



## SPECIAL ARTICLE

# Recommendations of the Working Groups from the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC) for the management of adult critically ill patients in the coronavirus disease (COVID-19)<sup>☆</sup>



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**PALABRAS CLAVE**

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**Abstract** On March 11, 2020, the Director-General of the World Health Organization (WHO) declared the disease caused by SARS-CoV-2 (COVID-19) as a pandemic. The spread and evolution of the pandemic is overwhelming the healthcare systems of dozens of countries and has led to a myriad of opinion papers, contingency plans, case series and emerging trials. Covering all this literature is complex. Briefly and synthetically, in line with the previous recommendations of the Working Groups, the Spanish Society of Intensive, Critical Medicine and Coronary Units (SEMICYUC) has prepared this series of basic recommendations for patient care in the context of the pandemic.

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**Recomendaciones de «hacer» y «no hacer» en el tratamiento de los pacientes críticos ante la pandemia por coronavirus causante de COVID-19 de los Grupos de Trabajo de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC)**

**Resumen** El 11 de marzo de 2020 el director general de la Organización Mundial de la Salud (OMS) declaró la enfermedad causada por el SARS-CoV-2 (COVID-19) como una pandemia. La propagación y evolución de la pandemia está poniendo a prueba los sistemas sanitarios de decenas de países y ha dado lugar a una miríada de artículos de opinión, planes de contingencia, series de casos e incipientes ensayos. Abarcar toda esta literatura es complejo. De forma breve y sintética, en la línea de las anteriores recomendaciones de los Grupos de Trabajo, la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC) ha elaborado esta serie de recomendaciones básicas para la asistencia a pacientes en el contexto de la pandemia.

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## Introduction

Back on March 11, 2020 the director general of the World Health Organization (WHO) declared the disease caused by SARS-CoV-2 (COVID-19) as a pandemic.<sup>1</sup> Healthcare has changed dramatically ever since due to the rapid spread of the virus, the large number of critically ill patients it has produced, and the prevention measures necessary to avoid its transmission.

For the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC) providing quality of care for critically ill patients is one of its main objectives. In today's context, it is difficult to maintain quality standards like the ones we were providing barely two weeks ago. All Spanish hospitals have developed clinical protocols based on the early studies published on the management of coronavirus. Variability in clinical practice can affect morbidity and mortality and, in view of the changing scenarios, it is difficult to control.

Despite the current difficulties and in line with previous projects,<sup>2,3</sup> SEMICYUC has designed a number of recommendations to guide health professionals who are providing care for critically ill patients during the current COVID-19 pandemic. A contingency plan has been designed followed with some ethical and moral recommendations, guidelines on non-invasive ventilation systems and critical transportation within a context of overload and need to implement resource and patient allocation strategies.

With the objective of improving care for critically ill patients with COVID-19, the SEMICYUC Working Groups

(WG) have elaborated a series of basic recommendations.

## Methodology of recommendations

### Assignment

In view of how quickly events have been unfolding lately, back in February 2020, SEMICYUC Board of Directors urged the WG coordinators to design, by setting up ad hoc groups, a series of basic recommendations of actions «to take» and «not to take», with the premise that they should be prepared within a week. Two members were chosen to coordinate the assignment, put them in order, and avoid duplicities.

### Reference search and writing the recommendations

To elaborate these recommendations each group conducted reference searches, which resulted in a variable number of recommendations, from which they selected the 3 most relevant actions to carry out and the 3 most important actions that should be avoided.

## Results

The following are the basic SEMICYUC recommendations established for the management of critically ill patients in

view of the coronavirus pandemic that causes the COVID-19 disease.

## Bioethics working group

### Recommendations on actions «to take»

*Recommendation #1: decision-making processes of limitation of life-sustaining treatments (LLST) based on disease severity and need for resources in a pandemic situation on the grounds of distributive justice*

Adapting life-sustaining treatments is a clinical decision often made at the intensive care unit (ICU) setting to prevent therapeutic obstinacy and futile treatments.<sup>4</sup> In a pandemic situation, in addition to taking into account both the clinical facts and the patient's values, the resources available will be assessed as well as the cost of opportunity based on the principle of distributive justice and by maximizing common good for the largest number of patients possible. Because these are difficult decisions to make, they should be made collectively by the treating team following the recommendations established by scientific societies and with the participation of the healthcare ethics committee if necessary.<sup>4-6</sup>

*Recommendation #2: information to the patient and his family during the current pandemic will be considered an essential pillar in the ICU clinical care*

In cases where contacts test positive and/or are quarantined, communication strategies will be established such as phone calls to ensure daily and truthful information about the health condition of the family member hospitalized at the ICU. The person who holds the right for information is the patient and if he is incapacitated to understand or make any decisions about his own state of health, this right will pass on to his family or legal representative.<sup>7,8</sup>

*Recommendation #3: keeping the health professional safe is an ethical and moral obligation in a pandemic situation*

Health professionals will provide care for critically ill patients with COVID-19 with the protection measures recommended by the health organizations and scientific societies, and it will be both an ethical and moral obligation to protect themselves to avoid becoming vectors of the disease to other patients.<sup>9</sup>

### Recommendations on actions «not to take»

*Recommendation #1: patient information cannot be revealed outside the healthcare setting without consent from the patient or his legal representatives*

The patient's privacy is a value to be protected at all cost and also in pandemic situations like this one, except for information requirements justified for public health reasons.<sup>10</sup> Health professionals at the ICU setting will protect confidentiality. Disclosure of clinical data requires prior consent from the patient or his legal representative if he is incapacitated.

*Recommendation #2: clinical decisions will not be made and procedures will not be performed without prior consent from the patient or his family*

Palliative care should be administered after informing the patient or his legal representatives of the current lack of evidence-based references, possible side effects, and

possibilities of success, which would justify its clinical recommendation in pandemic situations.<sup>11</sup>

*Recommendation #3: healthcare professionals will not abandon a quarantined patient, during basic care or accompanying duties*

Health professionals providing care for patients who remain in quarantine due to their infectious disease, will do so with the protection measures indicated. Also, they will explain to them the reasons why visits have been restricted and provide for all their needs and care. Family accompaniment will be favored if the epidemiological situation allows it and always observing the protective quarantine measures recommended.<sup>12,13</sup>

## Cardiology critical care and cardiopulmonary resuscitation working group

### Recommendations on actions «to take»

*Recommendation #1: monitor cardiac enzymes to assess myocardial damage and the QTc interval if a combination of antiretroviral therapy and hydroxychloroquine is being used*

Both agents lengthen the QTc interval in different degrees and interfere with the metabolic clearance pathway; therefore, the appearance of possible synergic effects on the QTc prolongation should be observed. Secure correct K and Mg levels to prevent greater toxicity levels from these drugs is key too.<sup>14</sup> If the patient has high cardiac enzyme levels, a bedside echocardiography should be performed to rule out altered myocardial contractility or the presence of pericardial effusion.<sup>15</sup> It is advisable to rule out other cardiovascular alterations that may be triggering the patient's clinical signs. Measures should be taken to protect the equipment and the probe to avoid contaminating other patients.

