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Early mobilization and physical exercise in patients with COVID-19: A narrative literature review

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ABSTRACT

Background: Currently, little is known about early mobilization and exercise in individuals with COVID-19.
Objective: To describe the indication and safety of early mobilization and exercises in mild to severe COVID-19 patients and to investigate the use of telerehabilitation to deliver exercise programs to these patients.
Methods: This narrative literature review was conducted performing a comprehensive search of databases.
Results: 32 articles met the established criteria and the main findings were summarized and described, including indication, contraindication and recommendation for early rehabilitation and exercises prescription.
Conclusions: The literature suggests that early mobilization and physical exercise are beneficial for individuals with COVID-19. However, much of what has been published is based on expert opinion due to a lack of randomized trials, which are needed.

1. Introduction

The newly emerging human coronavirus named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the etiologic agent of human coronavirus disease 2019 (COVID-19) [1]. After the first outbreak in Wuhan, China, this virus spread very quickly through Hubei Province [2] and worldwide, causing the current pandemic [1]. The rapid spread of the disease caused an unprecedented increase in demand for health care services and hospitalization, raising work overload and requiring worldwide urgent efforts to reorganize every aspect of care [3]. This unexpected increase in demand for specialized acute care caused a deep crisis in the health system [4].

Although most people present mild forms of COVID-19, nearly 14% of individuals present severe forms, requiring hospitalization and oxygen therapy, and 5% need admission to intensive care units [5]. Depending on the COVID-19 severity, patients may suffer several dysfunctions, such as impaired lung function, physical deconditioning, muscle weakness [5], acute cerebrovascular diseases, venous thromboembolism [6], acute cardiac injury [7–9], neurological complications, psychological disorders, and cognitive impairments [5,8,10]. In general, critical COVID-19 patients present long length of hospital stay [5,11] and prolonged bed rest and immobilization inevitably lead to several negative consequences [12,13]. In addition, COVID-19 patients admitted to critical care often need long supportive care and mechanical ventilation, which put them at high risk to develop post-intensive care syndrome [14]. Furthermore, relatively young patients who survive acute respiratory distress syndrome can present persistent exercise limitations, reduced physical quality of life, and functional disability 5 years after their critical illness, which increases costs and use of health care services [15]. For all these reasons, early mobilization and exercises should be performed to prevent, relieve and/or recover these impairments and limitations, even in the acute stage of COVID-19 [5,11,16].

Early mobilization comprises different kinds of movements, from passive to resistive movements up to activities, which are started immediately after the clinical stabilization [17]. It is worth mention that the term "activity" is being used as the execution of a task or action by an individual, according to The International Classification of Functioning, Disability and Health definition [18]. Early mobilization requires interdisciplinary team cooperation [19] and can be performed by different health professionals, especially physiotherapists [11,16,17,20,21], nurses [20] and occupational therapists [21]. On the other hand, exercise is defined as a subcategory of physical activity that is planned,

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structured, repetitive, and purposive, in the sense that the improvement or maintenance of one or more components of physical fitness is the objective [22]. Most of times, the exercises are prescribed and supervised by physiotherapists [13,16,23–26] and exercise professionals.

The early mobilization and exercises are common routine in several health conditions [23–25], as well as in critically ill patients [26–31], and its effects are well established [23–31]. However, as COVID-19 is a new disease, little is known about how and when mild, moderate or severe COVID-19 patients should be submitted to early mobilization and exercises. Besides that, the crescent use of remote tools for health services during the pandemic scenario, in an attempt to reduce the virus spread [31–33], reveals the need to know whether and how telerehabilitation has been used in COVID-19 patients.

Thus, the primary aim of this narrative review was to describe the indication and safety of early mobilization and exercises in mild to severe COVID-19 patients. The secondary objective was to investigate the use of telerehabilitation to deliver exercise programs to these patients.

It is important to highlight that respiratory physiotherapy for acute COVID-19 patients and rehabilitation for chronic sequelae after COVID-19 will not be debated here, since these subjects are out of the scope of this review and already have been discussed elsewhere [11,34–43].

2. Materials and methods

This narrative review was done following the methodology described by Gasparyan et al. [44].

2.1. Search strategy

A comprehensive search was conducted on MEDLINE, SciELO, PEDro and Web of Science up to June 30th, 2020 to retrieve meta-analyses, systematic reviews, randomized trials, guidelines, recommendations, state of the art, and other peer-reviewed studies investigating the relationship between COVID-19 and early mobilization or exercises. Key terms, including Medical Subject Headings (MeSH) terms, were identified for each construct and combined using the Boolean operators "OR" within the construct and "AND" between constructs. The MeSH terms used were "COVID-19", "SARS-CoV-2", "severe acute respiratory syndrome coronavirus 2", "coronavirus", "exercise", "early ambulation", "physical therapy modalities", "rehabilitation", and "telerehabilitation". The other key terms used were: "2019-nCOV", "coronavirus pneumonia", "physical exercises", "physiotherapy", "physical therapy", "mobilization", and "early mobilization". All key terms were searched in titles and abstracts. All key terms were written in English, and when the database had the idiom filter tool, the language was restricted to English, Portuguese and Spanish (Table 1). To identify eligible papers that may not have been retrieved by the search described above, reference lists of included articles were manually checked. The search was conducted independently by two authors, who identified and remove duplicates, screened studies by title/abstract, and then reviewed full text, considering the inclusion and exclusion criteria by eligibility. Discrepancies were resolved via consensus with a third author.

