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Effect of Prone Position in Severe Covid-19 Patients in a Referral Center: A Cohort Retrospective Study

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Abstract

Introduction: Covid-19 is defined as a pandemic disease by WHO, in November 2023, WHO recorded 772.1 million confirmed cases and 6.9 million deaths, including 68,382 confirmed cases and 1426 deaths in Madagascar. The management of severe cases of Covid-19 remains a challenge for the healthcare system in a resource-limited country, due to the consumption of human resources, the shortage of medical resources and the lack of capacity in resource-limited countries. Prone position (PP) improves survival in acute respiratory distress, and numerous studies have shown that during Covid-19, it reduces mortality rates at 28 and 90 days, and increases the number of days without mechanical ventilation. However, data on the beneficial effects of PP remain limited in low-income countries. In this context, our study aims to evaluate the benefits of the prone position for severe Covid-19 patients in a referral center in Madagascar. **Method:** This is a retrospective cohort study, during the 2nd and 3rd waves of COVID-19, over a period of 11 months in two wards managing COVID-19 cases. We included all patients aged 15 and over with severe forms of COVID-19 who required 6 l/min of oxygen therapy. **Results:** We enrolled 123 patients, including 40 in the prone position and 83 in the supine position, with a mean age of 60.5 ± 12 years. The prone position (DV) reduced the risk of probable complications of COVID-19 with a strong association in terms of use of respiratory assistance (OR = 0.15; 95% CI = 0.05 - 0.47), respiratory deterioration (OR = 0.22; 95% CI = 0.09 - 0.58), shock (OR = 0.30; 95% CI = 0.11 - 0.79) and hemodynamic instability (OR = 0.33; 95% CI = 0.12 - 0.95). Univariate analysis of the effect of prone position on SpO_2 showed improvement with significant associations with SpO_2 at Day

1- Day 3, D4 - D7, D8 - D14, and persisting even at D15 - D21, D3 and D2 before discharge, and at discharge. In the overall population, the mean length of hospital stay was 22.8 ± 22.1 days, with extremes of 1 and 67 days. Univariate analysis of the effect of the prone position showed a reduction in length of hospital stay with a strong association (p = 0.001) and a mean difference of 14 days. The prone position reduced mortality with a significant association (OR = 0.44; 95% CI = 0.20 - 0.98). **Conclusion:** Awake prone position prevents complications of COVID, improves SPO_2 even up to hospital discharge and reduces hospital stay. This practice is simple, less costly and suitable in low income countries.

Keywords

Covid-19, Prone Position, Madagascar

1. Introduction

The 2019 novel coronavirus (2019-nCoV) is a newly emerging disease that was first reported in China and is still spreading around the world [1]. On 11 March 2019, the WHO defined it as a pandemic disease and in January 2024, 774,291,287 cases and 7,019,704 COVID-19 deaths were reported. Data show that Africa is less affected than other continents, and in Madagascar, there have been 59,319 cumulative cases and 1274 cumulative deaths [2]. Previous predictive models suggest possibly lower mortality from COVID-19 in Africa than in high-income countries otherwise Africa is the least equipped in terms of standard of care [3]. Studies have reported that the distinctive features of Covid-19 in Africa are 1) Insufficient diagnostic capacity (linked to gross national product); 2) A younger population limiting the population at risk and the number of deaths; 3) A favorable climate (hot and humid) which reduces viral transmission; 4) Certain socio-cultural factors which may reduce case reporting [4]. The management of severe cases of Covid-19 remains a challenge for the healthcare system due to the shortage of medical resources and insufficient capacity in resource-limited countries. Prone position improve survival in acute distress respiratory and numerous studies showed that during Covid-19 prone positioning reduced 28-day and 90-day mortality rates and extubation time and increased ventilator-free day [5]. However, data are limited to describe the effect of prone position in Madagascar. In this context, we aimed to evaluate the benefits of prone position for severe Covid-19 patients in a referral Center

2. Methods

The study will take place in two units that manage patients with severe COVID-19 and that do or do not apply the prone position as a therapeutic protocol, namely the Infectious Diseases Department and the Pneumology Department of Befelatanana University Hospital.

