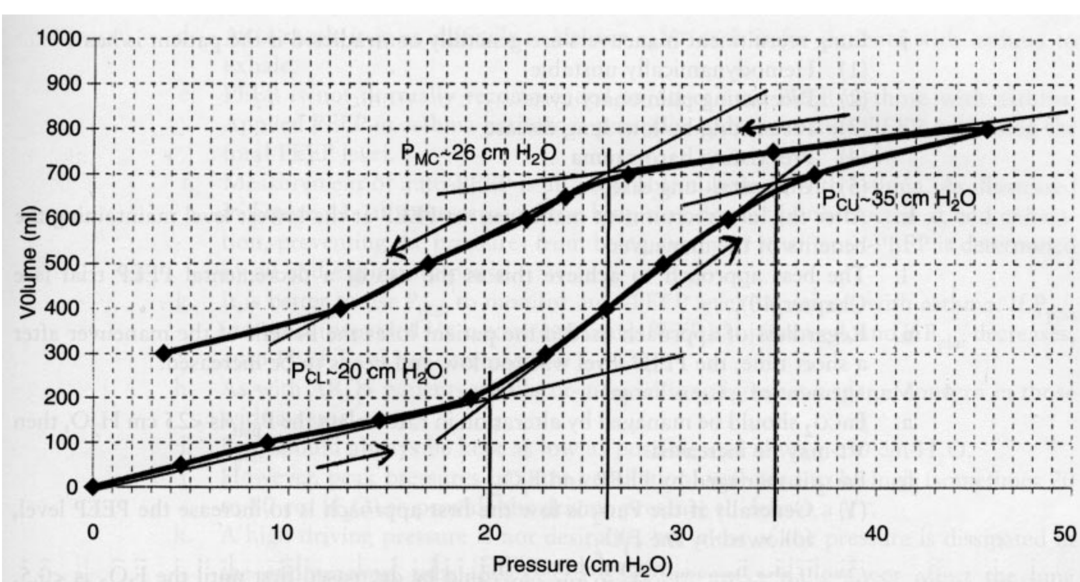

Fig. 1. Inflation and deflation pressure-volume curve of the lung of a laboratory animal with acute respiratory distress syndrome. The lower curve is the inflation limb. The upper curve is the deflation limb. P_{CL} = lower corner pressure (lower inflection point) P_{CU} = upper corner pressure (upper inflection point). PMC = point of maximum compliance change. Note the hysteresis (large difference between the 2 curves), which indicates that the lung is opened by a recruitment maneuver with a peak pressure of 45 cm H_2O and PEEP equal to P_{CL} set immediately after recruitment. Ventilation would now occur on the deflation limb, and a PEEP of 20 cm H_2O would maintain a larger lung volume than the same PEEP before lung recruitment (From Reference 8, with permission.)

mostly in nondependent positions; and (3) lung units on the borders of the latter 2 regions. It is this last group of alveoli that is most at risk of recruitment/derecruitment injury. Since peak pressure opens the lung, and airway opening pressure in both animal[12] and human[7,13] studies has a peak distribution at about 30 cm H_2O, unless plateau pressure is very low, the lung units at the borders between open and collapsed lung are exposed to an injurious stress level, unless the lung is recruited and PEEP is properly set. In addition, regardless of this potential for inducing additional mechanical injury to the lung, the unrecruited lung requires higher pressure to ventilate, higher fraction of inspired oxygen (F_{IO_2}) to oxygenate, has an increased likelihood of infection, has a decreased surfactant production, and has an increased likelihood of inducing an inflammatory mediator response.[14,15]

ARDS Mortality Is Still High

There is no question that the use of small V_T (6 mL/kg) reduces ALI/ARDS mortality; however, recent epidemiologic studies[16,17] indicate that mortality in ARDS is still over 50% and mortality in ALI is over 30%. Yes, the recent ARDS Network ALVEOLI study[5] indicated that mortality is 27–28%, but one must question the severity of illness of the patients studied by the ARDS Network.[3,5] Enrollment into the ARDS Network studies required a $P_{aO_2}/F_{IO_2} < 300$ mm Hg, regardless of the F_{IO_2} and PEEP setting. Two recent studies[18,19] indicate that patients with a $P_{aO_2}/F_{IO_2} < 200$ mm Hg, when placed on standard ventilator settings with defined PEEP and F_{IO_2} levels, separate into patients with high and low mortality. Villar et al[18] found that patients with persistent ARDS had a mortality of 68%, and those with a milder form of injury had a mortality of 23%. Ferguson et al[19] found similar results; patients with persistent ARDS had a mortality of 53%, and those with ALI had a mortality of 13%. The impact of standard ventilator settings is clearly seen in the more recently published randomized controlled trial by Villar et al,[4] which evaluated approaches to ventilating ARDS patients. In that study, 311 patients initially met ARDS criteria ($P_{aO_2}/F_{IO_2} < 200$ mm Hg). However, 24 hours later, on standard ventilator settings, only 103 patients still met ARDS criteria. As a result, it can be argued that the ARDS Network studied patients with a mild form of lung injury and that the mortality for persistent ARDS is still over 50%, which requires further innovative approaches to ARDS management to improve survival.

It is true that the immediate impact of lung recruitment is improvement in physiologic values, specifically oxygenation and lung mechanics, but as emphasized by Lachmann[20] in 1992, opening the lung and keeping it open is intended to change the course of ARDS and improve overall outcome. However, as emphasized earlier, randomized controlled trials have not yet been performed to evaluate this hypothesis.

Sustained Improvement in Lung Function

Ideally, the lung should be recruited with pressure high enough to open recruitable lung, sustained with adequate PEEP after lung recruitment, to avoid derecruitment, and performed on the appropriate patients early in the course of ALI/ARDS. Two different methods have emerged as the optimal approaches to recruiting the lung: high-level continuous positive airway pressure (CPAP),[21–23] and pressure control ventilation with high peak and end-expiratory pressure.[7,24] However, animal models[25] showed that pressure control ventilation to recruit the lung results in less cardiovascular compromise than does CPAP, so pressure control ventilation is considered the ideal approach to lung recruitment. With either approach it appears that the lung can be safely recruited with the short-term application of 40–50 cm H_2O peak alveolar pressure.

