






# Effectiveness of ECMO treatment for acute respiratory distress syndrome of patients with covid-19: a literature review

## Eficácia do tratamento com ECMO para síndrome do desconforto respiratório agudo em pacientes com covid-19: uma revisão da literatura



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### Abstract

**Introduction:** The highly virulent SARS-CoV-2 virus spread worldwide between 2020 and 2022, causing the covid-19 pandemic. The characteristics of easy transmission, difficulty to control, and severe respiratory conditions led to social isolation and the use of FFP2 masks, with hospitalizations and high mortality. Treatments such as medications, patient pronation, and invasive treatments, such as mechanical ventilation, were used to prevent the irreversibility. However, extracorporeal membrane oxygenation (ECMO) was a viable alternative for eligible patients who were unresponsive to conventional treatments. **Objective:** This study aimed to discuss the effectiveness of the ECMO treatment during the covid-19 pandemic. **Methodology:** Among the studies published between 2019 and 2023 and retrieved from databases (Google Scholar, SciELO, and PubMed), 21 met the inclusion criteria. **Final considerations:** The ECMO treatment demonstrated potential to contribute to the recovery of patients with severe respiratory failure despite its risks and the need for a trained multidisciplinary team combined with 24-hour care and monitoring, being an alternative to inefficient conventional treatments.

**Keywords:** Covid-19; Extracorporeal membrane oxygenation; ECMO; Respiratory failure; Therapeutic support.

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## Resumo

**Introdução:** O vírus SARS-CoV-2, altamente virulento, se espalhou pelo mundo entre 2020 e 2022, causando a pandemia de covid-19. As características de fácil transmissão, dificuldade de controle e quadros respiratórios graves levaram ao isolamento social e ao uso de máscaras PFF2, com internações e alta mortalidade. Tratamentos como medicamentos, pronação do paciente e tratamentos invasivos, a exemplo de ventilação mecânica, foram utilizados para prevenir a irreversibilidade. No entanto, a oxigenação por membrana extracorpórea (ECMO) foi uma alternativa viável para pacientes elegíveis que não responderam aos tratamentos convencionais. **Objetivo:** Discutir a eficácia do tratamento com ECMO durante a pandemia de covid-19. **Metodologia:** Entre os estudos publicados entre 2019 e 2023 e recuperados de bases de dados (Google Acadêmico, SciELO e PubMed), 21 atenderam aos critérios de inclusão. **Considerações finais:** O tratamento com ECMO demonstrou potencial para contribuir na recuperação de pacientes com insuficiência respiratória grave, apesar dos riscos e da necessidade de equipe multidisciplinar treinada, aliada a cuidados e monitoramento 24 horas, sendo uma alternativa aos tratamentos convencionais ineficientes.

**Palavras-chave:** Covid-19; Oxigenação por membrana extracorpórea; ECMO; Falência respiratória; Suporte terapêutico.

## INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused the coronavirus disease 2019 (covid-19) that emerged in China in December 2019. The SARS-CoV-2 spreads via aerosols, coughs, sneezes, and droplets from the respiratory tract containing viral load. The transmission mostly occurs by asymptomatic patients, and family environments and healthcare services are the focal points of contamination<sup>1</sup>.

The SARS-CoV-2 is a variation of the *Coronaviridae* family and expresses a single-stranded positive-sense RNA (RNA+)<sup>2,3</sup> that encodes approximately 29 proteins. Relevant proteins include the S protein (Spike), which promotes the viral cell infection; the N protein from the viral nucleocapsid, regulating replication; and the ORF7 protein, essential to viral release, triggers apoptosis in host cells and is associated with damage in alveolar cells<sup>3</sup>.

During transmission, the virus attaches to the mucosa of respiratory epithelium, binding the surface protein Spike with the angiotensin-converting enzyme 2 (ACE2) tissue receptor, highly expressed in pulmonary cells. Once bonded, the virus is endocytosed, and viral replication starts. The new particles are released by budding in the vascularized pulmonary parenchymal tissue, progressing to haematogenous spread and infection of other cells and tissues expressing ACE2<sup>4,1</sup>.

The viral tropism for cells of the respiratory system leads to classic symptoms, such as

fever and cough. However, the ACE2 receptor is expressed in other organs (e.g., kidneys, intestines, and heart), and its activation is associated with different clinical symptoms<sup>4</sup>.

Patients infected with the SARS-CoV-2 virus present a high chance of developing flu-like symptoms, except for asymptomatic cases. This acute respiratory condition includes fever, cough, sore throat, runny nose, or dyspnea due to the lack of a peak production of angiotensin<sup>5,6</sup>.