The hospital is a tertiary-level hospital located in the capital of Madagascar, with 350 beds and 584 staff. There are 22 technical departments, including pneumology and infectious diseases, which are referral departments for COVID-19 cases.

This was a cohort retrospective study during the second and third wave of COVID-19 in Madagascar from January 2021 to March 2022, 11 months.

Sampling: We included all patients older than 15 years with RT-PCR/TDR-Ag SARS-CoV-2 and/or typical chest CT presentation of COVID-19, presenting with a severe form of COVID-19 under high concentration mask with an oxygen requirement higher than 6 L/min, benefiting prone position for more than 16 hours per 24 hours associated with oxygen therapy and those receiving only oxygen therapy without prone position hospitalized during the two waves of COVID-19. We included also in the prone position cohort all patients that presented a respiratory worsening during hospitalization with an oxygen requirement greater than 6 L/min and were compliant with prone position for more than 16/24 hours. We excluded patients with an unexploitable medical record. The selection of patients according to these criteria is described in **Figure 1**.

Data collection is based on established questionnaires and medical record reviews applying these inclusion and exclusion criteria.

Variables: We studied the following variables:

- Socio-demographic characteristics of each group: age, gender
- Clinical characteristics at admission: comorbidities, clinical signs, vital parameters such as temperature, blood pressure, heart rate, respiratory rate, oxygen saturation, duration of onset of symptoms before admission of patients
- Univariate analysis: to study the effects of prone position versus supine position on complications of COVID-19, SpO_2, patients' outcomes

This national definition case categorized patients in three groups:

- Suspected cases: presence of clinical signs with epidemiological link but the PCR or RDT SARS COV were negatives
- Confirmed cases: presence of clinical signs with epidemiological link, the PCR or RDT SARS COV were positives
- Probable cases: presence of clinical signs with the epidemiological link, the PCR or RDT SARS COV were negatives but the CT scan reveals the image of COVID-19

A patient with a severe form of Covid-19 according to the national case definition and the WHO [6] is defined as patients who present fever, cough associated with an acute respiratory distress syndrome, tachypnea ≥ 30/min, SpO_2 ≤ 93% on room air, ground glass opacities on imaging > 50% involvement and a need for oxygen supplementation whether or not associated with septic shock: systolic pressure < 90 mmHg, mean arterial pressure < 60 mmHg, thready pulses, skin marbling, lack of response to adequate vascular filling, multi-visceral failure.

Statistics analysis: Data from the logbooks and medical records are collected using the established questionnaires. Census and Survey Processing System (CSPro) V7.7 was used for the data entry mask and data management. All statistical analyses and processing of the results (table and histogram) was done using

