

# PRONE POSITION IN PATIENTS WITH EXTRACORPOREAL MEMBRANE OXYGENATION: SERIES OF CASES

## POSIÇÃO PRONA EM PACIENTES COM OXIGENAÇÃO POR MEMBRANA EXTRACORPÓREA: SÉRIE DE CASOS

## POSICIÓN PRONA EN PACIENTES CON OXIGENACIÓN POR MEMBRANA EXTRACORPÓREA: SERIE DE CASOS

Nathália Ferreira Santos Tosti<sup>1</sup>  
Raelson Ribeiro Rodrigues<sup>2</sup>  
Danilo dos Santos Gomes<sup>3</sup>  
Henrique Mateus Fernandes<sup>4</sup>  
Francine Jomara Lopes<sup>5</sup>

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**Objective:** to describe the experience of the prone position in patients undergoing extracorporeal membrane oxygenation to manage refractory hypoxemia due to COVID-19, emphasizing complications and the evolution of ventilatory parameters after positioning. **Method:** medical records from between March/2020 and January/2022 were, retrospectively, analyzed. Seven male patients with a mean age of 57.7 years underwent the interventions and the main comorbidities found were cardiovascular and metabolic diseases. **Results:** after positioning, weaning from extracorporeal membrane oxygenation was successful and the association proved to be effective in recruiting posterior lung regions, amplifying the viable gas exchange region, with the main complication observed being the development of skin lesions. **Conclusion:** in the institution's experience, positioning was effective in managing refractory hypoxemia and hypercapnia, enabling weaning from extracorporeal membrane oxygenation. No serious or life-threatening complications were observed, demonstrating the importance of a trained team and well-designed protocols for safe interventions.

**Descriptors:** Extracorporeal Membrane Oxygenation. Prone Position. Severe Acute Respiratory Syndrome. COVID-19. Intensive Care Units.

*Objetivo:* descrever a experiência da posição prona em pacientes submetidos à oxigenação por membrana extracorpórea para manejo da hipoxemia refratária por COVID-19, ressaltando complicações e a evolução dos parâmetros ventilatórios após o posicionamento. *Método:* analisou-se, retrospectivamente, prontuários entre

Corresponding Author: Nathália Ferreira Santos Tosti, nftosti@gmail.com

<sup>1</sup> Hospital Sírio-Libanês. São Paulo, SP, Brasil. <https://orcid.org/0000-0002-7158-2947>.

<sup>2</sup> Hospital Sírio-Libanês. São Paulo, SP, Brasil. <https://orcid.org/0000-0001-9564-2046>.

<sup>3</sup> Hospital Sírio-Libanês. São Paulo, SP, Brasil. <https://orcid.org/0000-0001-9628-7154>.

<sup>4</sup> Hospital Sírio-Libanês. São Paulo, SP, Brasil. <https://orcid.org/0000-0003-1160-7089>.

<sup>5</sup> Hospital Sírio-Libanês. São Paulo, SP, Brasil. <https://orcid.org/0000-0001-8756-093X>.

março/2020 e janeiro/2022. Sete pacientes do sexo masculino com idade média de 57,7 anos foram submetidos às intervenções e as principais comorbidades encontradas foram doenças cardiovasculares e metabólicas. Resultados: após o posicionamento, obteve-se sucesso no desmame da oxigenação por membrana extracorpórea e a associação mostrou-se eficaz no recrutamento de regiões posteriores pulmonares, amplificando a região viável de trocas gasosas, sendo a principal complicação observada o desenvolvimento de lesões de pele. Conclusão: o posicionamento, na experiência da instituição, foi eficaz no manejo da hipoxemia e hipercapnia refratárias, possibilitando o desmame da oxigenação por membrana extracorpórea. Não foram observadas complicações graves ou potencialmente fatais, demonstrando a importância de uma equipe capacitada e protocolos bem desenhados para a segurança das intervenções.

*Descritores:* Oxigenação por Membrana Extracorpórea. Decúbito Ventral. Síndrome Respiratória Aguda Grave. COVID-19. Unidades de Terapia Intensiva.

