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What's the secret behind the benefits of whole-body vibration training in patients with COPD? A randomized, controlled trial

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ABSTRACT

Background: Several studies have shown that whole-body vibration training (WBVT) improves exercise capacity in patients with severe COPD. The aim of this study was to investigate the determinants of improved exercise capacity following WBVT.
Methods: Seventy-four COPD patients (FEV_1: 34 ± 9%predicted) were recruited during a 3-week inpatient pulmonary rehabilitation (PR) program. Conventional endurance and strength exercises were supplemented with self-paced dynamic squat training sessions (4bouts*2min, 3times/wk). Patients were randomly allocated to either a WBVT-group performing squat training on a side-alternating vibration platform (Galileo) at a high intensity (24–26 Hz) or a control group performing squat training without WBVT.
Results: Patients in the WBVT group significantly improved postural balance in several domains compared to the control-group (i.e. tandem stance: WBVT +20% (95%CI 14 to 26) vs. control −10% (95%CI 6 to 15), $p < 0.001$; one-leg stance: WBVT +11% (95%CI 4 to 19) vs. control −8% (95%CI -19 to 3), $p = 0.009$). Six-minute walk distance and muscle power but not muscle strength were also significantly improved compared to control group.
Conclusions: Implementation of WBVT improves postural balance performance and muscle power output. The neuromuscular adaptation related to improved balance performance may be an important mechanism of the improvement in exercise capacity after WBVT especially in COPD patients with impaired balance performance and low exercise capacity.

1. Introduction

Recently, there has been increased interest in whole-body vibration training (WBVT) as part of exercise therapy for patients with chronic obstructive pulmonary disease (COPD). During WBVT, subjects stand with both feet on a platform producing oscillating mechanical vibrations. The rapid up and down movement of the platform stretches the muscles of the lower extremities. The neuromuscular system reacts to these stretches in a reflexive chain of rapid muscle contractions [1]. Cardinale et al. proposed that the monosynaptic reflex-induced muscle contractile activities during WBVT would be an especially effective therapy in patients with impaired muscle performance, such as sedentary subjects with sarcopenia [2].

Since the 1990s WBVT has been widely studied in athletes, healthy subjects and patients with various chronic conditions [3,4]. However, the first study demonstrating benefits of WBVT in patients with COPD was published in 2012 [5]. In a recently published systematic review by our work group, in which six studies were

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Abbreviation

6MWD	six-minute walk distance
6MWT	six-minute walk test
APL	absolute path length
ATS	American Thoracic Society
BMI	body-mass-index
CON	control group
COPD	chronic obstructive pulmonary disease
FEV_1	forced expiratory volume in 1 s
FFMI	fat-free mass index
GOLD	Global Initiative for chronic Obstructive Lung Diseases
IVC	inspiratory vital capacity
LTOT	long-term oxygen therapy
PaO_2	partial pressure of oxygen
STST	sit to stand test
SpO_2	oxygen saturation
WBVT	whole-body vibration training

identified (including a total of 235 COPD patients), WBVT was applied using different approaches and settings [6]. It was found that WBVT was superior in improving functional exercise capacity (measured by the 6-minute walk test or sit-to-stand tests) in comparison to conventional exercise strategies. In other populations such as healthy elderly or patients with fibromyalgia, WBVT has been shown to improve balance performance [7,8]. However, the impact of WBVT on balance has never been investigated in patients with COPD. Furthermore, it is unknown whether potential improvements in balance are associated with benefits on exercise capacity after WBVT. Therefore, aim of this study was to evaluate the influence of a squat training protocol with and without WBVT on postural balance and exercise performance in patients with severe COPD. Our working hypothesis was that neuromuscular adaptation is largely responsible for the superior increases in exercise performance [6].

2. Material and methods

2.1. Study design

122 consecutive patients admitted to an inpatient rehabilitation program at the Schoen Klinik Berchtesgadener Land (Schoenau am Koenigssee, Germany) were screened for eligibility to participate in this three week randomized controlled trial (August 2015 until June 2016). All performance testing was done in same order at baseline (before randomization) and at three weeks. This study was conducted in accordance with the amended Declaration of Helsinki, was submitted to the German Clinical Trials Register (identification number DRKS7774) and approved by the Ethics Committee of the Bavarian Physician Association (ID15006).

