

Review Article

Effectiveness of physiotherapy techniques for rehabilitation after acute chronic obstructive pulmonary disease exacerbation: a meta-analysis

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Abstract: Chronic obstructive pulmonary disease is a major cause of mortality and morbidity worldwide with inflated costs for treatment and rehabilitation. Physiotherapy is clinically beneficial for rehabilitation of COPD patients but there is a lack of scientific analysis and comparison of physiotherapy effects in severe COPD patients. Therefore, we applied a detailed systematic approach to investigate the effect of all potential physiotherapy techniques on motor function in COPD exacerbation patients. We pooled data from 315 trials published in databases such as PubMed, etc. Colleagues independently reviewed these studies and any of the above study patients with exacerbated COPD were randomly allocated to receive diverse physiotherapy techniques. Primary outcomes were exercise distance and endurance time. Thirteen studies were eventually included in this study. Overall physiotherapy techniques contributed to significantly improved motor function (standardized mean difference 25.96, 95% confidence interval [CI]=19.08 to 32.85) including longer exercise distance (weighted mean difference), and longer endurance time (standardized mean difference). Specifically, results of TENS and HFCWO indicated a significant improvement of motor function of COPD patients (overall $P=0.003$ and <0.00001 , respectively) while ELTGOL did not statistically ameliorate motor function after COPD exacerbation (overall $P=0.43$). In general, physiotherapy techniques are effective in improving severe COPD patient motor function. Further research is needed to elucidate its effect on other outcomes and to determine the optimal use of physical therapy.

Keywords: Chronic obstructive pulmonary disease (COPD), transcutaneous electrical nerve stimulation (TENS), high-frequency chest wall oscillation (HFCWO), expiration with the glottis open in the lateral posture (ELTGOL), pulmonary rehabilitation

Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable pulmonary disease characterized by limitation in continuous air flow [1], according to a consensus document issued by World Health Organization-the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [2, 3]. However, extra-pulmonary manifestations of many COPD patients are various such as impairment of systemic motor functions at diverse levels, especially muscular dysfunction and muscular atrophy [4-6]. In addition, unfavorable impacts of COPD such as sarcopenia or acute onset, may last a long time. COPD is a major cause of mortality and morbidity worldwide with the prediction of be-

ing the third leading cause of deaths in 2030 according to the World Health Organization (WHO) [7, 8]. Moreover, costs for treatment of COPD and its complications remain about €60 billion annually, according to European Health Forum Gastein (EHFG, 2016) [9, 10]. The mean cost for each patient in Europe is about €500, reported by European Respiratory Journal (ERS) [11, 12]. These shocking situations draw the attention of each country so that better methods improving quality of life and lowering the mortality rate can be found.

Physiotherapy has been widely applied for treatment, rehabilitation, and prevention for healthy people and athletes [13-17]. Physiotherapy is clinically proven to be beneficial for rehabilita-

tion of COPD patients, especially in improving limb muscular functions [18-23]. Recent studies have even demonstrated that physical training can prevent cognitive function impairment and related complications of male COPD patients [24-26]. Physiotherapy intervention at this stage can relieve dyspnea, lower ventilation, improve lung capacity and volume, and reduce the impact of hospitalization period [16, 17, 21, 27]. However, it is still not known whether patients with severe COPD can tolerate physiotherapy because of intense respiration or the need of long-time work [28]. There is a lack of scientific analysis and comparison of physiotherapy effects in severe COPD patients, including many interventional measures and result measures. Despite diverse physiotherapy methods, the quality and extent of different practices are difficult to compare. Thus, evidence proving the effectiveness of most types of physiotherapy is rare. More comprehensive studies are urgently needed to figure out which technologies are effective and acceptable.

After studying important impacts of main physiotherapy technologies on COPD outcome, we collected the current data for a meta-study regarding effectiveness of physiotherapy technology on severe COPD.

Materials and methods

Literature retrieval strategy and learning identification

To obtain all relevant studies, literatures from Central Register of Controlled Trials, PubMed, ScienceDirect database, Google Scholar, and EMBASE until August 30, 2017, were retrieved by two of our colleagues. As for disease specificity, we combined the following terms in all of our retrievals: “chronic obstructive pulmonary disease”, “COPD”, and “physiotherapy technology”. All of the titles and abstracts have been examined by the two colleagues, respectively, for inclusion and exclusion criteria (**Figure 1**).