*Objetivo:* describir la experiencia de la posición prona en pacientes sometidos a la oxigenación por membrana extracorpórea para el manejo de la hipoxemia refractaria por COVID-19, destacando las complicaciones y la evolución de los parámetros ventilatorios tras el posicionamiento. *Método:* se analizaron retrospectivamente las historias clínicas entre marzo de 2020 y enero de 2022. Siete pacientes del sexo masculino con una edad media de 57,7 años fueron sometidos a las intervenciones y las principales comorbilidades encontradas fueron enfermedades cardiovasculares y metabólicas. *Resultados:* después del posicionamiento, el destete de la oxigenación por membrana extracorpórea fue exitoso y la asociación se mostró eficaz en el reclutamiento de regiones pulmonares posteriores, ampliando la región viable de intercambio gaseoso, siendo la principal complicación observada el desarrollo de lesiones cutáneas. *Conclusión:* en la experiencia de la institución, el posicionamiento fue eficaz en el manejo de la hipoxemia y la hipercapnia refractarias, permitiendo el destete de la oxigenación por membrana extracorpórea. No se observaron complicaciones graves ni potencialmente mortales, lo que demuestra la importancia de contar con un equipo formado y protocolos bien diseñados para realizar intervenciones seguras.

*Descriptores:* Oxigenación por Membrana Extracorpórea. Posición Prona. Síndrome Respiratorio Agudo Grave. COVID-19. Unidades de Cuidados Intensivos.

## Introduction

The use of extracorporeal membrane oxygenation (ECMO) was one of the strategies adopted for the recovery of patients affected by COVID-19 refractory hypoxemia. Venovenous ECMO (VV) is indicated in cases of hypoxemic respiratory failure ( $\text{PaO}_2/\text{FiO}_2 < 80 \text{ mmHg}$ ) after conventional treatment and/or hypercapnic respiratory failure ( $\text{pH} < 7.25$ ), even with the adoption of optimal invasive mechanical ventilation (IMV) strategies and/or ventilatory support as a bridge to lung transplantation<sup>(1-3)</sup>.

The prolonged prone position ( $\geq 16$  hours) was already recommended for patients affected by inflammatory syndromes that manifest with diffuse pulmonary edema and respiratory failure, and was able to significantly reduce mortality. During the pandemic, it was widely adopted by healthcare teams to improve oxygenation in severely affected patients, given the lack of curative treatments<sup>(4-5)</sup>.

Evidence on the adoption of the prone position during ECMO shows that, in addition to being feasible, the combination of interventions leads to a reduction in the 28-day mortality rate, from 32.8% to 16%, when adopted for periods  $\geq 16$  hours in patients with a  $\text{PaO}_2/\text{FiO}_2$  ratio  $\leq 150 \text{ mmHg}$  ( $p < 0.001$ )<sup>(4)</sup>. There are reports of improved oxygenation and compliance of the respiratory system and a reduction in the necessary levels of positive end-expiratory pressure (PEEP), to ensure alveolar viability with less propensity to pulmonary hyperdistension, aiding in successful ventilatory weaning and the adoption of protective strategies<sup>(2,6)</sup>.

The objective of this series of cases is to describe the experience of the prone position in patients undergoing ECMO to manage refractory hypoxemia due to COVID-19, highlighting complications and the evolution of ventilatory parameters after positioning.

## Method

This is an experience report of a series of cases conducted in the intensive care unit (ICU) of a tertiary hospital in the city of São Paulo, Brazil, affiliated with the Extracorporeal Life Support Organization (ELSO). The study information was collected retrospectively from the patient's electronic medical record and clinical information systems that follow the evolution of patients with a medical diagnosis of COVID-19 who underwent prone positioning during ECMO in the venovenous modality as a bridge to recovery, from March/2020 to January/2022.

The inclusion criteria for the convenience sample were patients aged  $\geq 18$  years undergoing extracorporeal membrane oxygenation with a medical diagnosis of Severe Acute Respiratory Syndrome (SARS) secondary to COVID-19, use of IMV and prone positioning. Those under the age of 18, with an ICU stay of less than 24 hours, on non-invasive mechanical ventilation and/or other non-invasive forms of oxygen therapy were excluded.

