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REHABILITATION AND COVID-19

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REVIEW

Rehabilitation and COVID-19: a rapid living systematic review 2020 by Cochrane Rehabilitation Field. Update as of October 31st, 2020

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ABSTRACT

INTRODUCTION: This living systematic review presents the monthly update of the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER Action Steering Committee. The aim of this study was to update the monthly COVID-19 and rehabilitation literature research up to October 31th, 2020.

EVIDENCE ACQUISITION: Methodology described in the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER action was applied. PubMed, Embase, CINAHL, Scopus, Web of Science, and PEDro databases were searched, and papers related to COVID-19 and rehabilitation were retrieved and summarized descriptively.

EVIDENCE SYNTHESIS: The database search retrieved 2704 publications. Duplicates were removed, and 1185 unique records were screened for inclusion. After screening titles, abstracts and full-texts, 22 papers were included in the present review. According to OCEBM 2011 Levels of Evidence table, 17 studies (77%) fall within the level of evidence 4 category, while the remainder (23%) are categorized as level of evidence 3. Most studies (N.=19; 86%) provided epidemiological data about the disease natural history/determining factor or the clinical presentation of COVID-19 infection, while only two studies focused on health service organization and intervention efficacy.

CONCLUSIONS: The most recent published COVID-19 research relevant to rehabilitation primarily provides data on the clinical course and the clinical presentation of the pathology, rather than on rehabilitation interventions or service delivery. Studies with high levels of evidence regarding the efficacy of interventions, long-term monitoring, or new health service organization models are lacking.

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Key words: COVID-19; Severe acute respiratory syndrome Coronavirus 2; Coronavirus; Rehabilitation; Physical and rehabilitation medicine.

Introduction

Rehabilitation – COVID-19 Evidence-based Response (REH-COVER) action is an initiative launched by Cochrane Rehabilitation Field aimed at summarizing and commenting the most recent evidence relating to Coronavirus disease 2019 (COVID-19) from a rehabilitation perspective.[1]

Ten months after the first reported cases of COVID-19, the number of randomized control trials (RCTs) and quasi RCTs (QRCTs) regarding COVID-19 and rehabilitation remains very limited.

The current systematic review aimed to provide an up-to-date overview of recent research relevant to rehabilitation and COVID-19. This paper represents the fourth update[2-4] of the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation REH-COVER action.[5]

Evidence acquisition

The present update follows the methodology applied in the second edition of the rapid living systematic review 2020 conducted by Cochrane Rehabilitation.[5]

We added all eligible papers available at the literature search performed on November 2, 2020 (publication date between October 1 and October 31, 2020). All results are also reported in the consolidated table of papers on the Cochrane Rehabilitation REH-COVER action website.[6]

Evidence synthesis

The search process identified 2704 publications. After the removal of duplicates and the screening of titles and abstracts, 63 studies were retained, of which 22 were suitable for qualitative synthesis (Figure 1). The studies published in October 2020 were conducted in the following World Health Organization regions: 10 in Europe (Italy,[7-10] UK,[11, 12] Belgium,[13, 14] Germany[15] and Spain[16]) and 10 in the Americas (USA,[17-23] Brazil[24, 25] and Canada[26]); one in Western Pacific (Australia[27]) and one in the African region (Morocco).[28] A detailed overview of this update is provided as Supplementary Digital Material 1: Supplementary Table I (available on Cochrane Rehabilitation website).[6]

Evidence level of included studies

Due to the heterogeneity of studies, a meta-analysis was not appropriate, and the results were described qualitatively. Based on the OCEBM 2011 Levels of Evidence table[29] the majority of studies (N.=17; 77.3%) were level 4 (six case report,[7, 11, 17, 19, 22, 28] eight case series,[9, 10, 13, 14, 16, 21, 24, 27] three historical cohort[20, 23, 26]), whereas the remaining five were level 3 (four cohort studies[8, 12, 15, 25] and one cross-sectional[18] study). No RCT or QRCTs were found in this update (Table I).