Safety and Timing. Ideally, the lung recruitment maneuver should be performed as early as possible in the course of ALI/ARDS. The longer ALI/ARDS is established, the greater the likelihood of adverse reactions and limited recruitment.[13,21,24] Grasso et al[21] very nicely demonstrated that patients who received a recruitment maneuver on day 1 $\pm$ 0.3 of ARDS could be recruited, versus patients recruited on day 7 $\pm$ 1. Similarly, Gattinoni et al[24] and Crotti et al[13] found limited recruitment in patients who were well along in the course of ARDS. Borges et al,[7] Tugrul et al,[23] and Girgis et al[9] all recruited patients early in the course of ARDS, and each found marked lung recruitment, on average, in all the patients studied.

Although the safety of lung recruitment maneuvers has been questioned, limited data in case series support this concern. The primary complications of lung recruitment maneuvers are hemodynamic compromise and barotrauma. Grasso et al reported a marked decrease in cardiac output (37 $\pm$ 2%) and mean arterial pressure (19 $\pm$ 3%) during recruitment maneuvers[21] in the non-recruitment-responder group. However, all of these patients had been ventilated long-term (7 $\pm$ 1 d) when recruitment was attempted. In addition, no protocol for ensuring adequate vascular volume was used prior to applying the maneuver. The study by Borges et al[7] recommends that pulse pressure variation should be limited to < 10–12% prior to performing a recruitment maneuver, to limit cardiovascular compromise. In the 26 patients studied by Borges et al,[7] with peak alveolar pressure up to 60 cm H_2O, none experienced hemodynamic compromise during the recruitment maneuver. Similarly the ARDS Network[25] reported only a 10.6 $\pm$ 1.2 mm Hg decrease in systolic blood pressure during lung recruitment in a negative recruitment study.

Barotrauma has rarely been reported following lung recruitment. Borges et al[7] used peak alveolar pressure of up to 60 cm H_2O in 26 patients, and reported one pneumothorax 48 hours after lung recruitment and one case of subcutaneous emphysema 12 hours after recruitment. Considering that the incidence of barotrauma in ARDS is about 10% in patients managed with lung-protective ventilation,[2–5] this barotrauma rate is consistent with that of these randomized controlled trials.[2–5]

Common sense must be used when considering which patients should receive a lung recruitment maneuver. Recruitment maneuvers should be avoided in patients with hemodynamic compromise, blebs or bullae on chest radiograph, or existing barotrauma. In addition, extreme caution should be exercised in patients with increased intracranial pressure, which should be considered a relative contraindication to lung recruitment.

Ability to Recruit the Lung. Recent data from Gattinoni et al[24] indicate that limited lung can be recruited. These data directly conflict with data from Borges et al,[7] Tugrul et al,[23] Girgis et al,[9] and Grasso et al,[21] all of whom found marked lung recruitment in patients recruited early in the course of ARDS. The most definitive data that support lung recruitment in ARDS (regardless of whether the ARDS is of pulmonary or extra-pulmonary origin) are from Borges et al.[7] They studied 11 patients with computed tomography (CT) and 15 patients in the intensive care unit during and after recruitment maneuvers. They defined maximum recruitment as a $P_{aO_2} + P_{aCO_2} > 400$ mm Hg, and, by that definition, recruited 24 of the 26 patients they studied. Figure 2 illustrates the results from one patient. Before lung recruitment, over 50% of the lung mass was collapsed, whereas following recruitment < 1% of the lung mass remained collapsed.

The data from Borges et al[7] conflict with those from Gattinoni et al,[24] for the following reasons:

1. Borges et al studied patients ventilated for a median of 2 days, whereas Gattinoni et al studied patients ventilated for 5 ± 6 days before they received the recruitment maneuver.

2. Borges et al used a peak alveolar pressure of 60 cm H_2O, whereas Gattinoni et al used a peak alveolar pressure of 45 cm H_2O.

3. During and after recruitment, Gattinoni et al allowed PEEP to decrease to 5 cm H_2O, whereas Borges et al maintained a minimum PEEP of 25 cm H_2O during recruitment and during the post-recruitment CT. If PEEP is not maintained after recruitment, the recruited lung is almost immediately derecruited.

Thus, the data from Gattinoni et al[24] can easily be dismissed as not representative of the response to lung recruitment properly performed in an appropriate patient.

