Does Whole-Body Vibration Improve the Functional Exercise Capacity of Subjects With COPD? A Meta-Analysis

Adriane B Cardim MSc, Patrícia EM Marinho PhD, Jasiel F Nascimento Jr MSc, Helen KB Fuzari MSc, and Armèle Dornelas de Andrade PhD

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Whole-body vibration (WBV) is considered a type of physical activity based on the assumption that it results in an increase in muscle strength and performance and, therefore, may be a promising way to exercise patients with COPD. A comprehensive database search (PubMed/MEDLINE, LILACS, CINAHL, Web of Science, Scopus, and COCHRANE Library) for randomized trials, including original articles, that compared WBV groups versus control groups was conducted and studies were selected for comparison. The effect of WBV treatment was compared for minimum clinically important differences. The statistical heterogeneity among the studies was assessed using the I² statistic; the results are expressed as percentages. Inconsistencies of up to 25% were considered low, those between 50 and 75% were considerate moderate, and those > 75% were considered high. Risk of bias was classified based on the Cochrane Collaboration tool, the meta-analysis was conducted using RevMan 5.3 software, and the level of evidence was assessed using the GRADE system. The primary outcome was functional exercise capacity. Secondary outcomes were quality of life, performance in activities of daily living, muscle strength of the lower limbs, and possible adverse effects assessed clinically or by subject reports. We included 4 articles involving 185 subjects for analysis. All subjects in the groups undergoing WBV showed improvement in distance walked in the 6-min walk test compared with the control group (57.85 m, 95% CI 16.36-99.33 m). Regarding the secondary end points, just one article reported improved quality of life and activities of daily living. The only article that assessed muscle strength found no difference between the groups. The quality of evidence for functional exercise capacity outcome was considered moderate. WBV seems to benefit subjects with COPD by improving their functional exercise capacity, without producing adverse effects. The quality of evidence is moderate, but the degree of recommendation is strong. (International Prospective Register of Systematic Reviews, http://www.crd.york.ac.uk/prospero, 2015:CRD42015027659.). Key words: COPD; dyspnea; exercise tolerance; quality of life; therapeutic use; vibration. [Respir Care 2016;61(11):1552–1559. © 2016 Daedalus Enterprises]

Introduction

COPD is among the leading causes of chronic morbidity and mortality, representing a major challenge to global public health. Although preventable and treatable, continuous exposure to risk factors, such as smoking, environmental pollution, and/or occupational irritants, and the increase in life expectancy of the population, underlie the rising prevalence of COPD globally.¹⁻³ Characterized by persistent limitation in air flow, this disease is defined by major chronic inflammation.⁴

COPD is associated with various local and systemic complications, and the high frequency of exacerbations and multiple comorbidities that follow the disease contribute to its severity in patients. In this context, the extrapulmonary aspects of COPD are increasingly being recognized as important contributors to morbidity and mortality. Skeletal muscle dysfunction is of particular interest, because it directly influences exercise performance.⁵⁻⁷

Whole-body vibration (WBV) has gained popularity in the rehabilitation of several populations.⁸⁻¹¹ WBV is a method of physical activity during which an individual is on a platform that generates vertical sinusoidal vibrations. The oscillations are transmitted to the body and stimulate muscle spindles to produce muscle contractions, with physiological responses similar to those produced by other modes of physical activity, such as aerobic conditioning and strength training.^{12,13} Based on the assumption that increases in muscle strength and performance are the main effects of WBV,¹⁴ this may be a promising mode of exercise in patients with COPD.¹⁵⁻²²

However, a systematic review on the topic²³ showed no conclusive data on the effectiveness of WBV at improving exercise capacity in these subjects. In the review presented by Gloeckl et al,²³ important aspects are missing for a review of this nature, such as linguistic restriction, analysis of the risk of bias in the selected studies, and the lack of summarizing the results and quantitative analysis through meta-analysis, thus compromising the interpretation of the data.

The systematic review and meta-analysis presented here aimed to assess the quality of evidence from the literature

The authors are affiliated with the Universidade Federal de Pernambuco, Post Graduate Program in Physical Therapy, Physical Therapy Department, Recife, PE, Brazil.

