Pronation in acute respiratory distress syndrome (ARDS) secondary to COVID-19

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Abstract: In March 2020, the outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was declared a pandemic by the World Health Organization. Patients with SARS-CoV-2 infection can develop coronavirus disease 2019 (COVID-19), the most concerning complication of which is acute hypoxaemic respiratory failure requiring mechanical ventilation and intensive care unit (ICU) admission. In this context prone position ventilation is an established method to improve oxygenation in severe acute respiratory distress syndrome (ARDS), and its application was able to reduce mortality rate. Prone position has been used since the 1970s to treat severe hypoxemia in patients with ARDS because of its effectiveness at improving gas exchange. Compared with the supine position, placing patients in prone position effects a more even tidal volume distribution, in part, by reversing the vertical pleural pressure gradient, which becomes more negative in the dorsal regions. Prone position also improves resting lung volume in the dorsocaudal regions by reducing the superimposed pressure of both the heart and the abdomen. In contrast, pulmonary perfusion remains preferentially distributed to the dorsal lung regions, thus improving overall alveolar ventilation/perfusion relationships. Moreover, the larger tissue mass suspended from a wider dorsal chest wall effects a more homogeneous distribution of pleural pressures throughout the lung that reduces abnormal strain and stress development. This is believed to ameliorate the severity or development of ventilator-induced lung injury and may partly explain why prone position reduces mortality in severe ARDS. In this review we investigate the physiological aspects of the pronation.

Keywords: Pronation; respiratory mechanics; gas exchange

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Introduction

The first description in the literature of the use of the prone position for the treatment of acute respiratory failure dates back to the mid-1970s. However, the actual widespread use of the prone position in patients with acute respiratory distress syndrome (ARDS) takes place in the second half of the 1980s. In fact, at that time the first studies on the use of computed tomography (CT) in patients with ARDS were published, which showed the heterogeneous character of the disease at the level of the lung parenchyma: sparing of the ventral lung regions (not dependent), which maintained good ventilation, while the dorsal (dependent) regions were those actually affected (1,2). Subsequent observations showed that the aerated lung parenchyma maintained normal mechanical characteristics and led to the formulation of the concept of "baby lung", namely that in ARDS the lung parenchyma which actually participates in gas exchanges is reduced to the size of the lung of a child of about 6 years (3). Since the "baby lung" in CT scans appeared to be located in the ventral region, ventilation in the prone position began to be used, in order to redistribute blood flow to the ventilated lung regions and thus reduce shunt, improving oxygenation. Subsequently, by performing CT scans in patients with ARDS in the prone position, it was seen that the atelectatic areas were found in the ventral (dependent) region, while the parenchyma in the dorsal region recovered aeration (4,5). These observations then lead to the concept of "Baby lung" from anatomical entity to functional entity and to the development of the pathophysiological model of the "sponge lung" that accounts for density distribution in prone position, for which the unloaded dorsal regions are recruited, while the loaded ventral region, collapses (6).

Etiology

It is possible to distinguish two forms of ARDS: the first in which the primary damage is to the lung parenchyma (pulmonary ARDS), the second resulting from an acute systemic inflammatory response such as sepsis (extrapulmonary ARDS), severe trauma, massive transfusion of blood components. In pulmonary ARDS the damage primarily involves the alveolar epithelium, while in the extrapulmonary form the main pathogenetic mechanism seems to be the formation of interstitial edema associated with a systemic inflammatory response. Patients with extrapulmonary ARDS have diffuse pulmonary edema due to inflammatory mediators that originate in extrapulmonary inflammatory foci; the increase in the weight of the lung causes compression atelectasis in the dependent lung areas (with a prevalence of ground glass opacity). On the contrary, patients with pulmonary ARDS tend to have a less homogeneous pulmonary alteration, the main feature of which is not lung collapse but the presence of areas of parenchyma consolidation. As a consequence of the aforementioned etiological and pathophysiological forms there is also a diversity of response to therapies; the extrapulmonary forms tend to respond more to recruitment, positive end-expiratory pressure (PEEP) and pronation maneuvers (7); the explanation probably lies in the fact that the increase in pressure mainly causes hyperinflation of the alveoli already open in cases where there is a prevalent aspect of consolidation, while it tends to be effective in recruiting previously closed alveoli where diffuse opacity is present.

