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Rehabilitation and COVID-19: a rapid living systematic review 2020 by Cochrane Rehabilitation Field. Update as of September 30th, 2020

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Abstract

Background. The COVID-19 outbreak response requires identifying and understanding the long-term consequences of this new pathology, and how to manage these. This living systematic review presents the most current and seminal information coming from the scientific literature. It is the monthly update of the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER Action Steering Committee.

Objective. The aim of this review is to update the monthly COVID-19 and rehabilitation literature research up to September 30th, 2020.

Methods. Methodology described in the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER Action was applied. The most important medical databases were searched, and papers related to COVID19 and rehabilitation were retrieved and summarized descriptively.

Results. The database search retrieved 2526 publications. Duplicates were removed, and 1150 unique records were screened for inclusion. After screening titles, abstracts and full-texts, 37 papers were included in the present review. According to OCEBM 2011 Levels of Evidence Table, most studies (78.4%) fall within the level of evidence 4 category, while the remainder (22.6%) are categorized as level of evidence 3. Most studies described patients in acute (51.4%) or subacute (35.0%) phase, while no studies described the chronic consequences of COVID-19. Just one study dealt with rehabilitation interventions regarding COVID-19, and two discussed reorganization of rehabilitative services.

Conclusions. The most recently published COVID-19 research focuses more on describing the clinical presentations and the natural history of the pathology, rather than rehabilitation interventions or service delivery. Studies with high levels of evidence regarding the efficacy of interventions, long-term monitoring, or new organization models remain lacking.

Keywords: COVID-19; Severe Acute Respiratory Syndrome Coronavirus 2; Coronavirus; Rehabilitation; Physical and Rehabilitation Medicine.

Introduction

REH-COVER (Rehabilitation – COVID19 Evidence-based Response) Action aims to inform the rehabilitation community on the growing evidence relating to COronaVirus Disease 2019 (COVID-19) and rehabilitation management¹. Cochrane reviews focus on randomized control trials (RCTs) and quasi RCTs (QRCTs) and are published in the Cochrane Library by a Cochrane Review Group. At this stage, RCTs and QRCTs are rare in rehabilitation; therefore, a classical Cochrane review is not possible.

The Cochrane Rehabilitation Field produces this systematic review of all studies relevant to its REH-COVER action to provide an up to date overview of recent research relevant to Rehabilitation and COVID-19. This paper is the third update of the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER Action².

Methods

The present update was conducted according to the methodology described in the first review². The literature search was performed on October 2nd, 2020 and included all eligible papers published between September 1st and September 30th, 2020.

Topic search filters covered a wide range of papers including studies about people with disabilities and chronic diseases who suffered the consequences of pandemic lockdown and movement restriction, without developing COVID-19 infection.

As of this update we excluded the above category of studies and restricted the focus to papers conveying specific information about the rehabilitation needs and management of people with or recovering from COVID-19 and the direct effects of pandemic on rehabilitation services.

The results are synthesized and described in detail in the comprehensive table that was gradually upgraded in all editions of this rapid living systematic review on the Cochrane Rehabilitation REH-COVER action website (https://tr.im/rr_dyn)³.

Results

Evidence synthesis

We identified 2526 publications. After removal of duplicates, we retained 1150 unique records. Based on screening of title and abstract, 1065 publications were excluded, while 85 items were deemed eligible; eventually, full-text screening led to the inclusion of 37 publications (Figure 1). A detailed overview of the new evidence is provided as Supplementary Digital Material 1: Supplementary Table I (available on Cochrane Rehabilitation website: https://tr.im/rr09_20).

The studies published in September 2020 were conducted in the following World Health Organization regions: 16 in Europe (Italy⁴⁻¹², United Kingdom¹³⁻¹⁵, Belgium¹⁶, Germany¹⁷, Switzerland¹⁸, and Netherlands and Belgium together¹⁹), 14 in the Americas (11 in the United States of America (USA)²⁷⁻³⁷, 2 in Brazil^{38,39} and 1 in Canada⁴⁰), 6 in Western Pacific (China²⁰⁻²¹, Japan²², Republic of Korea²³, Singapore²⁴, Australia²⁵), and one in the South-East Asia region (India²⁶).