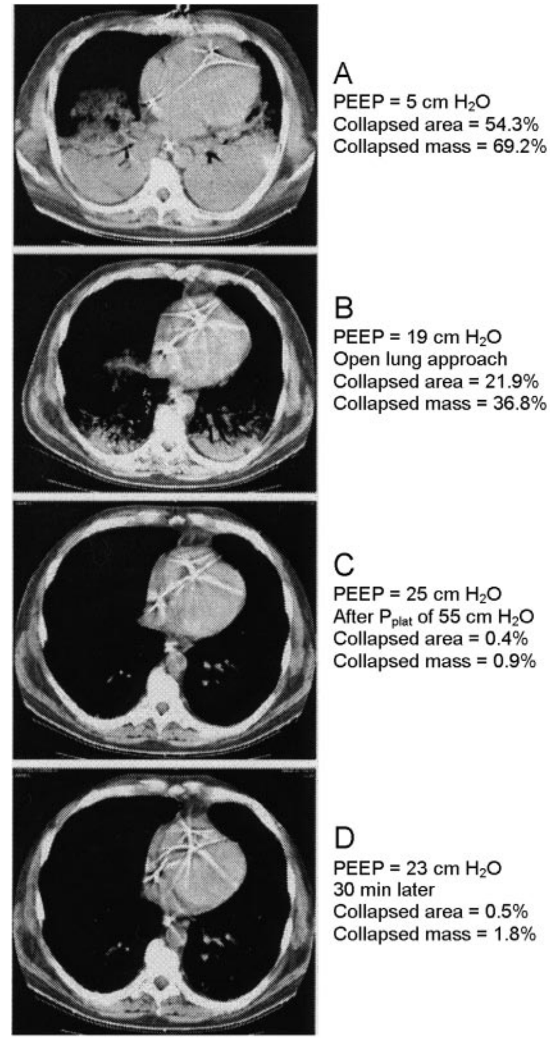

Fig. 2. Sequential computed tomograms (CTs) from a patient undergoing a series of lung recruitment maneuvers. A: Baseline at positive end-expiratory pressure (PEEP) of 5 cm H_2O. B: After a recruitment maneuver with 40 cm H_2O continuous positive airway pressure (CPAP) for 40 seconds, followed by PEEP set at 2 cm H_2O above the lower inflection point. C: Following a recruitment maneuver with pressure control ventilation, plateau pressure (P_{plat}) 55 cm H_2O, PEEP 40 cm H_2O, for 2 min; CT obtained at CPAP of 25 cm H_2O. D: After decremental PEEP trial identified optimal PEEP of 23 cm H_2O. (From Reference 7, with permission.)

Sustained Benefit of Lung Recruitment

All of the studies that have evaluated the effects of lung recruitment maneuvers that were unable to sustain the benefit of the maneuver did not determine the specific PEEP required to sustain the recruited lung open.[6,21,22,26–29] A prime example of this is the recruitment study associated with the ARDS Network ALVEOLI study.[26] After the lung was recruited, the study focused on decreasing the PEEP and F_{IO_2}, down the ARDS Network's PEEP/F_{IO_2} table. They deemed it a positive response only if 2 hours after the recruitment maneuver the PEEP/F_{IO_2} could be moved 2 steps down the table. Based on that protocol, the study was doomed to failure. The specific PEEP needed to maintain the recruited lung open was never determined. Similarly, none of the other studies[6,21,22,27–29] attempted to identify the PEEP that would maintain the benefit of lung recruitment. The only approach that allows the identification of the correct PEEP is a decremental PEEP trial.[30] The benefits of a recruitment maneuver have persisted for 4–6 hours in both animal[31–33] and human[7,9,21] studies that used a decremental PEEP trial. In all of these trials, the post-recruitment PEEP was initially set higher than was expected necessary to sustain the benefit of lung recruitment (20–25 cm H_2O), then decreased in 2-cm H_2O steps every 5–20 min while oxygenation (P_{aO_2} or oxygen saturation measured via pulse oximetry) or compliance was monitored. With both of these variables, the values increase as PEEP decreases, then decrease or plateau as PEEP is further decreased. The optimal PEEP is the one associated with the best compliance or oxygenation during the decremental trial. Once the optimal PEEP is identified, the lung is again recruited, and PEEP is set at 2 cm H_2O above the PEEP identified in the decremental PEEP trial. Only then is F_{IO_2} reduced to the lowest level that maintains P_{O_2} in the target range. Since it is easy to underestimate the correct PEEP, most recommend setting PEEP 2 cm H_2O higher than the PEEP identified in the decremental PEEP trial.[7,9,23] During the decremental PEEP trial, ventilation is maintained (via pressure or volume ventilation) with a small V_T (4–6 mL/kg predicted body weight). Compliance is the ideal variable to monitor during the decremental PEEP trial, because it rapidly equilibrates (within 3–5 min) after each PEEP reduction, which decreases the duration of the trial and identifies the same PEEP level as does P_{aO_2}.[31] The decremental PEEP trial is needed because, as shown by Girgis et al,[9] the final PEEP may be higher than, lower than, or equal to the PEEP that was used before the recruitment maneuver was applied.

If the oxygenation or compliance worsens, the PEEP is inadequate. This is, however, rarely observed if a decremental PEEP trial is conducted. The frequency that recruitment maneuvers should be applied is an unanswered question. If the benefit is sustained, no additional recruitment maneuvers are needed, but if the ventilator circuit is disconnected and the lung derecruited, the lung should be rerecruited.

Con: Lung Recruitment Should Not Be Used Routinely

The issue of whether recruitment maneuvers should be incorporated as routine therapy for patients with ALI/ARDS is made uncertain by several issues, which can be summarized as follows:

1. The existence and prevalence of repetitive shear injury in ALI/ARDS has not been firmly established, and, in this context, recruitment maneuvers have not been shown to reduce either morbidity or mortality.
2. Recruitment maneuvers provide only temporary improvement in lung function.
3. There are several methods of recruitment maneuver, and the most effective method has not been determined.
4. It has not been firmly established under what specific conditions of ALI/ARDS recruitment maneuvers should be used.
5. Recruitment maneuvers carry substantial risks.
6. There is the overarching question of whether optimization of physiological functioning during acute illness is synonymous with optimal therapy.

Theoretical Uncertainties

Recruitment maneuvers and high PEEP, which are the cornerstones of open-lung ventilation,[20] are based on a particular interpretation of the CT and the respiratory system pressure-volume curve, and the supposition that lung weight is an important determinant of the topographic distribution of regional lung volume. Open-lung ventilation is based on several assumptions:

1. The weight of edematous lung in ALI/ARDS causes compression atelectasis of the dependent zones, which results in regional variation of lung volume.
2. The increased vertical gray scale on chest CT correlates with alveolar size and hence local stress.
3. The lower inflection point on the inspiratory pressure-volume curve represents the beginning of lung recruitment.

However, uncertainties are associated each of these assumptions.