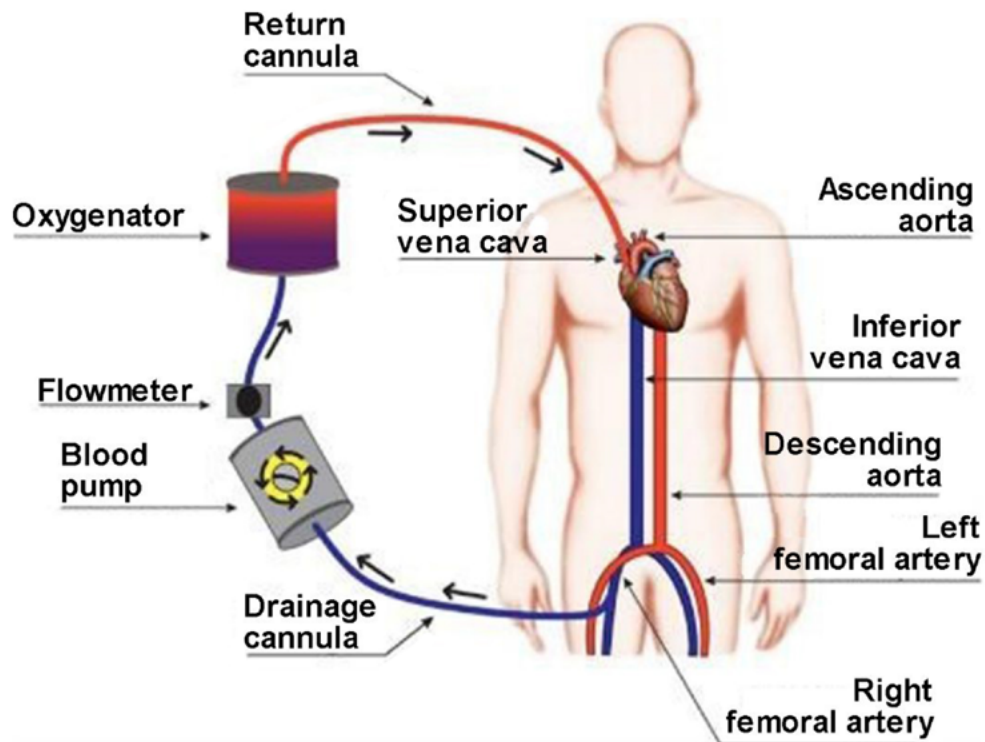
The pre-existing comorbidities considered as risk factors for severe progression of covid-19 include diabetes, high-risk pregnancies, immunosuppressive conditions, and respiratory, cardiovascular, liver, and chronic kidney diseases<sup>5</sup>. However, the presence of one or more symptoms is related to the interaction between host cells and SARS-CoV-2 since the immune response of the patient is crucial to disease evolution<sup>4</sup>. According to the Ministry of Health of Brazil (2020), 80% of cases were mild, whereas severe cases ranged from 5% to 10%<sup>7</sup>.

The high virulence of SARS-CoV-2 is responsible for the progression to acute respiratory distress syndrome (ARDS), especially in patients with old age or with pre-existing conditions<sup>7</sup>. Consequently, patients over 60 years old (physiologically immunocompromised due to aging) or with hypertension, diabetes, respiratory diseases, or heart conditions have increased risk factors, and one or more factors increase three to four-fold the odds of hospitalization<sup>8,9</sup>.

Patients with covid-19 have symptoms related to cellular distress due to hypoxia (oxygen saturation below 95%), hypotension, respiratory distress, and increased respiratory rate. Additionally, underlying diseases may present worse clinical evolution, such as chronic obstructive pulmonary disease<sup>7</sup>. This requires intensive and continuous care by a multidisciplinary team with mechanical ventilation, pronation, neuromuscular blocking agents, pulmonary vasodilators, high positive end-expiratory pressure, and recruitment maneuvers<sup>10</sup>.

The last therapeutic resource is the extracorporeal membrane oxygenation (ECMO), the main device for extracorporeal life support for pulmonary or cardiac failure. The two classic configurations are the venovenous ECMO (ECMO-VV) or venoarterial ECMO (ECMO-VA), which require a cannula for drainage and the other for return of oxygenated blood<sup>11</sup>.