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Correspondence: Armèle Dornelas de Andrade PhD. Universidade Federal de Pernambuco, Departamento de Fisioterapia. Av. Jornalista Anibal Fernandes, s/n. Cidade Universitária. CEP: 50740–560, Recife – PE, Brazil. E-mail: armeledornelas@yahoo.com.

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on the effects of WBV on the functional exercise capacity in subjects with COPD.

Methods

This study was performed at the Universidade Federal de Pernambuco. The protocol for the systematic review and meta-analysis is registered with the International Prospective Register of Systematic Reviews (PROSPERO, http://www.crd.york.ac.uk/prospero, 2015: CRD42015027659).

Study Eligibility and Outcomes

The study eligibility criteria included original articles, such as randomized clinical trials without language restriction, with planned research to evaluate the effects of WBV training, compared with the control group, on exercise capacity of subjects with clinical and functional diagnoses of COPD.

We considered articles whose primary outcome included functional exercise capacity tests. The secondary outcomes were quality of life, performance in activities of daily living, muscle strength of the lower limbs, and possible adverse effects, assessed clinically or by patient reports. Articles were excluded if they only reported acute effects or were compared with other interventions.

Search Strategy

We comprehensively searched the PubMed/MEDLINE, LILACS, CINAHL, Web of Science, Scopus, and CO-CHRANE Library databases during the period from February to March 2015. For surveying, the following descriptors were used: chronic obstructive pulmonary disease; vibration/therapeutic use; exercise tolerance; dyspnea; quality of life; activities of daily living; and muscle strength. Two independent reviewers (ABC and JFNJ) identified the eligible studies and extracted the data. The terms and their combinations were used in the search of each database field. Refining tools, such as MeSH terms in PubMed/MEDLINE and Decs in LILACS were used when available. The reference lists in each article selected were examined to identify other potentially relevant studies.

The titles and abstracts were screened to weed out irrelevant studies. Original articles were obtained and read in detail to assess the eligibility when the summary suggested a relevant study or when the summary was incomplete. To assess the concordance inter-evaluator of the selected studies to enter the qualitative assessment, we used the Kappa index.

Data Extraction

The main aspects of the selected articles were extracted and summarized in tables. These data included the study design, the characteristics of the samples, the characteristics of the intervention and the control groups, the measured outcomes, and relevant results. Analytical data missing from the primary reports were requested from the authors

The following training characteristics of WBV, when they were described by the respective authors, were also obtained for comparison: type of activity to be performed on the vibration platform, frequency (hertz), amplitude (mm), cycles (number of series and period of each series), repetitions (number of sessions performed), and cumulative dose (total training time in min).

Quality Assessment of Studies

The risk of bias in selected articles was classified based on the Cochrane collaboration tool by using RevMan 5.3 software. Two authors subjectively reviewed all the studies and assigned a value of "high," "low," or "unclear" to selection bias, blinding, attrition bias, reporting bias, and "other" bias. Because the type of intervention does not allow masking of the patient, it was determined that for this domain, the nonblinding was not a source of a high risk of bias. For the other biases, the presence or absence of sample calculation and/or small sample size was the main determining factor for their classification.

The level of evidence was evaluated using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system GRADEpro software. The following items were considered: study design, risk of bias, inconsistency, indirectness, imprecision, and magnitude of treatment effect. The quality of evidence was interpreted as high, moderate, or low; and the strength of the recommendation was classified as strong or weak.

Data Analysis

Our study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.²⁴ All data and statistical analyzes were combined and conducted using RevMan 5.3 software (The Cochrane Collaboration, SoftwareUpdate, Oxford, UK). The continuous variable distance covered on the 6-min walk test is expressed in the meta-analysis as average difference with 95% CI. All measurements were collected through the random effects model. The heterogeneity among the studies was tested by measuring the inconsistency (I²); the results are expressed as percentages; and inconsistencies of up to 25% were considered low, between 50% and 75% were considered moderate, and > 75% were considered high.²⁵ Data for each

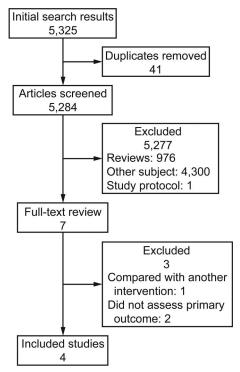


Fig. 1. Flow chart.

group are presented as mean \pm SD, and P < .05 was considered statistically significant. The effect size of the treatment was compared with its minimum clinically important difference.

