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Musa Güneş, Meral Boşnak Güçlü, Ayşenur Güvenir & Hatice Ayşe Tokçaer Bora

Effects of Inspiratory Muscle Training on Oxygen Consumption, Muscle Oxygen, and Physical Activity Levels in Patients with Parkinson's Disease

Musa GÜNEŞ[1,2*], Meral BOŞNAK GÜÇLÜ[3], Ayşenur GÜVENİR[1,4], Hatice Ayşe TOKÇAER BORA[5]

[1]Gazi University, Institute of Health Sciences, Physiotherapy and Rehabilitation Department, Ankara, Türkiye,

[2]Karabük University, Faculty of Health Sciences, Physiotherapy and Rehabilitation Department, Karabük, Türkiye,

[3]Gazi University, Faculty of Health Sciences, Cardiopulmonary Physiotherapy and Rehabilitation Department, Ankara, Türkiye,

[4]Yozgat Bozok University, Faculty of Health Sciences, Ergotherapy Department, Yozgat, Türkiye,

[5]Gazi University, Faculty of Medicine, Department of Neurology, Ankara, Türkiye.

Musa GÜNEŞ, PT, PhD[1] (musagunes@karabuk.edu.tr), (ORCID: 0000-0001-8532-2575)

Meral BOŞNAK GÜÇLÜ, PT, PhD[2] (meralbosnak@gazi.edu.tr), (ORCID: 0000-0002-3861-9912)

Ayşenur GÜVENİR, PT, MsC[3] (aysenur.guvenir@bozok.edu.tr) (ORCID: 0009-0005-0566-3051)

Hatice Ayşe TOKÇAER BORA, MD[4] (tokcaer@gazi.edu.tr) (ORCID: 0000-0003-4363-724X)

***Corresponding Author:**

Musa GÜNEŞ[1], (musagunes@karabuk.edu.tr, Phone: +90 531 513 2482)

[1]Karabük University, Faculty of Health Sciences, Physiotherapy and Rehabilitation Department, Karabük, Türkiye.

Abstract

To investigate the effects of inspiratory muscle training (IMT) on maximal exercise capacity, muscle oxygenation, peripheral and respiratory muscle strength, respiratory muscle endurance, pulmonary function, physical activity level, and quality of life in patients with Parkinson's disease (PD). A randomized, controlled, triple-blind study. Twenty patients with PD were randomly included in each group: the IMT group (50% of MIP) and the control group. Maximal exercise capacity (CPET), respiratory muscle strength (MIP and MEP) and endurance, pulmonary function, peripheral muscle strength, muscle oxygenation, physical activity level, and quality of life (Parkinson's Disease Questionnaire-39 (PDQ-39)) were evaluated before and after. Peak oxygen consumption, MIP, MEP, respiratory muscle endurance, peripheral muscle strength, active energy expenditure, and PDQ-39 scores of the IMT group improved statistically significantly compared to the control group, $\%FEF_{25-75\%}$ improved within both groups ($p<0.05$), and there was no statistically significant difference within and between groups in muscle oxygenation ($p>0.05$). IMT improves oxygen consumption, respiratory muscle strength and endurance, small airway obstruction, peripheral muscle strength, physical activity level, and quality of life in patients with PD and preserved pulmonary function. Similar muscle oxygen levels, even at higher workloads, may indicate an improvement in oxygenation. ClinicalTrials number: NCT06017336 (date: 15/08/2023).

Keywords: Parkinson's disease; inspiratory muscle training; oxygen consumption; muscle oxygenation; physical activity; quality of life.

Introduction

Parkinson's disease (PD) is a multifactorial, chronic, and progressive neurodegenerative disease manifested by motor and non-motor symptoms[1]. Postural deformities, chest wall rigidity, diaphragmatic dyskinesia, and fatigue resulting from these symptoms in patients lead to respiratory muscle weakness, decreased lung volumes, and deterioration in pulmonary function[2,3].

Respiratory muscle strength and endurance decrease from the early stages of PD. Patients experience restrictive or obstructive type pulmonary dysfunction, with approximately 50% reporting dyspnea[3]. Dyspnea, hypoxia, and motor symptoms lead to inadequate oxygen delivery to the muscles, resulting in physical inactivity[4,5]. Respiratory muscle weakness, in addition to these disorders, may limit exercise capacity[3,6]. Previous studies have shown that submaximal exercise capacity is decreased in patients with PD[7,8], and that maximum oxygen consumption is 34% lower than that of healthy controls[8].

Decreased inspiratory muscle strength in PD may increase metaboreflex activity during exercise, leading to reduced blood and oxygen flow to peripheral muscles[3,9]. Consequently, the contractile performance of skeletal muscles declines[10]. Studies have shown that as inspiratory muscle strength diminishes, peripheral muscle strength decreases, and mortality risk rises[11,12]. These factors negatively affect the quality of life of patients with PD[3]. Additionally, mitochondrial dysfunction and hypoxia affect skeletal muscle oxidative metabolism, impairing the oxygen utilization capacity of skeletal muscle during exercise[5]. Inspiratory muscle training (IMT) may enable respiratory muscles to work longer without fatigue at higher workloads, improving oxygenation and exercise capacity[9,13,14]. Thus, IMT

may be an important rehabilitation strategy to improve pulmonary and extrapulmonary symptoms and quality of life in Parkinson's disease.

The beneficial effects of IMT have been reported in various groups with chronic diseases, including chronic obstructive pulmonary disease (COPD), heart failure, hypertension, and multiple sclerosis[13-16]. However, the effect of IMT on patients with PD has been examined in only a few studies. IMT enhances respiratory muscle strength and endurance while reducing dyspnea in patients with PD[17,18]. Nevertheless, the effects of IMT on PD remain uncertain due to variability in training intensity and frequency[19,20]. Furthermore, the effect of IMT on maximal exercise capacity, peripheral muscle strength, muscle oxygenation, and physical activity levels in individuals with PD is unknown.

Therefore, this study aimed to investigate the effects of IMT on maximal exercise capacity, muscle oxygenation, respiratory muscle strength and endurance, peripheral muscle strength, pulmonary function, physical activity level, quality of life, motor function, and disease severity in patients with PD.

Methods

Study population

Forty patients with PD referred from the Gazi University, Faculty of Medicine, Department of Movement Disorders and PD of Neurology Clinic, for pulmonary rehabilitation to the Department of Cardiopulmonary Physiotherapy and Rehabilitation, located in the Faculty of Health Sciences, between September 2023 and December 2024, were included.

The inclusion criteria were as follows: a diagnosis of idiopathic PD according to the MDS Clinical Diagnostic Criteria for PD[21], conducted by a neurologist, aged 45 to 80 years, classified as stages I-III on the Modified Hoehn & Yahr (M. H&Y) scale, the ability to walk independently, and a stable clinical condition. Exclusion criteria included the presence of

additional neurological diseases, any diagnosed lung disease, cardiac, orthopedic, and psychological problems that affect physical functions, cognitive impairment (Mini-Mental State Examination test score <24), any contraindications for exercise testing and/or training as outlined by the American College of Sports Medicine[22], and a diagnosis of COVID-19 in the previous year. The study was approved by the University Ethics Committee (2023-903, date: 27/07/2023) and was conducted in accordance with the Declaration of Helsinki. (Clinical trial registry number: NCT06017336, Registry date: 15/08/2023). All patients provided written informed consent to participate in the study.