First, only 20% of the ventral-dorsal pleural pressure gradient normally can be attributed to superimposed lung weight.[34,35] Stress distribution within the lung primarily depends on the weight of the chest wall and mediastinal structures. Furthermore, the injured lung is more resistant to gravitational shape deformation than is normal lung.[36]

Second, the vertical gray-scale gradient observed in chest CT represents tissue density and relative gas content, but gives no information regarding the state of lung tissue. In other words, the increasing density along the ventrodorsal gradient may represent either increasing amounts of fluid-filled alveoli (noncollapsed) or atelectasis (collapsed).[36] Interpretation of chest CT images is further complicated because areas that appear consolidated may include aerated alveoli, whereas areas that appear normal may result from the combination of consolidated and overinflated alveoli.[37]

Third, the lower inflection point observed on the pressure-volume curve does not necessarily reflect recruitment of collapsed alveoli. Although congestive atelectasis has been described in ARDS,[38] exudative alveolar edema and hemorrhage are the more salient pathologic features on microscopic examination.[38–44] Use of a parenchymal marker technique in an oleic acid model of lung injury found that, even though gas volume was reduced by edema fluid, regional lung volume at functional residual capacity was not diminished.[45] This suggests that the lower inflection point may not represent the reopening of collapsed airspaces, but rather signifies the pressure needed to break liquid menisci in the small airways and shift fluids peripherally during gas inflation.

Moreover, the most widely-cited study[46] that implicated "atelectrauma" as a source of ventilator-associated lung injury utilized a nonperfused, saline-lavage model that induced alveolar collapse, but without the alveolar flooding typically found in ALI/ARDS. This may have exaggerated shear injury more than what occurs naturally during mechanical ventilation in humans with ALI/ARDS. In the presence of alveolar flooding, variable amounts of air remain trapped behind foam-blocked airways, in addition to alveoli that are either partially or completely fluid-filled. In this situation the critical airway-opening pressure would be dissipated over a series of menisci, so that local stresses to the lining cells would be relatively small.[36] Therefore, shear stress may play a smaller role in the generation of ventilator-associated lung injury than what has been suggested by proponents of open-lung ventilation. Interestingly, a recent animal study found that recruitment maneuvers did not reduce alveolar epithelial injury following oleic acid injury.[47]

Limited Temporal Efficacy

Several studies have shown that a recruitment maneuver with high-level CPAP, pressure-controlled ventilation, and high PEEP or sigh breaths of 45 cm H_2O did not result in sustained improvement in oxygenation,[6,21,26–29,48,49] lung volume,[21,28] or lung compliance.[21,27,28] However, there is some clinical[50] and laboratory[25,51] evidence that a recruitment maneuver with pressure-controlled ventilation with step-wise increasing PEEP is more effective in stabilizing lung function than is sustained CPAP.

More importantly, theoretical predictions based on animal modeling do not always match clinical reality. Recently, it was suggested that if full recruitment can be achieved with a sustained inflation recruitment maneuver, so that the lungs are placed on the deflation arm of the pressure-volume curve, then lung-protective ventilation can be achieved with PEEP set below the lower inflection point.[52] Yet it is increasingly apparent that PEEP must be titrated *upwards* following a recruitment maneuver, to preserve the gains in lung function. This incongruity probably stems from the fact that animal models of lung recruitment based on surfactant washout do not comport with clinical reality. In ALI/ARDS the lungs are flooded and obstructed with particulate, tenacious fluid, in addition to the compressive effects of an edematous chest wall, distended abdomen, and engorged mediastinal structures (as commonly occurs during sepsis, necrotizing pancreatitis, and trauma). These clinical features often are not adequately captured in animal modeling. This may explain why some investigators are now advocating recruitment with extraordinarily high inspiratory levels of pressure-controlled ventilation to achieve adequate recruitment.[53] Therefore, it becomes difficult to support the adoption of recruitment maneuvers into *routine* practice when the modeling is inadequate and the treatment approach is unsettled.

Limited Efficacy in Subtypes of ARDS

In ALI/ARDS, the percentage of recruitable lung tissue is highly variable between patients.[24] Furthermore, not all forms of lung injury appear amenable to substantial lung recruitment. In particular, patients who present with severe pneumonia and extensive consolidation,[28,29,54] and animal models of direct lung injury[25] do not have an appreciable amount of recruitable lung tissue. For example, in both an oleic acid model of lung injury[12] and in patients with primary forms of ARDS,[13] the majority of recruitable lung tissue opens at alveolar pressure below 25 cm H_2O. This suggests that a recruitment maneuver may not improve lung function any better than use of a small V_T with moderately high PEEP. In patients with small capacity for recruitment, a recruitment maneuver paradoxically may worsen oxygenation by overdistending aerated lung units and redistributing pulmonary blood flow to areas of consolidation.[6] Furthermore, use of a recruitment maneuver in this situation may needlessly expose the lungs to stretch-related lung injury.[6] Other studies suggest that categorizing the potential effectiveness of a recruitment maneuver based on direct or indirect lung injury is too simplistic, and that the particular derangements in lung and chest wall compliance are more important.[21] Therefore, it is unclear how broadly recruitment maneuvers should be applied in ALI/ARDS, and how to identify patients likely to benefit from recruitment maneuvers.

Which Method of Recruitment Maneuver Should Be Used?

The most well known method of recruitment maneuver is sustained application of CPAP of 30–50 cm H_2O for 30 seconds.[26,27,55] However, other methods include periodic recruitment with a series of traditional sigh breaths,[28] intermittently raising PEEP over several breaths,[48] and an extended sigh maneuver with step-wise increase in PEEP while V_T is decreased.[29,56] Recently, interest has focused on the intermittent application of pressure-controlled ventilation with incremental high PEEP[53] as a more effective way to reestablish functional residual capacity. Therefore, the best method of recruitment maneuver remains uncertain, and for each method the optimal pressure, duration, and periodicity is unknown.[57] These uncertainties suggest that advocating routine use of recruitment maneuvers for patients with ALI/ARDS is premature.