Evidence level of included studies

Due to the heterogeneity of published studies, a meta-analysis was not appropriate, thus the results are described qualitatively. Based on the OCEBM 2011 Levels of Evidence table⁴¹ most studies (78.4%) were Level 4 (15 case reports^{4,6,8,15,17,18,20,23-25,27,28,34,39,40}, 7 case series^{11,12,21,29,30,36,38}, and 7

historical cohort^{5,7,16,26,31,32,35}), whereas the remainder 8 papers (21.6%) were Level 3 (4 cohort^{9,13,14,22} and 4 cross sectional studies^{10,19,33,37}) (Table I). No RCT or QRCT were found.

According to the research question, most studies (70.3%) investigated the natural history/determining factors of the disease (3 cohort studies^{9,13,14}, 1 cross-sectional³³, and 22 descriptive studies^{5,7,8,11,12,15–18,20,23–26,28,29,32,34–36,38,40}). Five descriptive papers reported epidemiological data on the clinical presentation of COVID-19 infection^{4,6,27,30,39}, and 3 described disease prevalence (2 cross sectional studies^{10,19}, and 1 case series²¹). Finally, 2 papers described data on health service organization (1 cohort study²² and 1 cross-sectional study³⁷) and only 1 historical cohort study speculated about intervention efficacy³¹.

Clinical characteristics of included studies

Thirty-two studies (86.5%) included COVID-19 patients who were assessed in the acute (19 studies)^{5,7,11,13,14,16–18,23,25–27,30–32,35,36,39,40} or post-acute phases (13 studies)^{4,6,8,10,12,15,19,20,24,28,29,34,38}.

No studies described patients in the chronic phase of COVID-19. Three studies (8.1%) reported data on the impact of COVID-19 infection on people with pre-existing health conditions, i.e. patients with severe neurological impairments⁹, Parkinson's Disease (PD)³³ or underlying rheumatologic diseases²¹. Finally, 2 papers (5.4%) studied the effect of COVID-19 on rehabilitation services for people with pre-existing disease (heart failure²²) or disability³⁷.

Sixteen papers (43.2%) provided data about the type of rehabilitation service: 8 acute care^{13,17,18,23,26,31,38,40}, 6 general post-acute^{4,6–8,24,29}, 2 specialized post-acute rehabilitation⁹ including outpatients²².

According to the ICF-based classification of the Limitations of Functioning of Rehabilitation Interest (LFRI), most studies (n=26; 70.3%)^{5–9,11–13,16–18,20,23,25–30,32–36,38,39} described the impact of COVID-19 on nervous system structure and related functions, 4 (10.8%) on respiratory structures and related

functions^{14,15,24,40}, 2 (5.4%) on activity limitation and participation restriction^{19,31}, 2 (5.4%) on any other body structures and functions^{21,37}, 2 on digestive functions^{4,10} and 1 on cardiovascular functions²². The following section summarizes the main evidence.

Epidemiology - Impairment in respiratory structures and related functions

Most studies regarding impairment of respiratory structures and related functions were case reports (3) and 1 was a cohort study. The case reports described the benefit of self-proning⁴⁰, respiratory and musculoskeletal rehabilitation²⁴ and of intravenous thrombolysis in cases of post-COVID-19 massive pulmonary embolism¹⁵, respectively. The cohort study by Halifax et al. followed up 48 patients admitted to a respiratory high-dependency unit and described their discharge setting after treatment¹⁴.

Epidemiology - Impairment in nervous system structures and related functions

Three analytical studies reported on impairment of nervous system structures and related functions. Two cohort studies concerned severe COVID-19 patients undergoing rehabilitation¹³ or neurorehabilitation inpatients developing COVID-19 during their hospital stay⁹, while one cross-sectional study provided data on the effect of the COVID-19 pandemic on people with PD³³.

Twenty-two descriptive studies reported on impairment of nervous system structures and related functions (11 case reports, 6 case series and 6 historical cohort studies). They described the clinical course of patients with COVID-19 and the development of possible neurological complications such as stroke^{6,25,32,35,36}, Guillain-Barré syndrome^{5,8,17}, refractory status epilepticus³⁴, postherpetic neuralgia²⁰, meralgia paresthetica²⁸, multisystem inflammatory syndrome³⁹, pituitary apoplexy²⁷, encephalopathy³⁰, peripheral nerve injury²⁹, delirium⁷, agitation and spatial disorientation¹¹, cognitive impairment¹².