Study design

This study is a prospective, randomized, controlled, triple-blind design and followed the Consolidated Standards of Reporting Trials (CONSORT) statement guidelines[23]. Patients were randomly assigned to either the IMT group (n = 20) or the control group (n = 20). The IMT group underwent IMT at 50% of maximum inspiratory pressure (MIP) for eight weeks, whereas the control group performed thoracic expansion exercises. Patients were evaluated on two consecutive days before and after the eight-week training period. Pulmonary function, respiratory muscle strength and endurance, peripheral muscle strength, and quality of life were assessed on the first day. Maximal exercise capacity and muscle oxygenation were evaluated on the second day. Following these assessments, an activity monitor was attached on the second day. All patient evaluations and treatments occurred during the “on” period, approximately 1 hour after medication administration. The primary outcomes included maximal exercise capacity, muscle oxygenation, and physical activity, while the secondary outcomes included respiratory muscle strength and endurance, peripheral muscle strength, pulmonary function, and quality of life.

Randomization

Patients were randomized using a six-block design to assign eligible patients to either the IMT or the control group. The study director kept computer-generated random allocation sequences in sealed, opaque envelopes until the group assignments were completed. A physical therapist (not a researcher) assigned patients to groups by opening each envelope in the order of study entries. Patients were assigned to the IMT and control groups according to the order of allocation in the envelope.

Blinding

In the triple-blind study, patients were not informed of their group assignment (IMT or control) and were assessed and educated at different times and locations. The pre- and post-assessments and training sessions were conducted by two different physiotherapists. Furthermore, patient groups were coded prior to statistical analysis, and the code meanings were not disclosed to the statistician. In this way, a triple-blind study was conducted, ensuring that patients, assessors, and analysts remained blinded.

Measurements

Demographics and clinical characteristics were recorded. The patient's motor symptoms were evaluated using the Movement Disorder Society's Unified Parkinson's Disease Rating Scale-III (UPDRS-III)[24], and disease staging was assessed using the M. H&Y scale[25].

Pulmonary function test

Pulmonary function was evaluated using a portable spirometer (MIR® Spirobank) according to the American Thoracic Society/European Respiratory Society (ATS/ERS) guidelines. FEV_1, FVC, FEV_1/FVC, PEF, and $FEF_{25–75\%}$ were measured. The decrease in predicted FEV_1/FVC and FVC were classified as obstructive and restrictive lung abnormality[26].

Respiratory muscle strength

The MIP and maximum expiratory pressure (MEP) were evaluated using the mouth pressure device following the ATS/ERS guidelines[27]. Reference values were utilized to calculate the percentage of predicted values for MIP and MEP, which helped identify respiratory muscle weakness[28].

Respiratory muscle endurance

Respiratory muscle endurance was evaluated using the maximal incremental loading technique with a device (POWERbreathe® Classic, IMT Technologies Ltd., Birmingham, UK). The tests started at 30% MIP and increased by 10% every 2 minutes until the load became intolerable. Endurance was determined by multiplying the maximum peak pressure by the total time (cmH_2Oxsec)[29].

Maximal exercise capacity

Maximal exercise capacity was assessed using a Cardiopulmonary Exercise Test (CPET) conducted on a treadmill ergometer (Trackmaster, 3017 Full Vision, Newton, USA) with an analyzer interface (Cosmed Quark CPET®, Rome, Italy). Electrocardiography was performed using a 12-lead system (COSMED® C12x/T12x). The test load was increased to 1 km/h with a 1% elevation rate per minute, using the "breath by breath" method. When the respiratory exchange ratio (RER) reached ≥ 1.10, heart rate reserve (HRR) was < 10, or any abnormal ECG changes or signs of exhaustion were observed, the CPET was terminated[30]. Dyspnea, leg fatigue, overall fatigue perceptions, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were recorded at rest, during testing, and during recovery.

Muscle oxygenation

The oxygen saturation of the quadriceps femoris (QF) muscle and total hemoglobin in muscle capillaries were measured using a near-infrared spectroscopy device (Moxy®, Fortiori, Design LLC, Minnesota, USA), a valid and reliable non-invasive method. Prior to the CPET, the

Moxy® monitor was positioned on the lower one-third of the motor point of the QF muscle. Muscle oxygen saturation (SmO_2), minimum (SmO_{2min}) and maximum muscle oxygen saturation (SmO_{2max}), total hemoglobin (THb), minimum (THb_{min}) and maximum (THb_{max}) total hemoglobin values at rest, during the test, and during recovery were measured and recorded[31].

Peripheral muscle strength

The isometric muscle strength of the QF and shoulder abductors were assessed using a digital pressure dynamometer (JTECH® Power Track Commander, Baltimore, MA, USA). Measurements were repeated three times on each side, and the highest values were recorded[32].

Quality of life

Quality of life was evaluated using the Parkinson's Disease Questionnaire-39 (PDQ-39). The PDQ-39 comprises eight domains, each scored from 0 to 4: mobility, daily activities, emotional well-being, stigma, social support, cognition, communication, and physical discomfort. The total score varies from 0 to 100, with lower scores signifying a better quality of life[33].

Physical activity level

Physical activity levels including duration of physical activity (min/day) (>3 metabolic equivalents (METs)), total and active energy expenditure (joules/day), average METs (METs/day), number of steps (steps/day), lying time (min/day), and sleep time (min/day), were assessed using an activity monitor (Sensewear®, BodyMedia, Inc., Pittsburgh, USA). The activity monitor was attached to the patient's non-dominant triceps brachii for five consecutive days each week. Physical activity level was categorized by METs and the number of steps[34,35]. Physical activity level was classified according to the number of steps as <5000 steps/day: inactive, 5000–7499 steps/day: low active, 7500–9999 steps/day: somewhat active,

10000–12499 steps/day: active[35]; and according to MET as <1.5 MET: inactive, 1.5–2.9 MET: low active[34].

Inspiratory muscle training protocol

The training utilized a pressure threshold loading device (POWERbreathe® Classic Low Resistance) to provide consistent pressure loads during each inhalation, thereby strengthening the diaphragm and rib cage muscles. The IMT group participated in IMT at 50% of the measured MIP during supervised sessions each week, with this percentage representing their new training workload[36]. Patients were instructed to practice diaphragmatic breathing for 10–15 breaths and to rest for 5–10 seconds following each set. All groups engaged in training for 30 minutes per day, seven days a week, over eight weeks, with one supervised session and six sessions conducted at home. Vital signs were monitored throughout the sessions. The total training time was calculated from patients' diary entries. It is reported that training workloads of at least 8 weeks with weekly graded evaluations at 50% or more of MIP are more effective[37,38]. Patients were advised to refrain from participating in any physical activities or exercises outside their usual routine during the study period.

The control group completed thoracic expansion exercises at home for eight weeks, performing 30 times per session, four sessions per day, and seven days a week. Patients received weekly calls and were asked to record their exercise sessions in a diary. Additionally, for ethical reasons, we invited patients in the control group to participate in IMT after completing the initial protocol.

Statistical analysis

Data were analyzed using SPSS 25.0 (SPSS, Chicago, Illinois). The sample size was estimated with the G*Power v3.1 (Universitat Kiel, Germany) program. According to

peakVO_2, 20 people per group were required to achieve 80% power, a 5% type 1 error, and a Cohen's F=0.40 effect size.