The project was approved by the Human Research Ethics Committee in accordance with Resolution 466/2012 of the National Health Council, with Certificate of Submission for Ethical Appraisal (CAAE) no. 34652820.0.0000.5461. A waiver was requested from the use of the Informed Consent Form (ICF) in view of the retrospective nature of the research, involving data collection based on electronic medical records and the institution's information systems. In order to guarantee the confidentiality of patient information, the data was treated in such a way as to prevent the recording of sensitive information that could lead to the identification of study patients.

Data was collected from electronic medical records by the research team after training with the institution's ECMO team, using an instrument developed on the REDCap platform with sociodemographic, hemodynamic and ventilatory variables and the patients' clinical outcomes.

## Results

### Case 1

Male, 60 years old, hypertensive and obese. Cannulated after 34 days of IMV, with multiple attempts to optimize protective ventilatory support, maintained with ascending parameters on ECMO. Posterior collapse was observed on impedance tomography and he was prone for 18 hours. When supine, he had facial edema. The patient was decannulated eight days after the maneuver and died as result of meningoencephalitis.

### Case 2

Male, 73 years old, with no known comorbidities. Transferred by air transport, with an unknown duration of mechanical ventilation and cannulated after 24 hours. The patient developed bleeding from cannula insertion sites, venous access and lower digestive bleeding, ascending parameters on ECMO and posterior collapse on impedance tomography. Prone positioning was chosen for 23 hours. He presented facial edema and stage II pressure injury in the thoracic region when supine, sustaining significant enterorrhage. He died secondary to refractory hemorrhagic shock.

### Case 3

Male, 53 years old, hypertensive and dyslipidemic. Cannulated after 19 days of IMV and optimization of ventilatory support. He evolved without significant improvement and with posterior collapse on impedance tomography. Prone positioning was chosen for 20 hours, with no complications when supine, and evidence of improvement in refractory hypoxemia. Decannulated after 48 hours, he progressed with ventilator weaning and was discharged after 27 days for rehabilitation.

#### Case 4

Male, 46 years old, obese. Cannulated after 15 days of IMV and optimization of ventilatory support. He evolved without an effective response to ECMO and failed the autonomy test. A prone test was carried out to recruit the posterior regions, enabling decannulation, and he underwent a 23-hour cycle. Positioning without effective response, decannulated after 33 days, evolved with respiratory failure refractory to support measures and death.

#### Case 5

Male, 51 years old, no known comorbidities, transferred from another institution with unknown duration of mechanical ventilation. Cannulated after hypoxemia refractory to ventilatory optimization maneuvers and hypercapnia. He responded with an improved PaO<sub>2</sub>/FiO<sub>2</sub> ratio and success in the autonomy test, and was decannulated after 11 days on ECMO. He continued to suffer from worsening respiratory symptoms, evidence of a pneumothorax requiring drainage and a further worsening of the infection. He was recannulated and submitted to prone for 25 hours in an attempt to rescue the posterior regions. He evolved with a significant improvement in hypoxemia. When supine, he had facial edema. After 24 hours, a new prone positioning test was carried out for 23 hours, showing improved gas exchange and no new complications. Decannulated after 13 days, he progressed with ventilator weaning and was discharged to an inpatient unit.

#### Case 6

Male, 60 years old, with no known comorbidities, transferred from another institution, already on mechanical ventilation and cannulated on ECMO. After 27 days, he was highly dependent on extracorporeal support. Proning was performed for 24 hours, with consequent radiological improvement and the possibility of reducing tidal volume and FiO<sub>2</sub> in IMV and ECMO. When supine, he presented with edema of the face and

upper limbs. After five days, it was opted for a new 24-hour cycle in prone, and his hypoxemia improved. When supine, he had a stage 2 pressure injury in the thoracic region. Attempts were made to wean him off the ventilator and to test his autonomy, but the patient progressed to multiple organ dysfunction and irreversible lesions in the lung parenchyma, with an indication for transplantation. The palliative care team was called in and comfort was prioritized. He died secondary to asystole, after 116 days of circulatory assistance.

