# The Assessment of Prone Position in Severe Acute Respiratory Syndrome

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## Abstract

Introduction: Acute respiratory distress syndrome (ARDS) is a frequent condition associated with high mortality, acute alveolar damage, loss of lung compliance and hypoxemia. The prone position has been used to improve oxygenation in patients with moderate to severe hypoxemia with PaO2/FiO2<150, with this maneuver the lung compliance increases, associated with more homogeneous lung expansion and better gas exchange.Aims: Primary: To evaluate the effectiveness of the prone position in patients with acute respiratory distress syndrome. Secondary: Understand the respiratory physiology involved in the use of prone position in patients with acute respiratory distress syndrome.Methods: This work is a narrative review of literature in the Google academic, Scientific Electronic Library Online (Scielo), Medline and Cochrane databases, 22 articles were selected between 2001 and 2020. The keywords used were "prone position", "respiratory distress syndrome" and "acute lung injury".

***Index terms***— ?prone position?, ?acute respiratory distress syndrome? e ?acute lung injury?.

# 1 Introduction

cute respiratory distress syndrome (ARDS) is a common condition with high mortality rates in patients in critical state and it is related with acute alveolar damage, loss of lung compliance and hypoxemia 1 .

For many years, prone position has been used to improve oxygenation in patients with ARDS that need mechanical ventilation support, being recommended to patients with moderate to severe hypoxemia with PaO2/FiO2<150 2 .

The improvement of oxygenation associated with prone position is related to the decrease of aspects that contribute to alveolar collapse, alveolar ventilation redistribution and perfusion. There is a reduction in pulmonary stress and tension, reducing over distension of non-dependent aerated zones and recruit dependent and atelectasis zones. Lung compliance increases, but with a decrease of the rib cage compliance associated to a more homogenous lung expansion and better rates of ventilation/perfusion 2 .

The prone position is a maneuver that can be used on patients with acute respiratory distress syndrome aiming to diminish hypoxemia, was used for many years in the management of this disease. Prospective randomized studies and meta-analyzes have increase the evaluation of the scientific evidence of the use of the prone position connected to the reduction of mortality rates, its efficiency as well as the necessary time to accomplish the adequate ventilatory parameters. 3 II.

# 2 Aims

Primary: Evaluate the efficiency of the use of the prone position in patients with acute respiratory distress syndrome.

Secondary: Understand the respiratory physiology involved in the use of the prone position in patients with acute respiratory distress syndrome.

# 3 III.

# 4 Methods

This work was elaborated through a revision of the literary narrative present on the Scientific Eletronic Library Online (Scielo), Medline e Cochrane databases. Twenty-two articles published between 2001 and 2020 were selected to this endeavor. The descriptors used for this were ”decúbito ventral”, ”síndrome do desconforto respiratório” and ”lesão pulmonary aguda” in Portuguese and its English translations ”prone position”, ”respiratory distress syndrome” and ”acute lung injury”, found on ”Medical Subject Headings-MeSH” list.

Through the research methods used, there were no studies that approached the efficiency of this conduct on acute respiratory distress syndrome in mild cases, including nevertheless, moderate to severe cases in the twenty-two articles mentioned.

The criteria used in this research included articles both in English and Portuguese, with the complete text provided online excluding articled published before 2001, thesis, chapters of thesis, seminary and conference proceedings.

To measure outcomes in the use of the prone position maneuver in patients with acute respiratory distress syndrome, variables like mortality were evaluated, following studies and metanalyses trough statistic parameters, like risk motive, trust interval and p value.

# 5 IV.

# 6 Results and Discussion

Acute respiratory distress syndrome is a potentially devastating form of hypoxemic respiratory insufficiency caused by acute inflammatory lung affection. It is marked by a sudden beginning and by the presence of triggering factors (bilateral diffuse pulmonary infiltrate), that generally constitute a noncardiogenic pulmonary edema 4 .

Even though the clinical significance of acute respiratory syndrome is undeniable, its global prevalence is uncertain. Approximately 10-20% of hospitalized patients on mechanical ventilation fit the diagnosed criteria for ARDS 4 .