*Recommendation #2: cardiopulmonary resuscitation (CPR) maneuvers during the management of COVID-19 should be started only with compressions, heart rate should be monitored, and the personal protection equipment (PPE) should be worn at all times*

While performing the CPR maneuvers there is always the possibility that the resuscitators performing them will be exposed to bodily fluids. Also, procedures similar to this (eg, tracheal intubation, ventilation or chest compressions) generate infectious aerosols that can favor the transmission of the virus among those performing CPR maneuvers. In these conditions it is considered crucial to maximize protection with the PPE recommended and have medical staff trained in PPE donning and doffing techniques to avoid possible self-contamination.<sup>16-18</sup> The quick recovery of circulation after defibrillation can avoid the implementation of other more invasive resuscitation maneuvers, thus avoiding the generation of infectious aerosol particles that can favor transmission among the healthcare personnel performing the resuscitation maneuvers.<sup>17</sup>

*Recommendation #3: in case of cardiac arrest (CA) in patients ventilated in the prone position, start CPR maneuvers modified and adapted to the current situation*

This is a special situation of which we don't have a lot of medical evidence available. The use of reverse chest compressions in patients who remain in the prone position

has been described especially in patients in the surgical setting,<sup>19</sup> but it could be used in patients with COVID-19 who are ventilated in this prone position. For defibrillation purposes under this scenario, the location of the adhesive patches that better favors the vector of depolarization generated by the defibrillator would still be the conventional one (right subclavicular/left apical). If this is not possible, the antero-posterior (left precordium/left subscapular location), latero-lateral or left dorsal/left apicolateral location of the self-adhesive patches are feasible alternatives that can facilitate defibrillation maneuvers in these cases.<sup>20</sup>

#### Recommendations on actions «not to take»

*Recommendation #1: do not administer amiodarone together with chloroquine or lopinavir/ritonavir due to the existing high-risk of adverse effects*

The co-administration of amiodarone and chloroquine or lopinavir/ritonavir is associated with a risk of accumulation of the former since these antiretrovirals interfere with their clearance pathway through the inhibition of P450 isoforms.<sup>21</sup> The US Food and Drug Administration (FDA) recommends plasma controls in cases of acute administration.<sup>14</sup> In the management of supraventricular arrhythmias, cardioversion can be attempted (using drugs, electricity or both in a sequential manner) if the arrhythmia is new and due to the patient's hemodynamic situation. A second strategy here would be to control heart rate with betablockers and digoxin.<sup>22</sup> The use of selective short-term  $\beta_1$  betablockers is advisable. It is convenient to explore the possible interactions of all the drugs administered that can have negative chronotropic effects.

*Recommendation #2: do not start extracorporeal membrane oxygenation (ECMO) support without a prior echocardiographic study of cardiac function*

It is advisable to assess cardiac function by performing an echocardiography before starting ECMO support to choose the most appropriate modality (VV or VA).<sup>23</sup> The indication for ECMO has to be rigorous and adjusted to the patient's clinical situation since an inadequate indication could lead to failed therapy and a significant use of resources. The use of ECMO in the current pandemic is very scarce, meaning that its indication should be individualized and adjusted to the reality of every moment.

*Recommendation #3: the «hear/feel» strategy to assess respiration should not be used during CPR in patients with suspected or confirmed COVID-19*

It is advisable to look for signs of life, normal breathing or, if the person is skilled and trained, carotid pulse. When in doubt, and only after calling for help and communicating the situation of suspected cardiac arrest in a patient with suspected or confirmed COVID-19, start CPR maneuvers with chest compressions only.<sup>17</sup> Any manipulation and/or intervention on the airways of patients with COVID-19 should be performed by expert medical personnel with proven skills in advanced airway management. Also, the airway devices that will be used should be those for which they are trained in order to minimize the risks.<sup>16,17</sup>

## Nephrological intensive care working group

#### Recommendations on actions «to take»

*Recommendation #1: early examination of the risk factors to develop acute kidney injury (AKI)*

The early identification of patients at risk of developing AKI can help implement the interventions needed to avoid or reduce the appearance or progression of AKI. The possible risk factors associated with AKI in patients with COVID-19 are similar to the rest of the ICU population<sup>24,25</sup>: old age, arterial hypertension, previous chronic kidney disease, ischemic heart disease and heart failure, shock at admission, and nephrotoxic drugs.

*Recommendation #2: close monitoring of renal function*

The incidence of AKI in patients admitted with COVID-19 has not been well-established, but it is between 0.1% and 29%. The development of AKI is associated with a higher mortality rate of up to 91% in cases of severe acute respiratory distress syndrome (SARS) with AKI.<sup>26,27</sup> Etiopathogenesis includes: 1) It is known that the new coronavirus binds to the angiotensin-converting enzyme 2 receptor (ACE2) damaging the renal tubules that highly express the ACE2<sup>28</sup>; 2) Immunomediated damage (pulmonary-renal crosstalk) due to the well-described associations between the SARS and AKI in relation to inflammatory mediators and kidney tubular injury, and 3) AKI already known due to tubular ischemia and the new mechanisms described of apoptosis and mitochondrial stress in patients with shock or hypovolemia.

*Recommendation #3: titrate the drug dose in patients with AKI paying special attention to drugs prescribed for the management of COVID-19*

The dose of hydroxychloroquine should be adjusted to glomerular filtration rates (GFR) < 30 mL/min. In patients on hemodialysis, peritoneal dialysis or continuous renal replacement therapies between 25% and 50% of the dose should be administered. The QT interval should be monitored in patients on hydroxychloroquine, especially with GFR  $\leq$  50 mL/min, and concomitant treatment with azithromycin.<sup>29</sup> The dose of IFN- $\beta$ 1b should be titrated in cases of chronic kidney disease. Dyselectrolytemia and effective blood volume due to diarrhea secondary to lopinavir/ritonavir should be assessed particularly in patients with AKI. Remdesivir is contraindicated with GFR < 30 mL/min or when using extracorporeal techniques (ECT).<sup>30</sup>

#### Recommendations on actions «not to take»

*Recommendation #1: extracorporeal clearance treatment should not be delayed*

According to the medical literature published on this regard, the percentage of patients with COVID-19 who require ECT is between 1.5% and 9%. This percentage goes up to 5.6%-23% in patients with seious disease who end up being admitted to the ICU with COVID-19. ECT should be considered in patients with KDIGO  $\geq$  2 and, in particular, in patients with an increased fluid balance and serious SARS.<sup>31,32</sup>

*Recommendation #2: do not use nephrotoxics in critically ill patients unless it is strictly necessary and do not use agents that cannot be replaced for similar drugs without renal adverse events*

Nephrotoxic drugs are responsible for around 20%–30% of all AKIs. They are especially important in patients with COVID-19 treated with non-steroidal anti-inflammatory drugs (NAID) or certain nephrotoxic antimicrobials due to possible bacterial coinfections or superinfections. The recommendation here is to avoid starch with resuscitation fluids. Exposure to these agents should be limited, if possible, and weighed against the risk of developing or worsening AKI as long as there are alternative therapies and procedures.<sup>33,34</sup>

**Recommendation #3: do not underestimate AKI in the context of a SARS-CoV-2 infection during the long-term progression of the disease**

Data on the long-term recovery of renal function after AKI in the context of a COVID-19 infection are scarce. That is why renal function should be reassessed between 3 and 6 months after discharge. The reason why is to determine the patients' degree of recovery and be able to establish rehabilitation and renal protection measures to improve the long-term prognosis.<sup>35,36</sup>

## Donation and transplant working group

### Recommendations on actions «to take»

**Recommendation #1: prioritize potential optimal donors in situations of brain death or controlled asystole in hospitals of areas most affected by COVID-19**

In hospitals of areas most affected by COVID-19 it may be necessary to prioritize certain processes of donation such as those based on optimal donors on criteria of age (< 60) and lack of comorbidities that may affect the viability and survival expectations of the transplant.<sup>37</sup> Here potential donors in situations of brain death such as controlled asystole should be taken into consideration. In this epidemiological context, hospitals may temporarily suspend processes of greater logistical complexity and lower chances of organ use such as donation-oriented intensive care,<sup>38</sup> and donation in uncontrolled asystole<sup>39</sup> with the added problem of the impossibility of performing the timely screening of donors to rule out SARS-CoV-2 cannot be done and living donation considered a scheduled, non-emergent surgery in most of the cases.

