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Diagnostic Assessment of Respiratory and Hemodynamic Changes Related to Prone Position in COVID-19 Patients

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Abstract

Objective: To study the respiratory patterns and the hemodynamic variations related to postural changes in inpatients with coronavirus disease (COVID-19).
Methods: This report is a prospective study in a cohort of inpatients admitted with COVID-19. We recruited 10 patients admitted to the hospital with moderate or severe COVID-19 who showed improvement in oxygen saturation with prone positioning. We performed cardiorespiratory polygraphy and hemodynamic evaluations by thoracic electrical bioimpedance.
Results: We observed a median minimum oxygen saturation of 85.00% (IQR: 7.00) in the supine position versus 91.00% (IQR: 8.00) ($P = 0.173$) in the prone position. The airflow restriction in the supine position was 2.70% (IQR: 6.55) versus 1.55% (IQR: 2.80) ($P = 0.383$) in the prone position. A total of 36.4% of patients were classified as having a normo-hemodynamic state in the supine position, whereas 54.5% were classified in this group in the prone position ($P = 0.668$). A decrease in vascular resistance was observed in the prone position (18.2% of vasoconstriction) compared to the supine position (36.4% of vasoconstriction) ($P = 0.871$).
Conclusion: This brief report describes the effects of prone positioning on respiratory and hemodynamic variables in 10 patients with moderate or severe COVID-19.

The world is currently facing a global health crisis caused by the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This new virus has caused more than 600 million confirmed cases of coronavirus disease (COVID-19), leading to more than 6 million deaths worldwide. The main cause of these deaths is the development of severe acute respiratory syndrome.[1]

One of the most relevant findings regarding COVID-19 is that pulmonary damage and low blood oxygenation lead to acute respiratory distress syndrome during the course of the disease.[2] Previous reports have described the effect of the patient's position on central apnea in case of airway disturbance.[3] These studies reported an increase in oxygen saturation after changing from the supine to the lateral or prone position; these results suggest that respiratory control instability and decreased pulmonary oxygen storage are associated with the supine position.[4] Furthermore, the myocardial damage described in COVID-19 patients could improve with the expansion of the left heart chambers' capacity associated with the prone position.[5]

To investigate COVID-19 physiopathology, we analyzed the respiratory patterns and the hemodynamic variations related to postural changes in inpatients with COVID-19.

Materials and Methods

We conducted a prospective study, performing cardiorespiratory polygraphy and hemodynamic evaluations on inpatients with moderate-to-severe COVID-19 who showed improvement in oxygen saturation when switched from supine to prone position.

The inclusion criteria were:

- Age > 18 years
- COVID-19 disease confirmed by a positive polymerase chain reaction test from a nasopharyngeal swab
- Any improvement in respiratory function according to oxygen saturation related to postural changes

- Moderate-to-severe respiratory COVID-19 disease assessed by oxygen saturation values: severe disease ≤ 94% and moderate disease > 94%[6]
- Patients' (or their legal guardians') consent and signatures on the informed consent document to accept participation in this study

The exclusion criteria were:

- History of chronic lung disease and/or heart disease before diagnosis with COVID-19
- Current tobacco abuse or previous tobacco abuse within the past 10 years

Study Protocol

Respiratory parameters were evaluated by cardiorespiratory polygraphy, with oronasal flow and airflow limitation recorded through an infranasal thermistor, surface electrodes to assess heart rate, and thoracic-abdominal respiratory bands to determine the ventilatory effort. This setup allowed the acquisition of oxygen saturation readings by pulse oximeter simultaneously with the other respiratory variables. The recording was performed using the Nox T3 respiratory polygraph (Nox Medical®). The filter setting was low-pass and high-pass filters of 70 Hz and 0.3 Hz, respectively, in the electrocardiograph recordings and 15 Hz and 0.1 Hz, respectively, to assess oronasal flow and ventilatory efforts. We used a "notch" filter at 50 Hz.

