

# Respiratory Rehabilitation in Patients with SARS-COV-2. Current State of Knowledge

## *Rehabilitación respiratoria en pacientes con SARS-COV-2. Estado de conocimiento actual*

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### INTRODUCTION RATIONALE AND JUSTIFICATION OF THE DOCUMENT

In December 2019, the first case of the disease caused by the SARS-Cov-2 virus was detected in the city of Wuhan, China.<sup>1</sup> Unlike the limited character of the two previous epidemics, the Middle East Respiratory Syndrome (MERS) and the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), the rapid expansion of SARS-CoV-2 forced the World Health Organization (WHO) to declare the pandemic in March, 2020.<sup>2</sup>

According to the reports on the evolution of the pandemic available at the John Hopkins University (JHU), at the time this document was written, around 160 million cases and 3.3 million deaths had been reported.<sup>3</sup> During the first year, the pandemic caused 1.8 million deaths around the world, compared to 2.6 million deaths produced by all the lower respiratory tract infections in 2019.<sup>4</sup>

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The mortality produced by all the respiratory infections in 2017 (last available record) was 64,869 deaths, and the mortality produced by SARS-CoV-2 only within one year of the pandemic accounted for 53,741 deaths.<sup>5,6</sup>

Apart from the mortality produced by SARS-CoV-2, we must consider two other levels of impact: the first one, generated by the acute disease, requires the early intervention of the rehabilitation tool, such as in the ICU (Intensive Care Unit) and in-patient wards. The second level of impact refers to the chronic disease, the multiple physical, psychological and neurocognitive functional sequelae that are usually expressed as Post-Intensive Care Syndrome (PICS) in critically ill patients.

A national study conducted on a sample of 207,000 patients with complete data, treated between March and October 2020, allows us to have an approximate estimation of how many patients who suffered from the disease caused by SARS-CoV-2 required rehabilitation.<sup>7</sup> 20.1% of them (41,703 patients) were hospitalized, out of which 2.7% (5,652 patients) were admitted to the ICU. Only among these ICU survivors (around 2,800 patients), then in the intermediate care ward, and finally with the outpatient in-person or remote modality, would rehabilitation be justified in that context.

Apart from the patients admitted to the ICU, the indication should also include patients with moderate or severe forms of the disease who required different levels of oxygen therapy in intermediate care or general wards.

In view of the above, an *early* intervention is urgently needed, mainly in the respiratory, cardiovascular, neuromotor, cognitive and psychological areas, in order to minimize sequelae and try to reach maximum patient's autonomy and the best possible quality of life.<sup>8</sup>

In any case, the most important thing is that rehabilitation becomes a *continuous* intervention. We recommend to keep a common line of work throughout the different stages of disease evolution. This applies to both patients who begin this intervention in the ICU, continue in the general ward and then during the outpatient period, and to those who begin in the general ward and continue on an outpatient basis.

The *objective* of this document is to offer the professionals involved in the respiratory rehabilitation of these patients a set of recommendations

supported by the current state of knowledge and endorsed by our specialized experts that can be feasibly used in centers of different complexity levels in our country.

## CLINICAL PRESENTATION OF INFECTION BY SARS-CoV-2

Infection by SARS-CoV-2 can be symptomatic or asymptomatic. Symptomatic patients may show mild and moderate or even severe forms of the disease with pneumonia and ARDS (acute respiratory distress syndrome), with respiratory failure and multi-organ failure. Also, long-term complications could occur after SARS-CoV-2 infection, causing the post-COVID syndrome (pCS) or the persistent COVID syndrome (PC).

Around 80% of patients with COVID-19 develop mild to moderate disease; 15% progress to severe stages and require oxygen support, and 5% develop a critical disease including ARDS, septic shock and multi-organ failure.<sup>9</sup> Age and various comorbidities such as diabetes, obesity, lung and cardiovascular diseases and some genetic polymorphisms correlate with a higher risk of respiratory failure.<sup>10-12</sup>

We must also take into account that approximately 50% of people with severe pneumonia caused by COVID-19 develop ARDS, with pulmonary fibrosis as a common complication.<sup>13</sup> These patients will have damaged lung function with irreversible respiratory failure associated with bad prognosis.<sup>14</sup>

## A. RESPIRATORY REHABILITATION IN COVID-19 PATIENTS ADMITTED TO THE CRITICAL CARE UNITS

Patients with COVID-19 whose treatment requires hospitalization in the Intensive Care Unit (ICU) with or without invasive mechanical ventilation (IMV) need early kinesiology care, not only for the management of the ventilatory treatment, but also for the motor rehabilitation that is necessary for the patient to go back to his/her regular activities after discharge.

In this section we suggest that general guidelines are established regarding the way in which we should evaluate the impact of rehabilitation upon these patients, which tests can be done, and how to address the rehabilitation process of COVID-19 patients in the ICU.