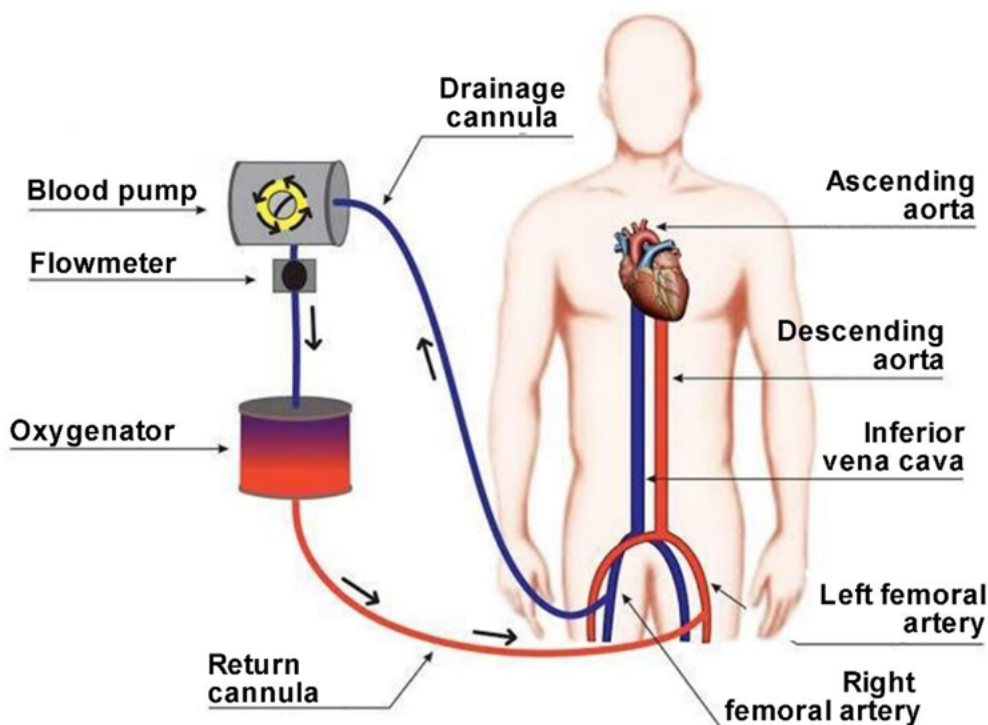
The ECMO-VV is used for respiratory failure with preserved cardiac function. In this procedure, blood is drained from the right femoral vein, flows via an oxygenator, and is infused in the right internal jugular vein, the first option for vascular access. The oxygenated blood perfuses the lungs to assist the impaired pulmonary tissue (Figure 1)<sup>10,11</sup>.

**Figure 1. Venovenous ECMO**

Source: Chaves (2019)<sup>11</sup>.

The ECMO-VA is indicated for cardiac support with or without preserved pulmonary function with central (i.e., after post-thoracotomy) or peripheral implantation. In central ECMO-VA, blood is drained from the right atrium and is infused in the ascending aorta. Meanwhile, in peripheral ECMO-VA, blood is drained from the femoral or jugular vein and is infused via the axillary, femoral, or carotid arteries (Figure 2)<sup>10,11</sup>.

Figure 2. Venoarterial ECMO.



Source: Chaves (2019)<sup>11</sup>.

The ECMO treatment was performed in the Middle East during the respiratory syndrome coronavirus (MERS-CoV) outbreaks in 2012 and the H1N1 influenza pandemic in 2009. Due to its effectiveness in the treatment of severe cases, ECMO was considered an option for covid-19<sup>10</sup> because of the alarming epidemiological data reported by the Ministry of Health of Brazil<sup>12</sup>.

Thus, this study aimed to discuss the effectiveness of ECMO as a therapeutic alternative for the treatment of severe ARDS in hospitalized patients with covid-19, supporting its clinical relevance.

## METHODS

This study is an integrative review conducted using articles indexed in databases such as Google Scholar, the Scientific Electronic Library Online (SciELO), and Medline (PubMed). The inclusion criteria were studies published in Latin America between 2019 and 2023 in Portuguese, English, and Spanish.

Keywords were used combined and individually in Portuguese (*oxigenação por membrana extracorpórea*, *ECMO*, *falência respiratória*, and *suporte terapêutico*), English (*extracorporeal membrane oxygenation*, *intensive care*, and *ARDS*), or Spanish (*terapia*, *recuperación*, and *oxigenación por membrana extracorpórea*).

Original articles, case reports, systematic reviews and meta-analyses, and randomized and non-randomized clinical trials were included. Studies that were duplicated and did not meet the theme were excluded. A total of 68 articles were found, and 21 met the criteria (Table 1).

**Table 1.** Characteristics of the included studies and the analysis of clinical aspects of infection in patients with covid-19 and the use of ECMO-VV.

