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Perioperative management of the patient with suspected or confirmed COVID-19 infection

Manejo perioperatorio del paciente con sospecha o confirmación de infección por COVID-19

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Keywords: COVID-19, perioperative management, personal protective equipment, cytokines.

Palabras clave: *COVID-19, manejo perioperatorio, equipo de protección personal, citoquinas.*

ABSTRACT

SARS-CoV-2 affects the host using the angiotensin-converting enzyme 2 (ACE2) receptor. The first step in virus entry is the binding of the trimeric protein S (spike) of the virus to the human ACE2 receptor, which is expressed in multiple organs, including the lung, heart, kidney, and intestine, and most importantly in endothelial tissue. Within the main pathophysiology is the cytokine storm, the uncontrolled systemic inflammatory response that results from the release of large amounts of proinflammatory cytokines and chemokines by immuno-effector cells. The cytokine storm is coupled with the metabolic response to the trauma of surgery, resulting in an inflammatory hyper-response that can lead to multiple organ failure. Management of the patient with COVID-19 disease and surgery involves different medical and surgical specialties.

RESUMEN

El SARS-CoV-2 afecta al huésped utilizando el receptor de la enzima convertidora de angiotensina 2 (ACE2). El primer paso en la entrada del virus es la unión de la proteína trimérica S (spike) del virus al receptor ACE2 humano, el cual se expresa en múltiples órganos, como pulmón, corazón, riñón e intestino, y aún más importante, en el tejido endotelial. Dentro de la fisiopatología principal está la tormenta de citocinas, que da lugar a una respuesta inflamatoria sistémica no controlada que resulta de la liberación de grandes cantidades de citocinas proinflamatorias y quimiocinas por células inmunoefectoras. La tormenta de citocinas se une a la respuesta metabólica que implica el trauma de una cirugía, lo cual ocasiona una hiperrespuesta inflamatoria que puede llegar a la falla orgánica múltiple. El manejo del paciente con la enfermedad de COVID-19 y cirugía implica diferentes especialidades médicas y quirúrgicas.

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INTRODUCTION

In our academic lives we may have read about the pandemics that had struck mankind centuries before. We may have read about and perhaps managed patients with SARS, MERS, and even influenza; however, we had not faced such a large and difficult to control pandemic. We are facing a new virus, the SARS-CoV-2 virus which produces COVID-19. It is a virus with a positive single-stranded RNA genome.[1]

There are four groups of coronaviruses: alpha, beta, gamma, and delta. The genome of the SARS-CoV-2 betacoronavirus has 80% homology with the earlier SARS-CoV and 96% homology with the bat coronavirus Bat-CoV RaTG13, so it is thought that it may

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be derived from a coronavirus originating from bats.[2]

During the 21st century, coronaviruses have evolved three times to be able to infect people: in 2002 with SARS-CoV and in 2012 with MERS-CoV, both beta coronaviruses. The outbreak of the current coronavirus in 2019 has resulted in a global pandemic with unpredictable consequences.

The main route of transmission is by person-to-person contact and respiratory droplets produced by talking, coughing, or sneezing. "Flügge droplets" are tiny droplets (more than 5 microns) produced naturally when talking, coughing, or sneezing by an infected person. When discharged from the nose or mouth, these droplets can reach the mucous membranes of the mouth, nose or eyes of another person and transmit the virus to them if they are nearby.[3] It is important to know that these droplets do not remain suspended in the air but are deposited rapidly up to just under one meter. Once deposited, the virus can be detected up to three hours after aerosol administration, four hours on a copper surface, 24 hours on cardboard, and up to two to three days on plastic and steel.[3] Therefore, the most effective way to stop transmission is to increase hygiene and social distancing measures and individual protection.

PATHOPHYSIOLOGY

SARS-CoV-2 affects the host using the angiotensin-converting enzyme 2 (ACE2) receptor. The first step in virus entry is the binding of the trimeric protein S *(spike)* of the virus to the human ACE2 receptor, which is expressed in multiple organs, including the lung, heart, kidney, and intestine, and most importantly in endothelial tissue. The virus is internalized using the endocytic pathway into endosomes using a clathrin-and caveolin-independent mechanism, while requiring cholesterol and sphingolipid-rich microdomains or *lipid rafts*. Endothelial cells are found throughout much of the body, including blood vessels. The cause of the alterations caused at the vascular level by COVID-19 is still not fully understood. However, the damage at the vascular level of different organs affecting human engineering through endothelial tissue has been proven.