Hemodynamic parameters were determined using the HOTMAN® system (HOTMAN® System, Hemo Sapiens Medical Inc., San Ramón, CA, USA), a thoracic electrical bioimpedance measuring set that collects data on blood volume, inotropic and chronotropic states, and vascular resistance. Measurement of these hemodynamic parameters was performed through the generation of a very low current circulating between 2 pairs of solid gel electrodes. We placed 8 surface electrodes, with 4 located in the supraclavicular region, and recorded blood volume and vascular resistance as the alveoli were filled with air (non-conducting medium), and the electrical current was conducted mainly through the thoracic aorta and the venae cavae. The other 4 electrodes were placed in the costal area bilaterally, which recorded the electrocardiogram and the voltage of the electrical current that crossed the thorax.[7]

The examination lasted a total of 60 minutes. We recorded changes in variables for a minimum of 30 minutes in the supine position and 30 minutes in the prone position.

Variables

The main respiratory variables were oronasal flow, oxygen saturation, and airflow limitation. Regarding the hemodynamic variables, we analyzed heart rate (beats per minute), cardiac index (L/min/m^2), stroke index (ml/beat/m^2), stroke systemic resistance index (dyn·sec·cm^{-5}·m^2 = F$^{\Omega}$), left stroke work index (g·m/m^2), inotropic state index (sec^{-2}), ejection phase contractility index (s^{-2}), and thoracic fluid content (KΩ^{-1}). The device also allowed analysis of blood volume, inotropism, chronotropism, vasoactivity, hemodynamic state, and blood pressure as a percentage based on normal values, classified into 3 groups: hypo, normo, and hyper.[8]

Table 1. Respiratory parameters in the prone and supine postural positions

Variable	Supine median (IQR)	Prone median (IQR)	Difference	*P* value
Minimum oxygen saturation (%)	85.00 (7.0)	91.00 (8.0)	6.00	0.173
Oxygen saturation median (%)	92.00 (6.0)	92.30 (5.5)	0.30	0.579
T90 median (%)	0.20 (65.93)	0.00 (30.5)	−0.20	0.486
Airflow restriction (%)	2.70 (6.55)	1.55 (2.8)	−1.15	0.383

IQR, interquartile range.

Statistical Analysis

Qualitative variables were expressed as a frequency distribution, and quantitative variables were expressed as a median and interquartile range (IQR). Student's t-test was used for parametric samples and the Mann–Whitney test was used for non-parametric samples. The threshold of statistical significance was set at 2-sided $P \leq 0.05$. Statistical analysis was performed using Stata16 software (StataCorp LLC, College Station, TX, USA).

Ethics

The research ethics committee of La Princesa University Hospital (local reference number 4096) approved this study, and it was conducted following the legislation regarding confidentiality.

Results

In total, 10 patients were recruited. They had a median age of 55.0 years (IQR: 15.0); 6 of them were women and 4 were men. All patients required supplemental oxygen as part of their treatment, with a wide variety of modalities; some patients required oxygen administered through a nasal cannula and others through an oxygen mask or high-flow oxygen device. More details can be found in Supplementary Table 1.

Regarding respiratory variables, no statistically significant differences between supine and prone positioning were found. As for oxygen saturation, we observed a trend toward a higher median minimum oxygen saturation (minSatO2) in the prone position (91.00% [IQR: 8.00]) compared with the supine position (85.00% [IQR: 7.00]) ($P = 0.173$) and a higher median of median oxygen saturation (SatO2m) in the prone position (92.30% [IQR: 6.00]) than in the supine position (92.00% [IQR: 5.50]) ($P = 0.579$) (Supplementary Figure 1). Furthermore, the median T90 (time with oxygen saturation below 90%) was higher in the supine position (10% [IQR: 58.70]) than in the prone position (0.00% [IQR: 19.50]) ($P = 0.486$), although this was statistically insignificant. A trend toward a reduction in airflow restriction in the prone position (1.55% [IQR: 2.80]) compared with the supine position (2.70% [IQR: 6.55]) ($P = 0.383$) was evident (Table 1; Supplementary Figure 2).