Title	Author (Year)	Objective	Main considerations
Description of covid-19 cluster: isolation and testing in asymptomatic individuals as strategies to prevent local dissemination in Mato Grosso state, Brazil, 2020	Silva <i>et al.</i> (2020) <sup>1</sup> .	To describe a covid-19 cluster and the strategies used to contain the virus in a municipality in the countryside of the state of Mato Grosso, Brazil.	The covid-19 cases should not be dismissed, even with negative molecular test results. The inclusion of complementary serological tests was proposed as a beneficial approach to clarify these cases and identify asymptomatic patients. This approach may support strategies for controlling and preventing covid-19.
SARS-CoV-2 as the causative agent of covid-19: Epidemiology, genetic characteristics, clinical manifestations, diagnosis and possible treatments	Bezerra <i>et al.</i> (2020) <sup>2</sup> .	To conduct an integrative review of the main characteristics of SARS-CoV-2 and the epidemiological, clinical, and diagnostic aspects of covid-19 and possible treatments.	The high rate of viral spread and the lack of effective vaccines or treatments available highlighted the need for further studies.
Coronavirus SARS-CoV-2 and Covid-19	Uzunian <i>et al.</i> (2020) <sup>3</sup> .	To explain the structure and function of the agent responsible for covid-19 in ARDS.	A prophylactic immunization against this virus was unknown. In severe hospitalized patients, intubation combined with oxygenation was performed to ensure adequate ventilation of the alveoli.
Immunopathological mechanisms involved in SARS-CoV-2 infection	Brito <i>et al.</i> (2020) <sup>4</sup> .	To gather evidence regarding the main mechanisms of transmission and immunopathology of SARS-CoV-2 infection.	The immune response of the host plays a crucial role in the pathogenesis of covid-19. In vitro studies are essential to elucidate the pathogenic mechanisms of SARS-CoV-2 and to the development of vaccines and therapeutic targets.
Suspected covid-19 case definition: a narrative review of the most frequent signs and symptoms among confirmed cases	Iser <i>et al.</i> (2020) <sup>5</sup> .	To describe the most frequent signs and symptoms of SARS-CoV-2.	Considering the lack of diagnostic tests and a wide spectrum of symptoms, health services should employ a sensitive case definition for appropriate surveillance, prevention, and treatment.



Does angiotensin II peak in response to SARS-CoV-2?	Xavier <i>et al.</i> (2020) <sup>6</sup> .	To address the covid-19 severity and to analyze the relationship between symptoms and angiotensin-converting enzyme 2, providing an accurate understanding of the prognostic of the disease.	The ARDS plays a critical role in the early response to SARS-CoV-2 infection, affecting the prognosis of covid-19.
Comorbidities and deaths by covid-19 in Brazil	Souza <i>et al.</i> (2021) <sup>8</sup> .	To describe the cases of patients who died due to covid-19 in Brazil, highlighting age, sex, and comorbidities.	The presence of one or more comorbidities, particularly heart diseases, was associated with a poor prognosis of covid-19. Additionally, the age of the patient was a relevant aspect.
Covid-19 and hospitalizations for SARI in Brazil: a comparison up to the 12th epidemiological week of 2020	Bastos <i>et al.</i> (2020) <sup>9</sup> .	To investigate the pattern of hospitalizations due to SARI in Brazil since the outbreak of SARS-CoV-2, comparing the temporal and age profiles and laboratory results from 2010 to 2019.	The increase in hospitalizations due to SARI, the lack of specific information regarding the etiological agent, and the predominance of cases among older adults during the rise of covid-19 cases suggest that severe cases were identified via SARI surveillance, overloading the healthcare system. The inclusion of tests for SARS-CoV-2 in the SARI surveillance protocol and its effective implementation is crucial for monitoring the progression of severe covid-19 cases in Brazil.
Evidence on the effectiveness of ECMO in adults hospitalized with covid-19	Carvalho <i>et al.</i> (2021) <sup>10</sup> .	To inform on the anesthetic, surgical, and intensive care during the start and management of ECMO in patients with respiratory failure, disseminating knowledge on its efficacy.	The ECMO should be the last resource after the failure of other ventilatory support strategies, including prone positioning, use of high positive end-expiratory pressure, alveolar recruitment maneuvers, pulmonary vasodilators, and neuromuscular blocking agents.
Extracorporeal membrane oxygenation: a literature review	Chaves <i>et al.</i> (2019) <sup>11</sup> .	To present the theoretical and practical concepts on the use of ECMO for refractory respiratory or cardiac failure in conventional clinical management and critical patients.	The ECMO is one of the main devices of extracorporeal life support currently used and requires a multidisciplinary team with expertise for this support.

Brazilian Guidelines for the pharmacological treatment of patients hospitalized with covid-19	Falavigna <i>et al.</i> (2022) <sup>13</sup> .	To elaborate recommendations to support decisions regarding the pharmacological treatment of patients hospitalized with covid-19 in Brazil.	Few therapies were efficient in the treatment of hospitalized patients with covid-19, being recommended corticosteroids and prophylaxis for thromboembolism.
The use of ventilators in the covid-19 pandemic	Barbosa <i>et al.</i> (2020) <sup>14</sup> .	To present challenges in the use of ventilators during the pandemic in different countries.	Challenges, such as difficulty in social distancing, increased infection rates, and reduced availability of ventilators, potentially overwhelmed healthcare systems worldwide, especially in Brazil. Thus, alternatives emerged to address the demand for this resource.
Clinical characteristics and predictors of mechanical ventilation in patients with covid-19 hospitalized in Southern Brazil	Bastos <i>et al.</i> (2020) <sup>15</sup> .	To describe the clinical characteristics and predictors of mechanical ventilation in adult patients hospitalized with covid-19.	Advanced age was the main predictor of respiratory insufficiency, with a need for mechanical ventilation in the Brazilian population. The presence of comorbidities, especially systemic arterial hypertension, diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease, malignancies, and obesity, was associated with worse prognosis and death.
Use of conscious pronation in the respiratory management of patients with covid 19: a literature review	Campos <i>et al.</i> (2022) <sup>16</sup> .	To evaluate the indications and advantages of the use of conscious pronation in the management of non-intubated patients with respiratory impairment due to covid-19.	Conscious pronation is a simple and easy intervention that patients may perform with proper guidance and minimal assistance. Furthermore, conscious pronation does not require institutional resources or have associated costs.
Pronation in ARDS due to covid-19: more pros than cons	Battagliani <i>et al.</i> (2022) <sup>17</sup> .	To identify the factors that contribute to improve oxygenation and mortality after pronation in patients with covid-19 using mechanical ventilation.	The use of a prone position in covid-19 patients with severe hypoxemic respiratory failure was important. This technique should be maneuvered early and regardless of the oxygenation response. However, results still need validation in comprehensive randomized controlled trials.