The first thing to decide is how the rehabilitation plan should be organized, taking into account that it has to be individualized and customized. In order to do that, several aspects are to be considered:

1. Setting suitable titration of analgesia and sedation, depending on the ventilatory mode that is being used, disease evolution, and the patient's oxygenation state.
2. Using a ventilator mode and setting that are adequate for the patient (avoid the patient/ventilator asynchrony), on distension and hypoventilation.<sup>15</sup>
3. Providing the kinesiology treatment gradually, taking into account the clinical status of the patient.
4. Monitoring with strict safety criteria.<sup>16</sup>
5. Planning early rehabilitation together with the interdisciplinary team.

When addressing the important aspects described in this section, we use four trigger questions for educational purposes.

#### 1. Which are the objectives of a rehabilitation process in the ICU?

The main objective of an early rehabilitation program (ER) (defining the ER as an intervention to provide motor, sensitive and proprioceptive stimuli that generate in the patient a less negative impact of the ICU admission), is to avoid losing the functionality the patient had before being admitted to the critical care area.<sup>17</sup>

Also, the objectives related to the ER must be proposed, for example, reducing sedation and analgesia, maintaining the range of motion, sitting position, standing position and walking. Then come the DLAs (daily living activities).

These goals have to be proposed upon the patient's admission to the critical care area, and must be evaluated upon discharge.

For the correct organization of the proposed objectives, the measures known as the "ABCDEF Bundle" can be used, especially when there is early weaning, prevention and treatment of delirium and early rehabilitation.<sup>18</sup> This allows for the coordination of patient care in order to wean him/her from IMV and discharge him/her from the ICU.

#### 2. Which are the necessary criteria to begin rehabilitation?

The kinesiologist has to adapt to the patient's conditions: whether he/she has orotracheal intubation

or tracheotomy, invasive or non-invasive mechanical ventilation, humidified high-flow therapy or any other form of oxygen therapy support. It is essential to consider the presence of drug administration routes, drainage, hemodynamic stability and monitoring.

The patient must have a stable medical condition, one airway free of complications and ensured oxygen requirement, and he/she should also begin the respiratory rehabilitation (RR) session, ensuring the use of drugs if necessary.

The criteria are defined in the following way:<sup>19</sup>

1. Heart rate of less than 50% of the theoretical maximum heart rate (TMHR).
2. Blood pressure with a variability of less than 20% (avoid hemodynamic decompensation).
3. Normal electrocardiogram.
4. Partial oxygen saturation > 90% with a reduction of less than 4 points at the time of the ER.
5.  $\text{PaO}_2/\text{FiO}_2 > 300$  (ER tolerance index with good reserve volume; lower values reduce such volume, state of alert).
6. Adapted respiratory pattern.
7. Stable mechanical ventilation.
8. Stable airway.
9. Absence of fever.

#### 3. How is the patient who begins rehabilitation in the ICU evaluated?

The evaluation must include respiratory and muscular functions and state of consciousness. The recommended instruments are:

1. Evaluation of dyspnea through the mMRC (Modified Medical Research Council) scale.<sup>20</sup>
2. Evaluation of the muscular state through the MRC scale.<sup>21</sup>
3. Assessment of sedation and analgesia and patient's state of alert: Visual Analog Scale (VAS), Pain Behavior Scale (PBS) Richmond Agitation-Sedation Scale (RASS), and delirium scale (CAM-ICU, Confusion Assessment Method for the Intensive Care Unit).<sup>22-24</sup>

#### 4. Which are the elements of the ICU's early rehabilitation plan?

Stages must be respected according to the Morris model of complexity levels<sup>25</sup>.

The plan consists of the following steps:

- Including two daily stimuli from the patient's admission to the critical care area until discharge.

- The initial level (deeply sedated patient) includes passive movement of the limbs and postural control.
- Once the patient regains consciousness, he/she begins with active-assisted exercises and functional progression as he/she meets the objectives. Such progression includes: sitting on the corner of the bed, trying the standing position once he/she controls his/her trunk, and then walking around with assistance and doing activities outside the bed.<sup>25,26</sup>
- Including family members in the rehabilitation process through videocalls and helping the patient both with functional progression and providing the patient's elements (watch, glasses, books, radio, etc.)
- Recording adverse events so as to avoid repeating them.

## B. RESPIRATORY REHABILITATION ON THE IN-PATIENT WARD

As we already mentioned, it is estimated that between 14% and 20% of patients infected with SARS-CoV-2 will require hospitalization in a general in-patient ward, so complications associated with immobilization could generate a negative impact on the patient's quality of life.<sup>7,27</sup> Thus, it is essential that the patient receives respiratory rehabilitation treatment during hospitalization, for the prevention and timely management of physical deconditioning effects and effects related to the appearance of sequelae.<sup>28</sup>

When the patient is transferred from the ICU to Intermediate Care or to the in-patient ward, the RR has to be continuous and in-line with the treatment that had already begun in the ICU; in the case of patients initially admitted to the in-patient ward, they have to meet the following conditions once they are included in the rehabilitation program:

1. Patients coming from the ICU, will continue with their RR treatment but those who are directly admitted to the in-patient ward have to establish their corresponding treatment.
2. An evaluation will be carried out to identify prognostic factors of PICS syndrome, chronic damage caused by COVID, post-COVID syndrome and persistent COVID syndrome, in patients coming from the ICU.<sup>29</sup>

3. Rehabilitation goals have to be set.<sup>27,30</sup>
4. Patient's evolution has to be monitored.
5. The comparison between the RR parameters and applications in its different stages is recommended.

