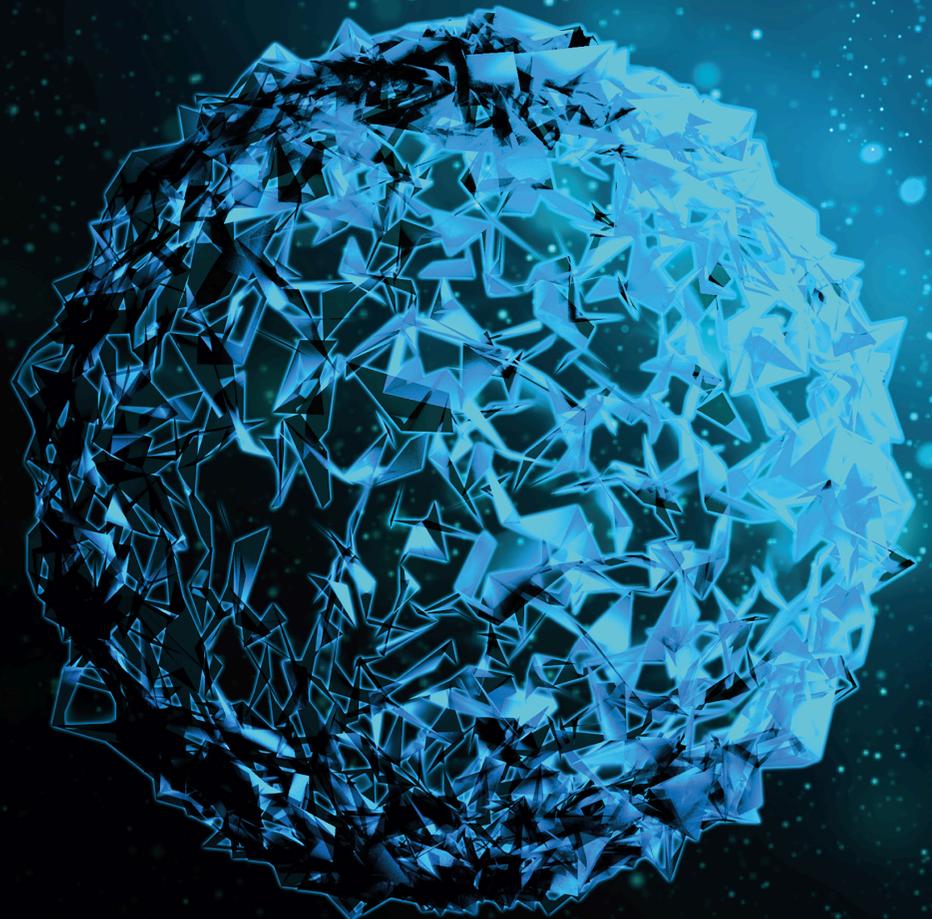


Integrated Role of Nonpharmacological Interventions for Rehabilitation of Individuals with Musculoskeletal Disorders 2021

Lead Guest Editor: Mario Bernardo-Filho

Guest Editors: Borja Sañudo, Adérito Seixas, Danúbia Sá-Caputo, and
Redha Tair





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BioMed Research International

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Research Article

Effects of Muscle Energy Technique and Joint Manipulation on Pulmonary Functions, Mobility, Disease Exacerbations, and Health-Related Quality of Life in Chronic Obstructive Pulmonary Disease Patients: A Quasiexperimental Study

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Chronic obstructive pulmonary disease (COPD) is primarily a disease of the lungs; however, extrapulmonary comorbidities like rib cage stiffness, decreased thoracic spine mobility, postural changes, and skeletal muscle dysfunctions also coexist. Muscle energy technique (MET) and joint manipulation (JM) may help alleviate these musculoskeletal problems. This study was aimed at evaluating the effectiveness of MET and JM on pulmonary functions, dyspnea, chest wall mobility, disease exacerbations, and health-related quality of life in COPD patients. A total of 16 patients (7 women and 9 men) suffering from COPD between the ages of 35 and 65 years participated in the study. Pretest-posttest quasiexperimental design was used. MET was applied to the sternocleidomastoid, anterior scalene, pectoralis major muscles, and at the C4-C6 level of the cervical spine. Maitland JM was performed in the thoracic region at the intervertebral, costovertebral, and costotransverse joints. The treatment intervention lasted for 3 weeks. FEV₁/FVC, maximum inspiratory pressure (MIP), SpO₂, modified Borg dyspnea scale (MBDS), COPD assessment test (CAT), mMRC dyspnea scale, BODE index, right and left hemidiaphragm excursion, and chest wall expansion at T4 and T10 levels were the outcome measures. Significant improvement ($p < 0.05$) was observed in FEV₁/FVC, MIP, SpO₂, MBDS, CAT, mMRC dyspnea scale, BODE index, and chest expansion at T4 and T10 levels. Only for the hemidiaphragm excursion, no significant ($p > 0.05$) improvement was observed. Combined application of MET to accessory respiratory muscles and cervical spine and JM to thoracic spine improved pulmonary functions, chest wall mobility, and health-related quality of life and reduced dyspnea and disease exacerbations in patients with mild to moderate COPD.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is among the leading causes of mortality and morbidity in low-, middle-, and high-income countries [1]. In COPD, obstruction

or limitation in airflow occurs due to emphysema (parenchymal destruction), a mixture of small airway diseases, and in many cases asthma (increased airway responsiveness) [1]. In addition to the involvement of the lungs in COPD, there are also extrapulmonary comorbidities [2, 3]. These

extrapulmonary comorbidities may include stiffness of the rib cage [4], reduced spinal motion [5], increased muscle sensitivity [5], postural changes [5], cervicothoracic pain, muscle loss, osteoporosis, and/or skeletal muscle dysfunction [6, 7]. The activity-limiting dyspnea that occurs in COPD patients may be caused by mechanical restrictions [8, 9]. Reduced thoracic axial rotation and altered neck posture in COPD patients were found to be associated with poorer pulmonary functions [5]. There is evidence to show that pathophysiological changes in COPD are related to the inflammatory status and oxidative stress that occurs in COPD [10]. Skeletal muscle wasting and weight loss in COPD patients have been proposed to be related to the imbalance of oxidative stress status [11, 12]. One recent study concluded that COPD-related sarcopenia is related to increased oxidative stress-related factors [13].

Regarding the treatment of COPD, international guidelines recommend that the management and treatment of COPD should be individualized to reduce symptoms, improve exercise tolerance and quality of life, and reduce the chances of exacerbations [3, 14]. Physical therapy has an important role to play in addressing musculoskeletal disorders in COPD patients.

Previous studies have evaluated the use of manipulative osteopathic treatments [15, 16], soft tissue techniques [17], myofascial release techniques [18], and spinal joint manipulation (JM) [19, 20] in the treatment of patients with COPD with varying results. Muscle energy technique (MET) and spinal JM are used to treat musculoskeletal problems in patients with COPD. MET is a form of manual therapy in which the patient performs voluntary contraction against the counterforce applied directly by the therapist [21]. MET is used to increase the length of the spastic, shortened, or contracted muscles. Localized edema can also be reduced with MET by muscle pump action. MET can also increase the strength of physiologically weakened muscles [21] and can be used to mobilize articulation whose mobility is reduced [22]. Previous studies have shown that MET can increase shoulder range of motion (ROM) [23, 24], spinal ROM [25, 26], and muscle flexibility [27, 28]. Another technique, spinal manipulative therapy (high-grade JM), was found to improve chest wall compliance when applied to paravertebral tissues or the region of spinal stiffness [29]. JM of the spine consists of high-velocity low-amplitude thrust to the thoracic intervertebral, costovertebral, and costotransverse joints. Spinal JM is hypothesized to decrease the rigidity of the chest wall and increase the mobility of the costal and spinal joints [30]. However, a systemic review reported that there was insufficient evidence to support or refute the use of manual therapy in the treatment of COPD [31].

Due to the pathophysiology of COPD, where several musculoskeletal dysfunctions coexist, MET or spinal JM alone may not be able to provide desirable improvements. If both techniques are applied to patients, which is conveniently possible in clinical settings, then we may get better results.

To our knowledge, no study has examined the effects of MET and JM, when applied together, on lung functions, dyspnea, chest wall mobility, disease exacerbations, and health-

related quality of life in patients with COPD. Therefore, a study was warranted that examined the cumulative effects of MET and JM. The present study was aimed at assessing the effects of MET and JM on pulmonary functions, dyspnea, chest wall mobility, disease exacerbations, and health-related quality of life in patients with COPD. We hypothesized that MET and JM when applied together improve pulmonary functions, chest wall mobility, and health-related quality of life and reduce dyspnea and disease exacerbations, in patients with COPD.

2. Materials and Methods

2.1. Study Design and Participants. A single-group pretest-posttest quasiexperimental design was used. Due to the COVID-19 pandemic, COPD patients were not easily available; therefore, a convenient sampling method was performed. In retrospect, the minimum sample size was calculated to be 12 for a quasiexperimental study, using the software G*Power 3.1.9.4. (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany; <http://www.gpower.hhu.de/>), from the data obtained in the present study (effect size = 0.99; $\alpha = 0.05$; power $(1 - \beta) = 0.80$; Wilcoxon signed-rank test). A total of 22 participants aged 35-65 years were screened for the study; however, two participants declined to participate and four participants could not complete the 3-week protocol; therefore, data of the 16 participants were analyzed. Patients diagnosed with COPD were recruited from the Department of Respiratory Medicine of the tertiary care hospital and referred to the Musculoskeletal Physiotherapy Research Laboratory. The selected participants were currently nonsmokers and had $FEV_1/FVC < 0.70$ and oxygen saturation of $>95\%$. Patients diagnosed with severe and very severe COPD, osteoporosis, thoracic joint instability, scoliosis, neurological disease, cardiovascular disease, cognitive disorder, recent abdominal or chest surgery, pneumothorax, haemothorax, tuberculosis, pneumonia, lung carcinoma, and high anxiety level related to treatment were excluded from the study. This study was prospectively registered before recruiting participants in the Indian Clinical Trial Registry with the registration number CTRI/2020/04/024648 and obtained its Universal Trial Number U1111-1247-6630. The protocol copyright related to the study was registered with the unique registration number L-97600/2020 under the Copyright Office of the Government of India. The risks and benefits of the study were discussed with all participants who participated voluntarily, and informed consent was obtained. The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Research Ethics Committee at Maharishi Markandeshwar (deemed to be University), Mullana, Ambala (Protocol ID: MMDU/IEC-1547 and 10 December, 2019).

2.2. Outcome Measures

2.2.1. Primary

- (i) FEV_1/FVC ratio measured by spirometer [32]

2.2.2. Secondary

- (i) Maximum inspiratory pressure (MIP), measured by a portable capsule sensing pressure gauge [33]
- (ii) SpO₂, measured by pulse oximeter [34]
- (iii) Modified Borg dyspnea scale (MBDS) [35]
- (iv) COPD assessment test (CAT) [36]
- (v) mMRC dyspnea scale (modified Medical Research Council) [37, 38]
- (vi) BODE index (body mass index, airflow obstruction, dyspnea, and exercise) [39]
- (vii) Right and left hemidiaphragm excursion measured by chest radiograph [40]
- (viii) The expansion of the chest wall was measured at the level of the fourth thoracic vertebra (T4) and the tenth thoracic vertebra (T10) using a measuring tape

2.3. Instrumentation

- (i) RMS PC-Based Spirometer Helios-401 (Recorders & Medicare Systems Pvt. Ltd., Haryana, India) [41]
- (ii) Portable capsule sensing pressure gauge (Gauges Bourdon (India) Pvt. Ltd., New Delhi, India) [33]
- (iii) Pulse oximeter (Choicemmed MD300C2, China) [42]
- (iv) Chest radiographs [43]
- (v) Measuring tape [44]

2.4. *Study Protocol.* The study protocol was divided into three phases.

2.4.1. *Preintervention Evaluation.* The baseline measurement of all primary and secondary outcome measures was taken before the application of the intervention.

Lung volumes (FEV₁ and FVC): in the sitting position, participants were asked to first inhale as deeply as possible and then exhale from the mouth into the spirometer tube as forcefully as they could. Then, the exhaled volume of air in the first second (FEV₁) [45] and total volume of air exhaled (FVC) [46] were recorded. FEV₁ was also used for the calculation of the BODE index

MIP: participants were made to sit comfortably, and then, a nose clip was applied to the participants' nose to avoid air leaks. They were asked to hold the gauge with both hands and close their lips firmly around the mouthpiece. Then, they were asked to exhale as much as possible and then to inhale maximally for more than 1 sec against the resistance of the gauge. MIP reading in the portable capsule sensing pressure gauge was recorded [47]

MBDS/CAT/mMRC scale: each participant was asked to complete these scales

SpO₂: a fingertip pulse oximeter was used to measure SpO₂ [48]

6-minute walk distance for BODE index: each participant was asked to walk as far as possible for 6 minutes [49]. The distance walked was measured in meters and used to calculate the BODE index

Hemidiaphragm excursion: excursion of the right and left hemidiaphragm was measured by anteroposterior chest radiographs in the supine position. A radiopaque ruler was placed on the chest and abdominal area of the participants in the midline in the craniocaudal direction. X-ray films were obtained during maximum inspiration and expiration. Then, the distance between the two levels of both hemidiaphragm was noted [50]

Chest wall expansion: the participants stood with feet 5 cm apart and arms elevated. Chest wall expansion was measured at two levels, upper and lower. For the upper level, a measuring tape was placed around the chest at the T4 spinous process and the fourth intercostal space. For the lower level, a measuring tape was placed at the T10 spinous process and the xiphoid process. The participants were asked to maximally inhale and exhale. The difference between these two extremes was noted [51]

2.4.2. *Intervention.* MET followed by JM was applied to all participants. MET was applied to the following muscles and regions: sternocleidomastoid (SCM), anterior scalene, pectoralis major, and at the C4-C6 level of the cervical spine. Grade V (high velocity, low amplitude) Maitland JM was performed in the thoracic region at the intervertebral, costovertebral, and costotransverse joints. This intervention was carried out twice a week for a total of 3 weeks.

(1) *MET.* For SCM, the participants were made to lie in a supine position with arms on their sides. The physical therapist (PT) performed stretching of SCM with his arms crossed and hands stabilized the participant's mastoid area and shoulder. The participants were asked to perform the action of SCM with 20% of the maximum strength, from both ends against the resistance of PT. The participants put effort for 7-10 seconds followed by relaxation, and then, the PT took it to the new barrier to increase the degree of side bending and rotation, where it was stabilized, and then, the shoulder was stretched caudally. Once the muscle was in a stretched position, the patient relaxed, and the stretch was held for up to 30 seconds [22].

For the anterior scalene muscle, the participants were made to lie supine with a cushion or towel under the upper thoracic area. The PT placed his hand on the side of the participant's face/forehead to resist the isometric contraction and the other hand on the sternum. The participants were asked to perform the action of the anterior scalene muscle against PT resistance and hold it for 7-8 seconds followed by relaxation [22].

For pectoralis major, the participants were supine and the PT was on the ipsilateral side. The PT placed one hand on the sternum and applied the lateral compression force, placed another hand on the anterior shoulder, and applied

the force in the posterolateral direction. Then, the participants were asked to exert force in the anterior direction towards the ceiling for 5-7 seconds, followed by relaxation, and then take it to the new barrier by taking up the slack 2-3 times [22].

For the cervical spine (C4-C6), in the supine position, the neck of the participants was slightly flexed, completely bent on the side, and rotated to the ipsilateral side. The middle fingers of the PT's right hand were placed over the pillars of C4-C6. The PT placed his other hand on the left parietal and temporal area of the patient. The participants were asked to bend and rotate the neck towards the contralateral side against the resistance of the PT, for 5-7 seconds, followed by relaxation, and then taken to its new barrier, and the same procedure was repeated 2-3 times [22].

(2) *Joint Manipulation (Thoracic Spine)*. The participants were made to lie in the prone position. The PT placed his hands parallel to each other on both sides of the participants' thoracic spine over their back. One hand was placed caudal and another cephalad to the joints to be mobilized. Then, the PT applied the posteroanterior and rotational component with the right hand towards the caudal direction and with the left hand towards the lateral and cephalad direction. The technique was performed rhythmically along with the participant's breathing pattern, and the manipulative thrust was administered at the end of the expiration. This technique consisted of oscillatory movements applied in three directions: posteroanterior, caudal, and lateral. This manipulation mobilized the intervertebral, costovertebral, and costovertebral joints [52].

2.4.3. *Postintervention Evaluation*. All outcome measures were measured again after a 3-week intervention similar to the case of preintervention evaluation.

2.5. *Data Analysis*. Data analysis was performed using SPSS version 26 statistical software (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk normality test was used to assess the normal distribution of the data. For normally distributed data, a paired *t*-test was used. The paired *t*-test is a parametric test, used to test if the means of two paired measurements (e.g., pretest/posttest) are significantly different [53]. For ordinal and not normally distributed data, the Wilcoxon signed-rank test was used. The Wilcoxon signed-rank test is a non-parametric test used as an alternative to the paired Student's *t*-test. This test does not assume that the samples are normally distributed [54]. The confidence interval was established at 95%, and the *p* value < 0.05 was considered significant. For variables having normal distribution, arithmetic mean was used; however for variables that did not have a normal distribution, geometric mean was used.

3. Results and Discussion

Data from 16 participants were analyzed. Table 1 includes some demographic characteristics of all participants.

Wilcoxon signed-rank test: this test was performed for the following variables: FEV₁/FVC, MBDS, BODE index,

TABLE 1: Demographic characteristics of the participants (*n* = 16), mean (LL-UL).

	Mean (LL-UL)
Age (years)	49.25 (43.70-54.80)
Height (meter)	1.65 (1.60-1.70)
Body mass (kg)	62.2 (56.4-67.98)
BMI (kg/m ²)	23.07 (20.7-25.5)
Male/female	9/7

LL: lower limit; UL: upper limit; BMI: body mass index.

mMRC dyspnea scale, SpO₂, CAT (COPD assessment test), and hemidiaphragm excursion (right and left). Significant improvement (*p* < 0.05) was observed in all variables except for both hemidiaphragm excursions (right and left) (Table 2). For significant values, Cohen's *d* showed a large effect size

Paired *t*-test: this test was performed for the following variables: MIP and chest expansion at levels T4 and T10. A significant improvement was observed in all variables (Table 3). For significant values, Cohen's *d* showed a large effect size

The present study was aimed at evaluating the effectiveness of MET and JM when applied together, on pulmonary functions, MIP, SpO₂, dyspnea, diaphragm excursion, disease exacerbations, chest wall mobility, and health-related quality of life in patients with COPD. The results of the present study showed that application of MET (on accessory respiratory muscles and C4-C6 spine) and JM (on thoracic spine joints) improved spirometry (FEV₁/FVC ratio), MIP, SpO₂, chest wall mobility, and health-related quality of life and reduced dyspnea and disease exacerbations in patients with COPD.

In the current study, geometric mean (GM) was calculated for nonparametric variables as the values were altered by the outliers, and the mean of data tended to make large fluctuations. Thus, GM gave an appropriate mean of the data set by neglecting the factors that provided values in negative and zero and obstructed the mean data. In the case of a skewed distribution of the data, by GM, the symmetry of data was made by log transformation [55]. The GM provides values less than the actual arithmetic mean, as the arithmetic mean gives a sum of the total number of values and is sensitive to outliers, while the effect of outliers on the geometric mean is mild [55]. Thus, in the case of a nonparametric test, the exact mean was obtained by GM.

To the best of our knowledge, no study has used both MET and JM simultaneously in COPD patients. Therefore, it is difficult to compare this study with the previous studies. However, several previous studies have used either MET or JM along with other interventions for the management of COPD patients. One of the previous studies in COPD patients reported an improvement in lung function after the application of MET to the accessory respiratory muscles in conjunction with other soft tissue manual therapy techniques [17]. The study by Putt et al. [23] reported an increase in lung capacity in COPD patients after applying the hold-relax technique (PNF) to the pectoralis major

TABLE 2: Dependent variable data, AM (LL-UL) and GM at baseline and postintervention, Wilcoxon signed-rank test p values, and Cohen's d values.

Variables	Baseline		Post-intervention		p value	Cohen's d
	AM (LL-UL)	GM	AM (LL-UL)	GM		
FEV ₁ /FVC (%)	57.94 (54.1-61.8)	57.49	68.88 (63.16-74.59)	68.17	0.001*	0.99
MBDS (n)	4.38 (3.95-4.80)	4.30	2.87 (2.45-3.30)	2.75	<0.001*	0.99
BODE (n)	6.0 (5.3-6.7)	5.88	3.8 (3.13-4.5)	3.56	0.002*	0.99
mMRC (n)	2.06 (1.70-2.42)	1.943	0.875 (0.60-1.14)	1.054	<0.001*	0.99
SpO ₂ (%)	98.50 (98.2-98.8)	98.49	99.3 (99.0-99.6)	99.31	<0.001*	0.99
CAT (n)	11.5 (10.5-12.5)	11.35	6.06 (5.4-6.7)	5.94	<0.001*	1.00
Left hemidiaphragm excursion (cm)	1.5 (1.45-1.6)	1.52	1.55 (1.5-1.6)	1.54	0.157	0.6
Right hemidiaphragm excursion (cm)	1.7 (1.6-1.8)	1.67	1.7 (1.6-1.74)	1.66	0.480	0.58

*Significant ($p < 0.05$). AM: arithmetic mean; LL: lower limit; UL: upper limit; GM: geometric mean; FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; MBDS: modified Borg dyspnea scale; BODE: body mass index, airflow obstruction, dyspnea, and exercise; mMRC: modified Medical Research Council dyspnea scale; SpO₂: peripheral capillary oxygen saturation; CAT: chronic obstructive pulmonary disease evaluation test.

TABLE 3: Dependent variables data, mean (LL-UL) at baseline and postintervention, paired t -test p values, and Cohen's d values.

