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The effectiveness of physiotherapeutic procedures on patients diagnosed with COVID-19

Master Thesis

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Declarations

I declare that the work on which this thesis is based, in my original work under the direction of Doc. Paed Dr. Dagmar Pavlů, CSc. I declare that neither the entire work nor any part of it has been, is or will be submitted for another degree at this or any other university.

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Abstrakt

Background

Fyzioterapie představuje cennou intervenci aplikovanou u pacientů s COVID-19 trpících respiračními příznaky.

Cíl

Zhodnotit účinnost fyzioterapeutických metod na plicní funkce, fyzické funkce a psychosociální účinek pacientů s diagnózou covid-19.

Metody

Bylo provedeno komplexní systematické prohledávání literatury CINAHL, PubMed, Embase, Cochrane library a Scopus s cílem získat potenciální recenzované články, které hodnotily účinnost fyzioterapeutických modalit na plicní funkce, fyzické funkce a psychosociální účinek pacientů s diagnózou covid-19.

Výsledek

Z 1093 potenciálních hodnocených článků 9 splnilo kritéria pro zařazení. Výsledky ukázaly, že respirační rehabilitace zlepšuje respirační funkce, kapacitu cvičení a kvalitu života u pacientů s diagnózou covid-19.

Závěr

Respirační rehabilitační a telerehabilitační programy jsou účinné při zlepšování funkční kapacity, kvality života a respiračních funkcí pacientů s diagnózou covid-19.

Klíčová slova: fyzioterapeutické postupy; telerehabilitace; funkční kapacita; kapacita dušnosti; plicní funkce.

Abstract

Background

Physiotherapy represents a valuable intervention applied to COVID-19 patients suffering from respiratory symptoms.

Objective

To assess the effectiveness of physiotherapeutic modalities on pulmonary function, physical function, and psychosocial effect of patients diagnosed with COVID-19.

Methods

A comprehensive systematic literature search of CINAHL, PubMed, Embase, Cochrane library, and Scopus was done to retrieve potential peer-reviewed articles that assessed the effectiveness of physiotherapeutic modalities on pulmonary function, physical function, and psychosocial effect of patients diagnosed with COVID-19.

Results

Of the 1093 potential articles assessed, 9 met the inclusion criteria. The results demonstrated that respiratory rehabilitation improves respiratory function, exercise capacity, and quality of life in patients diagnosed with COVID-19.

Conclusion

Respiratory rehabilitation and telerehabilitation programs are effective in improving the functional capacity, quality of life, and respiratory function of patients diagnosed with COVID-19.

Keywords: physiotherapeutic procedures; telerehabilitation; functional capacity; dyspnea capacity; pulmonary function.

List of abbreviations

30STST: Thirty Second Sit To Stand Test

ACBT: Active Cycle of Breathing Techniques

ACE2: Angiotensin-Converting Enzyme receptor

AKI: Acute Kidney Injury

ARDS: Acute Respiratory Distress Syndrome

BS: Borg Scale

CG: Control Group

CNS: Central Nervous System

COVID-19: Coronavirus disease

COPD: Chronic Obstructive Pulmonary Disorder

CT: Computer Tomography

DAD: Diffuse Alveolar Damage

DSI: Dyspnea Severity Index

FEV1: Forced Expiratory Volume in a minute

FEV: Forced Expiratory Volume

FVC: Forced Vital Capacity

IG: Intervention Group

ICU: Intensive Care Unit

INPTRA: International Network of Physical Therapy Regulatory Authorities

IMT: Inspiratory Muscle Training

LMS: Lower limb Muscle Strength

MERS-CoV: Middle East Respiratory Syndrome Coronavirus

MRI: Magnetic Resonance Imaging

NOS: Newcastle Ottawa Scale

NRCT: Non-Randomized Controlled Trial

NTEP: Non-Specific Conditioning Exercise Program

Rep: Repetitions

ROM: Range Of Motion

PT: Physiotherapy

QOL: Quality of Life

RCTs: Randomized Controlled Studies

RHB: Rehabilitation

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus

SARS: Severe Acute Respiratory Syndrome

SpO2: Oxygen Saturation

V/Q: Ventilation/Perfusion Ratio

WCPT: World Confederation for Physical Therapy

WHO: World Health Organisation

Table of content

1. Introduction

Coronavirus disease (COVID-19) outbreak was first reported in the Hubei provenance of China in December 2019. COVID-19 is a highly contagious respiratory tract disease commonly caused by severe acute respiratory syndrome 2 (SARS-CoV-2). The World Health Organization (WHO) report suggests more than 753 million confirmed cases, including 6.8 million deaths, as of 31 January 2023. (39;58)

COVID-19 individuals have varied clinical manifestations. WHO classify the COVID-19 as a moderate and severe disease based on clinical signs. Patients with moderate COVID-19 have clinical manifestations of pneumonia (i.e., cough, fever, rapid breathing, and dyspnoea) with peripheral oxygen saturation (SpO2) $\geq$ 90% in room air. Moreover, patients with severe COVID-19 have a fever, cough, and dyspnoea with respiratory distress (i.e., SpO2 $<$ 90% on room air or respiratory rate $>$ 30 breaths/min). Most symptomatic patients appear as mild (40%) or moderate (40%) COVID-19 diseases. It is estimated that 15% of symptomatic patients will develop a severe state requiring oxygen support. In comparison, 5% of patients appear a critical COVID-19 state with complications such as acute respiratory distress syndrome (ARDS), respiratory failure, thromboembolism, septic shock, or multi-organ failure. The most frequently observed COVID-19 symptoms are fever, fatigue, dyspnea, muscle pain, lung problems, joint pain, altered taste, and altered smell. (33;34;39;56;60)

Recent studies suggest severe cases of COVID-19 manifest as viral pneumonia (i.e., fever, cough, hypoxemia, and dyspnoea with bilateral infiltrates on chest radiographs . Moderate to severe acute COVID-19 is characterised by respiratory distress, necessitating immediate referral to healthcare setting. (32) In addition, severe COVID-19 cases causing ARDS can be fatal if not treated promptly with ventilation in the intensive care unit. The COVID-19 mortality rates range from 0.15%, 2,3% and 17% for the age groups 18-49, 49-75 and over 75yo, respectively. (24;33;34;39;61)

A meta-analysis demonstrated 80% of infected cases have at least one residual clinical symptom even after 6 months after discharge from the hospital, suggesting the need for assessment and rehabilitation. (51)

Numerous studies, guidelines, and expert consensus have designed the pathway for physiotherapists treating COVID-19 patients in both intensive care units and during the hospital stay, specifying the most satisfying treatment modalities. (23;27;43:57) Physiotherapy (PT) benefits the functional recovery of COVID-19 patients at the motor and respiratory levels at different recovery phases. The short-term goal of physiotherapy in patients with the mild-moderate respiratory process is restoring physical and psychological conditions with sequences of aerobic exercise to restore their pre-hospital exercise capacity. The physiotherapy modalities among severe-critical COVID-19 patients include patient education, strength and training exercise, aerobic exercise, ventilatory techniques, and secretion drainage when clinical stability permits. (43;51;57:59)

Numerous guidelines, such as the Chinese Medical Association of Rehabilitation and European Respiratory Society/American Thoracic Society, have recommended the application of pulmonary rehabilitation in treating the long-term critical clinical consequences associated with COVID-19. (28;55) Respiratory rehabilitation comprises respiratory muscle training and breathing exercise using body position exercise, pursed lip breathing and diaphragmatic breathing that ameliorates pulmonary disease's physical and psychological manifestations. (27;30;53;54;59) The recovery of COVID-19 patients occurs with respiratory rehabilitation (RHB) during acute, mild and severe phases. (57) Initially, PT prioritises the COVID-19 patients to return to normal daily activities at a safe level and within the limits of symptoms. Increasing exercise intensity is not advisable due to the associated risk of post-exercise fatigue. (25;51)

Earlier studies revealed that supervised pulmonary RHB improves exercise capacity, exertional dyspnea, pulmonary function, psychological function and quality of life (QOL) in both mild/moderate and severe COVID-19 patients. (31;37;44;62) Physiotherapy reduces psychological stress, improves oxygen exchange, and alleviates pulmonary failure and the need for artificial ventilation. (36;38;40) A recent review of 40 literatures emphasised that pulmonary rehabilitation in COVID-19 survivors appeared beneficial in reducing hospital stay and improving overall pulmonary function. The author reported a lack of high-quality studies regarding physiotherapy in COVID-19 patients. (53) A 6-week randomised controlled trial assessing the effect of pulmonary rehabilitation in COVID-19 elderly patients without any comorbidities disease found significant improvement in forced vital capacity (FVC), forced expiratory volume (FEV), QOL and psychological status (45). Several studies demonstrated the limited cardio-respiratory recovery from respiratory rehabilitation in an acute COVID-19 phase of therapy. (29;42;43;63) The possible cause includes breathing problems in COVID-19 patients from another pulmonary disease, such as dry cough and rapid deterioration of lung to acute respiratory failure in COVID-19 patients. (33;34;39;56)

Recent studies found long-term clinical consequences from COVID-19 even though the individual recovered. (46;52) Computer tomography (CT) of recovered COVID-19 patients had abnormal pulmonary findings and impaired pulmonary function even after 1 month of hospital discharge. Additionally, this pulmonary damage leads to reduced limb muscle strength, impaired pulmonary function and diminished exercise capacity (64). Few individuals revealed dyspnea, fatigue, fever, cough, and diminished functional capacity even 2 months after hospital discharge. (23;52) A study found that 39% of COVID-19 survivors had reduced overall health. (46;52;64) It becomes crucial to explore novel approaches to alleviate the residual symptoms. The evidence about the effect of pulmonary rehabilitation on physical and respiratory function in COVID-19 patients are not sufficiently studied. Therefore, I perform systematic review to synthesise the available evidence about the effectiveness of physiotherapy on exercise capacity, dyspnea, pulmonary function, and quality of life in individual with COVID-19.

2. Theoretical background

2.1. Coronavirus overview

COVID-19 is an enveloped positive-single-stranded ribonucleic acid (RNA) virus of the Coronaviridae family of viruses caused by SARS-CoV-2, Betacoronavirus genus, Sarbecovirus subgenus. Representatives of the Coronaviridae family are characterised by club-shaped spikes (peplometers) that look like a crown, which are detected on the surface of a viral particle during electron microscopy. The original strain, isolated from samples from patients hospitalised in China in December 2019, is the reference genome for all subsequent sequences obtained by sequencing. (1)

The number of SARS-CoV-2 variants currently exceeds 1,000 different genetic lines. Most reported SARS-CoV-2 mutations have no functional significance. Only individual lines have a pronounced epidemiological significance.