Three triggering questions are included in this section that intend to address *to whom*, *how* and *when* to perform the RR in a general in-patient ward.

### 1. Which are the conditions for COVID-19 patients to begin RR on the in-patient ward?

According to the aforementioned, around 3-5% of moderately ill patients will develop severe or even critical disease 7 to 14 days after the onset of the infection<sup>31,32</sup>.

The parameters that should be evaluated in patients coming from the ICU are:<sup>31-33</sup>

1. Time since the onset of symptoms.
2. Type and number of symptoms.
3. Oxygen saturation values.
4. Intensity and extent of pulmonary involvement.
5. Supplemental oxygen requirement and types of administration.
6. Need to use invasive or non-invasive mechanical ventilation.
7. Ventilation time and possible complications.
8. Coexistence of renal, hematologic, neurologic or any other type of complication and type of treatment received.
9. In patients directly admitted to the in-patient ward, an observational behavior must be set, depending on the patient's evolution.

## A. EXCLUSION AND TERMINATION OF EXERCISE CRITERIA

### A.1 EXCLUSION CRITERIA<sup>27,31</sup>

- Patient with fever.
- Time of initial consultation  $\leq 7$  days in patients directly admitted to the in-patient ward.
- Duration of the disease  $\leq 3$  days from onset to appearance of dyspnea, due to disease progression or fully active clinical condition.
- Progression of opacities in chest X-ray of at least 50% in 24 to 48 hours.
- $SO_2 \leq 90\%$  with supplemental oxygen.
- Heart rate  $< 40$  or  $> 130$  bpm.
- Blood pressure at rest  $< 90/60$  or  $> 140/90$  mmHg.
- Respiratory rate  $> 24$  bpm.
- Lack of consent from the patient.

## A.2 TERMINATION OF EXERCISE CRITERIA<sup>27,31,33</sup>

- Modified Borg Scale value > 3 for dyspnea score at the initial stage of RR.
- Drop in SpO<sub>2</sub> > 4%.
- Signs of chest tightness.
- Alterations in ventilatory mechanics and/or use of accessory muscles.
- Breathing difficulty, dizziness, headache, blurry vision, palpitations, excessive sweating and balance disorder.
- Other conditions determined by the physician as inadequate for doing the exercise.

### 2. How should patients included in the rehabilitation intervention be evaluated?

The different evaluations described below shall be selected depending on the working context of each professional.

There are different fields within the scope of the evaluation:

#### 1. EVALUATION OF THE PATIENT'S GENERAL CONDITION

It will observe the breathing rhythm, the state of muscular masses, mobility and range of motion, state of consciousness and the possibility to cooperate in the rehabilitation.

#### 2. EVALUATION OF DYSPNEA

In order to evaluate the level of dyspnea, many validated, simple scales can be used.

**2.1 Modified Borg Scale:** to evaluate the level of effort perceived by the patient and to be able to prescribe and control the intensity of the activity<sup>27</sup>.

**2.2 Visual Analog Scale**<sup>34</sup>

#### 3. EVALUATION OF EXERCISE CAPACITY

If allowed by the respiratory, cardiac and metabolic reserves of the patient, the following tests can be done:

**3.1 1- MIN SIT-TO-STAND TEST (STS1'):** this test will allow the evaluation of desaturation induced by exercise.<sup>35</sup>

**3.2 5R-STTS:** normal cut-off point ≤ 12 seconds.<sup>36</sup>

**3.3 TEST TIME UP and Go (TUG):** abnormal cut-off point for fall risk shall be ≥ 16 seconds.<sup>37</sup>

**3.4 4 - METRE GAIT SPEED:** this test will evaluate the time needed to walk 4 meters at a normal speed. A value > 0.8 m/sec shall be considered abnormal.<sup>38</sup>

## 4. STRENGTH ASSESSMENT

**3.1 Medical Research Council Scale (MRC)**<sup>27</sup>.

**3.2 Repetition method.**<sup>39-41</sup>

## 4 EVALUATION OF DAILY LIFE ACTIVITIES (DLAS)

**4.1 PCFS**<sup>29</sup>

**4.2 Barthel Index**<sup>42</sup>

**4.3 Katz Index**<sup>43</sup>

### 3. When and how should these patients undergo the peripheral muscle training?

We suggest early rehabilitation in patients coming from the ICU and in those who are directly admitted to the in-patient ward during the first 3 days after the patient was stabilized. It is also important to have good pain control, in order to favor the achievement of objectives.<sup>27</sup>

The design of RR programs for patients with COVID-19 must respect the general principles of training, which are related to intensity, duration, frequency, specificity and exercise reversibility.<sup>30,44</sup>

To do that, the training objectives and scope have to be planned with each patient, taking into account their exercise capacity tests.<sup>45</sup>

**PATIENT MONITORING:** patients should be monitored before, during and after the rehabilitation session. Variables to monitor are:

