Research

Ventilation in the prone position: For some but not for all?

Luciano Gattinoni MD, Alessandro Protti MD

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Shortly after acute respiratory distress syndrome was first described, it was soon realized that mechanical ventilation, aside from being essential for the treatment of the disease, can also harm the lungs by increasing the stress and strain applicable to the parenchyma. Stress is the tension developed in the lungs' fibrous skeleton when a distending force is applied, and strain is the volume increase caused by the applied force relative to the resting volume of the lungs. Supporting a patient's diseased lung with very high airway pressures can rupture alveoli, causing pneumothoraces and pneumomediastinum. This stress is referred to as barotrauma. In much the same way, very high tidal volumes distend and strain alveoli, causing volutrauma. Remaining normal portions of the lungs are especially vulnerable to this effect. Secondary lung injury can be induced by mechanical ventilation. Increased inflammation as a result of positive-pressure ventilation has recently been termed biotrauma. Repetitive opening and closing of collapsed parts of the lung can amplify local stress and produce damage (atelectrauma).[1] The major mechanisms in the pathogenesis of ventilator-induced lung injury are summarized in Figure 1.

Indeed, the focus of mechanical ventilation has progressively shifted from ensuring normal gas exchange to protecting the lungs from excessive stress and strain. Any survival advantage resulting from the way mechanical ventilation is delivered is likely to depend on a decrease in ventilator-induced lung injury.[3] If correctly performed, mechanical ventilation "buys time" to allow other therapies to take effect; if performed incorrectly, it may kill the patient.

Why should ventilation in the prone position compared to the supine position improve survival? Physiologically, for ventilation in the prone position to increase survival, it must be less harmful than in the supine position. More specifically, the stress and strain induced by ventilation in the prone position must be lower relative to the supine position. Does prone positioning ensure lower pulmonary stress and strain? If so, why have no major trials demonstrated any survival benefit associated with ventilation in the prone position?

Inflammatory pulmonary edema that occurs during acute lung injury and acute respiratory distress syndrome increases lung weight. As a consequence, if a patient is in a supine position, the dorsal regions of the lungs collapse under the weight of the ventral regions, and the gas contents of the dorsal regions are squeezed out (compression atelectasis) (Figure 2). During mechanical ventilation, most of the air goes to the ventral, open parts of the lungs, increasing their stress and strain. A minor part of the tidal volume goes to the dorsal parts of the lungs, causing their cyclic opening and closing, thus amplifying the local stress and strain. In contrast, if the patient is in a prone position, the ventral regions become dependent and collapse under the weight of the dorsal regions, which inflate to a different extent. Because of their shape, more parts of the lungs are open to ventilation in the prone position than in the supine position (Figure 2).[4] Therefore, in the prone position, air is distributed more homogeneously throughout the lungs, and stress and strain are decreased. This is the main reason why prone positioning can delay the appearance of ventilator-induced lung injury and increase survival, as suggested by animal studies.[5]

To detect any advantage of ventilation in the prone position, the pulmonary inflammatory edema must be severe enough to, in the supine position, produce an abnormally heterogeneous distribution of air and considerably increase the interface between the open and collapsed regions, which are possibly undergoing repetitive, cyclic opening and closing. It is obvious that without these conditions, such as in patients with only minimal inflammatory edema, we cannot expect any increased benefit from prone positioning.

In this issue of *CMAJ*, Sud and colleagues[6] report the results of their meta-analysis of 13 randomized or quasi-randomized controlled trials (1559 patients) comparing ventilation in the prone and supine positions in acute hypoxemic respiratory failure, including acute lung injury and acute respiratory distress syndrome. Mechanical ventilation for patients assigned to the prone group lasted a median of 12 hours per day (range 4–24) for 4 days (range 1–10). Sud and colleagues conclude that prone positioning cannot be recommended in the routine management of acute lung injury and acute respiratory distress syndrome because, despite improv-

Key points

- Prone ventilation is not recommended in the routine management of acute lung injury and acute respiratory distress syndrome, but it can be used as a rescue manoeuvre in cases of severe hypoxemia.
- Experimental evidence suggests that prone ventilation can prevent or attenuate ventilator-induced lung injury.
- The possible survival benefit of prone ventilation in subgroups of patients with acute lung injury or acute respiratory distress syndrome remains to be determined.

From the Istituto di Anestesiologia e Rianimazione, Fondazione IRCCS – Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Università degli Studi di Milano, Milan, Italy.

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ing oxygenation, they found no evidence of improved survival. We feel that this conclusion is appropriate based on the results of all the major studies of ventilation in the prone position published to date. However, were those studies designed in the most appropriate way to detect a possible survival advantage of prone positioning?

