Acute lung injury/acute respiratory distress syndrome is a syndrome of low respiratory compliance. However, longstanding knowledge of applied respiratory mechanics and refined imaging techniques have shown that this is clearly an oversimplified view. Though the average compliance of the respiratory system is reproducibly low, regional mechanics may vastly differ; lung, airway, and chest wall mechanics may be variably affected; finally, these abnormalities may be very dynamic in nature, being influenced by time, posture, and the way positive-pressure ventilation is applied. Modern mechanical ventilators are equipped to display pressure, flow, and volume waveforms that can be used to measure respiratory compliance, airway resistance, and intrinsic positive end-expiratory pressure. These basic measurements, once the domain of applied physiologists only, are now available to aid clinicians to choose the appropriate ventilator settings to promote lung recruitment and avoid injury during lung-protective ventilatory strategies. High-resolution lung imaging and bedside recording of physiologic variables are important tools for clinicians who want to deliver specialized care to improve the outcome of critically ill patients in acute respiratory failure.

**Key words:** acute lung injury, acute respiratory distress syndrome, lung recruitment.
maintain adequate gas exchange and to offset the increased ventilatory load. However, endotracheal intubation and mechanical ventilation are themselves associated with other problems, including injury to the airway and lungs, the need for pharmacologic sedation and paralysis, and increased risk of nosocomial infections and prolonged weakness.2,3

Although low lung compliance has long been recognized as characteristic of ARDS,4 only recently has it become possible to apply physiologic principles of respiratory mechanics to the bedside. In our opinion, that progress is due mainly to 2 events: (1) the introduction of sophisticated lung imaging such as computed tomography (CT) of the chest, and (2) the ability to record and immediately display basic ventilatory variables, such as tidal volume (VT), flow, airway pressure (Paw), and esophageal pressure. These tools improve our ability to properly ventilate these patients, using the ventilator settings that can best support respiration while minimizing the risk of iatrogenic injury.

In this article we will first review the changes in respiratory mechanics that are characteristic of ALI/ARDS, with particular attention to aspects of their dynamic evolution. We will then see how some of our current methods of ventilating these patients (eg, recruitment maneuvers and prone-position ventilation) affect respiratory mechanics. The authors hope that this review will encourage clinicians to use the physiologic waveforms displayed on ventilators to adjust the level of mechanical ventilation to the best advantage of each patient with ALI/ARDS.

ARDS: A Syndrome of Low Compliance

Figure 1 shows the lungs of a patient who died with ARDS. Even in this macroscopic, 2-dimensional view, we can see how the lungs are enlarged, swollen, and covered with hemorrhagic exudate. These pathological phenomena substantially decrease lung compliance. A more detailed and real-time view of the ARDS lung is provided by CT, which identifies the areas of collapse and/or edema responsible for the low lung compliance. Furthermore, CT reveals a more complex distribution of the injury than might be inferred from Figure 1 or from a traditional, standard portable chest radiogram. That is, consolidated areas of the lung alternate with seemingly normally aerated areas. The work ofGattinoni et al5–8 over the past 2 decades has correlated CT images of ARDS lung with measurements of respiratory mechanics, and their research suggests that the low lung compliance that we measure in the early phase of ARDS is an averaged approximation of different regional mechanics, which are affected by factors such as the pressure applied at the airway and patient position.5–8
Figure 2 shows CTs from 2 different patients, both of whom had bedside-measured respiratory-system compliance of approximately 25 mLs/cm H₂O. Despite similar compliance, the difference between the 2 CTs is striking. In panel A the lungs are diffusely affected by an acute pneumonitic process (Aspergillus infection of the lung). In panel B, bibasilar dense consolidations from repeated nosocomial pneumonias spare much of the ventral portions of the lungs. Clearly, a given pressure applied at the airway will distribute very differently across the lungs of these 2 patients, resulting in different patterns of lung recruitment, gas exchange, and injury.