Results

The systematic search results are summarized in Figure 1. From 5,325 articles identified, following the established criteria after the withdrawal of repeated articles and reading the titles and abstracts, only 7 were selected for full text analysis and potentially considered for the review. Of these, 3 were excluded, because they did not fit the inclusion criteria. The reasons for exclusion of these studies were the comparison with another intervention²¹ (1 study) and failure to assess the primary end point^{17,18} (2 studies). The concordance index of articles selected among the reviewers was $\kappa = 0.72$.

Authors and year of publication, type of study, sample characteristics, outcomes, and main results found are described in Table 1. The training characteristics of whole-body vibration are summarized in Table 2.

All included studies showed improved functional capacity in the group undergoing WBV training compared with the control group. Greulich et al¹⁶ also showed improvement in the performance of activities of daily living through the sitting-to-standing from the chair test.

Regarding quality of life, Greulich et al¹⁶ showed improvement in the WBV group based on the St George

Table 1. Summary Description of the Studies

Variables	Gloeckl et al ¹⁵ (2012)	Pleguezuelos et al ¹⁹ (2013)	Greulich et al ¹⁶ (2014)	Braz Júnior et al ²⁰ (2015)		
Design			Randomized clinical trial	Randomized clinical trial crossover		
Groups	Intervention: Pulm. rehab + WBV	Intervention: WBV	Intervention: Physiotherapy + WBV	Intervention: WBV		
	Control: Pulm. rehab	Control: Recommendations	Control: Physiotherapy	Control: No physical activity		
Sample	72 COPD subjects	51 COPD subjects	40 COPD subjects	11 COPD subjects		
	Intervention $(n = 36)$	Intervention $(n = 26)$	Intervention $(n = 20)$	Intervention and Control $(N = 11)$		
	$\text{FEV}_1(\%\text{predicted})$: 39 ± 11	FEV_1 (%predicted): 37.1 \pm 11.9	FEV ₁ (%predicted): 32.71 ± 13.18	FEV ₁ (%predicted): 14.63 ± 11.14		
	Age: 64 ± 11 y old	Age: $68.4 \pm 8.9 \text{ y old}$	Age: 66.4 ± 9.93 y old	Age: 62.9 ± 8.82		
	Sex (M/F): 18/18	Sex (M/F): 26/0	Sex (M/F): 14/6	Sex (M/F): 8/3		
	Control $(n = 36)$	Control $(n = 25)$	Control $(n = 20)$			
	$FEV_1(\%$ predicted): 38 ± 12	FEV_1 (%predicted): 32.0 \pm 6.8	FEV_1 (%predicted): 38.4 \pm 17.82			
	Age: 65 ± 7 y old	Age: $71.3 \pm 8.0 \text{ y old}$	Age: $70.4 \pm 10.1 \text{ y old}$			
	Sex (M/F): 19/17	Sex (M/F): 25/0	Sex (M/F): 12/8			
Outcomes	Functional exercise capacity	Functional exercise capacity	Functional exercise capacity	Functional exercise capacity		
	Performance in daily activities Quality of life	Performance in daily muscle strength of the lower limbs	Performance in daily activities Quality of life	Quality of life		
Results	6MWD: ↑ Intervention > ↑ Control Treatment effect: 26.7 m [95% CI, 0.5–52.9] ($P = .046$)	6MWD: Intervention > Control Treatment effect: 80.2 m [95% CI 68.4-92.0](P < .001)	6MWD: Intervention > Control Treatment effect: 89.42 m [95% CI 38.84,140] (P = .007)	6MWD: Intervention > Control Treatment effect: 64.18 [-27.72 to 156.08]($P = .005$)		
	Test sit/stand from the chair: ↓ Intervention and ↓ Control CRQ: ↑ Intervention and ↑ Control	Isokinetic test of flexion and knee extension: ns	Test sit/stand from the chair: Intervention $<$ Control Treatment effect: $-6.21s$ [95% CI -11.82 to -0.6]($P = .003$)			
	1		Total SGRQ: Intervention < Control	Total SGRQ: ↓ Intervention		
			Treatment effect: -12.02 [95% CI -22.8 to -1.21]($P = .049$)			
Pulm. rehab = M = male F = female 6MWD = 6-m CRQ = Chroni	body vibration pulmonary rehabilitation in walk distance c Respiratory Questionnaire ge Respiratory Questionnaire icant					

