ORIGINAL RESEARCH

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Effects of High-Frequency Chest Wall Oscillation on Acute Exacerbation of Chronic Obstructive Pulmonary Disease: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Purpose: This study aimed to evaluate the efficacy of high-frequency chest wall oscillation for sputum expectoration and hospital length of stay in patients with acute exacerbations of chronic obstructive pulmonary disease. The improvements in pulmonary function and oxygenation were also investigated.

Patients and Methods: This systematic review and meta-analysis followed the Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) guidelines. Automated literature database searches were conducted from the earliest records to March 31, 2022. The methodological quality of the included studies was assessed using the Cochrane Risk of Bias tool (RoB 2.0), and meta-analysis software (RevMan 5.4) was used to analyze the data.

Results: From 5439 identified articles, 13 studies (with 756 patients) were included in this meta-analysis. Compared to other airway clearance techniques, HFCWO significantly increased expectorated sputum volume by 6.18 mL (95% CI: 1.71 to 10.64; $I^2 = 87\%$), shortened hospital stay by 4.37 days (95% CI: -7.70 to -1.05; $I^2 = 84\%$). However, FEV₁ (%), PaO₂, and PaCO₂ did not improve significantly.

Conclusion: AECOPD patients may benefit from HFCWO therapy. HFCWO enables AECOPD patients to excrete more sputum and shorten their hospital stays. However, due to heterogeneity among the included research, these results should be interpreted with caution. **Keywords:** acute exacerbation of chronic obstructive pulmonary disease, AECOPD, high-frequency chest wall oscillation, HFCWO, sputum expectoration, length of hospital stay

Introduction

Excessive sputum obstruction of the airway is a common problem in chronic obstructive pulmonary disease (COPD) patients. Mucus hypersecretion is associated with an increased bacterial load, a more rapid decline in lung function, exacerbations, and an increased risk of hospitalization for COPD.^{1,2}

Patients with COPD who are experiencing an acute exacerbation must be able to expel sputum more effectively since their sputum and mucus issues are more demanding during such episodes. Airway clearance techniques (ACTs) are required for COPD patients in order to improve mucus clearance and gas-exchange efficiency through the airways. Airway clearance techniques use external forces to help eliminate sputum from the airway and are available in a variety

of forms, such as conventional chest physical therapy, including clapping percussion, postural drainage, and nebulizer inhalation; as well as mechanical chest percussion, positive expiratory pressure devices, and high-frequency chest wall oscillation (HFCWO) therapy, which are all clinically available options.³

Although HFCWO was initially prescribed to patients with cystic fibrosis, it is now used to treat a variety of respiratory, neurological, and neuromuscular diseases.⁴ HFCWO is simple to use and saves time and labor, making it a viable alternative to conventional chest physical therapies for patients.⁵ An air pulse generator and an inflatable vest comprise HFCWO. The vest receives air pulses, which compress the chest wall and facilitate in tracheal mucus evacuation.⁵ HFCWO has been shown to be efficient in removing sputum in numerous international studies. The impact of HFCWO in acute execrations of COPD and how effective it is comparing to other ACTs, however, are not well understood. Furthermore, existing research indicates that HFCWO has varying effects on COPD patients. As a result, it is necessary to conduct a systematic examination of HFCWO use in AECOPD patients.

This meta-analysis was conducted to summarize the current evidence regarding the efficacy of HFCWO in enhancing sputum expectoration and reducing hospital length of stay in COPD patients hospitalized for acute exacerbations. In addition, we also investigated the effects that HFCWO had on pulmonary function, arterial blood gases (ABGs), and the improvement of symptoms in AECOPD patients to gain a more in-depth and comprehensive understanding of the effects of HFCWO on AECOPD patients' airway clearance.

Material and Methods

This systematic review and meta-analysis adhered to the Preferred Reporting Items for Systematic Review and Metaanalyses (PRISMA) statement (the full checklist is given in <u>Supplementary Table 1</u>: PRISMA 2009 checklist).⁶

Search Strategy

Cochrane Library, Excerpta Medica Database (Embase), PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), China National Knowledge Infrastructure (CNKI), Airiti Library, and the National Digital Library of Theses and Dissertations in Taiwan were searched from their inception to March 2022 to identify publications of interest. The search terms were keywords, Medical Subject Heading (MeSH) terms, and suitable variants of COPD and HFCWO. Searches were conducted with a combination of terms using Boolean logical operators (AND/OR) as follows: "pulmonary disease, chronic obstructive" [MeSH] OR "Lung Diseases, Obstructive" [MESH] OR "Pulmonary Emphysema" [MESH] OR "Chronic obstructive pulmonary disease" OR "AECOPD" OR "Chronic obstructive pulmonary disease exacerbations" OR "Exacerbation" AND "chest wall oscillation" [MeSH] OR "High-frequency chest wall oscillation" OR "Physiotherapy" OR "physiotherapy intervention."

Study Selection

Two researchers independently conducted preliminary study screening and selection, including titles and abstracts. Then, full-text articles were accessed and assessed for their eligibility. Articles were included if they (1) described inpatients with acute exacerbation of COPD (AECOPD) or COPD; (2) used HFCWO therapy as an intervention; (3) were randomized control trials (RCTs); and (4) were published in English or Chinese.