Join Society of Critical Care Medicine- Extracorporeal Life Support Organization task force position paper on the role of the intensivist in the initiation and management of Extracorporeal Membrane Oxygenation	Della-Volpe <i>et al.</i> (2020) <sup>18</sup> .	To define the role of the intensivist in the initiation and management of patients on ECMO.	The role of the intensivist in the care of patients on ECMO is in development, especially regarding patient selection, cannulation, and management of ECMO.
ECMO use in covid-19: Case report of a venovenous ECMO in an adult patient with covid-19	Máximo <i>et al.</i> (2021) <sup>19</sup> .	To report a clinical case of an adult patient diagnosed with covid-19 submitted to ECMO in a private hospital in the metropolitan area of Belo Horizonte, Minas Gerais.	The ECMO treatment was designed to restore vital function and reduce adverse outcomes. Additionally, the ECMO supports vital organ systems during the recovery of the patient since it is not a direct treatment.
In search of the ideal monitoring of heparin in mechanical circulatory support	La Guerra <i>et al.</i> (2020) <sup>20</sup> .	To analyze the correlation between rTTPa and anti-Xa to describe the therapeutic range in the anticoagulation with UFH in patients under short-term mechanical support and to describe the complications and hematological disorders after this period.	The study observed a limited correlation between rTTPa and anti-Xa, with a more solid trend with anti-Xa. The use of anti-Xa monitoring may be safer and reduce hemorrhagic complications despite the quick laboratory results for rTTa. Therefore, the team and service should provide training and standardized management of the quality of care.
Extracorporeal respiratory support in patients	Oliveira <i>et al.</i> (2020) <sup>21</sup> .	To address aspects associated with ECMO in patients and describe clinical involvement.	The decision not to offer ECMO is equivalent to denying conventional ventilation since ECMO is used during diagnosis and in the search process for effective therapeutic strategies. Thus providing the opportunity to improve cardiorespiratory conditions and increase chances of recovery.
Effectiveness of extracorporeal membrane oxygenation (ECMO) therapy in critically patients with covid-19	Lavezzo <i>et al.</i> (2022) <sup>22</sup>	To conduct an integrative review of the literature on the investigation of ECMO therapy efficacy in critically ill patients with covid-19.	The ECMO might improve outcomes for patients with severe covid-19, mainly in cases of patients aged under 71 years and with fewer comorbidities. However, evidence associates ECMO with an increased risk of thrombosis.

ARDS: acute respiratory distress syndrome, SARI: severe acute respiratory illness, ECMO: extracorporeal membrane oxygenation, rTTPa: activated partial thromboplastin time-ratio, anti-Xa: activated anti-factor X, UFH: unfractionated heparin.

## DEVELOPMENT

### Epidemiology

According to the Ministry of Health of Brazil (2023)<sup>12</sup>, 660 million cases of covid-19 and more than six million deaths were reported worldwide until December 2022. The incidence and mortality rate in Brazil was 17,153.2 cases and 327.7 deaths per 100,000 inhabitants, respectively. From February 2020 to December 2022, Espírito Santo recorded the highest incidence rate (32,262 cases per 100,000 inhabitants), with a mortality rate of 368,2 deaths per 100,000 inhabitants. However, Rio de Janeiro had an incidence rate of 15,555.4 cases per 100,000 inhabitants, with the highest mortality rate in Brazil (440.6 deaths per 100,000 inhabitants) (Table 2)<sup>12</sup>.

### Therapeutic resources

The recommendation for mild cases of covid-19 is rest, a balanced diet, hydration, medication when needed (e.g., analgesics and antipyretics), and social distancing for five days from the onset of symptoms<sup>7</sup>. Moreover, for hospitalized patients on oxygen therapy, dexamethasone (a steroidal anti-inflammatory drug) was prescribed for ten days due to the inflammatory process associated with increased cytokine production to reduce pulmonary edema<sup>13</sup>.