**Recommendation #2: prioritize the transfer of patients in clinical situations of an emergency or high clinical severity and major difficulties. Also, if there are major issues when accessing the transplant in hospitals of epidemiological scenario #4**

In hospitals of areas most affected by COVID-19, it may be necessary to reduce the transplant activity due to the saturation of hospital and ICU services and guarantee patient safety post-transplant regarding nosocomial and community-acquired infections due to COVID-19.<sup>40</sup> It is advisable to limit the transplant activity to patients who meet the emergency criteria established nationwide<sup>41</sup> and to patients in situations of greater clinical severity<sup>42</sup> or with greater difficulties to access transplant therapies due to their immunological and/or anthropometrical characteristics (eg, pediatric, renal, and hyperimmunized patients). In any case, the decision to perform each transplant procedure should be made on an individual analysis of the risk

to proceed with the transplan and on the patient's clinical situation.<sup>40</sup>

**Recommendation #3: perform a thorough and close monitoring of all patients who are potential organ and tissue donors regarding SARS-CoV-2 infection and of all potential transplant recipients**

For the screening of patients, the RT-PCR technique is used by obtaining a single swab specimen from the patient's upper and/lower respiratory tract. Screening should be performed in bronchoalveolar lavage when the donation of the lungs is being considered. If these circumstances don't apply and in order to avoid fibrobronchoscopy, it is advisable to perform 1 nasopharyngeal swab followed by an oropharyngeal one. Regardless of the type of specimen obtained in these swabs, such specimen should be obtained 24 h prior to the extraction of the organ/s. Screening for COVID-19 should be performed among recipients. Pre-transplant tests should include information on when is the recipient admitted to the hospital, especially when he shows compatible symptoms or any other epidemiological situation. If a patient in the waiting list is a COVID-19 case, it is advisable to exclude him temporarily from the transplant program until he is fully recovered from the disease.<sup>40</sup>

### Recommendations on actions «not to take»

**Recommendation #1: always remember the possibility of donation and keep the notification systems of the possible donors alive and updated in advance**

Because transplant therapy is an essential part of health-care systems,<sup>40,43</sup> the standard of considering the option of donation systematically should still be applied.<sup>2</sup> In the current COVID-19 pandemic, the donation process is more complex: 1) possibility that certain organs will not be transplanted due to the saturation experienced by the health services and the security issues associated with the most affected regions; 2) restrictions to the mobility of the organ extraction and transplant health team, and 3) need to screen for COVID-19 in the potential donor and in potential recipient prior to the transplant.<sup>40</sup> The early notification of the possible donor will allow the transplant coordinator to complete a thorough assessment regarding COVID-19 by ruling out donation, when appropriate, scheduling a COVID-19 detection test to have the results available before transferring the organ extraction and transplant health team, and establishing the logistical and human feasibility of the entire process.

**Recommendation #2: the process of donation should not be initiated without securing the availability of the necessary means and resources and checking the safety of the potential recipients**

The early notification of possible donors to the transplant coordinator and the Spanish National Transplant Organization (ONT) will allow the ONT to offer the potentially implantable organs in advance in accordance with the allocation criteria implemented nationwide.<sup>41</sup> If the ONT does not identify adequate recipients in hospitals that are capable of performing the transplant with all the safety measures for the potential recipients, the donation process can be cancelled in the donor hospital. Similarly, the viability of the entire process from the logistical and human standpoint should be assessed before starting the process.

*Recommendation #3: remember to observe the safety of your team by implementing the routine preventive measures to avoid transmitting coronavirus to the health workers involved in the processes of donation and/or transplant*

The process of donation and transplant is basically multidisciplinary with the participation of a significant number of healthcare professionals from different disciplines and specialties. It requires interaction among health professionals, the potential donor, his family, and the potential organ recipients and their families. Added to the usual preventive measures to avoid transmitting SARS-CoV-2 to the healthcare workers,<sup>44</sup> there are additional measures that need to be observed before proceeding with the program of organ donation and transplant.<sup>45</sup>

## Infectious diseases and sepsis working group

### Recommendations on actions «to take»

*Recommendation #1: obtain nasal and pharyngeal specimens from the lower respiratory tract in patients intubated to perform the polymerase chain reaction test to rule out SARS-CoV-2*

The diagnosis of COVID-19 requires positivity for SARS-CoV-2 in the PCR test. The specimen is initially obtained from a nasal or pharyngeal swab. However, in highly suspicious cases, if the test is negative, it is advisable to obtain the specimen from the lower respiratory tract.<sup>46</sup>

*Recommendation #2: start empirical antibiotic treatment to rule out the possibility of bacterial co-infection*

Both in the current COVID-19 pandemic and in former flu epidemics, a significant rate of infection has been confirmed. Regarding the flu, this rate of infection went up to 20%. In the current COVID-19 pandemic this information is still unknown but given the severity of our patients starting empirical antibiotic treatment followed by patient re-assessments based on the microbiological results seems completely justified.<sup>47</sup>

*Recommendation #3: close monitoring of the adverse events and interactions of the drugs used to treat SARS-CoV-2*

Currently, there are no therapies to treat SARS-CoV-2 with the slightest bit of scientific evidence. The drugs that are being used (lopinavir/ritonavir, hydroxychloroquine, interferon, azithromycin, remdesivir...) have side effects, toxicities, and drug interactions.<sup>48</sup> If, with the best intentions, any of these drugs is used, we should be very cautious and monitor the disease progression of each patient closely. When in doubt, the most reasonable thing to do will be to suspend treatment.

### Recommendations on actions «not to take»

*Recommendation #1: always follow the prevention protocols of infections associated with healthcare at the ICU setting (Zero Projects)*

Although the PPE complicates the entire healthcare process, the measures implemented by the Zero Projects (Zero Bacteremia, Zero Pneumonia, Zero Resistance and Zero UTI) should be observed given the good results of these programs.

*Recommendation #2: do not remove quarantine measures in a patient with highly suspected COVID-19 with just*

*a negative PCR test performed on a specimen obtained from the upper respiratory tract*

Given the low sensitivity of PCR tests with specimens from the upper respiratory tract obtained through nasal or pharyngeal swabs, when dealing with patients with highly suspected COVID-19, it will be necessary to repeat the test in a new specimen obtained from the upper respiratory tract or obtain a different specimen from the lower respiratory tract.<sup>48</sup>

*Recommendation #3: do not enter into contact with the patient without the proper PPE for every individual patient and situation and always follow the protocol of each center*

In situations that require care to several patients with, at times, urgent actions, healthcare workers should not forget that one of the first rules is self-protection.<sup>47</sup> When treating a patient with coronavirus, the PPE should include gown, gloves, eye protection, and mask (FFP2 or FFP3).

