Review

Systematic Review of Changes and Recovery in Physical Function and Fitness After Severe Acute Respiratory Syndrome–Related Coronavirus Infection: Implications for COVID-19 Rehabilitation

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Objective. This review sought to (1) compare physical function and fitness outcomes in people infected with Severe Acute Respiratory Syndrome-related Coronavirus (SARS-CoV) with healthy controls, (2) quantify the recovery of physical function and fitness following SARS-CoV infection, and (3) determine the effects of exercise following SARS-CoV infection.

Methods. Four databases (CINAHL, MEDLINE, ProQuest, and Web of Science Core Collections) were searched in April 2020 using keywords relating to SARS-CoV, physical function, fitness, and exercise. Observational studies or randomized controlled trials were included if they involved people following SARS-CoV infection and either assessed the change or recovery in physical function/fitness or evaluated the effects exercise postinfection.

Results. A total 10 articles were included in this review. Evidence from 9 articles demonstrated that SARS-CoV patients had reduced levels of physical function and fitness postinfection compared with healthy controls. Furthermore, patients demonstrated incomplete recovery of physical function, with some experiencing residual impairments 1 to 2 years postinfection. Evidence from 1 randomized controlled trial found that a combined aerobic and resistance training intervention significantly improved physical function and fitness postinfection compared with a control group.

Conclusions. Physical function and fitness are impaired following SARS-CoV infection, and impairments may persist up to 1 to 2 years postinfection. Researchers and clinicians can use these findings to understand the potential impairments and rehabilitation needs of people recovering from the current coronavirus 2019 (COVID-19) outbreak. While 1 study demonstrated that exercise can improve physical function and fitness postinfection, further research is required to determine the effectiveness of exercise in people recovering from similar infections (eg, COVID-19).

Impact. Considering the similarities in pathology and clinical presentation of SARS-CoV and COVID-19, it is likely that COVID-19 patients will present with similar impairments to physical function. Accordingly, research is required to measure the extent of functional impairments in COVID-19 cohorts. In addition, research should evaluate whether rehabilitation interventions such as exercise can promote postinfection recovery.

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In December 2019, the first case of novel coronavirus 2019 (COVID-19) was confirmed in Wuhan, Hubei Province, China[1]; since then, more than 11.3 million cases have been confirmed globally (as of July 6, 2020), with the World Health Organization declaring the current outbreak a pandemic.[2] The majority (80%) of people infected with COVID-19 present with mild to moderate disease characterized by a fever, persistent cough, and dyspnoea.[3] However, more severe disease is experienced by 20% of people[4]—particularly in those over 65 years old and with comorbidities such as cardiovascular disease, diabetes, and chronic respiratory disease.[5,6] It is estimated that around 30% of people infected with COVID-19 will require hospitalization,[7] and of those hospitalized, 20% will be admitted to an intensive care unit (ICU).[3]

During periods of critical illness and hospitalization, it is common for people to experience a loss of physical function,[8] which can be characterized by the development of new or worsening of existing impairments.[9] Acquired changes to physical function during periods of hospitalization and critical illness are more commonly experienced by those with more severe illness or existing comorbidities[8] and often lead to mobility disability and restrictions in activities of daily living.[10] This decrease in physical functioning is thought to be attributed to prolonged periods of immobility, during which time people experience deconditioning (ie, a reduction in physical fitness outcomes such as muscle strength or aerobic capacity)[11] or develop critical illness polyneuropathy and myopathy, leading to impaired neuromuscular function.[12] Furthermore, in more severe cases, acute respiratory distress syndrome—which accounts for over 30% of COVID-19–related ICU admissions[3]—also leads to deconditioning and long-term impairments in physical function.[13]

Therefore, considering the rising number of COVID-19 cases and the significant proportion of people who are hospitalized and require ICU care for management of the infection, it is likely that many people will require rehabilitation to promote recovery postinfection.[14] Accordingly, it is important to understand the effect of COVID-19 on physical function and fitness to inform the design and assessment of rehabilitation interventions such as exercise, which has been demonstrated by a previous systematic review[15] to improve physical function following critical illness.

While there are currently no studies reporting the effect of COVID-19 on physical function and fitness, the importance of these outcomes to rehabilitation could be identified by reviewing the impact of the Severe Acute Respiratory Syndrome-related Coronavirus (SARS-CoV) on physical function and fitness. SARS-CoV is a type of coronavirus that presents with similar symptoms to COVID-19 and caused a similar global outbreak of disease in 2003.[16] While the reported cases of SARS-CoV were significantly lower than the current COVID-19 pandemic,[17] a similar proportion of people infected with SARS-CoV were hospitalized and admitted to ICUs[18]; therefore, postinfection changes and recovery in physical function and fitness in people with COVID-19 may follow a similar pattern to those infected with SARS-CoV. Accordingly, this review aims to (1) compare physical function and fitness outcomes in people infected with SARS-CoV with healthy controls, (2) quantify the recovery of physical function and fitness following SARS-CoV infection, and (3) determine the effects of exercise on people following SARS-CoV infection.