Epidemiology - Any activity limitation and participation restriction

One cross-sectional study by Vaes et al. described the independence level of non-hospitalized COVID-19 patients¹⁹.

Epidemiology - Impairment of any other body structure and function

A case series described the incidence and outcomes of all COVID-19 patients with rheumatologic conditions in Hong Kong²¹.

Micro level – Interventions

Johnson et al conducted a historical cohort study where the association between physical therapy visit frequency and the probability of being discharged home, and mobility status at discharge were analysed³¹.

Meso level – Services

Two studies described the re-organization of services following COVID-19: Blauwet et al. in a cross-sectional study described how to design and implement a virtual adaptive sports program for people with disabilities³⁷, while Nakayama et al. demonstrated the feasibility of remote cardiac rehabilitation²², in a cohort study.

Discussion

The key points emerging from this update are summarized as follows:

- Focusing this update on studies that: 1) provide specific information about the rehabilitation needs and management of COVID-19 patients, or 2) evaluate the direct effects of the

pandemic on rehabilitation services, led to the inclusion of fewer studies than the previous edition (37 vs 51). It is now clear that the implementation of lockdown to contain the COVID-19 affected the routine life and health of subjects with chronic diseases like diabetes, cardiovascular diseases, and neurological disorders. These patients usually require regular follow up for diagnostic tests and physician consultations, as well as regular physical activity and recurring rehabilitation treatment. The impact of restrictions on rehabilitation services have given rise to various concerns in the scientific community, thus stimulating the growth of reports on the health status of people with chronic diseases^{42–45} and enhancing the interest towards telehealth and telerehabilitation^{46–48}. While we agree with the importance of such issues, they are considered outside the scope of this rapid living systematic review, which aims to inform on the direct consequences of COVID-19 on people that contracted the disease.

- The quality of evidence remains low. Compared to the previous edition, there are fewer studies at Level 3 (21.6% vs 23.5%) and more at Level 4 (78.4% vs 76.5%). There are no published RCTs or QRCTs as yet.
- On the other hand, the number of cohort studies investigating the natural history of COVID-19 and its outcomes are growing (70.3% vs 43.1% in the previous update). This will hopefully drive the scientific community to understand what impairments may result from the infection in the medium term, what clinical and functional parameters should be monitored over time and how healthcare resources can be targeted.
- There are frequent reports on the neurological manifestations during the first weeks of COVID-19 infection. These mainly include stroke^{6,25,27,32,35,36}, Guillain-Barré syndrome^{5,8,17}, agitation and spatial disorientation¹¹, delirium⁷.

- Surprisingly, there is only one micro-level cohort study³¹ that assessed the rehabilitation effects on functional outcomes of COVID-19 patients. The majority of studies describing the effect of treatment are based on case reports.^{4,18,23,24,38,40}
- Most studies describe subjects in the acute phase (51.4%) or post-acute phase (35%). No studies described patients in the chronic phase. The long-term consequences and prognosis of neurological, respiratory, cardiac damage incurred during COVID-19 are unknown.
- In the acute phase, inpatient rehabilitation, including pulmonary rehabilitation, should be recommended in COVID-19 patients²³, though it is not always possible to deliver it at the time of admission because of the severity of the clinical condition¹³. The amount and intensity of rehabilitation must be carefully planned, as it seems that the greater the frequency and duration of intervention, the better the outcomes in terms of improved mobility at hospital discharge and the higher probability of being discharged to home³¹.
- Prone positioning as an intervention has been shown to substantially improve the outcome of patients with acute respiratory distress syndrome. The use of full prone position is associated with lower mortality than failed or positioning COVID-19 patients semi-prone¹⁴. Slessarev et al., proposed high-flow nasal cannula combined with patient self-proning as a useful approach to preserving ventilator capacity in resource replete settings, but also in resource-limited countries where sophisticated ICU techniques may not be available⁴⁰. However, while the intervention of prone positioning is effective at very low costs, it may increase the rate of complications such as peripheral nerve injuries²⁹ and meralgia paresthetica²⁸. Health professionals must be aware of increased susceptibility to these complications and refine standard protocols in order to reduce the risk.
- Among preventable complications in adult patients hospitalized for COVID-19, malnutrition was reported by Pironi and colleagues¹⁰. Nutritional risk and malnutrition were more