Let us examine, from a physiological perspective, the largest trials included in the meta-analysis by Sud and colleagues. In a study previously performed by one of us (L.G.) involving 304 participants, patients remained in the prone position for an average of 7 hours per day.[7] There was no control for mechanical ventilation because, at that time, conclu-

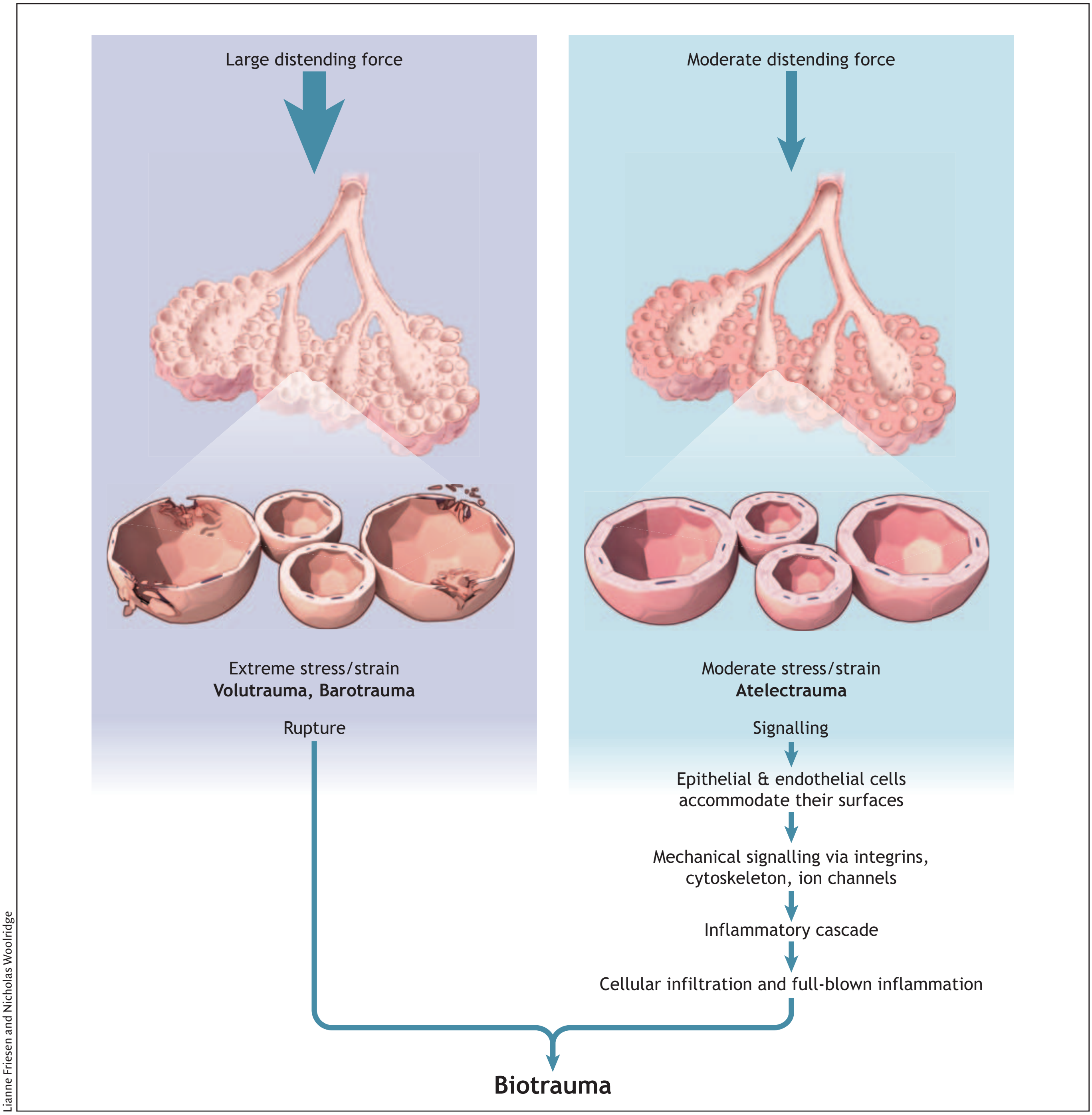

Figure 1: Ventilator-induced lung injury is initiated by the application of excessive stress and strain to the lung. High levels of mechanical stress and strain that occur when high airway pressures and volumes are delivered can disrupt the pulmonary fibroelastic skeleton (barotrauma and volutrauma) and trigger a secondary inflammatory response (biotrauma). Moderate degrees of stress and strain related to the cyclic opening and closing of parts of the lung (atelectrauma) may directly induce the release of inflammatory mediators and noxious proteinases. Modified from Marini and Gattinoni.[2]