Coronavirus disease shares the genetic similarity of the new virus to previously known coronaviruses- severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV), both viruses belong to the Betacoronavirus genus.

Prior to the outbreak of the first coronavirus epidemic in 2002, coronaviruses were considered agents of mild upper respiratory illness. Between 2002 and 2004 the SARS-CoV coronavirus was the first to cause the development of the so-called severe acute respiratory syndrome (SARS) epidemic and the confirmed cause of death of 774 people, in addition, since the end of this epidemic in 2004, no new cases of SARS-

CoV caused by SARS have been registered. The next epidemic caused by the MERS-CoV coronavirus began in 2012, by 2020 866 deaths were registered. At present, MERS-CoV continues to circulate and cause new cases. But both of these viruses were not as contagious and resistant to external factors as the new coronavirus. (1)

The high contagiousness of the coronavirus is provided by the S-protein of the SARS-CoV-2 virus, which is similar to the angiotensin-converting enzyme receptor (ACE2), and its affinity for this receptor is several times higher than that of SARS-CoV. (1)

The delta and omicron variants, which have become widespread, carry mutations in their genome that increase the contagiousness of the virus, mutations that increase the affinity of the S-protein of the virus for ACE-2 and reduce the recognition of viral antigens by post-infection and post-vaccination antibodies. The omicron variant, which carries multiple substitutions in the S-protein of the coronavirus, half of which are located in the receptor-binding domain, has the highest contagiousness among all SARS-CoV-2 variants.

The high pathogenicity of SARS-CoV, SARS-CoV-2 and MERS-CoV viruses allows them to be assigned to pathogenicity group II.

The ACE2 receptor has the ability to be expressed in cells of various organs, including the heart muscle and parts of the central nervous system (CNS), as well as in the epithelium of the respiratory tract, alveolar monocytes, vascular endothelium, macrophages, and other cells.

Despite how the coronavirus can affect the body as a whole, it tends to replicate most actively in the upper respiratory tract. The tropism of the coronavirus to the epithelium of the upper respiratory tract probably explains the continuous shedding of the virus from the pharynx and the highly efficient transmission of the virus. (1)

The course of the disease and progression of COVID-19 resemble SARS in terms of virus replication in the lower respiratory tract, as well as the development of severe immune disorders. This leads to damage to various organs and deterioration in the patient's condition approximately in the second week from the onset of the disease after the incubation of the virus has already passed. The most fundamental difference from previous viruses is the damage to the organs of the immune system, the development of microangiopathy and hypercoagulation syndrome with thrombosis and thromboembolism. (1)

Like other viruses, the coronavirus has the ability to replicate and mutate, and the more the virus circulates, the more it can change. A "variant" of the original virus is commonly referred to as a virus with one or more new mutations. These changes can result in a variant of the virus that is better adapted to the environment than the original virus. Some mutations can lead to changes in the characteristic features of the virus, such as the mechanism of transmission of the virus, the course or severity of the disease. (1;2)

2.1.1. Pathogenesis

Alveolar epithelial cells, in whose cytoplasm the virus replicates, are the main target cells for coronaviruses. They move to the cytoplasmic vacuoles after a direct encounter with varions, which, with the help of exocytosis, move to the cell membrane and exit into the extracellular space.

The production of antibodies together with the synthesis of interferon is stimulated rather late. This is due to the fact that the expression of viral antigens on the cell surface does not occur until the release of varions from the cell. The virus spreads rapidly into tissues due to the formation of syncytium by the virus. (2)

An increase in the permeability of cell membranes and an increased distribution of the transport of fluid, which is rich in albumin, into the interstitial tissue of the lungs and alveoli, is due to the action of the virus on the body. Due to this, the destruction of the surfactant occurs, resulting in the collapse of the alveoli, due to a sharp violation of gas exchange, acute respiratory distress syndrome develops. (2)

2.1.2. Pathophysiology

The autopsy of those who died from COVID-19 revealed pathological changes of varying severity and prevalence in the lungs. Despite this, lesions of other organs were also observed, which in some cases could prevail in severity over changes in the lungs and lead to death. In cases where COVID-19 was additional to another severe pathology, a combination of changes characteristic of different diseases is naturally observed. (5)

Depending on the stage of severity of the disease, various microscopic features were revealed in patients. For example, asymptomatic patients may present with nonspecific changes including pulmonary edema, focal pneumocyte hyperplasia, focal chronic inflammatory infiltrate, and multinucleated giant cells without prominent hyaline membrane formation. (4;5)

Further, as the disease progresses, diffuse alveolar damage (DAD) is observed with the formation of a transparent hyaline membrane and severe pulmonary edema. However, in coronavirus disease, there is a firbomyxoid exudate with visible fibrinous bands, as well as mucosal bronchiole occlusion, which is associated with oxygen therapy. Interstitial inflammatory infiltrates with severe epithelial damage and diffuse hyperplasia of type II pneumocytes, which are characteristic of acute ARDS, are also widespread. (5)

If the patient was on a ventilator for more than 7 days, a bacterial infection is characteristic in the form of viral-bacterial and mycotic pneumonia, as well as sepsis and septic shock. (4;5)

DAD in combination with involvement in the pathological process of the pulmonary vascular bed and alveolar haemorrhage syndrome is the main morphological manifestation in the lungs in severe infection. A feature of DAD in COVID-19 is dyschrony and prolongation with a frequent combination of its two phases - exudative and proliferative. (4;5)

The lungs are enlarged in volume and mass, doughy or dense consistency, low-air or airless; lacquered appearance from the surface, dark red in colour, when pressed from the surfaces of the cuts, a dark red liquid flows down, which is hardly squeezed out of the tissue. In addition to different sizes of haemorrhages, there are hemorrhagic infarctions obdurating blood clots, mainly in the branches of the pulmonary veins. In addition, inhomogeneous seals are observed along with fibrinous pleural exudate and fibrosis, often with purulent inflammation due to secondary bacterial infection with or without pericarditis. (5)

2.1.3. Histopathology

2.1.3.1. Respiratory system

Patients with upper respiratory tract infections usually have mild or moderate symptoms, however, in case of lower respiratory tract infection show symptoms of pneumonia, worsening the patient's condition can lead to organ failure. The severity of the disease also depends on the presence of concomitant chronic diseases. (6)

Alveoli: enlarged or damaged pneumocytes, type II pneumocyte hyperplasia, DAD, patchy desquamation, hyaline membrane formation, intra-alveolar haemorrhage, and intra-alveolar neutrophil infiltration.

Vessels: oedematous vessels with the formation of plugs, fibrinoid necrosis of small vessels, hyaline thrombi in micro-vessels.

Cellular components: focal infiltration of immune and inflammatory and an increase in the number of stromal cells, as well as the presence of syncytial giant cells.

Ultrastructural changes: virus particles were detected in the bronchial mucosal epithelium and type II alveolar epithelium. (7)

2.1.3.2. Urinary system

Factors contributing to acute kidney injury (AKI) include systemic hypoxia, abnormal coagulation, and possible drug or hyperventilation-related rhabdomyolysis. The incidence of AKI in COVID-19 ranges 1-30% with new onset proteinuria. (6)

Glomerulus: focal segmental glomerulosclerosis, ischaemic changes, podocyte vacuolation, accumulation of plasma in Bowman's space.

Vessels: increased accumulation of red blood cells obturating the lumen of the capillaries, without platelet or fibrinoid material with rare hemosiderin granules and pigmented cylinders, hyalinosis of arterioles, atherosclerosis of medium-sized arteries, fibrin thrombus, shrinkage of capillary loops in the glomeruli.

Renal tubules: necrosis and non-isometric vacuolar degeneration, oedematous epithelial cells, loss of brush border in proximal tubule

Ultrastructural changes: accumulation of viral particles in the tubular epithelium and podocytes. (7)

2.1.3.3. Gastrointestinal system

The most common gastrointestinal symptoms in covid patients were diarrhoea, decreased appetite, nausea, vomiting, abdominal pain, and gastrointestinal bleeding at onset and subsequent hospitalisation. (6)

Esophagus: Occasional lymphocytic infiltration in the oesophageal squamous epithelium.

Stomach: degeneration of the epithelium, necrosis and exfoliation of the gastric mucosa. Hyperemia with dilation of small blood vessels, edema of the lamina propria and submucosa with infiltration by immune cells.

Intestine: segmental dilatation, stenosis of the small intestine. A large number of infiltrating plasma cells and lymphocytes with syninterstitial edema in the lamina propria.

Pancreas: degeneration of the cells of islets. (7)

2.1.3.4. Digestive system-liver

Few microscopic changes in liver tissue have been reported in COVID-19, despite this, ACE-2 receptors have also been found in the hepatobiliary system, where cholangiocytes showed higher cell surface expression of the ACE-2 receptor compared to hepatocytes.

Given the fact that cholangiocytes express ACE-2 in the same way as type 2 alveolar cells, there is every chance that the liver could be a potential target for SARS-CoV-2. (7;19)

Liver: accumulation of nuclear glycogen in hepatocytes, dense atypical small lymphocytes in the portal tracts. Regenerative nodules and thick fibrous bands, mild sinusoidal dilatation of zone 3, mild lobular lymphocytic infiltration. Focal necrosis of the liver in the periportal and centrilobular areas. Degeneration of liver cells, biliary plugs in the small bile duct. (7)

2.1.3.5. Cardiovascular system-heart

Viral infections, which are one of the most common causes of infectious myocarditis, cannot be excluded from SARS-CoV-2 heart involvement.

Typical complications are foci of lymphocytic inflammation, acute myocyte necrosis, the presence of inflammatory cells and apoptotic bodies.

Ultrastructural observation: viral inclusion bodies in vascular endothelial cells. (7)

2.1.3.6. Blood vessels

Vascular endothelial cells are an easy target for the SARS-CoV-2 virus due to the presence of the ACE-2 receptor.

The presence of viral inclusions along with inflammatory cells and apoptotic bodies in endothelial cells was revealed. There is also evidence of edematous changes in the alveolar capillaries and small vessels with the presence of fibrin thrombi and neutrophils. (7)

2.1.3.7. Central nervous system

Patients frequently report neurological symptoms with COVID-19. Dizziness and headache were the most common CNS manifestations. Disturbances and changes in taste and smell are the most common symptoms of the peripheral nervous system. Stroke, acute encelopathy, seizures, ataxia, or nerve demyelination symptoms were neurological manifestations in some patients.

Possible routes of entry of the SARS-COV-2 virus into the CNS were by hematogenous way through penetration into the blood-brain barrier or retrograde spread of neurons involving the olfactory nerves.

A study of COVID-19 patients who exhibited neurological symptoms showed widespread brain lesions. Autopsy of the brain tissue showed signs of acute hypoxic-ischemic damage in the form of hyperanemia, edema and degeneration of neurons.