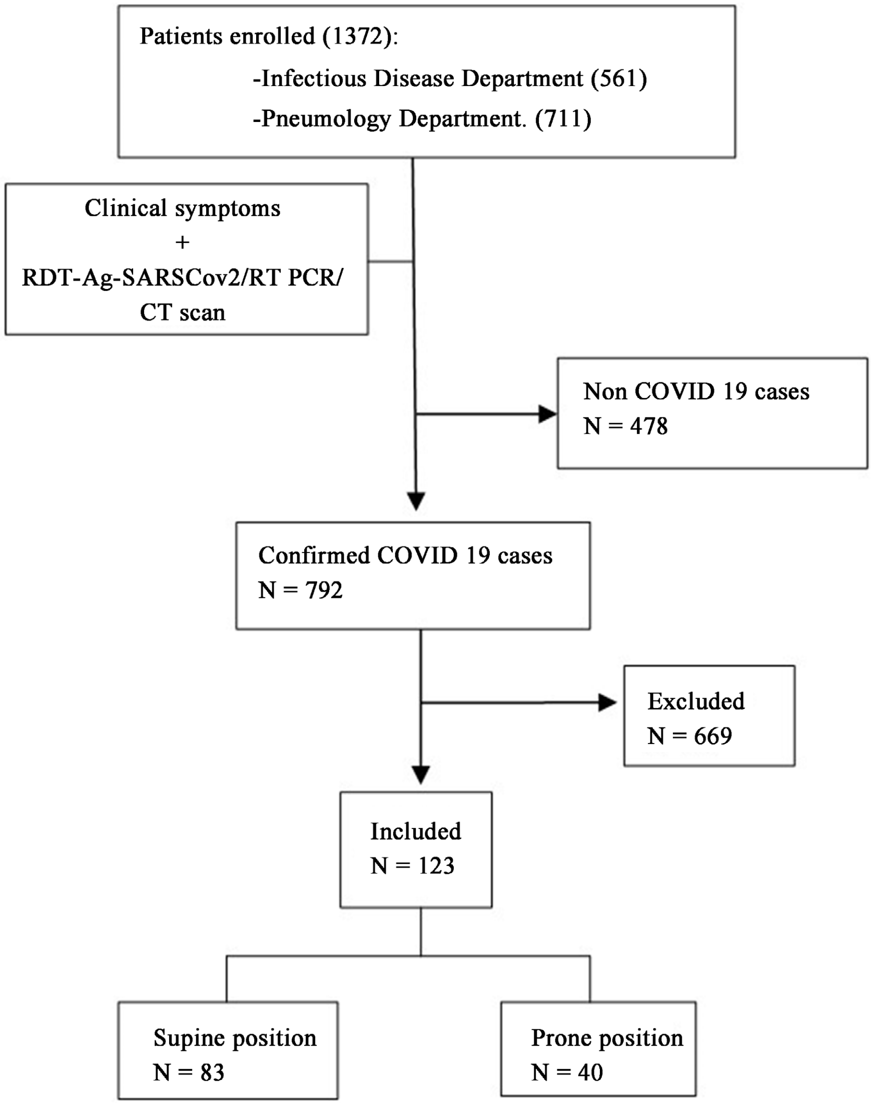

Figure 1. Flowchart of patients.

IBM SSPS Statistics V28.0.1.1 [7].

Text editing was done in Microsoft Word 2021 V2211 (16.0.15831.20208); Zotero V6.0.18 was used as bibliographic management software. All documents and computerized files was stored and secured on Microsoft One Drive and on I Cloud. Categorical data were reported as numbers and percentages, and continuous data as medians or interquartile ranges (IQR). A 95% confidence interval (95% CI) was set. A p-value $p < 0.05$ (5%) was considered significant for all associations. ANOVA will be used for association testing in generalized linear regression models.

Ethical considerations and data archiving: The implementation of this study was approved by the department heads and the Director of the Institution. Retrospective studies do not fall within the framework of the law of May 7, 2004, concerning experiments on the human person, so the present study do not take into account the validation of the Ethics Committee. The identities of patients in the collected data were coded in order to preserve anonymity and to respect total confidentiality. The data was used in compliance with medical confidentiality

3. Results

After applying inclusion and exclusion criteria (Figure 1) we enrolled 123 patients.

We identified two groups: 40 patients in the prone position and 83 in the standard position. Mean age was 60.5 ± 12.4 years, with extremes of 24 and 91 years. Among of the patients included, 61.8% were male, with a sex ratio (M/F) of 1.6. Among of symptoms before and on admission, cough was the most common at 100 (81.3%) followed by dyspnea 87 (70.7%) and fever 67 (61.8%), FR > 20 cycles per minute 99 (80.5%), room air SpO_2 < 90% 72 (58.5%) were the most reported (Table 1).

Severe lung involvement (50% - 75%) was most prevalent at 50.7%, followed by extensive involvement (25% - 50%) at 27.5%. There was no minimal involvement (<10%).

