

Evaluation and management of the patient with severe COVID-19

Evaluación y manejo del paciente grave con COVID-19

Ricardo E. Guido-Guerra¹, Jorge Morales-Hernández², Irene Balam-Lara³, Edith L. Nicolás-Martínez³, Jazmín G. Emeterio-Alcázar³, Gustavo Lugo-Goytia³, Iván A. Osuna-Padilla³, Carmen Hernández Cárdenas⁴, and Josué D. Cadeza-Aguilar^{3*}

¹Department of Anesthesiology; ²Department of Bronchoscopy and Endoscopy; ³Department of Critical Care; ⁴General Directorate. Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico

Abstract

COVID-19 exhibits a broad clinical spectrum, ranging from asymptomatic infection to critical illness associated with high mortality. This manuscript reviews the main risk factors, prognostic tools, and therapeutic strategies in patients with severe and critical disease. Severe illness is characterized by significant hypoxemia and respiratory compromise, whereas critical disease includes acute respiratory distress syndrome, septic shock, and multiorgan dysfunction. Key risk factors include advanced age, male sex, obesity, and smoking, as well as comorbidities such as chronic kidney disease, diabetes mellitus, hypertension, and cardiovascular disease. Several inflammatory (IL-6, C-reactive protein, ferritin), hematologic (lymphopenia, neutrophilia), and biochemical (lactate dehydrogenase, D-dimer, troponin) biomarkers are associated with worse prognosis. Clinical tools such as COVID-GRAM and the 4C Mortality Score enable risk stratification and guide therapeutic decisionmaking. Management involves a stepwise approach to oxygen therapy, starting with conventional devices and progressing to high-flow nasal cannula, noninvasive ventilation, or invasive mechanical ventilation according to clinical evolution. Pharmacologic treatment is based on systemic corticosteroids, particularly dexamethasone, which has demonstrated a mortality benefit. In selected cases, immunomodulatory agents may be added. Supportive measures include lung-protective ventilation strategies, prone positioning, prophylactic anticoagulation, hemodynamic management with vasopressors, and renal replacement therapy when indicated. Early identification and comprehensive multidisciplinary management are essential to improve clinical outcomes.

Keywords: COVID-19. SARS-CoV-2. Oxygen therapy. Respiratory failure.

Resumen

La COVID-19 presenta un espectro clínico amplio, desde formas asintomáticas hasta enfermedad crítica con alta mortalidad. Este manuscrito revisa los principales factores de riesgo, herramientas pronósticas y estrategias terapéuticas en pacientes graves y críticos. La enfermedad grave se caracteriza por hipoxemia significativa y compromiso respiratorio, mientras que la forma crítica incluye síndrome de dificultad respiratoria aguda, choque séptico y disfunción multiorgánica. Entre los factores de riesgo destacan la edad avanzada, el sexo masculino, la obesidad y el tabaquismo, así como comorbilidades como enfermedad renal crónica, diabetes, hipertensión y enfermedad cardiovascular. Diversos biomarcadores inflamatorios (IL-6, proteína C reactiva, ferritina), hematológicos (linfocitopenia, neutrofilia) y bioquímicos (LDH, dímero D, troponina) se asocian

*Correspondence:

Josué D. Cadeza-Aguilar
E-mail: jdcnm@gmail.com

Date of reception: 25-11-2025
Date of acceptance: 21-04-2026
DOI: 10.24875/NCTE.M26000033

Available online: 21-10-2026
Neumol Cir Torax (Eng). 2025;84(4):278-285
www.revistanct.org.mx

3082-0006 / © 2026 Sociedad Mexicana de Neumología y Cirugía de Tórax. Published by Permanyer. This is an open access article under the license CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

con peor pronóstico. Las herramientas clínicas como COVID-GRAM y 4C Mortality Score permiten estratificar el riesgo y guiar decisiones terapéuticas. El tratamiento incluye oxigenoterapia escalonada, comenzando con dispositivos convencionales y progresando a cánula nasal de alto flujo, ventilación no invasiva o invasiva según la evolución clínica. El tratamiento farmacológico se basa en corticosteroides sistémicos, principalmente dexametasona, con beneficio demostrado en la reducción de mortalidad. En casos seleccionados se añaden inmunomoduladores. Las medidas de soporte incluyen ventilación protectora pulmonar, posición prona, anticoagulación profiláctica, manejo hemodinámico con vasopresores y terapia de reemplazo renal en casos indicados. La identificación temprana y el manejo integral multidisciplinario son fundamentales para mejorar los desenlaces clínicos.

Palabras clave: COVID-19. SARS-CoV-2. Hipoxemia. Oxigenoterapia. Insuficiencia respiratoria.