2.2. Eligibility criteria

The inclusion criteria were studies in which early mobilization and/or exercises were discussed for patients diagnosed with COVID-19.

The exclusion criteria were papers regarding exclusively the pediatric population, exclusively the respiratory exercise, and those that approach exclusively the rehabilitation after COVID-19.

3. Results

A total of 567 studies were identified in the searches. After the exclusion of 111 duplicate studies, 456 articles were screened by title and abstract, and the remained 85 articles were full text reviewed. So, 32 studies were included in this narrative review (Fig. 1).

Table 1
Search strategies used in each database.

Database	Search strategy
Pubmed	("COVID-19" [Title/Abstract] OR "SARS-CoV-2" [Title/Abstract] OR "severe acute respiratory syndrome coronavirus 2" [Title/Abstract] OR "coronavirus" [Title/Abstract] OR "2019-nCOV" [Title/Abstract] OR "coronavirus pneumonia" [Title/Abstract]) AND ("exercise" [Title/Abstract] OR "early ambulation" [Title/Abstract] OR "physical therapy modalities" [Title/Abstract] OR "rehabilitation" [Title/Abstract] OR "telerehabilitation" [Title/Abstract] OR "physical exercises" [Title/Abstract] OR "physiotherapy" [Title/Abstract] OR "physical therapy" [Title/Abstract] OR "mobilization" [Title/Abstract] OR "early mobilization" [Title/Abstract]) Filters: English, Portuguese, Spanish
Web of Science	(("COVID-19" OR "SARS-CoV-2" OR "severe acute respiratory syndrome coronavirus 2" OR "coronavirus" OR "2019-nCOV" OR "coronavirus pneumonia")) AND (("exercise" OR "early ambulation" OR "physical therapy modalities" OR "rehabilitation" OR "telerehabilitation" OR "physical exercises" OR "physiotherapy" OR "physical therapy" OR "mobilization" OR "early mobilization")) Filters (Idioms: English OR Spanish OR Portuguese)
Scielo	ab: ((COVID-19 OR Sars-CoV-2 OR coronavirus OR "severe acute respiratory syndrome coronavirus 2" OR "2019-nCOV" OR "coronavirus pneumonia"))) AND (ab: ((exercise OR "early ambulation" OR "physical therapy modalities" OR rehabilitation OR telerehabilitation OR "physical exercises" OR physiotherapy OR "physical therapy" OR mobilization OR "early mobilization"))). Limits: English, Portuguese and Spanish
PEDro	Search 1: COVID-19 AND exercis*; Search 2: COVID-19 AND "early mobilization"; Search 3: COVID-19 AND physiotherapy; Search 4: COVID-19 AND "physical therapy"

Among the 32 included papers, there are: thirteen opinion/perspective/communication/special/commentary/correspondence/experience/document reports, four letters to the editor, four types of reviews, four guidelines, three position papers, three editorials, and one randomized controlled trial (RCT) protocol (Table 2). It is necessary to highlight that there is no RCT investigating early mobilization and exercises in COVID-19 patients. Therefore, this narrative review is mainly based on observational studies in COVID-19, and on opinions of the scientific community about how to deal with early mobilization and exercises in COVID-19 patients, with these opinions arising from literature findings for other health conditions.

The main findings of this review were grouped in the following topics: 3.1) COVID-19 manifestations and the need for early mobilization and exercises; 3.2) Early mobilization and exercises recommendations for mild to moderate COVID-19 patients; 3.3) Early mobilization and exercises recommendations for severe to critical COVID-19 patients; and 3.4) Telerehabilitation for COVID-19 patients.

3.1. COVID-19 manifestations and the need for early mobilization and exercises

Taking into account the multisystemic repercussions of COVID-19 [5,35,41,45–47] (Fig. 2), which are common to other disease conditions, it is easy to understand the need of early mobilization and exercises to prevent, relieve and/or recover these impairments in body structures and functions, that ultimately will lead to activity limitations. This need has been pointed out by recent guidelines [11,16,42,48,49] recommending early mobilization and exercises for COVID-19 patients to prevent and/or minimize these complications and to rehabilitate them. Besides the guidelines [11,16,42,48,49], all the other studies included in this review did also mention the importance of exercises for COVID-19 patients [35,40,46,50–52].

Although it is not yet possible to predict how many impairments will remain in post-acute and chronic phases, probably some patients will experience consequences during months or even longer, as observed on post intensive care syndrome cases [45]. Therefore, researchers,