#### Case 7

Male, 61 years old, dyslipidemic and kidney transplanted. He was transferred from another institution with an unknown duration of mechanical ventilation. Due to hemodynamic instability, ECMO cannulation was chosen at the service of origin. The patient's hemodynamic pattern worsened and therapy optimization was unsuccessful. Prone ECMO was chosen to recruit the posterior regions. He underwent a 16-hour cycle, with an improvement in the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, but with no effective response. He evolved with irreversible lung damage and consequent death secondary to multiple organ dysfunction and refractory shock.

### Discussion

The medical records of 81 patients diagnosed with SARS due to COVID-19 and undergoing ECMO were analyzed. Of these, seven were exposed to the prone position as a rescue maneuver during extracorporeal support. All the patients were male, with an average age of 57.7 years, of whom only two had no known comorbidities, totaling nine prone positions during VV-ECMO, with an average time of 21.8 hours in the position. Cardiovascular disease (CVD) was the most common comorbidity identified in the patients, associated with a greater likelihood of developing severe forms of COVID-19 and increased mortality<sup>(9)</sup>.

The patients underwent an ultra-protective mechanical ventilation strategy to reduce

ventilator-induced lung damage, adopting a volumetric flow of approximately 6 mL/kg of predicted weight, plateau pressure  $\leq 30$  cmH<sub>2</sub>O, PEEP titration to maintain PaO<sub>2</sub> between 55-80 mmHg and reduce collapsed areas<sup>(2,5)</sup>.

Table 1 summarizes the evolution of ECMO parameters pre- and post-maneuver. The RESP

Score<sup>(10)</sup>, developed to predict survival in adult patients undergoing ECMO, was used to stratify patients at the time of ECMO cannulation, with scores ranging from  $\geq 6$ , 3 to 5, -1 to 2, -5 to -2 and  $\leq -6$ , corresponding to risk classes and expected survival rates.

**Table 1** – Extracorporeal membrane oxygenation and ventilatory parameters pre- and post-prone maneuver. São Paulo, São Paulo, Brazil - 2020-2022. (N=7)

Case	RESP Score	Blood flow (L/min)	Carrier gas (L/min)	PaO <sub>2</sub> /FiO <sub>2</sub> ratio <sup>2</sup>	Blood flow (L/min)	Carrier gas (L/min)	PaO <sub>2</sub> /FiO <sub>2</sub> ratio <sup>2</sup>	Time on ECMO (days)
		Pre-maneuver parameters			Post-maneuver parameters			
1	-1	5	4	187	5	4	270	19
2	-3	4.4	3	167	4.45	3	490	15
3	3	4.4	3.5	158	2.9	3.5	242	13
4	2	4.7	5	104	4.7	3.5	100	46
5	2	2.4	3	150	4	3	276	39
6	NA	4.1	3	276	4.2	3	300	116
		3.4	3.5	240	3	3	222	
7	NA	3.5	3.5	182	3.2	3	372	33
		2.5	2.5	191	4.5	3	217	

Source: own elaboration.

PaO<sub>2</sub> - Arterial oxygen pressure; FiO<sub>2</sub> - Fraction of inspired oxygen; ECMO - extracorporeal membrane oxygenation; NA - not applicable.

The majority of patients were in classes II and III, with survival rates ranging from 76% to 57%, respectively. Only one patient obtained class IV, with a survival rate of 33%. Two patients were cannulated at other institutions, so it was not possible to calculate the RESP score.

An average pre-maneuver blood flow of 3.8 L/min was observed, characterizing the demand for high flows to guarantee oxygenation capable of meeting metabolic demands. At the same time, the carrier gas had a pre-maneuver average of 3.4 L/min. It should be noted that the ability to eliminate CO<sub>2</sub> depends mainly on the flow rate and the concentration of CO<sub>2</sub> in the blood, so the high parameter indicates a greater need for CO<sub>2</sub> removal to manage refractory hypercapnia<sup>(1-3)</sup>.

After prone, there was a mean blood flow of 4 L/min, but with a drop in the mean FiO<sub>2</sub> of the oxygenating membrane from 95% to 84%, and a drop in the mean FiO<sub>2</sub> of the mechanical ventilator from 38% to 36%. On the other hand,

carrier gas had a post-maneuver average of 3.1 L/min, correlated to the indirect effect of prone on refractory hypercapnia after the recruitment of perfused and previously collapsed units, resulting in a reduction in pulmonary shunt<sup>(4-5)</sup>.