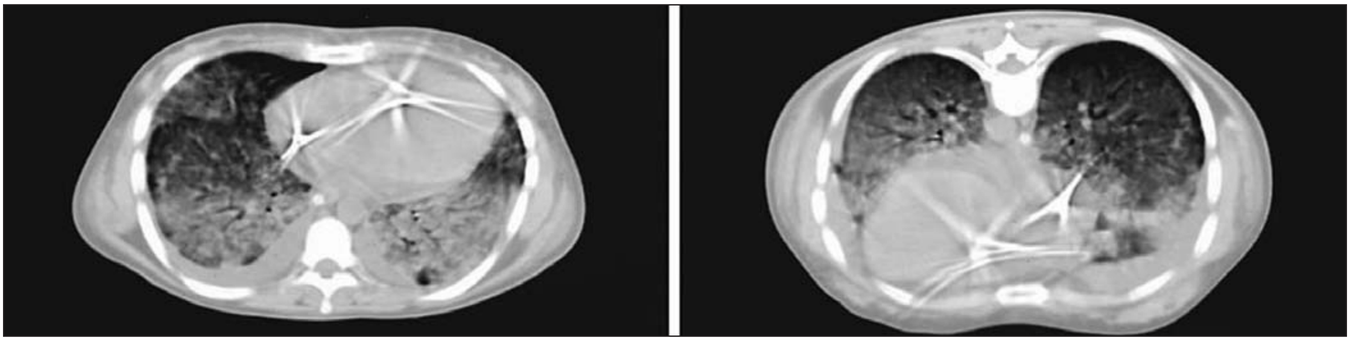

Figure 2: Computed tomography scan of the lungs showing acute respiratory distress syndrome when the patient is lying supine (left) and prone (right). Note the density redistribution in the prone compared with the supine position.

sive data supporting the delivery of low tidal volumes were not available. Despite the possibility of reduced pulmonary stress or strain, we limited the use of prone positioning to 7 hours per day. Moreover, the use of tidal volumes higher than those currently recommended could have eliminated any possible beneficial effect of prone positioning in some patients. Finally, only a small proportion of patients with acute lung injury or acute respiratory distress syndrome actually have a lung edema severe enough to expect an advantage from ventilation in the prone position.[8] Any beneficial effect of prone positioning in this subgroup could have been masked by the enrollment of patients lacking the physiological characteristics that warrant the use of the technique. Similarly recruitment of patients with different characteristics may have also affected the results of 2 other recent trials investigating the impact of high and low positive end-expiratory pressure on survival in patients with acute lung injury or acute respiratory distress syndrome.[9,10] It is possible that there may have been a significant benefit in a subgroup of patients, but this was not detected because of the enrollment of patients who did not warrant the use of positive end-expiratory pressure.[11]

These limitations are present at an even greater extent in the study by Guerin and colleagues,[12] who enrolled patients with inflammatory or cardiogenic lung edema ($n = 791$). Conversely, Mancebo and colleagues[13] enrolled 136 patients with relatively severe acute respiratory distress syndrome, used strictly controlled mechanical ventilation and maintained patients in the prone position for most of the day, reporting a strong, but nonsignificant ($p = 0.12$), tendency toward improved survival among patients in the prone group.

Although meta-analyses are fascinating, we must always remember that the final result strictly depends on the value of the studies retained for analysis. All of the randomized clinical trials studying ventilation in the prone position that have been published to date have been conducted without a clear understanding of the reason why prone positioning should improve patient outcomes. To correctly investigate the survival benefits associated with prone positioning, future studies will need to be designed in a way that considers the rationale behind the use of the technique, and researchers will need to appropriately select the study population and the timing of the intervention. We can conclude from the meta-analysis by Sud and colleagues that ventilation in the prone position for a few hours each day is very effective in relieving severe hypoxemia, but has no impact on survival in heterogeneous populations of patients with acute lung injury or acute respiratory distress syndrome — which is considerably different from concluding that ventilation in the prone position can never improve patient outcomes.

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Correspondence to: *Prof. Luciano Gattinoni, Istituto di Anestesiologia e Rianimazione, Fondazione IRCCS – Ospedale Maggiore Policlinico, Mangiagalli e Regina Elena, Università degli Studi di Milano, Via F. Sforza 35, 20122 Milano, Italy; gattinon@policlinico.mi.it*