2.2. Study population

Out of 122 eligible patients, 87 met the inclusion criteria and were included in the trial (Fig. 1). The inclusion criteria were: patients aged 50–80 years old with COPD stage III or IV according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines [9]. Exclusion criteria were defined as: major surgery, bone fracture or deep vein thrombosis (within the last 12 weeks) as well as existing arterial aneurysm, acute COPD exacerbation (within the last 4 weeks), or orthopedic co-morbidities that prevented patients from performing squat exercises, or inability to comply with the study protocol.

2.3. Intervention

Patients participated in a three-week multidisciplinary inpatient pulmonary rehabilitation (PR) program (standard duration in Germany), consisting of medical care, respiratory therapy, education, nutritional and psychological counseling. Patients performed conventional exercise training on 5 days per week consisting of endurance training (15 min cycling at 60% of peak power) [10] and strength training (four to six exercises at strength training machines with three sets of 15–20 repetitions for major muscle groups using the maximum tolerated load to momentary muscular failure) [11].

Furthermore, all patients underwent a supplemental supervised squat exercise program. Patients were randomized and allocated to either an experimental (WBVT) or a control group. The WBVT group performed squat exercises on a side-alternating vibration platform (Galileo®, Novotec Medical GmbH, Pforzheim, Germany) at high frequencies (24–26 Hz) and 5 mm peak-to-peak displacement (Fig. 2) wearing flat soled shoes. Controls performed the same squat exercises on a normal floor. The squat exercise consisted of four sets of 2-min duration, and was performed three times a week on non-consecutive days. An experienced exercise scientist supervised all sessions and corrected patients' movement if necessary. Patients performed knee and hip flexion between 90° and 120° during each squat movement without holding on to anything. Patients in both groups were instructed to perform squats at their own pace to increase comfort and feasibility. The number of repetitions within the allotted time (8 min/session) was recorded by the supervisor.

2.4. Outcomes and measures

2.4.1. Neuromuscular performance

Postural balance and muscular power were assessed using a ground reaction force platform (Leonardo Mechanograph®, Novotec Medical, Pforzheim, Germany). The platform uses 8 integrated force sensors (800 Hz each) to reliably calculate the center of force (= mean point where the patient generated forces are focusing on the plate) [12]. Each performance test on the platform was carried out three times but only the best test was used for analysis.

2.4.2. Postural balance

Patients were asked to stand as still as possible for 10 s while holding their arms against their sides in the following positions: 1) Romberg stance (eyes closed): feet side-by-side, 2) semi-tandem stance (eyes closed and eyes open): one foot beside and behind the other (Fig. 3) and 3) the one-leg stance (eyes open). During postural balance tests, the ‘absolute path length (APL)’ of the center of force induced on the force plate was measured in millimeters. The APL measures how much a subject sways during the 10 s period and its ability to stabilize in a specific posture (the smaller the APL, the better the balance capability and vice versa). The best test (with the lowest APL) out of three tests was used for analysis.

2.4.3. Muscle power (=muscular work per time)

A two-legged jump on the force plate was performed to assess muscle power. During this well-validated test [13] (also known as countermovement jump) patients were asked to jump as high as possible with using the arm-swing [14]. Outcomes are the jump height and peak Watt calculated by the force plate. The best test (highest jump height) out of three tests was used for analysis.