Data Extraction

Two investigators independently extracted data from the included studies. The extracted data included: (1) basic information (ie, the first author, year published, country, and study design); (2) participants (ie, no. of subjects, age, and sample size); (3) type of intervention (ie, type, duration, and frequency); and (4) types of outcome measures (ie, sputum expectoration, forced expiratory volume in 1 second (FEV₁), and length of hospital stay). In cases of a discrepancy in opinion, a third person served as a mediator, and a consensus was reached by discussion.

The risk of bias in the studies was evaluated using the revised Cochrane risk of bias tool for randomized trials (RoB 2), which includes five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result.⁷ We rated each domain as "low", "some concerns", or "high" and determined the overall ROB for each study based on the highest risk attributed to any one domain. All studies were independently reviewed by two reviewers. When the two reviewers had opposing opinions, a third researcher was brought into the discussion to assist in reaching a consensus.

Outcome Measurements

Patients with mucus hypersecretion and recurrent exacerbations have a faster rate of decline in lung function, which is a strong predictor of morbidity and mortality with COPD, as well as health-care utilization. In our review, we developed a comprehensive list of all of the parameters that were reported in the studies we examined, along with potential effects of HFCWO on lung function, physical endurance, quality of life, sputum expectoration, ventilation days, hospital stay, and mortality. Based on a combination of disease characteristics and the effectiveness of the intervention, we chose sputum expectoration and the length of hospital stay as the primary outcomes for this study; secondary outcomes included percentage of predicted FEV_1 (%) in the pulmonary function test; ABGs oxygenation and symptom assessment.

Statistical Analysis

The findings were extracted from selected studies. If the text did not disclose the numerical outcome data, we retrieved the data from available figures and graphs or contacted the authors. For continuous outcomes, the mean difference (MD) with a 95% confidence interval (CI) was used for outcome measurements in all studies unless otherwise stated. A random-effects model was used to estimate the overall effects of HFCWO, which incorporates an assumption that different studies were estimating different intervention effects. Forest plots were generated to assess the degree of the effect estimates of each research and their 95% CIs along with the pooled effect. Heterogeneity was assessed by the I² statistics for each comparison. An I² value of >75% or a $\chi^2 p$ value <0.1 was considered statistical heterogeneity.⁸ All data were pooled using the Cochrane software review manager (RevMan version 5.4; Cochrane, London, UK).

Results

Search Results

The search strategy yielded 5434 articles, and five more articles were added by manual review. All papers were imported into EndNoteX9, and 258 articles were removed because of duplications; 5128 papers were excluded after reviewing the titles and abstracts, leaving 53 papers. Six papers were excluded due to the full text being unavailable, leaving 47 papers to be filtered. Among them, 34 articles were excluded for the following reasons: subjects were not COPD or AECOPD inpatients; the intervention was not HFCWO; it was not an RCT, or it was not published in English or Chinese. The study selection procedure is presented in a flow chart (Figure 1). In total, 13 articles were included for review in this meta-analysis.

Study Characteristics

The characteristics of the 13 studies are shown in Table 1. The included studies were published from 2007 to 2021 and were carried out in China, Turkey, the United Kingdom, and the United States.^{9–21} There were 756 patients included across the 13 studies, with 381 in the intervention group and 375 in the control group. The mean sample size was 58, with a range of 22 to 86. Most of the studies recruited AECOPD patients, and only three studies mentioned the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages.^{9,10,13} Two of the studies were in patients at grade 3 or 4;^{9,13} one focused on GOLD stage 2 or 3 patients.¹⁰ In each of the 13 studies, HFCWO was used as an intervention in the experimental group, but the control groups did not receive the same treatment. Seven of the studies used mechanical percussion.^{14–17} One article was about oscillatory positive expiratory pressure (OPEP)¹³ and one article used sham HFCWO as the control group.¹² Two articles used two distinct experimental groups in their study design, and we included only the HFCWO group as the



Figure I PRISMA flow diagram of included studies.

Notes: Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. Creative Commons.⁶

experimental group to compare to the control group.^{20,21} The durations of the 13 RCTs ranged from 2 days to 4 weeks; two studies did not specify the number of days of the HFCWO intervention or the total number of treatments.^{19,20} The session frequency varied from once to three times a day.

Quality Assessment

The ROB assessments of the included studies are demonstrated in Figure 2. Thirteen studies had some concerns with the randomization process because of the randomized sequence generation process and whether the allocation sequence was concealed were not described.^{10–21} Two studies had some concerns with deviations from the intended intervention as they did not have good blinding of participants and operators or were unmasked.^{10,11} The risk of missing outcome data bias was high in one study when 13.75% of participants did not finish the trial. The ROB with measurement of the outcome