Introduction

The clinical spectrum of COVID-19 is highly variable, ranging from asymptomatic to critical disease. The objective of this article is to analyze the identified risk factors for severe disease and to establish the clinical approach to patients presenting with severe and critical COVID-19. Severe disease is defined when the patient presents with fever, dyspnea, or cough, accompanied by any of the following criteria: respiratory rate > 30 breaths per minute, severe respiratory distress, or oxygen saturation (SpO_2) $\leq 90\%$ on room air.¹ Other guidelines include a pulse oxygen saturation (SpO_2) < 93% on room air at sea level, or pulmonary opacities with involvement greater than 50%.²

Critical COVID-19 is considered when the patient develops moderate or severe acute respiratory distress syndrome (ARDS), septic shock, and/or multiorgan dysfunction. The World Health Organization (WHO) Clinical Progression Scale, scored from 0 to 10, provides a standardized severity stratification, where scores of 5 to 6 represent severe disease requiring oxygen support and scores of 7 to 9 indicate critical disease requiring mechanical ventilation.^{3,4}

As with any patient in the intensive care unit, success depends on treating both the initial medical condition and the underlying comorbidities and complications.²

Risk factors

The precise determinants remain unknown, but the principal factors appear to be host-related rather than attributable to viral mutations.⁵ Certain demographic factors are associated with a severe clinical course.⁶ Advanced age (particularly > 65 years) is an important predictor of mortality, and male sex is independently associated with disease severity; a body mass index (BMI) > 30 kg/m² and a history of smoking are considered additional risk factors for severe COVID-19.⁷⁻¹²

Comorbidities significantly increase the risk of disease progression. The strongest associations include chronic kidney disease (CKD) (odds ratio [OR]: 2.97), chronic obstructive pulmonary disease (COPD) (OR: 2.88), coronary artery disease (OR: 2.87), diabetes mellitus (OR: 2.40-3.68), systemic arterial hypertension (OR: 2.42-2.72), malignant neoplasm (OR: 2.60), and cerebrovascular disease (OR: 2.47).¹⁰⁻¹³ Kidney disease emerges as a particularly high-risk factor, with an adjusted OR of 7.71 for critical illness and 6.48 for mortality.¹³

Clinical manifestations predictive of deterioration include dyspnea or difficulty breathing (OR: 4.16), fever, and oxygen requirement upon hospital admission (OR: 2.9).^{12,14} The development of ARDS (OR: 39.59), shock (OR: 21.5), and acute kidney injury (AKI) (OR: 8.84) are the strongest predictors of unfavorable outcomes.¹⁰

Prognostic factors

An increase in the case fatality rate has been documented among patients with pre-existing conditions, with higher mortality recorded in individuals with cardiovascular disease (10.5%), diabetes (7.3%), COPD (6.3%), arterial hypertension (6.0%), and cancer – particularly hematologic and pulmonary malignancies (5.6%). In contrast, patients without pre-existing conditions had a case fatality rate of < 1%.¹⁵ Solid organ transplant recipients also appear to be at higher risk of complications.¹⁶

Chest imaging is indicated in patients with respiratory deterioration or in those considered at risk of disease progression. While chest radiography may be useful for detecting disease progression, computed tomography (CT) is more sensitive early in the course of the disease.¹⁷ The majority of patients who died from COVID-19 exhibited consolidation and air bronchograms. The CT score is based on the degree of attenuation and consolidation in specific pulmonary regions and

was higher in patients who died.¹⁸ Other findings with prognostic significance include traction bronchiectasis, extensive distribution, lymph node involvement, and increased pulmonary artery diameter.¹⁹

Likewise, inflammatory markers demonstrate strong prognostic value. Elevated interleukin (IL)-6 is the most precise inflammatory biomarker, with cutoff values of 42 pg/ml predicting severity with an area under the curve (AUC) of 0.97, and 83 pg/ml predicting mortality with an AUC of 0.94.^{20,21} Elevation of C-reactive protein (CRP), procalcitonin > 0.5 ng/ml (OR: 43.24), and elevated ferritin are consistently associated with severe disease and mortality.^{20,22-24}

Hematologic parameters include lymphopenia (OR: 1.91 for progression to severe presentation), elevated neutrophil count (OR: 2.62-6.25), neutrophil-to-lymphocyte ratio > 7.4, and thrombocytopenia.^{12,20-24} A neutrophil count > $3.74 \times 10^9/l$ demonstrates a sensitivity of 100% and a specificity of 81% for identifying high-risk patients.²⁴

Among biochemical markers with strong prognostic value, the following are included: lactate dehydrogenase (LDH) > 245 U/l (OR: 43.24), D-dimer > 0.5 mg/l (OR: 43.24 for progression; OR: 6.36 for mortality), elevated aspartate aminotransferase (AST) > 40 U/l (OR: 4.00), creatinine $\geq 133 \mu\text{mol/l}$ (OR: 5.30), and cardiac troponin I > 28 pg/ml (OR: 43.24).^{12,20,22,23,25}

COVID-19 has been associated with reports of severe systolic dysfunction and fulminant myocarditis;^{26,27} ST-segment elevation is associated with poor prognosis. Elevated troponin (serum levels > 99th percentile; > 28 pg/ml) may be an independent risk factor for in-hospital mortality.²⁸ Therefore, routine electrocardiography, troponin measurement, and transthoracic echocardiography may be important in evaluating the clinical course of COVID-19. Elevated glycated hemoglobin (HbA1c) values have been associated with inflammation, hypercoagulability, and high mortality (27.7%).²⁹

Clinical prediction tools

Early identification of COVID-19 patients who may develop critical illness enables the implementation of an appropriate clinical approach. Clinical tools such as COVID-GRAM and the 4C Mortality Score evaluate risk factors including age, comorbidities (obesity, diabetes, and hypertension), and biochemical markers to estimate the probability of hospitalization, intensive care unit admission, or mortality.