Cytokine storm: one of the main mechanisms of acute respiratory failure syndrome (ARDS) is the so-called cytokine storm, or also cytokine release syndrome. It is an uncontrolled systemic inflammatory response resulting from the release of large amounts of proinflammatory cytokines (interleukin [IL]-1b, IL-6, IL-10, IL-12, interferon [IFN]-alpha, IFN-gamma, TNF-alpha, and/or TGF-beta, etc.) and chemokines (CCL2, CCL3, CCL5, CXCL8, and/or CXCL10, etc.) by immunoeffector cells, e.g., macrophages activated by SARS-CoV, MERS, and SARS-CoV-2 infection.[4,5] The cytokine storm will cause ARDS and multiple organ failure, and ultimately lead to death in severe cases of infection.

Another important concept is secondary hemophagocytic lympho-histiocytosis (sHLH), also known as macrophagic activation syndrome,[6] which is a hyperinflammatory syndrome characterized by fulminant and fatal hyper-cytokinemia with multiorgan failure. HLHS is frequently triggered by viral infections.[6,7] The main features of sHLH include fever, cytopenias, and hyper ferritinemia. ARDS may be seen in up to 50% of patients.

A cytokine profile like sHLH is associated with severity of COVID-19 disease.[8] Indeed, in most patients, ferritin and IL-6 are found to be very elevated, being higher in patients who died, suggesting that mortality may be due to viral hyperinflammation.[8]

There is evidence of viral infection in endothelial cells along with diffuse endothelial inflammation. The virus uses the ACE 2 receptor expressed by pneumocytes in the alveolar epithelial lining to infect the host causing lung injury; it can also be expressed in other organs.[9]

Recruitment of immune cells, either by direct viral infection of the endothelium or immunomodulated, can result in generalized endothelial dysfunction associated with apoptosis. The vascular endothelium is an active paracrine, endocrine, and autocrine gland that is indispensable in the regulation

of vascular tone and maintenance of vascular homeostasis.[9,10]

Endothelial dysfunction is the primary determinant of microvascular dysfunction, causing increased vasoconstriction with subsequent organ ischemia, with inflammation associated with tissue edema and causing a procoagulant state.[11]

Viral elements have been found among endothelial cells and inflammatory cell accumulation with evidence of both endothelial and inflammatory cell death. This suggests that SARS-CoV-2 facilitates the induction of endothelitis in various organs as a direct consequence of viral development and host immune response. Likewise, apoptosis and pyroptosis also play an important role in endothelial injury.[11]

This endothelitis caused by SARS-CoV-2 may explain the microcirculatory alterations in the vascular bed and the clinical sequelae that occur in COVID-19 survivors. On the other hand, in the clinical presentation of severe cases of COVID-19, lymphopenia, higher levels of ferritin and D-dimer, as well as IL-2R, IL-6, IL-10 and TNF-alpha, among others, are observed. The absolute number of CD4+ and CD8+ lymphocytes decrease significantly more in severe patients, and the frequency of TCD4+ cells tend to be lower in severe cases. Somehow, it is as if the T cells remaining in the circulation, in addition to being decreased in number, appear to be functionally depleted.[12]

In short, the accumulated evidence so far indicates that patients with severe COVID-19 usually suffer a cytokine storm, and this altered immune response should be considered, as it has very relevant implications for the treatment of patients. Therefore, it is advisable to treat the hyperinflammatory state of these patients.

This hypothesis justifies the use of different treatments to stabilize the endothelium while viral replication is present, particularly with anti-inflammatory drugs, anti-cytokine drugs, ACE inhibitors, and statins.[9,13,14]

This strategy is particularly relevant for vulnerable patients with pre-existing endothelial dysfunction, which is associated with male sex, smoking, arterial hypertension, diabetes mellitus, obesity, and established cardiovascular disease, all associated with adverse outcomes in COVID-19.

HOW DOES ALL THIS HELP US IN SURGICAL PATIENTS?

Different studies have shown that surgical patients are part of a group vulnerable to SARS-CoV-2 exposure in hospitals and mainly susceptible to pulmonary complications, due to the proinflammatory cytokine response and immunosuppressive response to surgery and mechanical ventilation.