## Technology and research methodology assessment working group

### Recommendations on actions «to take»

*Recommendation #1: make sure you have the right clinical documentation despite the insufficient availability of healthcare resources*

Since the huge pressure exerted on the entire healthcare process can complicate access to the usual electronic clinical data due to the mismatch between the cases already taken care of and the resources available, make sure you keep your patients' clinical documentation up to date (past medical histories, prescriptions, and drug registries) in the format established.<sup>49</sup>

*Recommendation #2: keep a registry of cases already taken care of*

The existence of a proper and agreed registry in intensive medicine units is just essential. It is the only way to know what cases have already been taken care of and what progression they had, share the information obtained, and elaborate larger registries that can give us better overall information.<sup>50</sup>

*Recommendation #3: always administer experimental therapies according to clinical trials and following the recommendations established by these trials*

Experimental therapies should always be prescribed based on the clinical trials conducted in order to analyze their efficacy and always following the recommendations published to that date by public authorities, scientific societies or consensus documents.<sup>51</sup>

### Recommendations on actions «not to take»

*Recommendation #1: never oversee the recommendations and consensus documents of scientific societies based on the experience of countries that have already responded to the current pandemic*

Consensus documents serve 2 purposes: on the one hand, they administer the best treatment that contributes to a good clinical progression; on the other hand, they guarantee the right levels of infection prevention and control.<sup>16,52</sup>

*Recommendation #2: always authorize interhospital transfers with a centralized coordination of such trans-*

fers and always making sure that the clinical documentation required is available to the receiving center

It is essential to have the most relevant clinical information available of the patient transferred from the referral center as well as the clinical and therapeutic data administered during the transfer between the hospitals.<sup>53</sup> Similarly, it is essential to coordinate both hospitals in a centralized way by making sure the right flows of patients are being observed from the coordinating center while knowing the state of the resources available.

**Recommendation #3: never exclude critically ill patients assisted outside the ICU setting from your registries**

The identification of patients assisted outside the ICU while in a situation of healthcare stress should be based on recognizing, diagnosing, and treating early in time while keeping close collaboration with other clinical specialties and regardless of the place of hospitalization.<sup>54</sup>

## Acute kidney injury working group

### Recommendations on actions «to take»

**Recommendation #1: perform early orotracheal intubations (OTI) in patients with moderate-to-severe respiratory failure and/or signs of excessive respiratory work**

In patients with moderate-to-severe respiratory distress and signs of excessive respiratory work (respiratory rate > 30rpm) and  $\text{PaO}_2/\text{FiO}_2 < 200$  (with  $\text{FiO}_2 > 50\%$ ), delaying OTI leads to a worse prognosis. The decision to intubate the patient should be made after assessing the patient's potentiality to recover.<sup>55,56</sup>

**Recommendation #2: use the anticipated OTI with rapid sequence intubation without ventilation with mouth-to-bag resuscitator and implementing the protocol for difficult airway management**

Several attempts to perform OTI in patients with respiratory failure can lead to serious complications in these patients who already have low oxygen reserves.<sup>57,58</sup> This, added to the use of ventilation with mouth-to-bag resuscitators, increases the risk of contagion for the healthcare professionals.<sup>59</sup> If ventilation with the mouth-to-bag resuscitator is required, it is advisable to use a high-efficiency particulate air filter.

**Recommendation #3: perform the prone position maneuver within the first 24h in patients with SARS with  $\text{PaO}_2/\text{FiO}_2 < 150$  while assessing myorelaxation and repeat cycles until improvement**

The prone position maneuver improves oxygenation and mortality in selected patients.<sup>60</sup> Cycles of, at least, 16h should be performed. The use of myorelaxation in cases of asynchronies improves the adaptation to invasive mechanical ventilation (IMV) and eventually oxygenation.<sup>61</sup> Protective mechanical ventilation (tidal volume 4–8 mL/kg of predicted body weight, plateau pressure < 30, driving pressure < 15 cmH<sub>2</sub>O), and the use of optimal PEEP in patients with moderate-to-severe SARS is also associated with a lower mortality rate.<sup>62</sup>

### Recommendations on actions «not to take»

**Recommendation #1: avoid using non-invasive mechanical ventilation (NIMV). In selected cases you can contemplate**

**the use of high-flow oxygen therapy as non-invasive respiratory support**

NIMV can produce aerosols and increase the spread of the virus<sup>63</sup>; also, no benefits from hypoxemic respiratory failure have been confirmed to this day, which may delay OTI and increase mortality.<sup>64</sup> Under the current circumstances the use of non-invasive ventilation may be required. In this case the use of high-flow nasal cannula (HFNC) therapy is preferred.<sup>65</sup> In case of NIMV, prioritize the use of double limb respiratory circuits. In case of clinical impairment, do not delay OTI and start NIMV.

**Recommendation #2: do not use nebulized medications. If necessary, use a vibrating mesh to avoid particle dispersion**

Nebulizers generate aerosol particles of 1–5 μm that can carry both bacteria and viruses. The risk of transmitting the infection through aerosols is higher while a nebulizer is being used due to its potential to generate a high volume of respiratory aerosols that can be propelled to a greater distance compared to the pattern of natural dispersion. It is advisable to use vibrant mesh devices with a mouth pipette or mask to limit the spread of these respiratory aerosols and also put a surgical mask on. If possible, inhaled therapy with a metered dose inhaler (MDI) and a spacer/VHC will be prioritized too. Jet systems are ill-advised due to their greater capacity of particle dispersion into the air.<sup>63,66</sup>

**Recommendation #3: there is no scientific evidence on the use of a single ventilator for several patients or the use of prone maneuvers in non-intubated patients («awake prone positioning»)**

The use of a single ventilator for multiple patients is ill-advised because volume allocation can be unequal. Also, monitoring the pulmonary mechanics and other variables is not possible (and compromises security). It does not allow individual management and PEEP cannot be optimized. Also, the response and progression of each patient to the therapy is different, which can condition the care provided with unequal distribution, among other aspects. Therefore, its use is ill-advised as long as another clinically proven, effective, and safe therapy is available.<sup>67,68</sup>

There is no evidence on the benefits of the prone position compared to other strategies with scientific evidence in non-intubated patients. Only case studies exist. This maneuver is only possible in collaborative patients and patients who are capable of turning themselves for safety reasons. If performed, the patient will need to be closely monitored and OTI and IMV will have to be postponed.<sup>69</sup>

## Metabolism and nutrition working group

### Recommendations on actions «to take»

**Recommendation #1: Close monitoring of phosphate levels from admission, supplement with thiamine, and introduce nutrition gradually given the high risk of refeeding**

Identify and prevent refeeding syndrome in patients with COVID-19 or in those who have received low energy intake for more than 5 days. The main biochemical characteristic is hypophosphatemia, but it can occur together with sodium and abnormal fluids balances, thiamine deficit, hypopotassemia, hypomagnesaemia, and with changes in the glucose, protein and fat metabolism.<sup>70,71</sup> Its prevention

requires correcting hydro-electrolytic imbalances, supplementing with vitamins such as thiamine, and starting nutrition with low-calorie-protein intake increasing it every 72–96 hours if hypophosphatemia does not become worse until usual requirements are reached adjusted to disease progression.<sup>70–72</sup>

*Recommendation #2: estimate the calorie/protein requirements depending on disease progression and consider non-nutritional calories. If 60% is not obtained on the 4th day, start complementary parenteral nutrition (PN)*

The nutritional needs of the critically ill patient change over time and they should be adjusted based on disease progression despite the work overload in the current pandemic situation. In this type of patients, the main problem will be reaching the calorie and protein needs only through enteral administration, which is why it is necessary to resort to complementary PN if 60% of the requirements are not reached on the 4th day of disease progression.<sup>73</sup> The excessive administration of calories can lead to liver dysfunction and nonalcoholic fatty liver disease,<sup>74</sup> which is why we should take into account non-nutritional calorie intakes (glucose, propofol, citrate, etc.) to avoid «nutritrauma».<sup>75</sup>

*Recommendation #3: use fast-acting combined with short-acting insulin therapy (twice a day) to keep blood glucose levels < 180 mg/dL and to avoid blood sugar variability and hypoglycemia as much as possible*

Stress hyperglycemia is independently associated with mortality in critically ill patients.<sup>76</sup> Blood sugar levels should be kept < 180 mg/dL and, if possible, close to 150 mg/dL starting insulin therapy with blood sugar > 150 mg/dL. It is advisable to avoid both hypoglycemia and blood sugar variability because of the important repercussions it has on the morbimortality of the critically ill patient.<sup>77</sup> The use of slow-acting insulin therapy every 12 h, can help us to manage stress hyperglycemia avoiding hypoglycemia and reducing the need to start insulin perfusion<sup>78</sup> given the shortage of pumps and work overload among the health workers.