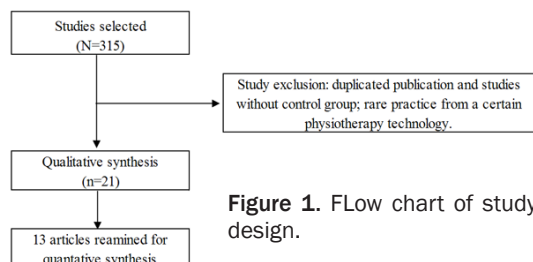


Figure 1. FLOW chart of study design.

Study selection

The inclusion criteria were: only English publications with random control trials and detailed data of exercise parameters for motor function comparison. Study exclusion criteria were: duplicated publications and studies without a control group. In the case of a rare practice from a certain physiotherapy technology, this technology was neglected due to failing to conform to our basic criteria of meta-analysis. As for articles reported in more than two publications, only the complete version was used for meta-analysis.

Data extraction

The following information was extracted from each study: the first author, publication year, patient ID, age, sex, COPD situation, FEV1%, physiotherapy technology, experimental and control measures (namely intervention category, training intensity, and duration), result parameters, and results. Patients who received stimulation or other treatments (namely sham stimulation) were included into the study group and motor ability as outcome was defined as traveling distance (6-minute walking test, 6MWT) and duration (constant work test, CWT).

Two of our colleagues (differing from those who screened the raw study data during literature retrieval) independently reviewed all of the studies. Any dispute was addressed through discussion with a third investigator. They cross-checked of all the data collected from the original articles. Duplication was eliminated and insufficient or inapplicable data was abandoned.

After data extraction described above, we selected three technologies which conformed to fulfil the inclusion criteria for meta-analysis: transcutaneous electric nerve stimulation (TENS), high frequency chest wall oscillatory ventilation (HFCWO), and glottis opened in lateral posture (ELTGOL).

Quality assessment

Results were assigned to the corresponding category according to comparable characteristics and expression. The preset primary outcome was motor function, for study convenience and comparison consistency. Motor

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Table 1. Characteristics of articles included in this systematic review

Author, year	Patients sample (m/f)	Grade	FEV1% (physiotherapy techniques/sham)	Age, years (physiotherapy techniques/sham)	Study design	Study intervention
Bourjeily-Habr 2002 [43]	18 (10/8)	Moderate-to-severe	35.6/40.7	58.5/61.5	RCT, double-blind	Transcutaneous electrical nerve stimulation (TENS)
Neder 2002 [44]	15 (9/6)	Moderate-to-severe	38/39.5	66.6/65	RCT, double-blind	High-frequency chest wall oscillation (HFCWO)
Basoglu 2005 [45]	27 (15/12)	Severe	N/A	69/51	RCT, single-blind	High-frequency chest wall oscillation (HFCWO)
Vivodtzev 2006 [46]	17 (11/6)	Severe	27/34	59/68	RCT, single-blind	Transcutaneous electrical nerve stimulation (TENS)
Kodric 2009 [38]	59 (39/20)	Severe	N/A	57/61	RCT, single-blind	Open glottis on lateral posture (ELTGOL)
Thierry 2010 [47]	30 (11/19)	Severe	N/A	59.3/68	RCT, single-blind	Transcutaneous electrical nerve stimulation (TENS)
Mahajan 2011 [39]	52 (41/11)	Severe	N/A	67/65.3	RCT, single-blind	Open glottis on lateral posture (ELTGOL)
Vivodtzev 2012 [48]	20 (13/7)	Severe	34/30	70/68	RCT, double-blind	Transcutaneous electrical nerve stimulation (TENS)
Kurzaj 2013 [21]	30 (16/21)	Severe	N/A	59/55	RCT, single-blind	Open glottis on lateral posture (ELTGOL)
Sillen 2014 [49, 50]	81 (43/38)	Severe	33/33	64.4/64	RCT, single-blind	High-frequency chest wall oscillation (HFCWO)
Vieira 2014 [51]	20 (20/0)	Moderate-to-severe	36.5/39.6	56.3/56.4	RCT, double-blind	High-frequency chest wall oscillation (HFCWO)
Tasdemir 2015 [37]	27 (24/3)	Moderate-to-severe	29/42.5	62.1/62.9	RCT, double-blind	Transcutaneous electrical nerve stimulation (TENS)
Maddocks 2016 [52]	52 (21/31)	Severe	30.8/30.7	70/69	RCT, double-blind	High-frequency chest wall oscillation (HFCWO)