Regarding the hemodynamic variables, we observed slight decreases in all parameters in the prone position; however, the differences were not statistically significant (Table 2). The hemodynamic state and its modulators were expressed as a percentage compared to normal values. The distribution of these parameters among the different groups is shown in Supplementary

Table 2. Hemodynamic parameters in the prone and supine postural positions

Variable	Supine median (IQR)	Prone median (IQR)	Difference	*P* value
Heart rate (bpm)	71.07 (3.1)	72.48 (3.9)	−1.41	0.352
Cardiac index (l/min/m^2)	3.38 (0.4)	3.4 (0.55)	−0.02	0.666
Stroke index (ml/beat/m^2)	47.55 (5.5)	46.09 (6.3)	1.46	0.512
Ejection phase contractility index (s^{-2})	0.04 (0.0)	0.04 (0.01)	0.00	0.525
Inotropic state index (sec^{-2})	0.95 (0.1)	0.93 (0.12)	0.02	0.488
Left stroke work index (g.m/m^2)	54.35 (6.4)	53.34 (2.61)	1.01	0.544
Stroke systemic Resistance index (FΩ)	176.6 (24.0)	176.38 (21.34)	0.22	0.401
Thoracic fluid content (KΩ^{-1})	0.04 (0)	0.04 (0)	0	0.959

IQR, interquartile range.

Figure 3. Regarding the hemodynamic state, 36.4% of patients were in the normo-hemodynamic state group in the supine position and 54.5% were in the normo-hemodynamic state group in the prone position ($P = 0.668$). A decrease in vascular resistance was observed in the prone position (18.2% of vasoconstriction) compared with the supine position (36.4% of vasoconstriction); however, this difference was not statistically significant ($P = 0.871$).

Discussion

Our report indicated a trend toward increased oxygen saturation and decreased airway resistance in patients with COVID-19 infection in the prone position. Moreover, our report revealed a trend between prone position and a normo-hemodynamic state with less vasoconstriction, which was observed using a non-invasive hemodynamic and oxygen transport management system. However, none of these findings were statistically significant.

COVID-19 patients often suffer from clinical symptoms compatible with central apneas/hypopneas due to the lack of thoracic-abdominal efforts and the deficit of respiratory changes in response to oxygen deficiency. Similarly, other data suggest the presence of obstructive apneas/hypopneas given the reported improvements related to positional changes, probably because of the decreased collapse of the upper respiratory tract.[9] Previous research described physiological changes in the prone position related to analytical respiratory variables, mainly PaO2 (partial pressure of oxygen), FiO2 (fraction of inspired oxygen), PaO2/FiO2 ratio, and SatO2; these studies reported relevant improvements in the prone position, such as a 5% increase in mean SaO2 from 90% in the supine position to 95% in the prone position.[10,11]

Our data showed a trend toward higher airflow restriction in the supine position compared to the prone position (2.7% vs 1.5%, respectively). We also observed an increase in median minimum oxygen saturation, although statistically insignificant. This trend is aligned with results reported by Gürün et al.[12] that show improvement in oxygenation after the change from supine to prone positioning. This change might be due to less collapse of the upper respiratory tract, a decrease in the difference in the dorsoventral transpulmonary pressure, improvement of pulmonary perfusion, and caudal displacement of the diaphragm and increase in functional residual capacity.[12]

Previous literature has described an expansion of left atrial diameter in the prone position, facilitating venous return, increasing cardiac output, and decreasing mean arterial pressure.[3,12] However, our results did not reveal statistically significant hemodynamic changes with prone positioning, and only a non-significant improvement in hemodynamic state was observed. One plausible explanation could be the interaction between SARS-CoV-2 and angiotensin-converting enzyme 2 (ACE 2). ACE 2 is expressed in type I and II alveolar cells, where it acts as the main receptor in the respiratory tract for viral entry. However, this receptor is also highly expressed in cardiac cells. The interaction of ACE 2 with the virus could cause excessive activation of the renin-angiotensin system, resulting in harmful cardiovascular effects.[13,14]

We evaluated cardiovascular and pulmonary function using 2 diagnostic techniques that to our knowledge have not been described in the literature for COVID-19 patients. These 2 approaches, cardiorespiratory polygraphy and thoracic electrical bioimpedance, may be useful in evaluating physiological variables in postural changes in cardiorespiratory diseases such as COVID-19 moving forward. The main limitations of this study include the small sample size and the 1-hour duration of analysis per patient, both of which may have affected the statistical significance of our results. Other limitations include the exclusion of patients with pre-existing chronic lung disease and/or heart disease as well as the absence of a control group. However, this study adds 2 novel techniques to this field that researchers may wish to further utilize in a more robust study.