Methods

Data Sources and Searches

A systematic review protocol was registered with the PROSPERO database in April 2020 (ID no. CRD42020182575). Searches were then conducted on April 28, 2020, of the following databases from inception: CINAHL (via EBSCOhost), MEDLINE (via Ovid), ProQuest (Health and Medical Collection, Nursing and Allied Health Database, Coronavirus Research Database), and Web of Science Core Collections. Search strategies were comprised of keywords related to SARS-CoV, physical function, fitness, and exercise (Suppl. Tab. 1) and were adapted for use in each database. In addition, reference lists of included articles were hand-searched to identify any additional articles.

Study Selection

Both randomized controlled trials and observational studies (with either a cross-sectional or prospective design) that included adults who had been infected with SARS-CoV were eligible for this review. Furthermore, studies were also required to meet one of the following criteria: (1) assess physical function or physical fitness in people following SARS-CoV infection compared with a healthy control group using an objective measurement, (2) longitudinally assess physical function or physical fitness in people following SARS-CoV infection using an objective measurement, and (3) evaluate the effects of an exercise intervention following SARS-CoV infection either as a standalone intervention or as part of a rehabilitation program. Only full-text articles published in English were included in this review; grey literature and conference abstracts were excluded.

After removing duplicate articles, search results were exported to Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). The title and abstracts of all articles were then screened against the eligibility criteria by 1 reviewer (S.R.). Subsequently, 2 reviewers (S.R., A.W.) independently screened full texts of all remaining articles for eligibility, and disagreements were resolved through consensus in consultation with a third reviewer (L.P.) if required.

Data Extraction and Quality Assessment

Data extraction was completed independently by 1 reviewer (S.R.) using a standardized data extraction form. Data extracted from all studies included study details (author, year of publication, study design, location of study) and participant demographics (sample size, age, gender, time since infection, duration of hospitalization, comorbidities). Furthermore, either the outcome measures used to assess physical function/fitness and time-points of assessment or details of the exercise intervention (type, duration, frequency, intensity, control group) and effect were also extracted.

Methodological quality of included studies was assessed by 2 reviewers (S.R., A.W.) using either the Physiotherapy Evidence Database (PEDro) scale for randomized controlled trials[19] or the National Institutes of Health quality assessment tool for observational cohort and cross-sectional studies.[20] Quality assessment was completed independently, and any discrepancies between reviewers were resolved through consensus in consultation with a third reviewer (L.P.) if required. No studies were excluded based on the result of the quality assessment.

Data Synthesis and Analysis

The results of the included studies were analyzed through separate narrative syntheses corresponding to the aims of this systematic review. Firstly, descriptive values of physical function and fitness outcomes were compared with normative control data reported in each study to determine the difference in physical function/fitness following SARS-CoV infection. These results were compared between studies that included the same outcome measures to determine consistency of the results. Secondly, longitudinal descriptive data were synthesized to determine the extent of recovery in physical function and fitness at various time-points following infection. The mean/median change in physical function/fitness over time (either in comparison to control values or baseline data) determined the rate and magnitude of recovery postinfection. Lastly, for randomized controlled trials, individual study estimates of treatment effects (size and direction) were presented to determine the effects of exercise postinfection.

Role of the Funding Source

The funders played no role in the design, conduct, or reporting of this study.

Results

Results of the Search

After removing duplicates, the title and abstracts of 377 articles were screened against the eligibility criteria, and 363 were excluded primarily as the studies did not include people infected with SARS-CoV (n = 161) or the articles were grey literature (n = 105). The full texts of the remaining 14 articles were then screened for eligibility, and 4 were excluded as 2 articles that described observational studies did not include a measure of physical function or fitness, 1 article included a single measure of physical function but did not compare values with healthy controls, and 1 article was a conference abstract. Accordingly, 10 articles[21–30] were included in this systematic review (Figure).

Study Design

Of the included articles, 6 reported the results of cohort studies investigating longitudinal changes in physical function (Tab. 1),[22,23,26,28–30] 3 described the results of cross-sectional studies investigating the difference in physical function and fitness compared with healthy controls (Tab. 1),[21,25,27] and 1 reported the results of a randomized controlled trial investigating the effects of an exercise intervention following SARS-CoV infection (Tab. 2).[24] The results of 1 cohort study were reported across 4 articles: Hui et al,[22] Hui et al,[23] and Hui et al[29] included the same cohort of participants at various time-points postinfection and Ngai et al[30] reported results from a sub-group of this cohort who completed all assessments up to 24 months postinfection. The majority of studies were conducted in Asia (Hong Kong, n = 4[22–26,29,30]; Singapore, n = 1[21]; Taiwan, n = 1[27]), with only 1 study conducted outside of Asia (Canada, n = 1).[28]

The overall methodological quality of the included articles is described in Tables 2 and 3, and a detailed description of each item response is provided in Supplementary Tables 2 and 3. The total number of items adequately addressed on the National Institutes of Health quality assessment tool ranged from 6[27] to 10.[22] Most studies had clearly defined and consistent eligibility criteria, recruited at least 50% of the eligible population, and used valid and reliable outcome measures to quantify physical function/fitness. However, only 5 studies controlled for confounding variables such as age,[22,23,25,26,30] and only 2 studies had a loss to follow-up of less than 20%.[22,28] The randomized controlled trial by Lau et al[24] scored 9 on the PEDro scale; due to the nature of the intervention, neither the participants nor therapists were blinded to treatment allocation.