In the univariate analysis, the prone position reduced the risk of probable COVID-19 complications, with a strong association in terms of less need for respiratory assistance (OR = 0.15; 95% CI = 0.05 - 0.47), respiratory deterioration (OR = 0.22; 95% CI = 0.09 - 0.58), shock (OR = 0.30; 95% CI = 0.11 - 0.79) and hemodynamic instability (OR = 0.33; 95% CI = 0.12 - 0.95) (Table 2).

Table 1. Characteristics of patients in the admission.

Characteristics of patients	Effectifs N = 123	Frequency %
Female	47	38.2%
Male	67	61.8%
Comorbidities		
Vaccinal status		
Vaccined	9	7.3%
Unvaccined	90	73.2%
Unknown	24	19.5%
High blood pressure	62	50.4%
Diabetes	47	38.2%
Ovreweight/obesity	16	13.0%
Heart disease	12	9.8%
Coronary aretery disease	4	3.3%
Respiratory chronic disease	9	11.4%
Tuberculosis	13	10.6%
Cerebrocardiovascular disease	4	3.3%
Neurological chronic disaes	0	0.0%

Continued

Chronic renal failure		1	0.8%
Chronic liver		2	1.6%
Cancer		2	1.6%
Auto immune disease		2	1.6%
Ethylisme		23	18.7%
Smoking		25	20.3%
Asthenia		69	56.1%
Fever		76	61.8%
Chills		7	5.7%
Cough		100	81.3%
Hémoptysis		10	8.1%
Expectoration		44	35.8%
Dyspnea		87	70.7%
Chest pain		30	24.4%
Arthromyalgia		61	49.6%
Rhinorrhea		37	30.1%
Odynophagya		2	1.6%
Diarrhea		20	16.3%
Abdominal pain		9	7.3%
Vomitting		5	4.1%
Digestive haemorrhage		2	1.6%
Other digestives disorders		6	4.9%
Headache		42	34.1%
Anosmia		10	8.1%
Agueusia		8	6.5%
Counscienceness disorder		16	13.0%
Convulsions		2	1.6%
Motor deficit		1	0.8%
External bleeding (hématurie, épistaxis)		2	1.6%
Vital parameters			
Temperature (˚C)	<35	2	2.1%
	35.1 - 37.7	66	68.8%
	>37.7	28	29.2%
PAS/PAD (mm Hg)	<090/060	2	1.8%
	090-140/060-090	94	84.7%

Continued

	>140/090	15	13.5%
Respiratory rate (cycles par minute)	<12	0	0.0%
	12 - 20	9	8.3%
	>20	99	91.7%
SpO_2 (%)	< 90	72	75.0%
	90 - 94	19	19.8%
	> 94	5	5.2%
Glasgow score	<9	0	0.0%
	9 - 14	15	13.8%
	15	94	86.2%

Table 2. Univariate analysis effect of prone position on Covid-19 complications.

COVID-19 Complications	Prone position n = 40 (100%)	Supine position n = 83 (100%)	OR (95% IC)
Use of respiratory aids	4 (10.0%)	35 (42.2%)	0.15 (0.05 - 0.47)
Respiratory degradation	26 (65.0%)	74 (89.2%)	0.22 (0.09 - 0.58)
shock	6 (15.0%)	31 (37.2%)	0.30 (0.11 - 0.79)
Hemodynamic instability	5 (12.5%)	25 (30.1%)	0.33 (0.12 - 0.95)
Pulmonary superinfection	10 (25%)	23 (27.7%)	0.87 (0.38 - 2.60)
Cardiac decompensation	2 (5.0%)	7 (8.4%)	0.57 (0.11 - 2.19)
Diabetes decompensation	4 (10.0%)	12 (14.5%)	0.66 (0.20 - 5.05)
Diabetic ketoacidosis	1 (2.5%)	9 (10.8%)	0.21 (0.03 - 1.73)
Vomiting	1 (2.5%)	4 (4.8%)	0.50 (0.05 - 4.68)
Épistaxis	1 (2.5%)	4 (4.8%)	0.50 (0.05 - 4.68)
Hemoptysis	2 (5.0%)	12 (14.5%)	0.31 (0.66 - 1.46)
Other infections	1 (2.5%)	5 (9.6%)	4.15 (4.47 - 37.02)

