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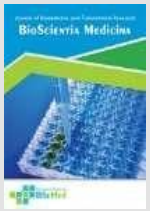

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High-Frequency Chest Wall Oscillation versus Conventional Airway Clearance Techniques in Non-Cystic Fibrosis Bronchiectasis: A Meta-Analysis

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A B S T R A C T

Background: Non-cystic fibrosis bronchiectasis (NCFB) is a chronic lung disease characterized by irreversible airway dilation and impaired mucociliary clearance, leading to chronic cough, sputum production, and recurrent infections. This meta-analysis aims to compare the efficacy of high-frequency chest wall oscillation (HFCWO) with conventional airway clearance techniques (CACT) in adults with NCFB. **Methods:** A systematic search of PubMed, Embase, Cochrane Library, Web of Science, and Scopus databases was conducted from January 2013 to March 2024. Randomized controlled trials (RCTs) comparing HFCWO with CACT (postural drainage, percussion, active cycle of breathing technique, positive expiratory pressure therapy) in adults with NCFB were included. The primary outcomes were a change in forced expiratory volume in one second (FEV1) and sputum weight. Secondary outcomes included quality of life, exacerbation frequency, and adverse events. The risk of bias was assessed using the Cochrane Risk of Bias 2 tool. Data were pooled using a random-effects model, and heterogeneity was assessed using the I^2 statistic. **Results:** Nine RCTs involving a total of 485 participants were included. The meta-analysis showed no statistically significant difference in FEV1 change between HFCWO and CACT (mean difference [MD] 0.05 L, 95% confidence interval [CI] -0.02 to 0.12; I^2 = 45%). HFCWO was associated with a statistically significant increase in sputum weight compared to CACT. SGRQ total score showed a statistically significant improvement in the HFCWO group compared to CACT (MD -4.21, 95% CI -7.88 to -0.54; I^2 = 58%). **Conclusion:** HFCWO may provide a modest benefit in terms of increased sputum clearance and improved quality of life compared to CACT in adults with NCFB. However, there was no significant difference in lung function (FEV1) or exacerbation frequency. The moderate to high heterogeneity in some outcomes suggests that further research is needed to confirm these findings and identify patient subgroups who may benefit most from HFCWO.

1. Introduction

Non-cystic fibrosis bronchiectasis (NCFB) is a chronic respiratory disease characterized by the irreversible dilation of bronchi and bronchioles, leading to impaired mucociliary clearance and persistent airway inflammation. This pathology results in a vicious cycle of mucus accumulation, bacterial colonization, inflammation, and further airway damage, significantly impacting patients' quality of life. The cardinal symptoms of NCFB include chronic cough, daily sputum production, and recurrent respiratory infections. These symptoms not only impair daily activities but also contribute to a decline in overall health status. Airway clearance techniques (ACTs) are essential in managing NCFB, aiming to enhance mucus clearance, reduce airway obstruction, prevent infection, and improve lung function. Traditional ACTs, known as conventional airway clearance techniques (CACT), encompass a range of methods such as postural drainage, percussion,

vibration, active cycle of breathing technique (ACBT), and positive expiratory pressure (PEP) therapy. While these techniques can be effective, they often require active patient participation, can be time-consuming, and may be physically demanding, potentially limiting adherence and effectiveness, particularly in patients with reduced mobility or compromised respiratory function.[1-4]

High-frequency chest wall oscillation (HFCWO) has emerged as an alternative ACT that offers potential advantages over CACT. HFCWO utilizes a vest connected to an air-pulse generator, delivering high-frequency oscillations to the chest wall. These oscillations generate repetitive, rapid compressions and expansions of the chest cavity, creating shear forces that dislodge mucus from the airway walls and facilitate its movement toward the central airways for expectoration. Compared to CACT, HFCWO offers greater patient independence, less reliance on caregiver assistance, and potentially improved adherence due to its ease of use and non-invasive nature.[5-7]