Physiological rationale for the prone position

In ARDS, widespread damage to the alveolar-capillary barrier leads to the accumulation of inflammatory edema in the pulmonary interstitium and, in part, in the alveoli. The weight gain of the whole lung parenchyma amplifies the hydrostatic pressure (called superimposed pressure) that weighs on the most sloping lung areas (the lower lung areas), thus causing atelectasis of the alveoli located in these regions (the dorsal ones in the supine position and the ventral ones in the prone position) (8). The redistribution of parenchymal aeration during the prone position shows us how at the basis of the significant improvement in gas exchange there is not a simple gravitational redistribution of the blood flow, as was initially believed, but a more complex mechanism that only thanks to pathophysiological studies it was possible to understand. In particular in the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) there is a severe ventilation/perfusion (V/Q) mismatch in which downregulation of angiotensin-converting enzyme 2 (ACE2) secondary to viral endocytosis plays a key role. There is low V/Q ratio in areas of injured lung parenchyma with ground-glass opacities or consolidation, secondary to loss of compensatory hypoxic pulmonary vasoconstriction (vasoplegia) and increased blood flow, which result in high perfusion to the areas of non-aerated lung, but there is also high V/Q ratio in areas of apparently healthy lung secondary to prominent vasoconstriction. The hypoperfusion of apparently healthy areas could be a consequence of vasoconstriction due to accumulation of angiotensin II, caused by decreased availability of ACE2, and that these changes in vascular resistance lead to a shunt or steal of vascular flow towards areas of non-aerated hyperperfused lung in moderate to severe COVID-19 cases. The pronation might improve V/Q mismatch with the redistribution of the blood flow (9).

Respiratory mechanics

CT studies have shown that in the supine position, in the healthy lung at the end of expiration, there is a progressive increase in radiological density starting from the ventral region and proceeding dorsally. This means that the gas/tissue ratio and consequently the parenchyma aeration tends to be maximum in the ventral region and to decrease as one proceeds towards the dependent areas. This alveolar aeration gradient seems to be due to the combination of the action of gravitational forces (and the consequent superimposed pressure acting on the dependent regions) with the uneven expansion of the alveolar units due to the discrepancy between the shape of the lung and that of the rib cage. In fact, the isolated lung with homogeneously expanded alveolar units has a shape similar to a cone (with the dorsal part more voluminous than the ventral part), while the thoracic cage is almost cylindrical (10). *In vivo* they occupy the same volume (the pleural space is virtual), consequently in the lung parenchyma there must be a greater increase in volume, with consequent greater aeration of the alveolar units, in the ventral areas compared to the dorsal ones (model of "shape matching"). There is therefore an additive effect of the two mechanisms mentioned in creating a gradual decrease in alveolar ventilation in the ventro-dorsal direction. In the prone position, the superimposed pressure gradient is inverted, with the ventral zones located in a dependent region with respect to the dorsals. However, the compression due to gravitational forces in the ventral region is counterbalanced by the expansion of the alveolar units due to "shape matching". The two mechanisms in the prone position therefore act in opposing ways, resulting in a more homogeneous aeration of the alveolar units (11). Another factor to consider is the compression on the lung parenchyma caused by the weight of the heart. In fact, in the supine position, a large part of the lung parenchyma is subjected to this compression (especially the left lower lobe). In the prone position, on the other hand, the fraction of lung parenchyma subjected to cardiac compression becomes negligible (12). However, the superimposed pressure can increase even 4 or 5 times its normal value, thus making the effect of "shape matching" and cardiac compression on the gas/tissue gradient of the lung parenchyma. In the prone position, the ventral areas become atelectatic, while the dorsal ones are recruited and then recover the ventilation. From the anatomical point of view, the amount of lung parenchyma is greater in the dorsal region, consequently the alveolar recruitment that occurs in this region tends to be greater than the derecruitment that occurs in the ventral region, with a net effect of gain in aeration of the parenchyma and improvement of lung compliance. This effect is greater the greater the total recruitability of the lung parenchyma, i.e., the amount of atelectatic lung parenchyma that can actually be reopened. Finally, considering the rib cage, the transition from the supine to the prone position causes a reduction in compliance, since the expansion of the ventral part is limited by the support surface and the dorsal part is more rigid; in addition, there is an increase in abdominal pressure. However, the improvement in lung compliance counterbalances the decrease in compliance of the rib cage, making sure that the total compliance of the respiratory system remains almost unchanged or tends to improve (11).