ARDS was defined in 1994 by the American-European Consensus Conference, and since then questions about this definition reliability and validity have been raised. In 2012, a new model of diagnose, known as the Berlin Definition, was proposed, being divided in three categories mutually exclusive based on its degree of hypoxemia: mild (200 mm Hg < PaO2/FIO2 ? 300 mm Hg), moderate (100 mm Hg < PaO2/FIO2 ? 200 mm Hg) and severe (PaO2/FIO2 ? 100 mm Hg),starting seven days after a known clinical insultor worsen respiratory symptoms, besides consistent bilateral opacities with pulmonary edema visible through chest Xrays or CT scans 5 .

To validate the criteria, it’s necessary that the minimal PEEP or CPAP configuration be 5 cm of water and that the relation Pao2/Fio2 is evaluated in patients with invasive mechanical ventilation (with the CPAP criteria being used to diagnose mild cases of ARDS) 5 .

As recognized by the Berlin definition, the development of ARDS is second to insults, that are mainly classified as pulmonary or systemic (indirect) factors of origin. Pneumonia (bacterial, viral, fungal, or opportunistic), aspiration of gastric contents and nonpulmonary focus sepsis together represent more than 85% of cases of ARDS 6 .

It is important to acknowledge that the acute respiratory distress syndrome is not a disease, but a syndrome characterized by many causes and by a great variety of clinical trajectories, with a physiopathology that can be divided into 3 sequential phases that overlap: exudative or inflammation phase, proliferative phase, and fibrous phase. In matters of histology, after the beginning of the primary disease, a diffuse lesion occurs, marked by innate immunity cells of the alveolar endothelium and epithelial barriers, with a flood of protein-rich plasma and cellular content in the interstitium and air space, occurring a rapid development of capillary congestion, the appearance of atelectasis, hemorrhage and alveolar edema, followed days later by the formation of a hyaline membrane, epithelial cell hyperplasia and interstitial edema 6 .

Considering the relevance of ARDS in a context of intensive therapy, clinical diagnose and the early adoption of therapeutic strategies (specially the use of protective ventilation) are determinant for the reduction of morbidity and the increase of patient survival rate 1 . The treatment for acute respiratory insufficiency is destined to the underlining disease, as well as a package of interventions destined to improve lung gas exchange, limiting secondary pulmonary lesion, with mechanical ventilation. In the initial phase of the mild respiratory insufficiency, non-invasive ventilation can be used to prevent orotracheal intubation and subsequent pulmonary lesions associated with mechanical ventilation 7 .

Prone position has been used for more than 30 years as treatment to patients with acute respiratory distress syndrome. This maneuver has shown that is capable to improve the oxygenation in patients with acute respiratory insufficiency. Studies done through metanalyses suggest that the use of the prone position is best used in patients on the subgroup with severe hypoxemia 8,9 .

Randomized studies confirm that prone position increases oxygenation when compared to the supine position, being recommended to patients with moderate to severe hypoxemia with PaO2/FiO2<150. The reasons behind the improvement on oxygenation are not completely defined and different potential mechanisms were identified 3,[10][11][12][13] .

Several clinical randomized studies investigate the evaluation of the use of prone position in patients with acute respiratory distress syndrome, observing the number of patients, duration of the trial, observed criteria, last follow-up evaluation and duration of the use of diverse maneuvers (TABLE **??**1).

To comprehend the respiratory physiology involved in the improvement of oxygenation during the use of the prone position, is fundamental to understand and recognize the importance of respiratory physiology, correlating with lung's West zone and alveolar pressure, of pulmonary arteries and veins (IMAGE 01).

West zone 1 correspond to the pulmonary peek, when alveolar pressure is higher than the pressure on the pulmonary artery, that in turn is higher than the pressure in the pulmonary vein. In this case, because the alveolar pressure is higher than the pressure on pulmonary vessels, the blood flow decreases in this pulmonary region. Being a ventilated area, but not well perfused, it impairs gas exchange there 18 .

Table 01: Characteristics of the randomized clinical studies that investigate the use of prone position in patients with acute respiratory distress syndrome Pronesupine I 2001 14 Guérin C et al 2004 15 Mancebo J et al 2006 16 Pronesupine II 2009 17 Guérin Adapted from Gattinoni L. 9 Lower, in the lung (zone 2) the arterial pressure increases because of the hydrostatic effect and now exceeds the alveolar pressure. Nevertheless, venous pressure is still very low, lower than the alveolar pressure. Under these conditions, blood flow is determined by the difference between alveolar and arterial pressure. Once the arterial pressure is increasing towards the bases, and the arterial pressure is the same for the whole lung, the difference in pressure is responsible for the increase of flow 18 .