frequent in ICUs, but also reported in intermediate care units and rehabilitation units, where patient energy and protein intake were at the lowest limit or below the recommended amounts, indicating the need for actions to improve the nutritional care practices. A foreseeable but less preventable complication is the acquired muscle weakness in critically ill COVID-19 patients. Its incidence in a cohort of 74 patients was high and led to persistent high disability, highlighting the need of tailored rehabilitation¹⁶.

- In the sub-acute phase, surveillance of previously detected abnormalities is important to follow the recovery or the progression of disease using validated outcome measures that are sensitive to change in this phase⁴⁹. The impact of COVID-19 on patients' daily lives is substantial, including for non-hospitalized patients with mild COVID-19, due to the persistence of non-specific symptoms like fatigue, muscle weakness, sleeping problems, and pain¹⁹. Moreover, the authors caution that a series of complications can occur in the recovery period or even after discharge, such as post-acute oropharyngeal dysphagia⁴, refractory status epilepticus³⁴, herpes zoster²⁰, cognitive decline¹² and acute massive pulmonary embolism¹⁵. The subjects most at risk are those with severe illness, pre-existing risk factors¹⁵ and longer length of ICU stay.¹²
- Three studies described the impact of COVID-19 infection on subjects with pre-existing health conditions, i.e. patients with severe neurological conditions⁹, PD³³, or underlying rheumatologic disease²¹. In the first study⁹, 1/14 patients died of COVID-19 related symptoms. PD patients did not show a greater risk of COVID-19 than subjects without PD but in positive cases, the complications were more frequent in those with longer PD duration³³. Finally, the authors of one study reported no notable signals of increased frequency or severity of COVID-19 for people with rheumatologic diseases²¹. Whether these disorders are poor prognostic factors for COVID-19 is still debatable²¹.

In conclusion, this month's update confirms that current literature production still focuses more on describing the clinical presentations and the natural history of the pathology associated with COVID-19. Studies with higher levels of evidence regarding the efficacy of interventions, long-term monitoring, or new organization models are lacking. This review will continue to inform researchers and clinicians about the best practices in rehabilitation treatment and clinical research on COVID-19.

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Conflicts of interest

All authors declare no conflict of interests, funding sources or consultant relationships with any organizations involved in this research.

Authors' contributions

Elisa Andrenelli and Francesco Negrini equally contributed to this work as first authors.

Database searching: Michele Patrini and Stefano G. Lazzarini; Study selection: Elisa Andrenelli, Francesco Negrini, and Alessandro de Sire; Data extraction: Elisa Andrenelli, Francesco Negrini, Alessandro de Sire, Michele Patrini, and Stefano G. Lazzarini; Data analysis and interpretation: Elisa Andrenelli and Francesco Negrini; Manuscript drafting: Elisa Andrenelli and Francesco Negrini; Study supervision: Maria G. Ceravolo; Critical revision: Elisa Andrenelli, Francesco Negrini, Alessandro de Sire, Michele Patrini, Stefano G. Lazzarini, Maria G. Ceravolo and the International Multiprofessional Steering Committee of Cochrane Rehabilitation REH-COVER action. Study submission: Alessandro de Sire. All authors read and approved the final version of the manuscript.