Pulmonary perfusion distribution

Classically, pulmonary perfusion has been described through a gravitational model, in which differences in regional blood flow are attributed to the hydrostatic pressure gradient in the vascular tree. However, the description of lung physiology by West is issued from patient without ARDS and not lying on their back. In particular, in the upper part of the lung, the pressure in the blood vessels (pulmonary arterioles and venules) would tend to be lower than in the alveolar one (West zone 1), with consequent collapse of the alveolar capillaries and ventilated but not perfused alveoli (physiological dead space); in the intermediate zones, (West zone 2), the alveolar pressure would be lower than that of the arterioles but greater than that of the venules, and the blood flow would depend on the difference in pressure between arterioles and alveoli; in the most sloping areas (West zone 3), the vascular pressures of the arterioles and venules would always be greater than the alveolar pressure, and therefore would represent the most perfused lung zones (13). According to West's model, therefore, lung segments located at the same height should receive the same perfusion. However, pulmonary perfusion studies performed with radio-labeled microspheres have shown that the apex-base perfusion gradient is maintained even in the supine or lateral position (14,15). Subsequent studies performed with the same method have shown that the differences in perfusion between lung segments located at the same height they can be up to 10 times greater than those between segments at different heights (16). It follows that the gravitational forces would be only a minor determinant of the uneven distribution of pulmonary perfusion, which would have as its main cause the same architecture of the pulmonary vessels. In fact, the asymmetry in the bifurcations along the entire vascular tree would be the main cause of regional perfusion differences (17). The latter model explains in a more complete way what happens when passing from the supine to the prone position. In fact, in the supine position, pulmonary perfusion is distributed according to a ventro-dorsal gradient. However, when passing into the prone position, this gradient does not reverse, but the dorsal regions remain the most perfused. In particular, among all the positions tested, the prone position is the one associated with a more homogeneous distribution of pulmonary perfusion. In SARS-CoV-2, as say below, the pronation might improve V/Q mismatch with the redistribution of the blood flow.

Gas exchanges

As already described, in the ARDS the prone position is associated with a marked improvement in arterial oxygenation. This finding has been confirmed by numerous studies, both clinical and in animal models of acute respiratory failure. The main reason why this occurs can be deduced from the pathophysiological mechanisms previously illustrated: in ARDS the prone position leads to the recruitment of the dorsal lung regions, which tends to be greater than the collapse that occurs in the ventral regions; moreover, the recruited dorsal regions tend in any case to be better perfused than the ventral ones, and this leads to an improvement in the ventilation/perfusion ratio and a reduction in shunt, which is the major determinant of hypoxemia (11). However, it seems to be the increase in dead space, and therefore the altered elimination of CO_2, the major determinant of patient outcome (18). The mechanism by which the prone position would reduce dead space, thus improving the elimination of CO_2, would seem to be due to the greater recruitment in the dorsal regions compared to the collapse of the ventral regions (and therefore to a "net gain" of ventilated alveolar units), associated with the reduction of overdistension that often occurs in the ventral alveolar, which tend to be hyperinflate and therefore have little or no ventilation (11). The passage to the prone position is not always associated with a decrease in arterial CO_2, since the fact that there are more alveolar units effectively ventilated (with consequent improvement in oxygenation) does not necessarily mean that these units are also well ventilated. In fact, it has been described how the change in arterial CO_2 levels after pronation is independent of the response in terms of oxygenation, and how a decrease in this level is associated with greater pulmonary recruitment and a better outcome (19,20).

There is a small proportion of patients who do not respond to prone position (in the range of 20%).

The improved oxygenation in prone position that has been described in patients with COVID-19 could be explained mainly through vascular redistribution towards the areas of apparently healthy lung with a high V/Q ratio, rather than alveolar recruitment.