The Shapiro-Wilks test was used to determine the normal distribution of numerical variables. Descriptive analyses were expressed as mean± standard deviation (X±SD), mean difference, and 95% confidence interval (95% CI) for normally distributed variables; median, interquartile range$_{25–75\%}$ (IQR$_{25–75\%}$) for normally undistributed variables, percentage (%), frequency (n) for categorical variables. Groups were compared to normally distributed variables using Student's t-test, non-normally distributed variables using the Mann–Whitney U test, and nominal data using a χ2-test. The effect of education on nominal variables was analyzed using Cochran's Q test. Analysis of covariance was used to determine whether there were significant differences between pre- and post-test variables and between the IMT and control groups; baseline measurements were used as covariates. Manually adjusted post-hoc comparisons were made for change in continuous variables within groups using the Bonferroni test. An intention-to-treat analysis was conducted; all patients received IMT or thoracic expansion interventions as allocated. Cohen's *d* effect size was calculated using the F test and categorized as trivial (≤0.20), small (0.21–0.49), moderate (0.50–0.79), or large (≥0.80)[39]. p≤0.05 was considered statistically significant.

Results

Sixty patients diagnosed with PD were screened, and 40 were randomly assigned to the IMT and control groups (Figure 1). There were no significant differences in baseline characteristics between the groups (p>0.05, Table 1). At baseline, 62.5% of patients had an obstructive type, 7.5% had a restrictive type, and 12.5% had mixed-type pulmonary function abnormalities. No adverse clinical effects were noted in any of the patients during the interventions. The treatment compliance for the IMST and control groups was 100% and 53.28%, respectively.

There were no significant differences in FEV_1% and FVC% in either group, both within and between groups, following the interventions ($p>0.05$). There was no significant difference in $FEF_{25-75\%}$ (8.58%, 95%CI [-6.16%–23.34] %, $FEF_{25-75\%}$; 1-β: 42.9%, Cohen's *d*=0.38) between the groups (p=0.246); however, significant differences were present within the groups ($p<0.05$).

The MIP (38.56 cmH_2O, 95%CI [30.26–46.87] cmH_2O, Cohen's *d*=3.05), MEP (31.25 cmH_2O, 95%CI [18.43–44.08] cmH_2O, Cohen's *d*=1.60), MIP%, and MEP% of the IMT group increased statistically significantly after the intervention compared to the control group ($p<0.05$, Figure 2, Table 2).

The respiratory muscle endurance (20519.10 $cmH_2O\times sec$, 95%CI [6686.67–34351.52] $cmH_2O\times sec$, Cohen's *d*=0.98) of the IMT group increased statistically significantly compared to the control group (p=0.005, Table 2). After training, the QF (30.02 N, 95%CI [2.80–57.24] N, Cohen's *d*=0.72) and shoulder abductor (29.12 N, 95%CI [0.42–57.82] N, Cohen's *d*=0.67) muscle strength of the IMT group increased statistically significantly compared to the control group ($p<0.05$, Figure 2, Table 2).

The total PDQ-39 score (-7.03 points, 95%CI [(-10.39)–(-3.67)] points, Cohen's *d*=1.39) and the mobility, daily activities, communication, and physical discomfort sub-parameters scores of the IMT group decreased statistically significantly compared to the control group ($p<0.05$, Table 2).

The active energy expenditure (890.44 joules/day, 95%CI [43.42–1737.47] joules/day, Cohen's *d*=0.69) of the IMT group increased statistically significantly compared to the control group (p=0.040, Figure 2, Table 2). There was no significant difference between the groups in total energy expenditure, physical activity duration (1-β: 46.2%, Cohen's *d*=0.62), average

METs (Cohen's *d*=0.38), number of steps (1-β: 13.1%, Cohen's *d*=0.27), and lying down (p>0.05, Table 2).

The number of patients classified as inactive to low active according to METs increased in the IMT groups (from 15% to 45% patients) compared to the control (from 5% to 15% patients) groups (p=0.038). There was no significant difference between the groups according to step count categories (p=0.281). Also, the number of steps increased clinically significantly after IMT, reaching 994.95 steps per day.

No significant differences were found in M. H&Y scale scores within and between the groups after interventions (p=0.187, Table 2). The UPDRS-III scores of the IMT group increased statistically significantly compared to the control group (p=0.050, Table 2).

The peakVO_2ml/min/kg (2.99 ml/min/kg, 95%CI [1.19–4.78] ml/min/kg, Cohen's *d*=1.09) and VO_2% (9.87%, 95%CI [5.21–14.53]%, Cohen's *d*=1.39) significantly improved between groups (p<0.05, Figure 2, Table 3). The power of this study, according to peakVO_2ml/min/kg (1-β=98.5%), was found to be statistically high.

At peak workload, VO_{2kg}, VO_2%, VCO_2, VE, VO_2/HR, speed, incline, and ΔSBP of the IMT group increased statistically significantly compared to the control group (p<0.05). CPET parameters of the IMT group at peak workload, VO_{2kg}, VO_2%, RER, VCO_2, MET, VE, VO_2/HR, breathing reserve (BR), speed, incline, and ΔSBP increased statistically significantly, and SBP at resting, Δdyspnea, Δfatigue, Δleg fatigue, and ΔSpO_2 decreased statistically significantly after intervention (p<0.05, Table 3).

There was no significant difference in resting, minimum, maximum, and recovery SmO_2, $SmO_{2average}$, and THb between and within groups for the QF muscle during CPET (p>0.05, Table 4). Effect sizes were small for SmO_{2max}% (1.03%, 95%CI [-7.37–9.45] %, Cohen's

d=0.25), trivial for $SmO_{2average-max}$% (-0.25%, 95%CI [-8.47–7.97] %, Cohen's *d*=0.06), and moderate for THbmax (g/dl) (-0.14 g/dl, 95%CI [-0.33–0.03] g/dl, Cohen's *d*=0.51).

Discussion

This study demonstrated that IMT significantly enhanced oxygen consumption, respiratory and peripheral muscle strength, respiratory muscle endurance, active energy expenditure, motor function, and quality of life in patients with PD. Maintaining the same oxygen level even at higher workloads may indicate that muscle oxygenation has improved. According to MET, the number of inactive patients decreased, while the rates of less active patients and the number of steps increased clinically significantly (994.95 steps/day); thus, the level of physical activity increased. Small airway obstruction improved similarly after training, whereas IMT did not significantly affect disease severity.

Pulmonary, cardiac, and musculoskeletal system involvement in patients with PD impairs maximal exercise capacity[7,8]. After IMT, $peakVO_2$ increased by 2.99 ml/min/kg and $\%peakVO_2$ by 9.87, with large effect sizes between groups. In the IMT group, $peakVO_2$ and $\%peakVO_2$ increased by 3.19 ml/min/kg and 11.10%, respectively.

IMT enhances respiratory muscle strength and endurance, maintaining ventilation and improving the metaboreflex[9]. In this study, the increase in minute VE at rest and the peak in the IMT group indicate improved ventilation. Additionally, increased peripheral muscle strength[40,41], decreased fatigue perception[4,6,42], and improved motor problems[43] may have increased $peakVO_2$ by alleviating limitations originating from the musculoskeletal system. As a result of all these adaptations, the increase in $peakVO_2$ in our study indicates that maximal exercise capacity improved.

In patients with PD, the heart rate may not increase sufficiently during exercise due to cardiac sympathetic denervation and reduced contractility, leading to chronotropic insufficiency[44].

Therefore, achieving a peak RER ≥ 1.1 at maximum effort during symptom-limited CPET may not be possible[30]. In the present study, IMT did not alter peak RER; however, maximal workload improved. Similar peak RER values may lead to reduced reliance on anaerobic metabolism, as a result of improved oxygen metabolism[30]. Thus, IMT may have increased exercise capacity by enabling the same effort at higher workloads. The patients' resting and peak heart rates remained unchanged after IMT. Similar heart rates, despite the increased peak workload, suggest enhanced cardiac function following IMT.