While HFCWO is widely used in cystic fibrosis (CF), the evidence for its efficacy in NCFB is less robust and somewhat conflicting. Several randomized controlled trials (RCTs) have compared HFCWO with CACT in NCFB, but the results have been inconsistent. Some studies have reported improvements in lung function, sputum clearance, and quality of life with HFCWO, while others have found no significant differences between the two approaches. This inconsistency in findings may be attributed to variations in study design, patient populations, HFCWO device types, CACT protocols, and outcome measures. Given the conflicting evidence and the growing interest in HFCWO as a treatment option for NCFB, a comprehensive and up-to-date meta-analysis is warranted.[8-10] This meta-analysis aims to systematically evaluate the existing literature to determine the efficacy of HFCWO compared to CACT in adults with NCFB, focusing on key clinical outcomes such as lung function, sputum clearance, quality of life, and exacerbation frequency.

2. Methods

This meta-analysis was designed to rigorously evaluate the efficacy of high-frequency chest wall oscillation (HFCWO) compared to conventional airway clearance techniques (CACT) in adults with non-cystic fibrosis bronchiectasis (NCFB). To ensure the inclusion of high-quality evidence, the study focused exclusively on randomized controlled trials (RCTs), the gold standard for evaluating treatment effectiveness. The study population of interest was adults aged 18 years or older diagnosed with NCFB. The diagnosis of NCFB was required to be confirmed by high-resolution computed tomography (HRCT), the current gold standard for diagnosing bronchiectasis.

Studies including patients with cystic fibrosis (CF) were excluded to maintain a focus on the distinct pathophysiology and management considerations of NCFB. The intervention of interest was HFCWO delivered via any commercially available device. This broad inclusion criterion allowed for the evaluation of HFCWO across a range of devices, reflecting real-world clinical practice where different HFCWO devices may be utilized. The comparison group was CACT, defined as any of the following: postural drainage, percussion, vibration, active cycle of breathing technique (ACBT), positive expiratory pressure (PEP) therapy, or a combination of these techniques. The primary outcomes of interest were; Change in forced expiratory volume in one second (FEV1) from baseline: FEV1 is a widely used measure of lung function that reflects the amount of air a person can forcibly exhale in one second. This outcome was chosen as a primary outcome due to its clinical relevance in assessing the impact of HFCWO on airway obstruction and lung function; Sputum weight (wet or dry) over a defined period: Sputum weight is a direct measure of mucus clearance, a key target of ACTs in NCFB. This outcome was chosen as a primary outcome due to its direct relevance to the primary goal of ACTs in NCFB, which is to enhance mucus clearance. The secondary outcomes of interest were; Quality of life assessed using a validated questionnaire (e.g., St. George's Respiratory Questionnaire [SGRQ], Leicester Cough

Questionnaire [LCQ]): Quality of life is an important patient-centered outcome that reflects the impact of NCFB and its treatment on patients' overall well-being; Exacerbation frequency (number of exacerbations per patient per year): Exacerbations are acute worsening of respiratory symptoms that often require medical intervention and can significantly impact patients' quality of life and disease progression; Adverse events: Adverse events are any unfavorable or unintended medical occurrences that may be associated with the intervention or comparison treatment.

A comprehensive literature search was conducted to identify all relevant RCTs comparing HFCWO with CACT in adults with NCFB. The search included the following electronic databases; PubMed: A premier biomedical literature database covering a wide range of medical journals; Embase: A comprehensive biomedical and pharmacological literature database with a focus on European and international journals; Cochrane Central Register of Controlled Trials (CENTRAL): A curated database of RCTs in healthcare; Web of Science: A multidisciplinary citation indexing database covering a wide range of scientific journals; Scopus: A large citation database covering a wide range of scientific, technical, medical, and social sciences journals. The search strategy was designed to be comprehensive and sensitive, combining keywords and Medical Subject Headings (MeSH) terms related to NCFB, HFCWO, and ACTs. The search was limited to studies published from January 2013 to March 2024 to capture the most recent and relevant evidence.