#### **Recommendations on actions «not to take»**

*Recommendation #1: formulas with high-lipid content should not be administered in the presence of hypertriglyceridemia (TG > 400 mg/dL) associated with severe inflammation*

In these patients, hypertriglyceridemia is caused by the severe inflammation that occurs in them, and it is exacerbated by an excessive dose of lipids in PN or by the drug-induced suppression of lipoprotein lipase or the stimulation of lipogenesis induced by an excessive intake of carbohydrates. Therefore, hypertriglyceridemia in patients with COVID-19 can become worse due to the mismatch between the administration of fats and the capacity to eliminate fat plasma. Based on experts' recommendation, the dose of lipids recommended is between 0.7 and 1.3 g/kg/day or between 25% and 40% of the calorie intake,<sup>79</sup> and it should be reduced in the cases where plasma triglyceride levels exceed 400 mg/dL.<sup>75</sup>

*Recommendation #2: do not delay or interrupt enteral nutrition (EN) only because the patient needs prone position or myorelaxation*

Prone position ventilation does not contraindicate nutrition via the enteral route. In a prospective study no higher rate of digestive or respiratory complications was found regarding the supine position, and 25° elevation of the headboard was recommended during IMV in the prone position.<sup>80</sup> Another prospective study of patients ventilated while in the prone position with relaxation concluded that EN is feasible, safe, and is not associated with a higher risk of gastrointestinal complications or pneumonia due to bronchoaspiration as long as EN tolerance is closely monitored. In both studies EN was administered through a nasogastric tube.<sup>81</sup>

*Recommendation #3: do not systematically attribute gastrointestinal complications to nutritional therapy without ruling out adverse reactions to polymedication in these patients*

Gastrointestinal complications of EN such as increased gastric residual volume, constipation, EN related diarrhea, vomits, regurgitation, abdominal pain or distension, and bronchoaspiration are cause for hyponutrition, which is why management protocols should be identified and implemented.<sup>82,83</sup> Diarrhea is common in critically ill patients, but only in between 10% and 18% of the cases it is due to EN, and it is mostly multifactorial.<sup>84</sup> Reviewing the polymedication these patients receive and even searching for possible infectious causes will allow us to rule out enteral diet as the culprit of diarrhea and avoid its interruption unnecessarily.

## **Trauma and neurointensive care working group**

### **Recommendations on actions «to take»**

*Recommendation #1: the assessment of patients with severe or neurocritical trauma should be performed taking the proper measures*

Pandemic situations result in an important number of critically ill patients that impact healthcare systems. In this context, the management of a patient with severe or neurocritical trauma should be provided taking the appropriate precautions based on the patient's characteristics (gown, distance...), but maintaining the priorities and objectives in his treatment.<sup>85</sup>

*Recommendation #2: in the differential diagnosis of headache, in addition to COVID-19, include structural, infectious and vascular causes*

Headache is one of the symptoms reported in COVID-19 infection. In the series published, its presence has been described in up to 8% of the patients with COVID-19.<sup>86</sup> The anamnesis should include symptoms and signs that will allow us to rule out structural, infectious injuries and subarachnoid hemorrhages and/or intraparenchymatous hemorrhages as the possible etiological causes.<sup>87</sup>

*Recommendation #3: design an action plan including coordination with the reference center and intrahospital transfers*

Planning care and triage should consider the referral of trauma and neurocritical patients. It is advisable to preserve hospital capacity.<sup>88</sup> In case of intrahospital transfers or radiodiagnosis or OR units, it is advisable to plan the itinerary and the personnel involved in the transfer



## Recommendations on actions «not to take»

*Recommendation #1: the assessment of neurocritical patients or with severe trauma should not be delayed for the sake of ruling out a COVID-19 situation*

Severe traumatic disease or strokes are time-dependent diseases: providing immediate care reduces mortality and improves functional results.<sup>89</sup> In a suspected COVID-19 situation, timely measures should be adopted until COVID-19 is ruled out or confirmed, but not delaying the patient's provision of care.

*Recommendation #2: do not perform additional tests that involve the transfer of traumatic or neurocritical patients with COVID-19 that will not bring significant changes to the therapeutic approach*

In the care of trauma or neurocritical patients with COVID-19 it is advisable to perform only the additional tests that are necessary. However, transfers should be avoided. Instead, these tests should be run preferably by using portable machines in the patient's room.<sup>16</sup>

*Recommendation #3: no-essential staff will not participate in the provision of care to severe trauma or neurocritical patients*

Initial care for this type of patients is characterized by being multidisciplinary in nature and with a large number of professionals being coordinated.<sup>90</sup> It is advisable to restructure the healthcare teams by limiting the number of people involved to minimize risk of contagion. The established quarantine, personal protection, and disinfection measures will be observed.<sup>16</sup>

## Planning, organization, and management working group

### Recommendations on actions «to take»

*Recommendation #1: implement a contingency plan of the intensive care service (ICS) within the local contingency plan*

ICS professionals should participate actively in the local crisis committees bringing their own contingency plans into the hospital plans.<sup>52</sup> It is necessary to plan the available resources proactively (structural resources, as well as equipment and professionals), paying special attention to the description of viable expansion areas to allow the use of therapy devices and respiratory support plus the ones often used in intensive medicine. The necessary logistics should always be available to be able to group patients and professional teams based on their needs, while trying to avoid the collapse of both the ICS and the hospital.<sup>91</sup>

*Recommendation #2: establish effective communication that secures good teamwork*

Effective communication creates a fully operational system, integrating the different health professionals to provide better quality of care and reduce issues with patient safety.<sup>92</sup> A specific, safe communication channel can be necessary. An information transfer protocol should be used.<sup>93</sup>

Single leadership with unity of action and organization is required, one that ensures clear treatment, procedural, and task system.

All health professionals should be trained in the processes and procedures associated with the disease, especially regarding personal protection and use of PPEs.<sup>94</sup>

Se requiere un sistema de detección precoz de enfermos con riesgo de deterioro en urgencias y plantas de hospitalización que evalúe al paciente de forma global.

*Recommendation #3: design triage and early detection protocols of patients at high-risk of deterioration outside the ICS*

There should be an early detection system of patients with risk of deterioration at the emergency services and hospital that evaluates the patient globally.

The criteria for assessing and admitting patients to the ICS should be agreed with other hospital departments to maximize the resources and prioritize global benefit.<sup>95</sup>

The action protocols should be dynamic and adaptable to modifications while under the crisis situation. Factors such as age, comorbidity, disease severity, compromise of other organs, reversibility, and ethical and moral considerations in effect should be taken into account while under the crisis situation.<sup>6,96</sup>

### Recommendations on actions «not to take»

*Recommendation #1: do not underestimate the emotional impact of the crisis on healthcare professionals*

The crisis situation can cause professional fatigue due to excessive workload, moral suffering, care perceived as inappropriate, and compassion fatigue. Also, post-traumatic stress disorder can occur.<sup>97</sup>

The ICS and the treating center should set up a protocol to take care of health professionals including, among others, assessing the exhaustion situation of each professional, tips to avoid or reduce it, a plan to arrange periods of rest and implement a preventive psychological system of support and treatment with psychologists at their disposal.<sup>98</sup>

This protocol should be perfectly structured and well-known by all healthcare professionals who should use it mandatorily and follow its instructions.