The COVID-GRAM predictive risk score was developed by the Chinese National Health Commission using

data from a retrospective cohort of patients diagnosed with COVID-19 to estimate the risk of developing critical illness (defined as requiring intensive care unit admission, mechanical ventilation, or death);³⁰ it includes 10 variables for risk calculation, which are typically available at hospital admission. If the estimated risk of critical illness is low, the physician may opt for monitoring, whereas high-risk estimates may justify aggressive treatment or intensive care unit admission.

The 4C Mortality Score is a tool for stratifying in-hospital mortality risk in patients with COVID-19. It uses clinical variables at admission (age, sex, comorbidities, respiratory rate, SpO₂, level of consciousness) to classify risk as low, intermediate, high, or very high, thereby facilitating therapeutic decision-making. It has demonstrated superior or comparable performance relative to other severity scales (such as CURB-65 or NEWS2) in predicting 30-day mortality and in-hospital mortality. It allows clinicians to identify which patients require more aggressive management and closer monitoring.³¹

The change in lymphocyte count has also been used as a prognostic scale and is classified as follows: 1) if the percentage was > 20% within 10 to 20 days after symptom onset, moderate disease can be predicted; 2) if the percentage decreased to 5-20% within 10 to 20 days after symptom onset, a severe disease presentation could be predicted; and 3) if the percentage decreased to < 5% within 17 to 19 days, a high risk of mortality could be predicted.³² Furthermore, there is a direct correlation between elevated CRP values – as a predictor of severity – and extensive involvement on CT.²²

Recommended interventions in critically ill patients

Recommended interventions for critically ill patients with COVID-19 include oxygen therapy, invasive mechanical ventilation (IMV), and noninvasive mechanical ventilation (NIV), additional interventions such as prone positioning and extracorporeal membrane oxygenation (ECMO), as well as pharmacologic interventions. These interventions are summarized in [table 1](#).

Oxygen therapy

Oxygen therapy should be initiated immediately using nasal prongs, a face mask, or an oxygen delivery device. Intensification of oxygen therapy involves a gradual progression of devices aimed at improving oxygenation and reducing the patient's respiratory effort.

Table 1. Interventions in critically ill patients with COVID-19

Intervention	Main indications	Clinical objective	Key recommendations	Bibliography
Strategies for improved oxygenation				
Conventional oxygen therapy	Initial hypoxemia ($\text{SpO}_2 \leq 90\text{-}93\%$)	Correct hypoxemia and reduce respiratory work	Use of nasal prongs, simple face mask, or reservoir mask with continuous monitoring	WHO ¹ , Long et al. ³³
Awake prone positioning	Persistent hypoxemia with conventional oxygen or HFNC	Improve ventilation/perfusion ratio	Recommended before escalating to invasive ventilatory support	Long et al. ³³ Attaway et al. ³⁴
HFNC	Acute hypoxemic respiratory failure	Improve oxygenation while avoiding intubation	Start FiO_2 at 100% and flow at 20 l/min, adjustable according to response	Long et al. ³³
NIV/CPAP	Persistent hypoxemia with increased respiratory work	Reduce respiratory effort and improve alveolar ventilation	CPAP improves alveolar recruitment and oxygenation	Long et al. ³³
IMV	Failure of oxygen therapy/NIV or intubation criteria met	Advanced respiratory support	Do not delay intubation in the setting of clinical deterioration	Attaway et al. ³⁴ SSC Guidelines ⁴²
Lung-protective ventilation	Moderate-to-severe ARDS	Reduce ventilator-induced lung injury	Tidal volume 4-8 ml/kg and plateau pressure < 30 cm H_2O	Meyer et al. ⁵⁷ SSC Guidelines ⁴²
Prone positioning on IMV	Refractory hypoxemia and moderate-to-severe ARDS	Improve oxygenation and pulmonary recruitment	12-16 hours/day in selected patients	SSC Guidelines ⁴² Berlin et al. ⁵⁸
Veno-venous ECMO	Refractory hypoxemia despite optimal management	Extracorporeal oxygenation support	Only at experienced centers and in selected patients	SSC Guidelines ⁴²
Pharmacologic				
Dexamethasone	Patients requiring supplemental oxygen or IMV	Reduce systemic inflammation and mortality	6 mg/day for up to 10 days; greatest benefit in IMV	SSC Guidelines ⁴² RECOVERY ^{47,48}
Remdesivir	Severe COVID-19 without IMV	Reduce clinical progression	May be combined with dexamethasone	NIH Guidelines ² Kim et al. ⁴⁵
Tocilizumab/Sarilumab	Severe/critical patients with elevated inflammation	IL-6 modulation and mortality reduction	Add to systemic corticosteroids	RECOVERY ³⁹ REMAP-CAP ^{36,40} IDSA 2025 ³⁵
Baricitinib	Selected patients with rapid progression	Inhibition of inflammatory response	In combination with glucocorticoids	IDSA 2025 ³⁵ Berger et al. ⁴⁶
Prophylactic anticoagulation	All hospitalized patients without contraindication	Prevent venous thromboembolism	LMWH or unfractionated heparin	SSC Guidelines ⁴² CHEST Guidelines ^{54,55}
Therapeutic anticoagulation	Selected moderate cases with elevated D-dimer	Reduce thrombotic events	Not routinely recommended in critically ill patients	REMAP-CAP/ ATTACC/ ACTIV-4a ⁵⁶
Fluid resuscitation with crystalloids	Shock or hypoperfusion	Restore tissue perfusion	Prefer dynamic parameters and avoid starches	SSC Guidelines ⁴² Attaway et al. ³⁴
Vasopressors (norepinephrine)	Fluid-refractory shock	Maintain MAP 60-65 mmHg	Vasopressin as second-line agent	SSC Guidelines ⁴² NIH Guidelines ²
Renal replacement				
CRRT	Acute kidney injury with dialytic indications	Renal support and metabolic control	Preferred over intermittent hemodialysis	Arabi et al. ⁵³ SSC Guidelines ⁴²

HFNC: high-flow nasal cannula; NIV/CPAP: noninvasive ventilation; IMV: invasive mechanical ventilation; CRRT: continuous renal replacement therapy.