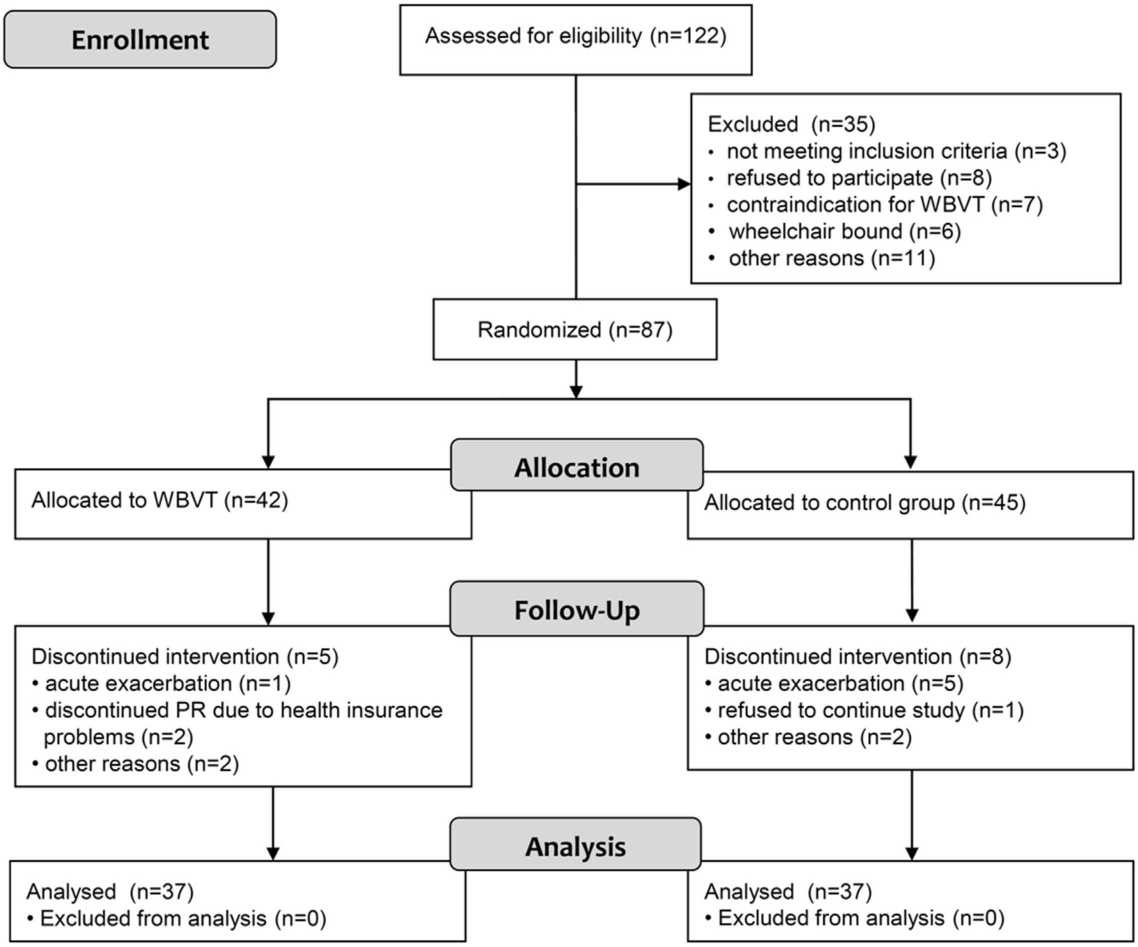

Fig. 1. Study flow chart (abbreviation: WBVT = whole-body vibration training).

2.4.4. *Maximal quadriceps muscle strength*

Peak isometric knee extension strength was measured at 90° knee angle using a dynamometer (MicroFET2, Hoggan Scientific LLC, UT) which was fixed in a leg curl training device.

2.4.5. *Sit to stand tests*

During sit to stand tests (STST) patients were asked to stand up and sit down from a bench (46 cm height) fixed on the force plate with their arms crossed in front of their chest. Patients performed a five-repetition STST (time to complete the test was recorded by the force plate) [15] and a 1 min STST (number of repetitions was recorded) [16].

2.4.6. *6-Minute walk test*

The 6 MWT were performed in accordance with the ATS/ERS guidelines [17]. Two 6 MWTs were performed (separated by 1 h) and the one with the longest 6 MWD was used for analyses.

2.4.7. *Adverse events*

Intervention-related adverse events were documented by the supervisor of the squat exercise sessions.

2.5. *Statistical analysis*

2.5.1. *Sample size calculation*

The a priori sample size computation was based on the results of an own pilot study (data not published) which was conducted using an equivalent methodology. This computation included the following assumptions: changes in the APL of the semi-tandem stance with closed eyes (=primary outcome) of −266 ± 478 mm (WBVT) and 2.6 ± 293 mm (control), power of 80%, alpha of 5% and two-sided, independent t-tests. Based on these assumptions, a sample size of 74 (37 per group) was necessary to achieve this power at this effect size.