With regard to the PaO<sub>2</sub>/FiO<sub>2</sub> ratio, the pre-maneuver average was 184, indicating that most patients had severe to moderate hypoxemia, while the post-maneuver average was 276, indicating mild hypoxemia. Thus, the prone position adopted during ECMO positioning proves to be effective in recruiting posterior lung regions by amplifying the viable gas exchange region, favoring the management of refractory hypoxemia and enabling the gradual weaning of ECMO in patients undergoing interventions.

The decrease in the ratio between ventilation and perfusion and the reduction in the total available surface area of the respiratory membrane, caused by SARS secondary to COVID-19, evidenced by the low PaO<sub>2</sub>/FiO<sub>2</sub> ratio, blood flow and

carrier gas pre-positioning in the cases described depict states of hypoxemia and hypercapnia found among the nursing phenomena that characterize the diagnosis Impaired gas exchange, presented in the NANDA International Nursing Taxonomy (NANDA-I) as a clinical condition that represents “excess or deficit in oxygenation and/or in the elimination of carbon dioxide in the alveolocapillary membrane”<sup>(11: 381)</sup>.

Thus, by carrying out clinical reasoning to identify existing problems together with the different care subjects, nurses are able to guide the discussion and prioritize the development of a care plan with interventions capable of optimizing the human response.

Consequently, the most common complication related to nursing care was the development of pressure injuries (PI). In COVID-19 patients undergoing ECMO, the presence of severe hypoxemia associated with microvascular lesions and a state of hypercoagulability stimulated by viral infection and the release of pro-inflammatory cytokines promote the appearance of ischemic lesions and contribute to the fragility of the cutaneous barrier<sup>(12)</sup>.

On the other hand, the institution studied implemented a checklist to minimize the incidence of PI attributed to the prone position, such as the use of a viscoelastic mattress; the use of cushions on the face, shoulders, chest, lower limbs and pelvis; the use of adhesive foam dressings with polyurethane to absorb moisture and redistribute pressure in areas at risk; and tilting the bed to redistribute global pressure.

There is also evidence in the literature showing that the consequent increase in nursing workload in critically ill patients is a risk factor for the occurrence of adverse events in care, when considering the adoption of the 1:2 scale made possible by current legislation<sup>(13)</sup>. However, based on the increased workload, the 1:1 scale was adopted in all patients undergoing ECMO, having a positive impact on nursing care and assuming a protective role in the development of adverse events related to care.

Thus, nursing actions focused on effective, closed-chain communication, defining roles for

safely performing the maneuver, checking and maintaining invasive devices and continuous skin assessment were decisive for the viability of the prolonged prone position, optimizing ventilatory weaning and improving gas exchange with a high impact on patient safety.

This study has limitations inherent to the method, however, due to the lack of data on the association of the two interventions in the national literature, it serves as a framework for structured studies that provide robust scientific evidence for improving nursing care and valuing the category in the scope of advanced practices.

## Conclusion

The ELSO center's experience with proning in ECMO was satisfactory in terms of improved gas exchange and weaning from extracorporeal oxygenation, and no potentially fatal complications were observed. The complications observed are related to the development of pressure damage due to prolonged positioning in the prone position and a disseminated inflammatory response, contributing to the fragility of the skin barrier in these patients, which demonstrates an opportunity for improvement when it comes to nursing care for critically ill patients.

At the same time, the high mortality rate observed in the cases presented can be explained by the severity of the patients who evolved with the need for ECMO and were refractory to other support measures. Its association, however, was effective in recruiting dorsal regions and managing refractory hypoxemia and hypercapnia.

## Collaborations:

1 – project conception and planning: Nathália Ferreira Santos Tosti, Raelson Ribeiro Rodrigues, Danilo dos Santos Gomes, Henrique Mateus Fernandes e Francine Jomara Lopes;

2 – data analysis and interpretation: Nathália Ferreira Santos Tosti e Raelson Ribeiro Rodrigues;

3 – writing and/or critical review: Nathália Ferreira Santos Tosti, Raelson Ribeiro Rodrigues e Francine Jomara Lopes;

4 – approval of the final version: Nathália Ferreira Santos Tosti, Raelson Ribeiro Rodrigues, Danilo dos Santos Gomes, Henrique Mateus Fernandes e Francine Jomara Lopes.