On zone 3, venous pressure exceeds alveolar pressure, and the flow is determined by the difference between the pressure on the pulmonary arteries and veins. Besides the growing of capillary recruitment, the increase of blood flow can be produced by capillary distension 18 .

Image 01: Lung's West zones and their correlation to alveolar, arterial and venous pulmonary pressure. PA: Alveolar pressure; Pa: Arterial pulmonary pressure; Pv: Venous pulmonary pressure. Source: Levitzky MG. 18 Various mechanisms can explain the respiratory physiology involved in the improvement of oxygenation with the use of prone position, like a homogenous alveolar distribution, reducing pulmonary tension and stress associated with mechanical ventilation, as well as the recruitment of zone with atelectasis, promoting a better recruitment of pulmonary dorsal regions related to ventral regions of the lung. So, pulmonary ventilation is more homogenous with better ratio of perfusion ventilation, improving gas exchange and preventing pulmonary lesion provoked by mechanical ventilation 2 .

Prone position contributes to an improvement of oxygenation in patients with severe respiratory distress syndrome in general due to the decrease of compression effects that favor alveolar collapse. Since the physiopathology of the disease is uniform throughout the lung, the edema is responsible for the increase of the weight of the lung, which associated with gravity, makes that the dependent regions collapse. The region that collapses the most, is the dorsal one. When the patient is put on prone position, the dorsal region does not suffer from the weight of the lung, becoming more expanded 9 .

Prone position enhances respiratory mechanics, through the improvement of the inspiratory kinetics, probably preventing the closing of smaller air ways before the final exhale 9 .

In normal individuals, the weight of the heart influences aeration of lungs' dependent regions, facilitating its collapse. On patients with ARDS, this effect can be aggravated by pulmonary hypertension that results from hypoxic vasoconstriction, releasing vasoconstrictive substances and remodeling pulmonary circulation, in addition to an enlargement of the right cardiac chamber. The improvement of the mechanics with the use of the prone position can result in the relief of cardiac and abdominal compression made by the lower lobes on the supine position 19 .

The compliance of the pulmonary system can increase, even though the thoracic wall compliance diminishes. Besides that, the driving pressure of the respiratory system (plateau pressure -PEEP)increased from the supine position to the prone one, and the augmentation of the directed pressure of the respiratory system was due to a growth of the elastance of the thoracic wall 19 .

However, in addition to the inherent benefits of the prone maneuver on the patient, we have the risks associated with the formation of pressure ulcers, obstruction of the orotracheal tube and dislocation of the tube 3 .

Two metanalyses and the PROSEVA study showed the beneficial effects on patients with moderate to severe acute respiratory distress syndrome with a decrease of mortality. Nonetheless the duration of the session remains unknown, being necessary additional research to a better understanding of the total time needed for this maneuver. While on the PROSEVA study, patients remained in position for about 17 hours, on both metanalyses, time ranged from 7 to 18 hours **??**,8,9. A cohort study analyzed arterial blood gases, pulmonary mechanics and capnography during the first prone position session. The results generally showed a significant increase of pH, static compliance and PaO2/FiO2 and a significant decrease of PaCO2, plateau pressure and pressure variation. Since it's a study mainly based on observations, it needs to be evaluated with care, since the absence of randomization may lead to a biased result. Nevertheless, it brings us an idea of the parameters that can be altered using this maneuver 2 .

Analyzing the PROSEVA study, multicentric, prospective, controlled, and randomized, we obtained a study that aimed to evaluate the early use of prone position in patients with ARDS, randomizing 466 patients with

PaO2/FiO2<150 mmHg, FiO2 higher or equal to 0,6 and PEEP higher or equal to 5cmH20 3 . 237 patients were subjected to the prone position and 299 subjected to the supine position. Taking into account the mortality in the first 28 days, the results showed a percentage of 16% of the prone position vs 32.8% of the supine position(HR 0,39;IC de 95%; 0,25-0,63; p<0,001)and until the ninetieth day, 23,6% in patients in prone position vs 41% in supine position(HR 0,44;IC de 95%; 0,29-0,67; p<0,001).This strongly suggest that in patients with severe ARDS, the early usage of prolonged prone position sessions lead to a significant diminish in mortality on days 28 and 90 3 .