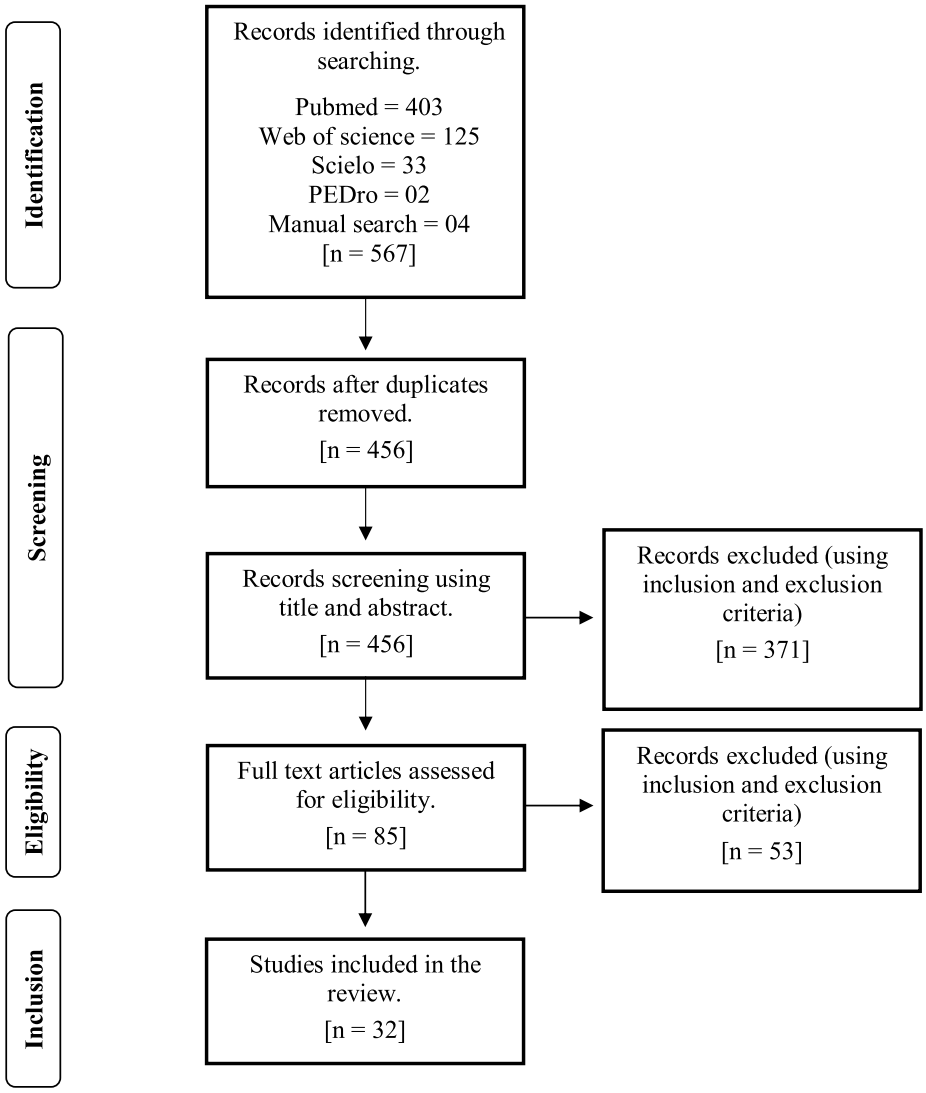

Fig. 1. Flowchart detailing the systematic search, screening, eligibility, and inclusion procedure.

considering previous studies with critically ill patients, suggested that, in COVID-19 population, early mobilization and exercise can prevent muscle atrophy, venous thrombosis, stiffness of joints and soft tissue [49], prevent and reduce polyneuromyopathy, improve quality of life, reduce time and mortality during hospitalization, contribute to the optimization of cognitive, respiratory, neuromuscular and osteo-articular function, shorten the duration of intensive care unit (ICU) stay and its clinical and functional sequelae [47], prevent and treat several adverse effects of sedation and bed rest [11,16,53,54]. Furthermore, the mechanical thromboprophylaxis (graduated compression stockings or intermittent pneumatic compression) additionally to pharmacologic thromboprophylaxis or as an option when pharmacological treatment is contraindicated was recommended for COVID-19 patients by the German Society of Angiology [55].

However, early mobilization and exercises prescription for COVID-19 patients should involve careful consideration of clinical conditions [11] and prescription parameters depend on the disease severity. As there are small variations regarding severity classification of COVID-19 [11,16,35,40], this review adopted the World Health Organization (WHO)'s classification and definition of COVID-19 severity for adults [1] (Table 3) and, its next topics will report the indication (exercise type, intensity, frequency and duration) and safety (parameters to be monitored, exercise initiation and interruption criteria and contraindications), of early mobilization and exercises according to WHO COVID-19 severity classification.

Still on exercise intensity, it is worth mention that moderate-intensity continuous training improves immune function biomarkers [56] and may optimize the functional integrity of the immune system to prevent or attenuate the severity of infection, especially among vulnerable populations with immune-compromised conditions [57]. Otherwise, high-intensity prolonged exercise leads to immunosuppression [58].

3.2. Early mobilization and exercises recommendations for mild to moderate COVID-19 patients

It is important to note that most of mild COVID-19 patients are not hospitalized [48,49], and then, they should be advised to stay home and balance rest and physical activity, paying attention to their symptoms. A home exercise program may be instituted, and an individualized approach is recommended specially in cases of immobility, neurologic, lung and cardiac diseases, and other complications.

For hospitalized COVID-19 patients, the modality, timing, and intensity of intervention for patients with COVID-19 must be tailored according to the individual patient's needs, especially for elderly, obese patients, and those with comorbidities [16]. Considering the individual's overall condition, the exercises intensity can be lowered to match the patients with reduced muscle strength [49]. Since some mild

Table 2
Characteristics of included studies (n = 34) and information about localization of papers findings in this narrative review.