*Recommendation #2: do not overlook the recommendations established by other scientific societies that have suffered the crisis previously or with experience in similar situations*

It is advisable to benefit from the experience of centers and professionals with experience in healthcare organization and provision of care for patients with COVID-19, and/or from the experience of professionals who have been dealing with this pandemic much longer. It is necessary to consider the evidence available in other countries and regions of the same country to provide proactive responses.<sup>99,100</sup>

Scientific societies such as SEMICYUC and SEEIUC have taken into consideration previous evidence and experience to envision a contingency plan whose main objective is to provide optimal care for patients, optimize resources, and bring the best recommendations to authorities and healthcare and clinical managers in the possible different scenarios.<sup>52</sup>

*Recommendation #3: do not detach yourself from a territorial approach in the management of critically ill patients with COVID-19*

Patient referral circuits should be set up for the transfer of these patients to other centers of the same or different autonomous communities for the proper and solidary distribution of them in order to avoid situations of healthcare

collapse and thus benefit patients, professionals and society in general.

Also, it is advisable to establish circuits to be able to transfer technological equipment, PPEs, etc., from ICS where there is a surplus to other ICS where there is shortage.<sup>91</sup> To this end, an ICS coordination team should be created to guarantee the fluidity and adequacy of these transfers or referrals.<sup>101</sup>

### Sedation, analgesia, and delirium working group

#### Recommendations on actions «to take»

*Recommendation #1: prescribe deep sedation to patients with severe SARS, BIS monitoring with proper analgesia and dose adjustment anticipating the possible pharmacological interactions*

Patients with COVID-19 and SARS need deep sedation to adapt themselves to the respirator and allow recruitment maneuvers including the prone position one.<sup>102</sup>

Multiple pharmacological interactions have been described with the usual treatments including the modification of plasma levels of sedatives and alterations on the electrocardiogram.<sup>103</sup> It is advisable to monitor the level of sedation closely followed by ECG monitoring, dose titration, and avoiding oversedation: keep BIS between 40–60. For more in-depth information visit: <http://www.covid19-druginteraction.org>

Consider other sedation strategies such as inhalation, when available, especially in cases of difficult sedation, and the healthcare professionals are experienced managing different sedation strategies like this one.

*Recommendation #2: use relaxation with neuromuscular blockers (NMB) in patients with moderate-to-severe SARS, respirator asynchrony, prone position or high plateau pressures*

Muscular relaxation is necessary in patients with SARS, especially in severe cases, to achieve a proper protective ventilation.<sup>104</sup> Also, in these patients we should guarantee the proper deep sedation. Due to the harmful long-term effects of NMB, it is usually advisable to administer boluses whenever possible to minimize these effects. However, in patients with COVID-19, due to the severity of SARS and to minimize the number of interventions, it is advisable to use continuous infusions, while monitoring by the use of TOF and the least possible time (preferably less than 48 h).<sup>105</sup> The NMB drugs with less pharmacological interactions of all with the treatments used in patients with COVID-19 are cisatracurium and vecuronium.

*Recommendation #3: use sequential and dynamic analgosedation during SARS mild stages after withdrawal of NMB, to achieve lighter levels of sedation*

In cases of improvement in the gas exchange with reduction of ventilatory parameters and withdrawal of neuromuscular blockade,<sup>26</sup> a sequential analgosedation strategy is recommended to achieve sedation levels that will make it easier to wean from IMV. At this point the objective is that BIS is between 60 and 80 or RASS between -3 and -1.<sup>106</sup> To achieve these goals we should minimize the use of drugs with the longest half-life such as midazolam replacing them for others with a shorter half-life such as propofol, remifentanyl or dexmedetomidine. We should also avoid prolonged

use of opioids and develop multimodal analgesia strategies with other types of painkillers (paracetamol, NSAID, metamizole).

#### Recommendations on actions «not to take»

*Recommendation #1: do not spread aerosols during OTI, reduce ventilation with resuscitation bags, and perform rapid sequence intubation*

Due to the clinical situation of these patients with severe hypoxemia and in order to reduce the cough reflex and the spread of microdroplets, rapid OTI sequences are recommended using rocuronium (1.2 mg/kg) and etomidate (0.2–0.3 mg/kg) or ketamine (1.5 mg/kg) almost simultaneously. In some cases, it can be necessary to add a sleep inducer like low-dose midazolam or propofol.<sup>107</sup>

*Recommendation #2: do not forget detection, prevention, and management of delirium during sedation withdrawal and weaning from IMV*

In these patients on deep sedation, withdrawing from sedation and weaning from IMV can be more difficult due to agitation and delirium, which is why it is of paramount importance to monitor them using validated scales such as the CAM-ICU (Confusion Assessment Method for the Intensive Care Unit) or the ICDS (Intensive Care Delirium Screening Checklist) and prevent its development.<sup>108</sup>

In these cases, drugs such as quetiapine and ziprasidone should be avoided since they lengthen the QT interval, being dexmedetomidine safer since it has fewer drug interactions. We should also be careful with haloperidol, which is commonly used, because of its pharmacological interactions.<sup>109</sup>

In cases of uncontrolled agitation with risk of self-extubation, the early tracheotomy could be an effective strategy.

*Recommendation #3: do not oversedate the patient performing dynamic and sequential sedation, goal-oriented, individualized, and adapted to the patient's clinical situation at all times*

Oversedation causes short and long-term harmful effects that make weaning from MV difficult and extend hospital stay.<sup>110</sup> Therefore, once the patient's hemodynamic and respiratory situation has improved, the dose of sedatives should be reduced, with an objective of light sedation to make weaning from IMV easier, preventing delirium, and promote early mobilization, thus avoiding the onset of long-term complications.

### Simulation for clinical training working group

#### Recommendations on actions «to take»

*Recommendation #1: conduct individual and collective formal training in personal protection measures and in the application of specific approach protocols, if possible, through clinical simulation*

We are facing crisis situations that are compromising the safety of both health professional and patients. We should minimize interpersonal variability and maximize safety measures through the implementation of protocols. It is important to establish formal training through clinical simulation on PPE donning and doffing and different clinical scenarios that will allow us to reinforce technical and non-technical skills (distributing roles, knowing the envi-

ronment, optimizing communication, using cognitive aids, planning, and anticipating). As an educational tool clinical simulation allows us to train interventions in a safe setting, minimizing mistakes, and increasing the safety of professionals and patients.<sup>94,111,112</sup>

**Recommendation #2: train multiprofessional teamwork while promoting mutual support behaviors**

Multiprofessional ICU teams work in a physically and emotionally challenging setting. The smallest number of professionals should be exposed without detriment to the patient safety. Also, the use of PPE in certain procedures can interfere with communication and change the management of some routine processes, which can lead to making more mistakes. In this sense, training teamwork is essential to understand the challenges of working in an unknown situation with additional PPE, identify unforeseen deficiencies, refine processes, improve communication, optimize care, increase the confidence of the staff, and be economically viable.<sup>113-115</sup>

**Recommendation #3: train the family on the disease progression**

Healthcare professionals play an educational role with the citizens by letting them acquire knowledge and skills on the disease that will eventually allow them to play a more active role in the defense of their own health and that of others, as well as in the decision-making process. Therefore, when healthcare professionals convey truthful, rigorous information about the disease, it is easier for the general population to be more prepared psychologically.<sup>116-118</sup>