Hemodynamic Compromise

Because a recruitment maneuver is a form of high-volume, high-pressure mechanical ventilation, the patient can be subjected to substantial hemodynamic compromise.[25,58-60] Extrapulmonary forms of lung injury, which are more amenable to recruitment, may carry a greater risk of hemodynamic compromise.[54] As the lung is recruited, and compliance returns toward normal, high airway pressure is more readily transmitted across the lung parenchyma to the pleural space, impeding venous return and reducing cardiac output.[61] Moreover, high alveolar pressure increases pulmonary vascular resistance and right-ventricular afterload, resulting in a leftward shift of the cardiac septal wall, which diminishes left-ventricular compliance, raises end-diastolic pressure, and decreases cardiac output.[62] Furthermore, cardiac compliance is reduced directly by the compressive effects of high lung volume on the cardiac fossa.[63]

Animal models have reported significant decreases in either cardiac output or blood pressure during various recruitment maneuvers,[47,64] whereas in humans substantial reductions (20–30%) in cardiac output and mean arterial blood pressure have been reported during sustained inflations of 40 cm H_2O.[21] Recruitment maneuvers with pressure-controlled ventilation of 40 cm H_2O and 20 cm H_2O PEEP resulted in a persistent decrease in gastric mucosal perfusion following the recruitment maneuver.[49] This raises concerns about using recruitment maneuvers in patients with gastrointestinal ischemia, as subsequent reperfusion may enhance the inflammatory response and potentiate multiple-organ system dysfunction. Of particular concern are the effects of recruitment maneuvers in head-injured patients with ALI/ARDS, in whom a 17% decrease in cerebral perfusion pressure, along with a marked, sustained decrease in jugular venous oxygen saturation, from 69 to 59%, were reported.[65]

Risk/Benefit Ratio

Because a recruitment maneuver is a form of high-pressure, high-volume ventilation, it may entail a substantial risk of barotrauma.[66,67] Ventilator-associated lung injury is produced primarily by excessive transalveolar pressure along with high end-inspiratory lung volume, which causes mechanical stress in both alveolar macrophages and epithelial cells.[68] This in turn stimulates mechanoreceptors in these cells to release pro-inflammatory cytokines into the pulmonary and systemic circulations.[69] Because lung injury in ALI/ARDS is heterogeneously distributed, high-pressure high-volume recruitment techniques invariably result in some degree of regional lung overdistention.[64,69–71] Thus, the injudicious and repeated use of recruitment maneuvers can exacerbate lung injury. Furthermore, whenever high airway pressure and end-inspiratory volume are generated, there is also a possibility of bacterial translocation into the systemic circulation, which may increase the risk of sepsis.[67,72–74]

Because a recruitment maneuver typically produces only transient improvement in oxygenation,[6,26,27,29,49] particularly if PEEP is not adjusted upward, there is a valid concern that frequent recruitment maneuvers may contribute to lung injury.[73] At present, therefore, the risk/benefit ratio does not appear to favor routine use of recruitment maneuvers in patients *without* life-threatening hypoxemia. It is important to bear in mind that recruitment maneuvers have not been shown either to prevent ventilator-associated lung injury or to improve outcome in ALI/ARDS.[53,67,75]

Finally, the promotion of recruitment maneuvers as a routine practice characterizes a therapeutic approach that believes that optimizing physiologic function is a worthy goal in the management of ALI/ARDS. However, optimizing physiologic function does not necessarily represent optimal therapy, particularly when the therapeutic maneuver carries substantial risks from adverse affects. Ultimately, optimal therapy is the treatment regimen that minimizes morbidity and mortality. To date there is no compelling evidence that optimizing pulmonary function in ALI/ARDS improves meaningful outcomes. The primary goal of mechanical ventilation is, and should remain, to stabilize pulmonary gas exchange at an oxygen concentration and airway pressure that minimizes the risk of ventilator-associated lung injury. An exaggerated, albeit well-intentioned, emphasis on maintaining optimal physiological function paradoxically may impede patient care, particularly if mechanical ventilation is unnecessarily prolonged, either from an unwillingness of clinicians to tolerate any deterioration in lung function, or from complications that arise from radical maneuvers to open the lung.

Summary

The use of recruitment maneuvers in ALI/ARDS is controversial without data from randomized controlled trials to guide our application. Advocates of lung recruitment argue that opening and sustaining the lung open will change the course of ALI/ARDS and improve outcome. When patients are selected properly (early in the course of ALI/

ARDS, with neither hemodynamic compromise nor the presence or high likelihood of barotrauma), recruitment maneuvers are safe. The application of a recruitment maneuver should always begin with a low peak alveolar pressure (40 cm H_2O) and only increase to a maximum pressure of 50 cm H_2O if the patient does not respond to lower pressure and tolerates the maneuver. For the benefit of a recruitment maneuver to be sustained, the specific minimum PEEP that maintains the recruited lung open must be identified. This is best determined with a decremental PEEP trial. However, as discussed in the con side of this debate, the limited outcome data and the potential for adverse reactions should limit the application of recruitment maneuvers to settings where patient response can be systematically evaluated and patient safety assured. Before recruitment maneuvers can be fully incorporated into clinical practice, appropriate randomized controlled trials must be performed.

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Discussion

MacIntyre: That was probably the most passionate presentation we've had in this conference.

Kacmarek: May I make a rebuttal? First of all, what I hope I was able to get across is that if you *do* recruit the lung and you *do* choose the correct PEEP, there shouldn't be a need to recruit the lung again; as long as you do not disconnect the patient from the ventilator, you should not see derecruitment. We should see the benefit sustained for a relatively long period, in some patients indefinitely. There is clearly the possibility that a patient could need multiple recruitment maneuvers, but there should not be a need for that unless there is some other intervention, or the first recruitment maneuver did not recruit enough alveoli, or the patient's condition worsens.

Comparing lung recruitment to the high-frequency ventilation trial unfairly compares activation of inflammatory mediators. We're talking about doing these lung recruitments maneuvers for 1–3 minutes, not for an 8-hour period. Although you may see a bump in inflammatory mediators during the recruitment procedure, it drops off very quickly.

It is interesting to compare the Gattinoni et al[1] study to that of Borges et al.[2] Gattinoni et al found an inability to recruit the lung, whereas we found a dramatic ability to recruit the lung. The most important reason is that Gattinoni et al used inadequate PEEP after recruitment; they dropped the PEEP to 5 cm H_2O. You can't sustain the benefit of recruitment unless the PEEP during and after the recruitment maneuver is higher than what you would need to maintain the lung open.