Univariate analysis of the effect of prone position on SpO_2 showed improvement with significant associations with SpO_2 at Day 1 - Day 3 (D1 - D3), D4 - D7, D8 - D14, and persisting even to D15-D21, D3 and D2 before discharge, and at discharge, compared with supine position (**Table 3**). In the overall population, the mean length of hospital stay was 22.8 ± 22.1 days, with extremes of 1 and 67 days. The modal class was 0-7 days (79.3%) (**Table 4**). Univariate analysis of the effect of prone position showed a reduction in length of hospital stay with a strong association (Fisher test = 13.31, p-value = 0.001) and a mean difference of 14 days (**Table 4**). The prone position reduced mortality with a significant association (OR = 0.44; 95% CI = 0.20 - 0.98) (**Table 5**).

Table 3. Univariate analysis prone position vs supine position in SpO_2.

SpO_2	Prone Position n = 40 (100%)	Supine Position n = 83 (100%)	Mean Difference	Test de Fisher	*p*-value
D0	39 (97.5%)	80 (96.4%)	8.7	0.00	0.40
D1 - D3	40 (100%)	83 (98.8%)	8.7	5.55	0.02
D4 - D7	35 (87.5%)	71 (85.5%)	13.7	12.80	0.001
D8 - D14	31 (77.5%)	59 (71.1%)	14.4	10.78	0.001
D15 - D21	23 (57.5%)	33 (39.8%)	23.9	13.01	0.001
D22 - D28	11 (27.5%)	17 (21.3%)	18.8	3.19	0.09
D29 - D39	3 (7.5%)	5 (6.0%)	−44.7	0.60	0.47
D40 - D47	3 (7.5%)	4 (4.8%)	−31.4	4.44	0.09
D48 - D55	2 (5%)	3 (3.8%)	−26.5	0.75	0.45
D56 - D63	2 (5%)	3 (3.8%)	−26.5	1.42	0.32
D3 before discharge	35 (87.5%)	73 (88%)	11.1	10.75	0.001
D2 before discharge	40 (100%)	77 (92.8%)	14.1	12.94	0.001
At discharge	40 (100%)	81 (97.6%)	39.4	26.45	0.001

Table 4. Univariate analysis prone position vs supine position in length of hospital stay.

Length of hospital stay	Prone position n = 40 (100%)	Supine position n = 83 (100%)	Mean of difference	*p*-value
0 - 7 days	21 (52.5%)	12 (26.8%)	−14.7	0.001
8 - 21 days	12 (30.0%)	50 (40.7%)		
22 - 30 days	5 (5%)	10 (8.1%)		
>30 days	5 (12.5%)	30 (24.4%)		

Table 5. Univariate analysis prone position versus supine position in patient outcomes.

Patient outcomes (N = 123)	Prone position n = 40 (100%)	Supine position n = 83 (100%)	OR (95% IC)
Living patients 70 (56.9%)	28 (40.0%)	42 (60.0%)	0.44 (0.20 - 0.98)
Dead patients 53 (43.1%)	12 (22.6%)	41 (77.4%)	