Variables	Mean (LL-UL)		t value	p value	Cohen's d
	Baseline	Postintervention			
MIP (cmH ₂ O)	42.56 (37.01-48.11)	49.37 (44.33-54.41)	-8.662	<0.001*	1.00
Chest expansion (cm) (T4)	2.4 (2.0-2.7)	2.6 (2.3-2.9)	-5.614	<0.001*	1.00
Chest expansion (cm) (T10)	2.5 (2.2-2.8)	2.7 (2.5-2.98)	-4.772	<0.001*	1.00

*Significant ($p < 0.05$). LL: lower limit; UL: upper limit; MIP: maximum inspiratory pressure; T4: fourth thoracic vertebra; T10: tenth thoracic vertebra.

muscle. Since the PNF technique and MET are similar in their principle of stretching and facilitating joints and muscles [56], therefore, the study by Putt et al. [23] supports the findings of the present study.

In the current work, improvement was observed in dyspnea scales (MBDS, mMRC dyspnea scale, and BODE index) also. The mechanism behind this improvement can be explained as follows: there is a feeling of breathlessness in patients with COPD, and to overcome this feeling, the patients continuously use accessory respiratory muscles, leading to shortening and tightening of these muscles [57]. MET stretching of these accessory muscles relaxes them and reduces the rate of muscle spindle firing in the lengthening phase. Due to this, the central respiratory motor command required for the given ventilation is decreased; thus, as a result, dyspnea may be alleviated [58]. MET corrects respiratory mechanics by correcting accessory inspiratory muscle dysfunctions; thus, diaphragmatic breathing is made more effective. This increases ventilation, which increases V/Q matching, resulting in an improvement in SpO₂ levels [56]. This may explain the increase in SpO₂ level in the present study.

The present study showed an improvement in the BODE index, which includes the BMI, FEV₁, mMRC scale, and the distance walked in 6 minutes. Marin et al. reported that dyspnea (modified MRC scale) was a good predictor of walking distance in their study [59]. Therefore, alleviating dyspnea and improving SpO₂ using the mechanisms mentioned above will explain the improved BODE index through an increase in walking distance in the 6-minute walk test,

improved FEV₁/FVC, and improved mMRC scores. The BODE index is reported to be a good predictor of mortality in COPD patients, in the medium to long term [60]. Therefore, the improvement in the BODE index after the application of MET and JM in the present study is significant from a functional status perspective of this population.

Spinal JM (high velocity, low amplitude) has been reported to increase spinal ROM [61] and decrease local hypertonicity of the muscles [62]. Previous studies in normal individuals have reported that increased mobility of the thoracic joints improved lung functions in the short term [63, 64]. Therefore, in the present study, manipulation of the thoracic joints may have increased mobility of the thoracic spine, which in turn may have resulted in increased lung functions.

In the present study, minimal clinically important difference (MCID) values were also calculated for comparison, but only for the variables whose MCID values were already provided in previous studies/literature. For FEV₁/FVC and MIP, MCID could not be found in the literature. For MBDS, a previous study reported an MCID value of 1 unit [65]. In the present study, MCID and standard error of measurement (SEM) for MBDS were found to be 2.536 and 0.915, respectively; therefore, both clinically and statistically significant improvements were found. For chest expansion, a previous study reported that MCID change scores should be greater than 3.60 for the upper chest and 4.40 for the lower chest expansion [66]. In the present study, the MCID for the upper (T4) and lower (T10) chest expansions was 0.684 and 0.554, respectively, and the SEM for the upper

(T4) and lower (T10) chest expansion was 0.247 and 0.2, respectively. Therefore, no clinically significant differences were found in the chest expansion in the present study after the application of the intervention. The previous study has cited ± 4 percentage points as MCID for SpO₂ [67]. In the present study, MCID and SEM were 6.5% and 0.237, respectively. Therefore, for SpO₂, statistically and clinically significant results were found. MCID for CAT is reported to be a change of 2 points [68]. The present study found MCID and SEM for CAT to be 3.045 and 1.099, respectively. Therefore, in the present study, for CAT, statistically and clinically significant results were obtained. A previous study reported MCID for mMRC as 1 [69]. In the present study, MCID and SEM for mMRC were found to be 0.70 and 0.25, showing that statistically and clinically significant results were observed on the mMRC dyspnea scale after the application of MET and JM.

No improvement was observed in diaphragmatic excursion in the present study. One of the recent studies by Jung et al. [70] reported improvement in diaphragmatic excursion after 8 weeks of thoracic mobilization in individuals with thoracic hyperkyphosis. The reason why there is no significant change in diaphragmatic excursion in the present study may be the short duration of the intervention. A longer duration intervention (8 weeks) may have brought the desired changes in diaphragmatic excursion.

The present study has several limitations also. Due to the limited availability of patients with COPD, no control group could be included in the study. Therefore, the lack of a control group limits the comparison of participants who received the intervention (MET and JM) with those who did not receive the same treatment during the same period. The present study did not include long-term follow-up; therefore, the improvements observed with the intervention may be temporary and short-lived. Therefore, future research is needed that includes a large sample size, a control group, and long-term follow-up. It may be possible that of the two interventions (MET and JM), only one of them is sufficient to bring about the desired improvements. Therefore, further studies should also evaluate the efficacy of MET alone versus JM alone in COPD patients.

4. Conclusions

Combined application of MET to accessory respiratory muscles and cervical spine and JM to thoracic spine (intervertebral, costovertebral, and costotransverse joints) improved pulmonary functions, chest wall mobility, and health-related quality of life and reduced dyspnea and disease exacerbations in patients with mild to moderate COPD. Therefore, a combination of MET and JM can be used as a physiotherapeutic intervention to improve the above-mentioned outcome measures in patients with COPD. These techniques can be an adjunct to breathing exercises and positioning techniques (postural drainage) to relieve symptoms and achieve a better quality of life in this population group; however, further experimental trials are needed to verify this claim.

Data Availability

The data associated with the paper are not publicly available but are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Research Article

Impact of Rehabilitation on Gait Kinematic following Grade II Anterior Cruciate Ligament Injury among Wrestlers

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Background. Anterior cruciate ligament (ACL) injuries are among the most common injuries in wrestling. Even though there are several studies available in the literature about the changes in gait kinematics following ACL injury and ACL reconstruction surgery, none of these studies investigated the changes in gait kinematics following nonoperative rehabilitation protocol. So, this study is aimed at investigating the changes in gait kinematic following a supervised ACL rehabilitation protocol among wrestlers following a grade II ACL injury. **Methods.** Fifteen male professional wrestlers with recent grade II ACL injury with mean age: 19.93 ± 2.01 years, weight: 72.33 ± 7.46 kg, and height: 173 ± 4.95 cm volunteered for this single-arm pretest-posttest study. Kinematic parameters during walking pre- and postrehabilitation were examined by two-dimensional (2D) video graphic analysis. Paired sample *t*-test and Cohen's *d* were used to determine significant differences and effect size of segmental angle, cadence, step length, stride length, etc. **Results.** Injured wrestlers after the rehabilitation program walked significantly faster and had a 10.13% higher cadence, a 10.89% faster gait velocity, a 05% greater step length, and a 4.69% longer stride length, compared with a prerehabilitation program of injured wrestlers. Furthermore, joint angles at the hip, knee, and ankle were significantly different between pre- and postrehabilitation. **Conclusion.** Research findings suggest that rehabilitation programs significantly impact the gait pattern of injured wrestlers. A 19-week supervised rehabilitation protocol can increase gait velocity and related parameters in ACL injured wrestlers.

1. Introduction

Wrestling is considered one of the most challenging sports globally, consisting of quick attack and defense moves that require high muscle power and force with an injury rate of 70 per thousand athletic exposures [1]. Compared to other sports, wrestling gets relatively less attention in terms of injuries. Epidemiological studies reported that wrestling does not cause as many injuries as soccer and taekwondo. At the same time, any part of the wrestler's body is prone to injury, with 65% of the injuries requiring surgery reported

in the knee, according to a previous study [2]. According to Ransone et al. [3], knee injury remains the most common injury in wrestling. Knee injuries frequently occur during the takedown or bottom positions, causing damage to collateral ligaments, meniscus, patella, and ACL. Among the reported knee injuries in wrestlers, up to 9.1% are ACL-related injuries [3].

It has been reported in previous studies that the gait pattern may affect following ACL injuries [4–6]. The ACL injury may result in loss of knee joint stability and abnormal movement patterns, leading to the early development of

degenerative changes such as osteoarthritis of the knee joint [7]. Evidence suggests nonoperative management (rehabilitation) as a viable alternative to operative management (ACL reconstruction surgery) and reported good functional outcomes [8, 9]. Conversely, biomechanical outcomes following ACL rehabilitation are not well understood. Compared to the uninvolved limb, the patient will walk with lower peak knee joint angle and moments that are obvious in the sagittal plane [10, 11]. It has been reported that patients with acute ACL injury (less than one month) produce a substantially distinct gait pattern from chronic ACL deficient (>2years postinjury) subjects [12, 13]. ACL injury patients may develop a “quadriceps avoidance” strategy to decrease anterior shear during gait.

A meta-analysis conducted by Culvenor et al. [10] reported no difference in peak knee flexion angle and movements after 1-3 years of ACL injuries. Button et al. [14] reported no difference in sagittal plane knee angle and movements in patients who undergone ACL rehabilitation compared to healthy controls. According to Khandha et al. [4], the patient who received rehabilitation protocol following ACL injury walked with 28% greater medial compartment contact forces and 28% greater peak knee adduction moment in the involved knee compared with patients who have undergone ACL reconstruction surgery. Even though there are several studies available in the literature about the changes in gait kinematics following ACL injury and ACL reconstruction surgery [11, 15], none of these studies investigated the changes in gait kinematics following nonoperative ACL rehabilitation protocol. So, this study is aimed at investigating the changes in gait kinematic following a supervised ACL rehabilitation protocol among wrestlers following a grade II ACL injury.

2. Materials and Methods

2.1. Sample. Fifteen male professional wrestlers from the republic of Iraq with recent grade II ACL injury age: 19.93 ± 2.01 years, weight: 72.33 ± 7.46 kg, and height: 173 ± 4.95 cm volunteered for this single-arm pretest-posttest longitudinal study. The sample size was calculated as 13 using a sample size calculator (<https://www.ai-therapy.com/psychology-statistics/sample-size-calculator>) based on a previous study [16] that investigated the gait parameters in ACL deficient knees with a 0.76 effect size 0.05 significant level and 0.8 statistical power. A 15% of the sample (2 participants) was added anticipating dropouts which made the sample size 15. However, there were dropouts in the study. The participants were recruited from the local wrestling federations registered under the Iraqi Wrestling Federation. The grade II ACL injury was confirmed by clinical assessment (Lachman test and anterior drawer test) and MRI scan by a senior orthopedic surgeon. Patients who have undergone ACL reconstruction, previous knee surgery, associated injuries to other ligaments or meniscus, and biomechanical abnormalities of the lower limb were excluded from the study. The participants were informed about the design, procedure, advantages, and disadvantages of the participation, and a written informed consent was taken from them. The

study was approved by the ethical research committee of Aligarh Muslim University (IRB no: 00/12/ss) and conducted as per the declaration of Helsinki.

2.2. The Experimental Approach to the Problem. Prior to the baseline measurement, all the participants have undergone a three-week initial rehabilitation following the ACL injury (acute phase). The initial rehabilitation focused on eliminating the residual symptoms such as pain, effusion, and reducing the impairment. All the participants have undergone initial rehabilitation under the same physical therapist and followed the same rehabilitation protocol. Details of the initial rehabilitation are available in supplementary Table 1. The baseline measurement was taken in the fourth week following the approval of the treating orthopedic surgeon and physical therapist. The criteria to perform the baseline measurement were full ROM of the knee joint, no joint effusion at the knee joint, and no joint line or patella-femoral pain.

2.3. Rehabilitation Protocol. The participants underwent a 19-week progressive rehabilitation protocol under the supervision of a senior physical therapist with experience in ACL rehabilitation. All the participants have undergone a similar rehabilitation protocol consistent with the literature consensus, and the details of the protocol are available in Table 1. The rehabilitation was primarily aimed to address the impairment, achieve functional stability, decrease the risk of reinjury, and return to sports activity [16, 17]. Neuromuscular training and perturbations are implemented in the second phase of rehabilitation. The final phase of rehabilitation focused on optimizing the neuromuscular strength and returning the athlete to the preinjury sports level by sports-specific training and improving the psychological readiness for sports participation.

2.4. Video Graphic Analysis. All of the A.C.L. grade-II injured wrestlers' gait patterns were captured by using two synchronized Nikon D-7000 video cameras in a field setting at the testing venue for a two-dimensional gait analysis (GA) examination. The first camera was positioned approximately 8.5 meters perpendicular to the sagittal plane and parallel to the mediolateral axis on their walking side (camera optical axes perpendicular to the sig plane), giving a 90° angle between their respective optic axes. The second camera was positioned (08) eight meters behind the stationary position, in an initial position with the camera's optical axis perpendicular to the frontal plane for measuring the upper and lower body segment motion of subjects during various phases of gait. Cameras were also raised (1.1 m) and tilted to get the biggest picture possible while keeping all of the things that were important in the picture in motion.

According to Davis et al.'s procedure [18], twenty-three passive markers were put on the subject's body. Each participant was asked to walk at their own pace on a 05-meter path. Each subject's starting position was selected and located on the pathway to reach the first platform on the right foot and the second platform on the left foot. The video

TABLE 1: The rehabilitation program (19 weeks) used in the study.

Subacute stage	
Goals	Maintain ROM and flexibility Restore muscle strength and proprioception Improve neuromuscular control Quadriceps sets (10 × 15 sec hold) Leg press (3 sets × 10 rep) Self ROM stretching (3 × 20 – 30 sec. hold) Front and side lunges (3 sets × 10 rep) Step up and squat progression
Activity/exercises	Planks (3 sets × 10 rep) Progressive resistance training Bicycle exercise for ROM (10 minutes) Eccentric quadriceps training (3 sets × 10 rep) Lateral lunges (3 sets × 10 rep) Progressive neuromuscular and proprioceptive drills
Advanced strengthening and neuromuscular control stage	
Goals	Full ROM and flexibility Maximal strength and neuromuscular control Improve balance and proprioception Restore limb function Progressive resistance training Leg press (3 sets × 20 rep) Lateral lunges and step-ups (3 sets × 20 rep) Step down (3 sets × 20 rep)
Exercises	Biodex stability system (stance—bilateral progress to unilateral, setup—dynamic balance, level 8—progress to level 4, duration—5 bouts of 30 sec. progress to 10 bouts) Pool exercises Advanced neuromuscular drills Perturbation training Dynamic stabilisation
Advanced activity stage	
Goals	Normalise strength Improve proprioception, balance, and neuromuscular control Sports specific training Advanced neuromuscular drills
Exercises	Plyometric training (start with a low rep, sets. 3 × 20 reps progress toward 30 reps. progress based on clinical judgment)
Return to sports stage	
Goal	Unrestricted sports activity Sports specific training Running and agility exercises
Exercises	Advanced plyometrics (progress based on clinical judgments) Strength and neuromuscular training

cameras were set to sports mode with a sampling rate of sixty (60) fields per second. The camera's shutter speed was set at high speed (1/2000 fast shutter speed enables rapid-moving subjects). A higher shutter speed will freeze the motion of a fast-moving image, whereas a slow shutter speed will blur the image to create the illusion of motion. Then, for each ACL, injured wrestlers performed three trials on a given specified area. For the following analysis, only the best trials were considered for further examination. The identified trails were played with the help of the software Silicon Coach Pro 8 (SCP) to make separate

clips of each player for separate gait phases. This software provides identification of angles, cadence (steps min-1), gait velocity (m s-1), step length (m), and stride length (m) and was considered as spatiotemporal parameters.

2.5. *Outcome Measures.* The following outcome measures were taken for analysis: (1) pre and postrehabilitation measurement of joint angles of the hip, knee, and ankle joint at each stage of swing (initial contact, loading response, mid stance, terminal stance, and toe-off) and stance phase (acceleration, midswing, and terminal swing) of the gait cycle. (2)

Pre and postrehabilitation measurement of spatiotemporal parameters of the gait which includes cadence, gait velocity step length, and stride length.

2.6. Data Analysis. SPSS (v24.0; IBM Corporation, Armonk, NY, USA) was used for analyzing the data. The normal distribution of the data was confirmed by the Shapiro-Wilk test ($p > 0.05$), and the equality of the variances was satisfied by the Levene test ($p > 0.05$). Paired sample *t*-test was used to determine significant differences in segmental angle, cadence, step length, stride length, etc., and used Cohen's *d* to calculate the effect size. The effect size was considered small, medium, and large if Cohen's *d* value was equal to 0.20, 0.50, and 0.80, respectively. A statistically significant difference was defined as a *p* value less than 0.05.

3. Results

The primary goal of this study was to determine the clinical impact of a rehabilitation program on specified kinematics of GAIT patterns in professional wrestlers with ACL (level-II) injury. A homogeneously distributed sample was identified using the Shapiro-Wilk test for normal distribution. The Paired Samples *t*-test was carried out to evaluate the significant mean variations in kinematics parameters of gait comparing injured wrestlers' before and postrehabilitation programs. Most of the kinematics parameters were significantly different between pre- and postrehabilitation program. (Tables 2–4).

The Paired Samples *t*-test was used to investigate the mean differences in joint angles (ankle joint, knee joint, and hip joint) at the stance phase of gait between the pre- and postrehabilitation programs of injured wrestlers. The results of Table 2 reveal that kinematic variables, hip joint angles at initial contact ($t = 2.85$, $p \leq 0.05$), loading response ($t = 4.1$, $p \leq 0.05$), midstance ($t = 3.23$, $p \leq 0.05$), terminal stance ($t = 4.17$, $p \leq 0.05$), and preswing phase ($t = -3.80$, $p \leq 0.05$) showed significant mean differences between pre- and postrehabilitation programs. The values of hip joint angles Cohen's *d* were 0.74 ($d > 0.50 - < 0.80$), which indicate medium effect size at initial contact phase, and 1.05 ($d > 0.80$) at loading response, 0.88 ($d > 0.80$) at midstance, 1.80 ($d > 0.80$) at the terminal stance, and 0.98 ($d > 0.80$) at preswing phase indicate high effect size, respectively. Knee joint angles at initial contact ($t = 4.29$, $p \leq 0.05$), loading response ($t = 5.7$, $p \leq 0.05$), midstance ($t = 5.67$, $p \leq 0.05$), terminal stance ($t = 11.47$, $p \leq 0.05$), and preswing phase ($t = -6.57$, $p \leq 0.05$) showed significant mean difference between pre- and postrehabilitation programs. The values of knee joint angles Cohen's *d* were 1.11 ($d > 0.80$) at initial contact, 1.50 ($d > 0.80$) loading response, 1.46 ($d > 0.80$) midstance, 2.4 ($d > 0.80$) terminal stance, and 1.70 ($d > 0.80$) preswing phase, which indicate high effect size, respectively. Ankle joint angles at loading response ($t = 4.1$, $p \leq 0.05$) and midstance phase ($t = 5.67$, $p \leq 0.05$) showed significant mean differences between pre- and postrehabilitation programs. The values of knee joint angles Cohen's *d* were 1.05 ($d > 0.80$) loading response and 3.30 ($d > 0.80$)

midstance, which indicates high effect size, respectively. Joint kinematic parameter revealed significant differences between pre- and postrehabilitation program in hip, knee, and ankle angles at stance phase with exception ankle angles at initial contact, terminal stance, and preswing phase. In particular, ACL injured wrestlers showed statistically significant change ROM at hip and knee joint compared to prerehabilitation program of injured wrestlers.

The Paired Samples *t*-test was used to investigate the mean differences in joint angles (ankle joint, knee joint, and hip joint) at the swing phase of gait between the pre- and postrehabilitation programs of injured wrestlers. The results of Table 3 reveal that kinematic variables, hip joint angles at acceleration ($t = 3.72$, $p \leq 0.05$), midswing ($t = 5.24$, $p \leq 0.05$), and terminal swing phase ($t = 6.38$, $p \leq 0.05$) showed significant mean differences between pre- and postrehabilitation programs. The values of hip joint angles Cohen's *d* were 0.97 ($d > 0.80$) at acceleration, 1.35 ($d > 0.80$) at midswing, and 1.62 ($d > 0.80$) at terminal swing phase, which indicate high effect size, respectively.

Knee joint angles at acceleration ($t = 5.94$, $p \leq 0.05$), midswing ($t = 6.95$, $p \leq 0.05$), and terminal swing phase ($t = 9.46$, $p \leq 0.05$) showed significant mean differences between pre- and postrehabilitation programs. The values of knee joint angles Cohen's *d* were 1.52 ($d > 0.80$) at acceleration, 1.59 ($d > 0.80$) at midswing, and 2.45 ($d > 0.80$) at terminal swing phase, which indicate high effect size, respectively. Ankle joint angles at the acceleration phase ($t = 3.18$, $p \leq 0.05$) showed significant mean differences between pre- and postrehabilitation programs. The values of knee joint angles Cohen's *d* were 0.82 ($d > 0.80$) at acceleration which indicates a high effect.

Paired Samples *t*-test was used to investigate the mean difference of spatiotemporal parameter between pre- and postrehabilitation program of injured wrestlers. Results of Table 4 reveal that kinematic variables, cadence ($t = -4.80$, $p \leq 0.05$), gait velocity ($t = -5.41$, $p \leq 0.05$), step length ($t = -4.15$, $p \leq 0.05$), and gait stride length ($t = -4.01$, $p \leq 0.05$) were showed statistically significant means differences exist between pretest and posttest of rehabilitation program of injured wrestlers. The spatiotemporal parameter Cohen's *d* was 1.24, 1.55, 1.06, and 1.03 ($d > 0.80$), which indicated a large effect size.

ACL injured wrestlers walk postrehabilitation program with a 10.89% increase gait velocity, with a 10.13% increase cadence, with a 5% longer step length and 4.69% greater stride length than prerehabilitation program. Furthermore, postrehabilitation program injured wrestlers showed significantly higher values in the prerehabilitation program, but all gait kinematics values did not reach the values of healthy subjects [19, 20].

4. Discussion

The rehabilitation of the ACL is a challenging task. Many therapeutic and sports scientific techniques are presently accessible. However, their usefulness is being scrutinized. Experimental studies were designed to find out the clinical

TABLE 2: Comparison of joints angles mean between pre- and postrehabilitation program at stance phase.