CT and magnetic resonance imaging (MRI) scans for COVID-19 patients with acute neurological symptoms showed signs of ischemia, haemorrhage, and increased cortical/subcortical grey matter and fiber tracts. Also, in some autopsied patients with COVID-19 who had neurological symptoms, SARS-CoV-2 RNA was detected in brain tissue and cerebrospinal fluid. (7)

2.1.4. Symptoms

A report by Davis et al. (9) similarly detailed over 200 symptoms in an international cohort of COVID patients. In this study, the likelihood of symptoms persisting beyond 35 weeks was 91%, with no statistically significant difference between men and women. 66% of respondents had experienced symptoms for at least 180 days. In addition, the likelihood of "severe" to "very severe" symptoms peaked during acute infection (<28 days), while the likelihood of "moderate" and "mild" symptoms increased gradually thereafter.

In patients who recovered in less than 90 days, the average number of symptoms peaked at week 2, and in those who did not recover within 90 days, the average number of symptoms peaked at month 2, with less decline over time. Respondents with symptoms for more than six months experienced an average of 13 symptoms over a 7-month period.

The overall prevalence of symptoms in 10 organ systems was estimated for 203 symptoms. Tables (1) and (2) summarises these prevalence estimates for 18 categories. Presented here (table 1) are 9 non-psychiatric organ systems: systemic, reproductive/genitourinary/endocrine, cardiovascular, musculoskeletal, immunological and autoimmune, HEENT, pulmonary, gastrointestinal and dermatological, and 9 neuropsychiatric subgroups (table 2): cognitive dysfunction, speech and language, memory , headaches, smell and taste, sleep, emotions and mood, hallucinations, sensorimotor. (9)

Musculoskeletal, cardiovascular, gastrointestinal, pulmonary, and neuropsychiatric symptoms predominated in 85% of participants. Based on a patient survey, the most debilitating symptoms were fatigue, breathing problems, and cognitive dysfunction.

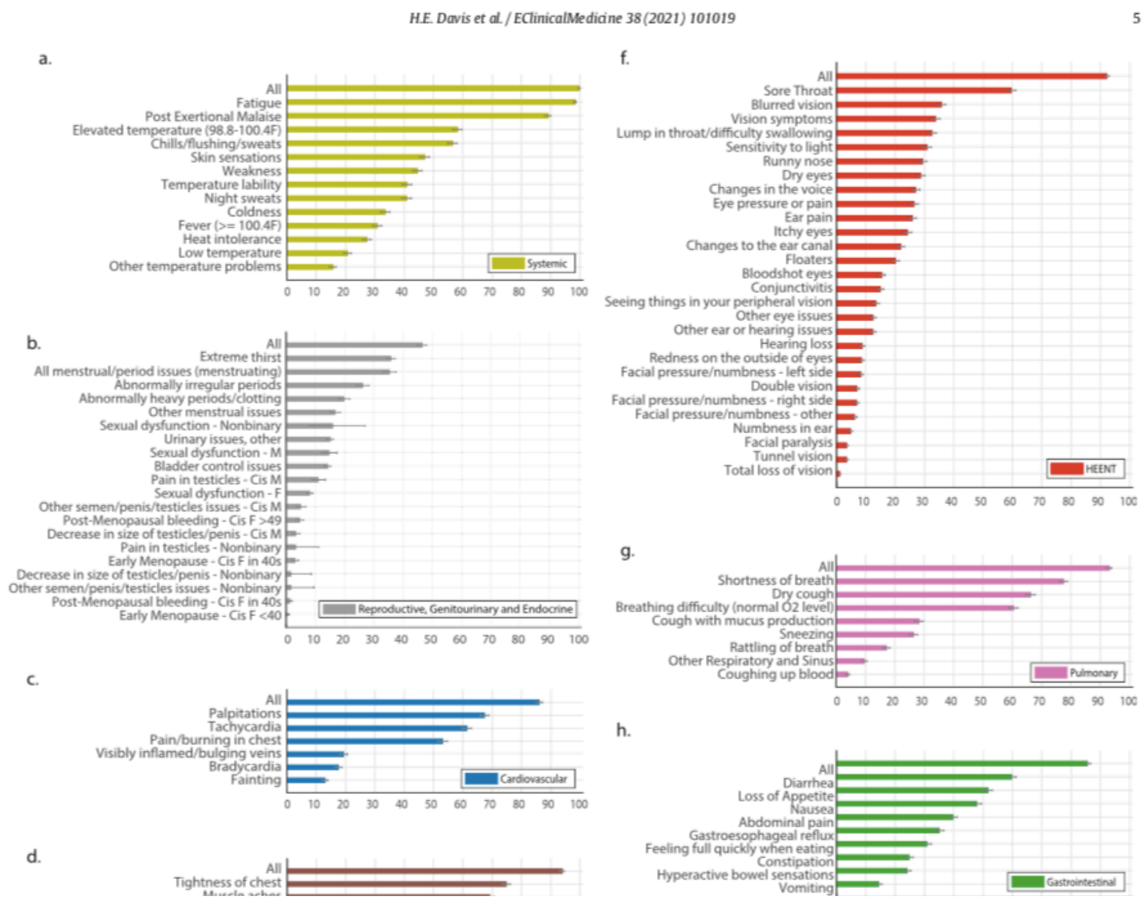

Table1. Symptom prevalence estimates for non-neuropsychiatric symptoms (9)

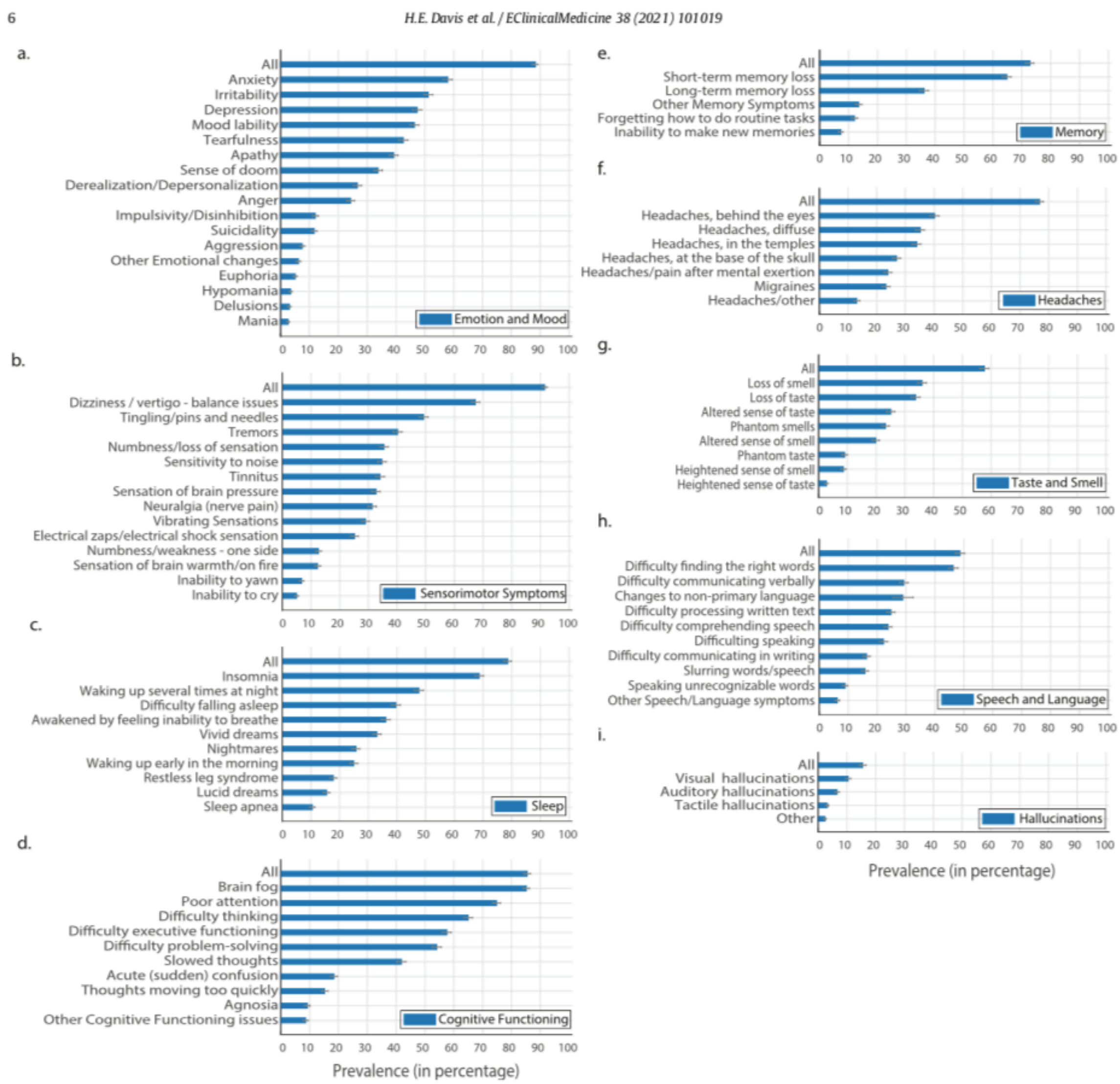

Table 2. Symptom prevalence estimates for neuropsychiatric symptoms (9)

2.1.5. Long-term effects in patients with COVID-19

In the study provided by Lopez-Leon et al (12) a total of 55 long-term effects associated with COVID-19 were identified. Most of the effects are consistent with clinical symptoms such as fatigue, headache, joint pain, anosmia, ageusia, etc. A meta-analysis of studies that included assessment of one or more symptoms showed that 80% of patients with COVID-19 have long-term symptoms.

The most common long-term manifestations were fatigue (58%), headache (44%), impaired attention (27%), hair loss (25%), shortness of breath (24%) and cough (19%). Also, lung CT abnormalities persisted in 35% of patients even 60 to 100 days after initial presentation.

