REUE | Review Article

Management of SARS-CoV-2 infection in the Emergency Department

Manejo de la infección por SARS-CoV-2 en urgencias

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Introduction

Infection by SARS-CoV-2 is having a major impact on public health, representing a continuous challenge in emergency departments due to increased patient volume, the need to establish dual care circuits, and the difficulty of making decisions regarding hospital admission or discharge.

In recent months, the high vaccination rate has led to a change in the natural history of the infection, since being vaccinated reduces the risk of disease progression and associated mortality. The impact of vaccination is clear. The emergence of treatments for patients with mild or moderate disease who do not require hospitalization further expands the tools available to fight the pandemic and improve outcomes for our patients.

Risk stratification for poor outcomes is one of the most important tasks of the emergency physician when making clinical decisions. Early in the pandemic, studies began to be published describing variables associated with increased mortality, and numerous risk-stratification models have since been published and presented as clinical support tools.

However, both the risk scales and the pivotal studies conducted to evaluate treatment efficacy have been conducted in unvaccinated populations, which are at higher risk of worse outcomes. Therefore, it may be difficult to assess the true effectiveness of treatments and to select those patients who should receive them because they are truly at risk of poor disease progression.

In this context, the Spanish Society of Emergency Medicine (SEMES) has decided to issue a position statement to help select patients eligible to receive specific COVID-19 therapy through the preparation of these recommendations. The document presented here also includes the evaluation procedures and risk-stratification tools that may be used in the daily clinical practice of emergency physicians.

Methodology

For the development of this document, the coordinator of the Infections Group (INFURG.SEMES) prepared an initial draft, which was presented and discussed in a meeting with the presidents or representatives of the SEMES groups from each Autonomous Community (Appendix). The version agreed upon in that meeting was distributed to all members of the Infections Group for review and commentary. Finally, the resulting manuscript was sent to three infectious disease specialists who acted as external reviewers.

Evaluation procedure

a) In all patients requiring hospital admission, a diagnostic test for active COVID-19 infection (PDIA) must be requested. The patient must remain under airborne isolation until the result is known. If an antigen test is performed and is positive, RT-PCR (polymerase chain reaction) is not required, and the patient should be considered positive.

b) Record comorbidities, especially those related to immunosuppression, as well as the patient's usual medications.

c) The COVID-19 laboratory profile in the emergency department should include at minimum: complete blood count, coagulation studies, urea, creatinine, sodium, potassium, glucose, C-reactive protein, transaminases, bilirubin, LDH, procalcitonin, and D-dimer.

d) Consider performing a baseline arterial blood gas analysis depending on oxygen saturation and the patient's clinical condition.

e) Ask and document the day of symptom onset and vaccination history.

f) Record respiratory rate and baseline oxygen saturation and saturation while receiving supplemental oxygen, indicating the FiO_2 being administered (if via nasal cannula, record liters per minute).

g) Consider obtaining microbiological samples if bacterial superinfection is suspected.

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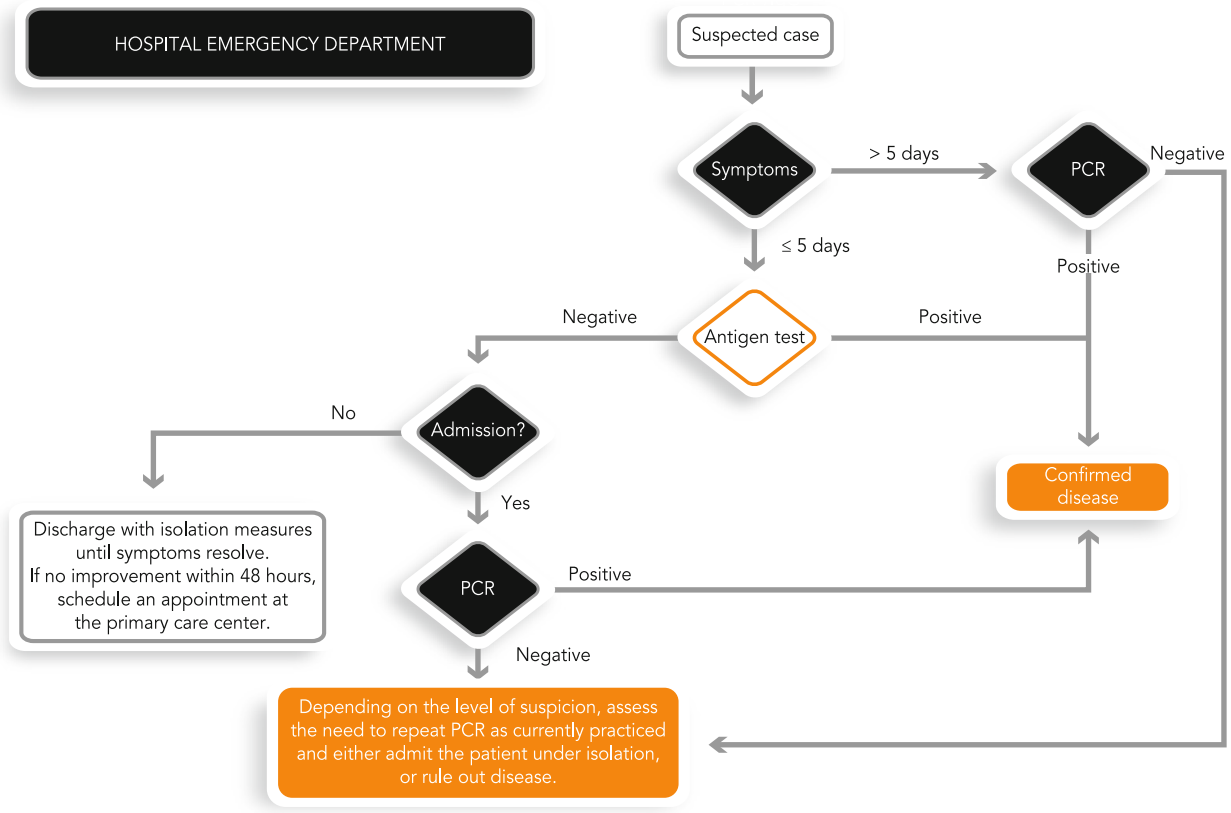

