



Effects of conventional versus virtual reality-simulated treadmill exercise on fatigue, cognitive function, and participant satisfaction in post-COVID-19 subjects. A randomized trial

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ABSTRACT

Background/objective: Post-COVID-19 subjects typically experience symptoms of fatigue, cognitive impairment, and sleep difficulty, which can be relieved by conventional aerobic exercise. Virtual Reality (VR) technology to support conventional exercise has recently gained much attention. Therefore, this study aimed to assess the effects of traditional treadmill exercise compared to virtual reality-simulated treadmill exercise on fatigue, cognitive function, sleep quality, and participant satisfaction with the exercise program in post-COVID-19 subjects.

Methods: This single-centered, randomized, parallel-group intervention study was conducted between December 2021 and March 2022. Sixteen of twenty post-COVID-19 subjects completed this study ($n_1 = 8$, $n_2 = 8$). Inclusion criteria were persistent dyspnea/fatigue, mild cognitive problems, and age from 30–60 years. Exclusion criteria were previous severe COVID-19 infection and ICU admission, concomitant respiratory or cardiovascular disease, and musculoskeletal or neurological disease. Eligible subjects were assigned randomly to two groups: a non-VR group that received traditional treadmill aerobic exercise only and a VR group that received treadmill exercise with non-immersive VR. Both groups received moderate-intensity exercise on a treadmill at $[50-60\% (\text{peak HR} - \text{resting HR}) + \text{resting HR}]$ for 30–45 min, three times per week, and for four weeks. The outcome measures were the Chalder Fatigue Scale, Montreal Cognitive Assessment (MoCA) questionnaire, Pittsburgh Sleep Quality Index (PSQI), and participant satisfaction with the exercise program rated on a 5-point Likert scale.

Results: Both groups showed significant improvements in the Chalder Fatigue Scale, the MoCA questionnaire, and the PSQI scores after training compared to baseline ($p < 0.05$), without significant differences between them ($p > 0.05$). However, participant satisfaction with the exercise program was significantly higher in the VR group than in the non-VR group ($p = 0.037$).

Conclusion: A moderate-intensity 4-week treadmill exercise program with and without non-immersive VR may improve fatigue, cognitive function, and sleep quality to the same extent in COVID-19 survivors. However, participant satisfaction with the exercise program could be greater after conventional treadmill training assisted by non-immersive VR than after conventional treadmill training alone in this cohort.

Trial registration: Pan African Clinical Trials Registry, PACTR202311561948428, retrospectively registered.

1. Introduction

Since its outbreak in late 2019, the novel Coronavirus disease 2019 (COVID-19) has been considered a major international epidemic.¹ After recovery from COVID-19 initial illness, a substantial proportion of

patients continue to experience persistent dyspnea/fatigue, cognitive problems or brain fog, and disordered sleep.² A large percentage of COVID-19 survivors showed persistence of at least dyspnea/fatigue.³ Exercise is an essential part of pulmonary rehabilitation programs after COVID-19 illness and can relieve symptoms of fatigue in post-COVID-19

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conditions.^{4,5}

Exercise can, however, be an unpleasant experience or obligation rather than a therapy, particularly in the presence of limiting symptoms such as fatigue. The unpleasant feelings while exercising can occur in patients with different conditions that cause pain or fatigue, resulting in low adherence to exercise.⁶ On the other hand, enjoyment while exercising is an immediate reward that can increase long-term adherence to exercise to a greater extent than delayed rewards such as health benefits.⁷ Hence, there is a need to design appealing exercise formats, making exercise an attractive therapeutic modality to increase participants' adherence. Virtual Reality (VR) has produced promising results with a higher level of contentment in COVID-19 patients.⁸ Additionally, VR games involving body movements can enhance physical performance in subjects with post-COVID-19 conditions.⁹ The VR can be either immersive VR achieved with VR viewers having a head-mounted display, or non-immersive VR achieved with a simulated VR scene played on a standard display.¹⁰

