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Prone Position in Non-intubated Patients with COVID-19, a Useful Maneuver to Avoid Mechanical Ventilation: A Literature Review

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Authors' contributions

All authors contributed in the same way and have read and approved the final manuscript.

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Review Article

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ABSTRACT

The spectrum of coronavirus disease 2019 (COVID-19) ranges from asymptomatic to acute respiratory distress syndrome (ARDS). Prone position has been widely used in ARDS patients with mechanical ventilation and its benefits have been proven. This maneuver can be extrapolated to non-intubated patients with COVID-19, avoiding mechanical ventilation in some patients. Previous reports have demonstrated the benefits of this intervention.

Keywords: *Prone position; COVID-19; acute respiratory distress syndrome; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2.*

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1. INTRODUCTION

COVID-19 is an infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), that was first reported in 41 people, all of whom were associated to exposure in one seafood market in Wuhan, China [1,2]. The spectrum of the disease ranges from asymptomatic infection to severe ARDS [3]; by Jul 06, 2020, it has infected over 11.3 million people, with a case fatality rate of 4.7% [4].

Approximately 20% of patients with COVID-19 presents with severe and critical disease [5]. Among those patients who progress to critical illness, ARDS is the most common complication, affecting 85% of patients admitted to an Intensive Care Unit (ICU) [6]. The mortality rate of patients who require invasive mechanical ventilation reaches 67% [7].

Prone positioning patients is maneuver widely used in the ICUs to improve oxygenation in intubated patients with ARDS. We noticed with the first patient at our center (case report under editorial evaluation), in whom prone position (PP) improved her oxygenation, delaying and eventually avoiding the need of mechanical ventilation. Since then, there have been case series consistent with these initial findings, where a subgroup of patients improved with this maneuver.

The purpose of this review, is to present general concepts of ARDS as the most common complication in critical patients with SARS-CoV-2, describe the physiological benefits of the prone position in non-intubated patients, and to propose an algorithm for its application in patients with COVID-19.

2. PRONE POSITION AND PHYSIOLOGICAL BENEFITS

In supine position, the posterior part of the lungs are compressed by the heart and abdominal viscera, and these components increase the dorsal pleural pressure, decreasing the transpulmonary pressure; this phenomenon is accentuated by the increase in lungs weight in a patient with ARDS [8]. Additionally, the conical shape of the chest cavity causes that a bigger proportion of the lung in the supine position (the dependent segments of the lungs) is compressed, thus exacerbating the ventilation/perfusion (V/Q) mismatch [8].

By placing a patient in PP, the changes in pendent and nondependent regions, as well as the conformational shape changing of the lung to the chest cavity, the lung aeration and strain distribution are more homogeneous, and more alveoli are aerated (Fig. 1) [8].

Prone position was first described in 1976 by Mellins, who found that in children with cystic fibrosis PP improved ventilation [9,10,11]. Since then, it has been used for over 40 years to improve oxygenation. In the early 2000's, several randomized controlled trials have been conducted [9,10,11], the PROSEVA trial in 2013 showed clear benefits regard not only in improving oxygenation but also decreasing mortality [11]. Nowadays, this strategy is used mostly in patients with ARDS [11,12].