The exact impact of surgical stress and anesthesia (with the expected associated inflammation as well as other common complications such as the occurrence of atelectasis) on the predisposition to new COVID-19 infection or exacerbation of infection in an asymptomatic COVID-positive patient undergoing surgery is unknown.[15] Based on current evidence, although the mortality of COVID-19 is believed to be between 1-3%, most deaths have occurred in elderly patients with underlying cardiopulmonary conditions, most of whom are hypertensive, diabetic, and obese.[15-17]

In a publication in *The Lancet*[16] investigators examined data from 1,128 patients with perioperative COVID-19 at 235 hospitals. Overall, the 30-day mortality rate in the study was 23.8%. Mortality was disproportionately high in all subgroups, including elective surgery (18.9%), emergency surgery (25.6%), minor surgery such as appendix surgery or hernia repair (16.3%), and major surgery such as hip surgery or colon cancer surgery (26.9%). Operated patients may be susceptible to subsequent pulmonary complications caused by inflammatory and immunosuppressive reactions to surgery and mechanical ventilation.[16]

Postoperative patients are another group of patients in whom COVID-19 infection is a diagnostic challenge and has a high mortality rate. A complicated postoperative course can be observed, especially in elderly patients with underlying health conditions.

In this context, the risk and benefit of performing elective surgical procedures should be carefully evaluated. In some

situations, postponing elective surgical procedures may be the right decision, with consideration also given to preserving resources, including personal protective equipment, and maintaining treatment space for critically ill patients.[18-20]

The main complication arises from the cytokine storm in the pulmonary epithelium (the organ where most of the epithelial tissue is located) and the immediate silent hypoxia in these patients, especially if they were intubated. It should be remembered that the complications that a patient infected with COVID-19 may present are ARDS (acute respiratory distress syndrome) 90%, respiratory failure 83%, secondary or nosocomial infection 27.3%, acute cardiac failure 9.1%, encephalopathy with hypoxia 18.2%, acute renal failure 18.2%, shock 9.1%, and hepatic failure 9.1%. If the patient is immunocompromised, complications may be more severe and multiple organ failure and death may occur.

If the patient is known to be infected with COVID-19, immediate treatment for SARS-CoV-2 should be given and treatment for the presenting surgical condition should be concurrent. But if the patient is not known to be infected but is in fact infected, or is an asymptomatic carrier, the problem may occur in the perioperative period.

The cytokine storm is coupled with the metabolic response to trauma, resulting in an inflammatory hyper-response, which can lead to multiple organ failure.

General surgery associations and societies have issued special considerations for the performance of surgical procedures[20-24] since the beginning of the health contingency.[21,22] There are no conclusive studies that indicate greater contamination by aerosols produced in laparoscopy compared to open surgery, but fewer infections have been observed when the surgical teams are wearing personal protective equipment, remembering that the greatest risk of infection occurs during intubation and extubation of the patient.

On the other hand, cases of time-sensitive diseases (oncologic) should be performed by carefully selecting surgeries and patients as well as emergency surgeries, since not performing them means condemning these patients to a poor prognosis regardless of the pandemic.[23,24] According to the ASA *(American Society of Anesthesiologists)* physical status, in time sensitive procedures the ASA I or II patient can be operated on; in the case of the ASA III patient with a history of diabetes, arterial hypertension, congestive heart failure, immunosuppression and in the case of ASA IV or higher patients requiring intensive care or massive transfusion, and where possible complications may outweigh the benefit, the recommendation is that they should be cancelled and other treatment alternatives should be sought.[15]

PROTECTIVE EQUIPMENT DURING THE PERIOPERATIVE PERIOD

Protection of personnel is a priority; if health personnel become ill, they deplete the workforce to fight the pandemic, becoming just another patient to be cared for, and putting other personnel at risk.

The recommendations are very clear when it is necessary to intubate COVID-19 positive or suspected patients, and complete personal protective equipment (PPE) is indispensable and care such as planning transportation routes from one room to another, and management protocols have already been universally proposed. However, there is another facet: the perioperative context of healthy or apparently healthy patients, since it has been estimated that the proportion of asymptomatic patients is 17.9%. However, this is variable, since experience has shown that there can be up to 80% of asymptomatic patients during an incubation period of the SARS-CoV-2 virus of five days or more and the development of symptoms, so there are COVID-19 positive patients who can be transmitters during this period[25] so precautions should be taken at the time of surgery to avoid infecting or infecting them.