### Recommendations on actions «not to take»

**Recommendation #1: do not expose the ICU staff unnecessarily**

Studies from other countries have shown a significant percentage of contagion among healthcare professionals. Therefore, the smallest possible number of them should enter into contact with the patient and use the PPE following the recommendations established by the institutions, adjusting the equipment to the indications given and optimizing the resources that could become scarce under the current circumstances. In case PPE have to be rationalized, face masks (FFP2 or equivalents) should be reserved for those procedures that generate aerosols, OTI among them, which should be performed by the most experienced staff and, if possible, with the use of a video laryngoscope.<sup>100,119,120</sup>

**Recommendation #2: do not inform the family without preparing in advance what you want to tell them or without empathy**

Prepare and anticipate the moment of briefing the family. It will make it easier for your message to be understood and accepted if you avoid resentment and confusion.<sup>121-123</sup>:

- Prepare the space where you will brief them: try to choose a place where intimacy and the absence of noise or interruptions is ensured, even if the information is to be given on the phone.
- Prepare yourself: be aware of your feelings, circumstances or emotions to prevent them from making you lose concentration during the briefing.

- Prepare your message: adjust your technical language to make it understandable, follow some protocol or strategy to help you.
- Prepare the family: introduce yourself and receive them with empathy. Respect the silences. Make sure that they understand the information that you are conveying to them and let them convey their questions and be ready to answer them.

**Recommendation #3: do not use PPE without specific training**

Protection of the medical staff is a priority. PPE is a barrier to avoid contagion of the healthcare personnel. It should be worn when the risk of infection cannot be avoided or limited enough through collective protection techniques or introducing changes in the routine organization of work. The effectiveness of PPE goes hand in hand with the selection of the equipment based on the type of exposure, and the appropriate donning and doffing. To prevent PPE from being a false barrier that worsens exposure, it is crucial to train the staff specifically on the equipment.<sup>124-126</sup>

### Toxicology working group

#### Recommendations on actions «to take»

**Recommendation #1: in case of combined treatment with lopinavir/ritonavir + hydroxychloroquine it is advisable to have a specific treatment protocol in place due to potential secondary effects**

Combined treatment with lopinavir/ritonavir + hydroxychloroquine has important secondary effects.<sup>48</sup> It is advisable to have a list of interactions of the most commonly used drugs to minimize adverse effects. Also, it is desirable to perform daily electrocardiogram (ECG) monitoring since both drugs lengthen the QT interval and increase the risk of arrhythmias. The white series can also be affected, which is why a daily hemogram follow-up is recommended.

Liver function tests should be monitored daily since the combination of lopinavir/ritonavir inhibits CYP3A of P450 with the corresponding risk of hepatopathy.<sup>127</sup>

### Transfusions and hemoderivatives working group

#### Recommendations on actions «to take»

**Recommendation #1: determine the D-dimer levels on admission and during disease progression to assess the prognosis of patients with COVID-19**

D-dimer levels > 1000 ng/mL on admission are associated with an 18-times higher mortality risk. Also, in non-survivors, the D-dimer levels increase during the hospitalization stay while they remain stable among survivors.<sup>102,128</sup>

Its determination can be useful together with other parameters such as age, the presence of comorbidities, q-SOFA, ferritin, and IL-6 for the assessment of these patients' treatment and prognosis.

It is advisable to make determinations every 24–48 h until achieving favorable disease progression or reduced values.

*Recommendation #2: start early prophylaxis of deep venous thrombosis. Think about the possibility of pulmonary thromboembolism (PTE) in view of shock and deterioration of respiratory failure*

Critically ill patients with COVID-19 are immobilized; they show an inflammatory state with hypercoagulability and there is also the possibility of endothelial activation due to the virus binding to ACE2 receptors.<sup>129</sup> Although it is not clear what the best antithrombotic strategy is for the management of COVID-19, it seems appropriate to use low-molecular-weight heparins early in time. If platelets are  $< 30\,000/\mu\text{L}$  or there is active bleeding and mechanical compression stockings should be worn. We should think and rule out thrombotic complications (PTE, cardiac complications, etc.) if there is sudden deterioration of the hemodynamic or respiratory condition.

*Recommendation #3: consider anticoagulating patients with high D-dimer levels ( $> 2000\text{ ng/mL}$ )*

In patients with COVID-19 there is a systemic inflammatory response with development of disseminated intravascular coagulation that causes thrombotic phenomena and ischemia in different territories. Anticoagulating is necessary if there is evidence of thrombosis or purpura fulminans. It is advisable to perform an echo-Doppler and echocardiography of the lower extremities. It is advisable to anticoagulate patients with increasing D-dimer levels over 4 times the peak value of normalcy as long as there are no contraindications.<sup>130</sup> It is advisable to use enoxaparin or unfractionated heparin. Use of direct-action oral anticoagulants or vitamin K antagonists should be avoided.

#### **Recommendations on actions «not to take»**

*Recommendation #1: do not transfuse patients with hemoglobin levels  $\geq 7\text{ g/dL}$  without active bleeding*

The restrictive transfusion strategy ( $\text{Hb} < 7\text{ g/dL}$ ) minimizes the use of blood bags without increasing morbidity or mortality in most critically ill patients.<sup>131</sup> A more liberal strategy ( $< 9\text{ g/dL}$ ) should be followed in patients with acute coronary syndrome.

There is not enough evidence to recommend one strategy over the other in patients with acute neurological damage, onco-hematological damage, the elderly or on ECMO. Due to lack of specific evidence in patients with COVID-19, we suggest following the general recommendations. We should bear in mind the importance of managing correctly scarce resources in times of sanitary crises.

*Recommendation #2: do not administer plasma for coagulation abnormalities without associated bleeding*

It is common to see coagulation abnormalities due to disseminated intravascular coagulation in patients with COVID-19. These abnormalities are associated with worse prognosis.<sup>129</sup>

Although no studies have been conducted in patients with COVID-19, the administration of plasma for prophylactic reasons to critically ill patients with coagulopathy has not improved hemostasis or brought any other benefit. On the other hand, plasma transfusion can be associated with risks such as liquid overload, transfusional reactions, lung injury (TRALI), and infections.

We should bear in mind the possibility of COVID-19<sup>128</sup> transmission and shortage of hemocomponents in times of healthcare crises.

*Recommendation #3: do not administer hyperimmune plasma or immunoglobulins outside of a clinical trial*

Although they have been used in several patient series, there is no evidence on the efficacy of hyperimmune plasma or IV immunoglobulin for the management of COVID-19. The administration of hyperimmune plasma has been used in other viral infections with respiratory distress syndrome and has been able to reduce the mortality rate.<sup>132</sup> However, no quality studies have been conducted with COVID-19 and we should keep in mind the ethical and moral connotations associated with its use and production in humans. The use of immunoglobulins can be associated with severe adverse effects such as anaphylaxis and thrombosis. Therefore, the use of hyperimmune plasma and immunoglobulins should be based on well-designed clinical trials where their efficacy and safety can be assessed rigorously.<sup>133</sup>

#### **Critical transfers working group**

##### **Recommendations on actions «to take»**

*Recommendation #1: design a strategic interhospital critical transfer plan establishing an ICU coordination head and a resource expansion plan*

Interhospital transfer plays a significant role in the correct allocation of resources during a pandemic but it collapses easily. It is necessary to create a strategic plan specific for this resource, determine logistic and human factors to expand the service adapting it to the current needs during the different stages of the process.