To date, little is known about the effectiveness of traditional aerobic exercises supported by VR technology in post-COVID-19 subjects. One recent study evaluated cycling exercise with and without a VR system in post-COVID-19 patients and found lower dyspnea and leg fatigue immediately after exercising with VR than exercise without VR.¹¹ Another recent study assessed cycling exercise assisted by an immersive virtual reality in post-COVID-19 patients and found that this training method was perceived as a highly motivating experience.¹² Also, to our knowledge, no previous study has investigated the effectiveness of treadmill exercise in a VR environment after COVID-19 illness. Based on the above, this study aimed to assess the effects of virtual reality-simulated treadmill exercise compared to conventional treadmill exercise on fatigue, cognitive function, sleep quality, and participant satisfaction with the exercise program in post-COVID-19 subjects. Considering that VR technology can offer a promising opportunity to enhance traditional exercise,¹³ we hypothesized that a potentially significant difference might exist between treadmill exercise with and without VR concerning the selected outcomes in post-COVID-19 subjects.

2. Methods

2.1. Study design, setting, and ethical considerations

This study is a single-centered, randomized, parallel-group intervention trial conducted in a private clinic from December 2021 to March 2022. It followed the principles of the Declaration of Helsinki, and its protocol was approved by the Ethics Committee of Scientific Research at the Faculty of Physical Therapy, Cairo University (No: P.T.REC/012/003455). All participants signed an informed consent form.

2.2. Randomization and concealed allocation

Simple randomization using a randomization table designed by a computer software program was used, with an allocation ratio 1:1. Sequentially numbered opaque sealed envelopes concealed the allocation sequence so that neither the recruiter nor the participant was aware of the upcoming assignment. A physiotherapist involved in research settings enrolled participants and assigned them to interventions.

2.3. Subjects

Sixteen of twenty post-COVID-19 subjects, recruited by referral from a pulmonologist, completed this study. Inclusion criteria were a history of COVID-19 infection within 3–4 months, persistent dyspnea and fatigue, oxygen saturation $\geq 94\%$, mild cognitive impairment (i.e., Montreal Cognitive assessment total score < 26),¹⁴ and age from 30–60 years. Exclusion criteria were a history of severe COVID-19 infection with ICU admission, concomitant respiratory disease, cardiovascular disease,

renal failure, smokers, musculoskeletal/neurological limitations to exercise, and contraindications to maximal exercise testing. Eligible participants were assigned randomly to a non-VR group and a VR group. Fig. 1 shows the flowchart of participants throughout the study.

2.4. Evaluation

2.4.1. Medical history taking and clinical examination

An experienced pulmonologist conducted the medical history taking and clinical examination at baseline for participant selection. Data on the baseline characteristics of participants were recorded.

2.4.2. Maximal treadmill exercise test

A symptom-limited maximal exercise test on a treadmill using the modified Bruce Protocol was performed at baseline. Subjects were instructed to avoid eating and strenuous activities before testing. The heart rate and oxygen saturation were continuously monitored during the test using a fingertip pulse oximeter (Contec Fingertip Pulse Oximeter, CMS50D, made in China, FDA approved). All participants underwent the test safely and stopped it because of maximal exhaustion. Upon test termination, the peak heart rate (HR_{peak}) was recorded. The HR_{peak} of each participant was needed to determine the targeted HR (THR) during exercise on an individual basis, as previously used.¹⁵

2.4.3. Outcome measures

2.4.3.1. The Chalder Fatigue Scale. This study used the Arabic version of the Chalder Fatigue questionnaire¹⁶ to assess overall fatigue at baseline and after four weeks through in-person interviews. McIlvenny et al.¹⁶ describe this questionnaire in detail. It includes 11 items with Likert-type responses from 0 to 3 and a total score of 33.