2.5.2. *Blinding*

Blinding of study participants was not possible within the study setting due to the nature of the intervention. However, investigators who performed pre and post intervention assessment as well as the statistician (WH) that performed all data analyses were blinded to group allocation.

2.5.3. *Randomization and allocation concealment*

Block randomization was based on a computer-generated random list including two permuted blocks of equal length with a ratio of 1:1. Stratification was done for baseline 6 MWD (using a threshold of 350 m). The investigator responsible for patient recruitment received group allocation by calling a third-party person who managed the randomization list.

2.5.4. *Statistical methods*

Results are reported as mean (standard deviation) and proportions (%). Repeated measures ANOVA with unpaired as well as paired Student t-tests as post-hoc tests were used to compare

Fig. 2. Patient during squat training on a whole-body vibration platform.

Fig. 3. COPD Patient performing a semi-tandem stance balance test on a force plate.

means among different groups and over time. Generalized linear models with a forward variable selection algorithm were used to test for significant predictors of change following the intervention. All reported tests were two-sided, and a p-value <0.05 was determined to indicate statistically significance. All statistical analyses in this report were performed by using STATISTICA 13 (StatSoft, Tulsa, OK) and were done by one of the authors (WH).

3. Results

Eighty-seven COPD patients were included in this trial. Thirteen patients dropped out of the study (for reasons see flow chart in Fig. 1) and 74 patients completed the study including all assessment tests. Enrolled patients had severe airflow obstruction (FEV_1: 35 ± 10 %predicted) and impaired exercise capacity (6 MWD: 342 ± 105 m, 52 ± 15%pred). For more baseline measures see Table 1.

Patients performed on average 8 ± 1 squat training sessions in the WBVT group and 8 ± 0 sessions in the control group (of the 9 possible) as well as a total of 843 ± 230 squat repetitions per patient in the WBVT group and 1073 ± 474 repetitions per patient in the control group ($p = 0.064$). All four balance tests improved significantly only in the WBVT group (all $p < 0.05$) (Table 2). Patients in the control group did not significantly improve balance in any of these tests. Furthermore, in three balance tests (semi-tandem stances and one-leg stance) the between-group improvements achieved significance and moderate to large effect sizes (Cohen's d from 0.48 to 1.04) in favor of the WBVT group (Fig. 4).

Several measures of exercise performance including 6 MWD (Fig. 5), two-legged countermovement jump, and the five-repetition STST significantly improved more in the WBVT group compared to controls (Table 2). However, peak muscle force of the lower extremities significantly improved to a similar extent between both groups (Fig. 4).

The generalized linear model identified the WBVT group ($p < 0.001$) and low baseline balance values for the semi tandem stance with closed eyes ($p < 0.001$) as significant predictors for improving balance performance. This model achieved a correlation of $R = 0.66$ and described 44% of the variance (R^2) of balance performance improvements. Furthermore, there was a significant ($p = 0.006$) relationship between an improved semi-tandem stance performance and an increase in 6 MWD (i.e. an improved APL of 300 mm was associated with a 15 m increase in the 6 MWD).

We did not observe any adverse events related to the study intervention.

4. Discussion

It has been previously demonstrated that supplemental WBVT on top of conventional endurance and strength training results in a superior increase in exercise capacity (i.e. 6 MWD) in patients with severe COPD [5]. The current study provides novel findings

Table 1
Demographic and clinical characteristics.