Author	Year	Country	Study design
Brugliera et al. [46]	2020	Italy	Letter to the editor (experience report)
Candan et al. [60]	2020	Turkey	Letter to the editor
Ceravolo et al. [41]	2020	Italy	Rapid living review
Chen et al. [52]	2020	China	Opinion articles
Devlin et al. [75]	2020	United States	Narrative review
Falvey et al. [64]	2020	United States	Perspectives
Gonzalez-Gerez et al. [68]	2020	Spain	RCT protocol
Greve et al. [47]	2020	Brazil	Special article (opinion of specialist)
Halabchi et al. [58]	2020	Iran	Editorial
Iannaccone et al. [61]	2020	Italian	Special communication
Kiekens et al. [45]	2020	Italian	Special article
Kurtaiş et al. [48]	2020	Turkey	Guideline
Laddu et al. [57]	2020	United States	Commentary
Lazzeri et al. [42]	2020	Italian	Italian position paper
Lee et al. [63]	2020	China	Case series (short communication)
Li et al. [35]	2020	China	Special article
Linnemann et al. [55]	2020	Germany	Position paper
Mukaino et al. [62]	2020	Japan	Letter to the editor
Nakamura et al. [59]	2020	Japan	Letter to the editor
Pan American Health Organization [05]	2020	United States	PAHO Document
Polastri et al. [53]	2020	Italy	Editorial
Polastri et al. [54]	2020	Italy	Editorial
Rahmati-Ahmadabad & Hosseini [56]	2020	Iran	Correspondence
Rayegani et al. [49]	2020	Iran	Iranian consensus (letter to the editor)
Righetti et al. [51]	2020	Brazil	Experience report and review
Simpson & Robinson [74]	2020	Canada	Review
Thevarajan et al. [66]	2020	Australia	Correspondence
Thomas et al. [11]	2020	Australia	Guideline
Vitacca et al. [16]	2020	Italy	Italian position paper
Vitacca et al. [76]	2020	Italy	Consensus
Zhao H-M e at [40].	2020	China	Guideline
Zhu et al. [50]	2020	China	Guideline

and moderate COVID-19 patients may rapidly progress to severe acute respiratory syndrome (SARS), it is recommended that interventions do not cause a further burden on breathing work, increasing the risk of respiratory distress [16].

The indication (exercise type, intensity, frequency and duration) and safety (parameters to be monitored, exercise initiation and interruption criteria and contraindications) of early mobilization and exercises in mild to moderate COVID-19 patients are summarized in Table 4.

As can been seen in Table 4, exercise intensity for mild COVID-19 patients should be limited to moderate. In fact, most of the studies recommended low-intensity exercise for these patients [16,35,51], represented by Borg category ratio (CR) 10 < 3 or MET values < 3. A single study advised low to moderate intensities (Borg CR 10 score ≤ 3) to mild COVID-19 patients [40], since the value 3 in the Borg CR 10 scale corresponds to moderate intensity.

Regarding patients with moderate disease, some studies proposed low-intensity exercise (Borg CR 10 scale < 3 or MET values < 3) [16,40], and other studies did not specify the intensity. However, the exercise intensity for moderate COVID-19 patients should not be high, since around 3%–5% of moderately ill patients develop severe or critical disease after 7–14 days of infection; therefore, the aim of the exercise is to maintain the physical status [40].

Concerning complementary therapies, it was observed that an exercise program including elements of Health Qigong, exercises of pulmonary rehabilitation and proprioceptive neuromuscular facilitation (PNF), performed in 30-min session, daily, during 14 days of hospitalization of mild to moderate COVID-19 patients, improves functional activity. The authors of this pilot study reported that a standardized clinical research will be carried out [52]. Other authors also indicated Chinese traditional exercises (Tai chi chuan, Ba-duan-jin) for mild to moderate COVID-19 patients [35,40].

3.3. Early mobilization and exercises recommendations for severe to critical COVID-19 patients

According to Li (2020) [35], there are still many doubts about rehabilitation of severe to critical COVID-19 patients; however, some consensus already have been achieved, such as the adoption of breath training at prone and/or semi recumbent bed position, moderate head elevation, limb mobilization, bed and bedside sitting and standing, as well as bedside walking when possible. Trying to better understand what "when possible" means, Kurtais et al. [48] recommended that only passive range of motion exercises and secretion management should be done in COVID-19 patients presenting acute respiratory distress syndrome (ARDS). However, Righetti et al. [51] strongly recommended 12–16 h/day of prone ventilation for severe ARDS patients and related that this maneuver can be repeated when the PaO_2/FiO_2 ratio of 150 mmHg is observed after 6 h in the supine position, and must be interrupted if the patient presents hemodynamic instability. According to Lazzeri et al. [42], as soon as clinical stability is reached, decubitus change, semi-prone, prone, semi-sitting and sitting position are recommended for severe patients spontaneously breathing or using non-invasive ventilatory support, and Kurtais et al. [48] postulated that active exercises and electrical muscle stimulation (EMS) should be considered for those recovering from ARDS.

EMS applied in the early acute phase of severe COVID-19 patients has been indicated to counter the ICU acquired weakness [59]. Among the various EMS modes, belt-type is suggested as more effective for critical care, because it can induce whole lower extremity exercise through whole muscle contraction between wrapped belts, and 50 min bouts, three bouts per day have presented good results in ventilated COVID-19 patients [59]. Righetti et al. [51] recommended that the EMS be associated with early verticalization and exercises in severe COVID-19 patients.