Consequently, oxygen consumption increased due to improved VE at peak exercise, leading to an increase in VO_2/HR. Both BR and peak VE/VCO_2, which indicate ventilatory efficiency, were preserved after IMT. These results suggest that, after IMT, higher workloads were achieved, and ventilation capacity was similarly utilized at these higher workloads, while BR and ventilation efficiency may have improved. Additionally, the enhanced oxygen utilization capacity of skeletal muscles may have contributed to the increase in ventilatory efficiency[45]. The VE/VCO_2 exceeded 34 in AT both before and after IMT, indicating that ventilation/perfusion mismatch persists throughout the exercise test. IMT alone may not influence ventilation-perfusion mismatch; further investigation into its effectiveness at varying intensities and frequencies is warranted.

IMT enhanced patients' peak workload during maximal exercise in CPET. The sustained reduction in dyspnea and fatigue at elevated workloads post-IMT indicates improvement in these symptoms. IMT also increased SBP at peak workload, indicating an improvement in sympathetic activity[7]. IMT attenuates metaboreflex activity by increasing blood flow and metabolite transport, thereby reducing fatigue[9]. Furthermore, as motor problems decrease, peakVO_2 increases[46].

This study suggests that IMT potentially improved respiratory and cardiovascular functions during peak exercise in patients with PD by enhancing the strength of respiratory and peripheral muscles, increasing ventilation, decreasing motor impairments, dyspnea, and fatigue, and alleviating autonomic dysfunction.

In this study, the impact of IMT on muscle oxygenation in patients with PD was first investigated using NIRS. After IMT, SmO_2 and THb levels in the quadriceps femoris were maintained during maximal exercise. However, patients achieved higher exercise workloads while maintaining the same muscle oxygen levels post-IMT. This result suggests that peripheral muscles may be able to better balance oxygen supply and demand by utilizing oxygen more efficiently during exercise. The enhancement in peripheral muscle strength after IMT may be attributed to increased mitochondrial activity, potentially improving the muscle's capacity to utilize oxygen[12,14]. This increased capacity is linked to improved oxygen diffusion, which refers to the movement of O_2 from hemoglobin to mitochondria[41]. Moxy measures the total hemoglobin content but does not differentiate between deoxyhemoglobin and oxyhemoglobin[31]. In the current study, the rise in blood oxyhemoglobin levels may have contributed to the muscle's enhanced oxygen-utilizing capacity. Furthermore, IMT may have diminished metaboreflex activity[9,42], allowing the QF muscle to maintain similar oxygenation levels despite higher breathing demands during maximal workload in CPET. This preservation of oxygenation is further evidenced by the reduced desaturation during CPET following IMT. However, studies are needed to clarify the underlying mechanism of muscle oxygenation.

IMT is used in patients with PD; however, its effectiveness is uncertain[19,20]. Inzelberg et al.[17] demonstrated that 12 weeks of IMT (MIP 15-60%) resulted in an increase of MIP by 16 cmH_2O. Mohammed Yusuf et al.[18] reported that six weeks of breathing exercises using volumetric incentive spirometry and threshold IMT at 30-55% of MIP led to increases in MIP of 9.66 and 16.22 cmH_2O, respectively, in patients with PD. Conversely, Reyes et al.[47] found

that home-based IMT at 50–75% of MIP did not enhance respiratory muscle function. In the present study, inspiratory muscle strength (MD=38.56 cmH_2O) increased with a large effect size (Cohen's *d*=3.05) and surpassed that reported in previous literature[17,18,47]. Furthermore, in the current study, patient compliance with the treatment was higher (100% vs. 65%), and the average disease duration was shorter compared to the study by Inzelberg et al.[17] In addition, the duration and training frequency in our study were greater than in the study conducted by Mohammed Yusuf et al.[18]. The weekly supervised sessions and training load increment may have increased patient compliance and could help explain the differences noted in the study by Reyes et al.[47]. Information regarding the effects of IMT on MEP in patients with PD is limited[47,48]. One study indicated a moderate effect size improvement in MEP (*d*=0.55) after IMT at 50-75% MIP over eight weeks[48]. Our study showed that IMT significantly enhanced MEP with a large effect size (Cohen's *d*=1.60), consistent with the existing literature. IMT has been reported to improve respiratory muscle endurance at 15–60% of MIP in patients with PD, in just one study[17]. In alignment with this finding, respiratory muscle endurance also improved with large effect sizes in our IMT group.

The effects of IMT on lung function in patients with PD remain unclear, according to two systematic reviews[19,20]. Previous studies did not show any improvement in FVC%, FEV_1% in one IMT study with 15-60% MIP[17] and in FVC%, FEV_1%, and PEF% in another study with 30-55% MIP [18]. In the current study, consistent with the literature, no improvement in dynamic lung volumes was detected. However, $FEF_{25–75\%}$ showed improvement in both groups after training. IMT enhances diaphragm activity, facilitating air distribution throughout the lungs[42]. In thoracic expansion exercises, intercostal muscles are rapidly stretched, aiding inhalation and potentially improving lung function[49]. These training effects may have led to similar enhancements in small airways. To further understand the impact of IMT on lung function, static lung volumes and diffusion capacity should also be assessed.

Increased motor symptoms and respiratory muscle weakness in patients with PD may affect peripheral muscle strength[11,12]. This study provides new evidence that IMT improves QF and shoulder abductor muscle strength in patients with PD with a moderate effect size. Studies show that IMT at 30% and 50% MIP increases QF muscle strength in patients with heart failure[14], and IMT at 30% and 50% MIP enhances QF and handgrip strength in those with hypertension[13]. Reduced muscle metaboreflex activity and improved oxygenation may lead to greater muscle strength[9]. Additionally, respiratory muscle training may enhance muscle activation and strength by alleviating motor symptoms in PD[43]. IMT may have increased peripheral muscle strength by positively affecting muscle oxygen utilization metabolism and reducing motor problems.

In the only study examining the impact of IMT on quality of life in patients with PD, IMT with 15-75% MIP did not enhance quality of life, according to SF-36[17]. In the present study, IMT improved quality of life (7.03 points), with a large effect size, through better mobility, daily living activities, communication, and reduced physical discomfort. This improvement surpassed the MCID (>4.72 points)[50]. This difference may stem from the variance in patient compliance with treatment (100% vs. 65.5%). Additionally, the shorter disease duration in our study may have led to less symptom burden for patients. Therefore, IMT can be integrated into rehabilitation to enhance the quality of life in PD.

In the present study, IMT increased physical activity levels in patients with PD by increasing active energy expenditure and the number of patients transitioning from inactive to low-active, as measured by METs, making a significant contribution to the literature. A clinically significant increase of more than 600 steps per day in step count after pulmonary rehabilitation in COPD has been reported[51]. Additionally, the MCID for PD was reported as 581 steps/day[52]. IMT significantly increased the number of steps (994.95 steps per day). In the present study, IMT may have increased physical activity levels by enhancing respiratory

muscle strength, improving motor symptoms, and reducing perceptions of fatigue and dyspnea[9,17,43], as well as increasing patients' confidence[14].