### Conflicts of interest

There are no conflicts of interest.

### References

1. Tonna JE, Abrams D, Brodie D, Greenwood JC, Mateo-Sidron JAR, Usman A, et al. Management of Adult Patients Supported with Venovenous Extracorporeal Membrane Oxygenation (VVECMO): Guideline from the Extracorporeal Life Support Organization (ELSO). *ASAIO J.* 2021;67(6):601-10. DOI: 10.1097/MAT.0000000000001432
2. Badulak J, Antonini MV, Stead CM, Shekerdemian L, Raman L, Paden ML, et al. Extracorporeal Membrane Oxygenation for COVID-19: Updated 2021 Guidelines from the Extracorporeal Life Support Organization. *ASAIO J.* 2021;67(5):485-95. DOI: 10.1097/MAT.0000000000001422
3. Barbaro RP, MacLaren G, Boonstra PS, Iwashyna TJ, Slutsky AS, Fan E, et al. Extracorporeal membrane oxygenation support in COVID-19: An international cohort study of the Extracorporeal Life Support Organization registry. *Lancet.* 2020;396(10257):1071-8. DOI: 10.1016/S0140-6736(20)32008-0
4. Guérin C, Reignier J, Richard JC, Beuret P, Gacoion A, Boulain T et al. Prone positioning in Severe Acute Respiratory Distress Syndrome. *N Engl J Med.* 2013;368(23):2159-68. DOI: 10.1056/NEJMoa1214103
5. Guérin C, Albert RK, Beitler J, Gattinoni L, Jaber S, Marini JJ, et al. Prone position in ARDS patients: why, when, how and for whom. *Intensive Care Med.* 2020;46(12):2385-96. DOI: 10.1007/s00134-020-06306-w
6. Roca O, Pacheco A, García-de-Acilu M. To prone or not to prone ARDS patients on ECMO. *Crit Care.* 2021;25(1):315. DOI: 10.1186/s13054-021-03675-6
7. Giani M, Martucci G, Madotto F, Belliato M, Fanelli V, Garofalo E. Prone Positioning during Venovenous Extracorporeal Membrane Oxygenation in Acute Respiratory Distress Syndrome: A Multicenter Cohort Study and Propensity-matched Analysis. *Ann Am Thorac Soc.* 2021;18(3):495-501. DOI: 10.1513/AnnalsATS.202006-625OC
8. Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med.* 2018;23(2):60-3. DOI: 10.1136/bmjebm-2017-110853
9. Harrison SL, Buckley BJR, Rivera-Caravaca JM, Zhang J, Lip GYH. Cardiovascular risk factors, cardiovascular disease, and COVID-19: an umbrella review of systematic reviews. *Eur Heart J Qual Care Clin Outcomes.* 2021;7(4):330-9. DOI: 10.1093/ehjqcco/qcab029
10. Schmidt M, Bailey M, Sheldrake J, Hodgson C, Aubron C, Rycus PT, et al. Predicting survival after extracorporeal membrane oxygenation for severe acute respiratory failure. The Respiratory Extracorporeal Membrane Oxygenation Survival Prediction (RESP) score. *Am J Respir Crit Care Med.* 2014;189(11):1374-82. DOI: 10.1164/rccm.201311-2023OC
11. Herdman TH, Kamitsuru S. Diagnósticos de Enfermagem da NANDA-I: definições e classificações 2018-2020. 11 ed. Porto Alegre: Artmed; 2018.
12. Moore Z, Patton D, Avsar P, McEvoy NL, Curley G, Budri A, et al. Prevention of pressure ulcers among individuals cared for in the prone position: lessons for the COVID-19 emergency. *J Wound Care.* 2020; 29(6):312-20. DOI: 10.12968/jowc.2020.29.6.312
13. Oliveira AC, Garcia PC, Nogueira LS. Nursing workload and occurrence of adverse events in intensive care: a systematic review. *Rev Esc Enferm USP.* 2016;50(4):679-89. DOI: 10.1590/S0080-623420160000500020

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