Prone position and mechanical ventilation damage

Numerous studies have shown a greater homogeneity of ventilation in the prone position compared to the supine position, furthermore, experimental studies have shown that the prone position affects the onset of the ventilator induced lung injury (VILI). The latter originates from the repeated application of forces that are generated and amplified at the interface between consolidated areas and ventilated areas or areas subject to cyclical opening and closing, in conjunction with mechanical ventilation (atelectrauma). The prevalence of these areas is predominant in the dependent regions of the lung parenchyma; the dorsal regions (dependent in the supine position, not dependent in the prone position) are therefore those most predisposed to the development of ventilation damage and consequently those most protected by the VILI in the prone position. The mechanisms by which this damage is limited are the reduction in the number of interfaces between the consolidated or atelectatic areas and the ventilated areas, but also the reduction or better distribution of transpulmonary pressure (the pulmonary parenchyma distension force) due to the improvement of compliance thanks to the pulmonary recruitment. In the event that the prone position is associated with recruitment of the lung parenchyma, ventilation will therefore be less harmful with a global reduction of "stress" (transpulmonary pressure) and "strain" (ratio between tidal volume and residual functional capacity) of the over-stretched areas. The damage from atelectrauma (the so-called "open and close") appears to be reduced especially in patients with high recruitment capacity ventilated with high PEEP. The use of the prone position also reduces damage from inflammation (a reduction in the concentration of pro-inflammatory cytokines has been demonstrated) and haemorrhagic pulmonary edema (21). Another important element to consider is the better drainage of secretions from the dorsal regions to the main airways (22). The main reason why the prone position has effects on mortality, as well as for the maneuver itself (considered life-saving in cases of very serious hypoxemia), is therefore probably related to the reduction of damage from mechanical ventilation.

Indications

There is no doubt that the prone position is to be considered as a life-saving therapy in cases of severe hypoxemia, especially if this maneuver is performed by expert and standardized teams. It is now known that the prone position is indicated for patients with "severe ARDS", formalized in the Berlin criteria (23). In clinical practice, the severity of the syndrome is assessed on the basis of the PaO_2/FiO_2 ratio. However, it is evident how this ratio can change according to the ventilatory strategy (for example the level of PEEP) and the level of FiO_2. Despite this variability, based on data available in the literature, deriving from randomized trials and meta-analyzes, long-term pronation in severe ARDS (characterized by a PaO_2/FiO_2 ratio <100) is recommended. Conversely, this is not suggested in mild forms of ARDS (300< PaO_2/FiO_2 <200) as it does not seem to bring any advantage in terms of improved survival. However, the use in moderate forms of ARDS (200 <PaO_2/FiO_2 <100) is still debated: the results of recent meta-analyzes suggest that pronation should be considered in patients with moderate ARDS in whom the PaO_2/FiO_2 ratio is below 150 mmHg with PEEP greater than or equal to 5 cmH_2O and FiO_2 greater than or equal to 0.6. Currently, therefore, PaO_2/FiO_2 values below 150 mmHg, measured with a PEEP level of at least 5 mmH_2O, represent a reasonable limit for the use of the prone position in ARDS (11,24). Pronation is maximized in the early stages of ARDS, in which edema, pulmonary parenchyma recruitment and the absence of structural changes in the lung are more prominent. This means that the advantages provided by the prone position, in minimizing ventilation damage in the early phase of the disease, are most likely greater than those provided in the late phase, when lung damage has already been induced.

Prone positioning was also feasible and effective in rapidly ameliorating blood oxygenation in awake patients with COVID-19-related pneumonia requiring oxygen supplementation. The effect was maintained after resupination in half of the patients (25).

Contraindications and complications

The absolute contraindications to pronation are very few and mainly represented by instability of the vertebral column and intracranial hypertension not monitored, since some methods of pronation require that the head be turned to one side or the other with possible compression of the jugular veins and consequent obstruction of the cerebral venous outflow. Relative contraindications are severe hemodynamic instability, open abdominal treatments, multiple unstabilized fractures, pregnancy, difficult airway management or the presence of vascular accesses (including dialysis catheters) although the latter should not be considered a contraindication to pronation as it is sufficient that they are adequately fixed to the patient and supervised during the pronation maneuver. The literature describes complications mainly related to pronation maneuvers such as extubation, accidental removal of vascular catheters or episodes of transient hypotension or desaturation. Other complications are related to the duration of pronation such as pressure ulcers, vomiting or the need to increase sedation. Particularly serious, albeit extremely rare, are the compression of the optic nerve and the retinal vessels with consequent blindness. The incidence of adverse events is reduced with the experience of the team and with the adoption of prevention measures or devices that facilitate the maneuver and prevent complications related to the duration of the positioning. In particular, with regard to pressure ulcers, it is advisable to use appropriate anti-decubitus devices along the body and appropriate eye protection.