Table I Characteristics of Included Studies

First Author, Year	Subject	Average Age (Years)	Treatment Group	И	Treatment Setting F, Frequency; P, Pressure	Duration
Chakravorty, 2011 ¹⁰	AECOPD GOLD 2 or 3	71	HFCWO	11	F: 13~15 Hz; P: NR 20 min/time; 2 times/day	4 weeks
			Conventional therapy	11	Followed their own COPD management regimen	4 weeks
Duan, 2019 ¹⁵	AECOPD	70.3	HFCWO	43	F: NR; P: NR 15~20 min/time; 2 times/day	7 days
		69.7	Mechanical percussion	43	F: 12~15 Hz 15~20 min/time; 2 times/day	7 days
Goktalay, 2013 ⁹	AECOPD, GOLD 3 or 4	63.6	HFCWO	25	F: 10 Hz; P: NR 20 min/time; 3 times/day	5 days
		66.5	Conventional therapy	25	Followed their own COPD management regimen	5 days
	COPD and pulmonary infection with endotracheal or tracheostomy tube	65	HFCWO	30	F: 8 Hz; P: 5 units 10~15 min/time; 2 times/day	3 days
		71	Mechanical percussion	30	F: 10 Hz 10~15 min/time; 2 times/day	3 days
,	AECOPD, CAP	78.7	HFCWO	15	F: 25 Hz; P: NR 10 min/time; 2 times/day	14 days
	Chronic bronchitis	84.9	Mechanical percussion	15	F: 25~35 Hz 10 min/time; 2 times/day	14 days
Li, 2020 ¹⁹	AECOPD	69.9	HFCWO and Conventional therapy	38	F: 6~15 Hz; P: 8~12 units 15~30 min/time; 3 times/day	NR
		68.5	Conventional therapy	32	Aerosol inhalation of an acetylcysteine solution 3 mL/time; 3 times/day	NR
Liu, 2014 ¹¹	AECOPD with mechanical ventilation	76	HFCWO	17	F: 10~15 Hz; P: 2~4 units 15 min/time; 3 times/day	7 days
		77	Conventional therapy	18	Followed their own COPD management regimen	7 days
Mahajan, 2011 ¹²	Acute COPD, acute asthma and COPD	46.5	HFCWO	25	F: 10~12 Hz; P: 4~6 units 15 min/time; 3 times/day	2 days
		50.4	Sham HFCWO	27	F: NR; P: NR 15 min/time; 3 times/day	2 days
Ouyang, 2020 ²⁰	AECOPD	65.3	HFCWO	38	F: 8~15 Hz; P: 4~6 kPa 15~30 min/time; NR	NR
		65.7	Conventional therapy	36	-	NR

(Continued)

First Author, Year	Subject	Average Age (Years)	Treatment Group	Ν	Treatment Setting F, Frequency; P, Pressure	Duration
Tan, 2020 ¹³	AECOPD GOLD 3 or 4	70.3	HFCWO	33	F: 10~14 Hz; P: 3~4 units 15 min/time; 3 times/day	5 days
		70.7	OPEP	36	P: 1-According to the patient's tolerance 15 times/session; 3 sessions/day	5 days
Wang, AE 2021 ¹⁸	AECOPD	61.0	HFCWO	42	F: NR; P: NR 15 min/time; 3 times/day	5 days
		60.6	Conventional therapy	42	Postural drainage 15 min/time; 3 times/day	5 days
Xie, 2017 ¹⁶	COPD accompanied by pulmonary infection	58.6	HFCWO	40	F: 8 Hz; P: 5 units 10~15 min/time; 2 times/day	3 days
		58.5	Mechanical percussion	40	F: 10 Hz 10~15 min/time; 2 times/day	3 days
Zhang, 2019 ²¹	AECOPD	65.9	HFCWO	24	F: 8~15 Hz; P: 4~6 kPa 15~30 min/time; 1 time/day	14 days
		65.7	Conventional therapy	20	-	14 days

Table I (Continued).

Abbreviations: AECOPD, acute exacerbation of COPD; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Pulmonary Disease; HFCWO, high-frequency chest wall oscillation; NR, not recorded; OPEP, oscillating positive expiratory pressure.

was high in four studies, as these studies were unmasked to the outcome assessors.^{15,19-21} Thirteen of all studies were rated as having some concerns about reporting bias, primarily due to the lack of availability of the protocol.^{9-14,16-21}

Outcome Analysis

Sputum Expectoration

Two different approaches were used to assess the effectiveness of sputum expectoration: sputum expectoration by treatment days and sputum expectoration by different control groups.

Sputum Expectoration by Treatment Days

Nine articles in the literature assessed the volume of sputum expectoration, but three were excluded from the meta-analysis due to the absence of the mean and standard deviation (SD) in two of them,^{10,12} and the other provided total sputum volume in 5 days, which could not be combined with single-day sputum expectoration of the other studies.¹⁹ Li et al reported that HFCWO significantly increased total sputum expectoration in patients over 5 days (p<0.05).¹⁹ Mahajan et al and Chakravorty et al reported no significant change in sputum expectoration.^{10,12} Six studies with a total of 409 patients were combined by the number of days of treatment received, as shown in Figure 3. ^{13–18} There was a significant increase in sputum expectoration after receiving HFCWO. A subgroup analysis was conducted based on the number of days of treatment received. After receiving 1 day of treatment, the sputum expectoration significantly increased (MD = 6.31; 95% CI: 0.31 to 12.30). Interestingly, there was no significant difference after 5 days of treatment (MD = 5.86; 95% CI: -3.66 to 15.38). There was high heterogeneity among the trials within subgroups (day 1: I² = 87%; day 5: I²=92%).