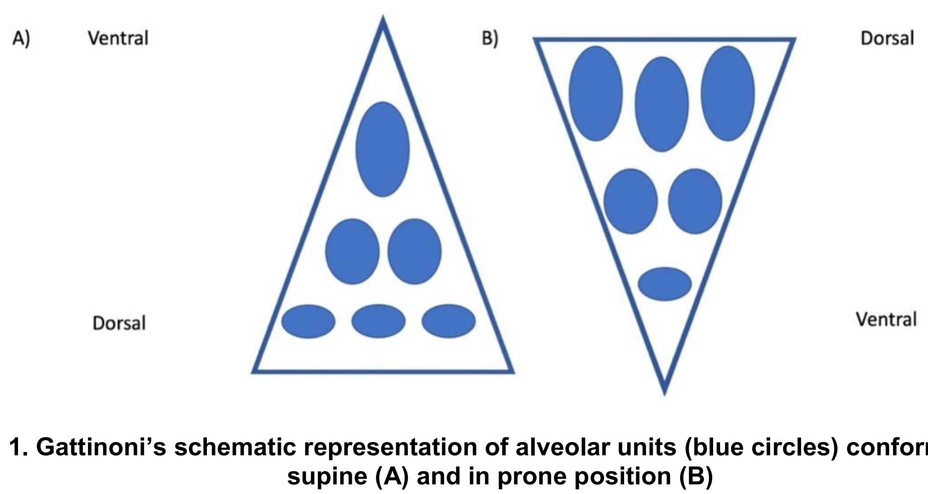

Fig. 1. Gattinoni's schematic representation of alveolar units (blue circles) conformation on supine (A) and in prone position (B)

When the patient is in prone position, a smaller fraction of alveolar units are compressed. Adapted from references [8,9]

As described by Gattinoni et al., while evaluating ARDS computed tomography scan (CT) of patients with ARDS, densities redistribute from the dorsal region (anatomic back) to the ventral region (anatomic front). This allows the dorsal region tends to reexpand while the ventral zone tends to collapse; this phenomenon is influenced by other components that lungs itself, such as heart weight and the abdominal pressure [12]. In prone position there is a more homogeneous distribution in stress and strain because the position of this components is modified. The result is a more homogeneous distribution of alveolar inflation [13]. Despite the widespread use in intubated patients and the physiological support of this maneuver, little is known about its use in non-intubated patients to improve oxygenation.

3. ARDS DIAGNOSIS

Initially ARDS was defined by the acute onset of noncardiogenic pulmonary edema, hypoxemia and the need for mechanical ventilation [14,15]. The first diagnostic criteria were made in 1992 by American–European consensus conference; these criteria were updated in 2012 in the so-called Berlin definition of ARDS in adults. Depending on the level of oxygenation, through the ratio partial pressure of arterial oxygen (PaO2)/ inspiratory oxygen fraction (FiO2), ‘mild’, ‘moderate’ and ‘severe’ descriptors can be added to the diagnosis of ARDS [14,15].

Since Berlin definition of ARDS requires a minimum positive end-expiratory pressure (PEEP), The Kigali ARDS definition was proposed in 2016 (Table 1). Because the Berlin definition may have difficulties to adapt the ARDS definition to the health care system conditions in the developing world. The minimum PEEP requirement was removed, whereas hypoxemia is evaluated using the ratio of arterial oxygen saturation measured by pulse oximetry (SpO2)/FiO2 ≤315 with SpO2 ≤97%.

The effectiveness in the early diagnosis of ARDS of the Kigali definition has been compared against the Berlin definition, showing a reliable method and can be considered as a potential

Table 1. Definitions of ARDS in adults

	Berlin definition	**Kigali definition**
Timing	Respiratory failure within 1 week of a known insult or new and/or worsening respiratory symptoms	Respiratory failure within 1 week of a known insult or new and/or worsening respiratory symptoms
Origin	Respiratory failure not fully explained by cardiac function or volume overload (need objective criterion such as echocardiography to exclude hydrostatic oedema if no risk factor is present)	Respiratory failure not fully explained by cardiac function or volume overload (need objective criterion such as echocardiography to exclude hydrostatic oedema if no risk factor is present)
Imaging	Bilateral opacities on chest radiograph or CT not fully explained by effusion, collapse or nodules	Bilateral opacities on chest radiography or ultrasonography scan not fully explained by effusion, collapse or nodules
Oxygenation	Acute onset of hypoxaemia defined as PaO2/FiO2 <300 mmHg on at least PEEP 5 cmH2O PaO2/FiO2 of 201–300mmHg is mild ARDS - PaO2/FiO2 of 101–200mmHg is moderate ARDS - PaO2/FiO2 ≤100mmHg is severe ARDS	SpO2/FiO2 <315; no PEEP requirement

CT, computed tomography scan; ARDS, acute respiratory distress syndrome; PaO2/FiO2, ratio partial pressure of arterial oxygen/inspiratory oxygen fraction; SpO2/FiO2, ratio of arterial oxygen saturation/inspiratory oxygen fraction; PEEP, positive end-expiratory pressure.

Adapted from references [14,15,16,17]

alternative for the diagnosis of ARDS [15,16,17,18].