2.4.3.2. Montreal Cognitive assessment (MoCA). The Arabic version of MoCA¹⁷ was used as a valid tool to assess cognitive function at baseline and after four weeks via face-to-face interviews. Rahman and El Gaafary¹⁷ described the MoCA Arabic version in detail. The total possible score is 30, with a score below 26 indicating mild cognitive impairment.¹⁴

2.4.3.3. Pittsburgh Sleep quality index (PSQI). The present study used the Arabic version of the Pittsburgh Sleep Quality Index (PSQI)¹⁸ to assess sleep quality at baseline and after four weeks through face-to-face interviews with participants. Suleiman et al.¹⁸ provide a detailed description of the PSQI Arabic version. The PSQI total score ranges from 0 to 21, with a higher score indicating poor sleep quality.¹⁸

2.4.3.4. Participant satisfaction with the exercise program. The satisfaction level of participants with the exercise program was assessed, as a secondary outcome, at the end of the interventions by a 5-point Likert scale,¹⁹ in which the participants specified their level of satisfaction with one of five answers as follows: (1) not at all satisfied, (2) slightly satisfied, (3) neutral, (4) very satisfied, (5) extremely satisfied.

2.5. Interventions

Participants received either a conventional treadmill exercise program without VR or a treadmill exercise program in a non-immersive VR environment under the direct supervision of a physiotherapist through face-to-face exercise sessions. The exercise program design followed the FITT-VP principle of exercise prescription laid down by the American College of Sports Medicine.²⁰ A moderate intensity and average duration were chosen for exercise training in both groups to avoid high-intensity or exhaustive prolonged effort, as per the Stanford Hall consensus statement for post-COVID-19 rehabilitation.²¹ The targeted intensity of exercise was prescribed in both groups based on the heart rate reserve