Joint angles	Stance phase	Mean ± SD.	Paired differences			<i>t</i>	<i>p</i> value	Cohen's <i>d</i>
			Mean %	SD	SEM			
HA (pre)	Initial contact	18.87 ± 2.85	13.08%↑	3.36	0.87	2.85	0.04*	0.74
H.A. (post)		21.33 ± 1.87						
KA (pre)		3.20 ± 1.65	58.43%↓	1.68	0.43	4.29	0.02*	1.11^
KA (post)		1.33 ± 0.49						
A.A. (pre)		1.33 ± 0.48	05.26%↓	0.59	0.15	0.44	0.67	0.10
A.A. (post)		1.27 ± 0.46						
HA (pre)	Loading response/foot flat	19.00 ± 3.02	22.10%↓	3.96	1.02	4.1	0.02*	1.05^
H.A. (post)		14.80 ± 2.21						
KA (pre)		18.33 ± 2.5	17.78%↓	2.18	2.05	5.7	0.01*	1.50^
KA (post)		15.06 ± 1.33						
A.A. (pre)		5.06 ± 0.88	25.09%↑	1.27	-1.44	2.21	0.04*	0.57
A.A. (post)		5.80 ± 1.37						
HA (pre)	Mid-stance	2.33 ± 1.23	48.49%↓	1.35	0.35	3.23	0.03*	0.88^
H.A. (post)		1.20 ± 0.41						
KA (pre)		8.93 ± 2.18	41.76%↓	2.54	0.65	5.67	0.01*	1.46^
KA (post)		5.20 ± 0.86						
A.A. (pre)		6.06 ± 1.27	20.79%↓	1.48	0.38	3.30	0.03*	0.85^
A.A. (post)		4.80 ± 0.56						
HA (pre)	Terminal-stance	14.06 ± 2.49	29.37%↑	3.83	0.98	4.17	0.02*	1.08^
H.A. (post)		18.20 ± 3.21						
KA (pre)		6.86 ± 1.40	73.76%↓	1.70	0.44	11.47	0.01*	2.94^
KA (post)		1.80 ± 0.86						
A.A. (pre)		1.93 ± 0.88	0.00%	1.25	0.32	0.00	1.00	0.00
A.A. (post)		1.93 ± 0.79						
HA (pre)	Preswing/toe off	12.20 ± 2.56	27.79%↑	3.39	0.87	3.80	0.03*	0.98^
H.A. (post)		15.53 ± 3.35						
KA (pre)		24.13 ± 2.97	35.64%↑	5.06	1.30	-6.57	0.01*	1.70^
KA (post)		32.73 ± 4.14						
A.A. (pre)		17.73 ± 2.43	-6.76%↑	3.54	0.91	1.30	0.21	0.34
A.A. (post)		18.93 ± 2.25						

HA: hip angle; KA: knee angle; AA: ankle angle; df = 14; *significant value if $p \leq 0.05$; SD: standard deviation; SEM: standard error mean; ^ effect size is large if $d = 0.8$.

implications of rehabilitation on the gait pattern of ACL grade-II injured wrestlers. Our study showed that a designed rehabilitation program is more effective in improving the gait pattern of injured wrestlers. The wrestlers' gait pattern shows significant changes in joint angles at different phases. Our results for joint angles at various gait speeds were not similar to previous researches [21, 22], which indicates that the significance in our dataset and highlights that our participants are representative of a nonhealthy population [22]. This combined dataset of joint angles could be useful for future work to compare with clinical cohorts and investigate the impact rehabilitation programs on body kinematics during walking have on clinical outcomes.

Hip joint flexion/hyperextension changes reported after the rehabilitation program at initial contact 18.87° to 21.33° (13.08%↑), loading response 19° to 14.8° (22.10%↓), midstance 2.33° to 1.20° (48.49%↓), terminal stance 14.06° to 18.20° (29.37%↑), preswing 12.20° to 15.53° (27.79%↑), initial swing/acceleration phase 16.26° to 19.93° (22.50%↑), midswing 23.86° to 23.86° (38.26%↑), and terminal swing 24.60° to 32.93° (33.86%↑) in line with the studies of Winter [23] showed that 20° hip flexion at initial contact, loading response 15°, mid-stance 0°, terminal stance 10-20°, preswing 10-20°, initial swing 20°, midswing 30°, and terminal swing 30° in the normal population. It can be seen that hip joint angles achieved maximum flexion due to rehabilitation program

TABLE 3: Comparison of joints angles mean between pre- and postrehabilitation program at swing phase.

Joint angles	Swing phase	Mean \pm SD	Paired differences			<i>t</i>	<i>p</i> value	Cohen's <i>d</i>
			Mean	SD	SEM			
HA (pre)	Acceleration phase	16.26 \pm 3.21	22.50% \uparrow	3.81	0.98	3.72	0.03*	0.97
H.A. (post)		19.93 \pm 3.08						
KA (pre)		45.00 \pm 6.4	21.46% \uparrow	6.29	1.62	5.94	0.01*	1.52
KA (post)		55.06 \pm 5.09						
AA (pre)		9.06 \pm 2.01	28.69% \uparrow	3.15	0.81	3.18	0.03*	0.82
A.A. (post)		11.66 \pm 2.84						
HA (pre)	Midswing (swing phase)	23.86 \pm 3.96	38.26% \uparrow	6.73	1.73	5.24	0.01*	1.35
HA (post)		33.00 \pm 4.48						
KA (pre)		23.66 \pm 3.67	36.34% \uparrow	5.40	1.39	6.15	0.01*	1.59
KA (post)		32.26 \pm 4.28						
AA (pre)		0.46 \pm 0.51	71.73% \uparrow	0.89	0.23	1.4	0.17	0.37
A.A. (post)		0.80 \pm 0.67						
H.A. (pre)		24.60 \pm 3.15	33.86% \uparrow	5.05	1.30	6.38	0.01*	1.65
H.A. (post)		32.93 \pm 4.14						
KA (pre)		Terminal-swing (swing phase)	5.86 \pm 2.06	94.3% \downarrow	2.26	0.58	9.46	0.01*
KA (post)	0.33 \pm 0.72							
A.A. (pre)	1.26 \pm 0.45		0.00	0.65	0.16	0.00	1.000	00.00
A.A. (post)	1.26 \pm 0.45							

HA: hip angle; KA: knee angle; AA: ankle angle; df = 14; *significant value if $p \leq 0.05$; SD: standard deviation; SEM: standard error mean; \uparrow effect size is large if $d = 0.8$.

TABLE 4: Comparison of spatiotemporal parameter of the study group.

Variables	Mean \pm SD	Paired differences			<i>t</i>	<i>p</i> value	Cohen's <i>d</i>
		Mean	SD	SEM			
Cadence (pre) s/m	95.33 \pm 5.69	10.13% \uparrow	7.78	2.01	4.80	0.02*	1.24 \wedge
Cadence (post) s/m	105.00 \pm 5.16						
Gait velocity (pre)	1.01 \pm 0.12	10.89% \uparrow	0.08	0.02	5.41	0.01*	1.55 \wedge
Gait velocity (post)	1.13 \pm 0.11						
Step length (pre)	61.97 \pm 5.04	5.0% \uparrow	2.89	0.74	4.15	0.02*	1.06 \wedge
Step length (post)	65.07 \pm 6.87						
Stride length (pre)	128.51 \pm 17.62	4.69% \uparrow	5.82	1.50	4.01	0.02*	1.03 \wedge
Stride length (post)	134.54 \pm 18.67						

*Significance value if $p \leq 0.05$; SD: standard deviation; SEM: standard error mean; df: 14; \wedge effect size is large if $d = 0.8$.

18.87° to 21.33° (13.08% \uparrow) around at initial contact with medium effect size at 0° of the gait cycle and reach most extended with high effect size in terminal stance position 14.06° to 18.20° (29.37% \uparrow) and preswing phase 16.26° to 19.93° (22.50% \uparrow) at about 50% of the gait cycle. Standard normal walking, hip ROM approximately 20° flexion to 20° extensions [23]. In the prerehabilitation program, the ACL injured wrestlers recorded hip joint flexion of 18.87° and extensions of 14.06° deviated from the standard norm [16]. The results of the study showed that the rehabilitation program played a significant role in normalizing hip joint ROM as per the standard normal population [23].

Knee joint flexion changes reported after the rehabilitation program of gait in ACL injured wrestlers at initial contact 3.20 to 1.33° (58.43% \downarrow), loading response 18.33° to 15.06° (17.78% \downarrow), midstance 8.93° to 5.20° (41.76% \downarrow), terminal stance 6.86° to 1.80° (73.76% \downarrow), preswing 24.13° to 32.73° (35.64% \uparrow), initial swing 45° to 55.06° (21.46% \uparrow), midswing 23° to 32.26° (36.34% \uparrow), and terminal swing 5.86° to 0.33° (94.30% \downarrow), in line with the study of reported that flexion at initial contact 0°, loading response 15°, midstance 5°, terminal stance 0°, preswing 30°, initial swing 60°, midswing 30°, and terminal swing 0° in normal population [16]. The knee joint standard normal ROM reported

by previous researches from 0° (straight) to 60° flexion [23]. Knee joints reached approximately straight position with high effect size 3.20° to 1.33° at initial contact phase and nearly straight again (6.86° to 1.80°) just before heel off at 40% of gait cycle [24–26].

During the swing phase, knee joint angles reached their maximum flexion with a high effect size of 45° to 55.06° of 70% of the gait cycle. Small knee flexion phases occur at 10 to 20% of the phase of the gait cycle. The study results show significant differences between the pre- and postrehabilitation program on knee joint ROM of the injured wrestlers, and the rehabilitation program played a significant role in normalizing knee joint ROM as per the standard norm reported [23]. The abovementioned results show that rehabilitation programs play a significant role in normalizing knee joint kinematics and gait patterns in ACL injured wrestlers [24–27].

Ankle joint plantar/dorsal flexion significant changes reported after the rehabilitation program at loading response 5.06° to 5.80° (25.09%), midstance 6.06° to 4.8° (20.79%), and initial swing/acceleration phase 9.06° to 11.66° (21.46%), in line with the study [22] showed that flexion at initial contact 0°, loading response 5°, midswing 0°, and terminal swing. Ankle joint angles reach maximum dorsal flexion of 6.06° to 4.8° at midstance phase at about 30% of the gait cycle and reach maximum plantar flexion of 17.73° to 18.93° at preswing phase (60%) with no effect on size. The ankle joint normal range of motion (ROM) is 7° dorsiflexion to 25° plantar flexion as reported [23]. The study results showed that the rehabilitation program played a significant role in the normalization of the ROM of the hip, knee, and ankle joints.

The cadence of gait was showed significant means differences with large effect size. In the current study, cadence significantly increased 10.13% from 95.33 s/m to 105 s/m. Results of the present study, in line with previous studies, have reported normal walking gait cadence 110 s/m by Boston and Sharpe [28], 111 s/m by Davis et al. [19], 117 s/m by Finley and Cody [29], and 112 s/m by Öberg et al. [30]. The abovementioned results showed that the rehabilitation program significantly affected gait cadence toward its normalization as per the standard normal population reported in the studies. Gait velocity was showed statistically significant means differences with large effect size. In the current study, gait velocity significantly increases 10.89% due to rehabilitation program from 1.01 m/s to 1.13 m/s in line with previous studies that have provided normal walking gait velocities 1.37 m/s [28], 1.22 m/s [29], and 1.34 m/s [30]. Gait step length and stride length were showed statistically significant means differences exist large effect size in gait pattern. In the current study, step length increased 5% from 61.97 cm to 65.07 cm, and stride length increased 4.69% from 128.51 cm to 134.54 cm significantly due to rehabilitation program in line with previous studies that have provided normal walking gait length of one stride 148 cm [28], 123 cm [29], and 141 cm [30, 31].

We acknowledge that our study has some limitations. The study was conducted on male professional wrestlers. So, the result of the study cannot be generalized to other

populations. The strength and flexibility of the lower limb muscles and preinjury gait characteristics may influence the gait kinematic following ACL rehabilitation. Due to the nature of the study, the researchers were not able to assess these factors in the current study. Due to ethical reasons, the researchers could not incorporate a control group in the current study. The baseline measurements were taken in the fourth week of rehabilitation after approval from the treating physician and physical therapist. Even though a similar rehabilitation protocol was given to all the participants in the first three weeks of rehabilitation, this might have influenced the baseline measurements. Psychological support and motivation are given to the patient during rehabilitation, and the individual motivation of the patients are important factors that influence the success of the rehabilitation. It is impossible to decide to what extent these factors influenced the rehabilitation outcome in the current study.

5. Conclusion

This study has provided that a 19-week supervised rehabilitation program significantly affected gait velocity, stride length, and step length. We believe this study may have potential implications for clinical practice to influence assessment and treatment methods. These findings show that exercise can increase gait velocity and related parameters in ACL injured persons. Future studies with larger sample sizes and longer follow-ups are required to determine the long-term impact of rehabilitation programs on gait kinematics.

Data Availability

The data set for the result of this study will be available from the corresponding author upon reasonable request.

Ethical Approval

The study was approved by the ethical research committee of Aligarh Muslim University (IRBNo:00/12/ss).

Consent

A written informed consent was taken from all the participants of the study.

Conflicts of Interest

The author certifies that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' Contributions

Conceptualization was done by Mohd Bari, Hussein Alghazal, Shibili Nuhmani, Ahmad Alghadir, Mohd Tafseer, and Amir Iqbal. Data curation was done by Mohd Bari and Hussein Alghazal. Formal analysis was done by Shibili Nuhmani and Amir Iqbal. Methodology was done by Mohd Bari, Hussein Alghazal, Shibili Nuhmani, and

Mohd Tafseer. Resources was done by Ahmad Alghadir and Amir Iqbal. Supervision was done by Ahmad Alghadir and Mohd Tafseer. Writing—original draft was done by Mohd Bari, Hussein Alghazal, Shibili Nuhmani, Mohd Tafseer, and Amir Iqbal. Writing—review and editing was done by Mohd Bari, Hussein Alghazal, Shibili Nuhmani, Ahmad Alghadir, Mohd Tafseer, and Amir Iqbal.

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Supplementary Materials

Supplementary Table 1: the three-week initial rehabilitation protocol used in the study during the acute phase of the injury. (*Supplementary Materials*)

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Research Article

Effectiveness of High Power Laser Therapy on Pain and Isokinetic Peak Torque in Athletes with Proximal Hamstring Tendinopathy: A Randomized Trial

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Athletes such as long-distance runners, sprinters, hockey, and/or football players may have proximal hamstring tendinopathy (PHT). Laser therapy has been shown to be effective in tendinopathies. High power laser therapy (HPLT) is used for the treatment of several musculoskeletal conditions; however, its efficacy on PHT has not been investigated. This study is aimed at examining the effects of HPLT on pain and isokinetic peak torque (IPT) in athletes with PHT. The two-arm comparative pretest-posttest experimental design was used with random allocation of 36 athletes aged 18–35 years into two groups (experimental and conventional group). The experimental group included the application of HPLT for 3 weeks. The conventional group included treatment with a conventional physiotherapy program including ultrasound therapy, moist heat pack, and home exercises for a total of 3 weeks. Pain and IPT of the hamstring muscle were measured before and after the application of the intervention. Pain score decreased, and IPT increased significantly ($p < 0.05$) after application of HPLT, by 61.26% and 13.18%, respectively. In the conventional group, a significant difference ($p < 0.05$) was observed in pain scores only, which decreased by 41.14%. No significant difference ($p > 0.05$) was observed in IPT in the conventional group. When HPLT was compared with conventional physiotherapy, a significant difference was found in pain scores only. HPLT for 3 weeks was found to be effective in improving pain in athletes with PHT. However, no significant difference was found between HPLT and conventional physiotherapy (US, moist heat, and home exercises) in improving the IPT of the hamstring muscle.

1. Introduction

Proximal hamstring tendinopathy (PHT) is tendinopathy of the semimembranosus and/or biceps femoris/semiotendinosus complex [1]. This condition is common among middle and long-distance runners, athletes who perform more sagittal plane activities (e.g. sprinters), and individuals including nonathletes, who routinely perform activities like leaning forward, sitting for

long periods, excessive static stretching, squatting, lunging, or changing the direction of running [2–4]. These activities compressively load the hamstring tendon at its proximal attachment. The main symptom of PHT is deep localized pain in the lower gluteal region near the ischial tuberosity, which may or may not radiate to the posterior thigh [5]. This pain often worsens during or after sitting, squatting, lunging, or running [4]. This condition may be present unilaterally or bilaterally [4].

Surgery is indicated for recalcitrant cases, and most cases are treated conservatively. Physical therapy treatment of PHT focuses on activity modification, effective tendon loading including eccentric training, addressing contributing biomechanical deficiencies, and electrotherapy including laser therapy. Two types of laser therapy are used as a part of physical therapy management: low power laser therapy (LPLT) which has an output power of less than 0.5 watts and high power laser therapy (HPLT) which has an output power of 0.5 watts or greater.

Previous studies have shown the efficacy of laser therapy in the treatment of tendinopathy. The study by Stergioulas et al. [6] showed that LPLT when added to an eccentric exercises regimen speeds up clinical recovery in patients with chronic Achilles tendinopathy. HPLT produces more powerful beams (power > 0.5 watts) and has longer laser emission intervals and shorter laser emission time in comparison to LPLT; thus, the deeper areas can be irradiated in a short time with HPLT [7, 8]. HPLT also creates heat on the skin surface due to its higher power density.

A recent systematic review by Taradaj et al. indicated the effectiveness of HPLT in decreasing musculoskeletal pain [9]. Other studies also showed that HPLT affects the repair of diabetic foot ulcer trauma [10], gonitis [11], shoulder pain [8], chronic low back pain [12, 13], chronic neck pain [14], and pain in the knee osteoarthritis [15, 16]. HPLT can also remove exudates through increased metabolism and blood circulation, thus helping in the quick absorption of edema [8]. Few physiological changes occur in tissues as a result of HPLT which do not occur in the case of a conventional physiotherapy program for tendinopathy including ultrasound therapy, moist heat pack, and eccentric hamstring exercises. HPLT radiation causes slow and small light absorption by the chromophores. The absorption by chromophores occurs with diffuse light in all directions, not with concentrated light, which is called the scattering phenomenon. This leads to the phenomenon of tissue stimulation (photobiology effects) and an increase in the mitochondrial oxidative reaction and DNA, RNA, or adenosine triphosphate production (photochemistry effects) [17].

To the best of our knowledge, no study has compared the effects of HPLT with conventional physiotherapy programs in athletes suffering from PHT. Therefore, this study is aimed at assessing the effects of HPLT on pain and isokinetic peak torque (IPT) of hamstring muscle in PHT patients. We hypothesized that HPLT is effective in reducing pain and improving the IPT of hamstring muscle in comparison to conventional physiotherapy program in patients with PHT. In the present study, the conventional physiotherapy program included ultrasound therapy [18], moist heat pack [19], and eccentric hamstring exercises [20].

2. Materials and Methods

2.1. Study Design. We used a two-arm parallel pretest-posttest experimental research design with random allocation of subjects into two groups (experimental and conventional group).

2.2. Participants

2.2.1. Sample Size Calculation. Before conducting the study, the sample size was calculated using the software G*Power 3.1.9.4. The pain score data from the study of Elsodany et al. [21], who used high intensity laser therapy on patients with rotator cuff tendinopathy, was used to calculate the effect size. Based on $\alpha = 0.05$, power $(1 - \beta) = 0.95$, and effect size $d = 3.89$, the minimum sample size was calculated to be 5 (including 12% drop out) in each group. Therefore, due to the availability of patients, a total of 36 participants aged 18-35 years were recruited in the present study (Table 1) (Figure 1).

2.2.2. Inclusion and Exclusion Criteria. The selected participants were diagnosed with PHT by a consultant physiotherapist. They were athletes, who took part in national level competitive track and field events more than once, with subacute onset of the buttock or posterior thigh pain for less than a year, tenderness in the ischial tuberosity, tightness deep of the hamstring muscle, deeper hip flexion such as squatting or sitting for long periods, repeated knee extension, and resisted knee flexion increased their pain. Other differential diagnoses like radiation due to lumbosacral radiculopathy, piriformis syndrome, or ischiofemoral impingement were ruled out by an expert physiotherapist. Participants who had a recent history of trauma to the posterior thigh, a musculoskeletal disorder or deformity of the ipsilateral lower extremity, lumbar prolapsed intervertebral disc, history of or currently taking pain medications, cardiovascular diseases, malignant tumor in the lower extremity, phlebitis, blood disorders, or tattoo over or around the area of treatment were excluded from the study because these conditions will affect the application of laser therapy or exercise of hamstring muscles. The repeated movement of the lumbar spine, sacroiliac joint provocation tests, SLR, and slump test did not aggravate their pain.

2.2.3. Randomization of Participants and Blinding. The selected participants were randomly assigned to an experimental and a conventional group using the lottery method and <http://randomization.com/> website with 18 participants in each group. The participants and outcome assessor were kept blind to the allocation.

2.2.4. Setting, Ethical Statement, Clinical Trial Registration, and Informed Consent. The study was carried out in the clinical setting of the University. The present study conformed to the "The Code of Ethics of the World Medical Association (Declaration of Helsinki)" and was approved by the ethical committee of the Institutional Review Board (file ID: RRC-2021-07; date of approval: 9 March 2021). This study had been retrospectively registered on Protocol Registration and Results System (PRS) clinicaltrials.gov (ID: NCT05100394) on 31st October 2021. The risks and benefits of the study were discussed with each participant before the start of the study, and informed consent was obtained from all participants involved in the study.

TABLE 1: Demographic data, baseline, and postintervention values of outcome variables in both groups ($n = 18$ each group), Shapiro-Wilk test, and independent t -test p values for baseline values.

	Experimental group	Conventional group	Shapiro-Wilk p value	Independent t -test p values
	Mean \pm SD	Mean \pm SD		
Age (years)	22.61 \pm 1.68	22.39 \pm 1.81		
Height (cm)	162.83 \pm 9.85	162.22 \pm 7.47		
Weight (kg)	58.78 \pm 4.91	59.44 \pm 3.95		
BMI (kg/m ²)	22.30 \pm 2.58	22.70 \pm 2.38		
Pre_NPRS (points)	6.17 \pm 1.42	6.61 \pm 0.97	0.004*	0.283
Pre_IPT (Nm)	251.17 \pm 78.00	236.89 \pm 40.34	0.254	0.495
Post_NPRS (points)	2.39 \pm 1.03	3.89 \pm 0.96		
Post_IPT (Nm)	284.28 \pm 109.23	240.44 \pm 44.03		

*Significant. SD: standard deviation; BMI: body mass index; NPRS: numeric pain rating scale; IPT: isokinetic peak torque.