Positioning

The positioning of a patient in prone decubitus requires the coordination of several team members present in intensive care. There are no standardized procedures to perform this maneuver, many centers are based on the sequence of movements envisaged for the log-roll, but there is equipment on the market that can assist and facilitate the movements, and there is also a bed designed specifically to facilitate pronation of ICU patients and minimizes the risks of the procedure. Regardless of the technique used for positioning, it is essential that the personnel carrying out the maneuver are adequately trained, in order to avoid injury to the patient or the removal of invasive devices. The patient's support areas must be protected to avoid the formation of pressure injuries. The number of people needed to perform the procedure depends on the patient's weight, the number and location of the devices, as well as the type of equipment used. Among the practical problems to be considered before pronation, there is therefore the need for adequate preparation of the patient with close surveillance of the endotracheal tube and vascular accesses. Due to the risk of accidental extubation, the endotracheal tube must be fixed in a stable manner. It is also advisable to ensure that the material necessary for emergency intubation is always readily available before starting the maneuver. It is also necessary to consider how the positioning of the endotracheal tube; during pronation maneuvers, in fact, excursions of the endotracheal tube are possible, therefore in order to avoid extubation or, on the contrary, intubation of a main bronchus, the distal end of the tube should be located 2–4 cm from the tracheal keel. Still with regard to the management of the airways, it is possible that during the pronation process there is an abundant drainage of secretions, resulting in bulk and difficulty in ventilation. We therefore recommend that you always have the necessary material for bronchial aspiration available. In prone positioning, a possible logistical difficulty could be represented by the presence of the tracheostomy, however there are several aids with which patients can be supported in such a way that the cannula has no direct contact with the bed or with the support padding and without the patient is subjected to excessive torsion of the neck and head. The head is usually turned to the left or right, to minimize orbital or facial pressure, and to avoid lip or nasal injury caused by the endotracheal tube. Lateral rotation of the head may be difficult to perform in some patients, such as elderly patients due to cervical spine stiffness. In these cases, it is possible to use foam donuts that suspend the head from the bed, without any lateral rotation. However, this type of control can lead to greater facial trauma. It should also be emphasized that it must be ensured, before starting the maneuver, that all cushions and devices, potentially necessary to support the head or other parts of the body during pronation, are readily available (26). As regards the management of vascular access. it is essential to ensure, during and at the end of the maneuver, the patency of the infusion routes, especially if the infusion of vasopressors is in progress.

Duration

In all the studies that demonstrated any validity of pronation, the protocols included cycles of at least 6 h up to a maximum duration of 20 h. However, it is important to note that the most recent trials have shown a relationship between favorable outcome and a longer duration of pronation (26-30). The PROSEVA study, for example, which demonstrated a reduction in mortality in the group of patients with severe ARDS undergoing pronation, it was designed with long pronation cycles, so much so that the average measured was about 17 h (28). Again, in this study the pronation cycles were repeated up to 28 days. The mortality reduction effect is probably attributable to a reduction in mechanical ventilation damage. Although among the various trials the criterion for determining the suspension of the use of pronation cycles was quantitatively different, the common denominator was the arbitrary interruption after a few days or the achievement of stability, in the supine position (during the daily interruptions of pronation), of oxygenation values above a predetermined limit. It is possible to consider the use of pronation even for short periods, this in fact, as already mentioned above, improves the drainage of secretions and is effective in re-expanding atelectatic areas refractory to recruitment maneuvers in the supine position. The benefits are particularly evident in the lower left lung lobe, as the prone position unloads the weight of the heart from the dorsal regions of the lung.

How to evaluate the response to pronation

It is important to evaluate the effectiveness of pronation in terms of lung parenchyma recruitment through the improvement of gas exchange, the appearance of crackles in the affected region and through the use of imaging methods also available at the patient's bedside such as lung ultrasound.