Severe forms of covid-19 potentially evolve into acute respiratory failure, requiring mechanical to replace totally or partially the involuntary ventilatory activity, which reduces respiratory work and enhances gas exchange efficiency. Mechanical ventilation presents as non-invasive with an external interface or invasive using intubation or tracheostomy. The maximum period of mechanical ventilation is 29.5 days<sup>14,15</sup>.

Pronation (i.e., the patient placed in a prone position) is indicated in cases of progression to ARDS with refractory hypoxemia to mechanical ventilation, reducing hypoxemia and improving the ventilation/perfusion ratio<sup>16,17</sup>. In Latin America, 72% of hospitalized patients required pronation before receiving ECMO<sup>23</sup>.

**Table 2.** Distribution of new covid-19 cases and deaths recorded in epidemiological week 52 (EW 52), total cases, incidence, and mortality coefficients (per 100,000 inhabitants) by Region/State, Brazil, 2022<sup>12</sup>

Region/State	Confirmed cases				Confirmed deaths			
	New	Total	Cumulative Incidence	Incidence in EW 52	New	Total	Deaths	Deaths in EW 52
<b>North</b>	<b>8.593</b>	<b>2.839.575</b>	<b>15.207,20</b>	<b>46.0</b>	<b>22</b>	<b>51.363</b>	<b>275.1</b>	<b>0.1</b>
AC	889	158.669	17.738,90	99.4	4	2.040	228.1	0.4
AM	138	624.864	14.850,40	3.3	3	342.7	14.418	0.1
AP	28	182.516	21.179,10	3.2	0	2.165	251.2	0.0
PA	823	861.041	9.907,60	9.5	8	18.953	218.1	0.1
RO	4.008	471.673	26.255,70	223.1	7	7.399	411.9	0.4
RR	180	181.245	28.715,20	28.5	0	2.180	345.4	0.0
TO	2.527	359.567	22.610,80	158.9	0	4.208	264.6	0.0
<b>Northeast</b>	<b>24.354</b>	<b>7.206.999</b>	<b>12.561,40</b>	<b>42.4</b>	<b>240</b>	<b>133.829</b>	<b>233.3</b>	<b>0.4</b>
AL	1.323	335.176	10.000,60	39.5	11	7.196	214.7	0.3
BA	6.116	1.769.063	11.848,50	41.0	82	31.230	209.2	0.5
CE	2.786	1.437.171	15.643,40	30.3	11	28.067	305.5	0.1
MA	759	488.093	6.860,40	10.7	6	11.034	155.1	0.1
PB	3.131	700.127	17.333,00	77.5	15	10.525	260.6	0.4
PE	5.926	1.122.935	11.677,00	61.6	22	22.579	234.8	0.2
PI	2.127	413.535	12.602,10	64.8	21	8.027	244.6	0.6
RN	1.395	582.618	16.485,30	39.5	71	8.689	245.9	2.0
SE	791	358.281	15.451,00	34.1	1	6.482	279.5	0.0
<b>Southeast</b>	<b>95.414</b>	<b>14.407.277</b>	<b>16.185,70</b>	<b>107.2</b>	<b>623</b>	<b>333.330</b>	<b>374.5</b>	<b>0.7</b>
ES	6.561	1.311.144	32.262,00	161.4	28	14.964	368.2	0.7
MG	52.536	4.079.422	19.158,80	246.7	189	64.447	302.7	0.9
RJ	10.121	2.701.378	15.555,40	58.3	167	76.508	440.6	1.0
SP	26.196	6.315.333	13.643,20	56.6	239	177.411	383.3	0.5
<b>South</b>	<b>55.012</b>	<b>7.712.937</b>	<b>25.546,00</b>	<b>182.2</b>	<b>144</b>	<b>109.809</b>	<b>363.7</b>	<b>0.5</b>
PR	14.773	2.861.213	24.843,70	128.3	47	45.718	397	0.4
RS	32.435	2.895.571	25.348,70	283.9	72	41.508	363.4	0.6
SC	7.804	1.956.153	26.972,10	107.6	25	22.583	311.4	0.3
<b>Central-west</b>	<b>23.571</b>	<b>4.164.493</b>	<b>25.232,80</b>	<b>142.8</b>	<b>81</b>	<b>65.522</b>	<b>397</b>	<b>0.5</b>
DF	4.114	888.063	29.067,70	134.7	0	11.838	387.5	0.0
GO	11.695	1.823.980	25.641,00	164.4	51	27.766	390.3	0.7
MS	2.549	593.209	21.115,20	90.7	17	10.903	388.1	0.6
MT	5.213	859.241	24.367,20	147.8	13	15.015	425.8	0.4
<b>Brazil</b>	<b>206.944</b>	<b>36.331.281</b>	<b>17.157,20</b>	<b>97.7</b>	<b>1.110</b>	<b>693.853</b>	<b>327.7</b>	<b>0.5</b>

Source: adapted from the Brazilian Ministry of Health<sup>12</sup>

## Indications for ECMO

Hospitalized patients on mechanical ventilation and in intensive care with worsening progression should be evaluated by a multidisciplinary team considering advanced support treatments. Patients with ARDS at high risk of death ( $\text{PaO}_2/\text{FiO}_2$  below 100) are indicated for ECMO<sup>18,24</sup>, and a trained team may immediately start ECMO at a specialized center when its benefits are evidenced<sup>19,24</sup>.