In the covid-19 era, some patients may have ARDS while on supplemental oxygen by conventional methods or non-invasive mechanical ventilation, so it is important to know Kigali's definition of ARDS.

Gattinoni et al. has described two phenotypes of ARDS in patients with COVID-19: Type 1 (or type L): near-normal lung compliance with isolated viral pneumonia; and type 2 (or type H) Decreased lung compliance. In type 1 phenotype prone positioning should be considered more as a rescue maneuver to facilitate the redistribution of pulmonary blood flow, rather than for opening collapsed areas and in type 2 phenotype PP could be used as a long-term treatment as in any form of severe ARDS [19,20].

4. PRONE POSITION IN NON-INTUBATED PATIENTS WITHOUT COVID-19

Previous studies suggested that prone position can increase the average ratio of PaO2/ FiO2 and reduce mortality in moderate to severe ARDS in intubated patients [21,22,23]. These benefits could also apply to non-intubated patients, in whom PP may improve oxygenation and therefore delay or even avoid the need for intubation.

Vittorio et al. demonstrated in fifteen non-intubated patients with acute respiratory failure, PP with non-invasive ventilation improved oxygenation measured by an increase in PaO2/FiO2 of up to 72 mmHg, with no changes in the pH nor in the partial pressure of carbon dioxide (PaCO2) [24].

Other studies showed benefit of PP plus noninvasive ventilation (NIV) or high flow-nasal cannula (HFNC), especially in patients with moderate ARDS who may avoid intubation. This was proven for infectious and non-infectious etiology. Of notice, in patients with severe ARDS, PP can increase the mortality [25,26].

5. PRONE POSITION IN NON-INTUBATED PATIENTS WITH COVID-19

Some clinical trials have been reported on awake PP in patients with COVID-19 and there are some trials in the recruitment phase [27,28,29]. Data from 631 confirmed cases of novel coronavirus pneumonia (NCP) in Jiangsu Province, China, showed that the awake prone position had significant effect on oxygenation and pulmonary heterogeneity, however, full details such as methods and complete results were not available in this letter to the editor [30].

The first reported trial was by Caputo et al.: in a pilot study, they included fifty patients, the median SpO2 at triage was 80%. When supplemental oxygen was given to patients through conventional methods (that includes non-rebreather mask and nasal cannula), SpO2 was 84%. After 5 minutes of prone position, SpO2 improved to 94%. Thirteen patients (24%) failed to improve or maintain their SpO2 and required endotracheal intubation within 24 hours of arrival to the hospital [31].

Xavier Elharrar et al. Made a prospective, single-center, before-after study was conducted among awake, non-intubated, spontaneously breathing patients with COVID-19. Six patients responded to PP, representing 25% of the 24 patients included. Among patients who sustained PP for 3 hours or more, PaO2 increased from a mean (SD) to 94.9 (28.3) mm Hg during PP. None of the included patients experienced major complications. While oxygenation increased during PP in only 25% and was not sustained in half of those after resupination. This study has several limitations that were written by its authors such as: The sample was small, a single episode of PP was evaluated, the follow-up was short, clinical outcomes were not assessed, and causality of the observed changes cannot be inferred [32].

Dong et al. reported a retrospective cohort of 25 COVID-19 patients who received PP, lateral position (LP) and oxygen therapy or non-invasive ventilation, they included severe and critical patients. They found a decrease in the respiratory rate of 28.4 breaths/min to 21.3 breaths/min in the 25 patients. All patients tolerated PP and LP well without deterioration or severe adverse events. All patients survived and none of them required mechanical ventilation. Also, the computed tomography showed lung recruitment in all patients [33].

Xu and colleagues demonstrated the benefit of PP in ten awake patients with COVID-19 combined with high-flow nasal cannula (HFNC), all of them were survivors, they used as a target SpO2 >90% and 16 hours or more for prone position [34]. Bower and He propose an algorithm for use prone position while the patient maintains and SpO2 > 94%. [35].

We also found formal and non-formal guidelines and protocols recommending the use of the prone position in an awake patient, like the Intensive Care Society Guidance, the Massachusetts General Hospital guideline and the COVID Awake Repositioning Proning Protocol. On this basis, we designed the later proposed algorithm [35-39].