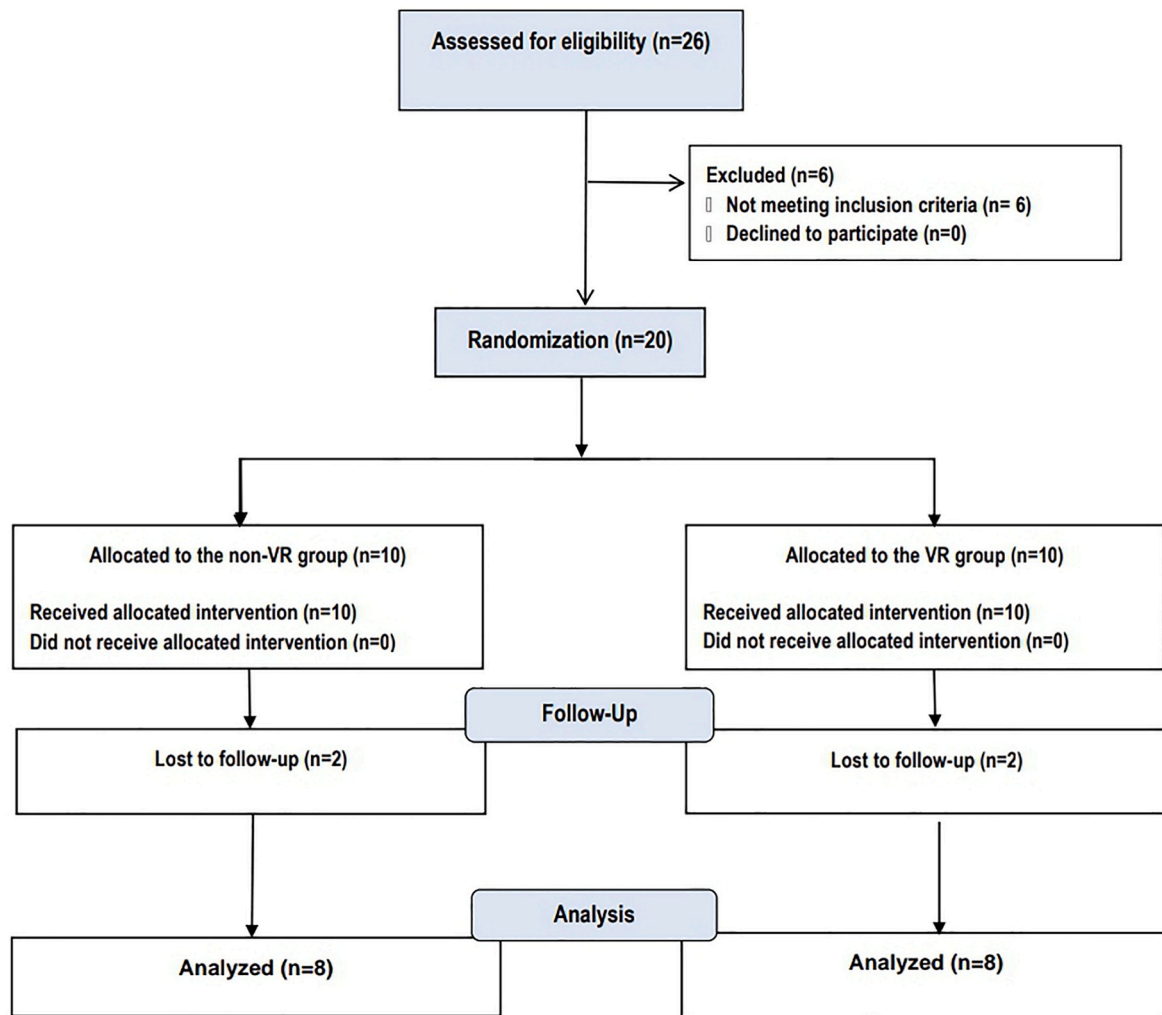


Fig. 1. The flowchart of the study.

method (i.e., Karvonen formula).²²

2.5.1. Treadmill exercise without VR

The participants in the non-VR group received a traditional treadmill

Table 1

Treadmill exercise prescription as per the FITT-VP principle.

FITT-VP principle	Exercise prescription
Frequency (F)	Three days per week
Intensity (I)	A moderate-intensity exercise was prescribed with the THR based on the Karvonen formula ²² ; $THR = 50-60\% (HR_{peak} - HR_{rest}) + HR_{rest}$. A fingertip pulse oximeter (Contec Fingertip Pulse Oximeter, CMS50D, made in China, FDA approved) was used to ensure that all subjects exercised at their individualized THR and to assess O ₂ saturation throughout the exercise session.
Time (T)/duration	The active phase of aerobic exercise was from 30 to 45 min. It was preceded by a 5-min warm-up and followed by a 3-min cool-down. The duration of the exercise program was 4 weeks.
Type (T)/mode of exercise	Continuous walking/jogging performed on a treadmill.
Volume/Progression (VP)	The overall exercise volume (i.e., exercise time and intensity) progressed gradually on an individual basis throughout the study, and by the end of it, all subjects exercised at the upper limit of their THR.

FITT-VP (frequency, intensity, time, type - volume, progression), THR: targeted heart rate, HR_{peak}: peak heart rate, HR_{rest}: resting heart rate.

exercise program without a VR system, designed as per the FITT-VP principle (Table 1).

2.5.2. Treadmill exercise with a non-immersive VR

The participants in the VR group received the traditional treadmill exercise program the same as the non-VR group as per the FITT-VP principle (Table 1), but while simulating a non-immersive VR scene (i.e., jogging in a virtual track with trees on the side) displayed on a screen, in front of the treadmill, connected to Nintendo’s Wii Fit Plus game console (Serial NO: BMH30001709/made in China). During the exercise, the Wii remote (i.e., the sensor controller for the Wii Fit Plus console) was fastened to the subjects to allow them to interact with the walker avatar displayed on the screen via motion detection sensing. The subjects interacted with the VR scene while having a complete perception of their real environment.