The criteria to interrupt the treatment were: improvement on oxygenation Pao2: Fio2 of ?150 mm Hg, with a PEEP of ?10 cm of water and a Fio2 of ?0,6, these criteria had to be attended on the supine position at least 4 hours after the end of the last prone position session; a decrease on PaO2/FiO2 in more than 20%, in relation to the supine position, before the two consecutive sessions in prone; or complications that occurred during the maneuver leading to its immediate interruption 3 .

The complications that involved an immediate interruption of the treatment in prone involved the nonscheduled extubation, obstruction of the orotracheal tube, less than 85% of oxygen saturation on pulse oximetry or PaO2 lower than 55mmHg for more than 5 minutes when the FiO2 were 1,0, cardiac arrest, cardiac frequency lower than 30 beats per minute for more than one minute, systolic arterial pressure lower than 60mmHg for more than 5 minutes and any other motive associated with a risk on life that lead the doctor to interrupt the treatment 3 . Hemodynamic compromise, a frequent condition associated with ARDS, does not represent, on its own, a contraindication to the use of the prone position. In the PROSEVA study, that showed the beneficial effect on survival rate, 72% of patients received vasopressors, with a result not so different from that noticed on the control group 3 . But all patients were hemodynamically stable when they were included on the study, since their average arterial pressure had to be ? 65 mmHg, or they would be excluded from the study. It is fundamental to emphasize that the prone position, when properly used, doesn't induce hemodynamics side effects, and can even improve hemodynamics 3 .

Even with an extensive literature about the handling of ARDS, COVID-19 constitutes a new viral infection of the lower respiratory tract, in which the physiopathology and treatment are not completely extended. The CT scan of these patients bring new and interesting information about the physiopathology and individualization of the mechanical ventilation, taking into account different phenotypes of the disease 20 .

Accordingly to the CT scans, there were 3 different phenotypes, with phenotype 1 being multiple, focal findings, ground-glass opacities in the subpleural region; phenotype 2 atelectasis and nonhomogeneously distributed peribronchial opacities and phenotype 3 with ARDS-like pattern. 20 .

In phenotype 1, pulmonary compliance was normal or even high, but with severe hypoxemia. Moderate PEEP can be used to redistribute the pulmonary flow and reduce the shunt. In this case, using the principles generally used for ARDS, and choosing the PEEP accordingly to a better driving pressure, lower PEEP can be used in case of normal compliance. Prone position may redistribute perfusion butis generally not very useful in this stage 20 .

In the phenotype 2, atelectasis is prevailing. In this case, moderate and high PEEP may be used, with or without the use of the prone position to recruit areas not aerated of the lung 20 .

In the phenotype 3, typical findings of moderate to severe ARDS, with alveolar edema and low pulmonary compliance were observed. Respiratory parameters must follow the same principles applied to ARDS, with the PEEP chosen accordingly to a better driving pressure, beyond the use of prone position and oxygenation trough the extracorporeal membrane (ECMO), if necessary 20 .

When hypoxemia and respiratory insufficiency persist or get worse after the use of oxygen, or in case of persistent hypercapnia, organic failure, coma, aspiration risk, orhemodynamic instability; the mechanical ventilation must be used as soon as possible 20 .

Hypoxemic respiratory insufficiency and the need for invasive ventilation must be considered when patients are under oxygen, but who show tachypnea (>30bpm) and hypoxemia (SatO2<90% or PaO2<60 mmHg), even with oxygen being administered through facial mask or reservoir bag with 10-15 L/min 20 .

In the current pandemic caused by the coronavirus (COVID-19), the prone position has been largely adopted by doctors and even used before intubation in patients that breath spontaneously 21 .

Patients with ARDS related to COVID-19 were included in a multicentric cohort study in Spain22, with 63% of patients with mild cases. Studies currently in progress indicate that the action mechanisms for pneumonia caused by COVID-19 (e.g., blood flow redistribution) may be different from other forms of ARDS, indicating that not all COVID patients intubated are benefited by the use of this maneuver 21 .

The use of prone position in patients not intubated and with spontaneous breathing was propelled by the COVID-19 pandemic. Up to this day, the results of studies, done through observation, about the viability and efficiency of this strategy on the oxygenation before intubating, in patients that received high flow of oxygen or noninvasive ventilation are inconclusive. New studies are necessary to verify if this strategy can reduce the intubation rate and improve the survival numbers 21 .