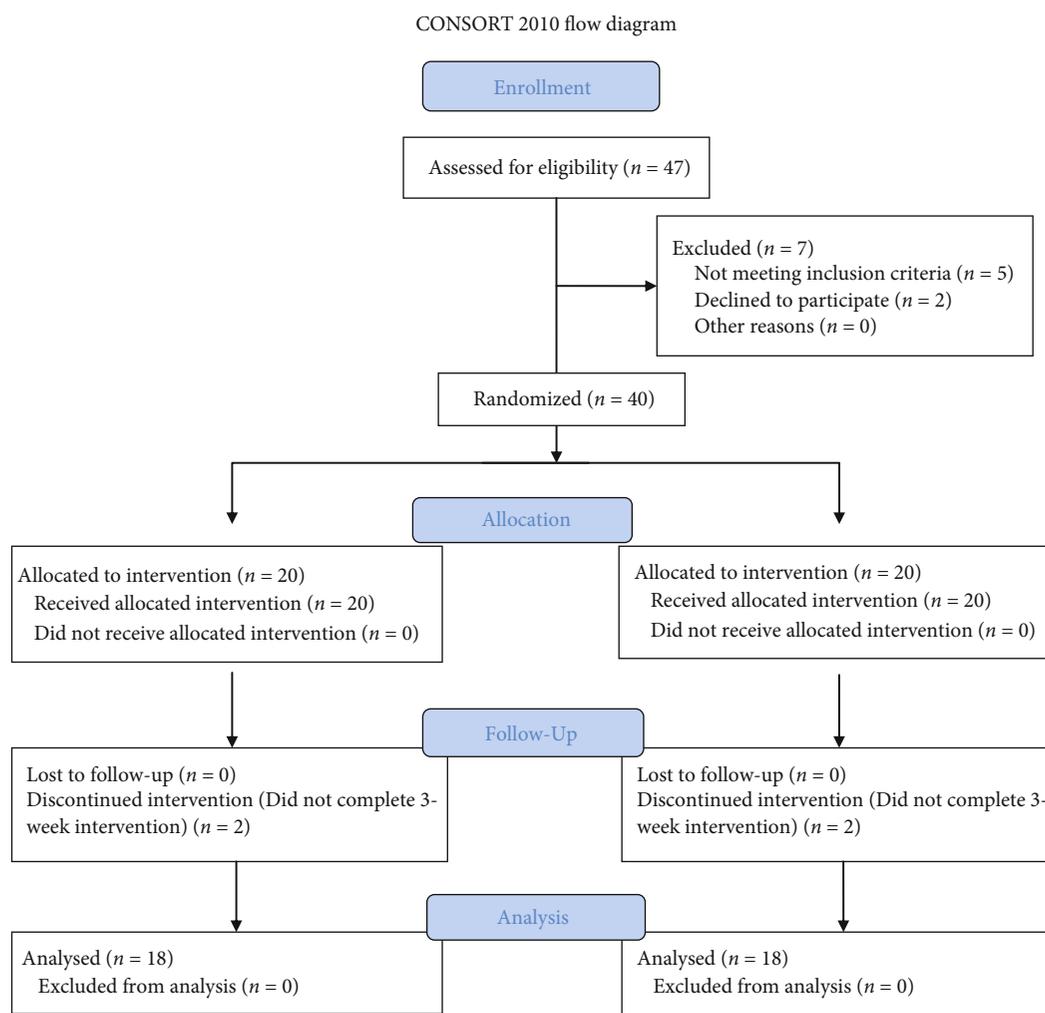


FIGURE 1: Consolidated Standards of Reporting Trials (CONSORT) flow chart of the study showing the recruitment of participants.

2.3. *Outcome Measures.* The following are the outcome measures:

- (i) Isokinetic peak torque of the hamstring muscle, assessed using an isokinetic dynamometer
- (ii) Pain, assessed using the NPRS (Numeric Pain Rating Scale) score

2.4. *Instrumentation.* The following are the instruments used:

- (i) LASER equipment (LiteCure, USA) [22]
- (ii) Isokinetic dynamometer (Easy Tech Biomed, India) [23]
- (iii) Ultrasound therapy equipment (Physiocare, India) [24]
- (iv) Moist heat pack [25]

2.5. *Study Protocol.* The study consisted of three phases:

2.5.1. *Preintervention Assessment.* Baseline NPRS (Numeric Pain Rating Scale) and IPT of hamstring muscle were measured before the start of the intervention. (i) The Numeric Pain Rating Scale (NPRS) is a subjective measure in which participants are asked to rate their pain on a scale of 0–10, where 0 represents “no pain” and 10 represents “worst pain imaginable” [26, 27]. The participants were asked to rate their pain on the NPRS scale. (ii) In the IPT of hamstring muscle, participants were asked to sit on the isokinetic dynamometer chair. Shoulders, chest, and hips were strapped to prevent unnecessary movements. The cuff of the dynamometer arm was attached near the ankle of the ipsilateral side. The back seat of the dynamometer was tilted 75–85° backward. The angle on the dynamometer was set from 0° (full knee extension) to 90° knee flexion, and the speed was selected at 90°/s. Before taking the readings for baseline measurement, each participant was asked to practice the movement thrice with submaximal effort. The participants were then asked to bend the knee with maximum effort. A total of three measurements were taken, and the highest reading was used for data analysis [28].

2.5.2. *Intervention*

- (i) Experimental group: the participants were made to lie prone, and the area around the ischial tuberosity was uncovered. Participants were asked to remove the excess hairs if present. HPLT was administered as monotherapy, in the area of ischial tuberosity where the hamstring tendons originate. The following parameters were used in laser equipment: average output power: 5 watts, dosage: 50 joules/cm², laser wavelength: 980/810 nm, total treatment area: 6 cm × 6 cm = 36 cm², and total energy: 50 × 36 = 1800 joules. Depending upon the total area to be treated and average output power and the total energy to be delivered, the total treatment time was calculated to be 6 minutes [29]. Therefore, HPLT

was applied in continuous mode for a total of 6 minutes. HPLT was administered 3 days a week for a total of 3 weeks [30].

- (ii) Conventional group: conventional physiotherapy treatment was administered that included ultrasound therapy (continuous mode, 1 MHz, 2 W/cm² for 5 minutes) in the area of the ischial tuberosity, moist heat packs (10 minutes) [31] over the ipsilateral buttock and posterior thigh region, and home exercises. The US and moist heat pack were applied in the prone position. Home exercises included Nordic hamstring exercise (eccentric hamstring contractions) [1]—2 sets of 5 repetitions. At home, participants were asked to stabilize their feet either under furniture/immovable objects or ask someone to hold their feet firmly. Then, they have to slowly lower their body from a vertical position towards the ground while maintaining a straight line from knees to head. Participants were allowed to use their hands to catch themselves if they cannot control the body movement from their knees. This treatment regimen was also administered 3 days a week for a total of 3 weeks [5].

2.5.3. *Postintervention Assessment.* After completion of the intervention, the NPRS score and IPT of the hamstring muscle were again measured similarly to the preintervention assessment.

2.6. *Data Analysis.* The baseline values of NPRS and IPT were compared between both groups using the independent sample *t*-test, which revealed no significant difference ($p < 0.05$); therefore, both groups were comparable for both variables. The Shapiro-Wilk normality test was performed to assess the normal distribution of the baseline NPRS and IPT values. The Shapiro-Wilk test revealed that the distribution of baseline NPRS values was not normal ($p < 0.05$); therefore, for further with-in and between-group comparison, nonparametric tests were used. Wilcoxon’s signed-rank test and Mann–Whitney *U* test were performed for within and between-group comparison, respectively. The confidence interval was set at 95%; $p < 0.05$ was considered significant (Table 2).

3. Results and Discussion

3.1. Within-Group (Wilcoxon’s Signed Rank Test) Analysis

3.1.1. *For the Experimental Group.* There was a significant difference ($p < 0.05$) in both variables (NPRS scores and IPT values) after the application of the intervention. NPRS scores decreased by 61.26%, and IPT increased by 13.18% after HPLT.

3.1.2. *For the Conventional Group.* There was a significant difference ($p < 0.05$) in the NPRS scores after application of intervention; however, for IPT there was no significant difference ($p > 0.05$). NPRS scores decreased by 41.14%, and IPT increased marginally by 1.49%.

TABLE 2: Within-group (Wilcoxon's signed-rank test) and between-group (Mann-Whitney *U* test) comparisons of outcome variables.

	Within-group, <i>p</i> values		Between-group, <i>p</i> values	
	Experimental group	Conventional group	Post_NPRS	Post_IPT
Post_NPRS-Pre_NPRS	≤0.001*	≤0.001*	Post_NPRS	≤0.001*
Post_IPT-Pre_IPT	0.028*	0.662	Post_IPT	0.113

*Significant. NPRS: numeric pain rating scale; IPT: isokinetic peak torque.

3.2. Between-Group (Mann-Whitney *U* Test) Analysis

3.2.1. *For Post_NPRS Scores.* There was a significant difference ($p \leq 0.001$) in post_NPRS scores between both groups.

3.2.2. *For Post_IPT Values.* There were no significant differences ($p = 0.131$) for post_IPT values between the two groups.

The results of the present study revealed that HPLT is effective in improving pain scores and hamstring IPT in athletes with PHT; however, compared to the conventional group (US, moist heat, and home exercises), a significant difference was found only in NPRS scores. With the application of HPLT, NPRS scores decreased and IPT increased. Conventional physiotherapy (US, moist heat, and home exercises), treatment also decreased NPRS scores; however, IPT remained unchanged. HPLT was more effective in reducing pain than the conventional physiotherapy program. With conventional physiotherapy treatment, no improvement in IPT was observed, perhaps because patients performed eccentric Nordic hamstring exercises, which may have put a strain on the hamstring tendons and prevented the muscle from being unloaded.

In earlier studies, laser therapy was found to be effective in relieving pain associated with several conditions such as knee injuries, shoulder pain, fibromyalgia, chronic arthritis, carpal tunnel syndrome, and tendonitis [32, 33]. A systematic review reported that acute neck pain decreased immediately after laser therapy and up to 22 weeks after complete treatment [34].

At different levels, several physiological effects of laser therapy have been reported that produce analgesic effects. At the tissue level, laser causes reduction of histamine and bradykinin release from the injured tissues [35], increases the pain thresholds [36], and reduces the secretion of substance P from peripheral nociceptors [37]. Laser therapy slows the transmission of pain signals by decreasing the conduction velocity and increasing the latency of sensory nerves, which in turn inhibit A δ - and C fiber transmission [38]. Furthermore, laser treatment inhibits pain centrally, by increasing the secretion of endogenous opioids (β -endorphin) [39]. Specifically, HPLT application has been found to assist in pain relief [15], recovery from nerve paralysis [40], and wound repair [41]. It was also used to provide relief from shoulder pain [8], low back pain [12], and chronic ankle pain [42]. HPLT has not been found to reduce inflammation, but it had an analgesic effect on nerve endings [43, 44].

The analgesic effects of HPLT obtained in the present study can be explained by two mechanisms. If it is used in pulse mode, it has analgesic effects on nerve endings [43,

44]. This mode of application inhibits nociceptive stimulation and produces low heat. If a continuous mode is used, then photochemical and photothermic effects are produced in deeper tissues. These effects increase vascular permeability, blood flow, and cell metabolism which result in the washing out of cytokines that justifies pain reduction [45].

In our study, HPLT resulted in improvement in IPT of the hamstring muscle. Not many studies have examined the effects of HPLT on muscle strength. A study by Santamato et al. reported improved muscle strength of shoulder joints affected with subacromial impingement syndrome after application of HPLT [8]. Some studies have reported no significant improvements in muscle performance with LPLT when combined with physical exercises [46, 47]. However, several other studies have reported improved muscle performance and reduced fatigue as a result of LPLT [47–49]. Lopes-Martins et al. reported that muscle damage and fatigue caused by tetanic contractions in the rat model are seemed to be reduced by LPLT [50]. In the present study, an increase in IPT after the application of HPLT may be due to reduced pain intensity. When pain intensity is reduced, then participants will be able to exert more force on the hamstring muscle.

In the present study, laser therapy was used as a monotherapy because its clinical benefits were reported when used alone [13, 51–54] and also when used in combination with stretching and regular exercises in orthopedic conditions [55, 56]. The clinical implications of the present study include the use of HPLT as an effective treatment modality for athletes with PHT.

The present study also has some limitations. No control group was included in the study where participants did not receive any treatment. Therefore, the reduction in NPRS scores may be due to time travel or avoidance of strenuous activities for 3 weeks and may not be due to the intervention applied. Moreover, the experimental group did not include the conventional physiotherapy treatment; therefore, it cannot be concluded that the improvements observed in the experimental group were additional effects of HPLT. Another limitation is the lack of long-term follow-up. The athletes were not assessed after their return to the sport. It may be possible that the improvement in pain and maximum torque was short-lived. Therefore, future research is needed that includes control group and long-term follow-up. In addition, only male athletes were recruited in the study. Therefore, the results of this study cannot be generalized to female athletes. More research is needed to recruit female athletes with large sample size. Future research should also compare HPLT with LPLT to examine which one is more effective for pain reduction in patients with PHT.

4. Conclusions

HPLT was effective in improving pain in athletes with PHT in comparison to conventional physiotherapy program (US, moist heat, and home exercises); however, due to the lack of a control group, the improvement cannot be solely attributed to HPLT. No significant differences were found between HPLT and conventional physiotherapy in improving hamstring IPT, although hamstring IPT increased with HPLT.

Data Availability

The data presented in this study are available in the supplementary material (available here).

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Supplementary Materials

Data associated with the study are submitted as supplementary materials. (*Supplementary Materials*)

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Research Article

Effectiveness of Interventions to Prevent Musculoskeletal Disorders among District Hospital Nurses in Vietnam

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Background. Nurses are one of the population groups with the highest prevalence of musculoskeletal disorders (MSDs). Preventive measures in Vietnamese hospitals on the job have not been proposed to study their effectiveness due to barriers related to the lack of knowledge about MSDs by health care administrators and the lack of human resources with expertise in MSD management in hospitals. **Objectives.** This study is aimed at evaluating the effectiveness of basic interventions (education, physical exercise) to prevent MSDs among district hospital nurses in Vietnam. **Material and Methods.** A quasi-experimental study was carried out before/after over a period of one year among two groups of nurses, one receiving the intervention ($n = 162$) and the other the control group ($n = 128$). The intervention includes 3 components: training on MSDs, ergonomics training, and instructions for physical exercise. The pre- and postintervention assessment tools included the Modified Nordic, Quality of Life Enjoyment and Satisfaction Short-Form (Q-LES-Q-SF), and the Kessler Psychological Distress Questionnaire (K6). A generalized estimating equation analysis was performed to assess the difference between the two groups at two points in time (before and after the intervention) on some indicators (prevalence of MSDs in the last 12 months and 7 days, score for quality of life and psychological distress). **Results.** There was a significant difference of the test on the prevalence of MSDs in the last 7 days between the 2 groups before and after the intervention with the p value = 0.016. This difference occurred in 4 anatomical sites: neck, shoulder/upper arm, wrists/hand, and lower back, with p values being 0.013, 0.011, 0.038, and 0.009, respectively. **Conclusions.** The intervention measures are probably effective in reducing the prevalence of MSDs at 4 anatomical sites in the last 7 days. More in-depth studies are needed with a combination of measures over a longer period of time to obtain stronger evidence of interventions.

1. Introduction

The global nursing workforce is 27.9 million and is the largest occupational group in the health sector, accounting for approximately 59% of health professions [1]. In this profession, nurses encounter a variety of occupational health problems such as biological hazards (hepatitis B, hepatitis non-A non-B, tuberculosis, AIDS...), chemical hazards (cytotoxic drugs, anesthetic agent, antibiotics, formaldehyde, ethylene oxide...), psychosocial hazards (stress, shift work, suicide...), and physical hazards (needle stick injury, back pain and back

injuries, radiation...) [2], especially musculoskeletal disorders (MSDs) with the prevalence of 71.9% [3]. Many studies have shown that the nursing profession is influenced by many environmental, working conditions, mental factors, and even personal factors that can contribute to MSDs [4, 5]. A review of the literature by Soyler and Ozer demonstrated that cumulative trauma and repetitive tasks included lifting, transferring, or repositioning patients; prolonged standing and also awkward postures (bending, lengthen) were highly associated with MSDs in nurses. These work-related health problems were also significantly associated with age, sex, BMI, type of

service worked, shift work, and hospital work. Studies have also shown that MSDs are mostly seen in operating room and intensive care nurses [6].

In developed countries around the world, there are many studies on MSD among nurses. On the contrary, in developing countries, including Vietnam, there are few published data. Several recent studies in Vietnam showed the high prevalence of MSDs in general [7] and of multiple musculoskeletal symptoms (MMS) [8] with the abundance of risk factors in hospital nurses. Another study has shown a negative impact of MSDs at multiple sites on the quality of life of nurses [9].

From that, it is clear that the burden of MSDs on nurses in Vietnam is large. This burden will affect their health and quality of life, thereby affecting the quality of their patient care. Therefore, it is necessary to take preventive measures systematically and comprehensively to reduce this burden. However, in Vietnam at present, the prevention of MSDs in nurses still faces many difficulties and barriers in implementation. There are many causes for this situation. Firstly, the field of occupational health in Vietnam in general has not received much attention and research. Second, occupational-related MSDs have not been included in the list of covered occupational diseases in Vietnam [10]. Third, there is a lack of suitable scientific evidence from studies on the feasibility and effectiveness of MSD interventions in nurses. For these reasons, the feasibility of intervention implementation is limited due to not being able to convince the experts, organizers, or even the trust of nurses about the effectiveness of interventions. A recent study by Khue et al. has shown that the lack of knowledge on MSDs by health care administrators inside and outside the hospitals and the lack of human resources with expertise in MSD management are important barriers to the implementation of an MSD prevention program in Vietnamese hospitals [11].

To address these issues, it is necessary first of all to obtain appropriate scientific evidence from studies on the effectiveness of preventive measures against MSDs in Vietnamese nurses.

In the context that the field of occupational health in Vietnam is still underdeveloped, and resources (human and material) for activities in this field are limited, the question arises as can simple and highly feasible interventions improve MSDs in nurses? If yes, how effective are those measures? In other words, what is the effect of basic interventions on MSDs on nurses? From there, it is the basis for further research in the future or for suggestions and recommendations for leaders in hospitals about the importance of preventing MSDs for their staff. This is the main reason why this study was conducted.

Haiphong is one of the largest cities in Vietnam with a very high population density (1,274/km²), but human resources for the health sector are short of supply with 7.7 doctors and 17.6 nurses per 10,000 inhabitants [12]. Therefore, the work pressure of medical personnel, especially nurses, is very high to meet the high demand for medical care of people. The evaluation of health risks to medical personnel and the effectiveness of preventive measures will contribute to improving their health status, thus improving the quality of health care services.

This study will answer whether the basic interventions (education, physical exercise) to prevent MSDs among district hospital nurses in Haiphong, Vietnam, are feasible, effective, or not and how effective are they?

2. Materials and Methods

A quasi-experimental before/after study was carried out over a period of one year between two groups of district hospital nurses, one receiving the intervention (intervention group) and the other being the control group.

The total number of district public hospitals in Haiphong is 15, divided into 2 types: 8 rural district hospitals (located in rural areas) and 7 urban district hospitals (located in urban areas).

Calculation of the number of subjects is needed.

The minimum sample size per group for a before/after intervention study was calculated using the formula [13].

$$n = 2(Z_{\alpha/2} + Z_{\beta})^2 \frac{p(1-p)}{(p_1 - p_2)^2}, \quad (1)$$

where α is 0.05 $\rightarrow Z_{\alpha/2}$ is 1.96; β is 0.10 $\rightarrow Z_{\beta}$ is 1.28; p_1 is the expected prevalence of MSDs in the control group = 81% or 0.81 (depending on the results of a previous study) [11]; p_2 is the expected prevalence of MSDs in the case group after the intervention = 60% or 0.60; p is the pooled prevalence = $(p_1 + p_2)/2 = (0.81 + 0.60)/2 = 0.705$.

The minimum sample size for each group was 99 nurses.

2.1. Sampling Technique. First, a list of nurses the number of available (who have a nursing degree, who have worked in the hospital for at least 12 months immediately prior to the start of the study) was established for each hospital. The number of nurses in each hospital was divided into 2 thresholds, either less than 45 or greater than 80 (see Table 1). In addition, to obtain an appropriate sample regarding the hospital type, four hospitals were selected (two hospitals per group, and each group contains one urban district hospital and one rural district hospital). Furthermore, to the guarantee the minimum sample size per group (99 nurses), only hospitals having 80 nurses or more were selected. Therefore, there are nine hospitals that meet this condition, including six rural district hospitals (An Duong, An Lao, Kien Thuy, Tien Lang, Thuy Nguyen, and Vinh Bao) and three urban district hospitals (Hong Bang, Le Chan, and Ngo Quyen). These 9 hospitals were divided into 2 branches (depending on the type of hospital). Then, a hospital per branch was randomly selected (random draw) for each group. The two hospitals, Le Chan (urban district) and An Lao (rural district), were finally chosen for the intervention group, while the control group included hospitals in Ngo Quyen (urban district) and Vinh Bao (rural district) (see Figure 1).

The total number of nurses in the two hospitals that received the intervention was 210, of which 197/210 agreed to participate. However, at the time of the pre- and post-intervention evaluation, only 162/197 nurses had fully participated in the evaluation. The reasons why the 35 nurses did

TABLE 1: Distribution of nurses by district hospital.

N°	Hospital	Hospital type	N
1	An Duong	Rural district	112
2	An Lao	Rural district	125
3	Cat Ba	Rural district	37
4	Cat Hai	Rural district	22
5	Duong Kinh	Urban district	45
6	Do Son	Urban district	33
7	Hai An	Urban district	30
8	Hong Bang	Urban district	87
9	Kien An	Urban district	45
10	Kien Thuy	Rural district	83
11	Le Chan	Urban district	85
12	Ngo Quyen	Urban district	130
13	Tien Lang	Rural district	85
14	Thuy Nguyen	Rural district	230
15	Vinh Bao	Rural district	130
Total			1 279

not participate are maternity leave (18/35), training (14/35), and change of job or work position (3/35).