Sputum Expectoration in Comparison to the Control Group

Six trials compared HFCWO treatment with various control groups to determine the efficacy of various methods for eliminating sputum (Figure 4). Four of the control groups used mechanical percussion,^{14–17} one compared HFCWO with conventional therapy,¹⁸ and the other study compared HFCWO with OPEP.¹³ When compared to mechanical percussion,

			ISK UI DIA	<u>s domain</u>	3	
Study	D1	D2	D3	D4	D5	Overall
Chakravorty 2011 ¹⁰	!	!	+	+	!	!
Duan 2019 ¹⁵	!	+	+	-	!	-
Goktalay 2013 ⁹	+	+	+	+	!	!
Huang 2013 ¹⁷	!	+	+	+	!	!
Li 2017 ¹⁴	!	+	+	+	!	!
Li 2020 ¹⁹	!	+	+	•	!	
Liu 2014 ¹¹	!	!	+	+	!	!
Mahajan 2011 ¹²	!	+	+	+	+	!
Ouyang 2020 ²⁰	!	+	+	-	!	-
Tan 2020 ¹³	!	+	•	+	!	-
Wang 2021 ¹⁸	!	+	+	+	!	!
Xie 2017 ¹⁶	!	+	+	+	!	!
Zhang 2019 ²¹	!	+	+	•	!	•
Domains: D1: Bias arising from the r D2: Bias due to deviations D3: Bias due to missing o D4: Bias in measurement D5: Bias in selection of the	from intend utcome data of the outco	led interven a. me.	tion.		- High ! Som + Low	e concerns
Bias arising from the rando Bias due to deviatio Bias due to missi Bias in measuremen Bias in selection of th C	ns from inte ng outcome t of the out	ended e data tcome result				

Risk of bias domains

Figure 2 Quality assessment of bias using Cochrane Collaboration 2.0.

the HFCWO group significantly increased sputum expectoration by 6.31 mL (95% CI: 0.31 to 12.30), and when compared to conventional therapy, HFCWO demonstrated its efficacy by increasing sputum expectoration by 10.59 mL (95% CI: 7.58 to 13.60). In contrast, when compared to OPEP, the difference was insignificant (95% CI: -3.49 to 5.23). Results showed that implementing HFCWO was significantly effective in helping sputum expectoration compared to other ACTs in COPD patients (MD = 6.18; 95% CI: 1.71 to 10.64).

■ Low risk ■ Some concerns ■ High risk

Length of Hospital Stay

There were four articles with a total of 179 participants that examined the impact of HFCWO on the length of hospital stay.^{11,14,19,21} The trial by Mahajan et al was not included due to the lack of an SD.¹² The pooled effect estimate showed

	н	FCWO)	c	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean SD Total		Mean SD Total		al Weight IV, Random, 9		IV, Random, 95% CI		
1.1.1 A. Day 1									
Duan 2019¹⁵	48.09	8.38	43	39.37	9.14	43	17.1%	8.72 [5.01, 12.43]	_ _
Huang 2013 ¹⁷	43.97	9.62	30	34.7	10.56	30	15.5%	9.27 [4.16, 14.38]	_
Li 2017 ¹⁴	9.1	7.7	15	11.7	2.6	15	16.7%	-2.60 [-6.71, 1.51]	
Xie 2017 ¹⁶	44.2	9.8	40	34.2	9.7	40	16.5%	10.00 [5.73, 14.27]	
Subtotal (95% CI)			128			128	65.8%	6.31 [0.31, 12.30]	
Heterogeneity: Tau ² =	32.59; C	Chi² = 2	23.78, 0	df = 3 (P	< 0.00	01); I² =	= 87%		
Test for overall effect:	Z = 2.06	(P = 0	0.04)						
1.1.5 B. Day 5									
Tan 2020 ¹³	35.45	8.63	33	34.58	9.83	36	16.4%	0.87 [-3.49, 5.23]	
Wang 2021 ¹⁸	48.05	6.23	42	37.46	7.76	42	17.8%	10.59 [7.58, 13.60]	
Subtotal (95% CI)			75			78	34.2%	5.86 [-3.66, 15.38]	
Heterogeneity: Tau ² =	43.59; C	chi² = '	12.94, d	df = 1 (P	= 0.00	03); I² =	= 92%		
Test for overall effect:	Z = 1.21	(P = (0.23)						
Fotal (95% CI) 203				206	100.0%	6.18 [1.71, 10.64]	-		
Heterogeneity: Tau ² =	26.70; C	Chi² = 3	37.34, d	df = 5 (P	< 0.00	001); l²	= 87%	-	
Test for overall effect:	Z = 2.71	(P = (0.007)	,		,,			-20 -10 0 10 20
Test for subgroup diffe	erences:	Chi² =	0.01, c	df = 1 (P	= 0.94), l ² = 0	%		Favours [control] Favours [HFCWO]

Figure 3 Forest plot of HFCWO vs control group treatment time, outcome: Sputum expectoration.



Figure 4 Forest plot of HFCWO vs mechanical vibration, conventional, and OPEP, outcome: Sputum expectoration (mL).

a reduction of 4.37 days in the length of hospital stay in COPD patients who received HFCWO (95% CI: -7.70 to -1.05, p=0.01) (Figure 5).

Pulmonary Function

The predicted FEV₁ (%) was utilized to assess pulmonary function (Figure 6). Six research reported the difference in the change in FEV₁ (%), 9,10,12,13,20,21 but the data by Mahajan et al could not be included in the meta-analysis because the SD was unavailable.¹² Mahajan et al observed no significant effect on the change of FEV₁ between the HFCWO group and the sham control group (*p*=0.69). The pooled mean difference in FEV₁ showed a trend toward improvement of 4.13%, (95% CI: -1.61 to 9.88, *p*=0.16) but it was not statistically significant. However, when the trials were divided by



Figure 5 Forest plot of HFCWO versus control group, outcome: Hospital stay (days).