Table 2. Overview of Whole-Body Vibration Parameters

Variables	Gloeckl et al ¹⁵ (2012)	Pleguezuelos et al ¹⁹ (2013)	Greulich et al ¹⁶ (2014)	Braz Júnior et al ²⁰ (2015)		
Activity	Dynamic squats	Static squat	Static squat	Static squat		
Amplitude	6 mm	2 mm	1.5–3 mm	2–4 mm		
Frequency	24-26Hz	35Hz	12-26Hz	35Hz		
Cycles	3 series of 3 min	6 series of 30 s	3 series of 2 min	Start: 20 series of 30 s		
				Progression: 15-20 series of 1 min		
Repetitions	9 (for 3 wk)	18 (for 6 wk)	-	36 (for 12 wk)		
Cumulative dose	81 min	54 min	-	540 min		

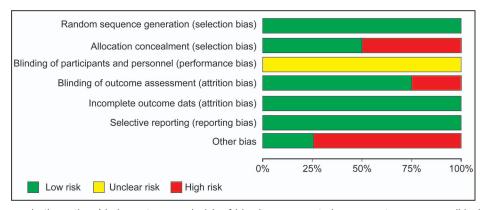


Fig. 2. Risk of bias graph: the authors' judgments on each risk-of-bias item, presented as percentages across all included studies.

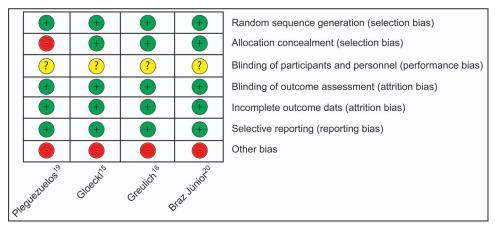


Fig. 3. Risk of bias summary: the author's judgments on each risk of bias item for each included studies.

Respiratory Questionnaire compared with the control group. However, Braz Júnior et al²⁰ found no difference in the final scores of the questionnaire between the 2 groups.

The study conducted by Gloeckl et al¹⁵ that compared training using a vibrating platform associated with a pulmonary rehabilitation program versus pulmonary rehabilitation program alone, showed improvement in all parameters investigated in both groups. The sitting-to-standing from the chair test as well as the quality of life questionnaire (Chronic Respiratory Questionnaire) showed no improvement at the end of the program.

Regarding muscle strength of the lower limbs, only Pleguezuelos et al¹⁹ investigated this outcome and found no differences between the WBV and control groups.

Regarding the methodological quality of the studies, Figures 2 and 3, respectively, show the chart and summary of each risk of bias for each selected study. The quality of evidence by the GRADE system was determined taking into account the risk of bias, inconsistency and inaccuracy of the results, indirect comparisons, and the possibility of publication bias. The quality of evidence for the outcome of the WBV functional capacity, measured by the distance

walked in the 6-min walk test, was determined to be moderate (Fig. 4).

The meta-analysis of the functional capacity outcome through the 6-min walk distance (Fig. 5) favored treatment with the vibrating platform compared with the control group. The analyzed studies showed a substantial level of heterogeneity ($I^2 = 64\%$).

Discussion

Our review found 4 studies comparing the effectiveness of using WBV versus a control in the functional exercise capacity of subjects with COPD, and all 4 articles showed improvement in distance walked in the 6-min walk test in the WBV group compared with the control group. Regarding the secondary end points, only one article reported improved quality of life and activities of daily living. The only study selected that evaluated muscle strength found no differences between the groups.