4. Discussion

During Covid-19, in low income countries like Madagascar, management of acute respiratory distress syndrome (ARDS) is very limited in healthcare system with insufficient intensive care services and equipment. Prone position is a treatment strategy indicated for patients with ARDS [8] [9]. By placing the patient in a prone position, the ventral-dorsal trans-pulmonary pressure difference is ameliorated, which helps reduce dorsal lung compression and improve lung perfusion [10] [11] [12]. This improves the mismatch between ventilation and perfusion, and therefore oxygenation. With this relatively constant regional perfusion in the supine position, and a significant improvement in lung homogeneity, the effect of the shunt fraction should reduce and lead to a marked improvement in oxygenation. This has been demonstrated in animal and human studies, where the relative shunt fraction of the supine position was reduced by 30% compared to the prone position [13] [14]. However, Gattinoni and colleagues reported that the improvement in oxygenation during prone position did not persist after the return to the supine position, and that the PaO_2/FiO_2 ratio returned to baseline 6 hours after return to the supine position [7]. This hypothesis may explain the improvement in SpO_2 in the prone group compared with the supine group. In our study population, the improvement of SpO_2 persisted until discharge as the patients included had benefited from a prone position within 6 hours and early at the start of hospitalization. This is a highly relevant criterion for determining the effectiveness of prone versus supine position as confirmed in various studies [15].

Our findings showed that there is a significant and strong decrease in the length of hospitalization associated with prone position. However, other studies showed other results. Indeed, a randomized trial of 1126 patients that enrolled and randomly assigned to prone positioning (n = 567) versus standard care (n = 559), showed that there is no difference in the length of stay on prone position group and standard care group [16] [17] [18]. However, the duration of prone position is variable from a study to another according the study methodologies and may be explain this difference.

In terms of mortality our study joined the literature showing that prone position decreased the mortality rate. A meta-analysis comparing the effect of prone and supine position described that five of thirty five studies (n = 688 patients) [18] [19] assessed the mortality rate in COVID-19 patients who received prone and supine position, the prone group had a lower mortality rate than the supine group (OR 0.44, 95% CI 0.24 to 0.80; $p = 0.007$, $I^2 = 31\%$), which was statistically significant. However, according to the World Health Organization, COVID-19 Clinical Management Living Guidance (25 Jan 2021), Intensive care Society Guidance suggested a conditional recommendation for awake prone position of severely ill Covid-19 patients with acute hypoxemic respiratory requiring supplemental oxygen (including high-flow nasal oxygen) [20] [21]. Furthermore, a recent expert consensus on the management of COVID-19 related acute respiratory failure concluded that awake self-prone position may be considered to improve oxygenation and should be used when additional oxygenation is required to maintain $SpO_2 > 90\%$ [22]. In that case, awake prone position may be used to delay the respiratory deterioration in selected patients who require oxygen supplementation. The evidence of prone position on mortality rate in intubated or non-intubated COVID-19 patients remains uncertain as the pathophysiology of classical ARDS and COVID-induced ARDS were different [23]. This implies that the early initiation and duration of prone position determines its long-term efficacy because ARDS during COVID-19 is quite specific. The lack of randomized trials limits the certainty of the effect of prone position by the fact that most studies were observational, with a high risk of publication bias, a low level of evidence, a non-standardized prone position regimen and different ventilation modes in all included studies [23] then the generalizability is controversial.

However, in low-income countries like Madagascar where ICU capacity is insufficient, or even non-existent in some regions, prone position can be an asset to improve the outcome of patients with ARDS, while respecting the required conditions, *i.e.*, at the start of hospitalization and for more than 6 hours.

This study produced statistically significant results showing the beneficial effects of the prone position in the management of respiratory distress during COVID-19. However, the beneficial effects reported depend on the methodology used in the literature. Our study is a retrospective monocentric study with a small sample size, which may limit the external validity of the study compared with a multicentric study with a larger sample size. In terms of methodology, the risk of selection bias in the selection and comparison of the two groups is not insignificant. The existence of confounding factors may limit also the value of the results.

Despite these limitations, this does not detract from the scientific value of the study and its interest in a country with limited resources.

This study is nevertheless of interest because it gave an insight into the difficulty of managing severe form of Covid-19 in a low-resource country, and may allow us to share the experiences of two different services involved in the management of COVID-19 in Madagascar, the benefit and the outcome of patients in prone position.