Characteristics	WBVT (n = 37)	Control (n = 37)	*p* value
General characteristics			
age, yrs	65 ± 8	63 ± 9	0.52
sex, women	10 (27%)	14 (38%)	0.60
BMI, kg/m^2	25.2 ± 5.2	25.6 ± 6.3	0.79
FFMI	19.5 ± 2.9	19.6 ± 2.6	0.90
FEV$_1$, % pred.	33.6 ± 8.5	36.6 ± 11.7	0.20
PaO$_2$, mmHg	62.5 ± 8.1	63.0 ± 7.3	0.82
Osteoporosis, n	22 (59%)	20 (54%)	0.35
LTOT, n	20 (54%)	25 (67%)	0.65
Balance tests			
Romberg stance/eyes closed, APL [mm]	446 ± 231	413 ± 273	0.59
Semi tandem stance/eyes closed, APL [mm]	971 ± 457	800 ± 364	0.09
Semi tandem stance/eyes open, APL [mm]	382 ± 161	349 ± 180	0.42
One-leg stance/eyes open, APL [mm]	898 ± 366	780 ± 257	0.12
Exercise performance tests			
6 MWD, m	335 ± 107	350 ± 104	0.55
6 MWD, % pred.[a]	51.0 ± 15.3	53.7 ± 14.8	0.44
Two-legged jump, peak W/kg body mass	23.1 ± 7.1	25.5 ± 6.0	0.13
Two-legged jump, jump height [cm]	21.2 ± 8.0	24.8 ± 8.4	0.08
5-rep STST [sec]	17.2 ± 6.9	13.0 ± 5.1	0.004
1-min STST [rep.]	17.2 ± 6.6	19.7 ± 7.0	0.12
Knee extension, peak force [N]	271 ± 90	294 ± 110	0.33

Data are presented in mean ± SD or percentages (%).
Abbreviations: 6 MWD = 6-minute walk distance, BMI = body-mass-index, FFMI = fat-free mass index, FEV$_1$ = forced expiratory volume (1 s), IVC = inspiratory vital capacity, PaO$_2$ = partial pressure of oxygen, KE = knee extension, LTOT = long-term oxygen therapy, STST = sit-to-stand test, WBVT = whole-body vibration training, APL = absolute path length, rep. = repetitions.

[a] The reference equation was used according to Troosters et al.[38].

Table 2
Comparison of treatment effects.

	mean changes from baseline (95% CI are given in brackets)						
	WBVT (n = 37)	*p* value	Control (n = 37)	*p* value	Between-group differences (95% CI)	*p* value	Cohen's d effect size
balance tests							
Romberg stance/eyes closed, APL [mm]	−92 (−174 to −10)	**0.029**	−16 (−99 to 66)	0.67	−76 (−202 to 30)	0.14	0.35
Semi tandem stance/eyes closed, APL [mm]	−272 (−382 to −162)	**<0.001**	67 (−45 to 179)	0.24	−348 (−504 to −193)	**<0.001**	1.04
Semi tandem stance/eyes open, APL [mm]	−78 (−133 to −23)	**0.005**	0 (−54 to 54)	0.99	−78 (−155 to −1)	**0.046**	0.48
One-leg stance/eyes open, APL [mm]	−124 (−221 to −27)	**0.012**	55 (−43 to 153)	0.27	−187 (−327 to −48)	**0.009**	0.61
exercise performance tests							
6-MWD, m	55 (43–69)	**<0.001**	32 (19–45)	**<0.001**	23 (4–42)	**0.020**	0.57
Two-legged jump, peak W/kg body mass	3.07 (2.09–4.05)	**<0.001**	1.66 (0.72–2.60)	**<0.001**	1.41 (0.03–2.79)	**0.042**	0.51
Two-legged jump, jump height [cm]	3.7 (2.0–5.4)	**<0.001**	−0.1 (−1.7 to 1.6)	0.94	4.1 (1.7–6.3)	**0.001**	0.87
5-rep STST [sec]	−5.4 (−6.9 to −4.0)	**<0.001**	−1.4 (−2.9 to 0.0)	0.053	−4.0 (−6.1 to −1.9)	**<0.001**	0.90
5-rep STST, avg. power [W]	1.23 (0.80–1.67)	**<0.001**	0.62 (0.17–1.06)	**0.006**	0.61 (−0.01 to 1.24)	0.054	0.48
1-min STST [repetitions]	4.9 (3.5–6.4)	**<0.001**	2.9 (1.4–4.4)	**0.004**	2.0 (−0.2 to 4.2)	0.060	0.46
Knee extension, peak force [N]	24.7 (11.6–37.8)	**<0.001**	23.7 (10.0–37.4)	**<0.001**	1.0 (−17.7 to 19.8)	0.912	0.027

Data are presented in mean (95% confidence interval); 6-MWD = 6-minute-walking-distance, APL = absolute path length, STST = sit-to-stand test, WBVT = whole-body vibration training. p-values with a significance level of <0.05 are shown in bold.