For the control group, the total number of nurses in the 2 hospitals was 260 people, of which 138 agreed to participate. During the survey, 128/138 fully participated from start to finish. The reasons given were similar to those of the intervention group: maternity leave [6], training [3], and change of job or position [1].

2.2. Research Instruments. The pre- and postintervention evaluation questionnaires included as follows:

- (1) *A Sociodemographic Questionnaire.* Collecting some personal information, such as gender, age, height, weight, seniority, and personal history of musculoskeletal diseases throughout their life
- (2) *The Standardized Nordic Questionnaire.* This questionnaire, which was developed by Kuorinka et al. in 1987 [14], evaluates the trouble (ache, pain, discomfort) of the locomotive organs at nine different positions on the body (neck, shoulder/upper arm, elbow/forearm, wrist/hand, upper back, lower back, hip/thigh, knee/lower leg, and ankle/foot) during the last 12 months and during the last 7 days and the impact of those problems on the work and life of the respondent
- (3) *The Short Form of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q-SF).* This was developed by Stevanovic et al. based on the original long-form Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) developed by Endicott et al. in 1993 [15]. The short form, with 14 elements, evaluates general enjoyment and satisfaction with physical health, mood, work, household activities, leisure activities, social and family relation-

ships, daily functioning, sexual life, economic status, and general well-being. The questions were rated on a five-point scale (from “very poor” to “very good”). The scoring of the Q-LES-Q-SF involves all of the 14 items to yield a total score (range from 14 to 70) with higher scores indicating better quality of life and vice versa

- (4) *The Kessler Psychological Distress Scale (K6).* This short questionnaire consists of six questions about a person’s emotional state (nervous, hopeless, restless, or fidgety, so depressed that nothing can cheer you up, everything is an effort, and worthless) [16]. Each question is scored from 0 to 4 (from “None of the time” to “All of the time”). The total score is calculated by calculating the score from the six questions, with total ranging from 0 to 24. A higher score indicates a more serious level of psychological distress

These questionnaires were used by our researchers for direct interviews ranging from 30 to 45 minutes in length before and after intervention.

For the intervention period, the following tools related to MSDs and preventive measures were used:

- (i) Presentations on MSDs, ergonomics, and physical exercise
- (ii) Documents and training material
- (iii) Leaflets, posters, and illustrations
- (iv) Instructional videos

2.3. Intervention Content and Implementation. The intervention contents were compiled based on the recommendations of the World Health Organization (WHO) on the prevention of MSDs on the workplace [17] and on the prevention of MSDs on the hospital sector of the General Directorate of Labor Humanization in Belgium [18] and the Guideline for ergonomics for the prevention of MSDs of the Occupational Safety and Health Administration, US Department of Labor [19]. The intervention includes 3 components:

- (i) *Training on MSDs.* Providing knowledge on MSDs such as definitions, symptoms, consequences, and preventive measures. This was a presentation with MSDs that lasted about 30 to 45 minutes
- (ii) *Ergonomics Training.* Providing knowledge of ergonomics, showing nurses how to correctly perform professional operations in patient care such as wound care, patient lifting, support, and transfer, as well as when handling medical equipment such as stretchers, wheelchairs, beds, trolleys... This component includes two forms: a presentation on ergonomics (30 minutes) and a practical session on handling and correct postures (30 to 45 minutes)

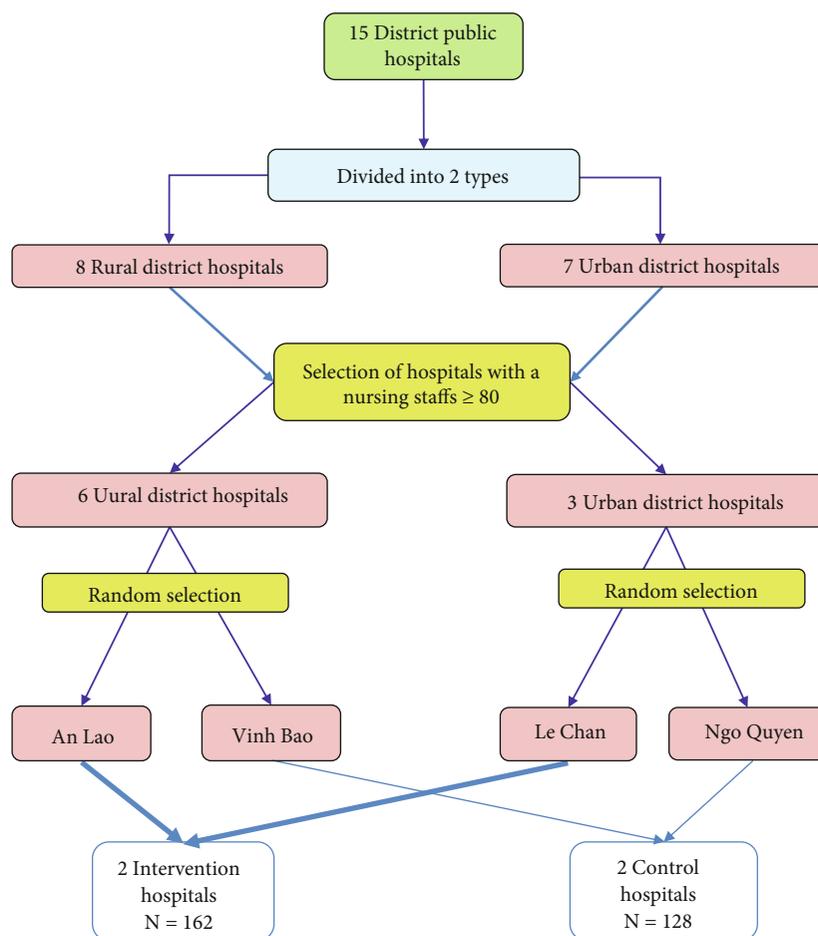


FIGURE 1: Flow chart of hospital selection.

(iii) *Instructions for Physical Exercises.* Stretching exercises (or relaxation), musculation training exercises, and back mobilization exercises. This is a practical session lasting about 30 minutes

Nurses from the 2 intervention hospitals were trained for the first time during the first week of the first month of the intervention period. This training included 2 sessions:

- (i) The first session, lasting about 60 to 75 minutes, contains two presentations (one on MSDs and the other on ergonomics)
- (ii) The second session also lasts from 60 minutes to 75 minutes, including 2 practice contents on ergonomics and physical exercise

These contents were repeated in the first weeks of the third and sixth month of the intervention period. Therefore, the intervention group received a total of three times of training. The last six months were the observation period. The aim was to see if the nurses were carrying out the training content correctly and fully. Leaflets, posters, and illustrations were introduced, distributed, and displayed in departments/services throughout the one-year intervention period.

2.4. Statistical Analysis. The SPSS version 22.0 software was used for data analysis. A chi-square test for qualitative variables and a Student's *t*-test for continuous variables were used to compare some characteristics between the intervention and control groups. A generalized estimating equation (GEE) analysis was performed to assess the difference between the two groups (intervention and control) at two points in time (before and after the intervention) on some indicators (prevalence of MSDs during 12 months, over the last 7 days, the score for quality of life and psychological distress), in the interaction of two variables (before/after intervention and intervention Yes/No), and adjusted for age, sex, BMI, and history of musculoskeletal diseases to control the impact of these variables on the model. The level of significance was set at a *p* value of less than 0.05.

3. Results

3.1. Profiles of Participants at Baseline. In this study, we carried out an intervention (full participation from start to finish) for 162 nurses and had a total of 128 nurses in the control group. Table 2 shows that some general characteristics of age, sex, BMI, and history of musculoskeletal disease between the intervention group and the control group at baseline were quite similar. This has been shown by the *p*

TABLE 2: Profiles of participants at baseline for the intervention and control group.

Characteristics	Intervention group, $n = 162$	Control group, $n = 128$	p
Age (year) ($M \pm SD$)	33.6 ± 6.8	34.4 ± 6.6	0.321*
Women ($n, \%$)	144 (88.9)	108 (84.4)	0.258**
BMI ($n, \%$)			
< 18.5	9 (5.6)	12 (9.4)	
18.5-24.9	144 (88.9)	109 (85.2)	0.459**
≥ 25	9 (5.6)	7 (5.5)	
Seniority			
Less than 5 years	44 (27.2)	17 (13.3)	
From 5 to 10 years	43 (26.5)	45 (35.2)	
From 10 to 15 years	40 (24.7)	40 (31.3)	0.054**
More than 15 years	35 (21.6)	26 (20.3)	
Have a history of musculoskeletal diseases ($n, \%$)	38 (23.5)	22 (17.2)	0.191**

*Student's t -test with two independent samples. **Chi2 test with two independent samples.

values in the Student's t -test and the Chi2 test, both higher than 0.05 (see Table 2).

3.2. Effectiveness of Interventions in the Prevalence of MSDs.

To assess the effectiveness of the intervention, we used generalized estimating equation analysis. The purpose of this analysis was to assess the difference between the two groups (intervention and control) at two time points (before and after intervention) on some study indicators in the interaction of two variables (intervention before/after and intervention yes/no) and adjusted for age, sex, body mass index, and history of musculoskeletal diseases to control for the impact of these variables on the model.

Regarding impact on the prevalence of MSDs, there was a significant difference of the GEE's test on the prevalence of MSDs in the last 7 days between the 2 groups before and after the intervention with the p value = 0.016. In more detail, the prevalence of MSDs in the last 7 days in the control group was 1.9 times higher than in the intervention group after the intervention. For the prevalence of MSDs in the last 12 months, the test did not provide significance by showing that the p value is equal to 0.059 (see Table 3).

In Table 3, the results of the test found positive changes in the prevalence of MSDs in the last 7 days. We would therefore like to know where these changes occur among the 9 anatomical sites studied. Using the same analysis, we found significant changes in the test between the 2 groups at the 4 anatomical sites: neck, shoulder/upper arm, wrists/hand, and lower back with p values lower than 0.05 (0.013, 0.011, 0.038, and 0.009, respectively) (see Table 4). This means that the intervention measures are probably effective in reducing the prevalence of MSDs at these 4 anatomical sites.

For the remaining anatomical sites, this analysis showed that the p values were greater than 0.05.

3.3. Effectiveness of Interventions in Quality of Life and Psychological Distress Scores. It is the same explanation for the quality of life and the psychological distress; Table 5

has shown that there is no significant change of the GEE's test on the score of quality of life and on the score of psychological distress between the 2 groups before and after the intervention with p values greater than 0.05 (0.344 and 0.789, respectively) (see Table 5).

4. Discussion

This is a quasi-experimental before/after study to assess the effectiveness of interventions by measuring the prevalence of MSDs, quality of life, and psychological distress scores before and after the implementation of the intervention for the 2 groups (intervention and control) to compare each other. According to the methodological guide concerning quantitative methods for evaluating interventions aimed at improving the practices of the French High Authority of Health (Haute Autorité de Santé Française (HAS)), this design has certain limitations. The results of a before/after study may overestimate the effects of interventions due to preexisting trends in improvement or variations related to another cause than intervention [20]. Therefore, to limit these drawbacks, on the one hand, to create a contemporary controlled site, the hospitals were divided into two groups representing two different types of hospitals (rural and urban districts). On the other hand, a random selection step (randomized) was applied to select 2 intervention hospitals and 2 control hospitals among the 2 hospital groups above (described in detail in the sampling technique section). This work made the characteristics between the two hospital groups participating in the study relatively similar and comparable. In addition, thanks to the choice of group (hospitals), the risk of contamination (occurs between nurses if the intervention and the control group occur in the same hospital—the learning effect of colleagues) did not exist. However, this trial exposes to the risk known as the Hawthorne effect [21]: the nurses in the group having benefited from the intervention may have improved their behavior because they still think that they are part of the intervention group, and the reverse occurs with the control group. In

TABLE 3: Difference in the prevalence of MSDs (at least one of the 9 locations) between the two groups at two points in time (before and after intervention).

Independent variables		In the last 12 months			In the last 7 days		
		β -Exponential (OR)	95% confidence interval	p	β -Exponential (OR)	95% confidence interval	p
Group	Intervention	1	—	—	1	—	—
	Control	1.6	0.9-2.6	0.059	1.9	1.1-3.3	0.016
Intervention	Before	1	—	—	1	—	—
	After	1.9	1.3-2.9	0.001	2.0	1.3-3.0	0.002
Gender (women)		1.1	0.6-2.1	0.776	0.6	0.3-1.1	0.118
Age		1.1	0.9-1.1	0.003	1.0	0.9-1.1	0.106
BMI		1.0	0.9-1.1	0.721	1.0	0.9-1.1	0.927
History of musculoskeletal diseases (yes)		2.1	1.3-3.3	0.001	2.7	1.7-4.4	<0.001

Binary dependent variables: MSDs in the last 12 months (yes/no) and in the last 7 days (yes/no). Method used: GEE: generalized estimating equation.

TABLE 4: Difference in the prevalence of MSDs at each anatomical site between the two groups before and after intervention.

Independent variables		Neck			Shoulder/upper arm			Wrist/hand			Lower back		
		OR	95% CI	p	OR	95% CI	p	OR	95% CI	p	OR	95% CI	p
Group	Intervention	1	—	—	1	—	—	1	—	—	1	—	—
	Control	1.9	1.1-3.3	0.013	2.5	1.2-4.9	0.011	2.5	1.1-6.1	0.038	2.0	1.2-3.3	0.009
Intervention	Before	1	—	—	1	—	—	1	—	—	1	—	—
	After	2.1	1.3-3.5	0.002	2.3	1.2-4.5	0.015	2.4	1.1-5.2	0.024	1.3	0.9-1.9	0.216
Gender (women)		1.8	0.9-3.6	0.076	1.0	0.5-2.2	0.915	1.3	0.5-3.4	0.664	1.0	0.5-2.0	0.969
Age		1.04	1.0-1.1	0.019	1.1	1.0-1.1	0.001	1.0	1.0-1.1	0.053	1.0	1.0-1.1	0.089
BMI		1.0	0.9-1.1	0.533	1.0	0.9-1.1	0.719	1.1	0.9-1.3	0.345	1.0	0.9-1.1	0.418
History of musculoskeletal diseases (yes)		1.9	1.2-2.9	0.007	1.5	0.9-2.6	0.121	1.4	0.7-2.8	0.301	2.3	1.4-3.8	0.002

Binary dependent variables: MSDs in the neck, shoulder/upper arm, wrist/hand, and lower back in the last 7 days (yes/no). Method used: GEE: generalized estimating equation. For the remaining anatomical sites: $p = 0.590$ for the elbow/forearm, $p = 0.328$ for the upper back, $p = 0.434$ for the hip/thigh, $p = 0.195$ for the knee/lower leg, and $p = 0.658$ for the ankle/feet.

TABLE 5: Difference in quality of life and psychological distress scores between the two groups before and after intervention.

Independent variables		In the last 12 months			In the last 7 days		
		β	95% confidence interval	p	β	95% confidence interval	p
Group	Intervention	1	—	—	1	—	—
	Control	-0.8	-2.4; 0.8	0.344	0.1	-0.6; 0.8	0.789
Intervention	Before	1	—	—	1	—	—
	After	-2.6	-3.8; -1.4	<0.001	0.7	0.1; 1.3	0.019
Gender (women)		-1.4	-3.6; 0.8	0.222	-0.7	-1.6; 0.3	0.172
Age		0.003	-0.1; 0.1	0.956	-0.05	-0.1; 1.0	0.047
BMI		0.2	-0.1; 0.5	0.161	-0.1	-0.3; 0.1	0.221
History of musculoskeletal diseases (yes)		-2.5	-4.3; -0.7	0.007	1.1	0.3; 1.9	0.007

Continuous independent variable: quality of life score and psychological distress score. Method used: GEE: generalized estimating equation.

addition to trying to limit the drawbacks of the before/after study, a generalized estimating equation was performed to limit confounding factors and make a direct change comparison between the intervention and the control group.

Before the study, the sample size for each group was calculated to ensure methodological optimization. The actual number of nurses who participated in the study ensured the minimum sample size condition. Then, four hospitals

were selected so that each group had a different type of hospital (rural district and urban district) to see the representativeness of the sample. Furthermore, sociodemographic characteristics such as age, sex, BMI, and history of musculoskeletal disease were similar and comparable between the intervention and control groups (no statistically significant differences). These conditions guarantee a good sample for this study.

After one year of intervention, the prevalence of MSDs in the last 12 months, the quality of life, and the psychological distress score were not statistically different between the 2 groups before and after the intervention, although that most of the changes are positive. It is possible that in the control group, although the nurses did not receive any interventions, their knowledge after answering many questions about MSDs was also improved. For that reason, they can apply good practices and postures or apply the acquired knowledge themselves to limit the risk of MSDs. This explains why the prevalence improved after the intervention but was not statistically significant in the tests.

The GEE has pointed out significant positive changes that have only occurred in the prevalence of MSDs in the last 7 days for 4 anatomical sites (neck, shoulder/upper arm, wrist/hand, and lower back) between the 2 groups after intervention compared with before intervention. Work-related MSDs clearly are a chronic disease that develops and evolves over a long period of exposure to risk factors. Therefore, the process of developing preventive strategies up to the time of intervention with preventive measures takes time to improve or reduce musculoskeletal symptoms. Additionally, this study only applied certain simple preventive measures (education, training, and physical exercise), and the duration of the intervention was not long enough (6 months of intervention then 6 months of observation). All of these reasons are likely to cause positive changes, but not statistically significant, in the prevalence of MSDs in the past 12 months, in the obstructive work, in the quality of life score, and in the psychological distress score. However, it is undeniable that the interventions used were also significant effective in relieving musculoskeletal symptoms of certain anatomical sites more commonly in nurses (lower back, neck, shoulder, and wrist) but only in the last 7 days. Therefore, it is necessary to have more effective preventive measures and a longer intervention time in future studies.

Therefore, although there have been many studies and trial studies of various interventions aimed at preventing MSDs, current data still show a high prevalence of MSDs among nurses, even in countries with developed occupational disease prevention systems [22–24]. This raises questions about the effectiveness of these interventions and how to apply them effectively in the hospital setting for nurses. Most studies around the world, especially in developed countries, have shown greater effectiveness when combining multiple interventions in parallel [25, 26]. However, the quality of most of these studies was poor, and the quality of randomized controlled trials was very low [26–28]. These studies mentioned many different interventions, which can be divided into different groups:

- (1) Education and training on patient care [29–32]
- (2) Provision of assistive devices for patient support and care (patient lifting systems, provision of manual handling equipment, etc.) [33–35]
- (3) Individual measures (physical exercise, stretching exercise [36, 37], cognitive-behavioral therapy

[38], wearing unstable shoes [39], or stress management [40])

- (4) Multicomponent intervention that includes two or more of the above interventions [25, 41, 42]

Regarding the application and feasibility of these measures to the practice of nurses, many elements must be taken into account to achieve the greatest efficiency, in particular for countries which are still limited in the prevention of occupational diseases. Ziam et al. examined the application of MSD prevention practices among nurses in Canada and identified organizational factors and sociodemographic variables that may or may not support [43]. In this survey, nurses stated that several factors that promote the application of preventive practices for MSDs in their work environment, including the availability of equipment in good condition for the transfer of patients (86%), training in MSD prevention practices (85%), and support for caregivers (85%), hold information sessions on the use of patient transfer and movement equipment (81%). In addition, several barriers to the implementation of preventive measures for MSDs are also reported: the lack of time to apply preventive measures, the lack of training, the unavailability of human resources (preventers, for example), the unavailability of efficient and sufficient patient transfer and movement equipment or the difficulty of accessing this equipment when needed, the discrepancy between training, and the reality of the work, as well as the lack of support of colleagues [43]. These results show that despite being a very developed country in terms of preventive measures in general and in the field of occupational health in particular, there are still limitations and difficulties in applying preventive measures for MSDs in the hospital setting. These difficulties also apply to Vietnam. The recommendations in the field of occupational health, as well as strategies for the prevention of occupational diseases for workers in general and for health workers in particular, there are still many limitations in Vietnam. In particular, the application of preventive measures in hospitals remains difficult when, on the one hand, the daily workload of nurses is essential with high work pressure [44], and on the other hand, there are barriers to the establishment of an MSD prevention program in Vietnamese hospitals due to poor recognition of the importance of the MSD problem by hospital managers, as well as lack of human resources with expertise in the field of MSD prevention [11]. For this reason, in this pilot study, only simple and feasible preventive measures were applied. Therefore, the effectiveness of these measures was therefore not high and controversial.

Another issue that needs further discussion here is about the educational interventions that were heavily used in this study. The field of occupational health in general and work-related MSDs has received little attention in Vietnam. That is, the first thing we did is in order to raise the awareness of nurses about this content. From that, they can understand the nature and importance of work-related MSDs, and how do they negatively affect the health of workers. Once they had the knowledge, we conducted training on daily work practices to change behavior and protect themselves

from the risk factors for MSDs. Besides, the suggested exercises to help strengthen the musculoskeletal system of nurses also contribute to reducing the risk of MSDs.

One of the limitations of the educational intervention in this study is that it only provides of theoretical information and knowledge to nurses but does not monitor the application of these measurements by nurses in their actual work. To ensure that we could provide the most complete knowledge of MSDs to nurses, as described in the research methods section, we flexibly used the recommendations of the World Health Organization (WHO) on the prevention of MSDs on the workplace [17] and on the prevention of MSDs on the hospital sector of the General Directorate of Labor Humanization in Belgium [18] and the Guideline for ergonomics for the prevention of MSDs of the Occupational Safety and Health Administration, US Department of Labor [19]. These recommendations cover most of the essential knowledge about MSDs and apply in the hospital setting to limit exposure to risk factors that can cause MSDs. In addition, repetition of these educational interventions is necessary to improve nurses' attitudes after different time periods [30, 32]. In fact, we repeated these interventions 3 times within the first 6 months. Educational interventions are not merely theoretical training to improve awareness and understanding but can also take other forms such as practical training in patient and manipulating with medical instruments [31] or training based on role-playing situations [30]. A study by Bos et al. [45] comparing approaches to knowledge education about MSDs for nurses, or as in Engels et al.'s study [46], showed that combining theoretical education with ergonomics will be more effective in the goal of reducing MSDs. We have tried to provide the most complete knowledge about MSDs for nurses. However, due to resource constraints (time, human resources, budget), it is also possible to negatively impact the effectiveness of these interventions. In addition, the application to practice in the daily work of Vietnamese nurses depends on many factors such as the workload, the will of each nurse, or the respect of the applied method. Furthermore, during the one-year intervention, hospitals have developed many innovative policies throughout the system based on the national patient satisfaction policy. This may have affected the interventional results.