The present study demonstrates that IMT alone improves motor symptoms measured by the UPDRS-III (3 points). Huang et al.[43] showed that 12 weeks of combined inspiratory (MIP 30-60%) and expiratory (MEP 15-75%) muscle training decreased UPDRS-III scores (from 21 to 7). In this study, the shorter training duration and IMT intervention alone may have led to less improvement in motor symptoms than Huang et al.[43]. Furthermore, the improvement in motor symptoms after IMT was close to clinical significance (MCID=3.25 points)[53]. Respiratory muscle training enhances lung function by stimulating the respiratory centers in the motor cortex, which may improve motor functions[43]. Additionally, the reduction in fatigue following IMT may have contributed to the improvement in motor symptoms.

There was no change in disease severity after IMT. One study reported that combined inspiratory and expiratory muscle training did not alter the H&Y stage[43]. Given the multifactorial pathophysiology of PD[1], although IMT has a positive effect on motor problems and exercise capacity, it may be insufficient to improve the underlying causes of the disease. The effects of IMT on disease severity should be investigated alongside various types of exercise training programs, such as aerobic and resistance exercise. Therefore, the effects of functional IMT in patients with PD could be explored in future studies.

This study has some limitations: patients with PD stages 4-5 according to the M. H&Y were excluded. Therefore, further studies are needed for advanced-stage patients with PD. In our study, only $\%FEF_{\%25-75}$ of the dynamic lung volumes of the groups showed similar improvement, with a power of 1-β: 42.9%. The duration of physical activity approached statistical significance; the number of steps increased significantly at a clinical level, with power values of 1-β: 46.2% and 13.1%, respectively. Based on these results, the sample size is

possibly insufficient to detect significant changes in pulmonary function and some physical activity parameters. In this study, thoracic expansion exercises applied to the control group may have some physiological effects on the respiratory system. Studies using passive controls can significantly contribute to the pure demonstration of IMT's effectiveness. Patients' adherence to their home programs was monitored daily and periodically by phone. However, adherence in the control group was low at 53.28%. While weekly face-to-face meetings and the perception of measurable progress increased adherence in the IMT group, the lack of similar feedback in the control group may have decreased adherence. This non-compliance may reflect the impact of the intervention on differences in outcomes between the IMT and control groups, as well as treatment adherence. Video interviews and patient education can improve adherence. Future studies could investigate the effect of IMT by minimizing this difference.

Conclusions

IMT enhances oxygen consumption, respiratory and peripheral muscle strength, respiratory muscle endurance, motor function, physical activity levels, and quality of life in patients with PD. IMT may also have contributed to improved muscle oxygenation by increasing workload at the same oxygen level. Small airway obstruction improved at a comparable rate following training. IMT is a safe, effective, and applicable treatment method that can significantly increase exercise performance by improving respiratory, cardiovascular, and motor problems. Therefore, IMT is considered beneficial as an adjunct to rehabilitation in patients with PD.

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Declarations

Acknowledgment

This project, of which only a part is presented here (due to word limitations), is a doctoral thesis titled “Investigation of the Effects of Inspiratory Muscle Training on Oxygen Consumption, Muscle Oxygen, and Physical Activity Level in Patients with Parkinson's Disease.”

The part of this study was presented as a poster at the European Respiratory Society International 2024 Congress and published in European Respiratory Journal 2024, 64: Suppl. 68, PA4139. DOI: 10.1183/13993003.congress-2024.PA4139.

Author Contributions

MG: Conceptualization, Data curation, Formal analysis, Methodology, Visualization, Writing – original draft, Writing – review & editing. **MBG:** Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. **AG:**

Data curation; Investigation; Writing, review, and editing. **HATB:** Data curation, Supervision, Writing – review & editing.

Data Availability Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors report no conflicts of interest.

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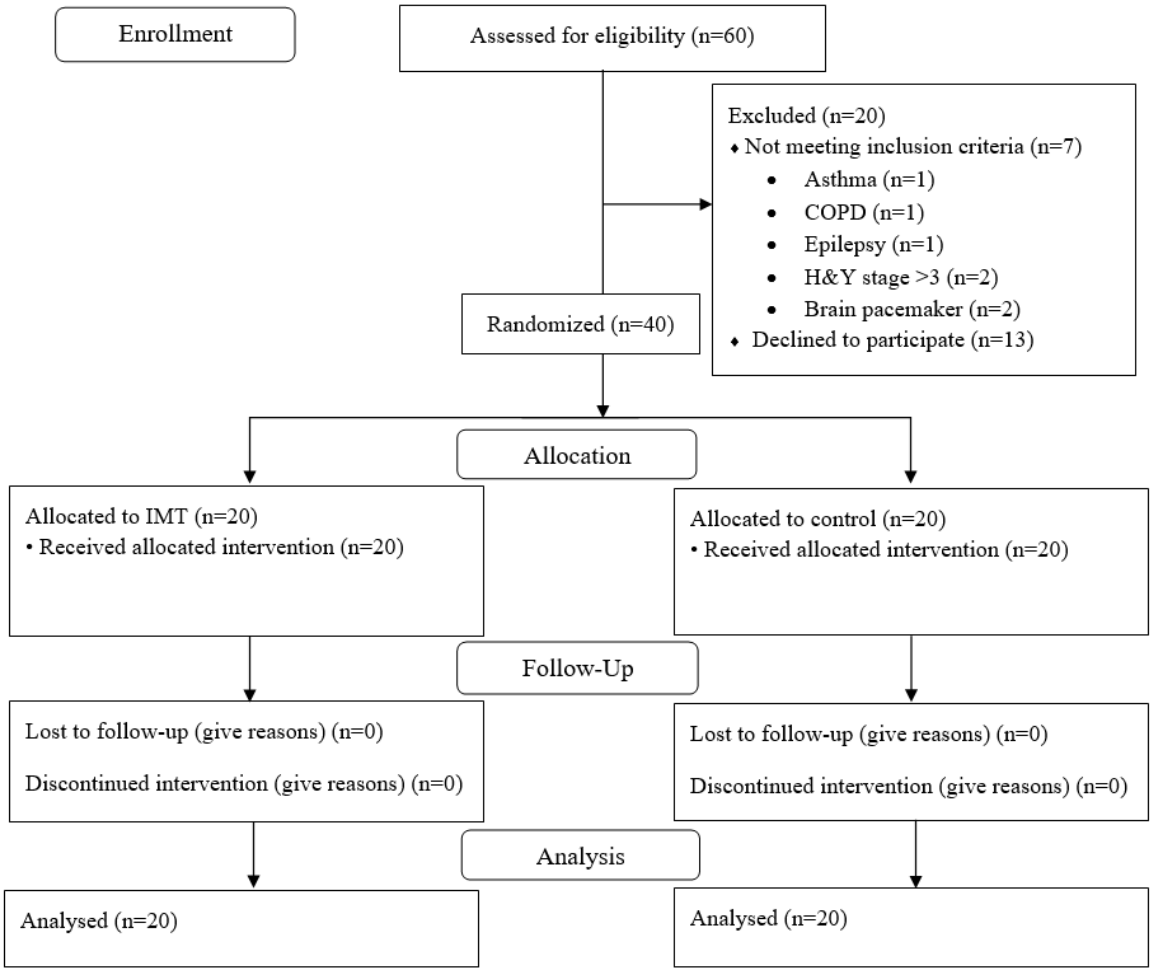