Figure 1. Microbiological diagnosis in patients with 0–5 days of symptoms. (Adapted from Candel FJ *et al.*[1]).

Microbiological diagnosis

Use antigen tests in patients with 0 to 5 days of symptoms1 (Figure 1).

Risk stratification

To stratify the risk of severe adverse events (including 30-day mortality), one of the following scales must be used:

Unvaccinated patients

– PrediCOVID-ED Scale. https://predicovid.shinyapps.io/RISK_MODEL_COVID/

– COVID-19 SEIMC Score.[2] https://covid19.seimc.org/index.php/seimc-score-mortalidad/

Vaccinated patients

– QCovid Risk – NHS.[3] https://bmjsept2021.qcovid.org

– Centers for Disease Control and Prevention.[4] https://www.cdc.gov/mmwr/volumes/71/wr/mm7101a4.htm

Admission criteria

Hospital admission is recommended for patients who meet any of the following criteria:

– Gasometric or clinical respiratory failure (consider RR > 24 rpm, oxygen saturation < 90%, or < 92% in those < 55 years).

– Severity criteria for pneumonia: PSI class 4–5.

– Hemodynamic instability.

– Organ failure: increase of ≥ 2 points in the SOFA score vs baseline.

– Active cancer under treatment or immunosuppression (Appendix 1) from any cause without the possibility of close home follow-up.

– Elevated inflammatory biomarkers: CRP > 75 mg/L.

Regardless of the above, there may be patients who, although not strictly meeting any criterion, require hospital admission due to their clinical condition. Similarly, some patients—after a period of observation in the emergency department and confirmation of good clinical evolution—may be safely discharged.

General therapeutic management

– Do not discontinue respiratory isolation in patients with a high clinical suspicion of COVID-19, even if PCR or antigen testing is negative.

– Avoid open-circuit aerosol therapies in the emergency department. When needed, use vibrating-mesh nebulizer systems. Prefer administration of bronchodilators via pressurized metered-dose inhaler with spacer, avoiding nebulization. If mechanical ventilation is required, ensure appropriate isolation conditions to protect other patients.

– Provide symptomatic treatment.

– Use conservative fluid management when there is no shock; avoid hypotonic solutions and gelatins.

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Table 1. Antivirals available for the treatment of patients with mild or moderate SARS-CoV-2 infection