Most studies (N.=13; 59.1%) analyzed natural history/determining factors of the disease (three cohort studies,[8, 12, 15] one cross-sectional,[18] nine descriptive studies[11, 13, 14, 19-22, 24, 27]). Six descriptive papers reported epidemiological data on the clinical presentation of COVID-19 infection,[7, 9, 10, 16, 17,

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[28] and one showed disease prevalence.[26] Two historical cohort studies described data on health service organization[23] and intervention efficacy.[25]

Clinical characteristics of included studies

Twelve studies included COVID-19 patients in the acute phase,[7, 9, 11, 13, 16-19, 21, 24, 25, 28] seven in the postacute,[8, 12, 15, 20, 22, 23, 27] whereas there were no studies in the chronic phase. One descriptive study[26] reported data on late-onset manifestations and two studies on the impact of COVID-19 infection on people with pre-existing neurological diseases.[10, 14] Seven studies reported the setting of rehabilitation service: according to the adopted classification,[5] they described four rehabilitation in acute care,[11, 14, 19, 25] one general postacute,[26] one outpatient,[23] and one rehabilitation in the home.[27] According to the ICF-based classification of the limitations of functioning of rehabilitation interest (LFRI), most papers (N.=12; 55%) described the impact of COVID-19 infection on nervous system structure and related functions,[7, 9-12, 16, 18, 19, 21, 22, 24, 28] four studies reported on generic body structures and functions,[13, 15, 17, 26] three on activity limitation and participation restriction,[20, 23, 27] two on respiratory structures and related functions,[8, 14] and one on digestive function.[25] The main evidence is summarized below.

Epidemiology – impairment in respiratory structures and related functions

A cohort study followed up 185 patients at 23 days (range: 20-29) post-discharge. The study found that respiratory impairment persisted in one third of patients, with the PaO_2/FiO_2 ratio and Body Mass Index (BMI) at presentation to the Emergency Department being the strongest independent predictors of persistent impairment and need for follow-up.[8] Authors of a case series warned that people with myotonic dystrophy type 1 are at high risk for severe COVID-19 disease and poorer outcomes.[14]

Epidemiology – impairment in nervous system structures and related functions

Two analytical and ten descriptive studies belong to this section. A cohort study found the presence of delirium as a significant predictor of worse functional outcomes in patients with COVID-19.[12] A cross-sectional study of 24,808 patients discharged from hospital in New York State – also including historical cohort data analysis – showed that patients with stroke with concurrent SARS-CoV-2 infection had increased case-fatality and a trend towards being discharged to rehabilitation;[18] on the other hand, they contended the hypothesis of an increased risk of stroke in young adults with COVID-19. Similar findings were reported by Requena *et al*. who showed a low frequency of acute stroke in patients with COVID-19 requiring hospital admission, and acknowledged usual causes for most stroke cases.[16] The remainder case report/series described neurological manifestations and/or their clinical course, such as palsy of the third[28] and the seventh[24] cranial nerves, myositis,[19] critical illness neuro-myopathy,[9] Guillain-Barré Syndrome,[7, 22] stroke,[10, 11, 21] delirium, and meningitis/encephalitis.[10]

Epidemiology – any activity limitation and participation restriction

A historical cohort study described age and COVID-19 severity as the most important factors leading to a loss in independence in ADLs in a postacute phase of the disease.[20] In a case series of three patients, a COVID-19 telehealth rehabilitation program delivered within a pulmonary rehabilitation setting was presented.[27]

Epidemiology – impairment of any other body structure and function

A cohort study by Daher *et al*.[15] did not find any impairment in pulmonary and heart function, or thromboembolic complications in 33 patients with COVID-19 six weeks after hospital discharge. A historical cohort[26] of 454 patients discharged from hospital after COVID-19 showed that the risk of thromboembolic complications diminished quickly after the acute phase.

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Other two descriptive papers reported the case of a 100-year-old patient with mild COVID-19 and hip fracture undergoing hemiarthroplasty without additional risk;[17] and the cases of four severe COVID-19 patients who exhibited heterotopic ossification (HO) in hips and shoulders after 30-40 days of hospital admission.[13]

Micro level – interventions

Lima *et al.*[25] conducted a cohort study describing the significant recovery in the functional pattern of swallowing in Intensive Care Unit (ICU) patients with COVID-19 who underwent swallowing intervention delivered by speech-language therapists, in the acute phase.