- 0.1 SpO<sub>2</sub>: it has to be higher than 90% with supplemental oxygen, with less than 4% variability tolerance during the session.<sup>27</sup>
- 0.2 Blood pressure: no more than 20% variability tolerance during the session.<sup>46</sup>
- 0.3 HR: no more than 80% variability tolerance of the TMHR is suggested<sup>22</sup>.
- 0.4 Respiratory rate: it shouldn't be higher than 24 bpm.<sup>46</sup>
- 0.5 If possible, the session must be restarted once the already mentioned parameters go back to normal.<sup>27</sup>

#### 1. MUSCULAR STRENGTH TRAINING:

- 1.1 It is suggested that patients begin with big muscle groups (shoulder girdle and pelvic girdle).<sup>43</sup>
- 1.2 Then, balance, proprioceptive and coordination exercises will be included. Fall risks will be monitored.<sup>27</sup>
- 1.3 Exercise intensity: patients will begin with active mobility exercises, and continue with sets of low intensity exercises using the body-weight (60% of the maximum intensity achieved with

the repetition method), and then will continue to increase intensity according to the muscular response of each patient. 3 sets per muscular group with a pause of 2 minutes between each set are suggested.<sup>47,48</sup>

- 1.4 Functional training is recommended.<sup>49-51</sup>
- 1.5 A frequency of two times a day is suggested.<sup>27</sup>
- 1.6 Regarding the duration of the session, it is recommended that the patient begins with 20 minutes and progresses to 30 minutes per session.

## 2. AEROBIC CAPACITY TRAINING

- 2.1 Given the small size of the rooms in the inpatient ward, exercises should be done with short displacement, also taking into account epidemiologic safety.
- 2.2 The intensity of exercise must be progressive until the patient reaches 80% of the TMHR.
- 2.3 Training methods can be continuous or intermittent.<sup>27</sup>
- 2.4 A frequency of two times a day is recommended.<sup>27</sup>
- 2.5 The duration of the session shall preferably be 20 minutes, minimum, and must progress to 30 minutes.

## RESPIRATORY REHABILITATION AFTER HOSPITAL DISCHARGE

It is extremely important that before hospital discharge, a report is made describing the most urgent needs of the patient, such as the safety of home mobility, symptom control, supplemental oxygen requirement, suitable nutrition, psychological and social support, and short- and long-term needs, for example, improvement in physical and emotional functions and return to work.<sup>17</sup>

## C. RESPIRATORY REHABILITATION IN OUTPATIENTS WITH POST-COVID-19 SYNDROME AND LONG OR PERSISTENT COVID SYNDROME

This section has the purpose of addressing respiratory rehabilitation in patients who suffered from the disease caused by SARS-Cov-2 and were discharged from hospital, as well as those who were treated on an outpatient basis but evolved and still have dyspnea.

This chapter uses five trigger questions about issues of interest to the professionals in charge of the Respiratory Rehabilitation Programs (RRPs) in outpatient modality.

### 1. What do post-COVID-19 syndrome and long or persistent COVID syndrome mean?

In accordance with different international studies, the duration of the symptoms caused by COVID-19 infection has a mean value of 11 days for patients who weren't hospitalized and 13 to 25 days for those who required hospitalization<sup>52</sup>. However, after the resolution of the viral infection, it has been observed that some signs and symptoms tend to prolong. The *post-COVID-19 syndrome* (hereinafter referred to as pCS) is defined as the group of signs and symptoms that appear after the acute infection has been resolved.<sup>53-61</sup> It includes persistent symptoms that could be related to residual inflammation (in the convalescent phase), organic damage, non-specific effects of hospitalization or prolonged ventilation (PICS) *and long or persistent COVID (PS)*.<sup>52-53</sup>

The first description alerting us to the importance of the pCS appeared in a patient survey conducted in the United States between April and May, 2020<sup>54</sup>. The name "pCS" came from that work and was endorsed by Greenhalgh in a subsequent publication.<sup>55</sup>

Spanish authors propose considering four stages of the SARS-CoV-2 disease and defining those clinical conditions depending on evolution.<sup>56</sup> Thus, symptoms related to the acute infection would be limited to the first 4 weeks; acute pCS would describe symptom persistence for 5-12 weeks; prolonged symptoms would be divided in two groups: long post-COVID syndrome (LS), of 12-24 weeks of evolution and persistent syndrome (PS), prolonging beyond 24 weeks from the onset of symptoms.<sup>56</sup>

However, there isn't any universally accepted name in the definitions of pCS and PS. Two Spanish guides define the pCS as the group of systemic findings beyond 4 weeks from the onset of the first symptom, with the signs and symptoms being part of the acute infection as essential requirement.<sup>52-53</sup> The NICE Guide (National Institute for Health and Care Excellence) from the United Kingdom takes the PS into consideration after 12 weeks, and the WHO Guide, as of the fourth or fifth week.<sup>57,58</sup>

The frequency of the PS is of approximately 10-35% of patients in general, even though in critically ill, hospitalized patients it can reach 80%.<sup>53,54,59</sup>

## 2. How to differentiate the pCS and PS from other similar clinical conditions?

It is important to differentiate the post-COVID symptoms from other situations that can be similar but don't share their temporal pattern and/or clinical presentation.