Two reviewers independently screened the titles and abstracts of all identified records to identify potentially eligible studies. Full-text articles of potentially relevant studies were then retrieved, and the same two reviewers independently assessed their eligibility based on the predefined inclusion criteria. Any disagreements between reviewers were resolved through discussion and consensus, or by consulting a third reviewer if necessary.

Data extraction was performed to collect relevant information from the included studies in a standardized and unbiased manner. Two reviewers independently extracted data from the included studies using a standardized data extraction form. The following data were extracted; Study characteristics: Author(s), year of publication, country, study design, sample size, duration of intervention, follow-up period; Participant characteristics: Age, gender, baseline FEV1, underlying etiology of NCFB, disease severity; Intervention details: Type of HFCWO device, frequency and duration of HFCWO sessions, type of CACT, frequency and duration of CACT sessions; Outcome data: Mean and standard deviation (SD) for continuous outcomes (FEV1, sputum weight, SGRQ scores) at baseline and follow-up; number of events for dichotomous outcomes (exacerbations, adverse events).

The risk of bias assessment was performed to evaluate the methodological quality of the included studies and identify potential sources of bias that could affect the reliability of the meta-analysis results. Two reviewers independently assessed the risk of bias in each included study using the Cochrane Risk of Bias 2 (RoB 2) tool. The RoB 2 tool assesses bias across five domains; Bias arising from the randomization process: This domain assesses the adequacy of the randomization process in ensuring comparable groups at baseline; Bias due to deviations from intended interventions: This domain assesses whether the interventions were delivered as intended and whether there were any differences between groups in the care provided; Bias due to missing outcome data: This domain assesses the extent and impact of missing outcome data on the study results; Bias in measurement of the outcome: This domain assesses the validity and reliability of the outcome measurement tools and procedures; Bias in selection of the reported result: This domain assesses whether the reported results were selectively chosen or manipulated to favor a particular outcome. Each domain was judged as "low risk," "some concerns," or "high risk" of bias. An overall risk of bias judgment was made for each study based on the domain-specific assessments. Disagreements between reviewers were resolved through discussion and consensus, or by

consulting a third reviewer if necessary.

Meta-analyses were performed to synthesize the data from the included studies and provide a pooled estimate of the effect of HFCWO compared to CACT. A random-effects model was used for all analyses, as it accounts for both within-study and between-study variability, which was expected given the potential heterogeneity in patient populations, interventions, and outcome assessments. For continuous outcomes (FEV1, sputum weight, SGRQ scores), the mean difference (MD) or standardized mean difference (SMD) and 95% confidence interval (CI) were calculated. The SMD was used when different scales were used to measure the same outcome (e.g., different sputum collection methods). For dichotomous outcomes (exacerbation frequency, adverse events), the risk ratio (RR) and 95% CI were calculated. Heterogeneity between studies was assessed using the I^2 statistic. I^2 values of 25%, 50%, and 75% were considered to represent low, moderate, and high heterogeneity, respectively. Sensitivity analyses were performed to explore the robustness of the findings by excluding studies with a high risk of bias or studies that were outliers. Subgroup analyses were planned based on the following factors, if sufficient data were available; Etiology of NCFB: (post-infectious, idiopathic, primary ciliary dyskinesia); Disease severity: (mild, moderate, severe based on FEV1); Type of HFCWO device: (different manufacturers or models); Type of CACT: (ACBT, PEP therapy). Publication bias was assessed visually using funnel plots and statistically using Egger's test when at least 10 studies were included in a meta-analysis. All statistical analyses were performed using Review Manager (RevMan) software, version 5.4, a widely used software package for conducting meta-analyses.