General anesthesia is recommended for patients with suspected or confirmed COVID-19 to reduce the risk of cough. Other types of anesthesia may be selected depending

on the type of surgery and individual patient needs. It should be remembered that intubation and extubation should be performed inside the operating room (with surgeons not required to be present in the room).[15,20]

Several studies have identified that immediate postoperative pulmonary complications occur in half of patients with perioperative SARS-CoV-2 infection and are associated with high mortality. This has direct implications for clinical practice worldwide. These increased risks associated with SARS-CoV-2 infection should be weighed in the balance and consideration given to decreasing these risks by delaying surgery. The patients most vulnerable to adverse outcomes are male, those aged 70 years or older, those with comorbidities (ASA grades 3-5), patients with cancer surgery, and those requiring major or emergency surgery.[18,19]

Greater care should be taken during the pandemic than is the case in normal or routine practice. Male patients aged 70 years or older who have surgery, whether emergency or elective, are at increased risk, particularly of high mortality, although minor elective surgery has also been associated with higher than usual mortality.

During SARS-CoV-2 outbreaks, consideration should be given to postponing non-critical procedures and promoting non-surgical treatments to delay or avoid the need for surgery.

However, if surgery must be performed, it should be remembered that postoperative outcomes in SARS-CoV-2 infected patients have higher morbidity and mortality than the pre-pandemic baseline rates of pulmonary complications and mortality. Thirty-day postoperative mortality of 23.8% has been reported, including all surgical patients. The highest mortality in SARS-CoV-2 patients was primarily in those who had postoperative pulmonary complications, which was approximately 50% of patients.[18] In the subgroups of elective surgery patients, mortality was 18.9%, in emergency surgery patients was 25.6%, in minor surgery patients was 16.3%, and 26.9% in major surgery patients.[18]

WHAT DOES THE SURGEON HAVE TO DO?

The first thing the surgeon should keep in mind is that any patient may be a carrier of COVID-19, even if he or she presents asymptomatic.

Therefore, the surgeon must keep relevant hygiene measures.[26]

1. Appropriate use of personal protective equipment (PPE): the use of personal protective equipment is recommended for every surgical procedure performed on a patient with a confirmed COVID-19 infection or a patient in whom infection is suspected *(Table 1)*.
2. N95 respirators, respirators or filters offering a higher level of protection should be used when an aerosol-generating procedure (e.g., patient intubation in the operating room, nasogastric tube placement) is to be performed on infected or suspected COVID-19 patients.
3. Disposable respirators and respirator masks should be removed and disposed of properly in the appropriate containers.
4. Perform hand hygiene after disposing of respirator or mask.
5. It is necessary to learn how to put on and remove the PPE (the ideal is to have an instructor). Fit testing is essential to ensure proper fit of the mask *(Table 1)*.
6. In the operating room or in the office or intensive care unit, the number of people should be as few as possible.
7. The transportation of the patient after surgery or from the emergency room to another destination must follow a strict protocol and with the minimum number of personnel and always with PPE.
8. Frequent hand hygiene is indispensable.[26]
9. Operating rooms with negative pressure and/or similar anterooms are recommended when available.
10. Appropriate PPE should be used according to the institution's policy as well as the intraoperative protocol.
11. It is necessary for all health personnel to be aware of the permanence of COVID-19 on different surfaces, being infectious (e.g.,

cardboard one day, plastic three to four days).

12. Have a minimum number of personnel in the operating room, including during intubation, as well as during the entire surgery or procedures. There should be no visitors or observers.
13. Use the smoke evacuator or aspirator when using electrocautery.
14. Post-operative/recovery: Transportation of a patient with COVID-19 or suspected COVID-19 infection to an outside recovery area or intensive care unit should be attended by a minimum number of transport personnel waiting outside the operating room. Personnel should wear personal protective equipment. This equipment should not be the same as that used during the procedure.
15. Recommendations for surgeon protection before and after separation from a patient with suspected COVID-19 infection vary from institution to institution. However, those that are universally called for are:
    a. Remove used clothing from home and store in a garment bag.
    b. Wear laundry after arrival at the hospital.
    c. After separating from the patient, remove clothing for laundering, and consider bathing before wearing clean suit or home clothes.
    d. Wash hands frequently and maintain safe social distancing.
16. Once at home: what should be done to keep the family safe?
    a. In some countries, health care institutions and/or systems have hotel or other accommodations for health