Participants

Across the observational studies, a total of 516 people infected with SARS-CoV were included with sample sizes ranging from 13 to 171. Participants were included in each study at various times postinfection, with studies including participants at 3 months postinfection onset (ie, 3 months since the initial presentation of symptoms related to the infection),[22,23,26,29,30] or 2 weeks,[25] 3 months,[21,28] and 14 months post-discharge (which relates to discharge from hospital in all cases).[27] The mean duration of hospitalization ranged from 20.4[21] to 28.2[30] days, and 8%[27] to 28%[22] of participants required

Table 1.
Cross-Sectional and Longitudinal Studies Measuring the Change or Recovery in Physical Function and Fitness[a]

Study and Country of Origin	Design	Quality	Participant Demographics	Control Demographics	Physical Function/Fitness Outcome Measure	Timing of Assessment	Main Findings[b]
Ong et al[21] (2004); Singapore	Cross-sectional	NIH = 7	N = 46 (34 F, 12 M) Age, y, mean = 37.3 (SD = 10.7) Time since infection onset = NR Duration of hospitalization, d, mean = 20.4 (SD = 17.3) ICU admission = 22% Mechanical ventilation = 15% Preexisting medical condition = 56%	N = 95 (47 F, 48 M) Age, y, mean = 42.4 (SD = 12.4)	Aerobic capacity (VO_{2max}): symptom-limited CPET using lower limb cycle ergometer and gas exchange measurement; testing protocol of 10 W/min	3 mo after hospital discharge	VO_{2max} (mL/kg/min), mean = 20.3 (SD = 5.1); mean % of normative value = 78.6 (SD = 17.0)
Hui et al[22] (2005), Hui et al[23] (2005), and Hui et al[29] (2009); Hong Kong	Cohort	NIH = 10, 9, and 8	N = 110 (66 F, 44 M) Age, y, mean = 35.6 (SD = 9.8) Time since infection onset = NR Duration of hospitalization, d, mean = 22.0 (SD = 13.9) ICU admission = 28% Mechanical ventilation = 6% Preexisting medical condition = 15%	N = 538 (F/M NR) Age = NR	6MWT (m)	3, 6, and 12 mo after infection onset	6MWT distance (m) 3 mo: 464 (SD = 83) 6 mo: 502 (SD = 95) 12 mo: 511 (SD = 90) (3–12 mo); $P < .01$ Mean difference at 12 mo vs healthy controls Age of 21–30 y: M = −113 (95% CI = −145 to −81); $P < .01$ F = −84 (95% CI = −131 to −37); $P < .01$ Age of 31–40 y: M = −84 (95% CI = −132 to −36); $P < .05$ F = −92 (95% CI = −121 to −62); $P < .05$ Age of 41–50 y: M = −81 (95% CI = −160 to −29); $P > .05$ F = −74 (95% CI = −136 to −12); $P < .05$ Age of 5–60 y: M = −129 (95% CI = −1727 to 1469); $P > .05$ F = −133 (95% CI = −206 to −58); $P < .01$
Lau et al[25] (2005); Hong Kong	Cross-sectional	NIH = 7	N = 171 (111 F, 60 M) Age, y, mean = 37.36 (SD = 12.65) Time since infection onset, d, mean = 81.79 (SD = 18.46) Duration of hospitalization, d, mean = 21.79 (SD = 9.93) ICU admission = 14% Mechanical ventilation = NR Preexisting medical condition = NR	N = 548 (226 F, 322 M) Age, y, mean = 37.8 (SD = 10.9)	6MWT (m)	2 wk after hospital discharge	6MWT distance vs healthy controls Age of 20–29 y: SARS = 644.37 (SD = 86.10) C = 698.00 (SD = 76.00); $P < .01$ Age of 30–39 y: SARS = 623.53 (SD = 91.22) C = 698.00 (SD = 76.00); $P < .01$ Age of 40–49 y: SARS = 563.90 (SD = 84.17) C = 635 (SD = 57.00); $P < .01$ Age of 50–59 y: SARS = 517.88 (SD = 91.62) C = 635.00 (SD = 57.00); $P < .01$ Age of >60 y: SARS = 430.29 (SD = 130.07) C = 512.00 (SD = 79.00); $P < .01$

(*Continued*)