Important differences in lung mechanics may also be present between the 2 lungs of the same patient. Figure 3 shows the example of a patient who suffered from acute rejection of a transplanted left lung. The patient’s underlying disease was emphysema, which can easily be seen in the native right lung. As the left lung developed an ARDS-like picture, an obvious discrepancy developed between the mechanics of the 2 lungs: a low compliance on the left, and a high compliance and high resistance on the right. The ventilator waveforms are compatible with a 2-compartment model: the initial part of the breath (which is best seen in the flow waveform during exhalation) has a fast time constant; that is, air goes in and out fast, because of the low compliance and approximately normal resistance of the transplanted and diseased lung. The second part of the breath has a very slow time constant, typical of terminal emphysema/chronic obstructive pulmonary disease (ie, air exits the airways extremely slowly and there is not sufficient time to exhale the entire VT).

Increased Resistance in ALI/ARDS

Although we described ARDS as a syndrome of low compliance, airway resistance may also be abnormal.9,10 Besides the possibility of developing ARDS in the presence of asthma/chronic obstructive pulmonary disease, as in the patient described above (see Fig. 3), a mild increase in airway resistance is found in patients with ALI/ARDS, independent of pre-existent airway disease. Figure 4 shows the waveforms from an end-inspiratory airway-occlusion maneuver in a representative patient with early ARDS, demonstrating increased airway resistance.10 Further analysis of resistance in that study revealed that its ohmic portion11 (peak inspiratory pressure minus pressure at 50 ms [P max − P1 in Fig. 4]) was increased in inverse proportion to the decrease in functional residual capacity, suggesting that it was not due to airway narrowing but to a reduced volume of ventilated lung. The additional resistance (plateau inspiratory pressure at the beginning of 1-second occlusion minus that at the end of the occlusion [P1 − P2 in Fig. 4]) was increased in all patients, indicating the presence of time-constant inequalities within the diseased lungs. Of particular interest in that study was the effect of positive end-expiratory pressure (PEEP). A low level of PEEP tended to decrease the average airway resistance, by normalizing the ohmic component, probably through an increase in lung volume. A higher PEEP (approximately 15 cm H₂O) increased the total resistance, almost exclusively through an increase of the additional component, hence increasing regional inequalities at high lung volumes.10 Appreciation of the effects of ALI/ARDS on airway resistance may be important in situations of high respiratory rate, such as during...
lung-protective low-$V_T$ ventilation. Recently, de Durante et al demonstrated that the high respiratory rate necessary to maintain an adequate minute ventilation during low-$V_T$ ventilation may lead to substantial intrinsic PEEP, suggesting that end-expiratory alveolar pressure during lung-protective ventilation may be higher than the level set on the ventilator.

**Time-Related Patterns of Recruitment in ARDS**

While CT analysis can provide sophisticated visual information about lungs with ALI/ARDS, bedside measurement of respiratory mechanics is still relatively unrefined. Although new methods will almost certainly be available in the future, respiratory mechanics are currently assessed in a rather simple way, by measuring changes in flow and pressure at the airway, occasionally supplemented by the measurement of esophageal pressure. Neverthe-

less, investigators have been able to assess the dynamic nature of respiratory mechanics in patients with ALI/ARDS and have provided a longstanding scientific background to aid our daily interpretation of ventilator waveforms at the bedside.

In a very intellectually stimulating study more than 2 decades ago, Katz et al demonstrated that the effects of PEEP on lung volume in patients with acute respiratory failure are complex. By measuring breath-to-breath $V_T$ changes following the application of PEEP, they found that the initial (1–4 breaths) increase in volume occurs at constant compliance, indicating an increase in the volume of already ventilated alveoli. A further increase in volume (about 10% of the ultimate volume change in that particular patient population) occurred at the same end-inspiratory pressure, indicating recruitment of newly opened alveoli over a 3–4 min period. This observation is exemplified in Figure 5, where the