Table 1: Recommendations for personal protective equipment. *University of Kansas Health System.*

Non-suspected COVID-19 patient care	Care of the suspected or confirmed COVID-19 patient (if the maximum distance is 90 cm between patient and physician, the patient should also wear a surgical mask)	Aerosolizing procedures in suspected or confirmed COVID-19 patients and in all patients submitted to airway procedures
When:		
• Asymptomatic patient • Minimum distance of 150 cm from the patient for less than one minute	• COVID-19 asymptomatic patient • Positive or pending COVID-19 test	• All procedures resulting in aerosolization
Where:		
• Medical offices • Emergency services • Acute care medical units • Intensive Care Units • Procedure rooms	• Medical offices • Emergency services • Acute care medical units • Intensive Care Units • Procedure rooms	• Medical offices • Emergency services • Acute care medical units • Intensive Care Units • Procedure rooms
PPE required:		
• Surgical mask	• Eye protection/face shield • Surgical mask • Coverall/gowns • Gloves	• Respirator N95 or PAPR + face shield + eye protection • Coverall/gowns • Gloves

All categories: hand washing before and after patient care regardless of isolation.
PPE = personal protective equipment, PAPR = powered air-purifying respirator.

care workers who cannot or prefer not to go home after their activities.
b. Make the family aware that viral contamination of surfaces is a known means of infection transmission.
c. Maintain hand sanitizer and/or disposable gloves for use of ATMs, vending machines, gas pumps, and transfer of items at the time of purchase.
d. Clean cell phones frequently before, during, and after patient care activities. Cell phones may be stored in a sealable bag during work activities. The phone can be used inside the bag.
e. You must remove your clothes and wash them when you get home.
f. Reduce physical contact with family members and wash hands frequently.
g. Clean hard surfaces at home with an effective disinfectant solution (e.g., 70% alcohol).[26]

TREATMENT OF PATIENTS CONFIRMED OR SUSPECTED OF COVID-19[27,28]

Fist consideration is that of the surgical pathology that the patient needs; however, as already explained, it should be given at the same time as the treatment for atypical viral pneumonia.

1. Hypoxemia management. If a patient is admitted to the intensive care unit (ICU) it is because his/her life is at risk, or he/she has failure of one or more organs, or the hemodynamics are altered. Respiratory failure is the primary and most common in COVID-19 cases and oxygen should be administered immediately. In adult patients with COVID-19 and acute respiratory distress syndrome (ARDS) and respiratory distress, hypoxemia, or shock (without intubation or mechanical ventilation), immediate supplemental oxygen is recommended until $SpO_2 \geq 94\%$ is achieved.
   The use of high-flow nasal cannula oxygen therapy and noninvasive mechanical ventilation (NIMV) should be restricted to units where only patients with suspected or confirmed COVID-19 are hospitalized in an adequate ventilation or negative pressure environment and if all personnel in the area correctly use aerosol protection measures. If this is not possible, mechanical ventilation with orotracheal intubation should be preferred. In adult patients under mechanical ventilation and ARDS it is recommended to use low tidal volumes (4 to 8 ml/kg predicted body weight) maintaining plateau pressures below 30 cm H_2O. Use positive end-expiratory pressure (PEEP) for alveolar recruitment (optimal PEEP) and if necessary, use the prone position for 12 to 16 hours (some articles mention up to 36 hours) to improve hypoxemia.[29]
2. Hemodynamic management. The hemodynamic pattern *per se* of patients with COVID-19 is not yet known; however, it is important to measure blood volume on admission and to initiate conventional hydric resuscitation according to the patient's clinical picture to avoid hydric over-resuscitation. The dynamic parameters normally used are internationally valid: central venous pressure, pulmonary pressure and occlusion (invasive), systolic volume variation, pulse pressure variation, skin temperature, capillary filling time, or lactate measurement. Hydric resuscitation is recommended to be done with balanced crystalloid solutions such as 0.9% saline or lactated Ringer's solution. It is not recommended to use hydroxyethyl starches, gelatins, or dextran, or to use albumin for hydric resuscitation and/or intravascular volume expansion.[29,30]
3. If shock persists despite hydric resuscitation, norepinephrine should be administered as a first-line vasoactive agent instead of other agents. In the absence of norepinephrine, epinephrine or vasopressin may be used as first line over other inotropic agents. The dose of the vasoactive drug should be increased until a mean arterial pressure (MAP) of 60-65 mmHg is reached. It is suggested that vasopressin be added (not

changed) as a second-line agent when vasopressor association is required if the expected MAP is not achieved by norepinephrine.[29]