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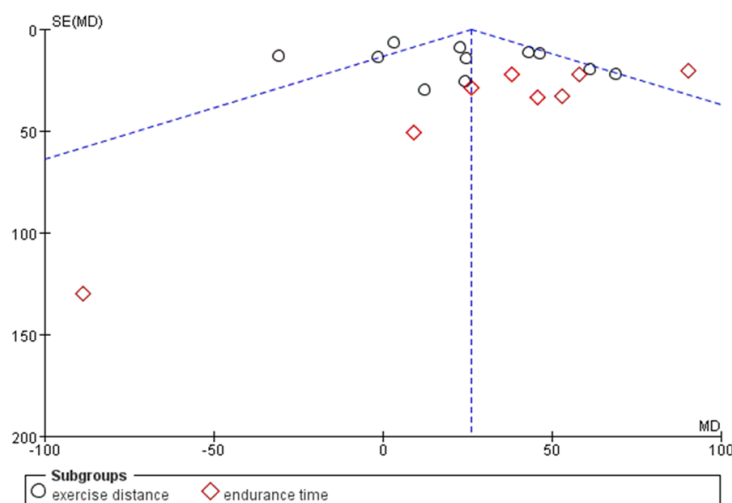


Figure 2. Degree of dispersion of samples used in comparing the effectiveness of all physiotherapy techniques on COPD. Abbreviations: SE, standard error; IV, inverse variance; CI, confidence interval.

function was compared mainly through 6MWT and CWT. The test parameters were exercise distance and endurance time.

Data synthesis and analysis

RevMan 5.3 software was used for meta-analysis. The weighted mean difference (WMD) or standardized mean difference (SMD) and 95% confidence interval (CI) were used for summarization and statistical analysis. After inter-trial differences were taken into consideration, the combined effects model and parameter random effects were adopted; as physiotherapy technology was expected to be heterogeneous, different stimulation parameters, treatment at different time points, different study designs, and study populations were included. Due to the limited quantity (lower than 10) of each technology, a complete funnel plot was constructed for all physiotherapy technologies. As for the data devices (\pm standard deviation), a two-sided p value <0.05 was considered statistically significant.

Results

Articles retrieved and characteristics of included trials

The studies collected through preliminary retrieval included 315 articles. After screening of titles and abstracts, 20 studies were excluded

due to irrelevancy and 17 studies were not random control trials. 237 articles were excluded due to insufficient or inapplicable data. 21 studies were eventually retained after the 20 repeated articles were excluded.

The collected articles were published from 2002 to 2017. Through collection of these trial data, 13 were assigned to physiotherapy technology. Characteristics of the participants, the interventional measures, and main results extracted from the corresponding studies are shown in **Table 1**.

Publication bias analysis

We used a funnel plot to investigate the potential source of heterogeneity. As shown in **Figure 2**, the funnel plot shows an asymmetry, however, the result was relative to Begg's insignificant ($P=0.06$) test (**Figure 2**). Therefore, all 13 studies were included in the meta-analysis.

Outcomes of all physiotherapy techniques on COPD

Comprehensive analysis indicates that application of all three physiotherapy technologies is beneficial to improvement of motor function by significantly prolonging the exercise distance (by 6MWT, WMD=21.99, 95% CI=14.64 to 29.34, $I^2=87\%$, subgroup $P<0.00001$), the walk endurance time (as shown in **Figure 3**), and (but of a high heterogeneity) motor tolerance time (by CWT, SMD=54.47, 95% CI=34.78 to 74.15, $I^2=7\%$, subgroup $P>0.05$). As for high heterogeneity, endurance time of the entire physiotherapy has not been concluded. However, the whole effect of physiotherapy technologies on COPD exacerbation was proven to be very effective in this meta-analysis (WMD=25.96, 95% CI=19.08 to 32.85, $I^2=80\%$, overall $Z=7.39$, $P<0.00001$).