2.6. Statistical procedures

Descriptive statistical analysis described the data as means and standard deviations for continuous variables and percentage and frequency distributions for nominal variables. The Kolmogorov-Smirnov normality test was used to assess the normality of the data. The Levene test was used to assess the homogeneity of variance between groups. Paired *t*-test was used to assess the changes within each group. The unpaired *t*-test was used to compare the means between the two groups at baseline and post-intervention. The Chi-square test was used to

compare the groups' categorical data (i.e., gender, participant satisfaction). P-values of less than 0.05 were considered statistically significant. Social Science Statistics and the GraphPad Prism software programs were used for statistical analysis.

3. Results

There were no significant differences in baseline characteristics between the two groups ($p > 0.05$), as shown in Table 2. In the non-VR group, there were significant improvements in Chalder fatigue score ($p < 0.001$), MoCA score ($p = 0.021$), and PSQI score ($p = 0.022$) compared to baseline values (Table 3). Likewise, in the VR group, there were significant improvements in Chalder fatigue score ($p < 0.001$), MoCA score ($p = 0.020$), and PSQI score ($p = 0.001$) compared to baseline values (Table 3). After the interventions, there were no significant differences between the two groups in the Chalder fatigue score ($p = 0.063$), MoCA score ($p = 0.640$), and PSQI score ($p = 0.921$) (Table 3). However, participant satisfaction with the exercise program was significantly better in the VR group than in the non-VR group post-intervention ($p = 0.037$), with one “neutral” response, three “very satisfied” responses, and 4 “extremely satisfied” responses versus 5 “neutral” responses, 3 “very satisfied” responses, and no “extremely satisfied” responses in the non-VR group (Table 3).

4. Discussion

The purpose of this study was to compare the effectiveness of traditional treadmill exercise versus virtual reality-simulated treadmill exercise concerning fatigue, cognitive function, sleep quality, and level of participant satisfaction with exercise programs in post-COVID-19 subjects. Contrary to our hypothesis, we found no significant difference between the two exercise forms in fatigue, cognitive function, and sleep quality. However, the significantly greater participant satisfaction with the exercise program found in the VR group agreed with our hypothesis. The main findings in this study can be summarized as: (a) a 4-week moderate-intensity treadmill exercise program, either with or without a non-immersive virtual reality, induced significant improvements in fatigue assessed by Chalder fatigue scale, cognitive function assessed by MoCA, and sleep quality assessed by PSQI compared to baseline in post-COVID-19 subjects, with no significant difference between them; (b) The participant satisfaction with the exercise program was significantly higher following VR-simulated treadmill exercise than following conventional treadmill exercise in this cohort.

A recent meta-analysis has underlined the importance of exercise-based rehabilitation in reducing fatigue in post-COVID-19 patients and called for further studies to highlight the effectiveness of rehabilitation in this population.²³ It has been reported that exercising in an immersive VR environment led to a lower perception of fatigue during exercise in post-COVID-19 patients.¹¹ In our study, however, overall fatigue was reduced similarly following 4-week treadmill exercises, either with or without non-immersive VR. Since the two exercise formats in the present study were at the same intensity (i.e., moderate intensity), similar cardiovascular demands could have been imposed during exercise,

Table 2
Baseline characteristics.

Variables	Non-VR group (n ₁ = 10)	VR group (n ₂ = 10)	p-value
Age (years)	50.00 ± 11.06	49.38 ± 12.24	0.916
Gender			0.531
male	1 (10 %)	2 (20 %)	
female	9 (90 %)	8 (80 %)	
BW (kg)	84.42 ± 12.30	87.37 ± 12.23	0.596
Height (cm)	159.80 ± 3.61	160.80 ± 6.03	0.658
BMI (kg/m ²)	32.91 ± 4.19	33.48 ± 2.90	0.728

Data are expressed as means ± SD and as frequency and percent distribution. VR: Virtual Reality; BW: body weight; BMI: body mass index.

Table 3

The results of the outcome measures in the two groups pre- and post-intervention.