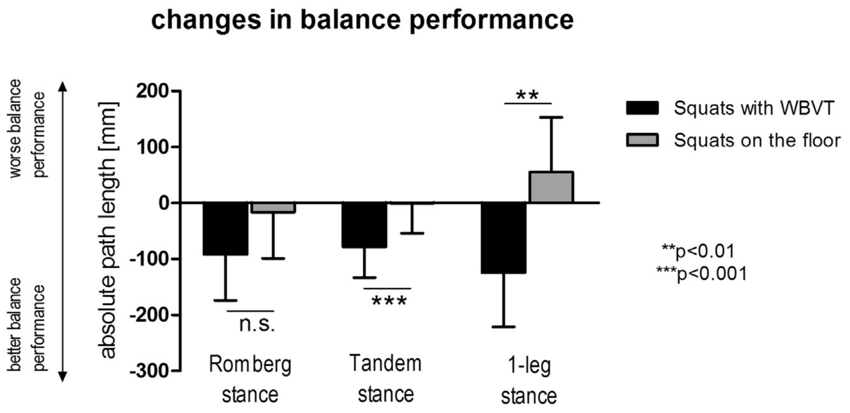

Fig. 4. Changes in balance performance following squat training with whole body vibration training (WBVT) or on the floor (data are shown as mean and 95%CI for mean).

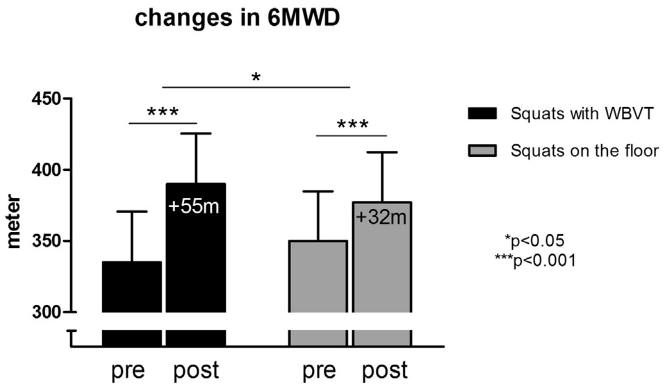

Fig. 5. Changes in 6-minute walk distance (6 MWD) following squat training with whole body vibration training (WBVT) or on the floor (data are shown as mean ± SD).

indicating that these WBVT are closely related to improvements in neuromuscular performance (postural balance and muscle power output) but not muscle strength.

4.1. Postural balance performance

COPD patients in our study showed a 50% worse balance performance compared to healthy age-matched historical controls [18]. This is in line with the findings of a recent systematic review [19].

Although patients in the control group were, as expected, able to significantly improve exercise capacity (albeit to a lesser extent than WBVT) following exercise training in PR, they were not able to improve balance performance. Only patients in the WBVT group significantly improved balance (in combination with a superior increase in exercise capacity). These findings concurred with the results of our generalized linear model and are supportive of the hypothesis that the beneficial effects of WBVT on exercise capacity are related to an increased balance performance. A former study has also found that dynamic balance parameters during gait such as stride length and velocity in COPD patients improve following WBVT [20].

In general, impaired balance and improving motor control are important issue in patients with impaired physical conditions and in the elderly. A decreased balance ability is associated with a lower physical activity in daily life [21] and a higher risk of falls [22]. The risk of falling with subsequent bone fractures is also higher in patients with osteoporosis [23], a common comorbidity in COPD (57% in the current study cohort). Also the risk for hospitalization is higher in patients with a history of falls [24]. Therefore, strategies to improve balance are needed. However, a comprehensive PR exercise training program including endurance and strength training without WBVT was not sufficient to improve balance in patients with COPD in the current study. This is consistent with findings from former studies in which it has been observed that balance performance only improves when specific balance training strategies are applied in the context of PR [25–27]. Hence, the implementation of WBVT in PR programs may be such a strategy to improve balance (and therefore exercise capacity) in patients with COPD. However, it remains unknown if conventional balance body exercises without additional equipment are as effective as WBVT for improving balance and exercise performance. This should be investigated in further studies.