- A. In cases in which signs and symptoms are present *before* the onset of COVID-19 clinical conditions.
- B. If signs and symptoms appear *after the infection* and weren't a part of it (post-viral symptoms).
- C. If signs and symptoms appear *after the infection* and weren't a part of the initial clinical condition and were caused by the organic damage generated by the infection (*COVID-19 sequelae*).<sup>52-53</sup> Unlike the PS, patients who have progressed with organic sequelae are usually older males with previous comorbidities that don't evolve in an outbreak like the PS.<sup>53</sup>
- D. Finally, the situation arising from systemic or organic damage due to a severe infection (*post-Covid-19 chronic damage*)<sup>52</sup>

## 3. Which is the presentation and clinical profile of the patient with PS who is referred to a Respiratory Rehabilitation Program?

López León et al conducted a systematic review and meta-analysis of the available literature on prolonged signs and symptoms caused by COVID-19 infection.<sup>60</sup> 6 of 15 studies belonged to hospitalized patients, and they had a follow-up of 14-110 days. 55 persistent signs or symptoms related to the viral infection were identified, the most common being: fatigue (58%), headache (44%), attention disorders (27%), hair loss (25%), and dyspnea (24%). In 7 studies (n = 1,915 patients), 80% of the subjects had at least one persistent symptom.<sup>60</sup>

Regarding the *profile of the patient* normally referred to RRP with a diagnosis of PS, a survey of 3,762 patients from 56 countries described symptoms up to 7 months after the onset of the acute infection.<sup>62</sup> Most patients had at least 3 months of evolution, a mean of 14 symptoms per patient and an average of 9 affected organs<sup>61</sup>.

With respect to the *degree of disability* that is usually self-perceived by the patients, a Spanish survey shows that patients reported 50% disability.<sup>62</sup> When describing each activity in detail, the most common limitations were found in personal hygiene and daily life activities, especially family duties and recreation activities.<sup>62</sup>

## 4. When, where, and how can a patient with pCS and PS be initially evaluated?

Evidence regarding which is the best approach for patients with pCS and PS referred to the RRP is scarce.<sup>30,52,57,58,63-65,66-70</sup> However, there are unanimous criteria about several important issues.

First, in this work we believe that patients who have been hospitalized for a long time or had oxygen requirement or ventilatory support need outpatient or home respiratory rehabilitation as a *continuous strategy* following the treatment that started in the ICU or general ward.

Secondly, given the multiplicity of organs affected by the PS, the high number of symptoms reported by patients and their time of evolution, it is necessary to have a *multidisciplinary approach* for those who suffered from COVID-19 and arrive at the RRP.<sup>30,53,57,58,63-70</sup>

In the third place, it's clear that, as far as is practical, rehabilitation must *focus on the patient*.<sup>30,53,57,63-70</sup> This means that the place *where* the patient is to be evaluated will depend on his/her needs and possibilities.

### A. Remote evaluation of patients with pCS and PS

Even though there is agreement on the usefulness of telemedicine in certain groups that apply to the RRP, at the moment there isn't any standardized, validated protocol on how to evaluate and train patients with pCS and PS remotely. The consulted literature relies on experts' recommendations.<sup>44,52,53,57,63,70</sup> We must take into account three basic aspects when a patient is going to be included in a distance RRP: *indication*, according to the particular situation of the patient; the *criteria* that the patient has to meet in order to access the intervention on equal terms; the *characteristics of the tools* that are going to be used for the evaluation.<sup>44,67-70</sup>

Table 1 describes the indications, inclusion criteria that ensure equality between patients and tools to be used in the process.

**TABLE 1.** Indicaciones, condiciones de inclusión y características de las herramientas a utilizar en el Evaluación No Presencial de pacientes externados con COVID-19<sup>17-21</sup>

Indications of remote evaluation	A. Patient under mandatory social lockdown due to the pandemic. B. Patient not physically capable of moving. C. Patient who rejects the institutional intervention or wasn't evaluated upon discharge.
Inclusion criteria	A. <b>Feasibility conditions</b> Availability, proper functioning and knowledge of the management of electronic devices or, if that's not the case, at least a tutor accompanying the patient. B. <b>Clinical conditions</b> Absence of comorbidities that prevent or limit the intervention (severe hearing loss, amaurosis, cognitive impairment, decompensated psychiatric disease). C. <b>Bioethical aspects</b> Information for the patient about the intervention scope and potential risks of not being supervised. Written informed consent, digital or audio format. Respect for the patient's privacy (position of the camera). Confidentiality of the relationship and consensus on the registration and management of the results.
Characteristics of the tools used for the evaluation	A. <b>Safety</b> The safety of the tool is prioritized over other aspects. B. <b>Simplicity</b> Use of everyday objects for the tests; accessibility and simplicity are prioritized over accuracy. C. <b>Reproducibility</b> The best possible tool is prioritized over the optimum or the most accurate one.