At each stage of escalation, respiratory rate, oxygen saturation, and clinical signs of dyspnea (nasal flaring, thoracoabdominal dissociation, and/or use of accessory respiratory muscles) should be monitored. If these symptoms do not improve, repositioning the patient (awake prone positioning) is recommended. High-flow nasal cannula is also more comfortable than noninvasive mechanical ventilation (NIV) and its various ventilatory modes. Guidelines recommend its use as a first-line strategy for patients with acute hypoxemic respiratory failure despite conventional oxygen therapy. When used, the fraction of inspired oxygen should be set at 100% with an initial flow of 20 liters per minute. The flow can then be adjusted according to patient comfort, provided that oxygen saturation remains above 88%.³³

NIV, along with high-flow nasal cannula, plays a role in the management of patients with hypoxemic COVID-19. Loss of pulmonary perfusion regulation, hypoxic vasoconstriction, and atelectasis are possible causes of hypoxemia in these patients. Continuous positive airway pressure may reduce respiratory effort and improve oxygenation, while positive airway pressure generally improves ventilation and may improve tidal volumes.³³

Patients with greater respiratory effort and hypoxemia who do not respond to escalation of oxygen therapy and present with severe respiratory distress should undergo IMV.³³ It is critically important to remember that at any point, if intubation criteria are met, the procedure should not be delayed.³⁴

Pharmacologic treatment

Treatment decisions should be made based on local guidelines, drug availability, and patient comorbidities. In patients receiving supplemental oxygen without high-flow support or mechanical ventilation, one of the following treatments is recommended: remdesivir as monotherapy, or dexamethasone plus remdesivir (for patients requiring increasing amounts of oxygen), or dexamethasone alone (when combination therapy with remdesivir cannot be used or is unavailable). If dexamethasone is not available, an alternative corticosteroid such as prednisone, methylprednisolone, or hydrocortisone may be used.²

Immunomodulatory therapies in critically ill COVID-19 patients have demonstrated benefits when combined with corticosteroids; for example, the 2025 Infectious Diseases Society of America (IDSA) guidelines recommend adding baricitinib or tocilizumab to systemic

glucocorticoids in hospitalized adults with rapidly progressing severe or critical COVID-19, as both agents demonstrate equivalent efficacy.³⁵ IL-6 receptor antagonists (tocilizumab, sarilumab) have a greater than 99.9% probability of improving 180-day survival compared with the control group, with an approximately 26% reduction in mortality.³⁶ The combination of corticosteroids plus tocilizumab shows better survival outcomes compared with corticosteroids alone or standard care.^{37,38}

The RECOVERY trial demonstrated that tocilizumab (an IL-6 receptor antagonist) improved survival and 28-day hospital discharge rates while reducing progression to IMV in patients with hypoxemia and elevated inflammatory markers (CRP $\geq$ 75 mg/L).³⁹ The REMAP-CAP trial confirmed that both tocilizumab and sarilumab improve organ support-free days and survival in critically ill patients, with effects sustained over six months.^{36,40,41} Tocilizumab is currently approved by the Food and Drug Administration (FDA) for hospitalized patients receiving systemic corticosteroids who require supplemental oxygen, NIV or IMV, or ECMO.⁴²⁻⁴⁴ Remdesivir is recommended for patients with severe COVID-19 who do not require mechanical ventilation but is not recommended for critically ill patients receiving mechanical ventilation.^{42,45} Baricitinib (a Janus kinase inhibitor) may be added to corticosteroids in selected patients.^{42,46}

Convalescent plasma and hydroxychloroquine are not recommended.^{44,45}

In patients requiring IMV or ECMO, one of the following treatments is recommended: dexamethasone as monotherapy or in combination; for patients who initially received remdesivir monotherapy and progressed to requiring IMV or ECMO, dexamethasone treatment should be initiated and remdesivir continued until the treatment course is completed; remdesivir or tocilizumab are not recommended as monotherapy in this patient group and should only be used in combination with corticosteroids.²

The use of systemic corticosteroids is recommended for severe and critical cases of COVID-19.⁴⁵ Dexamethasone 6 mg daily for a maximum of 10 days reduces 28-day mortality (OR: 0.69; 95% CI: 0.55-0.86), with the greatest benefit observed in patients receiving IMV (29 vs. 41% mortality; relative risk [RR]: 0.64).^{45,47,48}

Dexamethasone is the preferred corticosteroid based on available evidence, although hydrocortisone and methylprednisolone have also demonstrated benefits.⁴⁵ Higher doses (equivalent to more than 6 mg of

dexamethasone) do not provide additional benefit and may increase risk in patients requiring low-flow oxygen.⁴⁸ Corticosteroids should not be used in hospitalized patients who do not require supplemental oxygen (mortality of 18 vs. 14% with standard care; RR: 1.19).⁴⁸