Figure 1. Consort flow diagram of patients

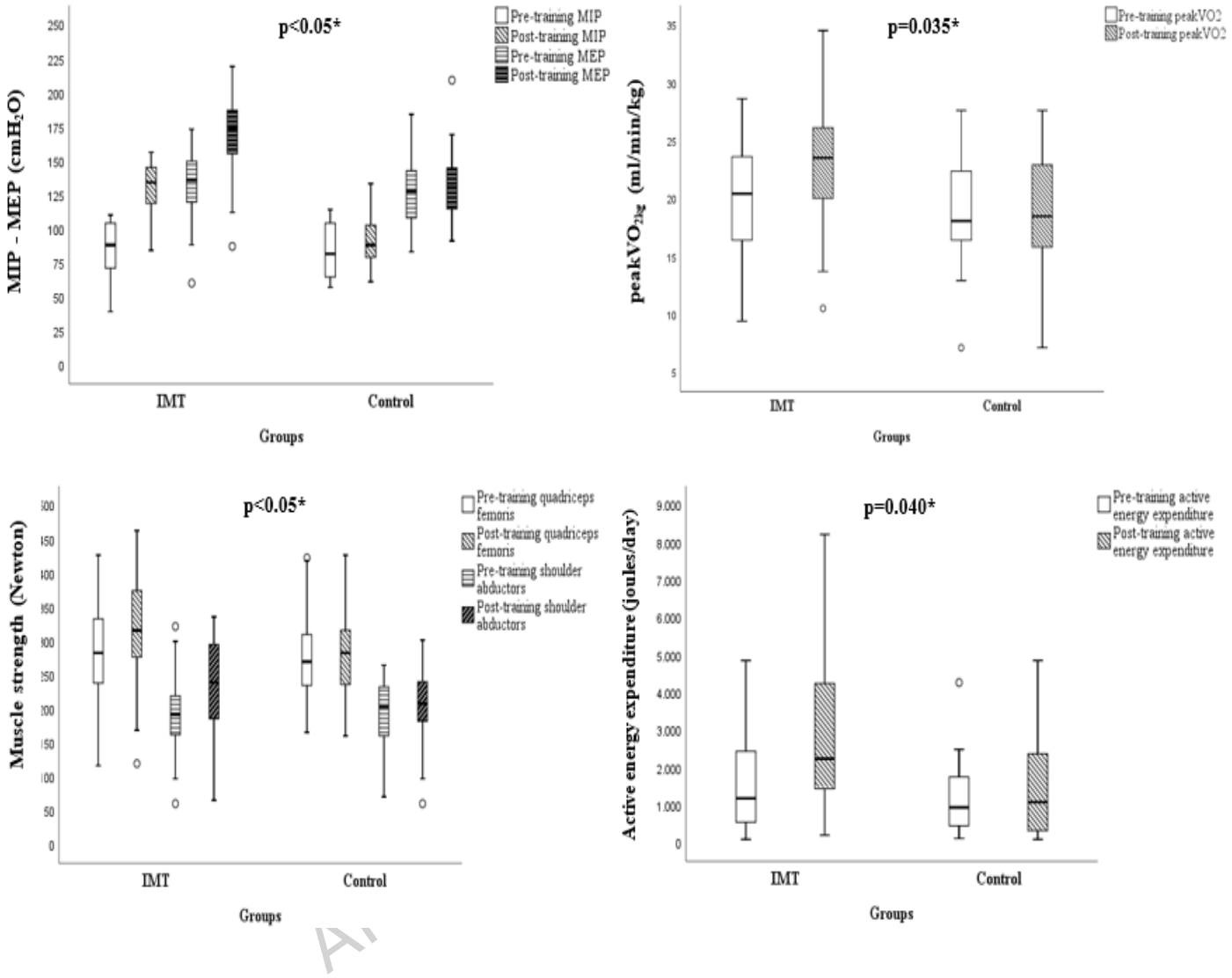

Figure 2. MIP, MEP, peakVO_2kg, peripheral muscle strength, and active energy expenditure before and after in groups

Table 1. Demographic characteristics of patients with Parkinson's disease

Characteristics	IMT (n=20)	Control (n=20)	Mean Difference %95CI/U	p
	X±SD/ Median (IQR25–75%)	X±SD/ Median (IQR25–75%)		
Age (years)	59.40±8.54	61.50±8.85	2.10 (-3.46-7.66)	0.450
Height (cm)	167.85±11.87	166.90±11.22	3.65 (-8.35-6.44)	0.796
Body weight (kg)	76.05±12.47	78.45±13.16	2.40 (-5.80-10.60)	0.557
Body mass index (kg/m²)	27.08±4.33	28.15±3.95	1.07 (-1.59-3.72)	0.421
• **Normal (18,6-24,9 kg/m^2), n (%)**	7 (%35)	4 (%20)	-	
• **Overweight (25,0-29,9 kg/m^2), n (%)**	7 (%35)	9 (%45)	-	
• **Obese (30,0-39,9 kg/m^2), n (%)**	6 (%30)	7 (%35)	-	
Gender (Female; male, n/%)	7/(35%); 13(65%)	9/(45%); 11(55%)	-	0.519
Smoking (pack-years)	5 (5-8)	5 (5-8)	57.5	0.563
Smoking (current/ex-smoker/non, n, %)	2/(10%); 11(55%); 7(35%)	1/(5%); 11(55%); 8(40%)	-	0.819
Comorbidities				
Hypertension, n (%)	7 (35%)	9 (45%)	-	0.519
Diabetes mellitus, n (%)	2 (10%)	4 (20%)	-	0.376
Coronary artery disease, n (%)	2 (10%)	4 (20%)	-	0.376
Charlson comorbidity index score (0-37 pts)	0 (0-0.75)	0.50 (0-1)	157.5	0.178
MMSE (0- 30 pts)	27.50 (24.25-30)	28 (25.25-30)	178.5	0.552
M. H&Y scale (0-5 points)	2 (2-3)	2 (2-2.37)	167	0.316
UPDRS-III (0-108 pts)	22.95±9.41	19.55±6.49	-3.40 (-8.57-1.77)	0.191
Disease duration (years)	4.50 (2-8)	4 (2-7)	176	0.513
Levodopa equivalent dose (mg)	609.35±244.58	652.20±328.44	42.85 (-142.51-228.21)	0.642

MMSE: Mini Mental State Examination scale, M. H&Y scale: Modified Hoehn & Yahr scale, UPDRS-III: Unified Parkinson's Disease Rating Scale-III

Table 2. Effects of inspiratory muscle strength training on pulmonary function, respiratory muscle strength and endurance, peripheral muscle strength, quality of life, and physical activity level