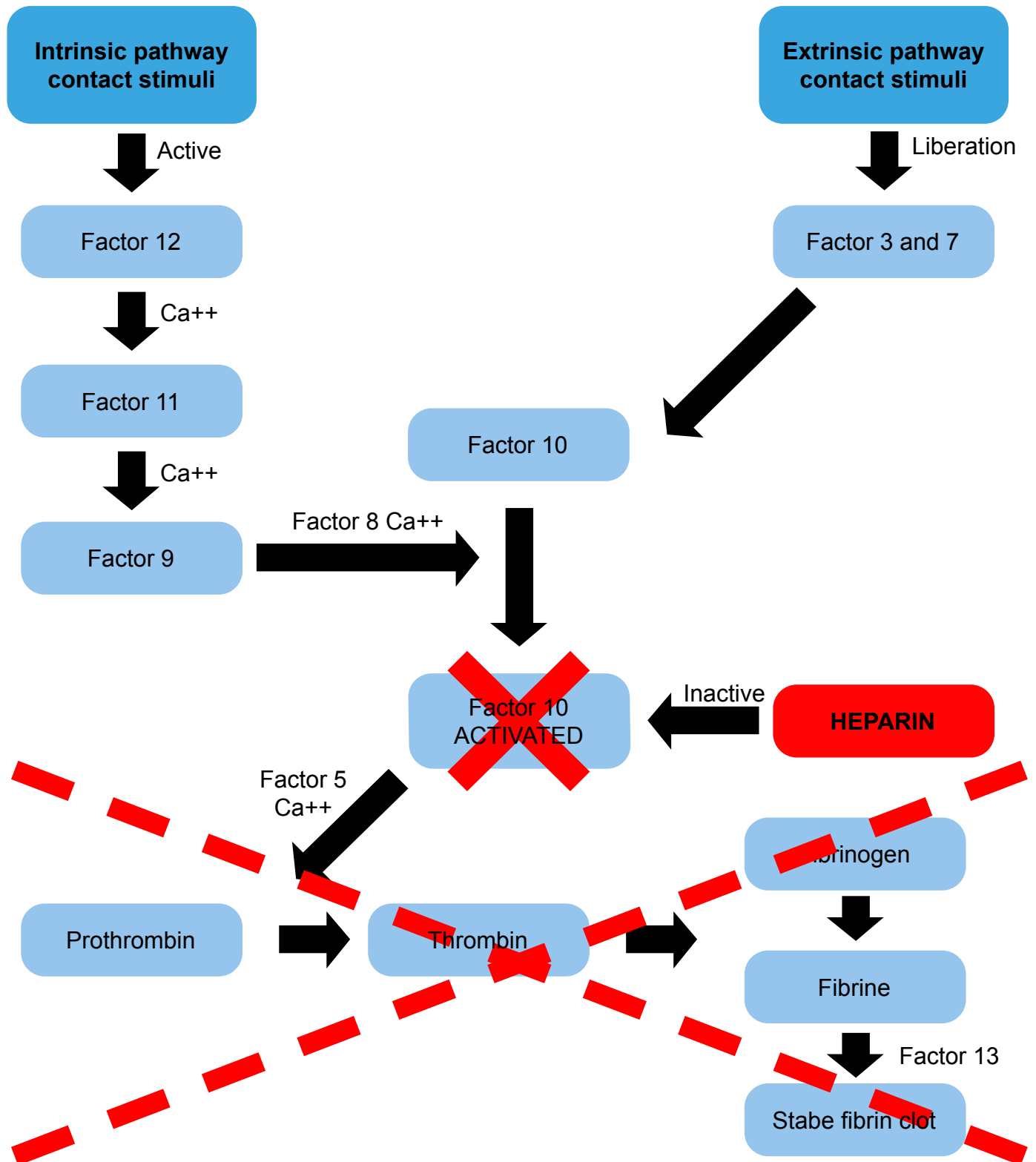
Despite ECMO treatment being an option, contraindication occurs on terminal illness, severe damage to the central nervous system, and do-not-resuscitate order<sup>24</sup>. The Extracorporeal Life Support Organization (ELSO) regulates and determines the exclusion criteria for ECMO treatment for patients with covid-19. Patients with comorbidities may be excluded due to a worse prognosis. The prognosis worsens with advanced age; however, this is a relevant factor when the potential for favorable outcomes and availability of resources are balanced. Thus, patients on mechanical ventilation for more than seven days must be evaluated for indication of ECMO treatment<sup>19,24</sup>.