Early mobilization and exercises, including positioning with 45° head up in bed [60], regular bed decubitus changes [60], passive movement for all joints [16,46,60], frequent posture changes [16,46] with gradual increase of antigravity position in order to achieve semi-sitting position [46], and/or neuromuscular electrical stimulation [16], are also recommended for unconscious or sedated critical COVID-19 patients. These therapeutic approaches have to be choose based on patient's clinical condition [46], and are important to prevent skin lesions, immobilization sequelae [42] and disability [16]. The rehabilitation team should discuss the possibility to start an active mobilization program as soon as patient sedation is reduced, to avoid critical illness myopathy and physical disability [42]. However, the active mobilization is not recommended for patients with clinical instability [42]. In these cases, the training of the skeletal muscle is contraindicated as it can impose an additional stress to the respiratory system, exposing the patients to an increased risk of respiratory distress [16].

Moreover, it already was demonstrated in severe COVID-19 patients that management of posture, passive and active mobilization, associated with respiratory and cognitive rehabilitation, depending on the clinical status, reduced the mean length of hospitalization and improved cognitive function in elderly who initially presented abnormal Mini-Mental State Examination or Montreal Cognitive Assessment scores [61].

Regarding safety, besides the contraindications and interruption criteria already described for mild to moderate COVID-19 patients (Table 4), severe to critical COVID-19 patients should also have the early

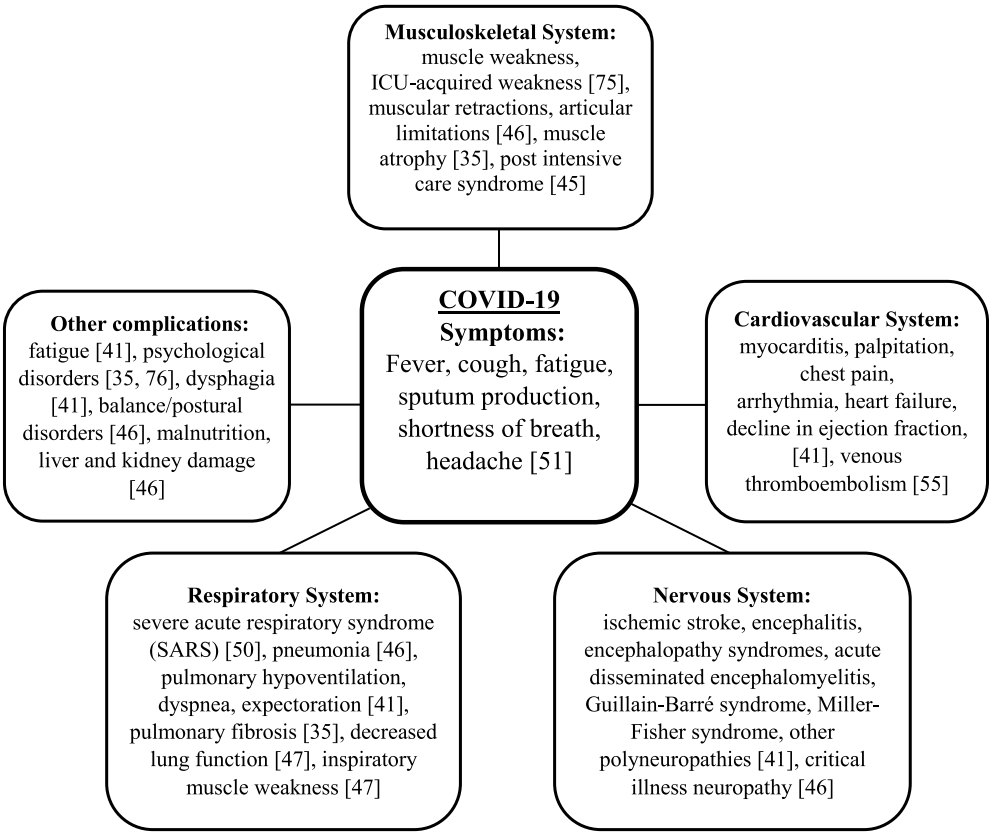

Fig. 2. Signs and symptoms of coronavirus disease 2019 (COVID-19) and possible acute and chronic complications associated with COVID-19 in different body systems.

mobilization and/or exercises stopped when disconnection of any device (intravenous access, endotracheal tube, feeding tube, etc.), irritability, heart palpitations, loss of consciousness, and falls appear [40].

3.4. Telerehabilitation for COVID-19 patients

An Australian guideline [11], that outlines recommendations for physiotherapy management for COVID-19 in the acute hospital setting, recommends the use of virtual tools to do an initial screening without direct contact with the patient whenever possible, calling the patient's isolation room telephone and conducting a subjective assessment and advising on patient mobility.

An editorial published [53] about physiotherapy in patients with COVID-19 also describe that, in collaborating with patients, it is possible to implement the execution of simple and low-intensity movements of upper and/or lower limbs in the sub-acute settings. In addition, a guideline for acute and subacute rehabilitation of COVID-19 patients [48], recommends that the choice of printed and visual materials during telerehabilitation should depend on the patient's cognitive status.