Other complications were associated with pulmonary disease (chest discomfort, decreased lung diffusivity), cardiovascular (arrhythmia and myocarditis), neurological (depression, anxiety, and impaired attention), other complications were non-specific, such as hair loss, tinnitus and night sweats. Most of the complications in patients were similar to the symptoms that developed during the acute phase of the disease. (10;11;12)

	Studies	Cases	Sample size	Prevalence % (95% CI)
Clinical manifestations				
1 or > symptoms	7	1403	1915	80 (65–92)
Fatigue	7	1042	1892	58 (42–73)
Headache	2	261	579	44 (13–78)
Attention disorder	1	32	120	27 (19–36)
Hair loss	2	178	658	25 (17–34)
Dyspnea	9	584	2130	24 (14–36)
Ageusia	4	108	466	23 (14–33)
Anosmia	6	210	1110	21 (12–32)
Post-activity polypnea	1	115	538	21 (18–25)
Joint pain	4	191	1098	19 (7–34)
Cough	7	465	2108	19 (7–34)
Sweat	2	144	638	17 (6–30)
Nausea or vomit	1	22	141	16 (10–23)
Chest pain/discomfort	6	264	1706	16 (10–22)
Memory loss	3	320	45,186	16 (0–55)
Hearing loss or tinnitus	2	64	425	15 (10–20)
Anxiety	4	2288	45,896	13 (3–26)
Depression	4	182	1501	12 (3–23)
Digestive disorders	1	15	130	12 (7–18)

Table 3. Long-term effects of COVID-19. (12)

2.1.6. Medical treatment

Based on clinical data, the results of the effectiveness of various drugs are presented. Drugs for the treatment of covid patients are constantly being updated, so it is necessary to keep track of current clinical studies.

Therapy/Mechanism	Authors	Country	Phase of trails	Methods	Primary outcome	Report findings
Remdesivir (RDV)/RNA polymerase inhibitor	Wang *et al*	China	III	Double-blinded RCT; RDV (n = 158) vs. placebo (n = 79)	Clinical improvement up to 28 days	RDV was not associated with a difference in time to clinical improvement (hazard ratio 1.23 [95% CI 0.87–1.75])
	Beigel *et al*	United States	III	Double-blinded; RDV (n = 538) vs. placebo (n = 521); hospitalized patients; favorable outcome in preliminary report	Time to recovery	Median recovery time: 11 days vs. 15 days, recovery rate ratio, 1.32; 95% CI, 1.12–1.55; $p < 0.001$
Lopinavir-ritonavir (LPV/r)/protease inhibitor	Cao *et al*	China	N/A	Hospitalized patients with COVID-19 and respiratory illness[a]; open-label RCT; LPV/r (n = 99) vs. placebo (n = 100)	Time to clinical improvement	Modified intention-to-treat population[b]: Median time to clinical improvement: 15 days vs. 16 days (hazard ratio, 1.39; 95% CI, 1.00–1.91)
Favipiravir (FPV)/RNA polymerase inhibitor	Chen *et al*	China	N/A	Adults with COVID-19 pneumonia; open-label RCT; FPV (n = 120, 116 accessed) vs. UFV (n = 120)	Clinical recovery rate on day 7	Clinical recovery rate on day 7: 71.4% vs. 55.9%; rate ratio (95% CI): 0.16 (0.03–0.28)
Ribavirin (RBV)/Guanosine analog	Tong *et al*	China	N/A	Adults with severe COVID-19; retrospective study; RBV (n = 44) vs. none (n = 71)	Time to viral negative conversion	12.8 ± 4.1 vs. 14.1 ± 3.5 days ($p = 0.314$)
Interferon (IFN) β-1b, RBV, LPV/r/ Combination therapy	Hung *et al*	Hong Kong	II	Adults with admitted COVID-19 patients; open-label RCT	Time to viral negative conversion	7 days vs. 12 days (hazard ratio,4.37; 95% CI (1.85 ~ 10.24), $p = 0.0010$)
Chloroquine (CQ) and *hydroxychloroquine* (HCQ)	Gautret *et al*	France	III	Hospitalized patients with COVID-19 (age >12 years) regardless of their clinical status; open-label, non-RCT; HCQ ± AZI (n = 26) vs. none (n = 16)	Viral clearance at day 6	70.0% vs. 12.5%, $p = 0.001$
	Mehra *et al*	Multinational	N/A	Hospitalized patients with COVID-19 received treatment of interest within 48 h; multinational registry analysis, CQ or HCQ ± macrolide (n = 14,888) vs. none (n = 81,144)	In-hospital mortality and *de novo* ventricular arrhythmias	Retracted owing to suspicious data sources
Tocilizumab (TCZ)/Interleukin-6 inhibitors	Klopfenstein *et al*	France	II	Hospitalized adult patients with COVID-19; TCZ (n = 20) vs. control (n = 25)	Death and/or ICU admission	Patients with TCZ presented with severe form; death and/or ICU admission: TCZ 25% vs. control 72%, $p = 0.002$
	Campochiaro *et al*	Italy	II	Severe non-ICU adult patients with COVID-19; TCZ (n = 32) vs. control (n = 33)	Survival and clinical improvement at 28 days	Clinical improvement: TCZ 69% vs. control 61%, $p = 0.61$; mortality rate: TCZ 15% vs. control 33%, $p = 0.15$
	Price *et al*	United States	II	Hospitalized patients with COVID-19; observational study; TCZ (n = 153) vs. control (n = 86)	—	TCZ-treated patients with similar survival rates to non-severe patients (83% vs. 91%, $p = 0.11$)
Convalescent plasma (CP)/Neutralizing antibodies	Li *et al*	China	II	Severe and life-threatening COVID-19; RCT; CP (n = 52) vs. standard treatment (n = 51)	Clinical improvement within 28 days	28-days clinical improvement: CP 51.9% vs. standard treatment 43.1%; hazard ratio, 1.40 (95% CI, 0.79–2.49), $p = 0.26$. Patients without life-threatening disease: 28-days clinical improvement, hazard ratio, 2.15 (95% CI, 1.07–4.32); 72-h negative conversion rate of viral nucleic acid detection was higher in the CP group (87.2% vs. 37.5%, $p < 0.001$)

Table 4. Drugs for COVID-19. (13)

Reductions in mortality, hospitalizations, and ventilator requirements have been observed with interferons and remdesivir, especially when given early, and also with bromhexine. (14)

Remdesivir and favipiravir may shorten recovery time for patients. Combination therapy with ribavirin, lopinavir and interferon β-1b shows early negative viral conversion, but the main effect may be related to interferon. Some studies have shown that inhibitors of interleukin-6 may show clinical improvement. (13)

Dexamethasone significantly reduced mortality, hospitalization, and ventilator requirements compared with standard care, especially in patients with severe disease. (14) Combination therapy with antiviral drugs and immunomodulatory drugs is reasonable, especially for critically ill COVID-19 patients with cytokine release syndrome. Despite this, drugs to slow down the release of cytokines may not be useful for patients at an early stage with a mild course of the disease or at a late stage with a critical illness. (13)

Combination therapy with antivirals and traditional Chinese medicine may relieve inflammation in patients with severe COVID-19. Also, traditional Chinese medicine with antiviral activity against SARS-CoV-2 and immunomodulation is being used to treat patients with COVID-19 in China and deserves further study. (13)

2.1.7. Physiotherapeutic treatment

RHB for patients in severe to moderate COVID-19 primarily includes positioning, respiratory exercises, active, semi-active or passive movements and verticalsations depending on current patients condition. Two main goals of rehabilitation in this stages are promoting airway clearance and preventing complications of acute illness-related immobilisation. (15;16)

2.1.7.1. Position management

Positioning of the patient can reduce the influence of sputum on the respiratory tract or change the position of the excessive secretions, that can help with the removal of this secretions by for example coughing and suctioning. It can significantly improve the patient’s condition. The best resting position for breathing is standing, it can increase patient's breathing efficiency and maintain lung capacity. In case that the patient is not able to achieve standing position, sitting in erect position with back support is recommended. (15)

2.1.7.2. Respiratory physiotherapy

Active Cycle of Breathing Techniques (ACBT): ACBT is an effective method for clearing bronchial secretions, improving lung function, increasing oxygenation, and reducing dyspnea. It involves three stages: breathing control, thoracic expansion, and exhalation. The breathing cycle should be adjusted based on the patient's current condition. (15;17)

Positive Expiratory Pressure Trainer: In patients with COVID-19, severe damage to the pulmonary interstitium can occur. To prevent this complication, mechanical ventilation is done with low pressure and low tidal volume. After discontinuing mechanical ventilation, a positive expiratory pressure trainer can be used to assist in moving secretions from low-volume lung segments to high-volume lung segments, making it easier to expectorate sputum. Positive expiratory pressure is generated by vibrating the airflow, which in turn vibrates the airways and helps to expel secretions as they are moved by the high-velocity expiratory flow. (15)

Chest Vibration and Percussion: Chest wall fluctuations, mechanical vibration, and chest percussion can promote the discharge of sputum. These techniques are effective at various stages of the disease, particularly in patients with excessive airway secretions. (19)

Flutter Breathing: This method involves using a device with a movable steel ball in a sealed tube. The patient forcefully exhales air into the tube, causing the steel ball to shake and create a rhythmic flow of air. Flutter breathing can help to loosen excessive secretions in the airways, making it easier to actively remove them. (18)

Huffing and Controlled Cough: Huffing is characterized by rapid exhalation of air without closing the glottis, while controlled coughing aims to prevent shallow and ineffective coughing. Both methods have been shown to reduce cough force and improve airway clearance. (18)

2.1.7.3. Breathing exercises

Different types of breathing exercises can improve lung function, promote the release of sputum from the alveoli and airways into the larger airways so that sputum does not accumulate in the lower part of the lungs, thereby making it difficult for the patient to breathe. (15;16)

Deep-slow breathing: The aim of this technique is to engage the diaphragm to its fullest extent during inhalation. The intensity of breathing should be adjusted based on the patient's condition, ensuring that the breaths are deep and slow enough to maintain efficient breathing. Unlike chest breathing, this type of breathing requires less muscle effort but results in improved tidal volume and V/Q (ventilation/perfusion) ratio. Deep-slow breathing can help correct dyspnea and overall breathing patterns in patients. (15;16)

Chest expansion breathing: This exercise is employed to enhance pulmonary ventilation. The patient should inhale slowly and deeply, expanding the chest and shoulders, and then exhale while retracting the chest and shoulders. It is important to avoid holding the breath for prolonged periods to prevent increased strain on respiratory function and the heart. If feasible, the respiratory rate should be maintained at 12-15 breaths per minute. (20)

2.1.7.4. Deterioration prevention

Immobilisation can lead to functional decline, including reduced muscle strength and cardiorespiratory endurance, in all patients, but particularly in the elderly and those with other severe health conditions. Once the patient's condition is stable, early encouragement of active or semi-active movements is important. During the period when active movements are not yet possible, passive mobilisation should be carried out. For patients with moderate to severe disease stages who are able to actively move their limbs, it is recommended to perform active exercises multiple times a day, depending on their condition. This helps maintain or improve joint mobility, prevent thromboembolism, joint contractures, and shortening of soft tissues, among other complications. (15)