Figure 6 Forest plot of HFCWO versus control group, outcome: FEV₁ (%).

control group interventions, the subgroup analysis revealed that HFCWO had a statistically significant effect on improving FEV_1 compared to conventional therapies (MD = 5.96; 95% CI: 1.08 to 10.84).

Arterial Blood Gases: Oxygenation

There were five trials with 307 participants which evaluated the partial pressure of oxygen (PaO₂) (Figure 7). ^{9,13,19–21} The results of all five studies indicated that HFCWO did not significantly increase PaO₂ levels (MD = 4.57; 95% CI: -1.81 to 10.96). Upon performing subgroup analysis, when HFCWO was compared to OPEP, it was evident that its efficacy was not as good as OPEP's. However, when we excluded the study with OPEP as the control group, the pooled data from the remaining four studies demonstrated that HFCWO significantly improved PaO₂ by 6.59 mmHg in comparison to conventional therapies (95% CI: 2.02 to 11.16).^{9,19–21} The same five studies also evaluated the value of the partial pressure of carbon dioxide (PaCO₂), and the results of PaCO₂ were in line with those of PaO₂, which was not significant in the pooled five studies, but in the subgroup excluding OPEP, the pooled results of four studies showed that HFCWO significantly lowered PaCO₂ (MD=-6.76; 95% CI: -13.42 to -0.10).

In addition to the studies mentioned previously, five additional studies compared the variations in SPO₂ between various sputum expectoration techniques. In the pooled results of five studies, HFCWO significantly increased SpO₂ by 1.78% (95% CI: 1.47 to 2.10).^{9,14–17}

Dyspnea Assessment

Three studies reported the modified Medical Research Council Dyspnea Scale (mMRC) (scale from 0 to 4; lower is better).^{9,13,18} There was a decreasing tendency in mMRC scores, but the results did not show statistical significance (MD=-0.22; 95% CI: -1.51 to 1.07, p=0.74) (Figure 8).

Α									D
		FCWC		Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV. Random, 95% Cl
4.1.1 HFCWO vs OP	EP								
Tan 2020 ¹³	1.9	1.9	33	4.5	2.1	36	22.4%	-2.60 [-3.54, -1.66]	
Subtotal (95% CI)			33			36	22.4%	-2.60 [-3.54, -1.66]	◆
Heterogeneity: Not ap	plicable								
Test for overall effect:	Z = 5.40) (P < (0.0000	1)					
4.1.2 HFCWO vs Cor	vention	al the	rapy						
Goktalay 2013°	63	9.11	25	61	14.06	25	18.2%	2.00 [-4.57, 8.57]	+=
Li 2020 ¹⁹	83.5	6.2	38	79.9	6.5	32	21.5%	3.60 [0.61, 6.59]	
Ouyang 2020 ²⁰	88.57	6.91	38	78.51	4.85	36	21.7%	10.06 [7.35, 12.77]	
Zhang 2019 ²¹	89.46	9.58	24	78.13	16.98	20	16.2%	11.33 [2.96, 19.70]	
Subtotal (95% CI)			125			113	77.6%	6.59 [2.02, 11.16]	
Heterogeneity: Tau ² =	15.12: 0	Chi² = ·	13.11. 0	df = 3 (P	P = 0.00	4): ² =	77%		
Test for overall effect:					5100	.,, .			
Total (95% CI)			158			149	100.0%	4.57 [-1.81, 10.96]	-
Heterogeneity: Tau ² =	= 47 08 [.] ($Chi^2 = 9$	92 69 0	df = 4 (F	< 0.00	001)· l²	= 96%	-	
Test for overall effect:				u + (i	0.00	,, i	0070		-20 -10 0 10 20
		•	,	df - 1 (D - 0 0	001) 12	- 02 20/		Favours [control] Favours [HFCWO]
Test for subgroup diff	erences.	TI	• 14.90,	ui – I (F - 0.0	001), I⁻	- 55.5%		

В

		HFCWO			Control			Mean Difference	Mean Difference				
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV. Random. 95% Cl				
4.2.1 HFCWO vs OPI	EP												
Tan 202013	-0.6	1.8	33	-5.3	2.2	36	20.6%	4.70 [3.75, 5.65]					
Subtotal (95% CI)			33			36	20.6%	4.70 [3.75, 5.65]	•				
Heterogeneity: Not ap	plicable												
Test for overall effect:	Z = 9.74	+ (P < 0	0.00001)									
4.2.2 HFCWO vs Cor	vention	al ther	ару										
Goktalay 2013 [°]	46	7.24	25	46	9.26	25	19.4%	0.00 [-4.61, 4.61]	_ 				
Li 2020 ¹⁹	50.2	5.8	38	52.6	5.5	32	20.3%	-2.40 [-5.05, 0.25]					
Ouyang 2020 ²⁰	42.35	5.21	38	55.39	5.26	36	20.3%	-13.04 [-15.43, -10.65]					
Zhang 2019 ²¹	43.54	7.24	24	54.98	8.74	20	19.3%	-11.44 [-16.24, -6.64]					
Subtotal (95% CI)			125			113	79.4%	-6.76 [-13.42, -0.10]					
Heterogeneity: Tau ² =	42.53; 0	$Chi^2 = 4$	7.63, c	lf = 3 (F	o.00 > 1	0001);	² = 94%						
Test for overall effect:	Z = 1.99	9 (P = 0	0.05)			,							
Total (95% CI)			158			149	100.0%	-4.38 [-12.60, 3.84]					
Heterogeneity: Tau ² =	84.99; 0	Chi² = 2	23.13,	df = 4 (P < 0.0	00001)	² = 98%	-					
Test for overall effect:	Z = 1.04	(P = 0)	0.30)						-20 -10 0 10 20				
Test for subgroup diffe	erences.	Chi ² =	11.16.	df = 1 (P = 0.0	0008)	² = 91.0%		Favours [HFCWO] Favours [control]				