A systematic review [41], cited the use of telrehabilitation to a patient with Charcot-Marie-Tooth disease who developed COVID-19 without major respiratory symptoms, and described one case series study, that applied a telerehabilitation system to deliver exercise to individuals who could not be assisted with the traditional face-to-face approach due to contagiousness concerns.

Most of the aforementioned studies [11,41,48,61] corroborate that the telerehabilitation system is an important alternative to exercise with selected patients, without increasing the exposure and risk of contamination of professionals and patients.

A letter to the editor [62] described the experience obtained with the use of telerehabilitation for 4 patients hospitalized with Covid-19 through a tablet connected to the Internet via Wi-Fi and a pulse oximeter (used by the patients) connected to the tablet via Bluetooth. A physical therapist guided each individual in a 20-min exercise program, which consisted of stretching, muscle strengthening, and balance exercises directed by a video program with real-time instructions. On a scale of 0–10, the participant graduated their overall satisfaction between 8 and 10, and when they were asked "whether they felt it meaningful for their health to participate in this program", and "whether they would recommend this exercise to others" the answers ranged from 7 to 10 and from 8 to 10, respectively.

Lee et al. [63] reported that at the time their manuscript was wrote, as part of the Singapore government's containment effort, all individuals with COVID-19 were admitted into hospitals, although most of them were asymptomatic or have mild symptoms. So, exercise videos were provided to all patients in the general medical wards to ensure that they remain active during their stay in the isolation facility [63]. The use of telerehabilitation in hospitalized patients with COVID-19 was also described for Falvey et al. [64], and has emerged as an important strategy during this pandemic.

4. Discussion

Since Covid-19 is a new disease, there is still no robust scientific evidence to define the different aspects of early mobilization and physical exercise in affected patients. However, through our search we were able to verify, based on previous knowledge of the physiological effects of exercise, as well as on studies that investigated the safety and efficacy in patients with clinical situations similar to Covid-19, that exercise can probably be beneficial throughout pandemic context.

Although in our results we restricted our search to articles that address the effects of early mobilization and exercise only in Covid-19, we noticed during the reading of the articles presented, that many of them [11,40–42,46,48] elaborated their recommendations based on

Table 3
WHO classification and definition of COVID-19 severity for adults [1].

Severity	Definition
Mild disease	Symptomatic patients meeting the criteria for diagnosis of COVID-19 without evidence of viral pneumonia or hypoxia.
Moderate disease (Pneumonia)	Adult with clinical signs of pneumonia, like fever, cough, dyspnea, tachypnea, however without signs of severe pneumonia, including $SpO_2 \geq 90\%$ (ambient air).
Severe disease (Severe pneumonia)	Adult with clinical signs of pneumonia, like fever, cough, dyspnea, tachypnea, with one of the following signs: respiratory rate > 30 breaths/min; severe respiratory distress; or $SpO_2 < 90\%$ (ambient air).
Critical disease	Onset: within 1 week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms. Chest imaging showing bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules. Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. (Assessment, e.g. echocardiography, to exclude hydrostatic cause of infiltrates/edema if no risk factor present).
(ARDS)	Classification of ARDS according to oxygenation impairment. Mild ARDS: 200 mmHg $< PaO_2/FiO_2 \leq$ 300 mmHg (with PEEP or CPAP $\geq$ 5 cmH_2O); Moderate ARDS: 100 mmHg $< PaO_2/FiO_2 \leq$ 200 mmHg (with PEEP $\geq$ 5 cmH_2O); Severe ARDS: $PaO_2/FiO_2 \leq$ 100 mmHg (with PEEP $\geq$ 5 cmH_2O).
(Sepsis)	Adults with acute life-threatening organ dysfunction caused by a dysregulated host response to suspected or diagnosed infection.
(Septic shock)	Adults: persistent hypotension despite volume resuscitation, needs vasopressors to maintain MAP $\geq$ 65 mmHg and serum lactate level > 2 mmol/L.

WHO: World Health Organization; COVID-19: coronavirus disease 2019; SpO_2: saturation of peripheral oxygen; ARDS: acute respiratory distress syndrome; FiO_2: fraction of inspired oxygen; PEEP: positive end-expiratory pressure; CPAP: continuous positive airway pressure; MAP: mean arterial pressure.

studies carried out in other diseases, and only a few studies and experience reports [52,59,61,63] cited effects and recommendations of exercise based on experience specifically with patients affected by Covid-19. The beneficial effects of exercise and mobilization in patients with other clinical conditions are well established in the literature [23,29,30]. However, mobilization is not recommended for patients with clinical instability [42], since it may not be well tolerated and cause rapid desaturation [45].

According to the guidelines of the American Association for Cardiovascular and Pulmonary Rehabilitation, the most challenging aspect of exercise prescription for pulmonary patients is the estimate of the appropriate intensity for each person to ensure that exercise is not too intense to cause adverse physiological effects, but it is enough to promote beneficial effects [26]. Therefore, in the case of a new disease, about which there is a lack of scientific evidence, clinical decision making on the ideal intensity of exercise is even a greater challenge.

The need for exercise to rehabilitate patients with pneumonia caused by other etiological agents has been consolidated by some studies [23,24]. Therefore, due the lack of RCTs about exercise on COVID-19, these studies about pneumonia have been considered for recommendations on COVID-19. Our results showed that most guidelines found [16,35,40,51] recommends performing low intensity exercises to mild patients.