It is necessary to create a central intensive care coordination chair that has availability of the resources need to know the actual status of ICU beds and with the capacity to analyze the situation, need for critically ill patient transfers, their prioritization and risk, and adjust the necessary means to perform safe transfers.<sup>134,135</sup>

*Recommendation #2: minimize transfers of patients with COVID-19 to avoid spreading disease and design an intra and interhospital transfer plan*

It is advisable to minimize the transfers of these patients and avoid the use of tests performed outside the ICU setting. It is necessary to set up an entry and exit patient circuit only for these patients plus a decontamination area for the professional transfer team.

Create an interhospital transfer protocol to simplify the transfer process: unify the phone contacts, use checklists, unify the transfer documentation, and inform the family about the risks involved in the transfer *per se*.<sup>135,136</sup>

*Recommendation #3: assess the risk of interhospital transfer and, in cases of saturation in your ICU, select patients with the lowest transfer risks of all*

It is necessary to assess the overall risk involved in the transfer and the benefit that the transfer to another center may bring. The risk of adverse events (AE) due to the transfer of critically ill patients has been associated with different aspects, among them, the patient's clinical severity. Other aspects that elevate the risk of AE are urgency of the transfer, personnel not properly trained, transfer time, inadequate or unchecked material, inad-

equate logistics, and lack of communication among the personnel involved.<sup>135,137,138</sup>

### Recommendations on actions «not to take»

*Recommendation #1: faster transfers are not always better regarding organization and execution*

Emergency transfers have a higher rate of AE than scheduled ones. On the other hand, we should know that working on a mobile means of transportation adds another difficulty. Therefore, despite the urgency and haste, we rather slow down and work in the cabin.<sup>135,137</sup>

*Recommendation #2: do not forget patient safety throughout the entire process from the planning itself to the patient's arrival at his destination*

Transfer of complex patients poses numerous challenges. It is necessary to pay attention to those points where there is a higher risk of adverse events such as availability of the necessary material (batteries, oxygen, perfusions), avoidance of accidental disconnections, suitable transmission of information, etc.<sup>139</sup>

*Recommendation #3: do not transfer patients without stabilizing them first or without having evaluated his risk of transfer*

Patients with pneumonia due to COVID-19 can be severely hypoxemic and deteriorate severely during the transfer. The transfer of deeply hypoxemic patients without ECMO cardiorespiratory support to reference centers in this therapy has been associated with mortality, which is why we should maximize precautions in this type of patients, stabilize them in advance, assess their risk, and adjust the means of transportation to every patient.<sup>140-142</sup>

## Discussion

These recommendations for the management of critically ill patients with COVID-19 have been elaborated with urgency and include aspects considered most important to this day on the issue at stake.

With these recommendations we seek to give key guidance in a moment in which novelty and urgency are causing high variability in the way routine activity is adjusted to the pandemic. On the one hand, advisable actions are indicated to be performed according to the evidence available. At the same time, we are advised to suspend, reduce or not to use practices that do not bring any proven benefits. This will certainly impact the patient clinical safety and the rational use of resources.

Este documento tiene limitaciones, fundamentalmente derivadas de la falta de conocimiento profundo de esta enfermedad y de la urgencia con la que están publicando los artículos científicos. La experiencia adquirida y los resultados de futuras investigaciones clínicas condicionarán que algunas de las recomendaciones puedan ser modificadas o eliminadas y que se incorporen otras nuevas.

This document has limitations, especially those that result from the lack of deep knowledge on this disease and the urgency with which scientific articles are being published. The experience acquired and the results of future clinical studies will modify or eliminate these recommendations or bring about new ones.

In conclusion, the recommendations for the management of COVID-19 elaborated by SEMICYUC intend to be a useful tool to be able to manage both the healthcare and treatment protocols of coronavirus infections. However, this pandemic situation is dynamic and the recommendations established will have to be adapted to the current and rapidly-changing situation.

## Conflicts of interest

None reported.

## Annex 1. Working Groups from the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)

*Bioethics Working Group:* Olga Rubio Sanchiz (Hospital Sant Joan de Déu, Fundació Althaia, Manresa).

*Cardiology Critical Care and Cardiopulmonary Resuscitation Working Group:* Miguel Ángel Rodríguez Yago (Hospital Universitario Son Espases, Palma); Virginia Fraile Gutiérrez (Hospital Universitario Río Hortega, Valladolid); M. Paz Fuset Cabanes (Hospital Universitario Bellvitge, Hospitalet de Llobregat), and Lluís Zapata Fenor (Hospital Sant Pau, Barcelona).

*Nephrological Intensive Care Working Group:* Manuel García Montesinos de la Peña (Complejo Hospitalario de Navarra, Pamplona); Ana Ortega Montes (Hospital Montecelo, Pontevedra); Ana Navas Pérez (Hospital Corporació Sanitària Parc Taulí, Sabadell), and María Dolores Arias Verdú (Hospital Carlos Haya, Málaga).

*Donation and Transplant Working Group:* Teresa Pont Castellana (Hospital Universitario Vall d'Hebron, Barcelona); Enrique Maraví Poma (Complejo Hospitalario de Navarra, Hospital Virgen del Camino, Pamplona); Juan José Rubio Muñoz (Hospital Universitario Puerta de Hierro, Majadahonda), and Francisco del Río Gallegos (Coordinación Autonómica de Trasplantes, Madrid. Hospital Clínico San Carlos, Madrid).

*Infectious Diseases and Sepsis Working Group:* Mercedes Catalán González (Hospital Universitario 12 de Octubre, Madrid), and Emili Díaz Santos (Hospital Universitario Parc Taulí, Sabadell).

*Technology and Research Methodology Assessment Working Group:* David Iglesias Posadilla (Hospital Universitario de Burgos, Burgos), and María Riera Sagrera (Hospital Universitario Son Espases, Palma).

*Acute Kidney Injury Working Group:* Claudia Vera-Ching (Hospital Universitario Dr. Josep Trueta, Gerona).

*Metabolism and Nutrition Working Group:* Carolina Lorencio (Hospital Dr. Josep Trueta, Girona), and Carlos González Iglesias (Hospital de Barbastro, Barbastro).

*Trauma and Neurointensive Care Working Group:* Marylin Riveiro Vilaboa (Hospital Universitario Vall d'Hebron, Barcelona), and Pedro Enríquez Giraudo (Hospital Universitario Río Hortega, Valladolid).

*Planning, Organization, and Management Working Group:* José Carlos Igeño Cano (Hospital San Juan de Dios, Córdoba); M. Cruz Martín (Hospital Universitario de Torrejón); Josep Trenado (Hospital Universitario Mutua Terrassa);

María Riera Sagrera (Hospital Universitari Son Espases, Palma); Juan Carlos Montejo (Hospital Universitario 12 de Octubre, Madrid), and Manuel Sánchez Sánchez (Hospital Universitario La Paz, Madrid).

*Sedation, Analgesia, and Delirium Working Group:* Carola Giménez-Esparza Vich (Hospital Vega Baja, Orihuela).

*Simulation for Clinical Training Working Group:* Jesús Priego Sanz (Complejo Hospitalario Universitario de Ourense, Ourense); María Jesús Broch Porcar (Hospital Universitario La Fe, Valencia); Miguel Valdivia de la Fuente (Hospital Universitario Puerta de Hierro, Majadahonda); M. Cruz Martín Delgado (Hospital Universitario de Torrejón); Diego Palacios Castañeda (Hospital Universitario Puerta de Hierro, Majadahonda), and Aida Fernández Ferreira (Hospital Universitario Álvaro Cunqueiro, Vigo).

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