We recommend that the evaluation of these patients is standardized in steps.

The *first step* consists in evaluating the patient's personal history and history of present illness, provided in the epicrisis of the hospitalization medical records.<sup>30,44,52,53,57,63,66,68-70</sup> The information to be included is: preexistent comorbidities, history of present illness, for example, time of evolution of the condition and initial symptoms, days of hospital stay, extension and severity of the disease, type of oxygen therapy, if so required (used devices and flows), application, if any, of invasive and non-invasive ventilation (days of effective ventilation), administered treatment and patient's response, laboratory anomalies of clinical and prognostic relevance and list of complications and potential sequelae registered after hospital discharge.<sup>44,66,68,69</sup>

The importance of the number of initial symptoms is related to a higher risk of suffering PS. The presence of five or more symptoms during the first week of evolution increases the risk of suffering from a prolonged disease by 3.53 times,

compared to patients who show less than five symptoms.<sup>44,64,66,68,69</sup>

The *second step* includes the remote estimation of the patient's general condition: his/her aspect, the state of muscular masses, the ventilatory mechanics, the identification of movement limitations and the state of consciousness<sup>69</sup>

With the *third step* we are able to establish the patient's level of dyspnea and exercise capacity.

The patient is asked to identify his/her level of dyspnea in accordance with the Borg dyspnea scale and the Modified Medical Research Council scale (mMRC).<sup>67-70</sup> In order to test if he/she needs oxygen, the patient is requested to measure oxygen saturation (SpO<sub>2</sub>) while sitting and at rest. If the values are  $\geq 96\%$ , the patient is asked to walk forty steps on a flat surface, with the oximeter. In the case of patients who don't have an oximeter, or as supplementary information of those who do, we recommend exercises that don't exceed 4 (four) points in the Borg Scale for perception of dyspnea.<sup>69</sup>

Apart from estimating dyspnea and SpO<sub>2</sub>, the patient's heart rate (HR) must be monitored, at rest and after each set of exercises. Since the activity isn't supervised, we suggest the formula of 220 beats minus the patient's age.

A second alternative to evaluate exercise capacity is the remote *Sit-to-Stand Test* (STS). Although it has been developed and validated for patients with COPD, given its safety and simplicity, it has been proposed in publications on distance rehabilitation.<sup>69-71</sup> From the less demanding modality of 5Rs, to the sit-to-stand in 30 sec (STS30") and 1-min sit-to-stand test (STS1'), these tests allow the evaluation of concentric and eccentric contraction of the quadriceps, the steady state and even the 1' variant correlates with the 6-Minute Walk Test (6MWT).<sup>65,71</sup>

The *fourth step* consists in evaluating muscle strength and nutritional status, commonly altered by the sarcopenia of pCS and PICS.<sup>30,44,52-55,57,60,64,66,68-70</sup>

We suggest the strength evaluation method in 8 MRs (maximum repetitions), the evaluation of 3-4 muscle groups of the upper and lower body and monitoring with the Visual Analog Scale of HR and SpO<sub>2</sub>. For the purpose of calculating the patient's capacity to face daily activities, we propose evaluating the weights using the patient's body weight.

With regard to the nutritional status, the Body Mass Index (BMI) is assessed and muscular masses are observed; that will allow us to have an approximate idea on the nutritional status of the patient.<sup>69</sup> Also a virtual follow-up must be performed, and the nutritionist must provide the most suitable diet for the patient.

The *fifth step* consists in evaluating Daily Life Activities (DLAs).

In accordance with the idea of using the simplest objects for the evaluation, we suggest the use of the functional status index of patients with COVID, called Post-COVID Functional Status, at the time of hospital discharge and 4, 8 and 24 weeks after (PCFS).<sup>29</sup>

The *sixth step* refers to the evaluation of the psychological sphere. There is a consensus on the use of the Hospital Anxiety and Depression Questionnaire (HAD), an instrument that has been validated for the Spanish language and suggested for virtual PS patients.<sup>68,72,73</sup>

The following table describes the steps of the remote evaluation of COVID-19 patients.

### B. In-person evaluation of patients with pCS and PS

The in-person evaluation of patients with pCS and PS shares the first steps with the remote evaluation, for example, the epicrisis information and general and particular observation of the patient.

With regard to the evaluation of dyspnea and exercise capacity, with this modality the patient can do the 6MWT or the Shuttle Test so as to calculate those variables and to identify the impact achieved by rehabilitation.<sup>75</sup>

To calculate the HR for exercise, we suggest the Karnoven formula which takes into account values at rest, heart reserve and maximum reached level.

The tests used to determine which intensity of aerobic exercise should be indicated are the Incremental Test (IT) with a treadmill or cycle ergometer and the Constant Load Test (CLT). The IT is sensitive to interventions and has prognostic implications depending on the severity of the patient.<sup>75</sup> The CLT is the most sensitive tool to detect the impact of RRP on respiratory diseases of various origins.<sup>75</sup>

In the evaluation of muscle strength and nutritional status, the in-person modality allows the use of machines, free weight or functional assessment implements such as suspension straps, exercise balls, bosu balls and body-weight exercise.<sup>44,45</sup>

Regarding the nutrition advice, if the necessary resource is available, it would be desirable to have an anthropometric measurements form that allows the analysis of the intervention effects on the patient's body composition.