Transcutaneous electrical nerve stimulation (TENS) significantly improved motor function of patients with COPD exacerbation

Transcutaneous electrical nerve stimulation works as a kind of physical stimuli. Specifically,

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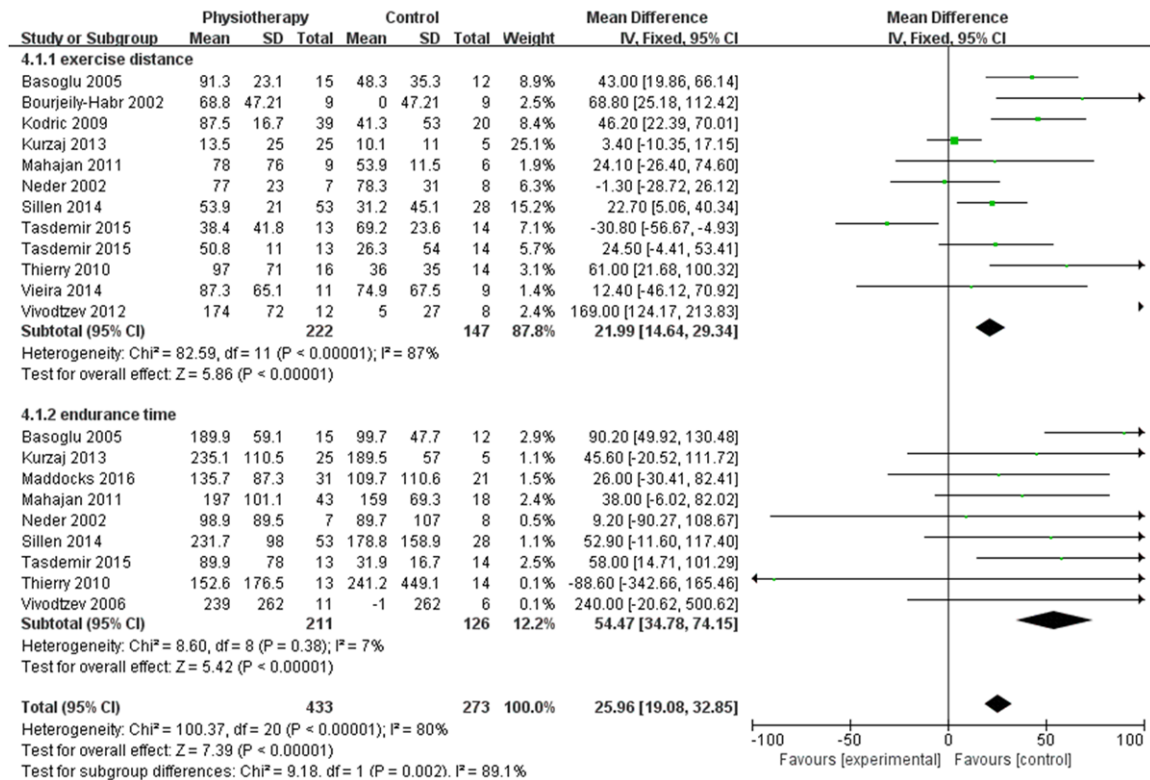


Figure 3. Effectiveness of all physiotherapy techniques on COPD. Abbreviations: SD, standard deviation; IV, inverse variance; CI, confidence interval.

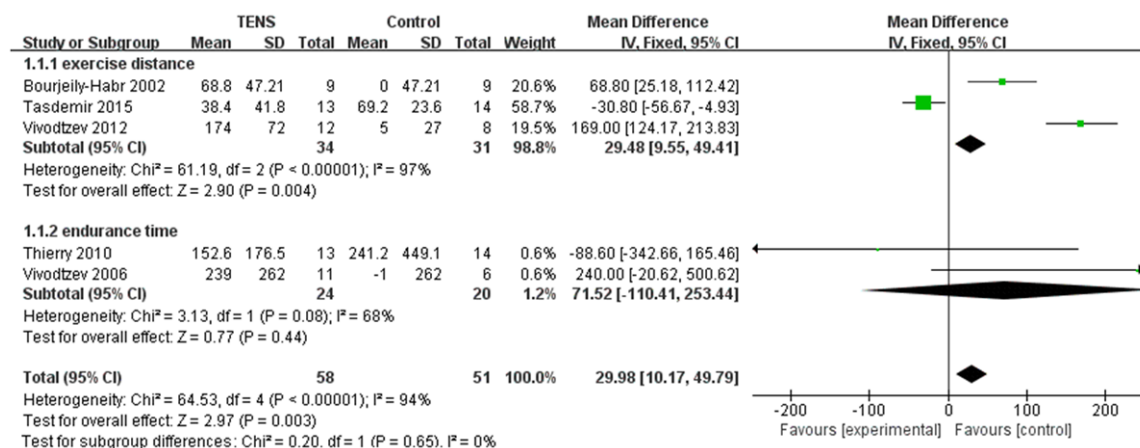


Figure 4. Effectiveness of transcutaneous electrical nerve stimulation (TENS) on COPD exacerbation. Abbreviations: TENS, transcutaneous electrical nerve stimulation; SD, standard deviation; IV, inverse variance; CI, confidence interval.