Additional considerations

The use of dynamic parameters, body temperature, capillary refill time, and/or lactate levels – rather than static parameters – has been recommended for assessing fluid responsiveness. Fluid resuscitation is recommended to be initiated with crystalloids; the initial use of albumin or starches for resuscitation is not recommended.³⁴ Approximately 20% of hospitalized COVID-19 patients have been reported to develop cardiac failure,⁴⁹⁻⁵¹ which is associated with a variety of pre-existing cardiovascular conditions, including acute coronary syndrome, myocarditis, and arrhythmias.⁵² Norepinephrine remains the first-choice vasopressor for shock that is unresponsive to fluid resuscitation; thereafter, vasoactive agents should be titrated to achieve a mean arterial pressure (MAP) of 60 to 65 mmHg. Vasopressin (up to 0.03 units/min) or epinephrine is recommended as a second-line vasopressor to raise MAP to the target in cases where the patient shows evidence of cardiac dysfunction and persistent hypoperfusion despite adequate fluid resuscitation and vasopressor use.² Critically ill patients are in a prothrombotic state, characterized by elevation of certain biomarkers, and there is an apparent increase in the incidence of venous thromboembolic disease.³⁹

In patients with acute kidney injury who develop indications for renal replacement therapy, continuous renal replacement therapy (CRRT) is recommended if available. If CRRT is unavailable or not feasible due to limited resources, prolonged intermittent renal therapy is recommended rather than standard intermittent hemodialysis. In a case series of critically ill patients, more than 15% required continuous renal replacement therapy.⁵³

Anticoagulation

Prophylactic anticoagulation with low-molecular-weight heparin or unfractionated heparin is recommended for all hospitalized COVID-19 patients without contraindications.^{45,47,54} In hospitalized patients with moderate severity (not requiring intensive care) and low bleeding risk, therapeutic-dose heparin may be considered instead of standard prophylaxis, particularly in

those with significantly elevated D-dimer levels (2-4 times the upper limit of normal) or a history of venous thromboembolism.⁵⁵ In critically ill patients, standard-dose prophylactic anticoagulation is recommended over therapeutic anticoagulation.^{45,54,55} The multiplatform REMAP-CAP/ACTIV-4a/ATTACC trial demonstrated no mortality benefit and an increased bleeding risk with therapeutic anticoagulation in intensive care unit patients.⁵⁶

Ventilatory support

In patients with moderate to severe ARDS undergoing mechanical ventilation, lung-protective ventilation strategies are recommended, with a preference for intermittent neuromuscular blockade as needed over continuous infusion.⁴⁵ Prone positioning should be used in cases of refractory hypoxemia.⁴⁵ Veno-venous ECMO should be considered in carefully selected patients with refractory hypoxemia despite optimized ventilation and rescue therapies, when available at experienced centers.⁴⁵

Ventilation strategies for critically ill COVID-19 patients follow the established principles for the management of acute respiratory distress syndrome (ARDS). Lung-protective ventilation with tidal volumes of 4-8 ml/kg of predicted body weight and plateau pressures < 30 cm H₂O is recommended.^{45,47,57} For moderate to severe ARDS, additional strategies include prone positioning for 12-16 hours daily, higher PEEP strategies (> 10 cm H₂O), conservative fluid management, and neuromuscular blockade as needed rather than continuous infusion.^{45,58}

Conclusion

The management of the critically ill patient with COVID-19 requires a comprehensive evaluation based on clinical factors, biomarkers, and prognostic prediction tools that enable timely identification of patients at highest risk of deterioration. The implementation of evidence-based therapeutic strategies – including stepwise respiratory support, appropriate use of corticosteroids and immunomodulatory agents, and intensive care unit supportive measures – is essential for reducing mortality. Favorable outcomes depend not only on the treatment of the viral infection but also on appropriate management of systemic complications and comorbidities, underscoring the importance of a multidisciplinary and dynamic approach to the care of the critically ill patient.

Funding

The present work received no funding.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of persons and animals. The authors declare that no experiments on human beings or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve personal patient data and does not require ethical approval. SAGER guidelines do not apply.

Statement on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence for the writing of this article.