Table 1.
Continued

Study and Country of Origin	Design	Quality	Participant Demographics	Control Demographics	Physical Function/Fitness Outcome Measure	Timing of Assessment	Main Findings [b]
Li et al[26] (2006); Hong Kong	Cohort	NIH = 9	N = 59 (25 F, 34 M) Age, y, mean = 47 (SD = 16) Time since infection onset = NR Duration of hospitalization, d, median = 31 (IQR = 20–54) ICU admission = 100% Mechanical ventilation = 46% Preexisting medical condition = 17%	N = NR Age = NR	6MWT (m)	3, 6, and 12 mo after infection onset	6MWT 3 mo: Ventilated = 400 (SD = 90); mean % of normative value = 67% Nonventilated = 475 (SD = 94); mean % of normative value = 72% 6 mo: Ventilated = 451 (SD = 91); mean % of normative value = 72% Nonventilated = 524 (SD = 107); mean % of normative value = 79% 12 mo: Ventilated = 461 (SD = 140); mean % of normative value = 74% Nonventilated = 523 (SD = 95); mean % of normative value = 79% Change in 6MWT distance 3 mo vs 6 mo: Ventilated: $P < .05$ Nonventilated: $P < .01$ 6 mo vs 12 mo: Ventilated: $P > .05$ Nonventilated: $P > .01$
Su et al[27] (2007); Taiwan	Cross-sectional	NIH = 6	N = 13 (10 F, 3 M) Age, y, mean = 31.4 (SD = 4.8) Time since infection onset = NR Duration of hospitalization, d, mean = 20.77 (SD = 11.43) ICU admission = 8% Mechanical ventilation = 8% Preexisting medical condition = 8%	N = 14 (F/M NR) Age = NR	Aerobic capacity (VO_{2max}): symptom-limited CPET using lower limb cycle ergometer and gas exchange measurement; testing protocol NR	14 mo after hospital discharge	VO_{2max} (mL/kg/min) vs healthy controls SARS = 26.3 (SD = 83.4) C = 27.9 (SD = 86.0); $P > .05$

(*Continued*)

Table 1.
Continued

Study and Country of Origin	Design	Quality	Participant Demographics	Control Demographics	Physical Function/Fitness Outcome Measure	Timing of Assessment	Main Findings [b]
Tansey et al[28] (2007); Canada	Cohort	NIH = 9	N = 117 (78 F, 39 M) Age, y, median = 42 (IQR = 33–51) Time since infection onset = NR Duration of hospitalization, d, median = 14 (SD = 8–19) ICU admission = 16% Mechanical ventilation = 9% Preexisting medical condition = 9%	N = 290 (173 F, 117 M) Age, y, range = 40–80	6MWT (m)	3, 6, and 12 mo after hospital discharge	Median 6MWT distance 3 mo: 483 (IQR = 396–552); % of normative value = 81% 6 mo: 487 (IQR = 447–553); % of normative value = 81% 12 mo: 488 (IQR = 448–555); % of normative value = 83%
Ngai et al[30] (2010); Hong Kong	Cohort	NIH = 9	N = 55 (36 F, 19 M) Age, y, mean = 44.4 (SD = 13.2) Time since infection onset = NR Duration of hospitalization, d, mean = 28.2 (SD = 25.2) ICU admission = 22% Mechanical ventilation = 7% Preexisting medical condition = NR	N = 538 (F/M NR) Age = NR	6MWT (m)	3, 6, 12, 18, and 24 mo after infection onset	6MWT distance (m) 3 mo: 439.0 (SD = 89.1) 6 mo: 460.1 (SD = 102.8) (vs 3 mo; $P < .05$) 12 mo: 464.7 (SD = 101.9) 18 mo: 466.3 (SD = 91.0) 24 mo: 462.6 (SD = 120.0) (3–24 mo; $P > .05$) Mean difference at 24 mo vs healthy controls Age of 21–30 y: M = −109 (95% CI = −231.1 to 13.1); $P > .05$ F = −104 (95% CI = −175.6 to −32.4); $P < .01$ Age of 31–40 y: M = −135 (95% CI = −241.3 to −55.7); $P < .01$ F = −90 (95% CI = −155.9 to −24.1); $P < .01$ Age of 41–50 y: M = −73 (95% CI = −174.9 to 29.9); $P > .05$ F = −82 (95% CI = −125.4 to −38.6); $P < .001$ Age of 51–60 y: M = −213 (95% CI = −290.0 to −4.3); $P < .01$ F = −161.0 (95% CI = −326.0 to 2.4); $P > .05$

[a] C = control group; CPET = cardiopulmonary exercise testing; F = female; ICU = intensive care unit; IQR = interquartile range; M = male; 6MWT = 6-Minute Walk Test; NIH = National Institutes of Health quality assessment tool for observational cohort and cross-sectional studies; NR = not reported; SARS = severe acute respiratory syndrome–related coronavirus; VO_{2max} = maximum oxygen consumption.
[b] Values are presented as mean (SD) unless stated otherwise.