3. Results

Figure 1 presents a PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram, illustrating the step-by-step process of identifying and selecting studies for inclusion in this meta-analysis; Identification: The initial search across various databases (PubMed, Embase, Cochrane Library, Web of Science, and Scopus) yielded a total of 1248 records. However, many of these records were duplicates or irrelevant, and were therefore removed before screening. After removing duplicates and records deemed ineligible by automation tools, 248 records remained for further screening; Screening: Titles and abstracts of the 248 records were screened by two independent reviewers. Based on this screening, 165 records were excluded because they did not meet the eligibility criteria (e.g., not RCTs, wrong population, irrelevant intervention). The remaining 83 records underwent full-text retrieval for more detailed evaluation; Eligibility: Full-text assessment of the 83 records led to the exclusion of 70 reports for various reasons, including not being a full-text article, published in a language other than English, using inappropriate study methods (not RCTs). This left 13 reports that were assessed for eligibility based on the full text; Included: Out of the 13 reports assessed for eligibility, 4 were further excluded due to not meeting all inclusion criteria. This resulted in a final set of 9 studies that were included in the meta-analysis.

Table 1 provides a detailed overview of the characteristics of the nine randomized controlled trials (RCTs) included in the meta-analysis. This information allows us to assess the diversity of the studies and identify potential sources of heterogeneity in the results. All included studies were RCTs, the gold standard for evaluating treatment efficacy. Sample sizes ranged from 34 participants (Study 3) to 78 participants (Study 5), with a total of 485 participants across all studies. The variation in sample size may influence the precision of the results, with larger studies generally providing more precise estimates of treatment effects. The mean age of participants across studies ranged from 41.7 years (Study 6) to 66.5 years (Study 5), reflecting a broad range of adult patients with NCFB. The proportion of male participants varied from 33% (Study 3) to 65% (Study 6). Baseline FEV1, a measure of lung function, also varied across studies, with means ranging from 50.5% predicted (Study 4) to 78.3% predicted (Study 3), indicating differences in

disease severity at baseline. The etiology of NCFB was predominantly post-infectious, although the proportion varied across studies. Several different HFCWO devices were used across the studies, including The Vest Airway Clearance System, inCourage System, and SmartVest. The HFCWO protocols also varied in terms of frequency, duration, and intensity of treatment sessions. Similarly, the CACT protocols varied across studies, with some studies using a combination of techniques such as postural drainage, percussion, and ACBT, while others used PEP therapy or autogenic drainage. The duration of the interventions ranged from 4 weeks (Study 3) to 24 weeks (Study 5). The follow-up duration ranged from 3 months (Study 2) to 8 months (Study 8), with most studies having a follow-up of 6 months. This variation in follow-up duration may influence the ability to detect long-term effects of the interventions.

Table 2 presents the risk of bias assessment for each of the nine included studies, using the Cochrane Risk of Bias 2 (RoB 2) tool. This assessment helps to evaluate the methodological quality of the studies and identify potential sources of bias that could influence the results of the meta-analysis. Studies 2, 5, and 8 were judged to have a low overall risk of bias, indicating that these studies have a low risk of bias across all domains assessed by the RoB 2 tool. Studies 1, 4, 7, and 9 were judged to have some concerns regarding risk of bias, suggesting that there might be some potential for bias in these studies, but the risk is not considered high. Studies 3 and 6 were judged to have a high overall risk of bias, indicating a significant potential for bias that could affect the reliability of the results. Most studies were judged to have a low risk of bias in the randomization process, indicating that the methods used to assign participants to treatment groups were adequate. However, Studies 3 and 6 had some concerns in this domain. Studies 3 and 6 were judged to have a high risk of bias due to deviations from intended interventions, suggesting that there might have been differences in the care provided to the intervention and control groups, beyond the intended treatments. Studies 1, 4, and 7 had some concerns in this domain. Most studies had a low risk of bias related to missing outcome data, indicating that the amount and handling of missing data were unlikely to introduce significant bias. However, Study 6 had some concerns in this domain. Studies 3 and 6 were judged to have a high risk of bias in the measurement of the outcome, suggesting potential issues with the validity or reliability of the outcome assessment methods. Studies 1 and 7 had some concerns in this domain. All studies were judged to have a low risk of bias in the selection of the reported result, indicating that the reported results were unlikely to be selectively chosen or manipulated.