С

-	H	FCWO)	Control				Mean Difference	Mean Difference				
Study or Subgroup	Mean SD Total			Mean SD Tota		Total	Weight	IV. Random. 95% CI		IV. F	andom, 959	% CI	
Duan 2019 ¹⁵	97.35	2.45	43	95.63	2.25	43	10.1%	1.72 [0.73, 2.71]					
Goktalay 2013 ⁹	90	4.63	25	90	5.15	25	1.4%	0.00 [-2.71, 2.71]		-			
Huang 201317	97.49	0.97	30	95.88	1.03	30	38.9%	1.61 [1.10, 2.12]			- I =		
Li 2017 ¹⁴	96	1.7	15	94.1	0.9	15	10.5%	1.90 [0.93, 2.87]					
Xie 2017 ¹⁶	97.8	1.2	40	95.8	1.1	40	39.2%	2.00 [1.50, 2.50]			•		
Total (95% CI)		153			153	100.0%	1.78 [1.47, 2.10]			•			
Heterogeneity: Tau ² = 0.00; Chi ² = 2.89, df = 4 (P = 0.58); I ² = 0%									-10	-5	0	5	
Test for overall effect:	. 0	Favours [coi	ntrol] Favou	irs [HFCW									

Figure 7 Forest plot of HFCWO versus control group, outcome: ABGs (A) PaO₂ (mmHg) (B) PaCO₂ (mmHg) (C) SpO₂ (%).

Discussion

The purpose of this meta-analysis was to summarize the current evidence regarding the efficacy of HFCWO in AECOPD patients. According to the findings of 13 studies with a total of 756 participants, there is evidence that HFCWO improves sputum expectoration and reduces hospital stays in AECOPD patients. In addition, subgroup



Figure 8 Forest plot of HFCWO versus control group, outcome: Dyspnea assessment.

analyses have shown that HFCWO has a significant effect on FEV_1 and oxygenation when compared to traditional therapies and mechanical percussion. However, the results are not significant when compared to relatively new devices such as OPEP, and since there is considerable heterogeneity in the results of this study, caution is advised when interpreting the results.

Coughing, sputum production, and shortness of breath are common COPD symptoms. These symptoms are particularly severe during an exacerbation episode. Excessive sputum retention in the lungs may cause more frequent exacerbations, which may decrease quality of life and increase mortality.²² Airway clearance to remove secretions is essential in managing COPD, and it is possible that more intensive airway clearance may be required during exacerbation. Breathing techniques, nebulizer inhalation, postural drainage, and pharmacologic therapy are all common airway clearance techniques in clinical patients. Ideal ACTs can aid in the increase of sputum elimination. This study demonstrated that compared to other ACTs, the use of HFCWO increased sputum elimination by an average of 6.18 mL, and noticeably even a short period of time was able to expectorate a significantly greater volume of sputum. The heterogeneity among the subgroups in this meta-analysis was high, so it is possible that the introduction of various devices into the control group had an impact. Additionally, only one study was conducted in the included study to measure the patients' baseline sputum volume for comparison, but this could have an impact on the experiment's outcomes.

In a 2012 Cochrane review, ACT use was associated with a shorter hospital length of stay in patients experiencing AECOPD, but the data were from only one study.²³ Weycker et al conducted a retrospective study which observed 135 COPD patients, and their analysis showed a 40% reduction in the average number of all-cause hospital admissions and also reductions in both outpatient visits and emergency department visits within 3 months of using HFCWO.²⁴ Daynes et al reported that ACT had no effect on the length of stay. However, ACT was not limited to HFCWO in that meta-analysis.²⁵ According to the pooled effect of this study, COPD patients who received HFCWO had a 4.37-day reduction in the length of their hospital stay. Gary Hansen et al conducted HFCWO in 219 COPD patients and found that the annualized hospitalization rate had decreased by 54.4% at 12 months (p=0.001).²⁶ Results of those studies are consistent with the combined analysis of this study.

A systematic review provided proof that a lower FEV₁ is significantly associated with risks of COPD exacerbation.²⁷ There is a negative correlation between sputum production and FEV₁.¹⁰ HFCWO intervention can increase the tidal volume of COPD patients, facilitate the inspiratory muscles, and aid spontaneous breathing.²⁸ The pooled effect of this study indicated that HFCWO did not improve FEV₁; however, when analyzed by subgroups based on four studies that used conventional therapies as the control group, HFCWO was associated with a statistically significant increase of 5.96% in FEV₁. The same observation was made when we examined the ABG oxygenation and observed that HFCWO had a notable impact on PaO₂ and PaCO₂ in the subgroup using conventional treatment as a control. A study in 2020 used HFCWO in 60 COPD patients receiving invasive mechanical ventilation and distinguished them into hypersecretive and normosecretive groups; their results showed that HFCWO improved lung aeration in hypersecretive patients.²⁹ Another study in 2014 showed that adding HFCWO to pharmacological therapy in patients with severe COPD significantly improved their pulmonary function tests and ABG analysis, which was in line with our study.³⁰ However, the studies included in this meta-analysis suggested that OPEP appeared to be more effective than HFCWO. Nevertheless, based on our inclusion criteria, only one of the thirteen studies included in this analysis compared the effective than HFCWO in AECOPD patients. OPEP is a positive-pressure expiratory device, and patients require cognitive and learning abilities to operate the device. Training

and ongoing evaluation are also needed to optimally operate OPEP.^{31,32} On the other hand, HFCWO can be used in patients who are unable to adequately use hand-held devices and can even be conducted without the assistance of skilled medical personnel. HFCWO has the benefit of being conducted early in the hospitalization of severely ill patients.¹²