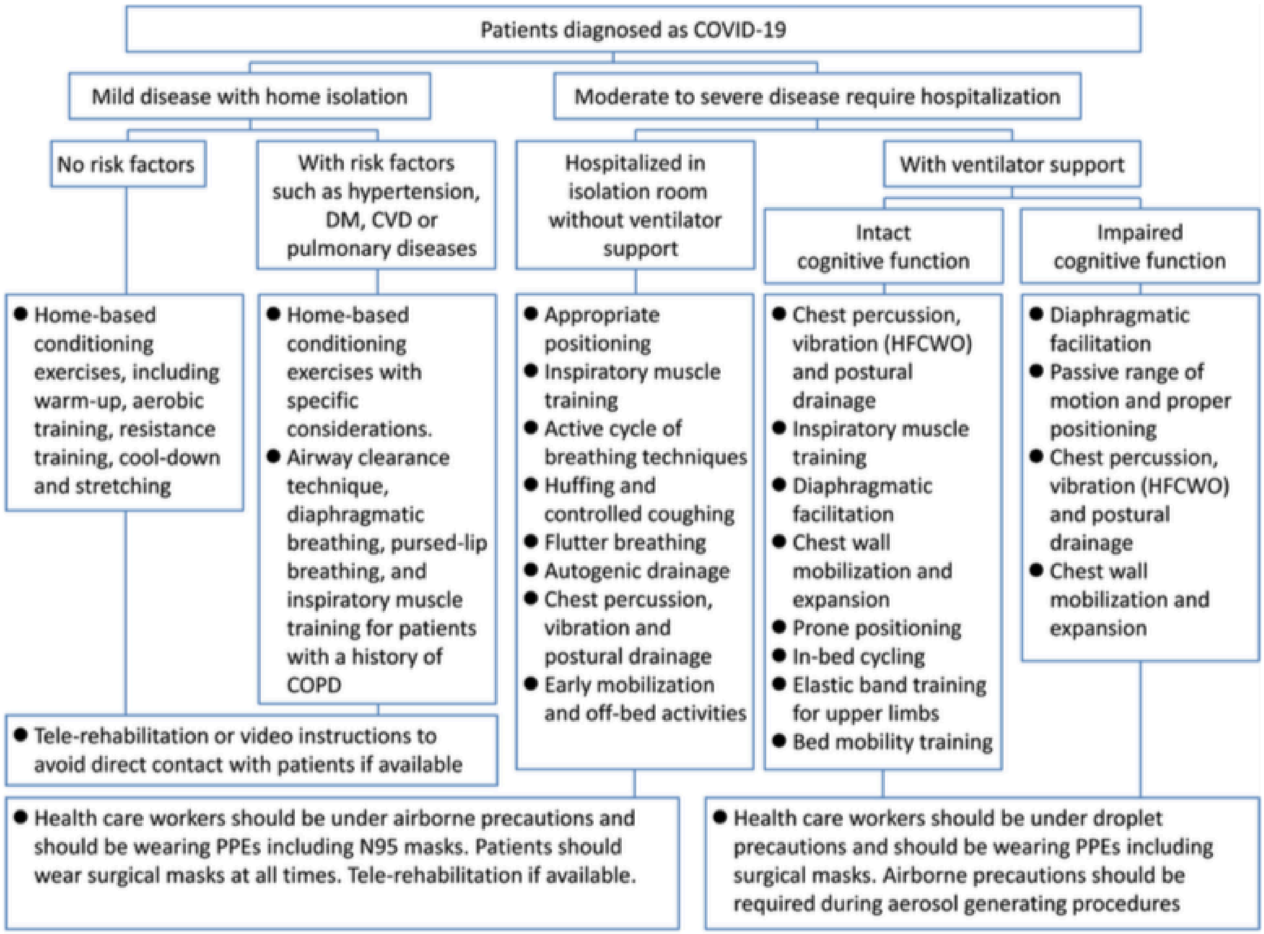

Table 5. The flowchart of suggested rehabilitation interventions and infection precautions for patients with COVID-19 (16).

2.1.8. Physiotherapy for mechanically ventilated patients

Physiotherapy has demonstrated effectiveness in improving long-term physical function in patients with COVID-19. For critically ill and post-critically ill patients, physiotherapy employs a multi-system approach that encompasses musculoskeletal rehabilitation to reduce morbidity, promote weaning from mechanical ventilation, and restore functional independence. (21;22)

Chest physiotherapy techniques for critically ill COVID-19 patients typically include airway clearance techniques, respiratory physiotherapy, vibration techniques, postural drainage, percussion, patient-ventilator interaction, inhalation therapy, and airway suction. These techniques are aimed at minimizing retention of pulmonary secretions and maximizing oxygenation. (21;22)

2.1.9. Telephysiotherapy

Telephysiotherapy or telemedicine is characterised as the clinical application of consultation for preventive action, diagnosis, and therapeutic approach with audio-visual links. (32;53;54) The International Network of Physical Therapy Regulatory Authorities (INPTRA) and the World Confederation for Physical Therapy (WCPT) suggest an international definition and highlight the importance of digital physiotherapy practice. Digital physiotherapy studies have reported positive effectiveness, validity, and benefits for neurological, musculoskeletal, cognitive and respiratory diseases. Digital physiotherapy provides an alternative approach to meet the patient's needs during respiratory problems with easy accessibility. (28)

Additionally, telemedicine programs significantly increased during the COVID-19 pandemic for maintaining organ function at acute and post-viral phases. (25;47) The requirement of physiotherapist and their training to deliver telerehabilitation services were enhanced. Furthermore, the use of telerehabilitation provides cardiac, pulmonary, psychological, and musculoskeletal benefits. Moreover, it reduced the cost of healthcare services and rates of spreading COVID-19. (25;26;51) Physiotherapy with digital practices is presented as complementary and promising modalities to standard physiotherapy in delivering services irrespective of time and healthcare setting. The higher acceptability and feasibility of digital physiotherapy may be satisfactory in obtaining an improved functional capacity for COVID-19 patients. (48)

3. Research problem

This systematic review aims to assess the effectiveness of physiotherapeutic modalities on pulmonary function, physical function and psychosocial effect of patients diagnosed with COVID-19.

The goal of the systematic review is to identify the recent available PT modalities that can be used on different stages of disease and evaluate its effectiveness.

Research question:

How effective physiotherapeutic procedures for treatment patients with COVID-19?

4. Methodology

This systematic review was conducted in accordance with preferred reporting items for systematic and meta-analysis guidelines to assess the effectiveness of physiotherapy modalities in COVID-19 patients. (50)

4.1. Literature search strategy

An electronic literature search includes the following databases: CINAHL, PubMed, Embase, Cochrane library and Scopus. The literature search was restricted to English-language articles published between 2019 to January 2023. PICOS was applied (P: population, I: intervention, C: Comparison, O: outcome, and study designs) strategy for the literature search. The search criteria used across PubMed were ("Chest physiotherapy" OR physiotherapy OR Huff OR "Forced Expiratory Technique" OR "postural drainage" OR "Drainage, Postural"[Mesh] OR percussion OR cupping OR clapping OR Exercise OR 'Assisted cough*" OR "Active cycle of breathing technique" OR "Autogenic drainage" OR "High-Frequency Chest Wall Oscillation" OR "Breathing exercises" OR "Breathing Exercises"[Mesh] OR "Respiratory Therapy"[Mesh]) AND (COVID-19 OR coronavirus or covid-19[Mesh]). The search criteria and Boolean operators were matched based on a database.

Moreover, cross-checking of references of potential articles and reviews was manually performed. Duplicate publications, case series, case reports, conference abstracts, or literature reviews were be eliminated. The literature search was restricted to human studies and English language articles.

4.2. Study criteria: Inclusion and exclusion

Studies report that patients with a confirmed diagnosis of either acute COVID-19, Chronic COVID-19 or recovered cases of COVID-19 with residual symptoms.

Included studies had to report on patients with a confirmed diagnosis of either acute COVID-19, chronic COVID-19, or recovered cases of COVID-19 with residual symptoms and the effects of physiotherapy in COVID-19 patients. PT includes position management, respiratory physiotherapy, flutter breathing, and breathing exercises. This physiotherapy was delivered either using online mode or face-to-face physiotherapy. Additionally, studies assessed the outcome before and after PT. Simultaneously, studies compared outcomes following post-intervention and control. Any physical parameter assessing the mean change of pulmonary function test, exercise capacity, dyspnea severity index (DSI), fatigue, or quality of life measure scales from baseline to post-therapy or follow-up. Additionally, the adverse effects experienced by patients during physiotherapy were also assessed. Studies were excluded if the patients suffered from MERS or SARS.

4.3. Study selection and data extraction

The Endnote 20.4 software imported all final search results across all databases and removed duplicate studies. Firstly, the title and abstracts of all the articles were screened to cross-check if they met the study criteria. Moreover, a full-text analysis of potential articles was performed for those whose abstracts failed to demonstrate clear and specific outcomes. Lastly, literature data such as stage, the severity of COVID-19, intervention, mode of intervention, intervention session, assessed outcomes, and summary of the study were extracted.

4.4. Data Synthesis

The characteristics (author, publication year, stage/severity of COVID-19, country, number of patients, intervention, intervention description, session and results) were extracted and summarised in the general study characteristic table (Table 7)). The assessed outcome included mean change in pulmonary function, exercise capacity, dyspnea capacity index, quality of life, and adverse effects during physiotherapy.

5. Results

5.1. Study selection

A total of 1093 articles were retrieved from the database search, and 152 duplicates were removed. After title and abstract screening, 903 articles were excluded. Subsequently, 38 articles were assessed for eligibility, and 29 of them were eliminated as they did not meet the inclusion criteria. Nine articles were deemed eligible for review after the screening process, as illustrated in Figure 1.

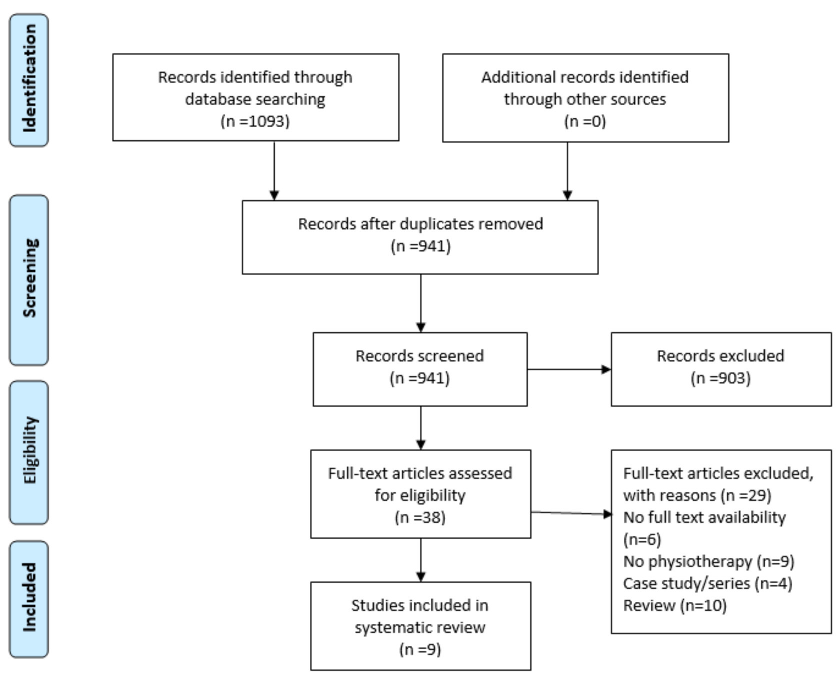

Figure 1: PRISMA flow diagram for literature search process

5.2. Data Synthesis

The characteristics (author, publication year, stage/severity of COVID-19, country, number of patients, intervention, intervention description, session and results) were extracted and summarised in the general study characteristic table (Table 7)). The assessed outcome included mean change in pulmonary function, exercise capacity, dyspnea capacity index, quality of life, and adverse effects during physiotherapy.