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**Fig. 3. Acute lung injury in a transplanted lung.** A: Computed tomogram shows severe emphysema in the right (native) lung and edema and consolidation in the left (transplanted) lung. B: Ventilator waveforms, compatible with a 2-compartment model. The initial part of the breath (seen best in the expiratory flow waveform) has a fast time constant, because of the low compliance of the acutely injured left lung; the second part of the breath has a very slow time constant, because of the high-resistance, high-compliance pattern of terminal emphysema. (Courtesy of Dean Hess RRT PhD FAARC, Massachusetts General Hospital, Boston, Massachusetts.)
compliance calculated using the end-expiratory and end-inspiratory P_{aw} difference (chord compliance) did not change at various levels of PEEP, while the compliance measured at functional residual capacity, once steady state was achieved, increased with each increase in PEEP, indicating that PEEP recruited alveoli, whereas tidal ventilation did not.

In another classic study of respiratory mechanics in ARDS, Matamis et al discerned different patterns of lung recruitment (Fig. 6). Early in the course of the syndrome (Fig. 6B) there is a large hysteresis, indicating potential for alveolar recruitment, associated with the initial exudative phase of ALI/ARDS, which remains present a few days later (Fig. 6C) but is now associated with a decreased compliance (decreased slope). Later in the course (Fig. 6A), during the fibroproliferative phase, the decrease in compliance becomes more apparent, with no substantial hysteresis, indicating a lower potential for recruitment. The pattern in Fig. 6D (low compliance, little recruitment potential) was observed in late ARDS and was associated with a high mortality.

Single-Breath Analysis of Recruitment

Setting the ventilator to provide lung recruitment and avoid injury is a complex and as yet unresolved task. ALI from mechanical ventilation can occur because of (1) alveolar overdistention due to high ventilating volumes and pressures, and (2) tidal recruitment/derecruitment due to insufficient PEEP. Recent evidence that low V_T may increase survival in ALI/ARDS has stimulated further discussion regarding how to use low V_T and maintain lung recruitment. A physiologically sound approach was used by Amato et al in the first published controlled study of low-V_T ventilation. They obtained static pressure-volume curves of the respiratory system to identify 2 important pressure values: the lower inflection point (the pressure above which end-expiratory alveolar collapse would not occur) was used to set the PEEP level, and the upper inflection point (the pressure below which end-inspiratory alveolar overdistention would not occur) was used to set the inspiratory plateau. Although widely used for several years thereafter, bedside measurement of pressure-volume curves has turned out to be a poor predictor of the appropriate degree of lung inflation in ALI/ARDS patients, both for physiologic and practical reasons.

A recent series of laboratory studies investigated an alternative method to set the ventilator with a lung-protective...
strategy, using analysis of the P_{aw}/time waveform as it can be displayed on the ventilator screen.\textsuperscript{21,22} This method is based on the observation that, during constant-flow insufflation, the rate of change of the pressure at the airway corresponds to the rate of change in respiratory-system compliance.\textsuperscript{23} Accordingly, a constant slope of the P_{aw} waveform suggests that there is no change in compliance during tidal ventilation (ie, the V_T is generated by elastic expansion of open alveoli that remain stable at end-expiration). A progressive increase of the slope indicates an increase in compliance (ie, lung recruitment during tidal ventilation). A progressive decrease of the slope indicates a decrease in compliance (ie, hyperinflation during tidal ventilation). The shape of the P_{aw} waveform can be further characterized numerically, using the stress index, which is derived from the equation that describes the relationship between P_{aw} and time during constant-flow insufflation.\textsuperscript{21,23} Figure 7 shows examples of those 3 types of P_{aw} waveform. In that particular study, the waveform with the linear slope (Fig. 7B) was associated with the lowest concentration of inflammatory cytokines in the bronchoalveolar lavage, indicating minimal lung injury.\textsuperscript{21} The appeal of this method resides in its potential bedside applicability. The P_{aw}/time waveform is routinely displayed on the ventilator screen, and the mathematical analysis of the slope could be carried out by the ventilator’s microprocessor and displayed in a way similar to how compliance and resistance are currently displayed.