	Nirmatrelvir–ritonavir	Sotrovimab	Casirivimab + imdevimab	Remdesivir	Molnupiravir
Mechanism of action	Viral protease inhibitor	Binds to the S protein, preventing viral attachment and cell entry	Binds to the S protein, preventing viral attachment and cell entry	Inhibits viral RNA polymerase	Catastrophic error due to accumulation of mutations in the virus via viral RNA polymerase
Efficacy	RR reduction 88% NNT: 18	RR reduction 85% NNT: 17	RR reduction 71% NNT: 19	RR reduction 87% NNT: 22	RR reduction 50-30% NNT: 35
Dose and duration	300/100 mg every 12 h 5 days	500 mg Single dose	600 mg/600 mg Single dose	Day 1: 200 mg Days 2–3: 100 mg	800 mg every 12 h 5 days
Route of administration	Oral	IV	IV	IV	VO
Therapeutic window	5 days	5 days	5 days	7 days	5 days
Advantages	High efficacy Oral administration	High efficacy Single dose	High efficacy Single dose	High efficacy Clinical experienceFew drug interactions	Oral administration No expected drug–drug interactions
Disadvantages	Drug–drug interaction Moderate renal impairment: 150 mg / 100 mg every 12 h Do not use if CrCl < 30 or Child-Pugh C	Requires IV infusion (30 min) with 1-hour observation	Requires IV infusion (30 min) with 1-hour observation	Must be given IV for 3 days Cannot be used if CrCl < 30	Lower efficacy
Notes	Effective against Omicron Carefully evaluate drug interactions: https://www.covid19-druginteractions.org/checker Monoclonal antibodies generally considered safe in pregnancy No data in pregnant women	Effective against Omicron Limited pregnancy safety data	Do not use for Omicron variant Monoclonal antibodies generally considered safe in pregnancy	Effective against Omicron Limited pregnancy safety data	Do not use in pregnancy

RR: relative risk; NNT: number needed to treat; Efficacy: reduction in progression to severe disease (composite of hospitalization + death); CrCl: creatinine clearance; RI: renal impairment; PO: oral route; IV: intravenous route.
(Adapted from Ghandi RT *et al.*[8]).

Emergency department treatment for patients requiring hospital admission

A. General measures

– Antibiotic therapy is not initially recommended. If bacterial superinfection is suspected—very uncommon—the antibiotic of choice is ceftriaxone (alternative: levofloxacin).

– In anticoagulated patients, switch to low-molecular-weight heparin (LMWH). If on acenocoumarol: switch when INR < 2. If on direct oral anticoagulants (DOACs): switch when the next dose is due. Doses: enoxaparin 1 mg/kg every 12 h SC or 1.5 mg/kg every 24 h; bemiparin 115 IU/kg every 24 h; tinzaparin 175 IU/kg every 24 h. Adjust dosing based on renal function.

– In clinically stable patients with mechanical heart valves, continuing acenocoumarol is suggested.

– In non-anticoagulated patients, prescribe LMWH thromboprophylaxis unless absolutely contraindicated (active bleeding, platelets < 30,000). In such cases, use intermittent pneumatic compression.

B. Anti-inflammatory treatment

– Dexamethasone 6 mg IV every 24 h. Recommended when low-flow oxygen is required to maintain SpO_2 > 94%.[5]

C. Antiviral treatment

– Remdesivir. Recommended if low-flow oxygen is needed to maintain SpO_2 > 94% in patients within 10 days of symptom onset. Early administration is recommended.[6]

– In patients with mild or moderate SARS-CoV-2 infection (respiratory and systemic symptoms but no hypoxia, tachypnea, or complications requiring hospitalization) who are admitted for another reason, but have risk factors for severe progression, consider remdesivir for 3 days[7] or a single dose of sotrovimab.[8]

Treatment in patients without admission criteria who will be discharged

A. General measures

– Bacterial superinfection is very rare in COVID-19, especially in mild outpatient cases.

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If clinically indicated: cefditoren 400 mg every 12 h ± azithromycin 500 mg every 24 h for 3 days, or amoxicillin 1 g every 8 h for 7 days ± azithromycin 500 mg every 24 h for 3 days, or levofloxacin 500 mg every 12–24 h for 7 days. Due to regulatory safety warnings on fluoroquinolones, levofloxacin is recommended as an alternative, not first-line.

– Venous thromboembolism prophylaxis: In general, it is not recommended. In patients with multiple risk factors [active cancer, history of deep vein thrombosis (DVT), pulmonary embolism (PE), immobilization], thromboprophylaxis at discharge is suggested.

B. Anti-inflammatory treatment

– Dexamethasone is not recommended.[5]

C. Antivirals

In non-admitted patients with risk factors for severe progression, antiviral therapy should be considered (Table 1).

Risk factors for severe disease progression include advanced age, chronic kidney disease, chronic liver disease, chronic neurological disease, chronic heart disease, chronic lung disease, diabetes, obesity (BMI > 35), and immunosuppression (Appendices 1 and 2).

Prioritization of Treatment Based on Availability:

1. Immunocompromised persons, regardless of vaccination status, prioritizing seronegative patients.

2. Unvaccinated individuals. Clinical trial inclusion criteria typically require age > 55–60 years or at least one comorbidity.

3. Vaccinated individuals. Given the impact of vaccination on disease evolution, treatment should be considered in older patients or those with multiple comorbidities.