5.3. Study Characteristics

Table 7 provides an overview of the included studies. These studies were published between 2020 and 2022. The severity of COVID-19 ranged from acute mild to severe in 6 studies and chronic-moderate to severe cases in 3 studies. All the studies were conducted in Asia and European continents, with Spain and China each represented by two studies. The remaining studies were conducted in Turkey and Saudi Arabia. The most common intervention method used was telerehabilitation which was employed in 6 of the studies, while face-to-face pulmonary rehabilitation was used in 3 studies. A total of 481 patients were included in the studies.

Reference Study	Stage/ severity of COVID-19	Country	Number of patients	Intervention	Intervention description	Session	Results
Abodonya et al., 2021	Chronic-moderate to severe cases	Saudi Arabia	42 (IG:21; CG:21)	Breathing exercise + inspiratory muscle training	IMT	2 times/day for 14 days	The intervention group demonstrated significant improvement of 6MWT, QOL, DSI and PFTs after breathing exercises
Estebanez -Pérez et al., 2022	Acute-mild to severe cases	Spain	32	Telerehabilitation	Active strength exercises, secretion drainage, ventilatory techniques, ladder breathing technique, walking	20-30 minutes/ session, 3-5 session/week for 4 week	Pulmonary rehabilitation exercises improved the functional capacity after 4 weeks of intervention
Gonzalez-Gerez et al., 2021	Acute-mild cases	Spain	38 (IG:19; CG:19)	Telerehabilitation	Breathing exercises, airway cleaning, exercise program	30-60min/ session, 1 session per day for 7 days	After 1 week of therapy: dyspnea, muscle performance and exercise capacity were improved in intervention group
Li Ja et al., 2022	Chronic-moderate to severe cases	China	118 (IG:59; CG:59)	Pulmonary rehabilitation	Breathing control and thoracic expansion, aerobic exercise, LMS exercise	3-4 sessions/ week, 40-60 minutes of exercise program for 6 weeks	Pulmonary functions, dyspnea, QOL, and exercise capacity were significantly improved after 6 weeks of pulmonary rehabilitation in intervention group than control group

Liu K et al., 2020	Acute-mild cases	China	72 (IG:36; CG:36)	Pulmonary rehabilitation	Cough exercise, respiratory muscle training, stretching exercise, diaphragmatic training, home exercise	10 minutes in a day with 2 sessions/week for 6 weeks	Pulmonary function, QOL, and exercise capacity were significantly improved after 6 weeks of pulmonary rehabilitation program
Pehlivan et al., 2022	Acute mild cases	Turkey	34 (IG:17; IC:17)	Telerehabilitation	Patient education, walking, breathing exercise, ROM exercise, active breathing techniques, wall squat exercise	10 min per session, 3 sessions/week for 6 weeks	Intervention group have improved dyspnea and QOL scores
Rodriguez-Blanco et al., 2021	Acute-mild cases	Spain	36 (IG:18; CG:18)	Telerehabilitation	NTEP of 10 exercises	1 hour/ session/day for 1 week	After 1 week of therapy: dyspnea, muscle performance and exercise capacity were improved in intervention group
Rodriguez-Blanco et al., 2022	Acute-mild cases	Spain	77 (IG:55; CG:22)	Telerehabilitation	Breathing exercises, stretching exercises	1 session/day for 2 weeks	Breathing exercise improved dyspnea and 6MWT
Teixeira et al., 2022	Chronic-mild cases	Brazil	32 (IG:12, CG:20)	Telerehabilitation	Aerobic exercise	5 sessions/ week for 12 weeks	Aerobic exercise improved forced expiratory volume, forced vital capacity

Table 7: Characteristics of eligible studies

IG: intervention group, CG: control group, 6MWT: 6 minute walk test, DSI: dyspnea severity index, PFTs: pulmonary function tests, LMS: lower limb muscle strength, IMT: inspiratory muscle training, ROM: range of motion, NTEP: non-specific conditioning exercise program.

5.4. Physiotherapeutic interventions used

Abodonya et al. (2021) used inspiratory muscle training as a PT intervention in recovered COVID-19 patients after weaning from mechanical ventilation. The intervention involved a 2 weeks inspiratory muscle training (IMT) program using a threshold loading device, which was started after weaning from mechanical ventilation. Estebanez-Pérez et al. (2022) used a digital physiotherapy intervention to improve functional capacity and adherence to intervention in patients with long COVID-19. The intervention was a 4-week program that consisted of personalised exercise videos and teleconsultations with a physiotherapist. The exercises aimed to improve functional capacity and included cardiorespiratory, strengthening, and stretching exercises. Gonzalez-Gerez et al. (2021) used respiratory telerehabilitation as a physiotherapeutic intervention in confined COVID-19 patients in the acute phase. The intervention involved a 1 week program comprising respiratory exercises and physical activity guidance delivered through telecommunication technology.

Li et al. (2021) used a telerehabilitation program as a intervention in post-discharge COVID-19 patients. The intervention consisted of a 6 weeks exercise program that consisted of personalized exercise videos, teleconsultations with a physiotherapist, and a mobile application for self-monitoring. The exercise program included breathing control and thoracic expansion exercises, aerobic exercises and LMS (lower limb muscle strengthening) exercises. Liu et al. (2020) used respiratory rehabilitation as a physiotherapeutic intervention in elderly patients with COVID-19. The intervention was a 6 weeks program that consisted of respiratory exercises, cough training, and physical activity guidance. Pehlivan et al. (2022) used telerehabilitation as a physiotherapeutic intervention in post-discharge COVID-19 patients. The intervention was a 6 weeks program that consisted of personalized exercise videos and teleconsultations with a physiotherapist, the program included patient education, walking, breathing exercises, range of motion (ROM) improvement exercises, active breathing techniques and wall squat exercise . The exercises aimed to improve cardiorespiratory fitness, muscle strength, and endurance.

5.5. Respiratory rehabilitation and telerehabilitation programs: primary and secondary outcomes

A thematic analysis, according to Braun and Clarke, 2006 was used to highlight and analyse dominant themes in the included studies. The qualitative analysis in this review considered all the included articles. The dominant themes in the study were clustered into three classes; respiratory functions, functional capacity, quality of life and fatigue. These outcomes are summarised quantitatively and presented in Tables 8, 9 and 10.

5.5.1. Respiratory Function

Some studies assessed respiratory function in patients diagnosed with COVID-19. The included studies used quantitative data to measure various aspects of lung function, including forced expiratory volume, forced vital capacity, and pulmonary function tests. FEV% measures the maximum air a person can forcefully exhale in one second expressed as a percentage of their total lung capacity. FVC% measures the maximum air a person can forcefully exhale after taking a deep breath expressed as a percentage of their total lung capacity.

Overall, these studies suggest that respiratory function, as measured by FEV% and FVC%, is significantly affected by COVID-19 and can be improved through various respiratory interventions, including inspiratory muscle training, respiratory exercises, and respiratory telerehabilitation programs. These interventions can effectively improve respiratory function in COVID-19 patients in the acute phase and during recovery.

5.5.2. Functional capacity

Some studies investigated functional capacity in patients diagnosed with COVID-19. Braun and Clarke (2006) defined functional capacity as "the ability to perform activities of daily living (ADL) with independence, safety, and comfort". Overall, the studies reviewed in this analysis suggest that various interventions such as inspiratory muscle training, digital physiotherapy, telerehabilitation, and respiratory rehabilitation can significantly improve the functional capacity of COVID-19 patients. The 6 minutes walk test (6-MWT) and dyspnea severity index (DSI) are valid tools used to assess functional capacity in these patients. Improving functional capacity is important for recovery and reducing the risk of future respiratory complications, and improving the QOL of COVID-19 patients.

5.5.3. Quality of life and fatigue

Some studies investigated the effectiveness of telerehabilitation programs on the quality of life and fatigue in COVID-19 patients. Braun and Clarke (2006) define the quality of life as an individual's subjective evaluation of their physical, emotional, and social well-being. Fatigue is a feeling of tiredness or exhaustion that impairs an individual's ability to perform daily activities. (66)

Several of the studies mentioned above focused on telerehabilitation that provides rehabilitation services through telecommunication technologies, such as video conferencing, to allow remote access to healthcare services.

For instance, Gonzalez-Gerez et al. (2021) and Rodriguez-Blanco et al. (2021) conducted pilot studies on the short-term effects of respiratory telerehabilitation programs in COVID-19 patients in the acute phase. Both studies found improvements in patients' respiratory function and QOL, with Gonzalez-Gerez et al. reporting reduced fatigue levels. Overall, the studies suggest that telerehabilitation and other rehabilitation interventions can improve the QOL and reduce fatigue levels in COVID-19 patients.