References

- World Health Organization. Clinical management of COVID-19: Interim guidance [Internet]. World Health Organization; 2020 May [citado: 2026 Apr 5]. Disponible en: <https://www.who.int/publications/item/clinical-management-of-covid-19/>.
- COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. Bethesda (MD): National Institutes of Health (US); 2021 Apr 21-2024 Mar 1. PubMed PMID: 34003615.
- Stroehlein JK, Wallqvist J, Iannizzi C, Mikolajewska A, Metzendorf MI, Benstoem C, et al. Vitamin D supplementation for the treatment of COVID-19: a living systematic review. *Cochrane Database Syst Rev*. 2021;5(5):CD015043. <https://doi.org/10.1002/14651858.cd015043>.
- Wagner C, Griesel M, Mikolajewska A, Metzendorf MI, Fischer AL, Stegemann M, et al. Systemic corticosteroids for the treatment of COVID-19: Equity-related analyses and update on evidence. *Cochrane Database Syst Rev*. 2022;11(11):CD014963. <https://doi.org/10.1002/14651858.cd014963.pub2>.
- Zhang L, Jackson C, Mou H, Ojha A, Rangarajan E, Izard T, et al. The D614G mutation in the SARS-CoV-2 spike protein reduces S1 shedding and increases infectivity. *bioRxiv* [Preprint]. 2020. 2020.06.12.148726. <https://doi.org/10.1101/2020.06.12.148726>.
- Imam Z, Odish F, Gill I, O'Connor D, Armstrong J, Vanood A, et al. Older age and comorbidity are independent mortality predictors in a large cohort of 1305 COVID-19 patients in Michigan, United States. *J Intern Med*. 2020;288(4):469-76. <https://doi.org/10.1111/joim.13119>.
- Booth A, Reed AB, Ponzio S, Yassaee A, Aral M, Plans D, et al. Population risk factors for severe disease and mortality in COVID-19: a global systematic review and meta-analysis. *PLoS One*. 2021;16(3):e0247461. <https://doi.org/10.1371/journal.pone.0247461>.
- Li X, Xu S, Yu M, Wang K, Tao Y, Zhou Y, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. *J Allergy Clin Immunol*. 2022;146(1):110-8. <https://doi.org/10.1016/j.jaci.2020.04.006>.
- Duan J, Wang X, Chi J, Chen H, Bai L, Hu Q, et al. Correlation between the variables collected at admission and progression to severe cases during hospitalization among patients with COVID-19 in Chongqing. *J Med Virol*. 2020;92(11):2616-22. <https://doi.org/10.1002/jmv.26082>.
- Li X, Zhong X, Wang Y, Zeng X, Luo T, Liu Q. Clinical determinants of the severity of COVID-19: a systematic review and meta-analysis. *PLoS One*. 2021;16(5):e0250602. <https://doi.org/10.1371/journal.pone.0250602>.
- Gao YD, Ding M, Dong X, Zhang JJ, Kursat Azkur A, Azkur D, et al. Risk factors for severe and critically ill COVID-19 patients: a review. *Allergy*. 2022;76(2):428-55. <https://doi.org/10.1111/all.14657>.
- Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. *J Infect*. 2020;81(2):e16-e25. <https://doi.org/10.1016/j.jinf.2020.04.021>.
- Meister T, Pisarev H, Kolde R, Kalda R, Suija K, Milani L, et al. Clinical characteristics and risk factors for COVID-19 infection and disease severity: a nationwide observational study in Estonia. *PLoS One*. 2022;17(6):e0270192. <https://doi.org/10.1371/journal.pone.0270192>.
- Bhargava A, Fukushima EA, Levine M, Zhao W, Tanveer F, Szpunar SM, et al. Predictors for severe COVID-19 infection. *Clin Infect Dis*. 2020;71(8):1962-8. <https://doi.org/10.1093/cid/ciaa674>.
- American College of Cardiology. COVID-19 Clinical Guidance For the Cardiovascular Care Team [Internet]. American College of Cardiology; 2020 Mar 6 [citado: 2026 Apr 7]. Disponible en: www.acc.org/-/media/665AFA1E710B4B3293138D14BE8D1213.pdf.
- Xie J, Covassin N, Fan Z, Singh P, Gao W, Li G, et al. Association between hypoxemia and mortality in patients with COVID-19. *Mayo Clin Proc*. 2020;95(6):1138-47. <https://doi.org/10.1016/j.mayocp.2020.04.006>.
- Rubin GD, Ryerson CJ, Haramati LB, Sverzellati N, Kanne JP, Raouf S, et al. The role of chest imaging in patient management during the COVID-19 pandemic: a multinational consensus statement from the Fleischner Society. *Chest*. 2020;158(1):106-16. <https://doi.org/10.1016/j.chest.2020.04.003>.