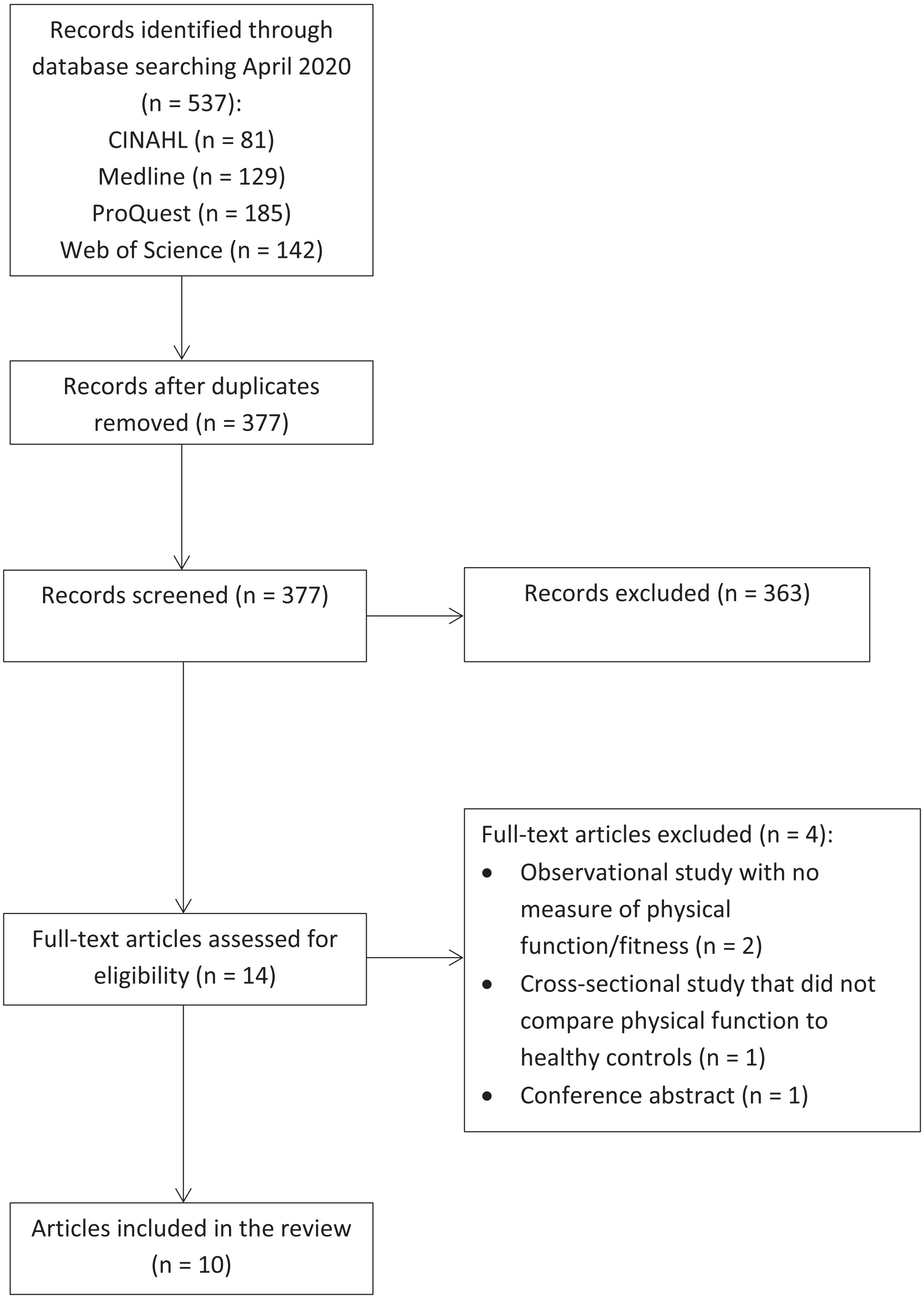

Figure.
PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram.

admission to an ICU with the exception of the study by Li et al,[26] where all participants were admitted to an ICU since the purpose of this study was to investigate people with acute respiratory distress syndrome caused by SARS-CoV. The proportion of participants with pre-existing medical conditions before SARS-CoV infection ranged from 8%[27] to 56%[21] across studies.

The sample size of the randomized controlled trial by Lau et al[24] was 133, of which 71 were assigned to the exercise

Table 2.
Details of the Randomized Controlled Trial Investigating the Effects of Exercise After Severe Acute Respiratory Syndrome-Related Coronavirus Infection[a]

Quality	Participants	Intervention (I)	Control (C)	Outcome Measures	Main Findings
PEDro = 9	N = 133 (88 F, 45 M) Age, y, mean (SD): I = 35.9 (9.3); C = 38.3 (11.2) Time since infection onset = NR Duration of hospitalization, d, mean (SD): I = 23.2 (11.3); C = 22.1 (10.9) ICU admission = NR Mechanical ventilation = NR Preexisting medical condition = NR	Exercise program: 6 wk; 2× supervised sessions/wk; 60–90 min 30–45 min aerobic exercise (60%–70% HR_{max}); resistance training, 3 sets of 10–15 repetitions maximum load	Educational session about general exercise and weekly telephone calls with physical therapist	6MWT; VO_{2max} (Chester Step Test); SF-36; MVIC of gluteus maximum, deltoids, and hand-grip (hand-held dynamometry) 0, 6 wk	Mean (SD) change at 6 wk 6MWT (m): I = 77.4 (71.3); C = 20.7 (98.6); $P < .05$ VO_{2max} (mL/kg/min): I = 3.6 (5.4); C = 1.0 (7.3); $P < .05$ MVIC gluteus maximus (kgf): I = 10.4 (12.3); C = 8.8 (14.7); $P > .05$ MVIC deltoids (kgf): I = 7.5 (6.1); C = 5.5 (10.1); $P > .05$ Right hand grip (kgf): I = 4.7 (6.0); C = 1.7 (5.2); $P < .05$ Left hand grip (kgf): I = 4.2 (5.9); C = 2.2 (4.8); $P < .05$ SF-36 (PF): I = 3.7 (18.4); C = 3.7 (16.1); $P > .05$ SF-36 (RP): I = 14.4 (40.2); C = 14.6 (37.2); $P > .05$ SF-36 (RE): I = 1.9 (38.2); C = 8.9 (42.0); $P > .05$ SF-36 (BPS): I = 0.0 (24.9); C = −5.0 (24.1); $P > .05$ SF-36 (SF): I = 12.9 (22.8); C = 14.2 (24.2); $P > .05$ SF-36 (GH): I = −0.8 (17.5); C = −2.5 (18.6); $P > .05$ SF-36 (MH): I = −1.6 (11.7); C = −0.3 (16.9); $P > .05$ SF-36 (V): I = 1.3 (18.0); C = 2.5 (14.2); $P > .05$