Outcomes	Reference Study	Outcome at baseline intervention (mean ± SD)	Post intervention (mean ± SD)
FVC %	Abodonya et al., 2021	78.7 ± 13.5	84.2 ± 10.3
FVC (L)	Li Ja et al., 2022	2.85 ± 0.75	2.86 ± 0.47
	Liu K et al., 2020	1.79 ± 0.53	2.36 ± 0.49
	Teixeira et al., 2022	3.74 ± 1.19	4.36 ± 0.715
FEV1%	Abodonya et al., 2021	76.2 ± 12.7	83.7 ± 10.5
FEV (L)	Li Ja et al., 2022	2.24 ± 0.74	2.24 ± 0.51
	Liu K et al., 2020	1.1 ± 0.08	1.44 ± 0.25
	Teixeira et al., 2022	3.1 ± 0.86	3.64 ± 0.52

DSI (q)	Abodonya et al., 2021	18.5 ± 4.3	14.2 ± 3.5
	Gonzalez-Gerez et al., 2021	12.26 ± 5.92	5.89 ± 3.48
	Rodriguez-Blanco et al., 2022	11.04 ± 6.49	5.32 ± 3.63
6MWT (m)	Abodonya et al., 2021	332.6 ± 34.5	376.5 ± 39.4
	Gonzalez-Gerez et al., 2021	374.72 ± 151.59	487.58 ± 133.36
	Li Ja et al., 2022	514.52 ± 82.87	927.16 ± 74.66
	Liu K et al., 2020	162.7 ± 72	212.3 ± 82.5
	Rodriguez-Blanco et al., 2021	440.17 ± 164.36	519.94 ± 135
	Teixeira et al., 2022	522 ± 107	543 ± 115
BS (q)	Gonzalez-Gerez et al., 2021	5.58 ± 2.32	2.95 ± 1.27
	Rodriguez-Blanco et al., 2021	4.78 ± 1.7	2.56 ± 0.85

30STST (rep)	Gonzalez-Gerez et al., 2021	12.68 ± 5.33	14 ± 5.47
	Pehlivan et al., 2022	9.9 ± 2.5	10.72 ± 1.67
	Rodriguez-Blanco et al., 2021	12.33 ± 4.81	13.83 ± 5.7
	Rodriguez-Blanco et al., 2022	11.18 ± 3.42	12.79 ± 4
Fatigue (q)	Pehlivan et al., 2022	2.2 ± 1.4	1.4 ± 0.84

Table 8: Within the intervention group (before and after intervention)
FVC: forced vital capacity, FEV: forced expiratory volume, FEV1: forced expiratory volume in 1 second, DSI: dyspnea severity index, 6MWT: 6 minute walk test, BS: Borg scale, 30STST: 30 second sit to stand test, SD: standard deviation, q: questioner, L: litres, rep: repetitions

Outcomes	Reference Study	Baseline control (mean ± SD)	Post control (mean ± SD)
FVC %	Abodonya et al., 2021	77.2 ± 12.6	76.8 ± 11.7
FVC (L)	Li Ja et al., 2022	2.69 ± 0.87	2.70 ± 0.4
	Liu K et al., 2020	1.77 ± 0.64	2.08 ± 0.37
	Teixeira et al., 2022	3.64 ± 1.14	4.2 ± 1.02
FEV1 %	Abodonya et al., 2021	75.4 ± 12.2	75.1 ± 12.4
FEV (L)	Li Ja et al., 2022	2.14 ± 0.69	2.14 ± 0.53
	Liu K et al., 2020	1.13 ± 0.14	1.26 ± 0.32
	Teixeira et al., 2022	3.23 ± 0.83	3.52 ± 0.86
DSI (q)	Abodonya et al., 2021	17.8 ± 5.1	17.1 ± 4.8
	Gonzalez-Gerez et al., 2021	9.74 ± 7.26	9.79 ± 7.47
	Rodriguez-Blanco et al., 2022	10.27 ± 6.49	10.59 ± 6.58
6MWT (m)	Abodonya et al., 2021	329.7 ± 37.8	334.8 ± 38.2

	Gonzalez-Gerez et al., 2021	393 ± 124.6	399 ± 126.07
	Li Ja et al., 2022	499.98 ± 93.41	585.42 ± 63.94
	Liu K et al., 2020	155.7 ± 82.1	157.2 ± 71.7
	Rodriguez-Blanco et al., 2021	379.72 ± 128.72	379.72 ± 136.01
	Teixeira et al., 2022	472 ± 98	490 ± 76
BS (q)	Gonzalez-Gerez et al., 2021	4.58 ± 1.89	4.26 ± 1.85
	Rodriguez-Blanco et al., 2021	4.78 ± 1.8	4.83 ± 1.54
30STST (rep)	Gonzalez-Gerez et al., 2021	11.42 ± 3.06	11.11 ± 3.78
	Pehlivan et al., 2022	10.7 ± 2.78	11 ± 2.22
	Rodriguez-Blanco et al., 2021	10.5 ± 2.25	9.94 ± 1.98
	Rodriguez-Blanco et al., 2022	10.45 ± 2.15	9.86 ± 1.88
Fatigue (q)	Pehlivan et al., 2022	1.88 ± 1.4	1.8 ± 1.4

Table 9: Within the control group (before and after intervention)
FVC: forced vital capacity, FEV: forced expiratory volume, FEV: forced expiratory volume in 1 second, DSI: dyspnea severity index, 6MWT: 6 minute walk test, BS: Borg scale, 30STST: 30 second sit to stand test, SD: standard deviation, q: questioner, L: litres, rep: repetitions

Outcomes	**Reference Study**	**Post intervention (mean ± SD)**	**Post control (mean ± SD)**
FVC %	Abodonya et al., 2021	84.2 ± 10.3	76.8 ± 11.7
FVC (L)	Li Ja et al., 2022	2.86 ± 0.47	2.70 ± 0.4
	Liu K et al., 2020	2.36 ± 0.49	2.08 ± 0.37
	Teixeira et al., 2022	4.36 ± 0.715	4.2 ± 1.02
FEV1 %	Abodonya et al., 2021	83.7 ± 10.5	75.1 ± 12.4
FEV (L)	Li Ja et al., 2022	2.24 ± 0.51	2.14 ± 0.53
	Liu K et al., 2020	1.44 ± 0.25	1.26 ± 0.32
	Teixeira et al., 2022	3.64 ± 0.52	3.52 ± 0.86
DSI (q)	Abodonya et al., 2021	14.2 ± 3.5	17.1 ± 4.8
	Gonzalez-Gerez et al., 2021	5.89 ± 3.48	9.79 ± 7.47

	Rodriguez-Blanco et al., 2022	5.32 ± 3.63	10.59 ± 6.58
6MWT (m)	Abodonya et al., 2021	376.5 ± 39.4	334.8 ± 38.2
	Gonzalez-Gerez et al., 2021	487.58 ± 133.36	399 ± 126.07
	Li Ja et al., 2022	927.16 ± 74.66	585.42 ± 63.94
	Liu K et al., 2020	212.3 ± 82.5	157.2 ± 71.7
	Rodriguez-Blanco et al., 2021	519.94 ± 135	379.72 ± 136.01
	Teixeira et al., 2022	543 ± 115	490 ± 76
BS (q)	Gonzalez-Gerez et al., 2021	2.95 ± 1.27	4.26 ± 1.85
	Rodriguez-Blanco et al., 2021	2.56 ± 0.85	4.83 ± 1.54
30STST (rep)	Gonzalez-Gerez et al., 2021	14 ± 5.47	11.11 ± 3.78
	Pehlivan et al., 2022	10.72 ± 1.67	11 ± 2.22

	Rodriguez-Blanco et al., 2021	13.83 ± 5.7	9.94 ± 1.98
	Rodriguez-Blanco et al., 2022	12.79 ± 4	9.86 ± 1.88
Fatigue (q)	Pehlivan et al., 2022	1.4 ± 0.84	1.8 ± 1.4

Table 10: Between groups (post-intervention)
FVC: forced vital capacity, FEV: forced expiratory volume, FEV: forced expiratory volume in 1 second, DSI: dyspnea severity index, 6MWT: 6 minute walk test, BS: Borg scale, 30STST: 30 second sit to stand test, SD: standard deviation, q: questioner, L: litres, rep: repetitions

5.6. Quantitative Results Analysis

5.6.1. Forced vital capacity

The study by Abodonya et al. (2021) shows for the intervention group a value of FVC% 78.7±13.5 as baseline while the corresponding post-intervention value was 84.2±10.3 (Table 8). This data demonstrates the effectiveness of the treatment regarding the FVC% when compared to the FVC% registered for the control group in which no difference was detected.

The other studies selected opted for the FVC metric measured in metres instead of the FVC% for evaluating the lung capacity. The results published by these studies showed no difference for the intervention and the control group displaying how the treatment didn't contribute to an overall improvement of the FVC test (Table10).

5.6.2. Forced expiratory volume

The analysis of data for the effectiveness of treatment on FEV is aligned to the one focusing the FVC data. In particular the published results by the the study conducted by Abodonya et al. (2021) displays the effectiveness of the treatment with the intervention group a value of FEV1% 76.2±12.7 as baseline while the corresponding post-intervention value was 83.7±10.5 (Table 8). The corresponding control group result data shows no difference in values (Table 9).

The other studies selected showed no difference for the intervention and the control group regarding the FEV data (Table 10).

5.6.3. Dyspnea Severity Index

The results of published studies that evaluated the DSI (using questionnaire) have shown an improvement for what concerns the difficulty breathing or shortness of breath in the intervention group (Table 8). For example in the study by Gonzalez-Gerez et al. (2021) the outcome at baseline registered as DSI value for the intervention group 12.26±5.92 while at post-intervention the same group registered a value of 5.89±3.48.

In contrast with the significant improvement in the intervention group the results for the control group didn't show any improvements (Table 9).

5.6.4. Six-Minute Walk Test

Every study evaluating the 6MWT agreed on the effectiveness of the PT treatment as demonstrated by a significant improvement of the cardiorespiratory fitness for the intervention groups compared to their respective control groups (Table 10). For example the study by Rodriguez-

Blanco et al. (2021) shows a value of 440.17m as 6MWT as baseline and a value of 519.94m as post intervention (Table 8). No significant change was measured for the control group (Table 9).

5.6.5. Borg Scale (BS)

The studies by Gonzalez-Gerez et al. (2021) and by Rodriguez-Blanco et al. (2021) have evaluated additionally how the PT treatment relates to the physical activity intensity level and demonstrated its effectiveness. For example in the study of Gonzalez-Gerez et al. (2021) the outcome at baseline registered as Borg scale value for the intervention group 5.58±2.32 while at post-intervention the same group registered a value of 2.95±1.27 (Table 8).

The related control group Borg scale value doesn't show any improvements. (Table 9)

5.6.6. Thirty-Second Sit-To-Stand Test (30STST)

The results of the selected studies that evaluated the 30STST have shown a minor improvement for what concerns the peripheral muscle performance of the lower limbs in the intervention group (Table 8). For example in the study of Gonzalez-Gerez et al.(2021) the outcome at baseline registered as 30STST value for the intervention group 12.68±5.33 while at post-intervention the same group registered a value of 14.00±5.47 (Table 8).

The related control group 30STST value doesn't show any improvements (Table 9).

5.6.7. Fatigue

The study by Pehlivan et al. (2022) researched the effects of PT treatment concerning the fatigue level which was evaluated using visual analog scale score from 0 to 10 as highest level of fatigue. The result published demonstrated the treatment effectiveness at lowering fatigue levels from a value of 2.2±1.4 as baseline to a 1.4±0.84 as post-intervention while no improvement was noticed for the control group (Table 8;9).