5. Conclusion

In this study, we aimed to evaluate the benefits of prone position. Our study showed that the prone position in patients with severe COVID-19 prevented complications of COVID-19, improved SPO_2 until hospital discharge and reduced the length of hospital stay. The prone position, performed under the required conditions, *i.e.* at the start of hospitalization and for more than 6 hours, can be used to manage severe forms of COVID 19 in oxygen-dependent patients. However, these results are debatable, as this is a study with a low level of scientific evidence due to its limitations but it has an impact on the management of severe forms of COVID-19, particularly in low-resource countries, where intensive care unit capacity is insufficient.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Dessie, Z.G. and Zewotir, T. (2021) Mortality-Related Risk Factors of COVID-19: A

Systematic Review and Meta-Analysis of 42 Studies and 423, 117 Patients. *BMC Infectious Diseases*, **21**, Article No. 855.
https://doi.org/10.1186/s12879-021-06536-3

[2] Organisation Mondiale de la Santé (2022) COVID-19—Data Dashboard Covid-19. https://covid19.who.int/

[3] Achan, J., Serwanga, A., Wanzira, H., Kyagulanyi, T., Nuwa, A., Magumba, G., Kusasira, S., Sewanyana, I., Tetteh, K., Drakeley, C., Nakwagala, F., Aanyu, H., Opigo, J., Hamade, P., Marasciulo, M., Baterana, B. and Tibenderana, J.K. (2022) Current Malaria Infection, Previous Malaria Exposure, and Clinical Profiles and Outcomes of COVID-19 in a Setting of High Malaria Transmission: An Exploratory Cohort Study in Ugand. *The Lancet Microbe*, **3**, E62-E71.
https://doi.org/10.1016/S2666-5247(21)00240-8

[4] Hardya, É.J.L. and Flori, P. (2021) Epidemiological Specificities of COVID-19 in Africa: Current or Future Public Health Concern? *Annales Pharmaceutiques Françaises*, **79**, 216-226. https://doi.org/10.1016/j.pharma.2020.10.011

[5] Koulouras, V., Papathanakos, G., Papathanasiou, A. and Nakos, G. (2016) Efficacy of Prone Position in Acute Respiratory Distress Syndrome Patients: A Pathophysiology-Based Review. *World Journal of Critical Care Medicine*, **5**, 121-136.
https://doi.org/10.5492/wjccm.v5.i2.121

[6] WHO (2023) Clinical Management of COVID-19: Living Guideline.

[7] Gattinoni, L., Tognoni, G., Pesenti, A., *et al.* (2001) Effect of Prone Positioning on the Survival of Patients with Acute Respiratory Failure. *The New England Journal of Medicine*, **345**, 568-573. https://doi.org/10.1056/NEJMoa010043

[8] Fan, E., Del Sorbo, L., Goligher, E.C., *et al.* (2017) An Official American Thoracic Society/European Society of Intensive Care Medicine/Society of Critical Care Medicine Clinical Practice Guideline: Mechanical Ventilation in Adult Patients with Acute Respiratory Distress Syndrome. *American Journal of Respiratory and Critical Care Medicine*, **195**, 1253-1263. https://doi.org/10.1164/rccm.19511erratum

[9] Guérin, C., Reignier, J., Richard, J.C., *et al.* (2013) Prone Positioning in Severe Acute Respiratory Distress Syndrome. *The New England Journal of Medicine*, **368**, 2159-2168.