Conclusion

This brief report describes the effects of prone positioning on respiratory and hemodynamic variables in 10 patients with moderate or severe COVID-19 using cardiorespiratory polygraphy and thoracic electrical bioimpedance.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/dmp.2023.152

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Competing interests. All authors declare no competing interest.

References

1. **Ha R, Sn B.** The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *J Autoimmun.* 2020;109:30-33. doi: 10.1016/j.jaut.2020.102433
2. **Alayash AI.** The impact of COVID-19 infection on oxygen homeostasis: a molecular perspective. *Front Physiol.* 2021;12:711976. doi: 10.3389/fphys.2021.711976
3. **Joho S, Oda Y, Hirai T, Inoue H.** Impact of sleeping position on central sleep apnea/Cheyne–Stokes respiration in patients with heart failure. *Sleep Med.* 2010;11(2):143-148. doi: 10.1016/j.sleep.2009.05.014
4. **Koulouras V, Papathanakos G, Papathanasiou A, Nakos G.** Efficacy of prone position in acute respiratory distress syndrome patients: a pathophysiology-based review. *World J Crit Care Med.* 2016;5(2):121. doi: 10.5492/wjccm.v5.i2.121
5. **Pump B, Talleruphuus U, Christensen NJ, *et al.*** Effects of supine, prone, and lateral positions on cardiovascular and renal variables in humans. *Am J Physiol Regul Integr Comp Physiol.* 2002;283(1):R174-R180. doi: 10.1152/ajpregu.00619.2001
6. **Clinical Spectrum**. The COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of Health. Accessed August 24, 2022. https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/.
7. **Faini A, Omboni S, Tifrea M, *et al.*** Cardiac index assessment: validation of a new non-invasive very low current thoracic bioimpedance device by thermodilution. *Blood Press.* 2014;23(2):102-108. doi: 10.3109/08037051.2013.817121
8. **Fadl Elmula FEM, Rebora P, Talvik A, *et al.*** A randomized and controlled study of noninvasive hemodynamic monitoring as a guide to drug treatment of uncontrolled hypertensive patients. *J Hypertens.* 2015;33(12):2534-2545. doi: 10.1097/HJH.0000000000000749
9. **Szollosi I, BAppl TR, Thompson B, Naughton MT**. Lateral sleeping position reduces severity of central sleep apnea/Cheyne-Stokes respiration. *Sleep*. 2006;29(8):1045-1051. doi: 10.1093/sleep/29.8.1045.
10. **Altinay M, Sayan I, Turk HS, *et al.*** Effect of early awake prone positioning application on prognosis in patients with acute respiratory failure due to COVID-19 pneumonia: a retrospective observational study. *Braz J Anesthesiol Elsevier.* 2022;72(2):194-199. doi: 10.1016/j.bjane.2021.07.029
11. **Ehrmann S, Li J, Ibarra-Estrada M, *et al.*** Awake prone positioning for COVID-19 acute hypoxaemic respiratory failure: a randomised, controlled, multinational, open-label meta-trial. *Lancet Respir Med.* 2021;9(12):1387-1395. doi: 10.1016/S2213-2600(21)00356-8
12. **Gürün Kaya A, Öz M, Erol S, *et al.*** Prone positioning in non-intubated patients with COVID-19. *Tuberk Ve Toraks.* 2020;68(3):331-336. doi: 10.5578/tt.70164
13. **Viveiros A, Noyce RS, Gheblawi M, *et al.*** SARS-CoV-2 infection downregulates myocardial ACE2 and potentiates cardiac inflammation in humans and hamsters. *Am J Physiol Heart Circ Physiol*. Published online November 11, 2022. doi: 10.1152/ajpheart.00578.2022
14. **Scialo F, Daniele A, Amato F, *et al.*** ACE2: the major cell entry receptor for SARS-CoV-2. *Lung.* 2020;198(6):867-877. doi: 10.1007/s00408-020-00408-4