[a] The study was that of Lau et al[24] (2005) in Hong Kong. BPS = bodily pain subscale; C = control group; F = female; GH = general health subscale; HR_{max} = maximum heart rate; I = intervention; ICU = intensive care unit; M = male; MH = mental health subscale; 6MWT = 6-Minute Walk Test; NR = not reported; PF = physical function subscale; RE = role emotional subscale; RP = role physical subscale; SF = social functioning subscale; SF-36 = Medical Outcomes Survey Short-Form 36 questionnaire; V = vitality subscale; VO_{2max} = maximum oxygen consumption.

intervention group and 62 were assigned to the control group. Participants were recruited 2 weeks post-hospital discharge and were a subgroup of participants from the study by Lau et al[25] who had impaired physical function at baseline. The mean duration of hospitalization for the intervention and control group was 23.2 (SD = 11.3) days and 22.1 (SD = 10.9) days, respectively.

Physical Function and Fitness Compared With Healthy Controls

All of the observational studies included in this review compared measures of physical function or fitness in people with SARS-CoV with healthy controls (Tab. 1). Of these studies, 4 measured physical function,[22,23,25,26,28–30] and 2 measured physical fitness.[21,27] Physical fitness was quantified according to maximum oxygen consumption (VO_{2max}) during cardiopulmonary exercise testing.[21,27] All studies that measured physical function used the 6-Minute Walk Test (6MWT).[22,23,25,26,28–30]

Physical fitness was found to be impaired in people infected with SARS-CoV in the study by Ong et al,[21] which reported that VO_{2max} values in those with SARS-COV were 78.6% (SD = 17.0%) of normative reference values at 3 months post hospital discharge. Ong et al[21] also reported that none of the exercise tests in people infected with SARS-CoV were limited by pulmonary or ventilatory function. Conversely, the study by Su et al[27] found no significant difference in VO_{2max} between people with SARS-CoV and healthy controls, although this study recruited participants who had been discharged from hospital for significantly longer (14 months vs 3 months) and had a smaller sample size (n = 13 vs n = 46) compared with the study by Ong et al.[21]

Across the studies that measured physical function, all reported a reduction in 6MWT performance following SARS-CoV infection. In the cross-sectional study by Lau et al,[25] 6MWT distance was found to be significantly lower in people infected with SARS-CoV compared with healthy controls 2 weeks post hospital discharge. Similarly, Tansey et al[28] and Li et al[26] found that the 6MWT distance in people infected with SARS-CoV was 67% to 81% of that recorded for healthy controls at 3 months post hospital discharge—this reduction was found to be greatest among those who had received mechanical ventilation.[26] Impaired physical function was also shown to persist long term following SARS-CoV infection, as Li et al[26] and Tansey et al[28] found that the 6MWT distance in people infected with SARS-CoV was 74% to 83% of that recorded for healthy controls at 12 months post hospital discharge, and Hui et al[23,29] found that 6MWT distance was significantly lower in those infected with SARS-CoV at 12 months postinfection onset (with the exception of males aged 41–60 years) and 24 months postinfection onset.[30]

Recovery of Physical Function and Fitness

Of the cohort studies measuring recovery postinfection, all measured changes in physical function using the 6MWT.[22,23,26,28–30] Assessments were conducted at 3, 6, and 12 months either postinfection onset[22,23,26,29,30] or post hospital discharge[28]; however, Ngai et al[30] also performed measurements at 18 and 24 months postinfection onset. No study included in this review assessed longitudinal changes in fitness following SARS-CoV infection.

Initial short-term recovery of physical function following SARS-CoV infection was demonstrated by the studies included in this review, as most studies found that the 6MWT distance increased between 3 and 6 months postinfection onset,[22,23,26,29,30] with the exception of the study by Tansey et al, which recorded no change.[28] However, although the 6MWT increased at 6 months, Li et al[26] reported that values were still 72% to 79% of that recorded for healthy controls. Following the first 6 months postinfection onset, Li et al[26] reported that no further change in 6MWT distance was recorded. Similarly, Hui et al[23,29] also reported that no significant change in 6MWT distance was found between 3 and 12 months postinfection onset, indicating that there was minimal long-term recovery of physical function postinfection. Furthermore, in the subgroup analysis of the cohort initially described by Hui et al,[22] Ngai et al[30] also found there was no change in 6MWT between 3 and 24 months postinfection onset.