Recruitment and ventilation

Across pronation and with the same ventilatory setting, monitoring of the ventilation pressures (plateau pressure and mean airway pressure) is useful if the patient is ventilated in a controlled volume, or the tidal volume if the ventilation is at controlled pressure. In fact, the effect of reducing the compliance of the rib cage, due to the prone position, could result in an increase in plateau pressure (in the case of volume-controlled ventilation) or a reduction in the tidal volume (if the ventilation is in controlled pressure). However, these effects are canceled out if the patient responds to pronation with recruitment of the dorsal regions prevalent over the derecruitment of the ventral regions. This leads to an increase in lung compliance and residual functional capacity (CFR). In this case there will therefore be a reduction in the ventilation pressures (if in controlled volume) or an increase in the tidal volume (if in controlled pressure). To evaluate the impact of pronation on the compliance of the respiratory system, it is necessary at least to wait for the conclusion of the cycle of pronation lasting at least 16 h.

Oxygenation

An improvement in PaO_2 in conjunction with prone positioning may depend both on the anatomical recruitment and re-ventilation of perfused but initially deflate areas, and on the improvement of perfusion/ventilation coupling in the dorsal areas, which prevails over the ventral ones. Therefore, an improvement in oxygenation will not necessarily correspond to "anatomical" recruitment of lung parenchyma and an improvement in ventilation. In fact, in order to observe an increase in oxygenation, the perfused areas must be inflated, however these do not need to be well ventilated because they can be overstretched.

Elimination of CO_2

In ARDS an altered elimination of CO_2 reflects structural changes at the level of the lung parenchyma such as destruction of the alveolar septa, microthrombosis, cysts, bubbles and edema. Dead space and $PaCO_2$ values do not always change in the transition from prone to supine position. However, an improvement in terms of mortality has been shown in the event that after the first pronation there is a reduction in pCO_2 values with the same minute ventilation (19). This phenomenon is probably attributable not only to the recruitment effect but also to the reduction of over-distension of hyperinflate areas in the ventral region, with consequent improvement of pulmonary ventilation. Both mechanisms lead to a reduction in ventilation damage and this is the possible explanation of why the reduction in pCO_2, but not in PaO_2, correlates with the outcome.

Outcomes

It has been shown in four randomized studies and two meta-analyzes that pronation significantly improves survival (16% reduction in relative risk of death) in patients with severe hypoxemia (PaO_2/FiO_2 ratio <100) at the time of randomization (31). It is therefore strongly the use of this procedure is recommended in cases of severe hypoxemia. However, its use should be emphasized especially in patients who demonstrate a response to pronation, in order to minimize the side effects in "non-responders" and maximize the benefits in "responders".

Conclusions

The use of the prone position in the ARDS improves oxygenation by optimizing lung recruitment and the ventilation/perfusion ratio. It also has a protective role in mechanical ventilation damage thanks to the more homogeneous distribution of ventilation and transpulmonary pressure, and so, the prone position provides an advantage in terms of survival in patients with severe ARDS. Long-term use is not indicated in mild or moderate forms of ARDS (PaO_2/FiO_2 >150 mmHg), due to the patient's exposure to the risk of complications in the absence of benefits.

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Footnote

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References

1. Gattinoni L, Presenti A, Torresin A, et al. Adult respiratory distress syndrome profiles by computed tomography. J Thorac Imaging 1986;1:25-30.