	IMT (n=20)			Controls (n=20)			Treatment effect p
	Before X±SD	After X±SD	Group difference p	Before X±SD	After X±SD	Group difference p	
FEV_1 (%)	85.96±14.47	90.47±16.20	0.139	90.56±14.74	94.62±19.55	0.110	0.932
FVC (%)	89.61±20.14	89.34±19.13	0.740	94.51±19.00	94.99±19.37	0.691	0.608
FEV_1/FVC (%)	75.91±7.02	81.08±8.42	**<0.001***	75.66±7.89	78.07±6.18	0.054	0.102
PEF (%)	86.52±23.40	96.94±20.71	**0.013***	93.39±25.02	95.18±21.30	0.366	0.244
$FEF_{25-75\%}$ (%)	84.47±25.29	104.56±28.62	**<0.001***	92.28±29.56	103.15±38.30	**0.035**	0.246
MIP (cmH_2O)	85.75±20.20	129.25±20.50	**<0.001***	83.40±20.00	88.95±18.55	0.078	**<0.001***
MIP (%)	75.72±17.10	114.71±19.31	**<0.001***	75.14±19.40	80.24±18.85	0.079	**<0.001***
MEP (cmH_2O)	130.95±29.07	165.75±30.29	**<0.001***	129.35±26.83	133.30±27.06	0.408	**<0.001***
MEP (%)	71.72±17.26	90.91±19.28	**<0.001***	73.11±16.95	75.79±20.11	0.335	**<0.001***
Respiratory muscle endurance ($cmH_2O \times sec$)	9973.58±7979.34	31213.08±29430.84	**<0.001***	13783.07±9324.92	12717.54±6332.60	0.971	**0.005***
Quadriceps femoris (D) (N)	284.55±80.03	315.40±86.52	**0.002***	279.15±64.36	280.45±69.39	0.911	**0.032***
% Quadriceps femoris (D) (N)	72.90±21.69	81.01±24.38	**0.005***	73.57±15.30	73.72±16.86	0.949	**0.046***
Shoulder abductors (D), N	195.04±65.58	233.70±70.90	**<0.001***	194.45±48.08	204.09±57.93	0.345	**0.047***
% Shoulder abductors (D), N	108.93±41.54	130.25±46.55	**0.001***	113.42±35.00	116.56±31.23	0.522	**0.032***
PDQ-39 (0-100 pts)	26.46±12.63	18.06±11.32	**<0.001***	22.21±11.33	21.50±11.34	0.379	**<0.001***
Mobility (0-100 pts)	27.87±16.16	16.93±15.25	**<0.001***	25.00±16.48	24.62±16.72	0.754	**0.002***
Daily activities (0-100 pts)	29.58±21.49	19.99±20.20	**<0.001***	24.36±19.87	22.91±18.95	0.340	**0.009***
Emotional well-being (0-100 pts)	32.95±15.85	22.70±15.50	**0.002***	30.57±16.14	26.87±15.49	0.158	0.206
Stigma (0-100 pts)	13.12±14.46	8.12±11.12	**0.021***	10.93±14.74	9.06±13.52	0.237	0.397
Social support (0-100 pts)	12.91±25.71	7.08±15.11	**0.023***	9.58±21.50	8.747±21.19	0.531	0.226
Cognition (0-100 pts)	34.06±17.38	28.43±21.11	**0.024***	29.06±14.80	28.95±16.45	0.949	0.117
Communication (0-100 pts)	21.66±16.97	12.91±13.37	**<0.001***	16.66±17.09	14.99±14.70	0.146	**0.018***
Physical discomfort (0-100 pts)	39.57±20.20	28.33±16.61	**0.004***	32.08±18.97	37.49±20.32	0.214	**0.005***
Total energy expenditure (joule/day)	9836.00±1928.93	10932.45±2472.95	**0.003***	9500.85±1762.51	9928.25±2278.22	0.226	0.178
Physical activity duration (>3 METs) minutes/day	144.70±283.55	147.55±110.96	0.072	64.55±52.47	81.60±70.47	0.384	0.063
Average METs (METs/day)	1.34±0.21	1.48±0.27	**0.002***	1.23±0.18	1.30±0.27	0.091	0.249
Active energy expenditure (>3	1634.25±1438.89	2909.55±2233.93	**<0.001***	1251.35±1049.47	1593.20±1502.05	0.224	**0.040***

METs) (joules/day)							
Number of steps (steps/day)	4610.60±2434.95	5605.55±2746.01	**0.015***	3740.70±2149.76	4381.75±2524.96	0.187	0.403
Lying down (hours/day)	473.90±135.38	486.85±135.95	0.666	482.85±138.81	487.40±130.37	0.794	0.904
According to average METs (n/%)							
Inactive (<1.5 MET/day)	17/85%	11/55%	**0.031***	19/95%	17/85%	0.500	**0.038***
Low active (1.5-2.99 MET/day)	3/15%	9/45%		1/5%	3/15%		
M. H&Y scale (0-5 points)	2.27±0.59	2.15±0.56	0.090	2.05±0.58	2.07±0.61	0.859	0.187
UPDRS-III (0-108 pts)	22.95±9.41	19.95±9.72	**0.005***	19.55±6.49	19.70±6.21	0.945	**0.050***

FEV_1: Forced expiratory volume in one second, FVC: Forced vital capacity, PEF: Peak expiratory flow, $FEF_{25-75\%}$: Forced expiratory flow from 25% to 75%, MIP: Maximum inspiratory pressure, MEP: Maximum expiratory pressure, PDQ: Parkinson Disease Questionnaire, UPDRS-III: Unified Parkinson's Disease Rating Scale-III, cmH_2O: centimeters of water, $cmH_2O \times sec$ centimeters of water×second, D: dominant side, N: Newton, X±SD: Mean±standard deviation, *p≤0.05.

Table 3. Effects of inspiratory muscle strength training on maximal exercise capacity

	IMT			Controls			Treatment effect p
	Before X±SD	After X±SD	Group difference p	Before X±SD	After X±SD	Group difference p	
VO_2kg (ml/min/kg)							
• Resting	4.81±1.54	5.89±1.12	**<0.001***	4.23±0.98	4.86±1.34	0.138	**0.031***
• Anaerobic threshold	16.06±6.77	17.69±6.78	0.458	14.51±5.10	16.06±6.77	0.160	0.636
• Peak workload	19.85±5.29	23.05±5.80	**0.001***	18.68±4.67	19.17±5.39	0.733	**0.002***
PeakVO_2 (% predicted)	76.93±19.25	88.04±16.96	**<0.001***	79.98±14.53	80.70±14.74	0.551	**<0.001***
RER							
• Resting	0.76±0.08	0.79±0.05	0.083	0.76±0.09	0.78±0.09	0.368	0.542
• Anaerobic threshold	0.88±0.11	0.89±0.13	0.430	0.82±0.12	0.89±0.15	0.055	0.417
• Peak workload	1.04±0.14	1.09±0.09	**0.002***	1.04±0.13	1.06±0.12	0.219	0.149
VCO_2 (ml/min)							
• Resting	299.30±86.72	382.30±79.36	**0.001***	334.45±121.16	306.55±88.65	0.556	**0.007***
• Anaerobic threshold	1200.45±582.70	1234.40±647.26	0.663	939.40±355.83	1114.50±542.63	0.051	0.280
• Peak workload	1507.50±552.12	1767.25±569.66	**<0.001***	1486.55±452.03	1548.80±521.31	0.232	**0.010***
MET							
• Resting	1.46±0.42	1.70±0.28	**0.001***	1.46±0.41	1.42±0.32	0.584	**0.006***
• Anaerobic threshold	4.94±1.69	5.01±1.88	0.702	4.16±1.46	4.55±1.90	0.238	0.574
• Peak workload	5.67±1.52	6.21±1.67	**0.010***	5.28±1.34	5.49±1.64	0.305	0.244
VE (l/min)							
• Resting	13.99±3.88	17.43±4.18	**0.006***	15.28±4.92	15.61±5.86	0.531	0.120
• Anaerobic threshold	45.56±20.71	46.60±23.49	0.694	37.22±14.35	43.10±21.33	0.130	0.428
• Peak workload	59.07±19.72	68.61±23.71	**0.002***	61.23±20.71	61.99±20.84	0.765	**0.039***
HR (beats/min)							
• Resting	84.30±9.82	83.30±10.62	0.536	84.90±10.84	83.75±9.98	0.558	0.981
• Anaerobic threshold	126.90±21.05	120.95±34.60	0.331	119.05±15.46	120.85±19.25	0.833	0.700
• Peak workload	144.45±20.29	145.75±18.51	0.638	142.65±19.97	138.90±19.69	0.263	0.262
HR (%predicted)	90.88±11.99	92.17±7.41	0.450	90.66±10.01	89.18±9.71	0.391	0.256
HR recovery (beats/min)	120.85±15.75	126.80±16.92	0.104	125.90±17.28	120.70±12.81	0.169	**0.037***
ΔHR recovery (beats/min)	23.45±16.92	19.00±9.15	0.284	16.90±10.26	18.90±11.85	0.958	0.475
HRR (beats/min)							
• Resting	73.80±9.98	73.30±15.09	0.873	72.95±12.34	70.65±12.24	0.334	0.566
• Anaerobic threshold	29.60±18.84	33.85±16.53	0.889	41.00±17.49	35.40±16.23	0.827	0.956
• Peak workload	13.65±19.24	12.15±11.59	0.418	15.90±15.73	17.30±14.95	0.438	0.265
VO_2HR (ml/beat)							
• Resting	4.35±1.56	5.53±1.32	**<0.001***	3.87±1.27	4.63±1.17	**0.024***	0.057
• Anaerobic threshold	10.49±4.20	10.94±3.47	0.225	9.26±3.17	10.23±3.12	0.221	0.995