- Yuan M, Yin W, Tao Z, Tan W, Hu Y. Association of radiologic findings with mortality of patients infected with 2019 novel coronavirus in Wuhan, China. *PLoS One*. 2020;15(3):e0230548. <https://doi.org/10.1371/journal.pone.0230548>.
- Spagnolo P, Cozzi A, Foà RA, Spinazzola A, Monfardini L, Bnà C, et al. CT-derived pulmonary vascular metrics and clinical outcome in COVID-19 patients. *Quant Imaging Med Surg*. 2020;10(6):1325-33. <https://doi.org/10.21037/qims-20-546>.
- Melo AKG, Milby KM, Caparroz ALMA, Pinto ACPN, Santos RRP, Rocha AP, et al. Biomarkers of cytokine storm as red flags for severe and fatal COVID-19 cases: A living systematic review and meta-analysis. *PLoS One*. 2021;16(6):e0253894. <https://doi.org/10.1371/journal.pone.0253894>.
- Sayah W, Berkane I, Guermache I, Sabri M, Lakhal FZ, Yasmine Rahali S, et al. Interleukin-6, procalcitonin and neutrophil-to-lymphocyte ratio: potential immune-inflammatory parameters to identify severe and fatal forms of COVID-19. *Cytokine*. 2021;141:155428. <https://doi.org/10.1016/j.cyt.2021.155428>.
- Zeng HL, Lu Q Bin, Yang Q, Wang X, Yue DY, Zhang LK, et al. Longitudinal profile of laboratory parameters and their application in the prediction for fatal outcome among patients infected with SARS-CoV-2: a retrospective cohort study. *Clin Infect Dis*. 2021;72(4):626-33. <https://doi.org/10.1093/cid/ciaa574>.
- Izovcovich A, Ragusa MA, Tortosa F, Marzio MAL, Agnoletti C, Bengolea A, et al. Prognostic factors for severity and mortality in patients infected with COVID-19: A systematic review. *PLoS One*. 2020;15(11):e0241955. <https://doi.org/10.1371/journal.pone.0241955>.
- Elshazli RM, Toraih EA, Elgaml A, El-Mowafy M, El-Mesery M, Amin MN, et al. Diagnostic and prognostic value of hematological and immunological markers in COVID-19 infection: a meta-analysis of 6320 patients. *PLoS One*. 2020;15(8):e0238160. <https://doi.org/10.1371/journal.pone.0238160>.
- Punzalan FER, Aherrera JAM, de Paz-Silava SLM, Mondragon AV, Malundo AFG, Tan JJE, et al. Utility of laboratory and immune biomarkers in predicting disease progression and mortality among patients with moderate to severe COVID-19 disease at a Philippine tertiary hospital. *Front Immunol*. 2023;14:1123497. <https://doi.org/10.3389/fimmu.2023.1123497>.
- Chen C, Zhou Y, Wang DW. SARS-CoV-2: a potential novel etiology of fulminant myocarditis. *Herz*. 2020;45(3):230-2. <https://doi.org/10.1007/s00059-020-04909-z>.
- Escher F, Pietsch H, Aleshcheva G, Bock T, Baumeier C, Elsaesser A, et al. Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies. *ESC Heart Fail*. 2020;7(5):2440-7. <https://doi.org/10.1002/ehf2.12805>.
- Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;5(7):802-10. <https://doi.org/10.1001/jamacardio.2020.0950>.
- Wang Z, Du Z, Zhu F. Glycosylated hemoglobin is associated with systemic inflammation, hypercoagulability, and prognosis of COVID-19 patients. *Diabetes Res Clin Pract*. 2020;164:108214. <https://doi.org/10.1016/j.diabres.2020.108214>.
- Liang W, Liang H, Ou L, Chen B, Chen A, Li C, et al. Development and Validation of a Clinical Risk Score to Predict the Occurrence of Critical Illness in Hospitalized Patients With COVID-19. *JAMA Intern Med*. 2020;180(8):1081-9. <https://doi.org/10.1001/jamainternmed.2020.2033>.
- Knight SR, Ho A, Pius R, Buchan I, Carson G, Drake TM, et al. ISARIC4C investigators. Risk stratification of patients admitted to hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: development and validation of the 4C Mortality Score. *BMJ*. 2020;370:m3339. <https://doi.org/10.1136/bmj.m3339>.
- Tan L, Wang Q, Zhang D, Ding J, Huang Q, Tang YQ, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. *Signal Transduct Target Ther*. 2020;5(1):33. <https://doi.org/10.1038/s41392-020-0148-4>.