Is fundamental to integrate the prone position with protective ventilation in patients with moderate to severe acute respiratory distress syndrome. It is not possible, though, to foresee which patients will have a real benefit with the use of prone position before, during and even after the maneuver. Studies are still needed to evaluate the pronation in patients with mild to moderate respiratory distress and on non-intubated patients, as well as to evaluate the proper duration of its use to improve oxygenation on patients 2 .

V.

# 7 Conclusions

Taken into account the collected data, we can conclude that the acute respiratory distress syndrome is a form of acute hypoxemic respiratory insufficiency, marked by an acute inflammatory process in the lung. The treatment for this condition varies accordingly to the base illness of the patient and his hemodynamic state. Patients with moderate to severe respiratory distress, with PaO2/FiO2< 150, have the therapeutic alternative of the use of the prone position, to improve their oxygenation.

The respiratory physiology involves the improvement of the oxygenation related to the decrease of pulmonary stress, pulmonary lesion induced by ventilation, with a more homogenous pulmonary expansion, improving ventilation parameters, as well as gas exchange. In this sense we achieve the secondary aim of this article.

We can conclude that various randomized clinical studies and metanalyses suggested the improvement of oxygenation on patients when they were subjected to the prone position, where primarily made in an early stage and in relative long sessions. We also attested an improvement on the mortality rates of these patients, with a highlight to the PROSEVA study that comparatively analyzed the mortality on days 28 and 90. The efficiency of the maneuver questioned in the primary aim of this article was also answered using scientific evidence and randomized studies as basis.

In the current pandemic of COVID-19, the use of the prone position has been extended to non-intubated patients, aiming the improvement of oxygenation, but more studies are still needed to evaluate if it can reduce the need for intubation and improve the survival rates.

With that, we path our way to a conclusive understanding that more studies are necessary to comprehend the use of the prone position to patients with moderate to mild respiratory distress, since the studies done up to now only prove the benefits for patients with moderate to severe cases, which limit our study. It's also fundamental to analyze the ideal duration of the maneuver to improve oxygenation and its ventilatory parameters. [1] [2]

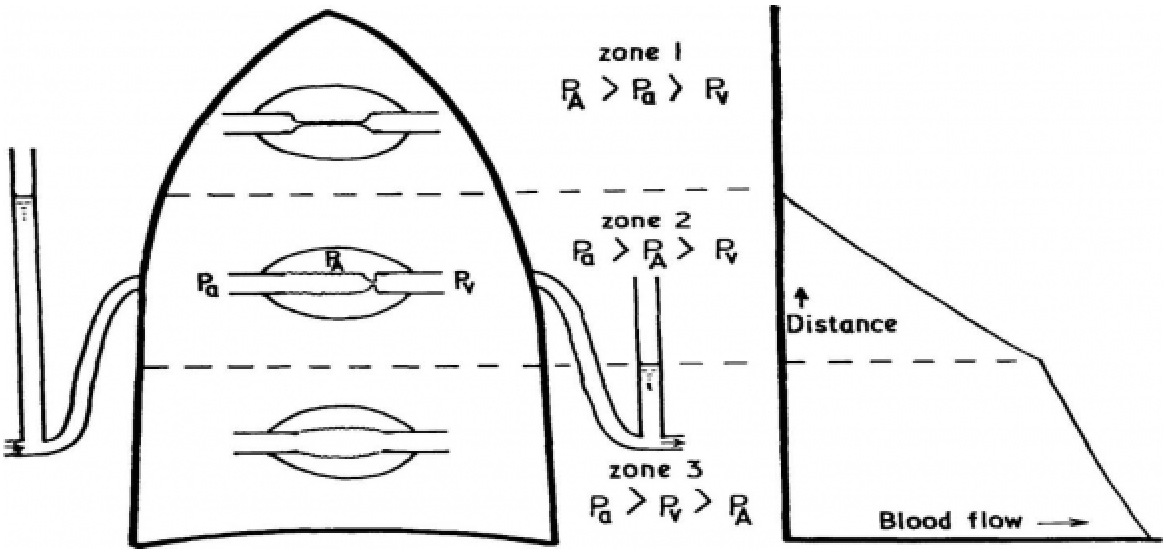


Figure 1: The

## .1 Acknowledgements

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