For the DLA evaluation we suggest the PCFS in the first place; the Barthel and Katz indices can be a second option, and finally, the 36-Item Short Form Health Survey (SF-36) and the Saint George's Respiratory Questionnaire (SGRQ) could be an alternative. The HAD questionnaire can be used for the psychological evaluation.

The following table summarizes the in-person rehabilitation aspects.

### 3. How to rehabilitate a patient with pCS and PS?

There isn't a generalized consensus on which is the best modality for the rehabilitation of patients

**TABLE 2.** Evaluation of patients with Post-COVID Syndrome/Persistent COVID through the remote respiratory rehabilitation modality

Stages	Remote evaluation
Step 1 Evaluation of personal history and history of present illness.	A. Evaluation of comorbidities as risk factors of unfavorable evolution. B. Evolution of clinical condition with interventions performed and list of complications, if any. C. Record of tests taken while evaluating the state of the patient upon discharge.
Step 2 Estimation of the patient's general condition	A. General observations: weight, height, state of muscular masses, BMI and mobility. B. Observation of the ventilatory mechanics. C. Observation of the state of consciousness and cognitive level
Step 3 Evaluation of dyspnea level and exercise capacity	A. mMRC and Borg dyspnea scales. B. Evaluation of supplemental oxygen requirement through 40-step walk. C. Evaluation of oxygen requirement and exercise capacity through 5R-ST <sub>S</sub> , ST <sub>S</sub> 30" and ST <sub>S</sub> 1'.
Step 4 Evaluation of muscle strength and nutritional status	A. Evaluation of range of motion. B. Evaluation of strength through the repetition method, eight (8) repetitions to estimate 1-rep max according to the Epley or Brzycki formula. C. Nutritional evaluation by BMI.
Step 5 DLA evaluation	Record of PCFS index values
Step 6 Psychological evaluation	Record of HAD test values

with pCS and PS. One concept must be emphasized in this section.

Several publications suggest which type of training could be used through telerehabilitation and in-person rehabilitation, and include not only peripheral muscle training but also nutritional and psychological support and aspects related to the patient's education.<sup>30,52,53,57,58,63,66-70</sup>

#### A. Respiratory rehabilitation with the remote modality

Telemedicine has provided recommendations for the section about respiratory rehabilitation, both in the case of an exercise program remotely supervised by a professional and also in the case of a non-supervised protocol.<sup>69,70</sup>

Exclusion criteria for remote respiratory rehabilitation of patients with pCS are:<sup>69</sup>

- Poor cognitive status (Mini-Mental State Examination  $\leq 24$  points).
- Presence of unstable heart or neurologic disease.
- Severely altered range of motion or other mus-

culoskeletal defects preventing the patient from making the requested gestures.

- Disabled patients who live alone and don't have any help.
- Patients with evident balance disorders.
- Patients without basic knowledge about the management of devices for remote contact.

#### A1. Asynchronous remote respiratory rehabilitation

Information about *which* type of exercise should be done and *how* to do it is provided through videos or workout charts that must be given to the patients. Also, a form must be given to patients containing all the exercises they have to do. The patient has to record the level of dyspnea and fatigue he/she felt in each exercise of the session, according to the Borg scale. If possible, the patient should also record SpO<sub>2</sub> and HR levels at the end of each walk or set of exercises.<sup>44,65,69</sup>

The educational and psychological support converge with muscular training to shape this remote RRP.

**TABLE 3.** Evaluation of patients with Post-COVID Syndrome/Persistent COVID with the in-person respiratory rehabilitation modality

Stages	In-person evaluation
Step 1 Evaluation of personal history and history of present illness	A. Evaluation of comorbidities as risk factors of unfavorable evolution. B. Evolution of clinical condition with interventions performed and list of complications, if any. C. Records of tests taken while evaluating the state of the patient upon discharge.
Step 2 Estimation of the patient's general condition	A. General observations: weight, height, state of muscular masses, range of motion and mobility in general, and patient's degree of disability. B. Observation of the ventilatory mechanics and ventilation type. C. Observation of the state of consciousness and cognitive level.
Step 3 Evaluation of dyspnea level and exercise capacity	A. mMRC and Borg dyspnea scales. B. Evaluation of supplemental oxygen requirement and exercise capacity through 6MWT or Shuttle Test. C. Evaluation of aerobic exercise weight according to the incremental protocol with treadmill or cycle ergometer (IT) and the Constant Load Test (CLT).
Step 4 Evaluation of muscle strength and nutritional status	A. Evaluation of muscle strength. 8 (eight) maximum repetitions, according to the Epley or Brzycki formula. B. Evaluation of angles and range of motion. C. Evaluation through BMI and interconsultation with Nutrition Department. Anthropometry study.
Step 5 DLA evaluation	A. Record of PCFS index values. B. As a second option, Katz or Barthel indices. C. SF-36 or SGRQ, and other options.
Step 6 Psychological evaluation	A. Record of HAD test values. B. Specialized psychological support.