Gattinoni et al also looked at patients who had had about 5 ± 6 days of mechanical ventilation. Those were long-term ventilator-dependent patients, as opposed to the patients we looked at, who were very early in the course of ARDS. The timing makes a difference in the ability to recruit the lung. In addition, Gattinoni only used one peak pressure: 45 cm H_2O. I would recommend starting at 40 cm H_2O peak pressure, with PEEP of 20–25 cm H_2O, in pressure control, then reassess the benefit, and if the patient is hemodynamically stable, then it is relatively safe going up to a pressure of 50 cm H_2O if the lung does not recruit at a lower pressure. I would not recommend—other than in a controlled experimental situation—going to a pressure higher than that.

When you say there are all these problems with recruitment, it's just not reflected in the literature where people have looked at case series of lung recruitment. Even the ARDS Network data does not show any significant problem associated with recruitment maneuvers.

1. Gattinoni L, Caironi P, Cressoni M, Chiumello D, Ranieri VM, Quintel M, et al. Lung recruitment in patients with the acute respiratory distress syndrome. N Engl J Med 2006;354(17):1775–1786.
2. Borges JB, Okamoto VN, Matos GF, Caramez MP, Arantes PR, Barros F, et al. Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome. Am J Respir Crit Care Med 2006;174(3): 268–278.

Steinberg: Very interesting arguments. I agree with you, Bob, that the goal of recruitment maneuvers should not be to improve oxygenation, but to reduce ventilator-induced lung injury and alter the course and severity of lung injury. I also agree that the current high mortality of 30–50% in some populations is unacceptable. But I think the evidence so far has failed to show that recruitment maneuvers can alter the course of lung injury, so I have to conclude that recruitment maneuvers should not be routine. We might find that there are patients in whom it's an important thing to do, but I don't think we're there yet. It remains a hypothesis. I think we all agree that repetitive opening and closing of alveoli may be harmful, but we haven't yet decided whether it's better to let alveoli stay closed or take the risk and effort to open them. It's a very interesting idea that maybe it's better to leave atelectasis alone unless it's a situation of severe life-threatening hypoxemia, when you need to recruit to keep the person alive.

MacIntyre: The ALVEOLI trial found that even though the higher PEEP clearly recruited lung and produced better P_{O_2} and better compliance, it did not change the outcome. We came up with the idea, and Ken coined the term (although I think I may have planted the seed) "permissive atelectasis." The idea is that it's not the atelectasis that hurts the lung; it's the repetitive opening and closing of alveoli. If it is that, then you could argue that reducing the V_T and leaving the atelectasis alone is all you need to do. Putting it another way, we could say recruit the easily recruitable lung but don't get too ambitious at trying to open up the tough, sticky, difficult-to-open alveoli.

Kacmarek: You're right; that is clearly where people stand. I obviously stand on one side of that argument and others stand on the opposite side. As you said, the lung opens at various pressures. We've ventilated patients at peak pressure of 25–30 cm H_2O, and then we maintain the open lung with a PEEP of 8 or 9 cm H_2O. I doubt that this is going to hold open those lung units that open at 20 or 25 cm H_2O, so you always have some lung units being recruited and de-recruited, even with small-V_T if you have atelectasis; you can't get away from it if you ventilate that way.

It's always the transitional units on the edges of the open and closed lung units that are most likely to develop lung injury. And it's those healthy lung units that are open next to those that are collapsed that are injured, by the shear force of opening the collapsed lung units. Mead et al[1] determined that these forces exert up to 140 cm H_2O of shear stress on the wall between open and closed lung units.

I don't believe that the ARDS Network studied patients who had ARDS, but, rather, I think that in both studies they looked at patients with ALI. I compared the data from the ALVEOLI trial to the Villar et al study,[2] in which, to be randomized the subject had to have a $P_{aO_2}/F_{IO_2} < 200$ mm Hg on standard ventilator settings 24 hours after meeting ARDS criteria ($P_{aO_2}/F_{IO_2} < 200$ mm Hg), whereas the ARDS Network only required a P_{aO_2}/F_{IO_2} of < 300 mm Hg, with no time or standard settings required. This difference is obvious when you compare the ARDS Network patients who had high PEEP on day 1 (PEEP 14.7 cm H_2O, F_{IO_2} 0.44, P_{aO_2}/F_{IO_2} 220 mm Hg) to the Villar et al patients on high PEEP on day 1 (PEEP 14.1 cm H_2O, F_{IO_2} 0.60, P_{aO_2}/F_{IO_2} 138 mm Hg). So it may have been a combination of issues that caused the appearance of no benefit from high PEEP in the ALVEOLI trial.

I don't think anybody has shown that recruitment negatively affects outcome. It hasn't been studied effectively with a randomized trial. It's a concept that needs to be systematically studied. So it's difficult for me to say that everybody ought to do lung recruitment maneuvers, although I think it is the right thing to do, based on the data we have.

1. Mead J, Takishima T, Leith D. Stress distribution in lungs: a model of pulmonary elasticity. J Appl Physiol 1970;28(5);596–608.
2. Villar J, Kacmarek RM, Perez-Mendez L, Aguirre-Jaime A. A high positive end-expiratory pressure, low V_T ventilatory strategy improves outcome in persistent acute respiratory distress syndrome: a randomized controlled trial. Crit Care Med 2006; 34(5):1311–1318.

MacIntyre: This morning we were talking about tidal stretch being an injury and arguing whether it's the repetitive physical stretch of alveoli above the normal V_T that causes injury. In thinking about it further, it occurs to me that maybe the benefit, or the harm to tidal stretch is just what you said. You're cycling through a whole series of openings and closings of alveoli that may not open until you get to a larger V_T. So forget the stretch injury—maybe the benefit of low V_T is a reduction in opening and closing injury.

Kacmarek: That is why you recruit the lung first. You set the PEEP properly, and then you adjust the plateau pressure to the lowest pressure you can get away with.

MacIntyre: I don't think you addressed what I just said. There's still going to be opening and closing of alveoli.