These prioritization groups are based on mortality data published by the Spanish Ministry of Health and emerging research on vaccinated populations.[9-11]

Adendum

Presidents of the SEMES groups in each Autonomous Community, or their representatives involved in the discussion and preparation of this manuscript:

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Annex 1. Definition of immunosuppression

- Recipients of hematopoietic stem cell transplantation (HSCT) or CAR-T therapy, vaccinated within 2 years after transplantation/treatment, receiving immunosuppressive therapy, or with GVHD regardless of the time since HSCT.
- Solid organ transplant recipients.
- Renal replacement therapy (hemodialysis or peritoneal dialysis).
- Chemotherapy or radiotherapy within the previous 6 months for any indication.
- Primary immunodeficiencies.
- HIV infection with CD4 < 200/µL (laboratory result within the past 6 months).
- Cystic fibrosis.
- Down syndrome in adults aged ≥ 40 years (born in 1981 or earlier).
- Treatment with immunosuppressive drugs (Annex 2).

Annex 2. Definition of immunosuppressive treatment

- Continuous high-dose oral corticosteroids (≥ 20 mg/day of prednisolone for ≥ 10 consecutive days in the 30 days prior to vaccination).
- Prolonged oral corticosteroids at moderate doses (≥ 10 mg/day of prednisolone for > 4 consecutive weeks in the 30 days prior to vaccination).
- High-dose oral corticosteroids (> 40 mg/day of prednisolone for > 1 week) for any reason in the 30 days prior to vaccination.
- Treatment within the prior 3 months with non-biologic immunomodulators such as methotrexate (> 20 mg/week, oral or subcutaneous), 6-mercaptopurine (> 1.5 mg/kg/day), or azathioprine (> 3 mg/kg/day).
- Treatment with biologic immunomodulators in the prior 3 months.
- Anti–TNF-α monoclonal antibodies or TNF-α receptor analogues: infliximab, adalimumab, certolizumab, etanercept, and golimumab.
- Anti-CD20 monoclonal antibodies: rituximab, ocrelizumab, obinutuzumab, and ofatumumab.
- B-cell proliferation inhibitors: ibrutinib.
- T-lymphocyte co-stimulation suppressor fusion proteins: abatacept.
- Interleukin-1 (IL-1) inhibitors: anakinra, canakinumab.
- IL-6 receptor–blocking monoclonal antibodies: tocilizumab, sarilumab.
- Anti-α4β1 integrin monoclonal antibody: natalizumab.
- Anti-α4β7 integrin monoclonal antibody: vedolizumab.
- IL-12, IL-23, IL-17 monoclonal antibodies: ustekinumab, guselkumab, ixekizumab, tildrakizumab, risankizumab, secukinumab, and brodalumab.
- Anti-CD52 monoclonal antibody: alemtuzumab.
- Calcineurin inhibitors: tacrolimus and sirolimus.
- Antimetabolites: mycophenolate and cyclosporine.
- Sphingosine-1-phosphate receptor modulators: fingolimod, siponimod, ozanimod, and ponesimod.
- Janus kinase (JAK) inhibitors: tofacitinib, baricitinib, upadacitinib, and filgotinib.

Annex 3. Monoclonal antibodies

- Monoclonal antibodies are useful for preventing progression from mild to severe disease when administered to patients with risk factors for poor outcomes and within 10 days from symptom onset.
- Indicated in adults and adolescents (≥ 12 years old and ≥ 40 kg) who do not require supplemental oxygen and are at risk of progression to severe disease.
- Currently, they must be requested as medications in special situations. The report must include: immunosuppression status, patient serologic status (when possible), risk factors for poor outcomes, and the MASS score.[12]

MASS score[12]

Age ≥ 65 (2 points)
BMI ≥ 35 (1 point)
Diabetes mellitus (2 points)
Chronic kidney disease (3 points)
Cardiovascular disease other than hypertension in ≥ 55 years (2 points)
Chronic respiratory disease in ≥ 55 years (2 points)
Hypertension in ≥ 55 years (1 point)
Immunosuppression (3 points)

- The activity of each compound against circulating viral variants must be considered. Only sotrovimab is effective against the Omicron variant, currently predominant. When possible, PCR-based variant suspicion should guide monoclonal antibody selection.
- Available monoclonal antibodies:
  1. **Sotrovimab.** Recommended dose: single IV infusion of 500 mg diluted, administered over 30 minutes. Monitor patients during infusion and for at least 1 hour afterward. No dose adjustment is required in elderly or renally impaired patients.[13]
  2. **Ronapreve.** Recommended dose: single IV infusion containing casirivimab (600 mg) + imdevimab (600 mg) over 30 minutes. Subcutaneous administration should not be used for treatment. No dose adjustment required for older adults or patients with renal or hepatic impairment.[14]

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