Regarding patients with severe and critical Covid-19 disease, our results also demonstrated that there are no RCTs that define which types of exercise and/or mobilization are safe and beneficial. However, all the articles selected in our search that addressed different forms of early mobilization [16,35,42,46,48,51,60,61], highlighted that, since the safety criteria are respected, all Covid-19 patients should be mobilized precociously. While the patient is sedated or unconscious, passive movement of the patient [16,42,48]) and postural exchanges [16,42,60] are recommended, however, once the patient‘ sedation is reduced, it is important to start the active mobilization program, to avoid physical disability and critical illness myopathy [42].

A systematic review demonstrated that early progressive mobilization in critically ill adults at Intensive Care Unit (ICU) is feasible and safe, improves functional ability and reduces ICU and hospital length of stay [30]. In addition, a RCT showed a reduction in delirium and duration of mechanical ventilation in critically ill patients who underwent early mobilization [65].

Since many patients with severe COVID-19 progress to mechanical ventilation and remain in hospital for long periods, they are likely to develop ICU-acquired weakness. In this context, early mobilization can help to improve functional, cognitive, and respiratory conditions, and contribute to the patient's early discharge from the hospital [60].

Some studies [50,56,57] included in this review, evidenced that exercise can have positive enhancing effects on immune system and may be helpful for healthy asymptomatic people and, therefore, its practice is suitable during this viral respiratory tract epidemic [66]. Among the immunological effects of moderate exercise that have already been described, we can mention: increases neutrophil and natural killer (NK) cell counts [67] and augments stress hormones levels, which lead to reduction in excessive inflammation [67].

RCT studies are need to investigate details about effect of exercise in patients with COVID-19, since, due to the unprecedented number of patients requiring intensive care, most publications addressing physical therapy and COVID-19 emphasize respiratory physical therapy. In the same way, there are several studies about exercise in post-discharge phase of COVID-19, since rehabilitation has been considered an urgent demand in this phase. The single RCT found during the screening process, about exercise in COVID-19 was conducted with patients after recovered from COVID-19 [36], however, it was excluded because it was an exclusion criterion. Our research also found a published protocol for a future RCT about the exercise in patients affected by COVID-19 confined to their homes, which will contribute to increase the knowledge about exercise in this population [68].

The restrictions imposed by the pandemic, can be a barrier to regular exercise and aggravate sedentary behaviors [69]. Special attention is deserved for the elderly population group, since exercise in older people positively affects and prevents frailty, sarcopenia, risk of falls, self-esteem and cognitive impairment [70].

Due to the aforementioned restrictions, typical rehabilitation programs need to be adapted [31,32,61,71] and, probably for this reason, our results indicated a breakthrough in the use of virtual tools for exercise program delivery to patients COVID-19 [11,63]. A RCT published before pandemic showed that telerehabilitation improved adherence to yoga in cardiac rehabilitation [72]. The use of telehealth technology is already a reality in many health services, with prospects for rapid expansion in the coming years, and development of different types of smart equipment, robots, wearable equipment for vital sign monitoring, among others, which are likely to perform a key role for prevention, treatment, and rehabilitation [35]. Telerehabilitation is an option for maintaining the mobility of the mild patients without increasing professional exposure, by mean of technologies to educate the patients on a safe exercise program and to encourage them to continue the exercise program independently [73]. For hospitalized and non-hospitalized stable patients in isolation, rehabilitation programs can be eventually conducted remotely by tele health system (educational videos, tele-consultation, webcams etc., with disinfectable tools) [73]. However, the virtual service also has many limitations, such as the need for equipment availability, risk of inadvertent disclosure of personal data and limitations for carrying out the physical examination [75].

In conclusion, this review highlights the need for early mobilization and exercise to hospitalized patients with COVID-19 to prevent, reduce and rehabilitate the consequences of the disease and of the post-intensive care syndrome. Recommendation about early mobilization and exercise was described for patients with the mild, moderate, severe, or critical disease. Exercise prescription for these patients should be

Table 4
Recommendations about exercise for hospitalized patients with mild and moderate COVID-19.