**Recruitment Maneuvers**

Low-V_T ventilation tends to produce alveolar derecruitment. This has long been known to anesthesiologists, who are accustomed to applying occasional prolonged manual insufflations, using the ventilator hand-bag, to reverse atelectasis and improve P_{aO_2}.\textsuperscript{24} More recently, as low-V_T ventilation has been used in the intensive care unit to limit lung injury, it is clear that low-V_T ventilation may be associated with alveolar derecruitment.\textsuperscript{25} However, the level of pressure necessary to generate recruitment, and how it can be safely applied to the injured lungs of patients...
with ALI/ARDS remains elusive. Since the studies by Mead et al, it has been known that the pressure needed to open collapsed alveoli in a nonuniformly expanded lung may be several times higher than the levels of PEEP commonly used in clinical practice. Because such pressures are well above the end-inspiratory pressure limits generally considered safe (30–35 cm H₂O), they cannot be delivered cyclically with each breath. Thus, lung-protective strategies of low-VT tend to include additional means to recruit the lung, by applying higher pressures at the airway for limited periods (recruitment maneuvers).

Amato et al included in their “open lung approach” of low-VT, pressure-limited ventilation with high PEEP, the occasional performance of 30–40-second sustained inflations at Paw above the inspiratory plateau pressure. Unfortunately, sustained inflations do not seem to improve gas exchange for more than a few minutes. Furthermore, it is not certain that repeated application of these high pressures is safe for the ALI/ARDS lung. Alternatively, other investigators have used the delivery of large cyclic breaths (sighs) at the rate of 1–3 per minute, in the attempt to minimize lung injury and adverse hemodynamic effects. Like sustained inflations, sighs increase PₐO₂ and lung compliance in the majority of ALI/ARDS patients. However, just as with sustained inflations, long-term effects have not been studied. There are various ways to deliver sighs, all with the aim to provide recruitment and limit lung damage. Figure 8 shows the method of Foti et al, in which the PEEP level is increased for 2 successive breaths, twice a minute.

An interesting application of the sigh is in the resolving phase of ALI/ARDS, when the patient has resumed spontaneous breathing on pressure-support ventilation, but due to the persistently low compliance of the lung, it is still prone to develop atelectasis. Patroniti et al...
found that the addition of 2 pressure-controlled breaths with an increased $P_{aw}$ and a longer inspiratory time increases compliance and $P_{aO_2}$ and decreases the overall ventilatory drive of patients with resolving ARDS. Figure 9 shows how one of those breaths appears on the flow, volume, and airway pressure waveforms.

Prone Positioning as a Recruitment Strategy

Ventilation in the prone position increases $P_{aO_2}$ in approximately 70% of patients with ALI/ARDS. Selective recruitment of collapsed alveoli accounts at least in part for the improvement in lung compliance and arterial oxygenation associated with the prone position. Measurements of pleural pressure in animal models have shown that the prone position overturns the physiologic gravitational pleural pressure gradient; in the presence of pulmonary edema (as in the acute exudative phase of ALI/ARDS) the effect of gravity is accentuated, and the benefit of prone ventilation is more apparent. Figure 10 illustrates changes in respiratory-system compliance in an experimental model of pulmonary edema; regional pleural pressure measurements significantly decreased in the gravitational pleural-pressure gradient. This redistribution of pleural pressure should result in a more homogeneous pattern of alveolar inflation and enhance the effects of a recruitment maneuver. This was confirmed by recent animal model and clinical studies of ALI/ARDS, which found a more pronounced effect from a sustained inflation and from cyclical sighs with the prone position than with the supine position.