33. Long B, Liang SY, Hicks C, Gottlieb M. Just the facts: what are the roles of oxygen escalation and noninvasive ventilation in COVID-19? *CJEM*. 2020;22(5):587-90. <https://doi.org/10.1017/cem.2020.396>.
34. Attaway AH, Scheraga RG, Bhimraj A, Biehl M, Hatipoğlu U. Severe covid-19 pneumonia: pathogenesis and clinical management. *BMJ*. 2021;372:n436. <https://doi.org/10.1136/bmj.n436>.
35. Nadig N, Bhimraj A, Cawcutt K, Chiotos K, Dzierba AL, Kim AY, et al. 2025 Clinical practice guideline update by the Infectious Diseases Society of America on the treatment and management of COVID-19: baricitinib vs. tocilizumab. *Clin Infect Dis*. 2026:ciaf681. <https://doi.org/10.1093/cid/ciaf681>.
36. Investigators WC for the RC, Florescu S, Stanciu D, Zaharia M, Kosa A, Codreanu D, et al. Long-term (180-Day) outcomes in critically ill patients with COVID-19 in the REMAP-CAP randomized clinical trial. *JAMA*. 2023;329(1):39-51. <https://doi.org/10.1001/jama.2022.23257>.
37. Narain S, Stefanov DG, Chau AS, Weber AG, Marder G, Kaplan B, et al. Comparative survival analysis of immunomodulatory therapy for coronavirus disease 2019 cytokine storm. *Chest*. 2021;159(3):933-948. <https://doi.org/10.1016/j.chest.2020.09.275>.
38. Ramiro S, Mostard RLM, Magro-Checa C, van Dongen CMP, Dormans T, Buijs J, et al. Historically controlled comparison of glucocorticoids with or without tocilizumab versus supportive care only in patients with COVID-19-associated cytokine storm syndrome: results of the CHIC study. *Ann Rheum Dis*. 2020;79(9):1143-51. <https://doi.org/10.1136/annrheumdis-2020-218479>.
39. RECOVERY Collaborative Group. Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2021;397(10285):1637-45. [https://doi.org/10.1016/s0140-6736\(21\)00676-0](https://doi.org/10.1016/s0140-6736(21)00676-0).
40. REMAP-CAP Investigators; Gordon AC, Mouncey PR, Al-Beidh F, Rowan KM, Nichol AD, Arabi YM, et al. Interleukin-6 receptor antagonists in critically ill patients with covid-19. *N Engl J Med*. 2021;384(16):1491-502. <https://doi.org/10.1056/nejmoa2100433>.
41. Derde L, Gordon AC, Mouncey PR, Al-Beidh F, Rowan KM, Nichol AD, et al. Tocilizumab, sarilumab and anakinra in critically ill patients with COVID-19: a randomised, controlled, open-label, adaptive platform trial. *Thorax*. 2025;80(8):530-9. <https://doi.org/10.1136/thorax-2024-222488>.
42. Park DH, Kang CK, Choe pg, Kim NJ, Park WB, Oh MD. How we have treated severe to critically ill patients with coronavirus disease 2019 in Korea. *J Korean Med Sci*. 2022;37(49):e353. <https://doi.org/10.3346/jkms.2022.37.e353>.
43. FDA. FDA Approved Drug Products with Therapeutic Equivalence Evaluations [Internet]. FDA [citado: 2026 Apr 7]. Disponible en: <https://www.fda.gov/drugs/drug-approvals-and-databases/approved-drug-products-therapeutic-equivalence-evaluations-orange-book>.
44. Kim MS, An MH, Kim WJ, Hwang TH. Comparative efficacy and safety of pharmacological interventions for the treatment of COVID-19: a systematic review and network meta-analysis. *PLoS Med*. 2020;17(12):e1003501. <https://doi.org/10.1371/journal.pmed.1003501>.
45. Alhazzani W, Evans L, Alshamsi F, Möller MH, Ostermann M, Prescott HC, et al. Surviving Sepsis Campaign Guidelines on the Management of Adults With Coronavirus Disease 2019 (COVID-19) in the ICU: First Update. *Crit Care Med*. 2021;49(3):e219-e234. <https://doi.org/10.1097/ccm.0000000000004899>.
46. Berger AC, Simchoni N, Auerbach A, Brode WM, Kuperman E, Raffel K, et al. Implementation of clinical practice guidelines for hospitalized patients with COVID-19 in Academic Medical Centers. *JAMA Netw Open*. 2022;5(4):e225657. <https://doi.org/10.1001/jamanetworkopen.2022.5657>.
47. Wiersinga WJ, Rhodes A, Cheng AC, Peacock SJ, Prescott HC. Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): a review. *JAMA*. 2020;324(8):782-93. <https://doi.org/10.1001/jama.2020.12839>.
48. Pirracchio R, Venkatesh B, Legrand M. Low-dose corticosteroids for critically ill adults with severe pulmonary infections: a review. *JAMA*. 2024;332(4):318-28. <https://doi.org/10.1001/jama.2024.6096>.
49. Sudre CH, Murray B, Varsavsky T, Graham MS, Penfold RS, Bowyer RC, et al. Attributes and predictors of long COVID. *Nat Med*. 2021;27(4):626-31. <https://doi.org/10.1038/s41591-021-01292-y>.
50. Logue JK, Franko NM, McCulloch DJ, McDonald D, Magedson A, Wolf CR, et al. Sequelae in adults at 6 months after COVID-19 infection. *JAMA Netw Open*. 2021;4(2):e210830. <https://doi.org/10.1001/jamanetworkopen.2021.0830>.
51. Townsend L, Dyer AH, Jones K, Dunne J, Mooney A, Gaffney F, et al. Persistent fatigue following SARS-CoV-2 infection is common and independent of severity of initial infection. *PLoS One*. 2020;15(11):e0240784. <https://doi.org/10.1371/journal.pone.0240784>.
52. Salama C, Han J, Yau L, Reiss WG, Kramer B, Neidhart JD, et al. Tocilizumab in patients hospitalized with Covid-19 pneumonia. *N Engl J Med*. 2021;384(1):20-30. <https://doi.org/10.1056/nejmoa2030340>.
53. Arabi YM, Mandourah Y, Al-Hameed F, Sindi AA, Almekhlafi GA, Hussein MA, et al. Corticosteroid therapy for critically ill patients with Middle East Respiratory Syndrome. *Am J Respir Crit Care Med*. 2018;197(6):757-67. <https://doi.org/10.1164/rccm.201706-1172oc>.
54. Moores LK, Tritschler T, Brosnahan S, Carrier M, Collen JF, Doerschug K, et al. Prevention, diagnosis, and treatment of VTE in patients with coronavirus disease 2019: CHEST Guideline and Expert Panel Report. *Chest*. 2020;158(3):1143-63. <https://doi.org/10.1016/j.chest.2020.05.559>.
55. Moores LK, Tritschler T, Brosnahan S, Carrier M, Collen JF, Doerschug K, et al. Thromboprophylaxis in patients with COVID-19: a brief update to the CHEST Guideline and Expert Panel Report. *Chest*. 2022;162(1):213-25. <https://doi.org/10.1016/j.chest.2022.02.006>.
56. Farkouh ME, Stone GW, Lala A, Bagiella E, Moreno PR, Nadkarni GN, et al. Anticoagulation in patients with COVID-19: JACC Review Topic of the Week. *J Am Coll Cardiol*. 2022;79(9):917-28. <https://doi.org/10.1016/j.jacc.2021.12.023>.
57. Meyer NJ, Gattinoni L, Calfee CS. Acute respiratory distress syndrome. *Lancet*. 2021;398(10300):622-37. [https://doi.org/10.1016/s0140-6736\(21\)00439-6](https://doi.org/10.1016/s0140-6736(21)00439-6).
58. Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. *N Engl J Med*. 2020;383(25):2451-60. <https://doi.org/10.1056/nejmcp2009575>.