[10] Lai-Fook, S.J. and Rodarte, J.R. (1991) Pleural Pressure Distribution and Its Relationship to Lung Volume and Interstitial Pressure. *Journal of Applied Physiology*, **70**, 967-978. https://doi.org/10.1152/jappl.1991.70.3.967

[11] Cornejo, R.A., Díaz, J.C., Tobar, E.A., *et al.* (2013) Effects of Prone Positioning on Lung Protection in Patients with Acute Respiratory Distress Syndrome. *American Journal of Respiratory and Critical Care Medicine*, **188**, 440-448.
https://doi.org/10.1164/rccm.201207-1279OC

[12] Nyrén, S., Mure, M., Jacobsson, H., Larsson, S.A. and Lindahl, S.G. (1999) Pulmonary Perfusion Is More Uniform in the Prone than in the Supine Position: Scintigraphy in Healthy Humans. *Journal of Applied Physiology*, **86**, 1135-1141.
https://doi.org/10.1152/jappl.1999.86.4.1135

[13] Richter, T., Bellani, G., Scott Harris, R., *et al.* (2005) Effect of Prone Position on Regional Shunt, Aeration, and Perfusion in Experimental Acute Lung Injury. *American Journal of Respiratory and Critical Care Medicine*, **172**, 480-487.
https://doi.org/10.1164/rccm.200501-004OC

[14] Pelosi, P., Tubiolo, D., Mascheroni, D., *et al.* (1998) Effects of the Prone Position on Respiratory Mechanics and Gas Exchange during Acute Lung Injury. *American Journal of Respiratory and Critical Care Medicine*, **157**, 387-393.
https://doi.org/10.1164/ajrccm.157.2.97-04023

[15] Kallet, R.H. (2015) A Comprehensive Review of Prone Position in ARDS. *Respiratory Care*, **60**, 1660-1687. https://doi.org/10.4187/respcare.04271

[16] Musch, G., Layfield, J.D.H., Harris, R.S., *et al.* (2002) Topographical Distribution of Pulmonary Perfusion and Ventilation, Assessed by PET in Supine and Prone Humans. *Journal of Applied Physiology*, **93**, 1841-1851. https://doi.org/10.1152/japplphysiol.00223.2002

[17] Lamm, W.J., Graham, M.M. and Albert, R.K. (1994) Mechanism by Which the Prone Position Improves Oxygenation in Acute Lung Injury. *American Journal of Respiratory and Critical Care Medicine*, **150**, 184-193. https://doi.org/10.1164/ajrccm.150.1.8025748

[18] Jagan, N., Morrow, L.E., Walters, R.W., *et al.* (2020) The Positioned Study: Prone Positioning in Nonventilated Coronavirus Disease 2019 Patients—A Retrospective Analysis. *Critical Care Explorations*, **2**, e0229. https://doi.org/10.1097/CCE.0000000000000229

[19] Padrao, E.M.H., Valente, F.S., Besen, B.A.M.P., *et al.* (2020) Awake Prone Positioning in COVID-19 Hypoxemic Respiratory Failure: Exploratory Findings in a Single-Center Retrospective Cohort Study. *Academic Emergency Medicine*, **27**, 1249-1259. https://doi.org/10.1111/acem.14160

[20] World Health Organisation (2021) Clinical Management Clinical Management: Living Guidance COVID-19.

[21] Messer, B., Antoine-Pitterson, P., Blundell, A., *et al.* (2021) BTS/ICS Guidance: Respiratory Care in Patients with Acute Hypoxaemic Respiratory Failure Associated with COVID-19. British Thoracic Society and the Intensive Care Society.

[22] Nasa, P., Azoulay, E., Khanna, A.K., *et al.* (2021) Expert Consensus Statements for the Management of COVID-19-Related Acute Respiratory Failure Using a Delphi Method. *Critical Care*, **25**, Article No. 106. https://doi.org/10.1186/s13054-021-03491-y

[23] Chua, E.X., Syed Mohd Zahir, S.M.I., Ng, K.T. and Teoh, W.Y. (2021) Effect of Prone versus Supine Position in COVID-19 Patients: A Systematic Review and Meta-Analysis. *Journal of Clinical Anesthesia*, **74**, Article ID: 110406. https://doi.org/10.1016/j.jclinane.2021.110406