Summary

The modern practice of critical care of patients with acute respiratory failure cannot be limited to the achievement of normal blood gases; it must include considerations of respiratory mechanics, hemodynamic consequences, adequate tissue perfusion, iatrogenic complications, and long-
term outcome. High-resolution lung imaging and bedside ventilator-measurement of physiologic variables have introduced to clinical practice principles of respiratory mechanics that used to be confined to the physiology laboratory. Clinicians need to take advantage of this technology in order to practice at a high, specialized level and improve the outcomes of critically ill patients with acute respiratory failure.

REFERENCES

Discussion

Harris: I am likewise impressed with the stress index and its potential, but I have a couple of questions about it because I think there may be some conceptual flaws in its interpretation. It seems to me that it assumes that resistance is constant throughout inflation and any deviation from a ramp indicates changes in compliance. And that ignores, perhaps, that there could be changes in resistance during the inflation. Also, perhaps, impedance, if that’s important at all. Did they discuss that?

REFERENCE

Bigatello: I don’t think they discussed it. I think you are probably right. Hopefully, one methodological part of this that might, at least in part, avoid the effect of resistance is that they selected a fairly limited part of the curve; they took away the initial part and the late part, which might be the part where low and high lung volume have the biggest impact on airway resistance. However, if I saw correctly in my research, all the studies so far have been in experimental models. So, I guess if you want to go into human experiments, these issues will probably come up.

Harris: The animals in those studies don’t have airway disease in addition to ARDS. So, if you had a patient, like you showed us—one of those complicated patients with heterogeneous time constants—I’m just wondering if it would hold up in situations like that.

Bigatello: I’m sure we would have to select a patient population, as with any other method.

REFERENCE
I think that measuring bladder pressure is very important. I don’t have any proof of that, but I can certainly say that in our practice we are doing it more and more. We have found that patients have higher bladder pressure than we expected. With classical abdominal compartment syndrome, of course, there is very high intra-abdominal pressure. Those are easy to tell, but there are a lot of patients who have an intermediate increase in abdominal pressure that in the past I certainly didn’t pay any attention to. They may have had an abdominal pressure of 10 to 15 cm H₂O or more, which may impact chest wall mechanics. So now we pay more attention to the problem of abdominal distention. We measure it more often.

Once we measure it, I have to admit that I don’t often place an esophageal balloon in that circumstance, because I imagine that, depending on the increase in abdominal pressure, some of it is going to affect chest-wall compliance. By adding an esophageal balloon to these patients who are supine, I don’t know how much more I’m going to learn in terms of precise measurement. Therefore, I empirically use higher plateau pressure and higher PEEP, if needed, in a patient who has increased abdominal pressure, because I think that not all the pressure applied at the airway will translate into transpulmonary pressure. So my approach is very empirical.

In terms of recruitment maneuvers, it just depends how badly the patient needs it. I still look at the \( P_{aO_2} \). If the patient requires and can tolerate low ventilator settings, then I don’t routinely do a recruitment maneuver.

I think Lluís is referring to the research by Musch et al., in which Scott Harris participated.

REFERENCE


That research was interesting. We initially were trying to look at blood flow and ventilation, since we have a PET [positron emission tomography] technique to look at blood flow and ventilation in an animal model of lung injury. We were thinking of using a model that was easily recruitable, so we chose a lavage model, but we ended up injuring the lungs too much, so we couldn’t recruit the lungs very well.

We had a decrease in \( P_{aO_2} \) when we did recruitment maneuvers, and it appeared from our images that the blood flow was being redistributed to the shunt regions—the collapsed lung regions—so that research suggested a possible deleterious effect from recruitment maneuvers. I think we’ve seen that sometimes you get a drop in \( P_{aO_2} \) or saturation that doesn’t get better, or it takes a long time to get better after doing a recruitment maneuver. Acute physiologic change may be one possible reason they can be deleterious, but the research was not saying that recruitment maneuvers are necessarily not good; I think we still don’t know.

Are the pressure-time waveforms from anesthetized or paralyzed patients?

They were done on animals, and they were anesthetized, yes.

That’s a good point. That would certainly be quite different if the subject was actively breathing.

Absolutely.