Meso level – services

In a historical cohort study, Steere *et al*.[23] described the outpatient rehabilitation service organization for previously hospitalized COVID-19 patients. They underlined that: 1) teams quickly developed physiatry-run outpatient COVID-19 recovery clinics *via* telehealth to address rehabilitation-related needs of patients who had become severely ill from COVID-19; 2) institutions differed in mechanisms for patient flow and referrals to the recovery clinic; and 3) patient demographics differed among institutions.

Discussion

This rapid living systematic review update to October 2020 presents the following key points:

- the lower number of studies included in the current update, compared to the previous one (22 *vs.* 37 studies) suggests a possible plateauing in the number of publications regarding rehabilitation needs due to COVID-19. However, taking into account the constant increase in the total number of the analyzed cases, more robust evidence on the direct consequences of COVID-19 could be available in the near future;
- Europe and the Americas are still the geographical areas providing most information on COVID-19 and rehabilitation needs. While this finding reflects the high prevalence of the pandemic in these areas, it might also represent a publication bias due to the fact that researchers from other geographical areas (like South-East Asia and Africa) have reduced access to English literature, or maybe express different health priorities or experience reduced availability of rehabilitation;
- the level of evidence continues to be low, lacking level 2 studies. Case reports (N.=6)[7, 11, 17, 19, 22, 28] and case series (N.=8)[9, 10, 13, 14, 16, 21, 24, 27] together represent 64% of the studies included in the systematic review;
- congruent with the above issue, more than half of the studies referred to the acute phase,[7, 9, 11, 13, 16-19, 21, 24, 25, 28] and 32% to the postacute phase.[8, 12, 15, 20, 22, 23, 27] With the exception of two studies reporting on the impact of COVID-19 infection in subjects affected by pre-existing diseases (*i.e.* neurological impairments,[10] myotonic dystrophy type 1[14]), no data were available concerning the chronic sequelae of the disease;
- regarding the natural history of COVID-19 infection, the case series concerning four severe COVID-19 patients with HO in hips and shoulders after 30-40 days of hospital admission suggests that the global inflammation associated to COVID-19 might play a role in the pathophysiology of HO, and enhances the need for an early monitoring of joint mobility and careful mobilization of patients in the acute phase;[13]
- based on a level 3 study,[8] it is suggested that a large proportion of patients still present with dyspnea at 3 weeks of hospital discharge, and that PaO_2/FiO_2 ratio and BMI at admission to the Emergency Department are the strongest independent

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predictors of persistent respiratory impairment and the need for follow-up in these patients;

- the rehabilitation component of acute care is reported by only seven (32%) studies, pointing to a limited involvement of the rehabilitation professionals in the acute phase of COVID-19 care;
- a large cross-sectional study[18] performed on 24,808 patients, and also including historical cohort data analysis, denied the association of COVID-19 with the risk of stroke; on the other hand, the study confirmed that stroke patients developing COVID-19 have a worse prognosis, with an over nine-fold increase in mortality and a higher probability of requiring rehabilitation;
- speech-language treatment was found effective at improving swallowing in ICU COVID-19 patients[25] in one cohort study, confirming the importance of an adequate assessment and management of oropharyngeal dysphagia in the ICU, for COVID-19 patients;
- finally, one study[23] describing the USA-based outpatient rehabilitation, supports the need for dedicated outpatient clinics aimed at addressing the rehabilitation needs of COVID-19 patients.

Conclusions

Findings of this rapid living systematic review updated to October 2020 reveal that there is still a lack of high-level evidence (level 1 and 2 studies) that might provide data on the functional limitations in the mid and long-term of COVID-19 course of infection and the effectiveness of rehabilitation in COVID-19 patients. Conversely, COVID-19 clinical presentation is better described through paradigmatic case reports and series, confirming that the involvement of nervous system structure and related functions is very frequent and deserves attention.