Outcome measures		Non-VR group (n ₁ = 8)	VR group (n ₂ = 8)	p-value	
Chalder fatigue scale score	pre	22.30 ± 4.39	21.50 ± 4.35	0.687	
	post	10.50 ± 0.66	13.12 ± 3.87	0.063	
	p-value	<0.001 ^a	<0.001 ^a		
MoCA questionnaire score	pre	18.44 ± 5.05	20.10 ± 6.08	0.530	
	post	21.37 ± 7.24	22.74 ± 5.20	0.640	
	p-value	0.021 ^a	0.020 ^a		
PSQI score	pre	10.10 ± 5.15	11.10 ± 3.75	0.625	
	post	5.75 ± 2.97	5.62 ± 2.53	0.921	
	p-value	0.022 ^a	0.001 ^a		
Participant satisfaction with the exercise program	Neutral	post	5 (62.5 %)	1 (12.5 %)	0.037 ^b
	Very satisfied		3 (37.5 %)	3 (37.5 %)	
	Extremely satisfied		0 (0 %)	4 (50 %)	

Data are presented as means ± SD and as frequency and percent distribution. VR: Virtual Reality; MoCA: Montreal Cognitive Assessment; PSQI: Pittsburgh Sleep Quality Index.

^a Significant p-value based on the paired t-test.

^b Significant p-value based on the Chi-square test.

resulting in similar adaptations after exercise for four weeks. Similarly, gaming console exercise did not differ significantly from traditional exercise in fatigue perception in cystic fibrosis.²⁴ Also, a recent meta-analysis reported a weak effect of VR interventions over traditional exercises for breathlessness in individuals with respiratory conditions.²⁵ However, Nascimento et al.,²⁶ in their meta-analysis, showed that VR exercises using video game consoles may seem superior to conventional exercises in reducing fatigue in Multiple Sclerosis.

Interestingly, persistent fatigue or exercise intolerance in post-COVID-19 subjects may not be related to central cardiopulmonary limitations or physical deconditioning but rather to reduced peripheral O₂ extraction or utilization by the muscles during exercise due to mitochondrial dysfunction, with resultant reduced ATP and energy production.^{27,28} Also, fatigue after COVID-19 infection may be due to neuro-inflammation processes, vagus nerve involvement, oxidative stress, and viral persistence.²⁹ Exercise can reduce fatigue via peripheral adaptations at the level of muscle in the form of greater O₂ extraction and utilization, increased muscle mass/strength, and improved inter-muscular coordination, resulting in improvements in respiratory efficiency and tolerance to exercise.^{30,31} This mechanism could explain the improvement in fatigue in the present study after a 4-week treadmill exercise program, whether combined with VR or not.

The present study also showed that cognitive function was significantly improved to a similar extent after treadmill aerobic exercise with and without VR compared to baseline in post-COVID-19 individuals. Exercise positively affects brain health and cognitive function via favorable actions on inflammatory markers, neurotransmitters, and neurotropic factors involved in the neurophysiological pathways likely disorganized by COVID-19 infection.³² Additionally, exercise can increase blood flow and improve glucose and lipid metabolism in the brain, thus enhancing cerebrovascular health.³³ Notably, since treadmill

exercises with and without VR were practiced moderately in the present study, cognitive function similarly improved following the two exercise formats. Within this context, Carbonell-Hernandez et al.³⁴ investigated the acute effects of aerobic, strength, and balance game exercises with similar intensity on cognitive function in older adults, and found that cognitive function was improved significantly following all exercise types with no significant difference between them. They concluded that different exercise types with the same intensity can lead to similar cognitive improvements.³⁴ Despite the discrepancy in exercise types and studied population between our study and that study,³⁴ its results may support the similar improvements in cognitive function found in the two exercise groups in the present study.