Kacmarek: The CT scan [see Fig. 2] I showed is representative of 24 of the 26 patients who were successfully recruited. The verification that the CT assessment was done accurately was performed by Gattinoni. We sent him the raw data, because he had concerns about our data. He calculated the changes and came up with the same level of change in collapsed lung volume. The Borges et al[1] data suggest that you can recruit the lung in many patients—I won't say everybody, but in many patients you can recruit to the level of virtually no collapse.

1. Borges JB, Okamoto VN, Matos GF, Caramez MP, Arantes PR, Barros F, et al. Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome. Am J Respir Crit Care Med 2006;174(3): 268–278.

MacIntyre: But if you haven't got them there, if you still have collapse present—

Kacmarek: But we're talking about recruitment maneuvers.

MacIntyre: OK, but in the run-of-the-mill patients you and I take care of, there's almost certainly going to be some collapse present in those lungs. All I'm suggesting is that in those atelectatic units we may reduce the opening and closing injury by reducing the V_T, regardless of the PEEP or plateau pressure.

Kacmarek: The V_T is only going to recruit if it generates a high pressure. If it doesn't generate a high pressure, it won't open any lung. It is pressure that opens the lung up, not necessarily volume.

MacIntyre: OK.

Kacmarek: So if that V_T does not generate a high peak alveolar pressure, it's only going to recruit lung with opening pressure at or below that pressure.

MacIntyre: But you are opening alveoli all the way through the pressure-volume curve.

Kacmarek: Absolutely.

MacIntyre: So regardless of how big the V_T is, it's going to open alveoli, many of which will subsequently close.

Kacmarek: There's no question that you have to have volume, but it's the transpulmonary pressure that opens the lung, not the particular volume you're delivering.

MacIntyre: But by minimizing V_T, by definition you will be opening and closing fewer atelectatic alveoli. You gotta spot me that one!

Kacmarek: I do. Reluctantly.

Kallet: I really want to emphasize the fact that our modeling and understanding of ventilator-induced lung injury are evolving and are far from being set in stone. And I would point out that a few years ago there were 2 very influential papers, by Rimensberger et al[1] and Borges et al,[2] that were based on a surfactant-washout model, and they demonstrated that if you fully recruit the lungs and move them onto the deflation limb of the curve, you actually need *less* PEEP to keep the lungs open. Your recent study[3] flatly contradicts that notion: once you re-recruit the lung, you in fact need a *higher* PEEP to sustain the effect. So the modeling we're using to look at this, to make decisions, is still being developed.

1. Rimensberger PC, Cox PN, Frendova H, Bryan AC. The open lung during small V_T ventilation: concepts of recruitment and "optimal" positive end-expiratory pressure. Crit Care Med 1999;27(9):1946–1952.
2. Rimensberger PC, Pristine G, Mullen JBM, Cox PN, Slutsky AS. Lung recruitment during small tidal volume ventilation allows minimal positive end-expiratory pressure without augmenting lung injury. Crit Care Med 1999;27(9):1940–1945.
3. Borges JB, Okamoto VN, Matos GF, Caramez MP, Arantes PR, Barros F, et al. Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome. Am J Respir Crit Care Med 2006;174(3): 268–278.

Kacmarek: I showed 3 studies, one of which required less PEEP after the lungs were recruited, although those patients were the least sick of the patients in the 3 studies I presented.

Kallet: OK. Now, again, with ARDS there are different pathological features: atelectasis with closed peripheral airways versus de-gassed lungs. Using a nonperfused, surfactant washout animal preparation to model what happens in patients with acute lung injury is not appropriate. There are other things going on that we still don't quite know. I think you guys are on the right track in terms of how to approach lung recruitment and stabilization with decremental PEEP trials, but I still think the whole subject is underdeveloped in terms of the theory and practice. We're still learning and we're still devising our models.

Rubin: Admittedly, I've been out of this literature for quite a while, but the surfactant study that most people quote for recruitment for treatment of ARDS, I think, was the old Exosurf study.[1] That study was negative, but they used a poor surfactant and an extremely poor aerosol delivery system. Has anybody looked at it now, with better surfactants and better delivery, using that as an adjunct to recruit airways, and perhaps at lower volume and lower pressure?

1. Anzueto A, Baughman RP, Guntupalli KK, Weg JG, Wiedemann HP, Raventos AA, et al. Aerosolized surfactant in adults with sepsis-induced acute respiratory distress syndrome. Exosurf Acute Respiratory Distress Syndrome Sepsis Study Group. N Engl J Med 1996;334(22):1417–1421.

Kacmarek: I don't know, but I do know of groups who are studying small volumes of perfluorocarbon to assist in the recruiting process—not to do partial liquid ventilation.

Rubin: We studied perfluorocarbon under both circumstances, and it's not the same thing. They are fairly *lower* surface tension, but that is not—

Kacmarek: I don't know if anybody's looking at surfactant as an adjunct to recruitment.

MacIntyre: There are trials ongoing, and one thing that has kept this field alive is the Willson et al study.[1] They studied pediatric—not neonatal—ALI/ARDS, and found that instilled surfactant improved gas exchange, presumably by improving recruitment, and this was associated with a mortality benefit.

1. Willson DF, Thomas NJ, Markovitz BP, Bauman LA, DiCarlo JV, Pon S, et al; Pediatric Acute Lung Injury and Sepsis Investigators. Effect of exogenous surfactant (calfactant) in pediatric acute lung injury: a randomized controlled trial. JAMA 2005; 293(4):470–476. *Erratum in: JAMA 2005; 294(8):900.*

Kacmarek: But it did not tie surfactant administration to doing a formal lung recruitment.

MacIntyre: It did not. That's true.

Rubin: I get the sense that people are worried about the high pressure involved, and concerned that we could be doing harm. Could we not be inducing more injury or pneumothoraces in these sick lungs? Aren't there are other ways of gaining some of these same benefits?