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Figure 1.—PRISMA Flow diagram.

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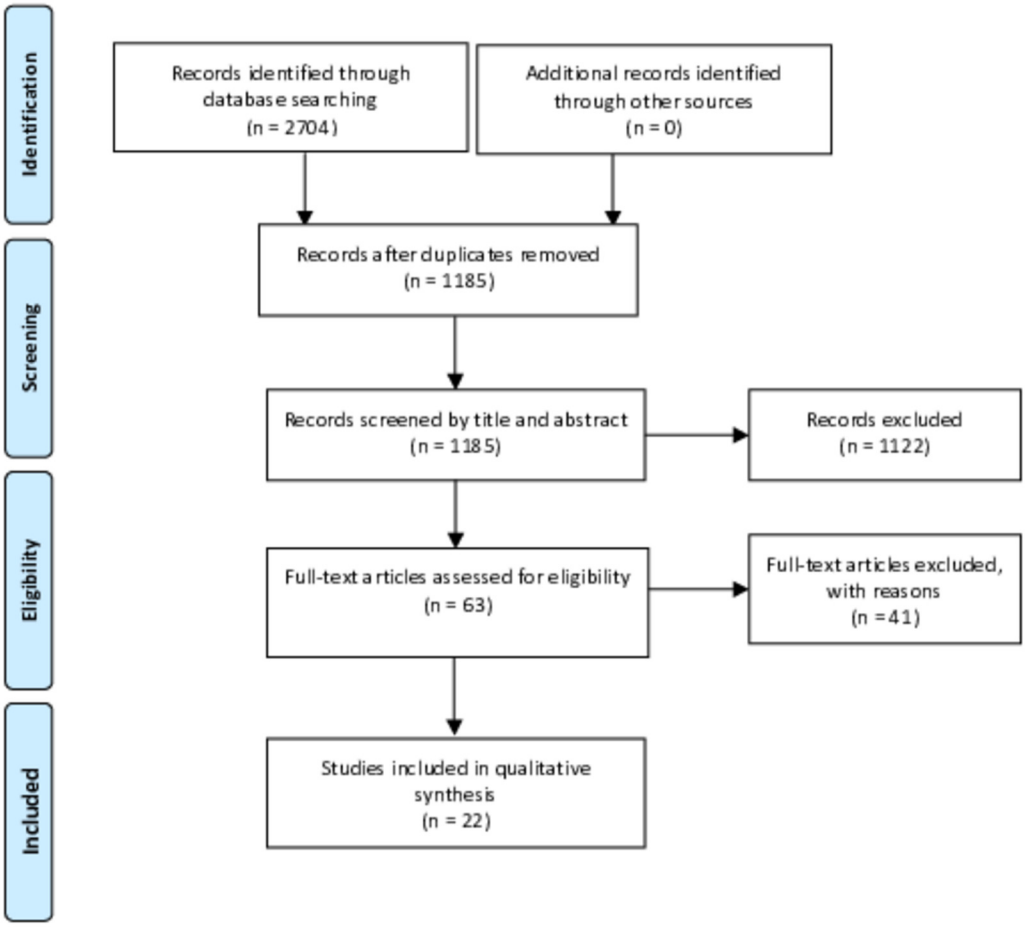
Table I.—Level of evidence of the studies included in the present rapid living systematic review.

Parameters	Level 1	Level 2	Level 3	Level 4	Total
Epidemiology – clinical presentation	0	0	0	6 (27.3%)	6 (27.3%)
Epidemiology – prevalence	0	0	0	1 (4.5%)	1(4.5%)
Epidemiology - natural history/determining and modifying factors	0	0	4 (18.2%)	9 (40.9%)	13 (59.1%)
Micro – interventions (efficacy/harms)	0	0	1 (4.5%)	0	1 (4.5%)
Meso level	0	0	0	1 (4.5%)	1 (4.5%)
Macro level	0	0	0	0	0
Total	0	0	5 (22.7%)	17 (77.3 %)	22 (100%)

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Figure 1. PRISMA Flow Diagram



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