The following table describes the important aspects of this rehabilitation modality.<sup>44,45,66,69,79,80</sup>

## A2. Synchronous remote respiratory rehabilitation

With this modality, the professional can supervise the work of the patient/s in two ways:

On one hand, by connecting to a video-conference with groups of 4-6 participants and observing how they are doing the activity. On the other hand, connecting individually with the patient and supervising him/her 2 (two) times a week while he/she does the activity, leaving other two weekly sessions in charge of the patient himself/herself.<sup>69</sup>

## B. Respiratory rehabilitation through the in-person modality

Once the patient finishes his/her evaluation, the professional has to be able to decide which training modality is most suitable for that patient in particular.

## B1. Aerobic resistance training

Although there isn't any specific protocol for this type of training in patients who suffered from COVID-19 disease, we suggest the training modalities commonly used for patients with diffuse interstitial lung diseases (DILDs), because they bear some similarity to the pulmonary damage caused by SARS-CoV-2 and PICS.

In this context, both the Continuous Variable Method (CVM) and the Intermittent Method can be used.<sup>81</sup>

A recent update of the Cochrane Database of Systematic Reviews regarding the RR in DILDs included 16 studies with 357 DILD patients and a control group of 319 individuals.<sup>81</sup> The rehabilitation improved the 6MWT with a mean of 40 ( $\pm$  32.7-47.4) meters, the capacity to work, oxygen consumption, dyspnea and DLAs measured by the SGRQ and CRQ (Chronic Respiratory Questionnaire), benefits which in five studies persisted between 6-12 months after finishing the intervention.<sup>82</sup>

**TABLE 4.** Suggested interventions for remote asynchronous respiratory rehabilitation

Domain	Intervention
Strength training	<ul style="list-style-type: none"> <li>• Frequency of 2-3 times a week, from 1.5 to 2 hours per session.</li> <li>• Duration of 8-12 weeks.</li> <li>• Strength exercises, 3-4 muscle groups of upper and lower body, using light, everyday objects. We propose 2-3 sets of exercises of 8-12 repetitions per set. Increasing weight according to degree of dyspnea and fatigue (level 5 of Borg scale).</li> <li>• Walking and other activities of less than 3 METS (Metabolic Equivalent of Task) (Ainsworth table).<sup>80</sup></li> </ul>
Educational support	Specially designed charts, videos and guides, for example the guide from the <i>NHS- Liverpool Health and Chest Hospital</i> . <sup>79</sup>
Psychological and nutritional support	Specialized remote support, by telephone or through virtual platforms

## B2. Muscle strength training

Whether they use training machines, free weights or functional training elements, patients can begin muscle strength training with weights that account for 50% of the maximal tolerated strength of the evaluation, commonly based on Epley or Brzycki 1-rep max formulas, then increasing up to 12 reps, and then 3 sets with 80% of maximum estimated strength.<sup>44,81,82</sup>

## B3. Psychological and nutritional support

With this in-person modality, we recommend educational meetings about the aspects related to posture, dyspnea and cough management in DLAs, breathing rhythm, energy-conservation techniques when doing physical exercise, suitable use of canulas and oxygen masks, how to recognize signs of alarm during physical activities, among other topics of interest.<sup>30,44,52,53,55,57,58,63,66,68,69,78,79,81</sup>

## B4. Psychological support

This in-person modality includes a psychopathologist who is familiar with the problems of these patients.<sup>30,44,52,53,55,57,58,63,66,68,69,78,79,81</sup>

## CONCLUSIONS

The approach to patients with moderate and severe forms of SARS-CoV-2 disease involves recognizing the systemic aspect of the condition, its frequently

incapacitating character and its wide community spread.

At present, the respiratory rehabilitation is the only intervention that has shown a positive impact on patients' dyspnea and fatigue and quality of life, as well as an improvement in the psychological sphere. Despite those benefits, both the indication and use of respiratory rehabilitation are still strongly underestimated.

Whatever the medical complexity level where it is to be applied, we suggest that it is administered at an early stage, in an integrated and continuous way, during the transfer from one level of care to another, and in so far as it is possible, with the participation of a multidisciplinary team consisting of kinesiologists, physicians, nutritionists and psychologists.

Evaluation and training must focus on the patient's needs and possibilities. This includes previous knowledge of the environment where the patient is going to continue the intervention, that is to say, if it is going to be remote or in-person; the use of safe and simple techniques with everyday objects, the analysis of the clinical condition of the patient starting the rehabilitation and the feasibility of the proposed strategy basing on the knowledge of the patient and his/her environment. Finally, the healthcare team must respect the ethical principles of privacy, confidentiality and of being informed about the expectations and results of the suggested intervention.

To conclude, this workgroup believes that the first duty of the rehabilitation team is to become the bridge that provides patients affected by SARS-CoV-2 accessibility to the only valid tool they can have in order to minimize their sequelae and improve their quality of life: respiratory rehabilitation.

#### Conflict of interest

Authors have no conflict of interest to declare.

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