Kacmarek: The counter to that is, when a nurse or therapist ventilates with a bag-valve-mask setup, they hit very high peak airway pressure, over 60 cm H_2O, in many adults. Use a manometer to check how much pressure the bag is delivering, and don't let the person doing the bagging see it; the pressure is much higher than they'd think.

Rubin: Although, if you're talking about trying to sustain both pendelluft and collateral ventilation, what you're really talking about is sustaining the PEEP level.

Kacmarek: No question. Lung recruitment and the correct PEEP for the specific patient based on their lung mechanics is essential.

Branson: How would you do that? I was trained to treat ARDS with the method of Kirby and Downs,[1] in which all patients receive a high PEEP and IMV [intermittent mandatory ventilation] with a minimum rate of 2 breaths/min. The average rate in the ARDS Network trial was 35 breaths/min, which is 2,100 breaths per hour, or 50,000 breaths a day.

If you put everybody on IMV of 2 breaths/min and let them breathe spontaneously, you could drop that to 120 breaths an hour, or 720 breaths a day. If tidal stretch is a problem, less frequent stretches might be less damaging than more frequent stretches, even if the stretches were bigger. What about the idea that we could put everybody on IMV, let them breathe on their own, and that that might reduce lung injury?

1. Kirby RR. Round and round we go, and where we stop, nobody knows: the open lung concept and high-level positive end-expiratory pressure (revisited). Crit Care Med 2000;28(5):1672–1673.

MacIntyre: If the patient can breath spontaneously, the V_T will be about 5 mL/kg. However, in most intensive care units, clinicians will probably put them on pressure support.

Branson: I'm saying no pressure support. Let the patient breathe spontaneously. I don't know of any studies where spontaneous breathing was compared to all-mandatory breaths.

MacIntyre: I often conclude my lung-protective strategy by saying that maybe the ultimate goal for everybody is CPAP. This is one of the arguments for high-frequency ventilation; it's CPAP with just a little wiggle.

Steinberg: Hotchkiss et al[1] found that in isolated rabbit lung the respiratory rate can contribute to ventilator-induced lung injury; the more frequent the breaths, the worse the injury. Those are the only data I'm aware of. Bob, in the study where you used CT to measure lung recruitment and found full recruitment at very high transpulmonary pressure, did you also see parts of the lung that were radiographically overdistended?

1. Hotchkiss JR Jr, Blanch L, Murias G, Adams AB, Olson DA, Wangensteen OD, et al. Effects of decreased respiratory frequency on ventilator-induced lung injury. Am J Respir Crit Care Med 2000;161(2 Pt 1):463–468.

Kacmarek: Yes. There clearly was overdistention. Remember, though, that that was done at a PEEP of 25 cm H_2O, and these patients were not necessarily maintained on a PEEP of 25 cm H_2O. We did a decremental PEEP trial, starting at 25 cm H_2O after the recruitment maneuver, and we left them at 25 cm H_2O during the CT scan, so we didn't lose recruitment.

Pierson:* I want to revisit the issue of safety. There's a discrepancy in the presentations between Bob's assurance that recruitment maneuvers, when properly done, are perfectly safe, and Rich's assertion that in clinical practice there's a lot of folks doing stuff that maybe aren't quite as careful as in your studies.

Actually, those points have come up numerous times in this conference, when the primary focus of our discussion in each case has been whether such-and-such intervention works and should we do it? And then somewhere along the line the people arguing one point or another say, "And it's safe." But the safety is always with the caveat, "in properly selected patients, and when done properly, according to the protocol." And Rich has reminded us, and it has come up at other times, that clinical practice isn't exactly what happens in studies.

I'd like to know more from you and the group about just how unsafe recruitment maneuvers are if you take them outside the context of your rigid requirements for your study—especially if we start applying them willy-nilly to people who are profoundly hypoxic, who *may* have some of the things Rich listed, such as unilateral lung disease, heterogeneity in the lung, and so forth.

Kacmarek: I agree. The more you deviate from the ideal set of circumstances, the greater the probability of problems. You absolutely will see patients who become hemodynamically unstable, and you will get pneumothoraces in the middle of a recruitment maneuver. The higher the pressure, the higher the probability that those things will occur. Should they be occurring in a high percentage of patients? Higher than the normal incidence of barotrauma in ARDS? I don't think so. But a lot has to do with who's doing it and how. It's like any technique in medicine. With a new fellow doing a bronchoscopy, the probability of problems is much greater than with a very experienced pulmonologist.

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Pierson: "Bronchoscopes don't kill people—people kill people!" That's the argument. That is, it's how they're used.

Kacmarek: It's the same thing here. I don't think of lung recruitment as a technique that results in injury. The key is using it on the right patient, at the right time, with the right technique, with the right safety measures to determine when to abort it. If a patient becomes hemodynamically unstable during recruitment, you stop it. We didn't talk about the practicalities of how to do recruitment maneuvers, but you can create guidelines that would avoid these problems during recruitment maneuvers.

Pierson: I think when we publish these discussions, and they get read by the 40,000 people who read RESPIRATORY CARE every month, we need to strongly emphasize that recruitment maneuvers, along with all the other therapies we're talking about in this Journal Conference, have the potential to do great harm if you don't do them carefully and abide by the usual guidelines.

Kacmarek: Agreed.

Kallet: Agreed. I want to point out that in your studies,[1,2] patients were adequately fluid resuscitated, very intensely monitored, and most were on pressors. You had clinicians present who were *extremely* careful in doing this.

1. Borges JB, Okamoto VN, Matos GFJ, Caramez MPR, Arantes PR, Barros F, et al. Reversibility of lung collapse and hypoxemia in early acute respiratory distress syndrome. Am J Respir Crit Care Med 2006; 174(3):268–278.
2. Girgis K, Hamed H, Khater Y, Kacmarek RM. A decremental PEEP trial identifies the PEEP level that maintains oxygenation after lung recruitment. Respir Care 2006; 51(10):1132–1139.

Kacmarek: A lung recruitment maneuver is not something a therapist should do by him or herself. There should be a physician at the bedside, and thoughtful discussion about what it is you're doing and how you're doing it. And it should be performed carefully.