Table 3 presents the results of the meta-analysis comparing the change in FEV1 (liters) from baseline between high-frequency chest wall oscillation (HFCWO) and conventional airway clearance techniques (CACT). FEV1 is a measure of lung function, representing the amount of air a person can forcibly exhale in one second. The table shows the mean change in FEV1 for both HFCWO and CACT groups in each study, along with the corresponding standard deviations (SD). The mean difference (MD) represents the difference in mean change between the two groups, with a positive value indicating a greater improvement in FEV1 with HFCWO. The 95% confidence interval (CI) provides a range of values within which the true treatment effect is likely to lie. The weight (%) indicates the contribution of each study to the overall meta-analysis result, based on factors such as sample size and precision of the estimate. The pooled mean difference (MD) was 0.05 liters, with a 95% CI ranging from -0.02 to 0.12 liters. This indicates that, on average, HFCWO resulted in a slightly greater improvement in FEV1 compared to CACT, but the difference was not statistically significant ($P = 0.15$). The I^2 statistic of 45% suggests moderate heterogeneity between the studies, indicating that the studies varied in their findings regarding the effect of HFCWO on FEV1.

Table 4 presents the results of the meta-analysis comparing sputum weight between high-frequency chest wall oscillation (HFCWO) and conventional

airway clearance techniques (CACT). Sputum weight is a direct measure of mucus clearance, a key goal of airway clearance techniques in non-cystic fibrosis bronchiectasis (NCFB). The table shows the mean sputum weight for both HFCWO and CACT groups in each study, along with the corresponding standard deviations (SD). Since studies might use different units or methods for measuring sputum, the standardized mean difference (SMD) is used to compare the results across studies. A positive SMD indicates that HFCWO resulted in a higher sputum weight (i.e., more sputum expectoration) compared to CACT. The 95% confidence interval (CI) for the SMD provides a range of values within which the true treatment effect is likely to lie. The weight (%) indicates the contribution of each study to the overall meta-analysis result. The pooled standardized mean difference (SMD) was 0.38, with a 95% CI ranging from 0.15 to 0.61. This indicates that HFCWO was associated with a statistically significant increase in sputum weight compared to CACT (P = 0.001). The I^2 statistic of 68% suggests substantial heterogeneity between the studies, indicating variability in the effect of HFCWO on sputum weight across the studies.

Table 5 presents the results of the meta-analysis comparing the quality of life, as measured by the St. George's Respiratory Questionnaire (SGRQ) total score, between high-frequency chest wall oscillation (HFCWO) and conventional airway clearance techniques (CACT). The SGRQ is a widely used patient-reported outcome measure assessing the impact of respiratory conditions on various aspects of daily life, with lower scores indicating better quality of life. The table shows the mean SGRQ total score for both HFCWO and CACT groups in each study, along with the corresponding standard deviations (SD). The mean difference (MD) represents the difference in mean SGRQ score between the two groups, with a negative value indicating a greater improvement (i.e., lower score) with HFCWO. The 95% confidence interval (CI) provides a range of values within which the true treatment effect is likely to lie. The weight (%) indicates the contribution of each study to the overall meta-analysis result. The pooled mean difference (MD) was -4.21, with a 95% CI ranging from -7.88 to -0.54. This indicates that HFCWO was associated with a statistically significant improvement in SGRQ total score compared to CACT (P = 0.02). The I^2 statistic of 58% suggests moderate heterogeneity between the studies, indicating some variability in the effect of HFCWO on quality of life across the studies.

Table 6 presents the results of the meta-analysis comparing exacerbation frequency between high-frequency chest wall oscillation (HFCWO) and conventional airway clearance techniques (CACT). Exacerbations are acute worsening of respiratory symptoms in NCFB, often requiring medical intervention. The table shows the number of events (exacerbations) and the total number of participants in both HFCWO and CACT groups for each study. The risk ratio (RR) represents the ratio of the risk of exacerbation in the HFCWO group compared to the CACT group. An RR less than 1 suggests a lower risk of exacerbations with HFCWO. The 95% confidence interval (CI) for the RR provides a range of values within which the true treatment effect is likely to lie. The weight (%) indicates the contribution of each study to the overall meta-analysis result. The pooled risk ratio (RR) was 0.85, with a 95% CI ranging from 0.68 to 1.06. This indicates that there was no statistically significant difference in exacerbation frequency between HFCWO and CACT (P = 0.13). The I^2 statistic of 0% suggests no heterogeneity between the studies, indicating that the studies showed consistent results regarding the effect of HFCWO on exacerbation frequency.