Despite these limitations, it is undeniable that on the one hand, these first results open the premise for future intervention studies to prevent MSDs to be carried out with more effective methods; on the other hand, it will pave the way for new and appropriate policies to more effectively apply the interventions for nurses in particular and workers in other professions in general.

5. Conclusion

This study is the first to examine the effectiveness of several simple MSD prophylaxes in Vietnamese nurses. The effectiveness occurred probably on the prevalence of MSDs in the last 7 days at 4 anatomical sites (neck, shoulder/upper arm, wrists/hand, and lower back) between the 2 groups before and after the intervention. More in-depth studies

are needed with a combination of measures over a longer period of time for more robust evidence on interventions.

Data Availability

The SPSS data used to support the findings of this study are available upon request from the corresponding author.

Ethical Approval

The study was approved by the Institutional Review Board of the Haiphong University of Medicine and Pharmacy and authorized by the Haiphong Department of Health to implement the study at its district hospitals.

Consent

All study participants provided their informed consent before enrollment in the survey.

Conflicts of Interest

The authors have no conflicts of interest to declare.

Authors' Contributions

All authors substantially worked on the conception, design, and process of the study. Minh Khue Pham and Thanh Hai Nguyen guided the study and contributed to the acquisition and interpretation of data. Thanh Hai Nguyen substantially contributed to the analysis and interpretation of data and writing of the manuscript. All authors worked on revising the manuscript for intellectual content and final approval of the version to be published.

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Research Article

Prolonged Application of Continuous Passive Movement Improves the Postoperative Recovery of Tibial Head Fractures: A Prospective Randomized Controlled Study

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Background and Purpose. Tibial head fracture (THF) rehabilitation is still a challenge in clinical practice. Short-term use of continuous passive motion (CPM) postoperatively for THFs can increase knee range of motion (ROM) immediately, and its effect on enhanced rehabilitation also ended when the CPM application was discontinued. The aim of this study was to investigate the effect on the recovery of prolonged use of CPM in the postoperative treatment of THFs. **Methods.** 60 patients with THFs were randomly and equally divided into the CPM group and non-CPM group. Both groups immediately received CPM and conventional physical therapies during hospitalization. After discharge, the non-CPM group was treated with conventional physical therapy alone, while the CPM group received conventional physical training in combination with CPM treatment. At 6 weeks and 6 months postoperatively, the primary outcome which was knee ROM and the secondary outcome which was knee functionality and quality of life were evaluated. **Results.** The CPM group had a significantly increased ROM at both follow-up time points. The Knee Society Score, UCLA activity score, and the EuroQoL as well as the pain analysis showed significantly better results of the CPM group than the non-CPM group. **Conclusions.** The prolonged application of CPM therapy is an effective method to improve the postoperative rehabilitation of THFs.

1. Introduction

Tibial head fractures (THFs) can be caused by high energy trauma incidents, mostly motor vehicle accidents, as well as low energy falls of geriatric patients with osteoporotic bone [1, 2]. They often require surgical treatment, and its main objectives are to restore the articular surface and axial relationships, avoid long-term immobilization, and ultimately restore the function of the injured knee joint as soon as possible [2, 3]. However, it is reported that the average motion of the knee is still limited 15 months after THF surgery, when compared with the healthy population (105° vs.

150°) [2, 4, 5]. Knee joint movement limitation caused by THFs severely restrict the patient's daily life, since high mobility is required to manage daily tasks, such as climbing stairs and sitting and standing from chairs requiring 90-120° of flexion and entering a bathtub requiring at least 135° of flexion [2, 6]. How to increase the range of motion (ROM) and the functionality of the knee as much as possible has become the focus of postoperative rehabilitation of THFs.

Continuous passive motion (CPM) is an external device that enables joints to move passively on a preset arc of motion [7]. Currently, CPM is widely used in postoperative rehabilitation that limits the ROM of joint, mainly including

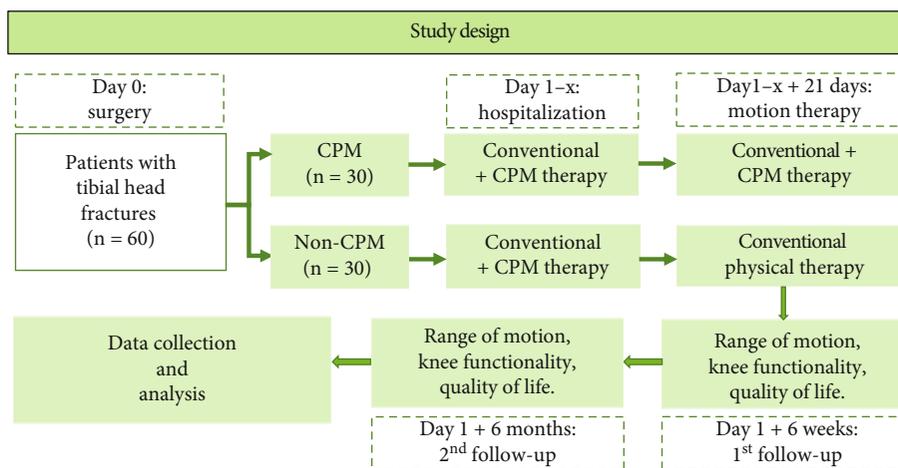


FIGURE 1: Schematic diagram of the processing method, timeline, and the evaluation parameters.

fracture repair [2, 8], rotator cuff repair [9], hand rehabilitation [10], reconstruction rehabilitation of the anterior cruciate ligament [11, 12], total knee arthroplasty (TKA) [7, 13], and adhesive capsulitis [14]. However, there is still no consensus on the clinical functional recovery outcome and standard intervention measures of CPM [7, 12, 15]. Regarding the rehabilitation of CPM for THFs, a study of intra-articular knee fractures involving proximal tibial fractures showed that, compared with the non-CPM group, the CPM group, which used CPM for 48 hours, had significantly increased knee ROM at short-term postoperation, but there was no significant difference at other longer follow-up time points [2]. However, whether prolonged CPM application affects postoperative rehabilitation after THFs remains unknown.

In addition, with the development of surgical technology and enhanced recovery after surgery, the patient's length of hospital stay has been reduced [16, 17], which led to a reduction of recovery time in the hospital. Rehabilitation at home becomes very important and a supplement to the insufficient time of rehabilitation in hospital. CPM is now more and more used in the postclinical home situation and has become a part of daily care plan [7]. The purpose of this study is to explore whether the prolonged application of CPM in the home situation will improve midterm postoperative rehabilitation after THFs. We hypothesized that prolonged use of CPM in the home situation is beneficial in the postoperative recovery of THFs.

2. Methods

2.1. Study Design. A prospective, nonblinded, controlled single-center trial of 60 patients who had been surgically treated for THF was performed at the University Hospital Carl Gustav Carus at TU Dresden, Germany. They were randomized into 2 groups of 30 patients each (CPM group and non-CPM group). CPM and conventional physical therapies started on the first postoperative day in both groups. Whereas the CPM group intensified its training with an additional CPM therapy for 21 days after discharge, the

non-CPM group received conventional physical therapy only. Follow-up points were set 6 weeks and 6 months post-operatively (Figure 1).

2.2. Participants. This trial included all patients undergoing tibial head surgery from February 2017 to October 2018 at the University Hospital Carl Gustav Carus at TU Dresden, Germany. All patients had open reduction and internal fixation (ORIF), with the operative and fixation method decided by their surgeons. Further inclusion criteria were an age of 18 years or older, a radiologically assured THF (OTA 41 type A/B/C), free motion of the knee joint prior to injury, and a healthy, freely movable contralateral knee joint. All patients with a previous knee injury, pathological fracture, open tibial physis, pelvic fracture, spinal injury, hip injury, and other diseases hindering the use of CPM were excluded. Patients were randomly divided into the CPM group and non-CPM group on a one-to-one ratio by the block randomization method.

2.3. Interventions. All patients received conventional physical therapy and CPM therapies from the first postoperative day. The conventional physical therapy comprising of 30 minutes of training with stretching exercises and muscle strength (2-3 times/week) and CPM therapy were performed 3 times a day per 30 minutes. The CPM therapy was performed by using a Kinetec Optima S4 device (S&U Medizintechnik GmbH, Zottenheim, Germany). After being discharged from the hospital, the non-CPM group was treated with conventional physical therapy alone. In addition to the conventional physical training, the CPM group continued the same rehabilitation program during the hospitalization to enable home training for 21 days after being discharged from the hospital. The ROM of CPM could be set individually using a remote control. Altogether, a ROM from -10° to 120° was covered by the CPM device. All patients were encouraged to move their knee joints on the first day after the operation, with partial weight-bearing within the first six weeks and full weight-bearing thereafter.

TABLE 1: Baseline data of the CPM and non-CPM group.

	CPM	Non-CPM	<i>p</i>
Age (years)	56.6 ± 16.1 (27–86)	56.0 ± 13.8 (27–81)	0.877
Gender	10 males 20 females	15 males 15 females	
Body weight (kg)	75.1 ± 11.8 (55–106)	81.4 ± 16.5 (57–118)	0.095
Operation time (minutes)	147.3 ± 55.2	140.6 ± 71.1	0.683
ASA classification	1.77 ± 0.6812 (1–3)	1.73 ± 0.6412 (1–3)	0.846
OTA classification of the fracture	B2: 3 B3: 12 C3: 15	A1: 1 B1: 3 B2: 2 B3: 11 C2: 2 C3: 11	
Time in hospital (days)	13.9 ± 1.2 (5–31)	15.4 ± 1.6 (7–49)	0.5

Abbreviations: CPM: continuous passive motion; ASA: American Society of Anesthesiologists; OTA: Orthopedic Trauma Association. Data are represented as mean ± standard deviation and range; significance was set at $p < 0.05$.

2.4. Outcomes. The therapy was assessed at 6 weeks and 6 months postoperatively. The primary outcome of the investigation was the ROM of knee. For this purpose, a goniometer was used which measured the ROM of the injured and contralateral healthy knee. Knee functionality and the patient's quality of life were determined as secondary outcome measurements which were assessed by the Knee Society Score (KSS) [18], the Oxford Knee Score (OKS) [19], the EuroQoL [20], and the University of California at Los Angeles (UCLA) activity score difference. Specially, the UCLA activity score difference was the difference between the preinjury status score and follow-up time point score, and the scoring rules were based on the previous standards [21].

2.5. Sample Size. When calculating the sample size, ROM was used as the main outcome parameter. The average knee ROM after tibial head fracture was 105°, and the clinically significant increase of ROM was 15°. Using an alpha of 0.05, a statistical power of 80%, 20% rate of dropouts, and combined with previous studies [2], sample size of 60 patients had statistical significance and was used in this study.

2.6. Statistical Methods. The data were performed by using SPSS software (SPSS Inc., Chicago, IL, USA). The normality of distribution of continuous variables was tested by one-sample Kolmogorov-Smirnov test. Continuous variables with normal distribution were presented as mean ± standard deviation and range. The mean of ROM, knee flexion, knee extension, functional outcome score, and baseline data of the CPM group and non-CPM group were compared at each follow-up time point by independent samples Student's *t* test.

The mean of ROM among 6 weeks and 6 months postoperative and the contralateral uninjured knee in the non-CPM group and CPM group were compared by a one-way ANOVA, followed by Tukey's post hoc test for multiple comparisons. A value of $p < 0.05$ was considered significant.

3. Results

3.1. Recruitment. From February 2017 to October 2018, 60 patients were recruited in this study. The follow-up ended 6 months postoperatively, because that is our typical follow-up time for every patient with THF. According to the internal hospital standards, follow-up of the patients was performed 6 months postoperatively. To assess short-term influence, a 6-week follow-up point was additionally chosen during which patients were just with partial weight-bearing. The trial was completed in April 2019. The baseline data for each group are represented in Table 1.

3.2. Participants. 60 patients were recorded and split into two treatment groups. All 60 patients completed 6-week follow-up. At 6 months postoperatively, group size of non-CPM group decreased from 30 to 24 due to follow-up loss. 27 out of the initial 30 patients were analyzed in the CPM group. Reasons were reoperation (non-CPM group: 4 patients and CPM group: 1 patient) and patients' request to discontinue the trial (non-CPM group: 2 patients and CPM group: 2 patients) (Figure 2).

3.3. Outcomes and Estimations. The ROM of the contralateral uninjured knee in the CPM group (133.4 ± 5.6) and the non-CPM group (134.1 ± 8.4) was equivalent ($p = 0.583$). At 6 weeks after surgery, the CPM group had a



CONSORT

TRANSPARENT REPORTING of TRIALS

CONSORT 2010 Flow diagram

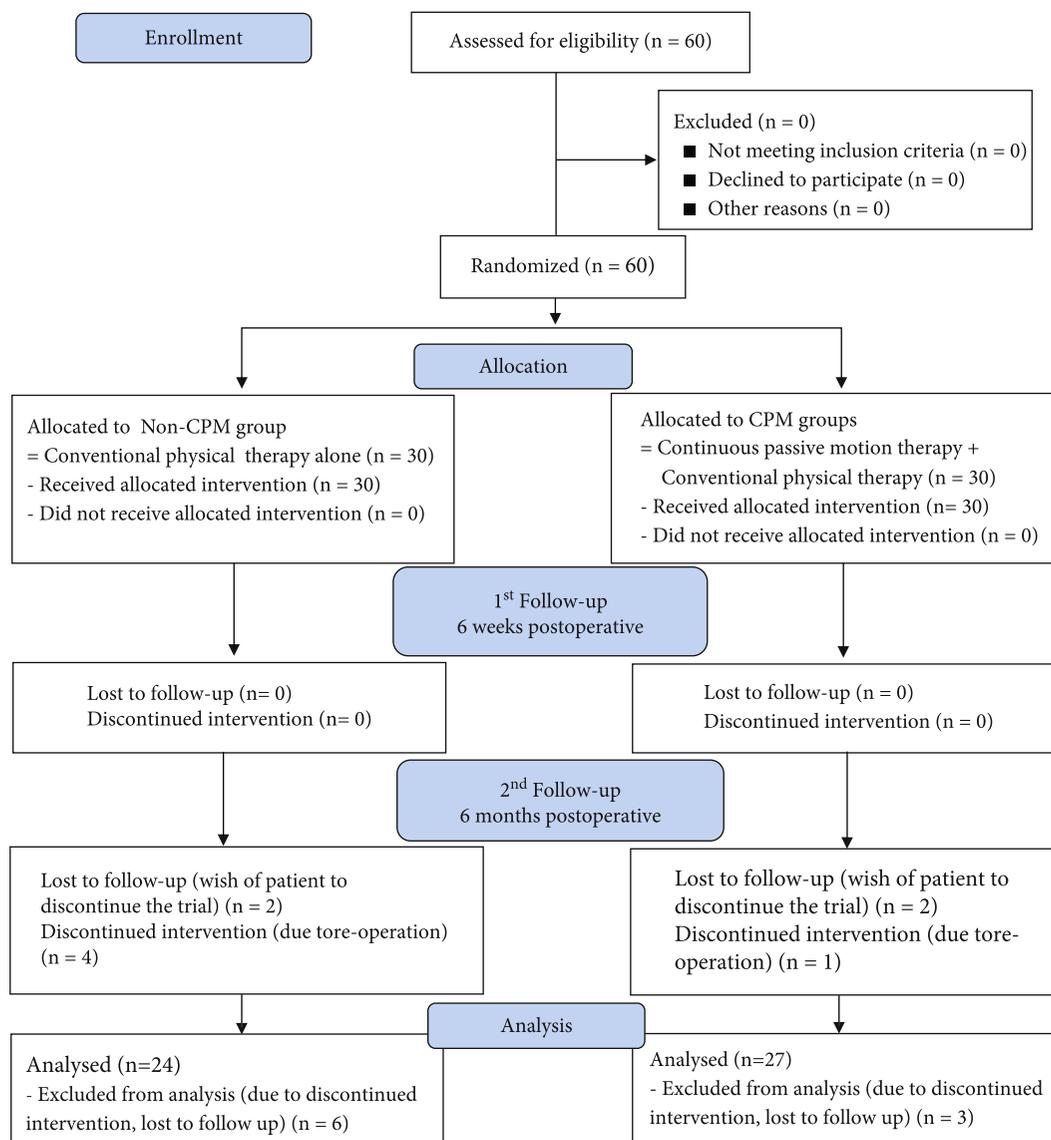


FIGURE 2: Consort (consolidated standards of reporting trials) flow diagram. Abbreviation: CPM: continuous passive motion.

significant increase in ROM compared with the non-CPM group (CPM group vs. non-CPM group; $96.7 \pm 14.8^\circ$ vs. $82.8 \pm 25.1^\circ$, $p = 0.012$). The different values could also be observed for knee flexion (non-CPM group vs. CPM group; $91.4 \pm 24.1^\circ$ vs. $102.0 \pm 14.5^\circ$, $p = 0.042$) and knee extension (non-CPM group vs. CPM group; $8.6 \pm 7.1^\circ$ vs. $5.4 \pm 6.4^\circ$, $p = 0.073$). At 6 months after surgery, the CPM group also had a significant increase in ROM compared with the non-CPM group (CPM group vs. non-CPM group; $122.4 \pm 13.2^\circ$ vs. $113.4 \pm 17.1^\circ$, $p = 0.040$). The knee flexion of the non-CPM group appeared to be significantly smaller than that of the CPM group (non-CPM group vs. CPM group; 116.7

$\pm 14.6^\circ$ vs. $124.8 \pm 11.6^\circ$; $p = 0.032$). The extension of CPM patients ($2.7 \pm 3.6^\circ$) was only marginally better than that of the non-CPM group ($3.3 \pm 4.5^\circ$) ($p = 0.633$) (Figure 3). In addition, both in the non-CPM and CPM groups, the recovery effect of 6 months after surgery was better than that of 6 weeks after surgery, including ROM, flexion, and extension of the knee. However, the ROM of injured knee joint in the two groups was still lower than the ROM of contralateral knee joint even after 6 months (Figure 4). Comparing the improvements from 6 weeks to 6 months after surgery, it was found that the motion of the knee, including ROM, flexion, and extension, in the CPM group was not better than

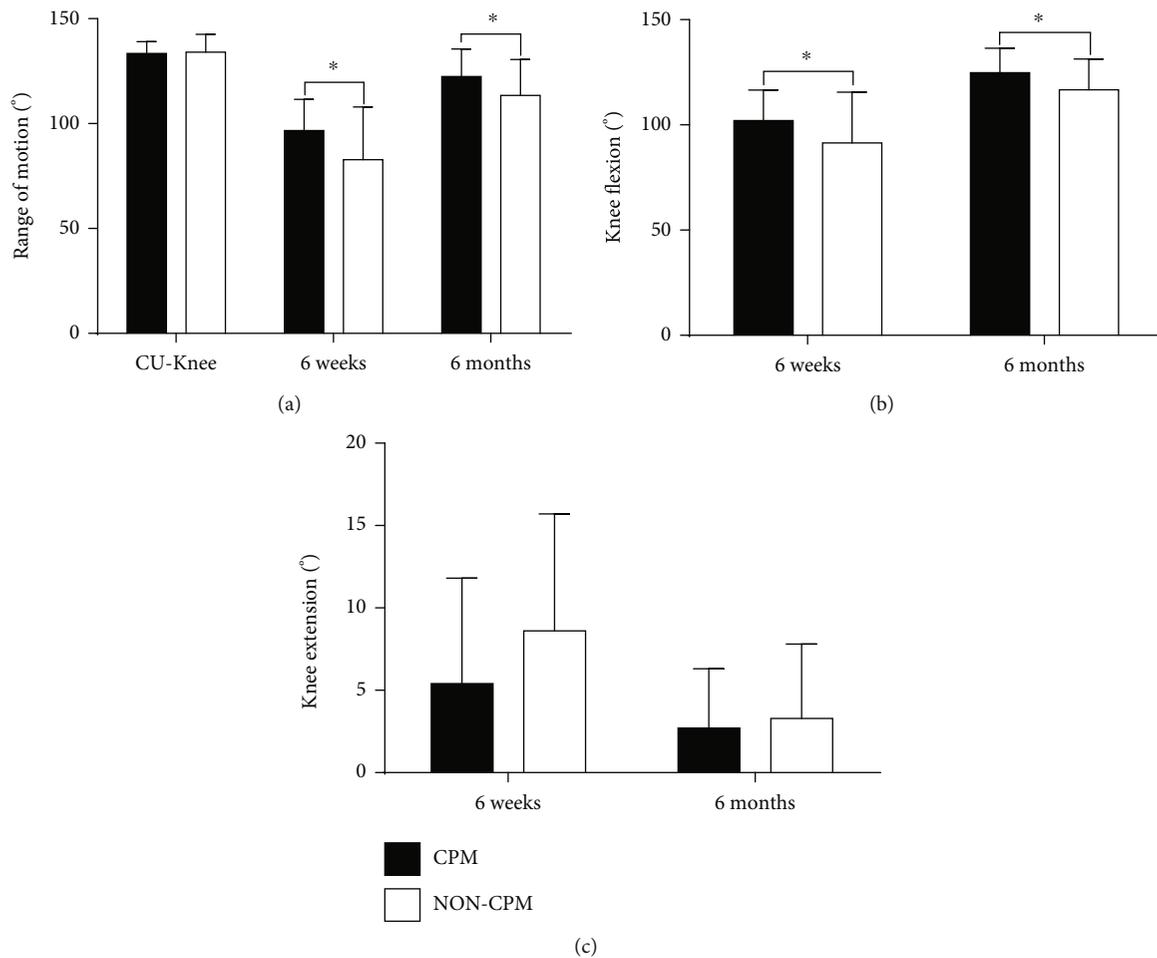


FIGURE 3: (a) Range of motion, (b) flexion, and (c) extension of the knee at 6 weeks and 6 months postoperatively and the range of motion of the uninjured knee. Abbreviations: CPM: continuous passive motion; CU-Knee: contralateral uninjured knee. Data are represented as mean \pm standard deviation, * $p < 0.05$.

that of in the non-CPM group (Figure 5). There were significant differences in the analysis of KSS and the EQ-5D-3L part of EuroQoL score at both follow-up time points. OKS and visual analog scale (VAS) part of the EuroQoL score in the CPM group showed better results than the non-CPM group, but there was only a significant difference at 6-month follow-up. At both follow-up time points, the pain score of the CPM group also showed better results in pain points of KSS. The UCLA activity score difference demonstrated better results in the CPM group, but there was no significant difference at both time points (Table 2). The improvements of knee functionality and the patient's quality of life from 6 weeks to 6 months postoperation showed that the results were similar between the two groups, and there was no statistical difference in all results (Table 3).