4. Steroids. There is discussion on the administration of systemic steroids: the first line is, if the administration of two vasoactive agents is necessary, corticosteroids are administered. The second: in patients with mechanical ventilation and respiratory failure without ARDS, administration of systemic corticosteroids is not suggested. However, in patients with ARDS, after the fifth day, it is suggested to start corticosteroids to avoid pulmonary fibrosis as much as possible.[29,30] Third: lately European studies, basically from the United Kingdom, suggest the administration of dexamethasone to reduce the hyperinflammatory state 6 mg IV for five days.[31]
5. Antibiotics. It is suggested to use antimicrobial agents empirically for five to seven days according to institutional protocols considering the clinical diagnosis (e.g., community-acquired/atypical pneumonia, sepsis) and local data of bacterial resistance. Third generation cephalosporins plus a macrolide may be used. Antibiotic administration should be initiated within one hour of patient evaluation. In surgical patients, if the underlying pathology is sepsis or associated with sepsis, the ideal is to start with first line carbapenems (such as ertapenem) and if anaerobic germs are suspected start metronidazole, always PLUS a macrolide (clarithromycin/azithromycin).
6. Antivirals. Lopinavir is a human immunodeficiency virus (HIV) type 1 aspartate protease inhibitor. Ritonavir inhibits CYP3A-mediated metabolism of lopinavir, thereby increasing serum concentration of lopinavir, hence the combination: lopinavir-ritonavir. Previously, during SARS and MERS outbreaks, they were used with some good results. Currently, in severe patients, the response is good.
7. Thromboprophylaxis/anticoagulation. Hospitalized patients, critical or not, can be complicated by sepsis-induced coagulopathy, disseminated intravascular coagulation, or venous thromboembolism due to prolonged bed rest, amongst other causes. However, critically ill patients with COVID-19 appear to be particularly predisposed to thrombotic complications. As in all surgical patients, antithrombotic prophylaxis should be managed; however, in the case of patients with SARS-COV-2 pneumonia, thrombosis is a continuous state, according to the physiology already explained. Ideally, D-dimer and fibrinogen should be measured, and prophylaxis or anticoagulation should be decided according to their test results. Conventional heparin or low molecular weight heparin is recommended. These drugs mainly prevent venous thromboembolism as well as micro embolism occurring at pulmonary, cardiac and cerebral levels (including ischemic attack, systemic arterial embolism and/or myocardial infarction).[29-31]
8. Interleukin-6 inhibitors (tocilizumab). Tocilizumab is a humanized immunoglobulin that blocks the IL-6 receptor. It is used to block severe T-cell response or life-threatening cytokine release syndrome (cytokine storm).[30,31]
9. Convalescent patient plasma. This is the blood plasma of a person who has recovered from an infection and contains neutralizing antibodies against the offending agent. It is considered as a form of passive immunotherapy. Convalescent patient plasma has been explored as a treatment option in SARS and severe influenza. It is still under study, and while initial results appear to be promising, the evidence is limited by the observational nature of the current studies and the size of the samples (very small). Recently, the FDA and here in Mexico studies are currently in place in selected specialized research centers and only in severe patients.

Severe SARS-CoV-2 pneumonia disease was defined as patient with dyspnea,

respiratory rate ≥ 30/min, SpO_2 ≤ 93%, Kirby index (PAFI) < 300, and/or pulmonary infiltrates > 50% in 24 to 48 hours. Life-threatening illness is defined as respiratory failure, septic shock, and/or multiple organ dysfunction or failure. Eligible plasma donors need to have a history of COVID-19 disease proven by positive PCR testing and be IgG positive; complete resolution of symptoms at least 28 days prior to donation or complete resolution of symptoms at least 14 days prior to donation and negative PCR testing for COVID-19; negative testing for human leukocyte antigen (HLA) antibodies, with defined SARS-CoV-2 neutralizing antibody titers (e.g., greater than 1:80).