6. INDICATIONS, CONTRAINDICATIONS, AND EQUIPMENT OF PRONE POSITION IN NON-INTUBATED PATIENT

The prone position in the awake patient is a different procedure than in the patient under invasive mechanical ventilation. In non-intubated patients, the most common reported complications are disconnection of vascular lines, hypotension, and arrhythmias, for which it is important to verify its indications, contraindications and the necessary equipment, as well as to carry out the procedure properly. These are summarized in Table 2 [40-43].

7. PROPOSED ALGORITHM TO PRONE POSITION AS RESCUE THERAPY IN CONSCIOUS PATIENTS WITH COVID-19

We propose a decision tree for a structured therapy of the prone position in non-intubated patients. This is based on the different formal and non-formal guidelines, as well as the available evidence about the prone position in the awake patient [35-39]. It consists of four blocks of questions with a binary answer (yes or no). This allows for a reduced time to decide if the patient is candidate to PP and if the procedure should continue (Fig. 2).

Table 2. Indications, contraindications and equipment of prone position in non-intubated patient

Indications	Contraindications	Equipment
• Necessity of oxygen to maintain SpO2 > 90% • Mild to Moderate ARDS	• Severe ARDS • Burn or injury on the face • Spinal instability • Facial or pelvic fractures • Open chest or unstable chest wall • Intracranial hypertension or head injury • Severe arrhythmias or acute hypotension • Multiple Trauma • Raised intraocular pressure • Massive hemoptysis • Recent tracheostomy <24hours • Respiratory distress (RR ≥ 30, PaCO2 ≥ 65, accessory muscle use) • Immediate need for intubation • Relative contraindications: delirium, confusion, inability to independently change position, recent nausea or vomiting, advanced pregnancy	• Pillow • Supplemental oxygen, as needed • Foam Dressings to protect pressure points (if indicated) • Continuous cardiac and oxygen saturation monitor • Registration documents

ARDS, acute respiratory distress syndrome; PaCO2, partial pressure of carbon dioxide; RR, respiratory rate; SpO2, peripheral capillary oxygen saturation.

Adapted from references [40-43]

The inclusion criteria for the procedure include patients with COVID-19 who present with hypoxemia or with a mild or moderate ARDS. The first block of questions is designed to know if the patient is candidate, including contraindications and the required material. For the candidates, five activities are described to be carried out before placing them in prone, followed by a second block of questions that is intended to answer whether these activities can be done and find out if the patient agrees with the procedure.

The affirmation to the questions of these two blocks allow us to advance with the intervention that is divided into four steps: I. Positioning and monitoring. II. The immediate evaluation of the intervention at 5-10 minutes. III. The continuation of the maneuver and its documentation during the first hour. And IV. Repositioning and evaluation of a complete cycle, comprising two to four hours in prone.

Once the complete monitoring is started and the appropriate position of the patient is adopted, there must be close monitoring during the first 5 to 10 minutes in order to answer the block of questions that define clinical instability, any variable present at this time determines the end of the algorithm and pronation must stop.

In the absence of instability, the procedure and its registration should be continued for sixty minutes, thereafter, it is suggested to do a second evaluation after half an hour to investigate the permanence of stability. This section also describes measures that must be taken to optimize the follow-up and ensure