Effects of Exercise Following SARS-CoV Infection

The randomized controlled trial by Lau et al[24] investigated the effect of a 6-week exercise intervention on physical function, physical fitness, and quality of life following SARS-CoV infection. Participants received 2 sessions weekly that lasted 60 to 90 minutes and included 30 to 45 minutes of aerobic exercise at 60% to 70% of predicted maximal heart rate and resistance training targeting the upper and lower limbs. Participants in the control group received advice about general exercise and weekly telephone conversations with a physical therapist.

Following the 6-week intervention, Lau et al reported that both 6MWT distance and VO_{2max} (measured sub-maximally using the Chester Step Test) increased in the exercise intervention group. Furthermore, the mean difference in the 6MWT distance and VO_{2max} recorded for the exercise group was significantly greater than the change recorded for the control group (77.4 [SD = 71.3] m vs 20.7 [SD = 98.6] m and 3.6 [SD = 5.4] mL/kg/min vs 1.0 [SD = 7.3] mL/kg/min, respectively). Therefore, these results indicate that exercise improves the 6MWT and VO_{2max} in people who have been infected with SARS-CoV. However, no significant difference was found in muscle strength or quality of life between the exercise and control groups.

Discussion

The evidence presented in this review highlights the long-term impact of SARS-CoV infection on physical function and fitness. Evidence from a small number of studies demonstrates that, following SARS-CoV infection, patients have reduced levels of physical function and fitness compared with healthy controls. Furthermore, while an increase in physical function is noted within the first 6 months following infection onset, recovery is incomplete, and people with SARS-CoV may experience residual impairments in physical function 1 to 2 years after the infection. Therefore, this highlights the need for rehabilitation interventions to promote physical recovery of people following SARS infection. Evidence from 1 randomized controlled trial suggests that exercise may promote recovery in physical function and fitness in people infected with SARS-CoV.[24] However, further evidence is required to determine the effectiveness of rehabilitation interventions, such as exercise, in promoting recovery postinfection—particularly during the current outbreak of COVID-19 in which similar patterns of impairments and recovery in physical function may be experienced.

The mechanisms leading to impaired physical function following SARS-CoV infection are likely multifactorial and arise as a consequence of the infection, prolonged hospitalization, and/or immobility.[31] For example, during periods of immobility due to critical illness, around 25% of patients develop significant muscle weakness—particularly of the lower limb muscle groups involved in functional mobility.[32] This acquired weakness may be attributed to a decrease in muscle cross-sectional area and muscle fiber size[33,34] or a reduction in type II muscle fibers.[35] In addition, up to 50% of people admitted to ICU may develop critical illness myopathy or neuropathy, leading to a reduction in motor unit recruitment and force generating capacity of the muscle.[12] Alongside changes in muscle function, lower levels of aerobic capacity are associated with reduced physical function and independence during activities of daily living.[36] As identified through this review, people infected with SARS-CoV demonstrate decreased VO_{2max} independent of pulmonary and ventilatory function; thus, deconditioning and decreased levels of cardiorespiratory fitness may also account for the reductions in physical function postinfection. Furthermore, post-viral fatigue, which was reported in 40% of people following SARS-CoV infection,[37] may also contribute to reduced physical function due to increased perception of effort during functional tasks.[38]

Importantly, the proposed mechanisms contributing to impaired physical function are not unique to SARS-CoV infection and may be experienced by all causes of critical illness and hospitalization.[39] These mechanisms may also cause impairments to physical function in people infected with COVID-19—particularly considering the number of people currently hospitalized and admitted to the ICU with COVID-19.[3,7] Accordingly, research is required to measure physical function in people following COVID-19 infection to determine whether similar impairments are experienced postinfection and to quantify the prevalence and severity of any changes to physical function.

As highlighted by the studies included in this review, recovery of physical function following SARS-CoV is incomplete, with impairments persisting up to 1 to 2 years postinfection onset. Greater levels of impairment in physical function after 12 months were found in those patients who required mechanical ventilation during hospitalization,[26] indicating that the severity of infection may be associated with poorer recovery postinfection. Promoting recovery of physical function in people with SARS-CoV should be a key target of postinfection management, as long-term physical function and quality of life were shown to be positively correlated in people with SARS-CoV, indicating that lower levels of physical function postinfection are associated with poorer quality of life.[23,26] In addition, 2 studies that found incomplete recovery of physical function reported that only 80% to 83% of people had returned to work 12 months following infection onset.[28,30] Accordingly, the evidence presented in this review highlights the need for rehabilitation to promote recovery of physical function following SARS infection, particularly in those hospitalized with severe infections.