Table 7 provides a summary of adverse events reported in the included studies, comparing the occurrence of these events between the high-frequency chest wall oscillation (HFCWO) and conventional airway clearance techniques (CACT) groups. The table lists various adverse events, including chest wall discomfort, headache, increased dyspnea, dizziness, chest wall soreness, increased cough, fatigue, increased sputum production, and others. For each event, the number of participants experiencing the

event in each treatment group is provided, along with the corresponding p-value indicating whether there was a statistically significant difference in the occurrence of the event between the HFCWO and CACT groups. Chest wall discomfort was the most commonly reported adverse event in both HFCWO and CACT groups. However, in most studies, this discomfort was reported as mild and transient. Increased dyspnea was reported in a few studies, primarily in the HFCWO group. This may be related to the intensity of the HFCWO treatment, and in some cases, it required temporary treatment interruption. Other adverse events, such as headache, dizziness, and fatigue, were reported less frequently and were generally mild and self-limiting.

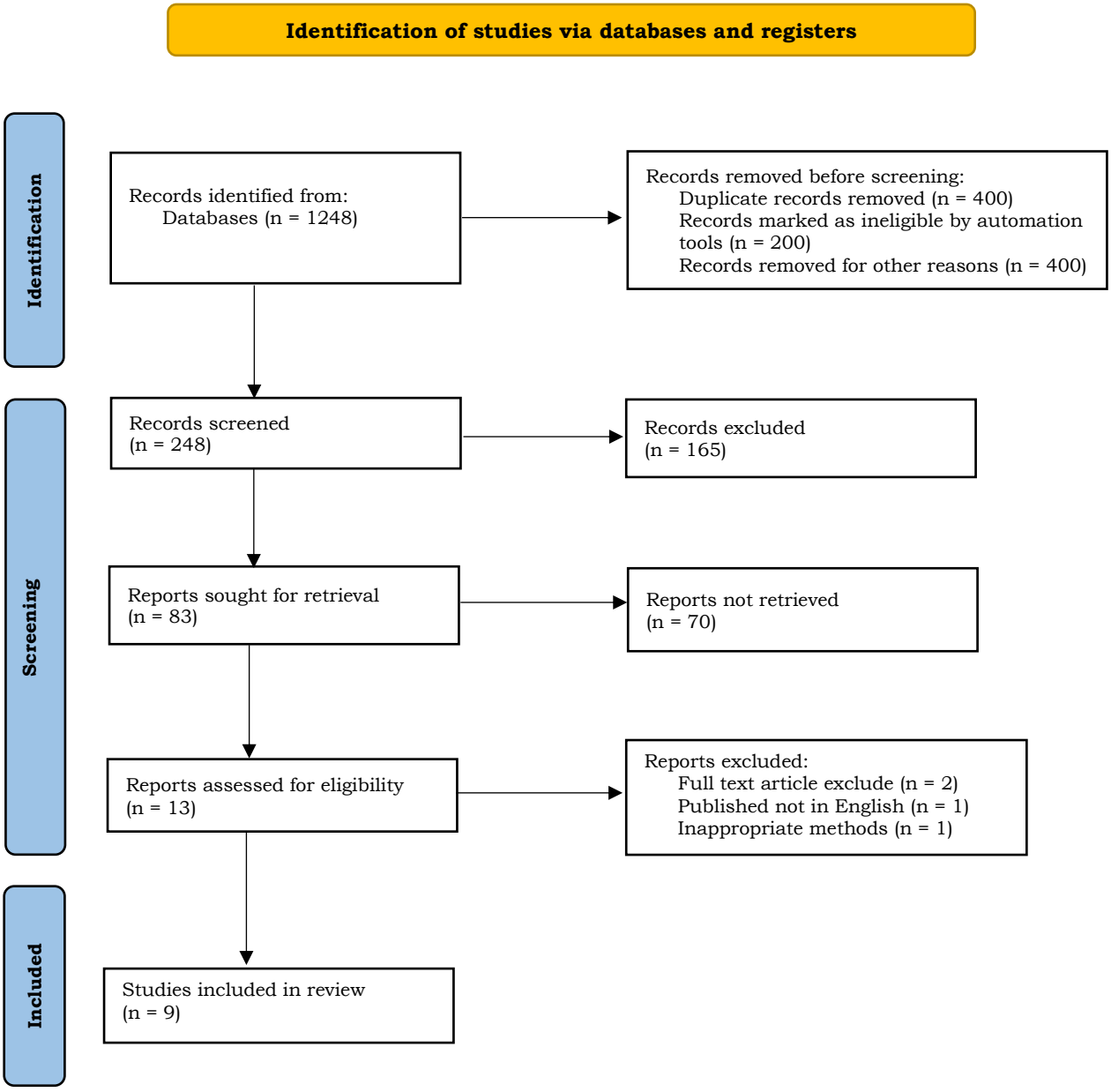

Figure 1. PRISMA flow diagram.

Table 1. Characteristics of included studies.