Potential risks of this plasma transfusion include pathogen transmission, anaphylaxis, transfusion-associated circulatory reactions; and transfusion-related acute lung injury and overload (TRALI).[30-32]

10. Remdesivir (GS-5734). A viral RNA-dependent RNA polymerase inhibitor with inhibitory activity against SARS-CoV and Middle East respiratory syndrome (MERS-CoV),[4-7] was identified early on as a promising therapeutic candidate for COVID-19 because of its ability to inhibit SARS-CoV-2 *in vitro*.[8] It has been observed that initiation of remdesivir 12 hours after inoculation with MERS-CoV9,[10] reduced pulmonary virus levels and lung damage. In the latest study reported in the *New England Journal of Medicine*, where remdesivir was administered for patients hospitalized with COVID-19 and requiring supplemental oxygen therapy, among its conclusions it highlights that despite a faster recovery and withdrawal of mechanical ventilation in fewer days, given the high mortality despite the use of remdesivir it is clear that treatment with an antiviral drug alone is not sufficient. Future strategies should evaluate antiviral agents in combination with other therapeutic approaches or combinations of antiviral agents to continue to improve patient outcomes in COVID-19.[31,33]

CONCLUSIONS

In conclusion, treatment should first address the underlying pathology and, depending on the severity of the pneumonia and the altered target organs, continue with comprehensive management. Always, the ideal is always team-making decisions (surgery + critical care + infectious diseases) for the patient's recovery.

Once hospitals resume routine surgery, it is likely to be in settings that remain exposed to SARS-CoV-2. In the future, routine preoperative screening for SARS-CoV-2 may be possible with rapid tests that have low false-positive rates, but hospital-acquired infection remains a challenge [27,28]. Strategies are urgently needed to minimize hospital transmission of SARS-CoV-2 and mitigate the risk of postoperative pulmonary complications in SARS-CoV-2-infected patients whose surgery cannot be delayed. In Mexico, some hospitals have been declared as COVID-19 sites in order to be prepared for the contingency; however, given the natural history of the disease, its dissemination and epidemiological prognosis, the initial organization does not exempt the rest of the hospitals from being involved in the care of patients infected with COVID-19, which implies the participation of the entire health system of the country. As specialists, we have a strong commitment, and knowing the disease and protecting ourselves will be our best weapons during this pandemic.

REFERENCES

1. Spanish Society of Immunology. Information about COVID-19. Version cov01. April 2020.
2. Guo YR, Cao QD, Hong ZS, et al. The origin, transmission, and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak-an update on the status. Mil Med Res. 2020; 7: 11. doi: 10.1186/s40779-020-00240-0.
3. Van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. N Engl J Med. 2020; 382:1564-1567. doi: 10.1056/NEJMc2004973.
4. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in