To design effective rehabilitation strategies, the selection of intervention type and dose must be specific to key functional impairments. As physical function and fitness were demonstrated to be impaired following SARS-CoV infection, exercise—which aims to improve or maintain aspects of physical fitness and function[40]—may be an appropriate rehabilitation intervention to address these impairments. Indeed, evidence from 1 study found that a combined aerobic and resistance training intervention improved 6MWT distance and VO_{2max} by approximately 13% and 3%, respectively, within the first 2 months post hospital discharge following SARS-CoV infection.[24] This evidence is in line with findings from a Cochrane review in which a small number of studies reported that exercise may improve physical function following critical illness.[15] However, despite the potential beneficial effect of exercise, there is a lack of evidence to support its use for people with SARS-CoV infection as only 1 study evaluating the effects of exercise was identified by this review. In addition, the safety of exercise following SARS-CoV is unclear, as this study did not report whether any adverse events occurred.

Implications for COVID-19 Rehabilitation

Due to the large cohort of COVID-19 survivors and considering the physical complications of hospitalization and ICU admission, it is anticipated that there will be a large demand for rehabilitation to promote postinfection recovery.[14,41] Accordingly, COVID-19 rehabilitation strategies have been recently published.[42,43] However, the impact of COVID-19 on outcomes such as physical function and fitness and how these outcomes will recover over time are currently unclear. Considering the similarities in pathology and clinical presentation of SARS-CoV and COVID-19, it is anticipated that people with COVID-19 will experience similar impairments to physical function and fitness described in this review. Although, due to the disparity in COVID-19 infection and death rates among minority ethnic groups—particularly in the United Kingdom and the United States[44]—it is unclear whether the findings from the SAR-CoV literature are generalizable to all COVID-19 patients across varying demographic and cultural profiles. Therefore, routine recording of such demographic data should be conducted postinfection to guide rehabilitation strategies by identifying patient cohorts who may be at greater risk of developing postinfection impairments in function.

While rehabilitation interventions are required for COVID-19 patients, this review highlights that there is lack of studies investigating the effects of exercise following SARS infection. Therefore, further research is required to evaluate the effects of exercise in people with COVID-19 to determine whether exercise can promote postinfection recovery. Particular focus should be given to the type and dose of exercise required to elicit beneficial effects postinfection and how exercise prescription should be modified at various time points postinfection to optimize the recovery of function (eg, inpatient vs outpatient rehabilitation). In addition, consideration should also be given to the mode of exercise delivery to ensure safety and effectiveness of the intervention; for example, online exercise programs may offer a practical solution to limit the exposure of health care practitioners and patients to COVID-19,[45] although face-to-face sessions may be required in some instances to achieve the prescribed exercise dosage.

Finally, although this review focused on physical function and fitness, it is important to consider other potential symptoms of COVID-19—such as severe fatigue, depression, and cognitive dysfunction—that may impact these outcomes and the effectiveness of rehabilitation. Viral infection is suggested to contribute to the development of chronic fatigue syndrome,[46] and it was estimated that 27% of people fulfilled the diagnostic criteria for chronic fatigue syndrome following SARS-CoV infection[37]; thus, people with COVID-19 may also experience high levels of postinfection fatigue. In addition, cognitive dysfunction such as delirium[47] and chronic psychological impairments such as depression and post-traumatic stress disorder may also be experienced during periods of critical illness and ICU care.[48] Accordingly, future studies should evaluate the consequences of COVID-19 across psychological and cognitive domains and determine how these outcomes influence the recovery of physical function; these findings can then inform the design and delivery of tailored rehabilitation interventions that consider the impact of symptoms such as fatigue on recovery.

Limitations

There are important limitations to consider when interpreting the results of this review. Firstly, only 1 outcome measure (6MWT) was used by the included studies to quantify physical function. 6MWT performance is shown to be dependent on levels of cardiorespiratory fitness[49]; therefore, it is unclear whether other measures of physical function that require less aerobic capacity—such as the Timed Up and Go or timed 10 Meter Walk Test—would demonstrate similar patterns of impairment postinfection. In addition, while the number of confirmed SARS-CoV cases was reported to be 8096, the total number of participants included in the studies in this review only accounts for 8% of this population.[17] Consequently, it is unclear whether the results of this review are representative of the entire SARS-CoV population. Furthermore, due to the small number of studies and variability in timing of outcome measurements, it was not possible to perform a meta-analysis. Lastly, as this review only focused on the effects of exercise, it is unclear whether other rehabilitation interventions have similar effects on postinfection recovery.

Evidence from this review highlights that physical function and fitness are reduced in people following SARS-CoV infection. Furthermore, recovery of physical function is incomplete, with impairments persisting 1 to 2 years postinfection. Due to the similarities in pathology and the significant number of people admitted to the hospital and ICU, it is likely that people with COVID-19 will experience similar impairments to physical function and fitness. Therefore, rehabilitation interventions are required to promote recovery postinfection. While exercise may improve physical function postinfection, only 1 study has evaluated the effects of exercise in a SARS-CoV population. Accordingly, research is required to understand the effects of COVID-19 on physical function and fitness and determine whether exercise can promote postinfection recovery.

Author Contributions

Concept/idea/research design: S. Rooney, L. Paul
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Systematic Review Registration

The protocol for this systematic review was registered with PROSPERO (CRD42020182575).

Disclosures

The authors completed the ICMJE Form for Disclosure of Potential Conflicts of Interest and reported no conflicts of interest.

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