Figures and Tables legend

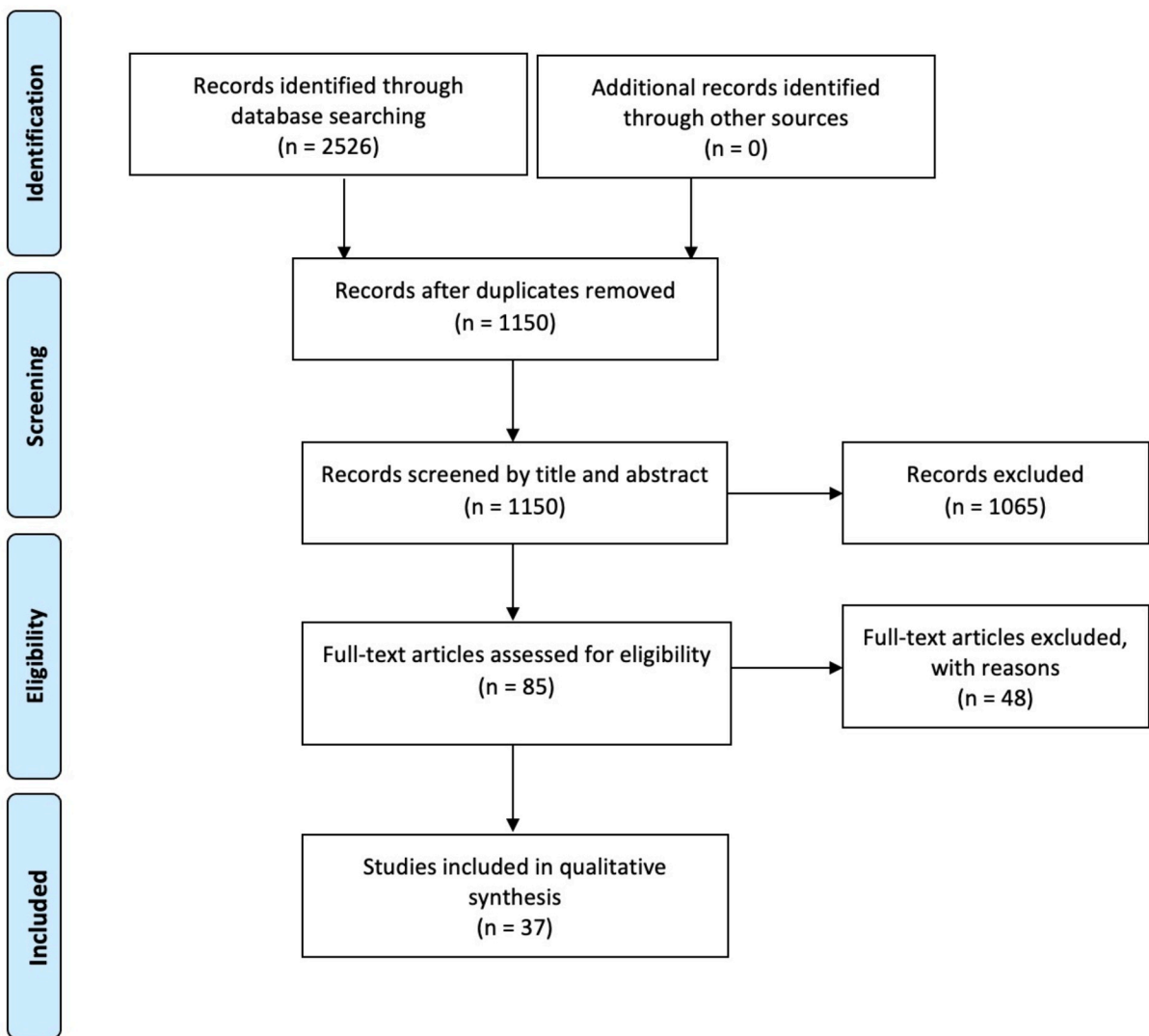
Table I. Level of evidence of the studies included in the present rapid living systematic review.

Figure 1. PRISMA Flow diagram.

Tables

Table I. Level of evidence of the studies included in the present rapid living systematic review.

	Level 1	Level 2	Level 3	Level 4	Total
Epidemiology - Clinical presentation	0	0	0	5 (13.5%)	5 (13.5%)
Epidemiology – Prevalence	0	0	2 (5.4%)	1 (2.7%)	3 (8.1%)
Epidemiology - Natural history / Determining and modifying factors	0	0	4 (10.8%)	22 (59.5%)	26 (70.3%)
Micro – Interventions (efficacy/harms)	0	0	0	1 (2.7%)	1 (2.7%)
Meso Level	0	0	2 (5.4%)	0	2 (5.4%)
Macro Level	0	0	0	0	0
Total	0	0	8 (21.6%)	29 (78.4%)	37 (100%)

Figure 1. PRISMA Flow Diagram

Supplementary Digital Material

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