In GOLD guidelines, mMRC is used to quantify respiratory distress-related disability.³³ There was a non-significant improvement in mMRC following the HFCWO intervention in this study. However, the research by Russo et al showed that HFCWO significantly improved mMRC in patients with severe COPD, which differs from our findings.³⁰ Moreover, a study by Kachel et al showed significantly higher treatment satisfaction, improved dyspnea, and a better quality of life in patients who consistently used HFCWO over a long period.³⁴ There was only one study lasting longer than 14 days in this study.¹⁰ It is possible that there was no significant effect on dyspnea improvement due to the relatively short experimental periods in the included literature.

Limitations

This study has a number of limitations that should be considered that may diminish the evidence for the findings of this study. First, this meta-analysis excluded outpatient studies and only included studies that evaluated the effect of AECOPD on key outcomes (eg, sputum expectoration and hospital stay). However, it is unlikely that excluding studies involving outpatients with stable COPD conditions would have an effect on the overall outcomes of this review. In this meta-analysis, the HFCWO intervention components varied across studies, as did the session durations and frequencies of the oscillations, potentially resulting in study heterogeneity. Thus, we carried out a subgroup analysis and applied a random effects model to the analysis in order to lessen the impact of heterogeneity. Moreover, our study includes both English and Chinese literature; however, some of the Chinese literature is unfamiliar outside of China, which may limit the generalizability of the study.

Conclusion

This meta-analysis suggests that the use of HFCWO may have the advantage of increasing the sputum clearance effectiveness and decreasing the length of hospital stays for AECOPD patients. However, due to the high degree of heterogeneity among the studies, these findings should be interpreted cautiously.

Disclosure

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References

- 1. Wedzicha JA, Donaldson GC. Exacerbations of chronic obstructive pulmonary disease. Respir Care. 2003;48(12):1204–1213.
- Vestbo J, Prescott E, Lange P; Copenhagen City Heart Study Group. Association of chronic mucus hypersecretion with FEV1 decline and chronic obstructive pulmonary disease morbidity. Am J Respir Crit Care Med. 1996;153(5):1530–1535. doi:10.1164/ajrccm.153.5.8630597
- 3. Holland AE, Button BM. Is there a role for airway clearance techniques in chronic obstructive pulmonary disease? *Chron Respir Dis.* 2006;3 (2):83–91. doi:10.1191/1479972306cd097rs
- 4. Fink JB, Mahlmeister MJ. High-frequency oscillation of the airway and chest wall. Respir Care. 2002;47(7):797-807.
- 5. Kempainen RR, Milla C, Dunitz J, et al. Comparison of settings used for high-frequency chest-wall compression in cystic fibrosis. *Respir Care*. 2010;55(6):695–701.
- 6. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ*. 2009;339: b2535. doi:10.1136/bmj.b2535
- 7. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:14898. doi:10.1136/bmj. 14898
- 8. Higgins JPT TJ, Chandler J, Cumpston M, Li T, Page MJ, Welch VA. *Cochrane Handbook for Systematic Reviews of Interventions*. John Wiley & Sons; 2021. Available from. www.training.cochrane.org/handbook. Accessed November 1, 2022.
- Goktalay T, Akdemir SE, Alpaydin AO, et al. Does high-frequency chest wall oscillation therapy have any impact on the infective exacerbations of chronic obstructive pulmonary disease? A randomized controlled single-blind study. *Clin Rehabil.* 2013;27(8):710–718. doi:10.1177/ 0269215513478226
- Chakravorty I, Chahal K, Austin G. A pilot study of the impact of high-frequency chest wall oscillation in chronic obstructive pulmonary disease patients with mucus hypersecretion. Int J Chron Obstruct Pulmon Dis. 2011;6:693–699. doi:10.2147/COPD.S22896
- 11. Liu Tingting KY, Zhaomin X, Yinxia L, Lingli J, Yun G. A study of the value of high frequency chest wall oscillation in patients with acute exacerbation of chronic obstructive pulmonary disease. *Chin J Tuberc Respir Dis.* 2014;37(4):255–259.