3.4. Harms. No direct harms and unintended effects due to physical therapy occurred in both groups. In total, 5 patients underwent reoperations for the following reasons: repeated trauma (non-CPM group: 1 patient), revision of osteochondral defect (non-CPM group: 1 patient), and revision by compartment syndrome (CPM-group: 2 patients and non-CPM group: 1 patient).

4. Discussion

Compared with the non-CPM group, the results of this study showed that the CPM group had a significant increase in ROM, enhanced knee functionality, lower pain, and improved quality of life at the two follow-up time points. Thus, the hypothesis that prolonged application of CPM in the home situation in the postoperative treatment of THFs is beneficial was verified.

THFs are a type of common and severe injury, and their later developmental complications such as traumatic arthritis, muscle and bone atrophy, and joint stiffness can cause functional problems in the knee of the patients and increase the socioeconomic burden [22]. A systematic review demonstrated that tibial plateau fractures have a lower return rates to sport compared with other types of fractures, and only 60% patients can recover to the preinjury level of sport [23]. Another study found that 88% of patients suffering from tibial plateau fractures involving the posterior column cannot recover to their preinjury levels of activity, and their restricting factors include pain (66%), fear of reinjury (37%), limited ROM (26%), and instability (21%) [24]. Therefore, the promotion of THF rehabilitation has important

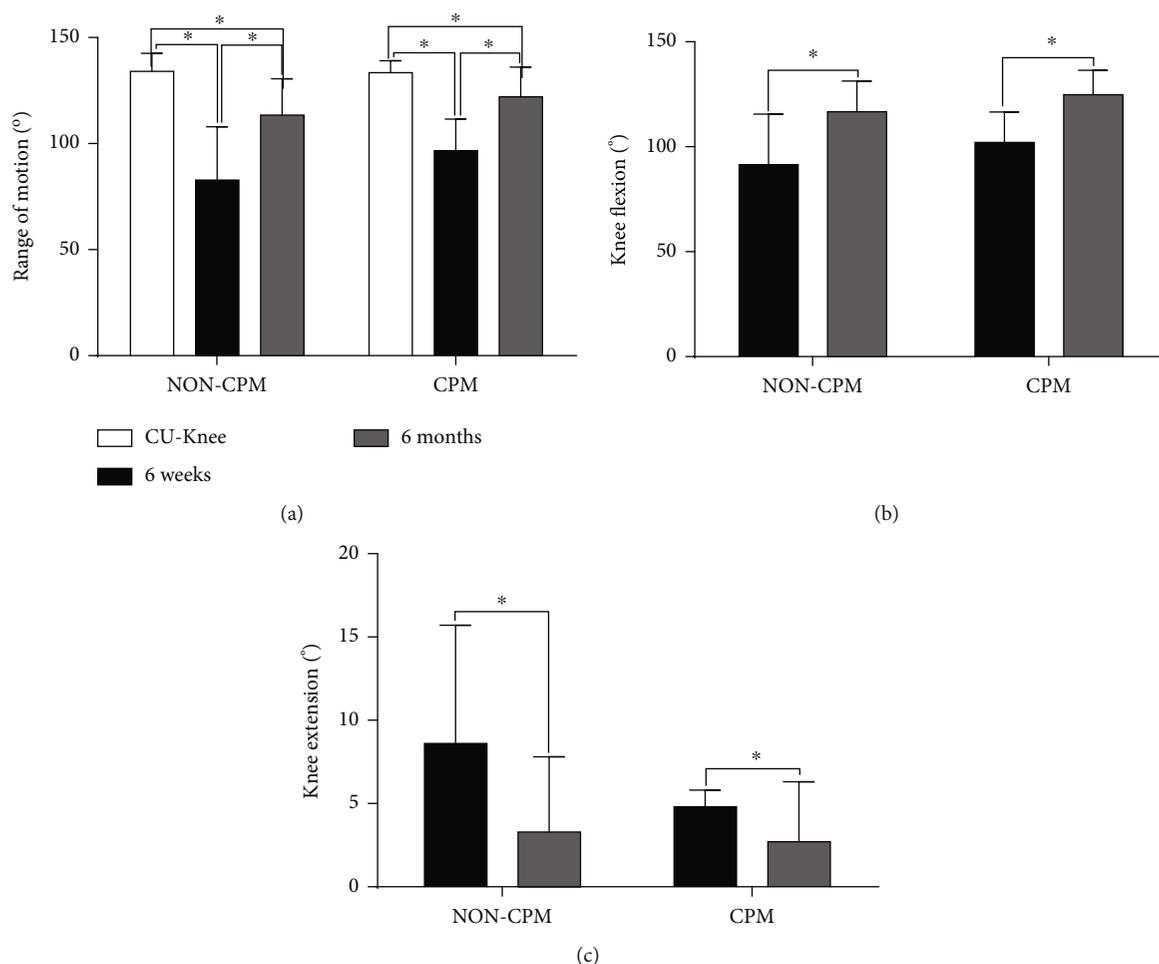


FIGURE 4: (a) Comparison of the range of motion among 6 weeks and 6 months postoperative and the contralateral uninjured knee in the non-CPM group and CPM group. Comparison the knee flexion (b) and knee extension (c) between 6 weeks and 6 months postoperative in the non-CPM group and CPM group. Abbreviations: CPM: continuous passive motion; CU-Knee: contralateral uninjured knee. Data are represented as mean \pm standard deviation, * $p < 0.05$.

significance, and the attention should be paid to not only ROM but also other restricting factors such as pain and quality of life in the process of rehabilitation of THFs.

Some preclinical studies demonstrated that CPM can prevent joint stiffness, and its underlying mechanics is that it can produce sinusoidal intra-articular pressure changes that promote trans synovial transport and clearance of the blood to prevent edema formation, halting granulation, and fibrotic tissue formation [15, 25]. In addition, CPM has the potential to limit muscle atrophy and relieve pain [15, 26, 27]. In clinical work, the early mobilization and increased ROM of the knee after THF surgery is important [22], and CPM is often used for postoperative rehabilitation of patients with tibial fractures after surgical fixation [28]. Surprisingly, there is only one report on this study between the CPM and THFs which showed that CPM therapy significantly increased the knee motion after short-term use of CPM, and its effect on enhanced rehabilitation after THF also immediately ended when CPM application was discontinued [2]. Another study showed that 3 days of CPM use could influence joint stiffness up to 24 weeks [29], so pro-

longed use of the CPM appears to be meaningful for post-THF rehabilitation. In this study, motion therapy started on the first postoperative day for both groups which can reduce the swelling and stiffness of the joints. However, there has been no consensus about the usage, duration, and timing of CPM therapy in all areas of application yet [30, 31]. A medium application duration of three times a day for 30 minutes during hospital and the continuing first 3 weeks after being discharged from the hospital was chosen, and this also enabled patients to have good compliance. A Cochrane review concluded that using CPM and physiotherapy has more beneficial short-term results than physiotherapy alone after TKA [32]. In our study, the CPM combination with conventional physical training was used for the recovery of THFs to hope for a good recovery for the patients. At 6 weeks and 6 months after surgery, the CPM group had a significant increase in ROM, extension, and flexion compared with the non-CPM group. This may be related to the prevention of edema, granulation tissue, and fibrotic tissue formation by CPM [15, 25]. In addition, it also may be related to CPM improving tendon strength,

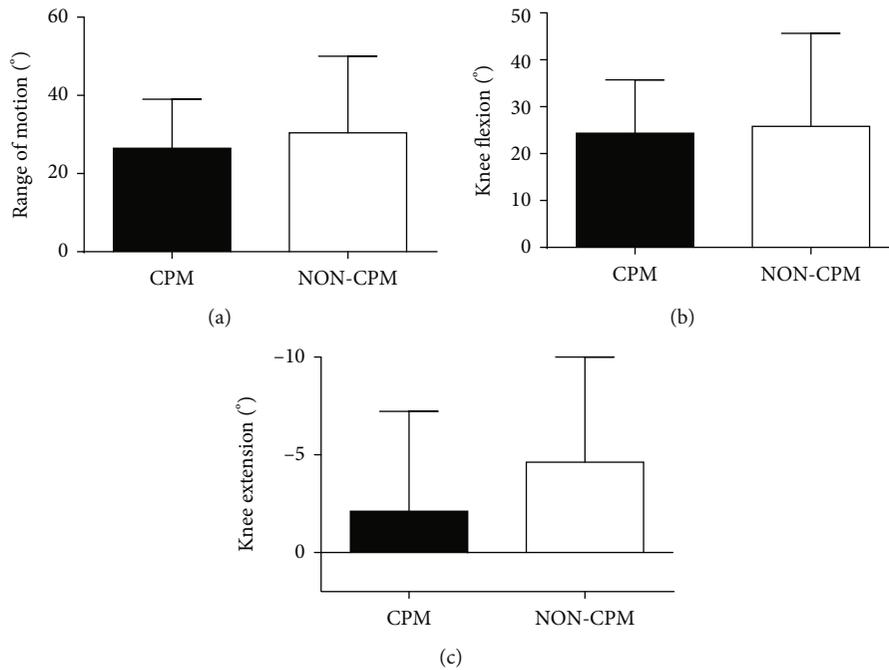


FIGURE 5: Comparison of the improvements from 6 weeks to 6 months (a, range of motion; b, knee flexion; c, knee extension) between non-CPM and CPM groups.

TABLE 2: Overview of the Knee Society Score, EuroQoL, Oxford Knee Score, and UCLA activity score difference results.

	6 weeks			6 months		
	CPM	Non-CPM	<i>p</i>	CPM	Non-CPM	<i>p</i>
KSS ¹	125.8 ± 33.3	105.8 ± 38.0	0.034	179.5 ± 29.3	151.1 ± 28.6	0.001
Pain points of KSS ¹	38.8 ± 11.0	30.7 ± 12.1	0.008	44.8 ± 7.0	36.7 ± 12.1	0.004
EQ-5D-3L of EuroQoL score	7.4 ± 1.6	8.6 ± 1.7	0.005	6.1 ± 1.4	7.1 ± 1.4	0.013
VAS ² of EuroQoL score	66.2 ± 17.0	58.2 ± 19.0	0.092	83.9 ± 11.4	75.8 ± 11.0	0.014
UCLA ³ activity score difference	3.2 ± 1.1	3.3 ± 1.4	0.686	1.0 ± 1.0	1.4 ± 1.1	0.190
OKS ⁴	28.0 ± 9.1	24.9 ± 9.8	0.207	39.3 ± 6.3	33.2 ± 7.1	0.002

Abbreviations: CPM: continuous passive motion; KSS¹: Knee Society Score; VAS²: visual analogue scale; UCLA³: University of California at Los Angeles; OKS⁴: Oxford Knee Score. Data are represented as mean ± standard deviation; significance was set at *p* < 0.05.

TABLE 3: Comparison of the improvements from 6 weeks to 6 months between the non-CPM and CPM groups.

	CPM	Non-CPM	<i>p</i>
KSS ¹	51.1 ± 18.6	44.3 ± 31.5	0.345
Pain points of KSS ¹	5.2 ± 8.5	5.8 ± 13.6	0.837
EQ-5D-3L of EuroQoL score	-1.2 ± 1.6	-1.5 ± 1.7	0.501
VAS ² of EuroQoL score	17.0 ± 15.5	14.1 ± 13.1	0.476
UCLA ³ activity score	2.1 ± 1.0	1.7 ± 1.0	0.109
OKS ⁴	11.0 ± 8.2	7.5 ± 8.8	0.142

Abbreviations: CPM: continuous passive motion; KSS¹: Knee Society Score; VAS²: visual analogue scale; UCLA³: University of California at Los Angeles; OKS⁴: Oxford Knee Score. Data are represented as mean ± standard deviation; significance was set at *p* < 0.05.

cartilage repair, and wound healing [33–35]. Apart from this, this study showed that CPM significantly decreased the patients’ level of pain which was consistent to other findings [11, 12]. The reasons might be a decreased inflammation and mitigated hyperalgesia [36–39]. The improvement in the CPM group from 6 weeks to 6 months after the operation was slightly lower than that of in the non-CPM group without a significant difference. One reason for the slightly slowed improvement may be due to the improved knee mobility in the early stage resulting in a lower increase in the later period in the CPM group. Another fact that cannot be ignored is that after 6 weeks postsurgery, all patients transitioned from partial weight-bearing to full weight-bearing exercise. A review study showed that weight-bearing after knee surgery can appropriately stimulate knee healing, reduce pain, and improve activity level [40]. However, the specific impact of weight-bearing on knee mobility, knee function, and quality of life after knee surgery needs further research. The

EuroQoL could provide mobility, self-care, main activity, social relationships, pain, and mood values [41]. The OKS and KSS for knee functionality suggested by the German Orthopedic Guidelines (Deutsche Gesellschaft für Orthopädie und Orthopädische Chirurgie 2018) and the UCLA activity rating are valid for clinical activity assessments [21]. All these findings have a positive impact on the patients' quality of life and knee functionality and were positively influenced by the prolonged CPM treatment. The fact that there was no significant difference between the CPM group and the non-CPM group in the development from 6 weeks to 6 months postoperative in quality of life and knee functionality shows that the positive effect of the additional CPM therapy in the first 3 weeks at home remains an advantage even after 6 months. The observed differences in knee flexion can also be seen as clinically relevant since a patient with 90° of knee flexion has difficulties to go down on his knees while 10° more flexion make that much easier.

Moreover, some studies could observe that hemarthrosis and deep vein thrombosis occurred less [42] and the number of manipulations under anesthesia were decreased [31] using CPM. In this study and another intra-articular fractures recovery study [2], the incidence of postoperative manipulations under anesthesia and thrombosis was rare regardless of whether CPM was used. Therefore, this study cannot draw similar conclusion, and it requires further research with large samples and multicenter trial.

5. Limitations

In this study, there were considerably more women than men in the CPM group, and it cannot preclude influence on the data. The last follow-up time point was set after 6 months postoperatively giving insufficient information about the long-term benefit of CPM therapy. This study was a single-center study with a small sample size, and a large sample multicenter randomized trial would be useful to further confirm our results.

6. Conclusions

The prolonged application of CPM therapy in combination with conventional physical therapy at home in treatment of THFs increased the ROM of the knee, reduced pain, and improved the knee functionality and quality of life of patients. In conclusion, the prolonged application of CPM therapy in the home situation is an effective method to promote postoperative rehabilitation of THFs.

Abbreviations

THF: Tibial head fracture
 CPM: Continuous passive motion
 ROM: Range of motion
 TKA: Total knee arthroplasty
 ORIF: Open reduction and internal fixation
 KSS: Knee Society Score
 OKS: Oxford Knee Score
 UCLA: University of California at Los Angeles

ASA: American Society of Anesthesiologists
 OTA: Orthopedic Trauma Association.

Data Availability

All data generated or analyzed during this study are included in this article.

Ethical Approval

The study was approved by the institutional ethical review committee of the Technical University Dresden (protocol no. EK 73022017) on February 14, 2017. The study has been performed with the appropriate participant's informed consent in compliance with the Helsinki Declaration.

Conflicts of Interest

The authors have no conflict of interest to declare.

Authors' Contributions

C.Ka., C.Kl., M.A., G.L., and Z.S. contribute to the conception or design and acquisition of data for the work; C.Ka., X.T., L.F., and Z.S. contribute to data analysis and manuscript drafting and revision; all authors contribute to the final approval of the version to be published.

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Research Article

Cardiac Autonomic Modulation in Subjects with Amyotrophic Lateral Sclerosis (ALS) during an Upper Limb Virtual Reality Task: A Prospective Control Trial

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Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease. As a result of the rapid progression and severity of the disease, people with ALS experience loss of functionality and independence. Furthermore, it has already been described presence of autonomic dysfunction. Despite the increasing use of virtual reality (VR) in the treatment of different diseases, the use of virtual reality environment as an intervention program for ALS patients is innovative. The benefits and limitations have not yet been proven. Our objective was to evaluate the autonomic function of individuals with amyotrophic lateral sclerosis throughout the virtual reality task. The analysis of autonomic function was completed before, during, and after the virtual reality task using the upper limbs; also, all steps lasted ten minutes in a sitting position. Heart rate variability (HRV) was taken via the Polar® RS800CX cardiofrequencymeter. The following questionnaire was enforced: Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFERS) and Fatigue Severity Scale (FSS). Different types of HRV were revealed for the groups, indicating that the ALS group has reduced HRV, with most of the representative indices of the sympathetic nervous system. Besides, the physiological process of reducing parasympathetic activity from rest to VR activity (vagal withdrawal), with reduction in HF (ms²) and an increase in HR from rest to activity, and a further increase throughout recovery, with withdrawal of sympathetic nervous system, occurs just for the control group (CG), with no alterations between rest, activity, and recovery in individuals with ALS. We could conclude that patients with ALS have the reduction of HRV with the sympathetic predominance when equated to the healthy CG. Besides that, the ALS individuals have no capability to adapt the autonomic nervous system when likened to the CG during therapy based on VR and their recovery.

1. Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease categorized by progressive loss of upper and lower motor neurons [1]. It affects the motor neurons of the cerebral cortex, brainstem, and spinal cord in adults [2–4]. Individuals with ALS live with continuous and multiple functional losses, presenting upper, lower, and trunk muscle atrophy, muscle weakness, fasciculation, and subsequently progressive loss of all movements [5, 6].

Although this population has chiefly motor symptoms, autonomic nervous system (ANS) disorders have also been reported, such as decreased heart rate variability (HRV) [7–10] with chronic cardiac sympathetic hyperactivity, that is, allied in this population with sudden cardiac death and stress-induced cardiomyopathy [11, 12].

As said by Vanderlei et al. [13], the ANS has a key role in regulating the physiological processes of the human organism throughout both normal and disease conditions. HRV has been established as a cheap technique that allows individual analysis of sympathetic and parasympathetic activity in many situations [14].

Deviations in HRV patterns provide a sensitive and early indicator of the physiological behavior of the human organism and the person's health [12]. A high HRV is a sign of good physiological adaptation, with efficient autonomic mechanisms, whereas a low HRV is an indicator of abnormal and insufficient ANS adaptation, both implying the presence of physiological changes in the individual [15].

In view of the above discussion, one possibility to analyze HRV is the use of physical activities where individuals are assessed during rest and movement activities. So, an innovative technology to offer physical activity for individuals with ALS is the use of virtual reality task. According to Dontje et al. [16], professionals involved in the rehabilitation of patients with ALS search for interventional ideas based on scientific evidence [16] and virtual reality has been considered an interesting option.

A bespoke technology, such as virtual reality (VR), defined as the use of interactive simulations, created with computer hardware and software, to present users with opportunities to perform in virtual environments that appear like real-world objects and events, has been promoted as a tool to stimulate movement and to support individuals to gain improvements in physical performance [17].

Few studies with ALS are directed to the computational technology. Chang et al. [18] analyzed three patients with ALS in a program using brain-computer interface (BCI) expertise, which offered the ability to verify accuracy and information transfer rate in the disabled group as compared to the typically developing group. Thompson et al. [19] and Silvoni et al. [20] steered research on BCI in ALS subjects and demonstrated possibilities for communication at advanced stages of the disease. Lancioni et al. [21] substantiated function in tasks with the use of computer mouse for interaction with written texts. Trevizan et al. [22] applied a VR task with alternative computer interfaces in ALS patients and attained some positive results in motor improvement with repetition.

Considering the lack of studies that analyze the ANS disorder in ALS subjects throughout physical activity, this study enforced HRV to investigate acute cardiac autonomic responses during rest, VR tasks, and recovery. Likewise, we organized a control group with a typical individual matched by gender and age with the ALS group that went through the same protocol to deliver a normal HRV pattern. Hence, if the HRV responses of ALS participants during virtual tasks are upgraded compared with the responses at rest, it provides new ways for research using technology that could be therapeutic by refining autonomic dysfunction in this cohort.

2. Materials and Methods

This is a prospective controlled trial. In this study, there were 41 age-matched individuals split into groups with diagnosis of ALS and healthy typically developed as a control group (CG). All subjects who were diagnosed with ALS were confirmed by medical analysis and regularly attended the Neuromuscular Disease Research Sector (SIDNM) of the Federal University of São Paulo, Brazil.

Subjects were omitted with severe motor problems and those with deviations in cognitive functions that would hinder the basic understanding of commands in the proposed activities. The research project (number CAAE: 80826217.0.0000.5390) was approved by the research ethics committee of the University of São Paulo and commenced after the signing of the Terms of Free and Informed Consent by the participants and was registered in the <http://ensaiosclinicos.gov.br> database with the subsequent number identifier: RBR-78zwm.

Data collection forms from their medical records were finalized in ALS individuals. It was enforced to acquire relevant information regarding patients' care, such as mass, height, date of birth, disease history, pharmacotherapies, and if they were a smoker or former smoker.

For the participants' clinical features, three scales referring to functional assessment, fatigue, and quality of life were necessary:

- (1) As a functional assessment tool, the Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFRS-R) was enforced, validated in Brazilian individuals with ALS which permits monitoring of symptoms and limitations of daily living activities. The scale has 12 questions, with scores ranging between 0 and 4 and a maximum score of 48 (where the participant is in his or her optimum state) [23–26]
- (2) To assess fatigue during the task implementation, we enforced the Fatigue Severity Scale (FSS). The FSS contains nine declarations, and for each item, subjects are instructed to choose a score ranging from 1 to 7, with 7 representing the highest level of agreement with a given statement. The total FSS score is obtained by calculating the mean of all items, with a score ≥ 4 indicating the presence of fatigue [27, 28]



FIGURE 1: Representative design of the accomplishment of the MoveHero software task in the use of the webcam interface, using the Polar RS800CX chest strap ECG measuring device. (a) Demonstration of hit performed by the participant. (b) Error performed by the participant.