The use of WBV has been adopted to improve exercise capacity in patients with COPD, but there is still little evi-

Quality assessment							Subjects, n		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Whole body vibration	Control	Relative (95% CI)	Absolute	Quality	importance
Functio	Functional capacity (measured with: 6MWD, better indicated by higher values)											
4	Randomized trials	Serious ¹		No serious indirectness	Serious ³	Very strong association⁴	93	92	-		⊕⊕⊕O Moderate	Critical

Fig. 4. GRADE evidence profile of the outcome functional capacity as measured by 6-min walk distance (6MWD). 1. Studies without allocation concealment, blinding and/or sample size calculation. 2. Meta-analysis with overlap in CI, statistical significance in heterogeneity test and high I2. 3. Studies with high CI and small sample size. 4. Magnitude of treatment effect above the minimally significant clinical difference.

	Treatme	nt group	Control group				Mean Difference	Mean Difference			
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year IV,	Random, 95%	CI
Gloeckl ¹⁵	349	112	36	344	104	36	26.1%	5.00 (-44.93-54.93)	2012 ———	-	
Pleguezuelos ¹⁹	493.1	31.7	26	410.4	31.2	25	39.1%	82.70 (65.44-99.96)	2013	7-	_
Greulich ¹⁶	263.45	124.13	20	198.67	101.37	20	19.0%	64.78 (-5.46-135.02)	2014	-	-
Braz Júnior20	413.09	101.56	11	337.85	95.62	11	15.8%	75.27 (-7.16–157.70)	2015		•
Total (95% CI)			93			92	100.0%	57.85 (16.36–99.33)			
Heterogeneity: Tau ² = 1068.85; Chi ² = 8.83, df = 3 (<i>P</i> = .04); ² = 64%											100
Test for overall effect: $Z = 2.73$ ($P = .006$)										Favors treatm	

Fig. 5. Meta-analysis of randomized, controlled trials in evaluating the effects of whole body vibration on 6-min walk test (6MWD) using the random-effects model. The area of each square is proportional to the precision of the mean treatment effect in the study. The horizontal line represents the 95% CI for the treatment effect in each study. The center of the diamond is the average treatment effect across studies, whereas the diamond width denotes its 95% CI.

RCT = randomized, controlled trial WBV = whole-body vibration

dence regarding its effectiveness. The studies found were conducted in Germany (2), Spain, and Brazil, with the oldest being published in 2012, which indicates the interest in the use of WBV in this specific population.

As for the training characteristics, each study had its own protocol, differing with regard to amplitude, frequency, cycles, and repetitions. Only 1 study, conducted by Greulich et al, 16 did not document the number of repetitions and the cumulative dose due to its development during hospitalization. 14

Functional Exercise Capacity

Gloeckl et al¹⁵ investigated the effects of WBV in subjects with COPD, assessing the effectiveness of this intervention in relation to exercise capacity, and observed improvement in walking distance in the WBV group compared with the controls. Because it is an intervention associated with a pulmonary rehabilitation program, the 2 groups were able to increase the 6-min walk distance above the minimum clinically important difference of 35m.²⁶ The pulmonary rehabilitation program consists of an interdisciplinary intervention, including structured physical training and behavioral interventions, and it is currently established as an accepted standard of care for patients with

COPD,²⁷ which explains the effectiveness of treatment in both groups.

The studies of Greulich et al, ¹⁶ Pleguezuelos et al, ¹⁹ and Braz Júnior et al, ²⁰ show a more significant increase in the distance walked on the treatment effect over the minimum clinically important difference. ²⁶ The 3 studies had as a characteristic a control group that did not undergo exercise training, which may explain this gain. When the intervention was compared with other types of training, such as in the Salhi et al study, ²¹ which compared WBV training with resistance training, both associated with aerobic training, it reported improved functional capacity and quality of life in both groups with no differences between them.

Quality of Life

The study conducted by Braz Júnior et al²⁰ showed a reduction in the total score on the quality of life questionnaire specific for respiratory diseases (St George Respiratory Questionnaire) over time in the WBV group, but at the end of the study there was no difference regarding the control group. Gloeckl et al¹⁵ also showed improvement on the questionnaire for chronic diseases (Chronic Respiratory Questionnaire) and did not differ from the control group that carried out the isolated pulmonary rehabilitation program.