• Peak workload	10.37±3.31	11.99±3.35	**<0.001***	10.81±2.51	11.11±2.82	0.358	**0.011***
VO_2HR (%predicted)	83.88±22.01	95.42±23.10	**0.001***	83.65±23.36	88.69±18.86	0.122	0.149
$ATVO_2$ (% predicted)	65.55±21.23	69.30±18.98	0.214	62.44±16.41	65.60±19.94	0.442	0.733
VE/VCO_2							
• Resting	40.46±7.22	39.62±5.96	0.361	40.96±7.19	41.22±7.57	0.737	0.378
• Anaerobic threshold	37.66±7.96	36.45±6.02	0.218	37.68±6.61	36.91±8.03	0.435	0.744
• Peak workload	38.61±8.90	37.11±7.21	0.288	38.04±7.18	36.94±10.18	0.396	0.878
VE/VO_2							
• Resting	31.06±6.09	31.73±5.63	0.576	31.39±5.90	31.69±7.09	0.755	0.861
• Anaerobic threshold	32.64±6.32	31.63±5.89	0.554	30.40±7.28	31.50±8.77	0.501	0.804
• Peak workload	39.15±9.50	40.10±6.92	0.576	39.40±7.98	38.45±12.60	0.577	0.431
BR (% predicted)	40.25±21.59	33.66±21.88	**0.032***	38.94±19.92	38.99±17.14	0.963	0.132
Speed (km/h), peak workload	8.34±2.17	8.52±2.35	**0.002***	8.18±2.35	7.69±2.07	0.099	**0.001***
Incline (%), peak workload	5.65±1.98	7.35±2.36	**0.001***	6.15±2.32	5.65±1.98	0.074	**<0.001***
ΔSBP (mmHg)	27.50±16.50	42.75±17.43	**<0.001***	31.25±14.67	30.50±16.37	0.904	**0.012***
ΔDBP (mmHg)	13.55±21.26	14.75±14.37	0.229	7.25±14.82	12.75±13.12	0.325	0.875
ΔDyspnea (M.Borg, 0–10)	2.67±1.83	2.17±1.20	**0.032***	2.75±1.93	2.22±1.47	**0.037***	0.963
ΔFatigue (M.Borg, 0–10)	3.00±1.45	2.20±1.64	**0.005***	3.05±1.93	2.80±0.95	0.395	0.138
ΔLeg fatigue (M.Borg, 0–10)	2.80±1.88	2.15±1.53	**0.034***	2.97±1.94	2.30±1.59	0.062	0.845
ΔSpO_2 (%)	5.65±6.39	2.20±4.58	**0.014***	4.10±5.06	3.80±5.16	0.395	0.230

RER: Respiratory exchange ratio, VO_2: Oxygen consumption, VO_2kg: Oxygen consumption per kilogram, MET: Metabolic equivalent, VE: Minute ventilation, HR: Heart rate, HRR: Heart rate reserve, O_2HR: Oxygen pulse, VCO_2: Carbon dioxide production, AT: Anaerobic threshold, $EqCO_2$: Ventilation to carbon dioxide ratio, EqO_2: Ventilation to oxygen ratio, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, M. Borg: Modified Borg Scale, SpO_2: Peripheral oxygen saturation, mmHg: millimeters of mercury, %: Percent, W: Watt, XX±SD: Mean±standard deviation, *p≤0.05.

Table 4. Effects of inspiratory muscle strength training on muscle oxygenation during CPET

	IMT			Controls			Treatment effect p
	Before X±SD	After X±SD	Group difference p	Before X±SD	After X±SD	Group difference p	
SmO_{2rest} (%)	46.80±19.89	48.80±17.74	0.423	46.15±17.52	48.55±15.00	0.390	0.967
SmO_{2min} (%)	29.40±19.62	23.80±17.83	0.178	26.75±16.98	30.40±16.83	0.418	0.130
SmO_{2max} (%)	53.35±22.37	54.25±20.57	0.901	56.20±20.29	55.00±16.41	0.821	0.804
Δ SmO_2 (%)	23.95±19.71	30.45±20.17	0.233	29.45±19.15	24.60±16.22	0.436	0.168
SmO_{2top} (%)	46.50±22.33	46.05±19.60	0.864	47.00±21.76	50.15±19.95	0.306	0.398
$SmO_{2ave-min}$ (%)	30.90±20.00	25.05±18.02	0.162	27.90±17.36	31.70±17.14	0.404	0.117
$SmO_{2ave-max}$ (%)	52.85±22.25	52.20±19.45	0.703	55.25±20.24	53.95±17.15	0.769	0.951
Δ SmO_{2ave} (%)	21.95±19.72	27.15±17.84	0.328	27.35±19.71	22.25±14.55	0.314	0.165
$SmO_{2recovery-ave}$ (%)	46.15±22.56	44.70±20.52	0.649	45.55±22.00	50.05±20.42	0.146	0.177
THb_{rest} (g/dl)	12.33±0.37	12.24±0.40	0.407	12.12±0.39	12.26±0.41	0.095	0.085
THb_{min} (g/dl)	12.01±0.36	11.92±0.41	0.394	11.87±0.40	11.96±0.44	0.401	0.237
Thb_{max} (g/dl)	12.48±0.34	12.35±0.36	0.099	12.36±0.33	12.41±0.36	0.595	0.127
Δ THb (g/dl)	0.47±0.21	0.43±0.17	0.336	0.48±0.28	0.45±0.22	0.462	0.870
$THb_{recovery}$ (g/dl)	12.20±0.31	12.17±0.33	0.726	12.16±0.45	12.21±0.38	0.531	0.491

SmO_2: Muscle oxygen saturation, SmO_2rest: Resting muscle oxygen saturation, SmO_{2min}: Minimum muscle oxygen saturation during the test, SmO_{2max}: Maximum muscle oxygen saturation during the test, $SmO_{2ave-min}$: Minimum mean muscle oxygen saturation during the test, $SmO_{2ave-max}$: Maximum mean muscle oxygen saturation during the test, SmO_{2top}: Recovery muscle oxygen saturation, $SmO_{2recoevry-ave}$: Recovery mean muscle oxygen saturation, THb: Total hemoglobin level, THb_{rest}: Resting total hemoglobin level, THb_{min}: Minimum total hemoglobin level during the test, Thb_{max}: Maximum total hemoglobin level during the test, $THb_{recovery}$: Recovery total hemoglobin level, *p<0.05.