2.1. Data Collection Instruments

2.1.1. MoveHero. The virtual reality task commenced was a computer game named “MoveHero” that provided an intervention via a virtual task. According to Martins et al. [29] and Silva et al. [30, 31], the game presents tumbling spheres on the computer screen, in four imaginary columns, with a musical rhythm chosen by the researcher. The action is to react (using the upper limbs) and not let the spheres pass from the fixed targets. The spheres ought to be only intercepted when they reach the targets allocated in parallel (at two height levels), two on the left (left position targets A and B) and two on the right (right position targets C and D) of the participant, as illustrated in Figure 1.

The virtual contact was accomplished by the individuals’ avatar, namely, a representation of the individual appeared on the computer screen. The individual motivated their upper limbs in front of the webcam to coincide with the moment the ball touched the target. The avatar’s hand must reach the target sphere together with the arrival of the ball, and the game proposes feedback on correctness and error by means of changing the spheres’ colour (green for correct and a red line for error). The game requires the subject to have a plan for the movement and its anticipation; this is likewise considered a coincident timing task. The subjects were located one meter from the computer monitor and they waited for the spheres to drop, which fell arbitrarily on each target.

2.1.2. Heart Rate Variability (HRV). We applied HRV to assess the autonomic nervous system before, during, and after the intervention. The data collection strap was situated on the participant’s chest, and the HRV was logged using the Polar RS800CX chest strap ECG measuring device (Polar Electro Oy, Kempele, Finland), formerly validated for beat-to-beat heart rate capture, with the heart rate receiver placed next to it.

Prior to HRV measurements, blood pressure, heart rate, and general state of the individual were measured, as measures regarding their activity. HRV was logged after the initial assessments, subjects persisted at rest in the sitting

position for 20 minutes, while practicing “MoveHero” for 10 minutes, and immediately after the practice for 10 minutes, we considered this the recovery period.

For assessment, HRV was logged for no less than 10 minutes, to assess at least 256 consecutive RR intervals (after filtering). Moderate digital filtering was completed in the program itself, to eliminate premature ectopic beats and artefacts [13, 32], and there was no substitution, only the elimination of artefacts. Only series within excess of 95% sinus beats were included in the study [33].

HRV analysis was executed using linear (time and frequency domain) and nonlinear methods, studied via Kubios HRV® software (Kubios HRV v.1.1 for Windows, Biomedical Signal Analysis Group, Department of Applied Physics, University of Kuopio, Finland).

2.1.3. HRV Indices. Time-domain analysis was achieved by RMSSD, which is the square root of the mean of squared differences between successive beat intervals, and PNN50 that corresponds to the percentage of adjacent RR intervals that differ by more than 50 milliseconds (ms), SDNN that corresponds to the standard deviation of all normal RR intervals, and similarly mean RR and mean HR [13, 34–36].

For the frequency domain, the spectral components of low frequency (LF: 0.04 Hz to 0.15 Hz) and high frequency (HF: 0.15 Hz to 0.40 Hz) were estimated, in milliseconds squared (ms^2) and normalized units (n.u.), LF/HF ratio. The spectral analysis was calculated via the fast Fourier transform (FFT) algorithm [37].

A Poincaré plot translates RR intervals into geometric patterns and permits HRV analysis via the geometric or graphic properties of the resultant patterns [38]. Thus, SD1 is the short-term variability of continuous RR intervals, SD2 is the long-term variability of continuous RR intervals, and then there is the SD1/SD2 ratio. The Poincaré plot analysis is considered based on nonlinear dynamics [39].

2.2. Collection Procedures. Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFERS) and Fatigue Severity Scale (FSS) were initial assessments to characterize the participants. The HRV receptor was situated on the patients’ wrist and strap placement on their chest; the individuals from both groups remained at rest and were seated in a chair with spontaneous breathing for 20 minutes. After this period, the computer screen was initiated, and the persons remained seated with a laptop computer to enable them to perform the game on the computer for 10 minutes. HRV was evaluated throughout three time periods: the period before (M1—rest), during (M2—“MoveHero” activity), and for ten minutes following the motor task (M3—recovery) (Figure 2). The participants were appraised individually in a suitable room with a laptop computer, desk, and chair (Figure 1) and evaluator involvement responsible for instruction and the data collection annotation.

2.3. Statistical Analysis. Descriptive statistics were completed. Categorical data was expressed as absolute and relative frequencies while continuous data were expressed as average (\bar{x}) and standard error (se). Data normality was

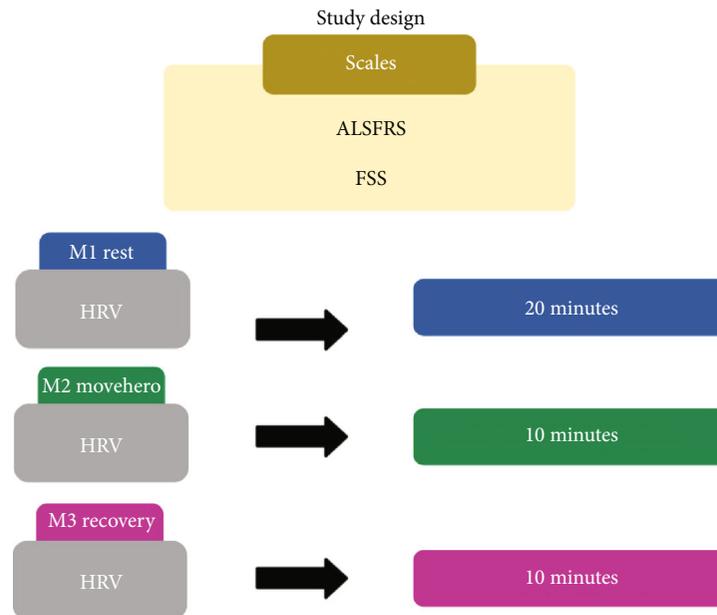


FIGURE 2: Flowchart of experimental design. ALSFRS: Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; FSS: Fatigue Severity Scale; HRV: heart rate variability; M1: first moment of HRV evaluation; M2: second moment of HRV evaluation; M3: third moment of HRV evaluation.

judged by a histogram with normality curve analysis. The following tests were enforced to verify the differences in each HRV index between the groups: multiple analysis of variance (MANOVA, intergroup evaluation) with repeated measures for comparison between the evaluation moments (M1—rest; M2—“MoveHero” activity; M3—recovery; intragroup assessment) with least significant difference (LSD) as a post hoc test. Partial eta-squared (η^2) was conveyed to measure effect sizes and interpreted as small (effect size > 0.01), medium (effect size > 0.06), or large (effect size > 0.14) [40]. Values of $p < 0.05$ (or <5%) were considered significant. The statistical package applied was Statistical Package for the Social Sciences (SPSS; IBM, Chicago, Illinois, USA), version 20.0.

3. Results and Discussion

Data collection was carried out from March 2017 to October 2018. A total of 49 potential subjects were requested to participate in the study. Six participants with ALS and 2 participants of the control group were omitted as they did not complete the protocol. Following exclusion criteria, 41 subjects were included in the data analysis, 21 with ALS and 20 from the control group. The groups were homogeneous concerning age, weight, and height. The sample characterization is represented in Table 1.

During HRV analysis, the MANOVA revealed a significant main effect for moments (Wilks' lambda = 0.300, $F_{56, 387} = 2.51$, $p < 0.001$, $\eta p^2 = 0.26$). No significant main effect for group or interaction between moments and group was found. Certainly, the separate ANOVAs presented a trend of difference in TINN (ms) and LF (ms^2) and significant effects for mean RR (ms), mean HR (bpm), and SD2 (Table 2).

Also, the post hoc analysis demonstrated some changes that were not found by the ANOVAs, in which the ALS group revealed reductions from rest to “MoveHero” activity on VR in mean RR, RR Tri, LF/HF ratio, and SD1/SD2 ratio and growths in RMSSD, TINN, HF ms^2 , and SD1. From the activity to recuperation, the ALS group subjects had increased mean RR, RR Tri, TINN, and LF/HF ratio, and from rest to recuperation, there were increases in RMSSD, TINN, and SD1. With regard the control group, from rest to activity, only mean RR and RR Tri decreased, and the matching indices increased from activity in VR to recuperation. Effects and measures of central tendency are represented in Table 2.

4. Discussion

The current study assessed HRV responses throughout a virtual task in ALS individuals (experimental group) and a control group (individuals presented with typical development) for three moments (rest, during VR activity, and recovery). We will now discuss the results.

4.1. HRV at Rest. The current study established that the experimental group at rest demonstrated lower HF n.u. and higher LF n.u. and LF/HF supporting Sachs et al. [41], suggesting larger sympathetic activation than the control group. Similarly, Dalla Vecchia et al. [42] revealed a greater sympathetic modulation at rest, related to a decrease in HF (ms^2), so ANS in ALS patients was impaired and these individuals had different baseline patterns, which can be elucidated by differences regarding the site of the lesion in the central nervous system (CNS); resultant in different behaviors of the ANS studies establishes that CNS damage in ALS can lead to degeneration of spinal cords' sympathetic

TABLE 1: Sample characterization.

	ALS ($n = 21$)	CONTROL ($n = 20$)	p value
	Mean (standard error) [confidence interval]	Mean (standard error) [confidence interval]	
Age (years)	51.3 (2.8) [31-74]	49.1 (10.7) [6.02-15.38]	0.542
Weight (kg)	73.8 (3.1) [55.5-102]	76.5 (3.9) [45-100]	0.602
Height (cm)	166.1 (2.0) [152-184]	170.8 (2.1) [158-185]	0.126
ALFRS	32.3 (0.9) [23-38]	—	—
FSS	40.4 (3.5) [11-61]	—	—
Symptom's time (months)	44.9 (9.9) [12-204]	—	—
	$\%(n)$	$\%(n)$	
<i>Gender</i>			
Male	71.4 (15)	70 (14)	0.545
Female	28.6 (6)	30 (6)	
<i>Ex-smoker</i>	28.6 (6)	0	0.006
Smoker	4.8 (1)	0	0.487
Arterial hypertension	23.8 (5)	0	0.049
<i>Education level</i>			
High school	28.6 (6)	50 (10)	0.333
Higher education	66.7 (14)	50 (10)	
Physiotherapy	47.6 (10)	—	—

Data presented as mean (standard error) and 95% confidence interval followed by p value of Student's t -test for continuous variables and chi-square test with posttest Bonferroni (for comparison between groups) for categorical variables. ALS: amyotrophic lateral sclerosis; CONTROL: control group; kg: kilogram; m: meters; cm: centimeters; ALFRS: Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised; FSS: Fatigue Severity Scale.

ganglia in the more progressive cases [43–45]. Thus, the presence of different autonomic profiles at rest reveals the new notion of ALS as a multisystem disorder with phenotypic heterogeneity.

According to Desport et al. [46], ALS subjects have a larger resting energy expenditure (i.e., energy vital for the maintenance of normal body functions and homeostasis) when likened to a control group, which can be linked with the presence of sympathetic overactivity at rest and can perhaps predict the rate of disease progression. While there is decrease in HRV with the severity of the disease, the subjects in our study were not in advanced disease stages (namely, they were able to move, climb stairs, and others), but nonetheless, there was an alteration compared to the control group.

It is recognized that incomplete autonomic system functionality can initiate a metabolic adjustment in ALS subjects [9]. Dupuis et al. [47] revealed that ALS patients have hypermetabolism, and nutrient ingestion and absorption are impaired [48]. It can be related to a pathophysiological process in the production of mitochondrial energy and in the sympathoadrenergic activation [46]. Additionally, ALS subjects regularly have high levels of plasma norepinephrine and catecholamines [42] and the sympathoadrenergic system can persevere when the heart is under stress [36], which occurs to those subjects even during rest.

4.2. HRV during VR Activity. Another significant discovery was during the performance of the virtual task (activity

moment); the parasympathetic modulation declined from rest to activity in the control group at various rates (RMSSD, pNN50, HF (ms^2), HF (n.u.), and SD1), while HR increased (as expected). Conversely, we revealed an increase in HR also in the experimental group, but there was only a reduction in the HF index (ms^2). This result highlights a parasympathetic nervous system dysfunction, which did not adjust to the demands of motor and/or cognitive activities in ALS individuals, in an identical intensity when equated to the control group. Yet, we can theorize that this dysfunction extends to the sympathetic system, as both need to act together, as revealed in LF n.u. index (that has part of its components representing sympathetic activation) a tendency to increase during the activity in the control group, but not the experimental group.

Consistent with Acharya et al. [49], sympathetic stimulation occurs in response to stress, exercise, and heart disease, triggering an increase in HR by elevating the rate of firing of pacemaker cells in the hearts' sinoatrial node and parasympathetic modulation, consequential on internal organ function, trauma, allergic reactions, and inhalation of irritating substances, decreasing the firing rate of pacemaker cells and HR, providing a regulatory balance in physiological autonomic function.

Therefore, the reduced HRV achieved in ALS subjects during VR task in this study demonstrated a sympathetic predominance in these individuals, which needs further investigation by reason of the cardiovascular neural profile that can initiate poor clinical results [42], for instance, loss

TABLE 2: Continued.

HRV indices	Groups	Moments				Main effect groups	Main effect moments	Interaction groups × moments
		Rest (M1) Mean (SE) [CI LL; UL]	VR activity (M2) Mean (SE) [CI LL; UL]	p (M1 × M2)	Recovery (M3) Mean (SE) [CI LL; UL]			
HF (ms ²)	ALS	130.5 (36.6) [55.3; 205.6]	78.8 (22.1) [33.5; 124.2]	0.059 * ↓	123.0 (35.8) [49.4; 196.6]	—	—	—
	CONTROL	190.7 (34.0) [120.8; 260.7]	134.5 (20.5) [92.3; 176.6]	0.029 ↓	196.1 (33.3) [127.6; 264.7]	0.022 ↑	—	6.52; 0.004; 0.20
	p value	—	0.076 *	—	—	—	—	—
LF n.u.	ALS	78.3 (3.6) [71.0; 85.7]	81.1 (3.1) [74.8; 87.5]	—	78.2 (2.7) [72.6; 83.9]	—	—	—
	CONTROL	66.3 (3.3) [59.5; 73.2]	74.1 (2.9) [68.2; 80.0]	0.077 * ↑	72.4 (2.6) [67.1; 77.6]	0.084 ↓	8.07; 0.009; 0.24	—
	p value	0.021	—	—	—	—	—	—
HF n.u.	ALS	21.6 (3.6) [14.3; 28.9]	18.8 (3.1) [12.5; 25.1]	—	21.7 (2.7) [16.1; 27.4]	—	—	—
	CONTROL	33.6 (3.3) [26.8; 40.4]	25.7 (2.9) [19.8; 31.6]	0.072 * ↓	27.6 (2.6) [22.3; 32.8]	0.083 * ↑	8.04; 0.009; 0.24	—
	p value	0.020	—	—	—	—	—	—
LF/HF	ALS	4.55 (0.63) [3.26; 5.84]	5.34 (0.77) [3.74; 6.93]	—	5.35 (0.88) [3.54; 7.16]	—	—	—
	CONTROL	2.68 (0.59) [1.48; 3.88]	4.03 (0.72) [2.55; 5.51]	—	3.11 (0.82) [1.42; 4.79]	—	4.77; 0.038; 0.16	—
	p value	0.038	—	—	0.073 *	—	—	—
SD1 (ms)	ALS	11.9 (1.6) [8.7; 15.1]	10.9 (1.3) [8.2; 13.7]	—	11.4 (1.6) [8.0; 14.8]	—	—	—
	CONTROL	15.3 (1.4) [12.3; 18.3]	13.7 (1.2) [11.1; 16.2]	0.060 * ↓	16.1 (1.5) [12.9; 19.3]	0.029 ↑	3.60; 0.069 *; 0.12	2.75; 0.079 *; 0.10
	p value	—	—	—	0.045	—	—	—
SD2 (ms)	ALS	27.9 (3.6) [20.5; 35.4]	27.9 (3.4) [20.9; 34.8]	—	30.6 (4.2) [22.0; 39.1]	—	—	—
	CONTROL	34.3 (3.4) [27.4; 41.3]	32.9 (3.1) [26.5; 39.4]	—	39.7 (3.9) [31.8; 47.7]	0.034 ↑	0.063 ↓	3.26; 0.050; 0.11
	p value	—	—	—	—	—	—	—

TABLE 2: Continued.

HRV indices	Groups	Moments				Main effect groups	Main effect moments	Interaction groups × moments
		Rest (M1) Mean (SE) [CI LL; UL]	VR activity (M2) Mean (SE) [CI LL; UL]	p (M1 × M2)	Recovery (M3) Mean (SE) [CI LL; UL]			
	ALS	2.51 (0.16) [2.19; 2.84]	2.83 (0.22) [2.39; 3.28]	—	2.88 (0.19) [2.50; 3.27]	—	—	—
	CONTROL	2.27 (0.15) [1.97; 2.58]	2.42 (0.20) [2.01; 2.84]	—	2.48 (0.17) [2.12; 2.83]	—	—	3.18; 0.052; 0.11
	p value	—	—	—	—	—	—	0.020 ↑

Data presented as mean (standard error (SE)) and 95% confidence interval (CI) presented in lower limit (LL) and upper limit (UL) followed by the p value of the post hoc LSD (least significance difference) test. Post hoc tests were calculated even when there were no significant interactions to find significant results; * marginally significant results ($p = 0.055 - 0.095$); arrows indicate whether the values represent an increase (↑) or decrease (↓) of the indices between moments. HRV: heart rate variability; M1–M3: moments 1 to 3; VR: virtual reality (during virtual task); bpm: beats per minute; HF: high frequency; LF: low frequency; LF/HF: low frequency and high frequency ratio; ms: millisecond; ms²: millisecond squared; n.u.: normalized units; RMSSD: square root of the mean squared differences of successive RR intervals; RR intervals: intervals between heartbeats; SDNN: standard deviation of the mean of all RR intervals over a period; pNN50: percentage of adjacent RR intervals with a difference in duration greater than 50 milliseconds; SD1: the standard deviation of the instantaneous variability of the beat-to-beat RR interval in ms; SD2: the standard deviation of the long-term continuous variability of the RR interval in ms; SD1/SD2: ratio of short and long variations of RR intervals; ALS: amyotrophic lateral sclerosis group; CONTROL: control group.

of left ventricular dynamics [50], increased cardiac arrhythmias, cardiovascular mortality [10, 51], and the possible risk of sudden death [12, 36].

4.3. HRV during Recovery. Regarding the recovery period, in the control group, there was an upsurge in PNS with a reduction in heart rate when associated to the moment of activity, but lacking the expected return to rest values, probably owing to the short rest time (5 min) after activity. Yet, in the ALS group, these ANS adjustments were not observed. We can speculate that the lack of ANS adaptation in ALS individuals during activity did not permit the PNS to reduce physiologically during activity, so the recovery response did not occur [52].

Another important corresponding finding of the current study was that ALS individuals presented several arrhythmia points during the analysis of the tracings. It has been advised that arrhythmias are marker of cardiac sympathetic denervation, usually present in ALS individuals, and it may possibly incline patients to fatal cardiac events. Pimentel et al. [10] suggested that autonomic dysfunction could affect the ALS clinical progression and increase the cardiac arrhythmia risk and sudden death. Otherwise, of the nonlinear HRV assessments, we used SD1 and SD2, but we know that several nonlinear HRV methods have been used and developed; evidence demonstrates a prognostic role of this analysis in identifying individuals at risk of cardiovascular events or mortality [53]. These analyses consider the application of complex system theory to physiology states and are associated with increased complexity variability when compared to healthy controls [54].

4.4. Final Comments and Limitations. Our study was a cross-sectional intervention, where a VR task was necessary to provide motor and/or cognitive activity; conceivably, for this short-term intervention the main results arose in the control group only; however, a limitation of our study is that although most participants from both groups (control and ALS) had completed higher education, without statistical difference between them, we were not able to obtain data on the participants' cognitive status; these data could have generated important responses to our study. A recent meta-analysis of Park et al. [55] demonstrates that therapeutic exercise seems beneficial for ALS patients, in longitudinal studies. While our results did not reveal any physiological adaptations of the ANS, VR tasks with demand for movement of the upper limbs and subjects with ALS similarly offered increased sympathetic activity at rest. We highlight that VR activities can be enforced to judge the ANS adaptation to characterize ALS patients and trace the prognosis and better clinical treatment and recommended in future studies. Moreover, as an alternative to physical activity, VR interpositions promote a more engaging and motivating modality, improving performance, wellbeing, and the recognized benefits of physical activity [22]. As such, VR should be investigated as a chance to heighten interactions and participation, similarly providing the medical clinicians and professionals the ability to modify the difficulty and repetitions of the

tasks, and thereby stipulate interaction along with the current and future physical requirements of the ALS patients.

It is important to mention that, although HRV is among the most sensitive and specific approaches currently available to evaluate cardiovascular autonomic neuropathy, its association with other forms of evaluation would be interesting since the interaction between the regulatory processes of the heart function and peripheral blood flow expands the possibilities of assessing autonomic dysfunction. The literature suggests the evaluation of baroreflex sensitivity, muscle sympathetic nerve activity, plasma catecholamines, and heart sympathetic imaging [56]. Besides that, the assessment by means of photoplethysmography could have been a great association to our analyses, for assessing the underlying status of peripheral blood vessels, and whenever possible, it is suggested using additional physiological cardiovascular measurements, increasing accuracy [57–59]. Additionally, by analysis of the phase coherence between the oscillations in microvascular blood flow and tissue oxygenation, it would be possible to study cardiovascular and microvascular dynamical processes [60]. Considering that in our study the focus was on the adaptation of ANS in people with ALS during physical activity in VR, we did not carry out in association with other assessments, so we suggest that this be done in future studies.

5. Conclusions

The results reveal that amyotrophic lateral sclerosis (ALS) subjects have reduced heart rate variability (HRV) with sympathetic predominance when likened to the healthy control group. Also, individuals with ALS do not express adaptive capacity of the autonomic nervous system when equated to the control group throughout virtual reality (VR) activity and recovery.

Data Availability

The heart rate variability data used to support the findings of this study are included within the article.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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