According to the Salman et al meta-analysis,²⁸ the improvement in exercise tolerance is due to neuromuscular adaptations and, above all, relief of dyspnea following a rehabilitation program, which may indirectly provide a better quality of life. Therefore, dyspnea is the main factor associated with quality of life in patients with COPD.^{28,29}

WBV consists of a method of physical activity that does not cause dyspnea, ¹⁸ allowing benefit to the most seriously ill patients who can not endure an intervention with greater intensity. Although the analyzed studies did not report a reduction in dyspnea during the walking test, Greulich et al ¹⁶ showed improvement in functional exercise capacity parameters reflected in the subjective questionnaire of quality of life with improvement for the WBV group compared with the control group.

Daily Activities

Greulich et al¹⁶ showed a reduction in the testing time of sitting-to-standing from the chair, indicating an improvement in the performance of daily activities. The clinical trial conducted by Furness et al,¹⁷ which compared the effect of 6 weeks of training on a vibrating platform with the sham training in a crossover study corroborates this result. However, Gloeckl et al¹⁵ did not find these results when comparing the WVB with a control group post participation in a pulmonary rehabilitation program.

Muscle Strength

Pleguezuelos et al¹⁹ showed no improvement in peripheral skeletal muscle strength of knee flexion and extension. The increase in muscle strength of the lower limbs is well documented in the literature as one of the main benefits of using WBV, especially in the elderly population.^{30,31} Although performed with healthy individuals, Petit et al¹⁴ concluded that frequencies and higher amplitudes are more effective for improving muscle strength of knee extensions.

However, skeletal muscle dysfunction observed in patients with COPD is caused by a complex series of interactions and many systemic and clinical inflammatory factors.^{7,32,33} These changes are reflected in several responses in relation to physical activity, which makes it necessary to create a specific protocol that meets the needs of this particular population. The conflicting findings may be due to differences in WBV protocols in different studies, especially pertaining to duration, amplitude, and frequency.

Adverse Effects

No serious adverse events, such as injury, cardiac symptoms, or increasing respiratory distress, were observed ac-

cording to the protocols of the 4 studies discussed. Only in the Pleguezuelos et al study, ¹⁹ did 2 subjects report knee pain, which was resolved with the administration of an anti-inflammatory drug and did not require discontinuation of training on the vibrating platform. The training was well accepted by subjects, and no changes in treatment costs were reported.

Quality of Evidence

Regarding the quality of the methodology, Greulich et al¹⁶ and Pleguezuelos et al¹⁹ had no sample calculations reporting sampling bias. The small sample size combined with the high CI, especially in the Greulich article, indicates an inaccuracy in the results. In addition to this inaccuracy, the Pleguezuelos et al study¹⁹ also had selection bias. Gloeckl et al¹⁵ besides not having undergone blinding of the cohort allocation, was the only study that did not have blinded reviewing, which resulted in the detection of bias.

For functional capacity outcome, the level of evidence of WBV was considered moderate. Although the risk of bias, the inaccuracy and inconsistency has led to a reduction in quality, direct comparison, the nondetection of publication bias and especially the effect size above the minimal clinically important difference, determined a moderate quality of evidence. This means that the true effect seems to be close to the estimate, but there is still a possibility that it could be substantially different.

The criteria for methodological quality and the presence of 2 independent reviewers, the calculation of the reliability coefficient, a wide search in multiple databases without language or y restrictions, and the use of specific tools for the analyses were carried out to minimize the biases involved in this review. Our study reinforces the findings of Gloeckl et al²³ and makes new contributions to the literature through the summarization of study results and quantitative analysis for this meta-analysis. However, they were not included in the research database of theses and dissertations, we could not rule out the publication bias. Based on this systematic review and meta-analysis, using WBV in the training of patients with COPD provides benefits to these subjects by improving their functional exercise capacity without generating significant adverse effects. The quality of the evidence was rated as moderate because of the different intervention protocols used, risk of bias, and heterogeneity. However, because of the magnitude of the treatment effect, combined with the low risk of undesirable consequences, the use of WBV in patients with COPD has a strong degreed of recommendation.

Conclusions

Based on this systematic review and meta-analysis, using WBV training provides benefits to patients with COPD,

improving their exercise capacity and producing no significant adverse effects. The quality of evidence was graded as moderate because of the different intervention protocols used, the risk of bias, and heterogeneity. However, because of the magnitude of the treatment effect, combined with the low risk of unintended consequences, WBV in patients with COPD can be highly recommended based on this meta-analysis.

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