a meta-study was carried out on the relationship of TENS application and COPD exacerbation outcome. The results showed that relatively long exercise distance (WMD 29.48, 95% CI=9.55 to 49.41, subgroup I²=97%, P=0.004) and longer endurance time (SMD 1.11, 95%

CI=0.14 to 2.08, subgroup I²=85%, P=0.44) (as shown in **Figure 4**) were connected. The overall effect of TENS on COPD exacerbation was also proven to be effective (WMD 29.98, 95% CI=10.17 to 49.79, subgroup I²=94%, P=0.003).

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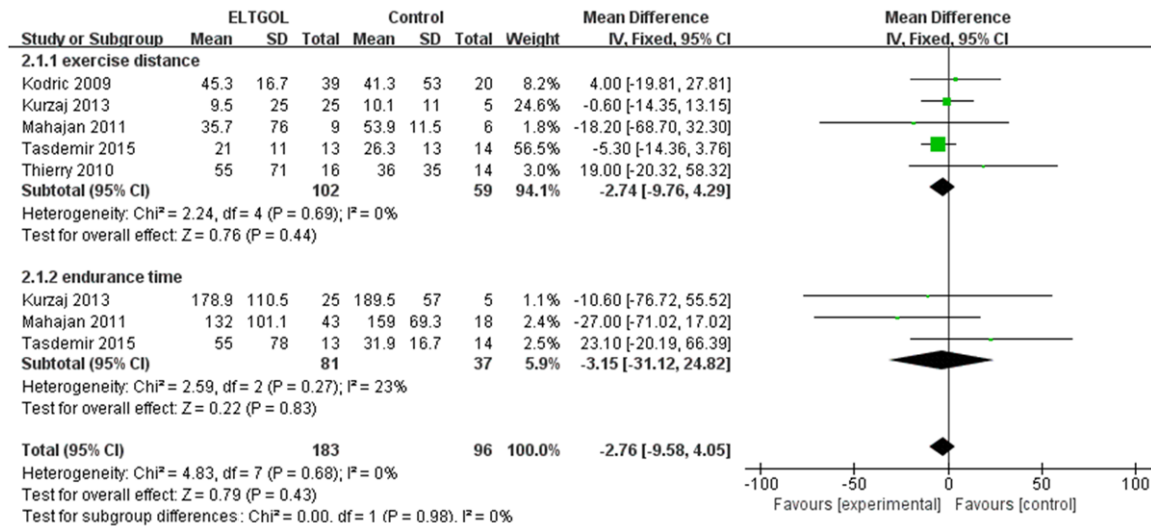


Figure 5. Effectiveness of expiration with open glottis on lateral posture (ELTGOL) on COPD exacerbation. Abbreviations: ELTGOL, expiration with the glottis open in the lateral posture; SD, standard deviation; IV, inverse variance; CI, confidence interval.