6.Discussion

This thesis provides a constructive analysis of quantitative and qualitative data on the effectiveness of physiotherapeutic modalities on pulmonary function, physical function, and psychosocial effects of patients diagnosed with COVID-19. It opens a bridge for further research on the effectiveness of respiratory RHB and telerehabilitation programs on patients diagnosed with COVID-19. The findings demonstrated that respiratory rehabilitation improves respiratory function, exercise capacity, and quality of life in patients diagnosed with COVID-19.

Respiratory and telerehabilitation programs have been effective in improving respiratory function and functional capacity in recovered COVID-19 patients. Inspiratory muscle training, a component of respiratory rehabilitation, has improved inspiratory muscle strength and pulmonary function in COVID-19 patients who have been weaned from mechanical ventilation. (68) According to Volpe et al. (2020) respiratory physiotherapy significantly decrease the time of patient stay in intensive care unit in acute stage of the disease.

Digital physiotherapy interventions, have been found to improve functional capacity and adherence to intervention in patients with long COVID-19. (69). Telerehabilitation programs, delivered remotely, effectively improve functional capacity and reduce the risk of readmission in post-discharge COVID-19 patients. (70;71)

The effectiveness of these RHB interventions can be attributed to their ability to target the specific impairments that COVID-19 patients experience. Respiratory rehabilitation can help improve respiratory muscle strength and endurance, lung function, and oxygen saturation levels. (44)

Telerehabilitation programs, which can be accessed remotely, allowing patients to participate in rehabilitation programs from the comfort of their homes, which may increase their adherence to treatment. (72)

Furthermore, these interventions can help mitigate the long-term effects of COVID-19, which include persistent fatigue, dyspnea, and reduced physical activity. (51) They focus on improving lung function, respiratory muscle strength, and physical fitness. A study by Pehlivan et al. (2022) found that telerehabilitation practices significantly improved exercise capacity, as measured by the 6MWT, in recovered COVID-19 patients. Another study by Rodriguez-Blanco et al. (2021) showed that a digital physiotherapy intervention significantly improved functional capacity and QOL in long COVID-19 patients. Inspiratory muscle training has also improved exercise capacity in recovered COVID-19 patients. (68) By improving respiratory function and functional capacity, rehabilitation interventions can help patients regain their independence and QOL.

The long-term effects of COVID-19 such as dyspnea severity index and persistent fatigue, among others were quantitatively analysed. DSI was used to measure difficulty in breathing or shortness of breath among patients diagnosed with COVID-19. Expectedly, difficulty in breathing reduced significantly within the intervention group. This implies that patients diagnosed with COVID-19 within the intervention group were better relieved from difficulty in breathing post-intervention than those in the control group. (51;68) Therefore, the interventions showed their effectiveness in reducing the difficulty of breathing.

Regarding persistent fatigue, there was an association between telerehabilitation and the reduction in fatigue level in the intervention group. This result must be interpreted cautiously since quantitative data on fatigue was only reported in a study by Pehlivan et al.(2022).

In addition, Sire et al. (2022) compared rehabilitation interventions on fatigue levels in patients at various stages of coronavirus disease. The study compared the effectiveness of high-intensity exercise, different types of respiratory exercises, passive/semi-active mobilisation of the extremities, aerobic exercises and strength exercises. The therapy was carried out both in the telerehabilitation mode and directly with a physiotherapist. Respiratory exercises in combination with aerobic exercises showed the highest effectiveness on fatigue levels on COVID-19 patients at different stages of the disease.

Airway clearance techniques (ACTs) were commonly used in studies conducted by Gonzalez-Gerez et al. (2021) and Liu K et al. (2020). ACTs can be effective in managing respiratory symptoms in COVID-19 patients by promoting the clearance of mucus and secretions from the airways. These techniques can improve ventilation, reduce airway obstruction, and facilitate the removal of mucus that may accumulate in the airways due to increased production from respiratory infections like COVID-19 and other respiratory diseases. Different procedures can be used to achieve airway clearance, including deep breathing exercises, huffing or forced expiratory technique, chest physiotherapy, coughing, postural drainage, intensive spirometry, suctioning, and more.

Gonzalez-Gerez et al. (2021) used coughing in combination with active cycle of breathing techniques for acute COVID-19 patients. The active cycle of breathing techniques involves alternate depths of breathing to move mucus from small airways in the bottom of the lungs to upper airways, where they can be more easily cleared by coughing. After a week of treatment, patients showed significant improvements in parameters such as DSI and BS. Additionally, the results of the 6MWT improved, which could be correlated with the decrease in DSI results as it represents the subjective sensation of difficulty or discomfort in breathing.

McWilliams et al. (2021) described the possibilities and importance of airway clearance techniques for severe COVID-19 patients. Coughing, when used in combination with other physiotherapy techniques such as deep breathing, is a very effective way to clear the airways.

In his study, Wang et al. (2020) highlighted the importance of clearing airways from sputum and excessive secretions as it is one of the symptoms that severely affects the condition of patients with COVID-19. If excessive secretions remain in the airways, they can be a severe aggravating factor in the development of other complications associated with COVID-19. (96)

Airway clearance is not only beneficial for patients diagnosed with COVID-19 at different stages of the disease, but also for patients suffering from chronic obstructive pulmonary disorder (COPD), bronchiectasis, and cystic fibrosis. Active cycle of breathing and assisted cough are useful interventions to decrease chest pain and dyspnea associated with respiratory diseases. (80) Lee et al. (2015) discussed the general benefits of ACTs for patients diagnosed with bronchiectasis, indicating that airway clearance techniques appear to be safe for adult patients and children with stable bronchiectasis and may result in improvements in sputum expectoration, selected measures of lung function, and quality of life. (97)

Lui et al. (2020) used respiratory muscle training in combination of the cough exercises and diaphragmatic breathing as an intervention for elderly patients in acute stage of coronavirus disease for 6 weeks. This study aimed to investigate the efficacy of combination of interventions mentioned above. Six weeks of respiratory rehabilitation significantly improved respiratory function, QOL, anxiety, and depression in elderly patients with COVID-19 and patients without COPD. (45)

Coronavirus patients may have residual fibrous lesions in the lungs as a complication of the disease, especially in older patients, and this can seriously affect respiratory function. Despite this, already after short period of therapy, patients showed a significant improvement in various indicators. The reason may be that the rehabilitation was aimed not only to clear the airways, but primarily target strengthening of the respiratory muscles such as the diaphragm and intercostal muscles, which play a crucial role inspiratory cycle. The weakening and reduction of the respiratory muscles function leads to changes in breathing pattern, shortness of breath, dyspnea, fatigue and excessive tiredness due to decreased ventilation in the lungs and drop of the saturation level. (45)

Ilie et al. (2022) investigated the effectiveness of PT interventions on patients with acute coronavirus disease in intensive care unit (ICU) after 2 week of daily treatment. Physiotherapy program was adjusted according to patients current state and included: different types of active movements of extremities in bed, diaphragmatic breathing and pursed lip breathing.

In patients receiving active physiotherapy, the disappearance of some symptoms such as dry cough and shortness of breath at the end of therapy was observed. The effectiveness of physiotherapy also depended on the condition of the patient and the type of PT intervention used, but it is important to note that all patients performed respiratory exercises, while physical exercises were subject to great adaptations. In addition to this, patients in the control group showed almost no improvement.

The results of this and many other studies indicate a significant role for physiotherapy in improving the condition of patients with COVID-19, both during hospitalisation and after discharge.

6.1.Possible Study Limitations

The articles included in this study were either written in English or could be translated into English; therefore, non-English studies could have been neglected. In studies by Gonzalez-Gerez et al. (2021) and Rodriguez-Blanco et al. (2021) intervention and follow-up durations were relatively short. Certain studies selected participants based on availability rather than the evaluation of sample size and power analysis. Additionally, certain studies used were non-randomized for ethical considerations. Therefore, randomized controlled studies are needed with larger sample sizes, longer duration, and follow-up observation.

7.Conclusion

In conclusion, based on the findings of this thesis, respiratory rehabilitation and telerehabilitation programs have emerged as effective interventions for improving the functional capacity, QOL, and respiratory function of recovered COVID-19 patients. Inspiratory muscle training, as a component of respiratory rehabilitation, has been shown to improve inspiratory muscle strength and pulmonary function in COVID-19 patients who have been weaned from mechanical ventilation. Digital physiotherapy interventions, delivered remotely, have also been found to improve functional capacity and adherence to intervention in patients with long COVID-19.

Furthermore, telerehabilitation programs have shown promising results in post-discharge COVID-19 patients by improving functional capacity and reducing the risk of readmission. These programs allow patients to participate in rehabilitation from the comfort of their homes, overcoming barriers such as transportation limitations, and potentially increasing their adherence to treatment. The convenience and accessibility of telerehabilitation make it a viable option for providing ongoing care to COVID-19 patients, especially in remote or underserved areas.

The effectiveness of these rehabilitation interventions can be attributed to their ability to specifically target the impairments that COVID-19 patients experience. Respiratory rehabilitation focuses on improving respiratory muscle strength and endurance, lung function, and oxygen saturation levels. Telerehabilitation programs, on the other hand, provide a tailored approach that can be adapted to the individual needs of patients, including exercise training, breathing exercises, and education on self-management techniques. These interventions can help COVID-19 patients regain their functional independence, improve their ability to perform daily activities, and enhance their overall QOL.

Importantly, these interventions have the potential to mitigate the long-term effects of COVID-19, such as persistent fatigue, dyspnea, and reduced physical activity. All selected studies have shown that telerehabilitation practices significantly improve exercise capacity, as measured by the 6MWT, in recovered COVID-19 patients. Digital physiotherapy interventions have also been shown to significantly improve functional capacity and quality of life in long COVID-19 patients. By addressing these long-term effects, rehabilitation interventions can contribute to the holistic management of COVID-19 patients, beyond the acute phase of the disease.

Given the positive outcomes observed in this thesis, RHB interventions, including respiratory rehabilitation and telerehabilitation programs, should be recognised as an essential component of the comprehensive care of COVID-19 patients, both during hospitalisation and after discharge. They have the potential to play a crucial role in optimising the recovery and rehabilitation process for COVID-19 patients, promoting better respiratory function, functional capacity, and overall well-being. Further research, implementation, and integration of these interventions into clinical practice are warranted to fully harness their potential and improve outcomes for COVID-19 patients.

To summarise, the findings of this thesis underscore the importance of incorporating physiotherapeutic modalities, such as respiratory rehabilitation and telerehabilitation programs, in the management of COVID-19 patients. These interventions have shown promising results in improving respiratory function, functional capacity, and quality of life in recovered COVID-19 patients, and have the potential to mitigate the long-term effects of the disease. Further research, implementation, and integration of these interventions into clinical practice can contribute to enhanced care for COVID-19 patients and better overall outcomes.

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