4.2. Exercise performance

Patients in the WBVT group increased 6 MWD significantly more compared to the control group (55 m versus 32 m) and this inter-group difference of 23 m almost reached the minimal important difference [MID] range of 25 m–33 m [28]. Furthermore, 68% of the patients in the WBVT group and only 45% of the controls exceeded the mean MID threshold of 30 m for improvement in the 6 MWD.

Patients in the WBVT group performed 27% fewer squat repetitions than patients in the control group. This may have been the case because standing on a WBVT platform requires more concentration and provides an intense stimulus, whereas standing on the floor provides no impact on the subject. However, even though patients in the WBVT group performed fewer squat repetitions they showed a larger increase in exercise performance.

During this study a variety of different exercise tests beyond the 6 MWT were applied to identify potential improvements in specific areas of muscle performance eventually explaining the WBVT effects. Average power during the two-legged jump is a well-validated parameter to determine muscle performance [13]. In one study, individuals with COPD had a 38% reduction in this parameter as compared to healthy elderly persons [29]. In our study, this parameter increased significantly more after PR in the WBVT group compared to controls. In healthy subjects it has been shown that squat training during WBVT elicits an alteration in neuromuscular recruitment patterns in terms of a significant increase in reflex amplitude (measured by electromyography) after a single bout of WBVT which apparently enhance neuromuscular excitability compared to squat training on the floor [30]. Although we did not perform electromyography in our study, this is an additional mechanism by which the benefits of WBVT may have been conferred. Notably, improvements in knee extension muscle force were not different between groups, suggesting that the benefits of WBVT on balance and exercise capacity did not solely relate to quadriceps strength, and the better performance during the STST in the WBVT group may have related to an improvement in postural control.

At baseline there was one significant between-group difference (5-rep STST). Since our study is a randomized trial this finding is likely to be a type 1 error. We tested 22 variables at baseline so the probability to find at least one significant difference – assuming independence - is 68%. Furthermore, the 5-rep STST is not the primary outcome. Therefore, and from a statistical point of view this finding is not unusual in a randomized controlled trial and does not influence the main finding and conclusions of this study.

4.3. Potential mechanisms of improved muscle performance following WBVT

Compared to voluntary muscle control (as in traditional resistance training), muscle contractions during WBVT are caused by passive stretch reflexes [31,32]. The micro movements during WBVT facilitate the excitability of the spinal reflex [33–35]. On WBVT platforms muscles are exposed to a very high frequency of nerve impulses [36]. It has been proposed that proprioceptive neuromuscular facilitation, tonic vibration reflex, increased gravitational forces on muscles and higher muscle contractile activities may all be responsible for the physiological changes induced by WBVT [36–38]. Interestingly, the ventilatory efficiency (VE/VCO2) is similar after 3 min of standardized squat training with (38.0 ± 4.4) or without (37.4 ± 4.1) WBVT in patients with severe COPD, hence does not explain the superior benefits on exercise capacity [39].

4.4. Limitations and strengths of this study

There are certain limitations to our study. First, only objective measurements of static but not dynamic balance performance were performed. However, it has been suggested that since there is a strong correlation between static and dynamic balance performance, the results may be transferable [40]. Furthermore, the long-term efficiency of WBVT benefits on neuromuscular performance or a potential reduction in risk of falls still remain unknown.

Despite these limitations, the most important strength of this study is that balance and exercise performance tests were objectively measured using well-validated equipment. Furthermore, the study was performed as a randomized, controlled trial and used an a priori calculated sample size to determine improvements in balance performance.

5. Conclusions

It seems that the secret behind the positive effect of WBVT on exercise performance in patients with COPD may be related to improvements in neuromuscular performance, as opposed to muscular strength or central cardiovascular adaption. WBVT may be highly beneficial when incorporated into PR programs for COPD patients [5,41] especially in those with impaired balance performance and low exercise capacity.

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Novotec Medical provided the force plate (Leonardo) for the study purpose. However, the company did not have any influence on study design, the conduct of the study, data analysis, interpretation of results or writing this manuscript.

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Contributorship statement

Study concept and design: RG and KK; acquisition of data: RG, UB, MC, TS, IJ; analysis and interpretation of data: WH and RG; drafting the article: RG, VA, JWC; providing scientific discussion and revising the manuscript critically for important intellectual content: all authors; RG had full access to all study data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Conflict of interest declaration

None declared.

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