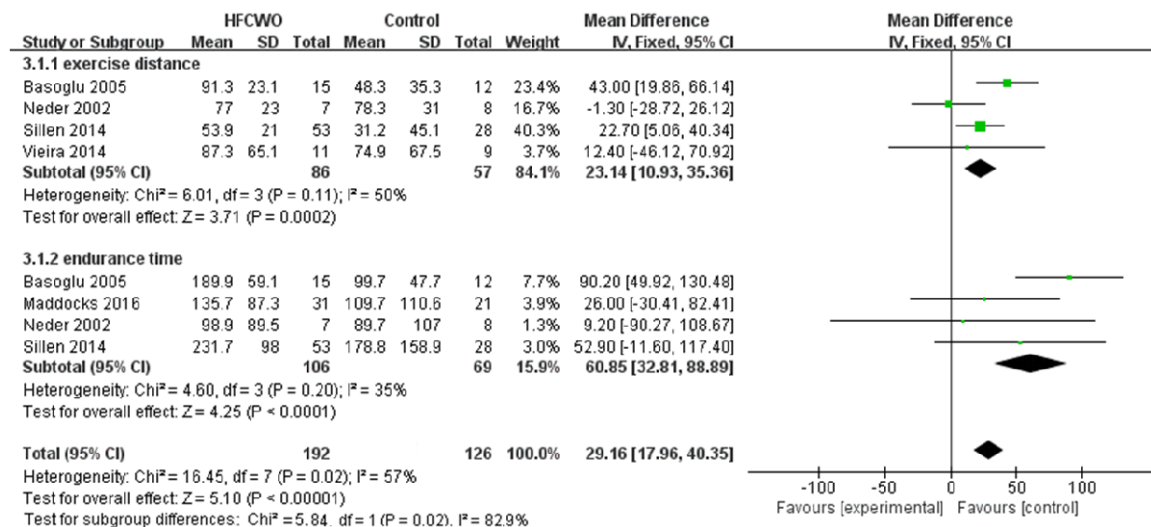


Figure 6. Effectiveness of high-frequency chest wall oscillation (HFCWO) on COPD. Abbreviations: HFCWO, High-frequency chest wall oscillation; SD, standard deviation; IV, inverse variance; CI, confidence interval.

Expiration with glottis open in the lateral posture (ELTGOL) significantly improved motor function of patients with COPD exacerbation

ELTGOL is a bronchial de-obstruction technique. Meta-analysis results demonstrated no different effect between ELTGOL and the control group in exercise distance (WMD -2.74, 95% CI=-9.76 to 4.29, subgroup I²=0%, P=0.44) or endurance time (SMD -3.15, 95% CI=-9.58 to 4.05, subgroup I²=0%; P=0.83) (as shown in **Figure 5**). Thus, the test of overall effect of

ELTGOL is undoubtedly insignificant (overall I²=0%; P=0.43).

High-frequency chest wall oscillation (HFCWO) significantly improved motor function of patients with COPD exacerbation

In addition, studies containing application of HFCWO in COPD exacerbation underwent meta-analysis. The results clearly showed increased exercise distance (WMD 23.14, 95% CI=10.93 to 35.36, subgroup I²=50%; P=0.0002) and

relatively long motor tolerance duration (SMD 60.85, 95% CI=32.81 to 88.89, subgroup $I^2=35\%$; $P<0.00001$) (as shown in **Figure 6**). Motor function improvement of HFCWO in COPD exacerbation was significantly higher than that in control group ($P<0.00001$).

Discussion

While screening articles for this review, applied techniques and/or resources as a treatment option on hospitalization applications for patients with COPD exacerbation were found to be different. In general, physiotherapy techniques widely applied in COPD patients included: electrical stimulation [28]; bronchial drainage technique [14]; thorax relaxation techniques [29, 30]; mechanical vibration [31, 32]; acupuncture [33]; active exercises of peripheral joints [34]; and strengthening of the quadriceps muscles and constant walks [35, 36]. Among the above categories, three main techniques in practice with enough participants and control groups (namely transcutaneous electrical nerve stimulation [37], expiration with the glottis open in the lateral posture [38], high-frequency chest wall oscillation [39]) were eventually taken into consideration for this meta-analysis of physiotherapy techniques effect on COPD exacerbation.

Compared with meta-analysis from Alvarenga et al. [40] and a review from Chen et al. [41], our study involved more physiotherapy techniques to be evaluated. Patients with COPD always developed varying degrees of peripheral function impairment [4, 6]. In this study, we included reports in which patients were only studied for impaired motor function alteration, to simplify the complexity of meta-data, as baseline levels of peripheral muscle dysfunction in COPD patients might exert an influential impact on the outcome of these physiotherapy techniques. We took exercise distance and endurance time as the primary outcome criteria. Although the small number of participants present in the few articles reflects the fragility of the evidence provided by the literature on diverse physiotherapy techniques, the funnel plot of all physiotherapy techniques indicated that all data from the 13 included studies showed an asymmetry (**Figure 2**). Moreover, it is significant to emphasize that all patients who

participated in these study samples were under clinically optimized pharmacological treatments. Our colleagues have made sure that treatment followed the guidelines of Global Initiative for Chronic Obstructive Lung Disease-GOLD [2] by serving patients with salbutamol, ipratropium bromide, theophylline, and methylprednisolone. Thus, we believe that our meta-analysis is more convincing with low heterogeneity, since inconsistent inclusion criteria leading to high heterogeneity were excluded.