Wuhan, China. Lancet. 2020; 395: 497-506. doi: 10.1016/S0140-6736(20)30183-5.
5. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: Causes and consequences of cytokine storm and immunopathology. Semin Immunopathol. 2017; 39: 529-539. doi: 10.1007/s00281-017-0629-x.
6. Karakike E, Giamarellos-Bourboulis EJ. Macrophage activation-like syndrome: a distinct entity leading to early death in sepsis. Front Immunol. 2019; 10: 55. doi: 10.3389/fimmu.2019.00055.
7. Kan FK, Tan CC, Von Bahr Greenwood T, et al. Dengue infection complicated by hemophagocytic lymphohistiocytosis: experiences from 180 patients with severe dengue. Clin Infect Dis. 2020; 70: 2247-2255. doi: 10.1093/cid/ciz499.
8. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020; 395: 1033-1034. doi: 10.1016/S0140-6736(20)30628-0.
9. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. Lancet. 2020; 395: 1417-1418. doi: 10.1016/S0140-6736(20)30937-5.
10. Ferrario CM, Jessup J, Chappell MC, et al. Effect of angiotensin-converting enzyme inhibition and angiotensin II receptor blockers on cardiac angiotensin-converting enzyme 2. Circulation. 2005; 111: 2605-2610.
11. Flammer AJ, Anderson T, Celermajer DS, et al. The assessment of endothelial function: from research into clinical practice. Circulation. 2012; 126: 753-767. doi: 10.1161/CIRCULATIONAHA.112.093245.
12. Chen G, Wu D, Guo W, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020; 130: 2620-2629.
13. Anderson TJ, Meredith IT, Yeung AC, et al. The effect of cholesterol lowering and antioxidant therapy on endothelium-dependent coronary vasomotion. N Engl J Med. 1995; 332: 488-493.
14. Feldmann M, Maini RN, Woody JN, et al. Trials of anti-tumour necrosis factor therapy for COVID-19 are urgently needed. Lancet. 2020; 395: 1407-1409. doi: 10.1016/S0140-6736(20)30858-8.
15. Garduño-López AL, Guido-Guerra RE, Guizar-Rangel MT, et al. Perioperative management of the patient with COVID-19. Rev Mex Anest. 2020; 43: 109-120.
16. COVIDSurg Collaborative. Mortality and pulmonary complications in patients undergoing surgery with perioperative SARS-CoV-2 infection: an international cohort study. Lancet. 2020; 396: 27-38. doi: 10.1016/S0140-6736(20)31182-X.
17. Myles PS, Maswime S. Mitigating the risks of surgery during the COVID-19 pandemic. Lancet. 2020; 396: 2-3. doi: 10.1016/S0140-6736(20)31256-3.
18. Peng PWH, Ho PL, Hota SS. Outbreak of a new coronavirus: what anaesthetists should know. Br J Anaesth. 2020; 124: 497-501. doi: 10.1016/j.bja.2020.02.008.
19. Aminian A, Safari S, Razeghian-Jahromi A, Ghorbani M, Delaney CP. COVID-19 outbreak and surgical practice: unexpected fatality in perioperative period. Ann Surg. 2020; 272: e27-e29. doi: 10.1097/SLA.0000000000003925.
20. Brindle M, Gawande A. Managing COVID-19 in surgical systems. Ann Surg. 2020; 272: e1-e2. doi: 10.1097/SLA.0000000000003923.
21. Zheng MH, Boni L, Fingerhut A. Minimally invasive surgery and the novel coronavirus outbreak: lessons learned in China and Italy. Ann Surg. 2020; 272: e5-e6. doi: 10.1097/SLA.0000000000003924.
22. American College of Surgeons. COVID-19: elective case triage guidelines for surgical care. 2020.
23. Ti LK, Ang LS, Foong TW, Ng BSW. What we do when a COVID-19 patient needs an operation: operating room preparation and guidance. Can J Anaesth. 2020; 67: 756-758. doi: 10.1007/s12630-020-01617-4.
24. Wong J, Goh QY, Tan Z, et al. Preparing for a COVID-19 pandemic: a review of operating room outbreak response measures in a large tertiary hospital in Singapore. Can J Anaesth. 2020; 67: 732-745.
25. Mizumoto K, Kagaya K, Zarebski A, Chowell G. Estimating the asymptomatic proportion of coronavirus disease 2019 (COVID-19) cases on board the Diamond Princess cruise ship, Yokohama, Japan, 2020. Euro Surveill. 2020; 25: 2000180.
26. American College of Surgeons. COVID-19: considerations for optimal surgeon protection before, during, and after operation. March 27, 2020.
27. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020; 395: 1054-1062.
28. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020; 323: 1061-1069.
29. Guidelines for the Critical Care of Critically Ill Adult Patients with Coronavirus (COVID-19) in the Americas. Pan American Health Organization (PAHO), World Health Organization (WHO). April 3, 2020.
30. Xu X, Ong YK, Wang Y. Role of adjunctive treatment strategies in COVID-19 and a review of international and national clinical guidelines. Mil Med Res. 2020; 7: 22. doi: 10.1186/s40779-020-00251-x.
31. Phua J, Weng L, Ling L, et al. Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations. Lancet Respir Med. 2020; 8: 506-517. doi: 10.1016/S2213-2600(20)30161-2.
32. COVID-19 Treatment Guidance Writing Group. JHMI Clinical Guidance for Available Pharmacologic Therapies 2020, 25 March 2020. Available at: https://www.hopkinsguides.com/hopkins/view/Johns_Hopkins_ABX_Guide/540747/all/Coronavirus_COVID_19__SARS_CoV_2_.
33. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19-preliminary report. N Engl J Med. 2020; NEJMoa2007764.

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