- 12. Mahajan AK, Diette GB, Hatipoğlu U, et al. High frequency chest wall oscillation for asthma and chronic obstructive pulmonary disease exacerbations: a randomized sham-controlled clinical trial. *Respir Res.* 2011;12(1):120. doi:10.1186/1465-9921-12-120
- 13. Tan X, Xu J, Luo W, et al. Comparison of effects of two airway clearance techniques in patients with AECOPD. *Chin Nurs Res.* 2020;34 (9):1662–1665.
- Li XZ. A comparative study between high-frequency chest wall oscillation expectoration and mechanical vibration expectoration in elderly patients with pulmonary infection. J Comp Nurs Res Care. 2017;16(3):241–244.
- Duan M, Liang Z, Wang K. Clinical observation of the expectoration drainage effect of high frequency chest wall oscillation to treat patients with AECOPD complicated with pneumonia. Sichuan Med J. 2019;40(10):1047–1049.
- Xie D, An D, Hu L, et al. Effects of high-frequency chest wall oscillatory device on sputum excretion in patient with chronic obstructive pulmonary disease accompanied by pulmonary infection. Nurs Integr Tradit Chin West Medi. 2017;3(2):78–80.
- 17. Huang B. Gao pin xiong bi zhen dang pai tan yi yong yu man xing zu sai xing fei ji bing he fei bu gan ran huan zhe pai tan xiao guo ping jia (Evaluation of the effectiveness of high-frequency chest wall oscillation sputum evacuation apparatus for sputum evacuation in patients with chronic obstructive pulmonary disease and lung infection). *West China Med J.* 2013;28(9):1446–1447.
- 18. Wang J, Shi -T-T. qi dao kuo qing ji shu zai man xing zu sai xing fei ji bing ji xing jia zhong qi huan zhe zhong de xiao guo guan cha [Effectiveness of airway clearance technique in chronic obstructive pulmonary disease patients with acute exacerbation]. *Med Diet Health*. 2021;19:4.
- 19. Li W-Q, Liu C, Xie -M-M, et al. Ti wai gao pin xiong bi zhen dong pai tan yi lian he wu hua xi ru zai AECOPD huan zhe zhong de ying yong xiao guo [Effectiveness of extracorporeal high-frequency chest wall oscillation combined with nebulized inhalation in patients with AECOPD]. Prac Med Pharm. 2020;37:3.
- 20. OuYang X-Y, Yao J-K, Li C-J. bu tong wu li Liao fa dui zhong du man xing zu sai xing fei ji bing ji xing jia zhong qi huan zhe fei kang fu de xiao guo guan cha [The effect of different physical therapies in pulmonary rehabilitation of patients with acute exacerbation of severe chronic obstructive pulmonary disease]. *Jilin Med J.* 2020;41(6):1333–1335.
- Zhang C, Liu L, Song S, et al. Efficacy of different physiotherapies for pulmonary rehabilitation in patients with acute exacerbation of severe chronic obstructive pulmonary disease. J Third Mil Med Univ. 2019;41(18):1782–1788.
- Martínez-García MA, Soler-Cataluña JJ, Perpiñá-Tordera M, Román-Sánchez P, Soriano J. Factors associated with lung function decline in adult patients with stable non-cystic fibrosis bronchiectasis. *Chest.* 2007;132(5):1565–1572. doi:10.1378/chest.07-0490
- Osadnik CR, McDonald CF, Jones AP, et al. Airway clearance techniques for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev.* 2012;(3):Cd008328. doi:10.1002/14651858.CD008328.pub2
- 24. Weycker D, Seifer F, Hansen G. Outcomes with High-Frequency Chest Wall Oscillation Among Patients with Bronchiectasis or COPD, in A37. American Thoracic Society; 2017:A1419–A1419.
- 25. Daynes E, Jones AW, Greening NJ, et al. The use of airway clearance devices in the management of chronic obstructive pulmonary disease. a systematic review and meta-analysis of randomized controlled trials. Ann Am Thorac Soc. 2021;18(2):308–320. doi:10.1513/AnnalsATS.202005-482OC
- Hansen G, Barto T, Caceres DM, et al. Outcomes of high frequency chest wall oscillation (hfcwo) in COPD patients without bronchiectasis. *Chest.* 2019;156(4):A1170. doi:10.1016/j.chest.2019.08.1065
- 27. Martin AL, Marvel J, Fahrbach K, et al. The association of lung function and St. George's respiratory questionnaire with exacerbations in COPD: a systematic literature review and regression analysis. *Respir Res.* 2016;17:40. doi:10.1186/s12931-016-0356-1
- 28. Piquet J, Brochard L, Isabey D, et al. High frequency chest wall oscillation in patients with chronic air-flow obstruction. *Am Rev Respir Dis.* 1987;136(6):1355–1359. doi:10.1164/ajrccm/136.6.1355
- Longhini F, Bruni A, Garofalo E, et al. Chest physiotherapy improves lung aeration in hypersecretive critically ill patients: a pilot randomized physiological study. Critical Care. 2020;24(1):479. doi:10.1186/s13054-020-03198-6
- Russo D, Romaggi C, Grecchi B, et al. Comparison of intrapulmonary percussive ventilation and high frequency chest wall oscillation in patients with severe COPD. Eur Respir J. 2014;44(Suppl 58):P3664.
- Morgan SE, Mosakowski S, Giles BL, et al. Variability in expiratory flow requirements among oscillatory positive expiratory pressure. CJRT. 2019;56:7–10. doi:10.29390/cjrt-2019-025
- Fagevik Olsén M, Olofsson P, Frejd P, et al. Technical aspects of devices and equipment for positive expiratory pressure with and without oscillation. *Respir Care.* 2021;66(5):862–877. doi:10.4187/respcare.08003
- 33. Vestbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013;187(4):347–365. doi:10.1164/rccm.201204-0596PP
- 34. Kachel DL, Davey CS, Kennedy TC, et al. Utility of a high-frequency chest wall oscillation (HFCWO) trial period to assess treatment satisfaction adherence and benefit in patients with COPD. Chest. 2005;128(4):252S.

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