This study also revealed that sleep quality, assessed by PSQI, improved significantly in both groups to the same extent. A recent systematic review by Alnawwar et al.³⁵ showed that exercise improves overall sleep quality, in terms of falling asleep easier and sleeping better, by increasing melatonin hormone levels, reducing stress, improving mood, and regulating body temperature. They also reported that moderate-intensity exercise, not high-intensity exercise, is the most effective for improving sleep quality.³⁵

Patient satisfaction is the state of contentment experienced by patients while receiving health care and has become a standardized measure to judge the efficiency and effectiveness of a treatment.³⁶ An important finding in this study was that participant satisfaction with the exercise program was significantly higher in subjects who performed VR-simulated treadmill exercise than their counterparts who performed conventional treadmill exercise alone. This finding could be supported by a systematic review reporting that physical exercises, such as cycling, running, and rowing, combined with VR, resulted in more enjoyment than physical exercises alone.³⁷ Though we did not measure enjoyment directly, it is reasonable to suppose that participants enjoyed treadmill exercises more when they used the VR system, which increased their satisfaction with exercise. In a similar context, Dimbwadyo-Terrer et al.³⁸ investigated the impact of combining VR with conventional therapy versus conventional therapy alone in tetraplegia patients. The study found that adding VR to conventional treatment resulted in greater patient satisfaction.³⁸ Also, Polat et al.³⁹ showed that the combination of virtual reality and cycling exercises led to higher levels of patient satisfaction in those with fibromyalgia syndrome. Furthermore, it has been recently reported that virtual reality exercises have a more motivational impact on healthy adults than traditional forms of exercise.⁴⁰

The clinical implications of this study could emerge from the greater participant satisfaction reported following the performance of conventional treadmill exercise with non-immersive VR. Since exercise programs can be physically challenging in post-COVID-19 subjects owing to persistent fatigue, making exercise a pleasant experience by augmenting non-immersive VR while exercising can improve patient compliance with exercise programs, particularly long-term rehabilitation exercise programs. A recent review reported that virtual reality could solve the challenges of conventional exercise training methods.⁴¹

Finally, the present study's findings should be viewed cautiously due to the small sample size, which may limit the generalized extrapolation of the results. Other limitations include the lack of a non-exercising control group and lack of assessment of dyspnea, exercise tolerance, peak oxygen consumption, or health-related quality of life. In addition, due to the nature of the interventions, neither the physiotherapist nor the participants were blind to the exercise programs. Likewise, the interviewer who administered the questionnaires was not blind to patient allocation for practical reasons. Furthermore, the participants were recruited by referral only. Nevertheless, the present study has several strengths, as follows: (i) This study is one of the few trials investigating the effectiveness of traditional aerobic exercise supported by VR technology in post-COVID-19 subjects and may provide preliminary results in this research area; (ii) The actual HRpeak determined from the maximal treadmill exercise test was used to calculate the THR

individually and precisely; (iii) The choice of assessment of patient-reported outcomes using questionnaires in the native language of participants came following the recent shift in the disease management plan from a disease-centered biomedical approach to a more comprehensive patient-focused biopsychosocial model.

5. Conclusion

A 4-week moderate-intensity treadmill exercise program with and without non-immersive VR may similarly lead to significant improvements in fatigue, cognitive function, and sleep quality in post-COVID-19 subjects. However, incorporating non-immersive VR as an adjunctive rehabilitation tool into a traditional treadmill exercise program may lead to greater participant satisfaction with the exercise program in this cohort. Nonetheless, a definitive conclusion cannot be reached due to the limited sample size, and future randomized controlled trials with a larger sample size are warranted to verify our findings.

Credit author statement

Ahmad Mahdi Ahmad: Conceptualization, Methodology, Validation, Formal analysis, Statistical Analysis, Writing Original Draft, Writing - Review & Editing, Visualization, Supervision, and Project administration; Sara Ali Awad Allah: Methodology, Investigation, Resources, Writing Draft, Editing; Gehad Abd Elhaseeb: Writing Draft, Editing; Dalia Elsharawy: Supervision; Hend Salem: Revision, Editing; Mona Ahmad Abdelwahab: Methodology, Supervision, Writing Draft, Editing.

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Declaration of competing interest

The authors declare no conflict of interest.

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