2. Maunder RJ, Shuman WP, McHugh JW, et al. Preservation of normal lung regions in the adult respiratory distress syndrome. Analysis by computed tomography. JAMA 1986;255:2463-5.
3. Gattinoni L, Pesenti A, Avalli L, et al. Pressure-volume curve of total respiratory system in acute respiratory failure. Computed tomographic scan study. Am Rev Respir Dis 1987;136:730-6.
4. Gattinoni L, Pelosi P, Vitale G, et al. Body position changes redistribute lung computed-tomographic density in patients with acute respiratory failure. Anesthesiology 1991;74:15-23.
5. Langer M, Mascheroni D, Marcolin R, et al. The prone position in ARDS patients. A clinical study. Chest 1988;94:103-7.
6. Gattinoni L, Pesenti A. The concept of "baby lung". Intensive Care Med 2005;31:776-84.
7. Gattinoni L, Carlesso E, Taccone P, et al. Prone positioning improves survival in severe ARDS: a pathophysiologic review and individual patient meta-analysis. Minerva Anestesiol 2010;76:448-54.
8. Pelosi P, D'Andrea L, Vitale G, et al. Vertical gradient of regional lung inflation in adult respiratory distress syndrome. Am J Respir Crit Care Med 1994;149:8-13.
9. Santamarina MG, Boisier D, Contreras R, et al. COVID-19: a hypothesis regarding the ventilation-perfusion mismatch. Crit Care 2020;24:395.
10. Hubmayr RD. Perspective on lung injury and recruitment: a skeptical look at the opening and collapse story. Am J Respir Crit Care Med 2002;165:1647-53.
11. Gattinoni L, Taccone P, Carlesso E, et al. Prone position in acute respiratory distress syndrome. Rationale, indications, and limits. Am J Respir Crit Care Med 2013;188:1286-93.
12. Albert RK, Hubmayr RD. The prone position eliminates compression of the lungs by the heart. Am J Respir Crit Care Med 2000;161:1660-5.
13. West JB. Ventilation-Perfusion Relationships. In: Respiratory Physiology: the Essentials. Wolter Kluwer/ Lippincott Williams & Wilkins, 1977:55-74.
14. Greenleaf JF, Ritman EL, Sass DJ, et al. Spatial distribution of pulmonary blood flow in dogs in left decubitus position. Am J Physiol 1974;227:230-44.
15. Reed JH Jr, Wood EH. Effect of body position on vertical distribution of pulmonary blood flow. J Appl Physiol 1970;28:303-11.
16. Glenny RW, Bernard S, Robertson HT, et al. Gravity is an important but secondary determinant of regional pulmonary blood flow in upright primates. J Appl Physiol (1985) 1999;86:623-32.
17. Galvin I, Drummond GB, Nirmalan M. Distribution of blood flow and ventilation in the lung: gravity is not the only factor. Br J Anaesth 2007;98:420-8.
18. Nuckton TJ, Alonso JA, Kallet RH, et al. Pulmonary dead-space fraction as a risk factor for death in the acute respiratory distress syndrome. N Engl J Med 2002;346:1281-6.
19. Gattinoni L, Vagginelli F, Carlesso E, et al. Decrease in PaCO2 with prone position is predictive of improved outcome in acute respiratory distress syndrome. Crit Care Med 2003;31:2727-33.
20. Protti A, Chiumello D, Cressoni M, et al. Relationship between gas exchange response to prone position and lung recruitability during acute respiratory failure. Intensive Care Med 2009;35:1011-7.
21. Broccard A, Shapiro RS, Schmitz LL, et al. Prone positioning attenuates and redistributes ventilator-induced lung injury in dogs. Crit Care Med 2000; 28:295-303.
22. Li Bassi G, Torres A. Ventilator-associated pneumonia: role of positioning. Curr Opin Crit Care 2011;17:57-63.
23. ARDS Definition Task Force; Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin Definition. JAMA 2012;307:2526-33.
24. Sud S, Friedrich JO, Adhikari NK, et al. Effect of prone positioning during mechanical ventilation on mortality among patients with acute respiratory distress syndrome: a systematic review and meta-analysis. CMAJ 2014;186:E381-90.
25. Coppo A, Bellani G, Winterton D, et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. Lancet Respir Med 2020;8:765-74.
26. Messerole E, Peine P, Wittkopp S, et al. The pragmatics of prone positioning. Am J Respir Crit Care Med 2002;165:1359-63.
27. Guerin C, Gaillard S, Lemasson S, et al. Effects of systematic prone positioning in hypoxemic acute respiratory failure: a randomized controlled trial. JAMA 2004;292:2379-87.
28. Guérin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med 2013;368:2159-68.
29. Mancebo J, Fernández R, Blanch L, et al. A multicenter trial of prolonged prone ventilation in severe acute

respiratory distress syndrome. Am J Respir Crit Care Med 2006;173:1233-9.

30. Taccone P, Pesenti A, Latini R, et al. Prone positioning in patients with moderate and severe acute respiratory distress syndrome: a randomized controlled trial. JAMA 2009;302:1977-84.
31. Guérin C. Prone position. Curr Opin Crit Care 2014;20:92-7.

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