## Patient care in ECMO

A multidisciplinary team constantly monitors patients on ECMO since complications are frequent due to the use of vasopressors and anticoagulants (e.g., heparin) drugs<sup>11</sup>. Although most lines are coated with anticoagulant-like molecules, patients on ECMO receive anticoagulants to prevent clot formation in the circuit and vascular thrombosis at the cannula insertion sites<sup>25</sup>. Heparin acts by inactivating factor 10a in the coagulation cascade (Figure 3), preventing clot formation<sup>20</sup>.

Anticoagulation is monitored using the activated coagulation time (ACT) or the activated partial thromboplastin time (aPTT) tests, performed every four to six hours<sup>25</sup>. Reference values are from 180 to 220 and 40 to 55 seconds for ACT and aPTT, respectively.

Figure 3. Heparin action in the coagulation cascade.



Source: authors.

## Complications of ECMO

Complications regarding ECMO are frequent and categorized as clinical or mechanical. Mechanical complications are triggered by issues in the extracorporeal circuit, such as failure of the oxygenation membrane, rupture of the system, and coagulation. Moreover, clinical complications include intracranial, intrathoracic, and retroperitoneal hemorrhages, acute kidney injuries, infections due to invasive devices, and thromboembolism<sup>11,21-22</sup>.

## Weaning from ECMO

Weaning from ECMO should only start when the patient autonomously performs gas exchanges to supply the needs generated by their body surface (peak pressure  $\leq 30$  cmH<sub>2</sub>O, positive end-expiratory pressure  $\leq 15$  cmH<sub>2</sub>O, tidal volume  $\leq 6$  mL /Kg of predicted body weight, respiratory rate  $\leq 35$  breath per minute e FiO<sub>2</sub>  $\leq 60\%$ )<sup>23</sup>. Additionally, radiography findings and pulmonary compliance should be improved.

After, an autonomy test for weaning from ECMO-VV is performed, suspending the fresh gas flow in the system. Arterial blood gas tests are evaluated in patients stable for six hours. Blood pH and PaO<sub>2</sub> levels within the expected parameters are considered to ECMO weaning after 12 hours of sustained stability without ventilatory support from the membrane and with stable hemodynamic parameters<sup>11</sup>.

## DISCUSSION

Hospitalized patients with covid-19 often need intensive treatments, including ECMO. In Brazil, the average length of ECMO treatment is ten days, and the survival rate is 57%, similar to the global rate reported by ELSO<sup>26</sup>.

The ECMO is an intensive treatment with benefits and risks, preventing multiple organ failure, worse respiratory insufficiency outcomes, and the disease progression to ARDS<sup>25</sup>. However, ECMO may be associated with a high risk of thromboembolism<sup>19</sup>.

During ECMO treatment, temporary support of pulmonary and cardiac function provided by the oxygenating membrane leads to changes in the body and respiratory system. This membrane provides gas diffusion between fresh gas flow and the venous blood, supplying oxygen-rich blood and exuding carbon dioxide<sup>11</sup>. However, ECMO can be recognized as a foreign body, resulting in severe conditions such as a systemic inflammatory response syndrome<sup>11,21</sup>. Despite risks, ECMO may enhance the chances of recovery for patients with ARDS or refractory cardio-circulatory impairment<sup>10,19</sup>.

Comorbidities are risk factors that affect ECMO treatment. In 2020, 31% of patients in Latin America had hypertension, and 48% were overweight and/or obese, which is contraindicated for



advanced therapeutic intervention, according to ELSO<sup>23</sup>. During the covid-19 pandemic, although used as a last resource, the ECMO treatment provided an important treatment for hospitalized patients with ARDS<sup>10</sup>.

## FINAL CONSIDERATIONS

The ECMO is one of the main treatments to save patients with severe respiratory failure, providing temporary support in conventional treatments of pulmonary or refractory cardiac function. Furthermore, the ECMO decreases the load on these organs and contributes to the recurrence of the condition and recovery of the patient.

The treatment followed ELSO recommendations and was supported by a trained multidisciplinary team during the pandemic. In this way, the treatment elicited positive results, improving the condition of 57% of patients with severe covid-19.

The ECMO treatment offers a high-efficacy alternative to treat severe patients of new pandemic diseases that cause severe respiratory failures. Thus, the potential described in case reports and others studies during the covid-19 pandemic was corroborated in the present study.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## AUTHOR CONTRIBUTIONS

**LSR e MPV:** Conceptualization, data curation, formal analysis, investigation, methodology, writing – original draft. **RCC:** Formal analysis, resources, supervision, validation, visualization, writing – review & editing. All authors read and approved the published version of the manuscript.

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