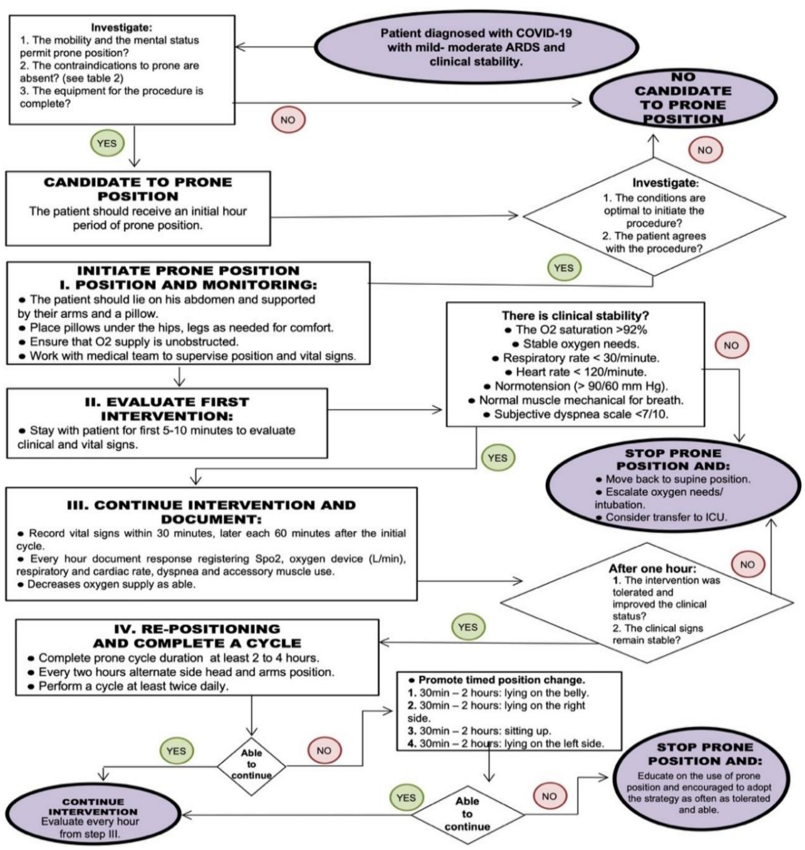

Fig. 2. Proposed algorithm to prone position as rescue therapy in conscious patients with COVID-19

ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; ECG, electrocardiogram; ICU, intensive care unit; L/min, liters per minute; mm Hg, millimeters of mercury; O2, oxygen; SpO2, peripheral oxygen saturation. Adapted from reference [35,39] patient safety. After an hour, the third block of questions have the purpose to evaluate the usefulness of the procedure. Negative answers to these questions indicate the need to interrupt PP.

The fourth step is applied to patients who were able to tolerate the initial one-hour intervention to extend the time until complete a cycle. Three sections are detailed for this step; the first one sets the measures to complete a cycle if the patient can continue. The second section describes a time-based method of position change for patients who are unable to complete a prone cycle, and the third specifies the actions to be carried out for the patients who was unable to adapt to timed position changes. The evaluation of the first two sections must be hourly, orienting again with all the elements of the third step. In the case of the third section of the fourth step the evaluation is suggested every half hour to try to perform from step two.

The goal of the algorithm is to complete, documenting benefit in clinical status, a cycle at least twice a day. Considering that it should be suspended at time of clinical imbalance to not delay treatment in the ICU and the need of other support measures, including mechanical ventilation.

8. WHEN TO DISCONTINUE PRONE POSITION?

There is no clear definition of proning failure. However, if the patient has an impending need for intubation (Respiratory rate ≥ 30, accessory muscle use, dyspnea > 7 of 10) there is no doubt that the maneuver has failed [44].

In patients without immediate need for intubation, we can use prediction tools such as the ROX index. ROX index was published by Oriol Roca et al in 2016, it can predict the failure to the use of HFNC in patients with pneumonia.[45] This index has not been validated in COVID-19. However, in the original study a small proportion of patients had viral pneumonia (14 patients out of 157).

The ROX index is defined as the ratio of oxygen saturation as measured by pulse oximetry/fraction of inspired oxygen to respiratory rate) for determining the need or not for intubation. The best cut off point is ROX Index ≥4.88, measured at 2, 6, or 12 hours after HFNC initiation: this value is associated with a lower risk for intubation. For a ROX Index <3.85, risk of HFNC failure is high, and intubating the patient should be assessed. [46,47,48] Also, we suggest ROX index as a tool to evaluate the response to prone position, although this has not been validated so far.

9. CONCLUSION

Some selected patients may benefit from the combination of prone position plus early non-invasive ventilation / High Flow Nasal Canula/ supplemental oxygenation by conventional methods, to avoid intubation and allowing patients to “buy time” to heal, or in case of ventilators shortage, it can buy us precious time while one is available. This maneuver must be closely monitoring to identify patients who will not respond adequately. More studies are in progress, and the advantages, disadvantages and benefits will be shown with the results.

CONSENT

As per international standard or university standard, patient’s consent has been collected and preserved by the authors.

ETHICAL APRROVAL

It is not applicable.

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To all the health workers in the fight against the novel coronavirus.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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