The way of motor function assessment may affect the outcome of our meta-analysis. According to review previously, 6MWT and CWT of patients were included as subgroups of the motor function outcome of physiotherapy techniques. To minimize deviations of different participates in every study, WMD were used to pool exercise distance and SMD to pool endurance time in the meta-analysis. Taking all physiotherapy techniques into consideration, physiotherapy techniques had a random significantly improved effect of exercise distance of 95% CI=14.64 to 29.34 (**Figure 3**). We also observed a clear prolonged endurance time 95% CI=34.78 to 74.15 (but of a high heterogeneity, subgroup $P>0.05$). As for high heterogeneity, endurance times of all physiotherapies were not concluded. However, the whole effect of physiotherapy technologies on COPD exacerbation was proven to be very effective in this meta-analysis (WMD=25.96, 95% CI=19.08 to 32.85, $I^2=80\%$, overall $Z=7.39$, $P<0.00001$), indicating that physiotherapy techniques result in a certain improvement on exercise tolerance, regardless of the type of physiotherapy technology.

Transcutaneous electrical nerve stimulation (TENS) use electric current to produce stimuli to the nerves for therapeutic purposes [37], generally at high frequency (>50 Hz) with an intensity below motor contraction (sensory intensity) or low frequency (<10 Hz) with an intensity that produces motor contraction. Bensten et al. [18] reported a case in which skin nerve stimulation (TENS) was performed on a 74 year old male patient, in which the acupuncture points and its efficacy were proven to effectively eliminate dyspnea induced by COPD exacerbations. In our study, the results showed that TENS treatment caused relatively longer exercise distance ($P=0.004$) and longer endur-

ance time ($P=0.44$) (as shown in **Figure 4**). We also observed high heterogeneity in endurance time, which may be attributed to different SWT measurements. Incremental SWT tests were applied in different trials. Sensitivity, response speed, and the repeatability of these tests are not the same. In most cases, more and more 6MWT and longer endurance allows us to consider the scale effect of physiotherapy techniques to improve motor function. However, heterogeneity didn't impair the overall effect of TENS on COPD exacerbation, still proven to be highly effective in improving patient motor function after COPD exacerbation ($P=0.003$).

Expiration with open glottis on lateral posture (ELTGOL) is a bronchial de-obstruction technique [38]. Previously, Kodric et al. [38] assessed the efficacy of ELTGOL in patients with acute exacerbation COPD, in which hospitalization time, dyspnea, and quality of life were found to be improved to different scale. Moreover, according to Guimaraes et al. [42], ELTGOL was performed with a slow expiration from residual function (FRC) residue and led to contraction or proximal contraction and eliminated the risk of secretion. However, our study demonstrated no different effect between ELTGOL and the control group in exercise distance ($P=0.44$), endurance time ($P=0.83$), or undoubtedly overall effect (overall $P=0.43$). The reason that ELTGOL doesn't improve motor function could be due to the fact that ELTGOL doesn't distinguish between mechanical stimuli to physical exercise.

High frequency chest wall shock (HFCWO) is a technique used to mobilize secretions of aviation [27]. One way to produce this oscillation is through an inflatable vest. The system allows people to clean their respiratory tract without requiring a specific positioning or coordination period and can use minimal treatment support. Mahajan et al. [39] conducted a study on the effect of HFCWO on inpatients with COPD exacerbations. Participants in the HFCWO group presented a higher level of comfort after a significant reduced dyspnea index. In accordance to Mahajan's study, the results of our meta-analysis clearly showed increased exercise distance ($P=0.0002$) and relatively long motor tolerance duration ($P<0.00001$) (as shown in **Figure 6**). Motor function improvement of HF-

CWO in COPD exacerbation is significantly higher than that in the control group ($P<0.00001$).

Conclusion

Physiotherapy techniques or measures used for COPD exacerbation patients include breathing exercises and techniques such as TENS, ELTGOL, and HFCWO. In general, physiotherapy techniques are effective in improving severe COPD patient motor function. Further research is needed to elucidate its effect on other outcomes and to determine its optimal use in regards to physical therapy.

Disclosure of conflict of interest

None.

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