Study	COVID-19 classification	Exercise type	Exercise intensity/frequency/duration criteria for interruption	Recommendation
Zhao et al. [34] 2020 China	**Mild**	Breathing exercises, Tai chi chuan, or square dancing.	Borg CR 10 scale dyspnea score ≤3 Twice a day, 15–45 min/session.	Start 1 h after meals; Fatigue should be absent on the next day (preferably).
Li [17] 2020 China	**Mild Acute phase**	Respiratory training, aerobic training, Chinese traditional exercises (Tai chi chuan, Ba-duan-jin), square dance.	Mild aerobic training.	
Kurtaiş et al. [48] 2020 Turkey	**Mild pneumonia**	Active-assisted or active ROM exercises, achieving mobilization, muscle strengthening exercises, incentive spirometry and other devices for patients having sputum and productive cough, breathing techniques.		Started when the virulence decreases and when patient's condition is stabilized: decreased fever, reduced dyspnea, RR < 30 breaths/min, SpO_2 > 90%.
Righetti et al. [36] 2020 Brazil	**Mild Acute phase**	Neuromuscular stimulation, therapeutic exercises, and early verticalization.	Light intensity exercises; the exercises can be for maintenance of a Borg CR 10 scale < 3.	To maintain minimal functional capacity. Start as soon as possible, as long as the patient presents suitable clinical conditions.
Zhu et al. [50] 2020 China	**Mild/ Moderate Stable period**	Respiratory training and RMT, mild exercise training, trying to walk, bedside bicycling, sitting and standing, resistance training, balance training; psychological support.	Exercises with intensity less than 3 Mets, maintaining a Borg score of 3–4 or visual analog scale (VAS) score 5–6. Progressive resistance training, three groups per day, 10 times per group, with a 1 repetition maximum of 50–70%. Criteria for exercise interruption: SpO_2 decreased by 4% points; or the patient had perspiration, nausea and vomiting, dizziness, blurred vision, etc.; severe sudden dyspnea; chest compression or pain; rapid heart rate or arrhythmia; unable to maintain balance.	Initiation Criteria: FiO_2 ≤60%; SpO_2 ≥93%; RR ≤ 30 breaths/min; PEEP ≤10 cmH_2O; SBP 90–180 mmHg; MAP 65–110 mmHg; HR 40–120 BPM; temperature <38,5°. No new arrhythmias or myocardial ischemia; no new unstable deep vein thrombosis and pulmonary embolism; no aortic stenosis; no severe hepatorenal disease or new, progressive impairment of liver and kidney function. Contraindications: Temperature >38°; severe dyspnea; resting heart rate >120 BPM; X-ray manifestations: progression of thoracic infiltration >50% within 24–48 h; SpO_2 < 95%; BP < 90/60 mmHg or >140/90 mmHg.
Vitacca et al. [7] 2020 Italy	**Mild/ Moderate Acute phase**	Mobilization to get patient out of bed, posture changes/rotational therapy, therapeutic postures (early sitting/ pronation), active limb exercises (also with devices), muscle reconditioning and strengthening, NES, RMT.	Criteria for exercise withdraw: high fever, worsening dyspnea, SpO_2 < 93% or 4-point drop during exercise, chest tightness, belching, dizziness, headache, unclear vision, palpitations, sweating, inability to keep balance, increased need for O_2 or NIV, radiological lesions' progression (>50%) within 24–48 h.	
Rayegani et al. [49] 2020 Iran		Rolls on the bed, gets out of bed, sits on a chair, stands up, walks a few steps, stroll up and down the stairs, tai chi, preventive exercises for venous thrombosis, and Zheng's recumbent exercises. Active and passive joints range of motion exercises. The passive exercises are carried out if a patient has a reduced level of consciousness (assistive device for mobilization, ROM and stretching exercises, NES and compression stockings to prevent venous thrombosis). A full surface massage while using infrared light and TENS therapy to reduce myalgia.	The intensity of physical activity between 1 and 3 METs. Twice a day, at least 1 h after eating, and between 15 and 45 min, as beyond that may cause fatigue in patients.	
Zhao et al. [34] 2020 China	**Moderate**	Breathing exercises, stepping, Tai chi chuan and exercises to prevent thrombosis.	1 < METs to <3 METs (from rest to light) Twice a day, 15–45 min/session. Patients who are prone to fatigue or are physically weak should perform intermittent exercise. 3–5% of these patients develop severe disease after 7–14 d. So, intensity should not be high (exercise objective: maintain previous physical state) Criteria for exercise interruption: Borg > 3 (dyspnea), breathlessness, chest tightness, headache, blurred vision, palpitations, profuse sweating, dizziness, balance disorder, etc.	Start 1 h after meals Exclusion criteria: T > 38 °C, initial consultation time ≤7 d, from disease onset to dyspnea ≤3 d, chest radiological scans >50% progression within 24–48 h, SpO_2 ≤ 95%, resting BP: <90/60 or >140/90 mmHg.
Thomas et al. [6] 2020 Australia		Range of motion (passive, active-assisted, active or resisted), muscle strength, bed mobility, sitting out of bed, sitting balance, sit to stand, walking, tilt table, standing hoists, upper/lower ergometry and exercise programs.	Mobilization and exercise prescription depends on the patient clinical status.	Direct physiotherapy interventions should only be considered when there are significant functional limitations, such as (risk of) ICU-acquired weakness, frailty, multiple comorbidities and advanced age.

BP: blood pressure; COVID-19: coronavirus disease 2019; CR: category ratio; h: hour(s); d: days; FiO2: fraction of inspired oxygen; HR: heart rate; ICP: intracranial pressure; MRC: Medical Research Council; MAP: mean arterial pressure; MET: metabolic equivalent of task; NES: neuromuscular electrical stimulation; NIV: non-invasive ventilation; PEEP: positive end expiratory pressure; RASS: Richmond agitation sedation scale; RMT: respiratory muscle training; ROM: range of motion; RR: respiratory rate; SpO_2: peripheral capillary oxygen saturation; SBP: systolic blood pressure; T: temperature.

done with caution, observing each stage of the disease and the clinical condition, to ensure that exercise is not too intense to cause adverse physiological effects, but it is enough to promote beneficial effects. Although the available exercise recommendation is based on specialists' consensus and studies with low evidence level, the exposed data may help to guide the clinical practice of physical therapists, and other health professionals until randomized controlled trials are published about exercise in COVID-19. Due to the occupational risk of contamination by the virus, telerehabilitation emerged as a valuable tool, especially in mild and stable COVID-19 patients.

Declaration of competing interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctcp.2021.101364.

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