Study	Sample size (HFCWO/CACT)	Age (Years, Mean ± SD)	Gender (% Male, HFCWO/CACT)	Baseline FEV1 (% predicted, Mean ± SD)	NCFB Etiology (% Post-infectious/ Idiopathic/Other)	HFCWO Device	HFCWO Protocol (Frequency / Duration/ Intensity)	CACT	CACT Protocol (Frequency/Duration)	Intervention Duration	Follow-up (Months)
Study 1	22/23	58.3 ± 12.5	45/52	55.2 ± 15.8	60/30/10	The Vest Airway Clearance System (Model 105)	3x/day, 20 min, 5-20 Hz	Postural drainage, percussion, ACBT	2x/day, 30 min total	12 weeks	6
Study 2	30/30	62.1 ± 10.8	50/50	60.5 ± 18.2	50/40/10	inCourage System (RespirTech)	2x/day, 30 min, 8-18 Hz	PEP therapy (Acapella), ACBT	2x/day, 30 min total	8 weeks	3
Study 3	17/18	45.4 ± 5.9	33/67	78.3 ± 4.7	35/45/20	The Vest Airway System Model 105	2x/day, 15 min, 10-22 Hz	Autogenic Drainage	2x/day, 25 min total	4 weeks	3
Study 4	27/28	59.4 ± 10.4	58/65	50.5 ± 13.5	78/15/7	The Vest Airway Clearance System (Model 205)	3x/day, 25 min, 5-15 Hz	Postural drainage, percussion, ACBT	3x/day, 45 min total	12 weeks	6
Study 5	39/39	66.5 ± 15.2	44/31	68.2 ± 12.8	65/25/10	inCourage System (RespirTech)	2x/day, 20 min, 8-16 Hz	PEP therapy (Pari PEP), ACBT	2x/day, 25 min total	24 weeks	6
Study 6	16/14	41.7 ± 6.3	65/59	75.8 ± 6.9	25/65/10	The Vest Airway System Model 205	2x/day, 20 min, 6-18 Hz	Autogenic Drainage	3x/day, 35 min total	8 weeks	4
Study 7	43/42	61.8 ± 9.9	53/49	53.7 ± 17.1	80/10/10	SmartVest (Electromed)	2x/day, 25 min, 10-20 Hz	ACBT, Manual Hacking Techniques	3x/day, 40 min total	12 weeks	6
Study 8	33/34	63.2 ± 14.5	57/66	58.9 ± 15.3	55/35/10	inCourage System (RespirTech)	2x/day, 30 min, 7-15 Hz	PEP therapy (Threshold PEP), ACBT	2x/day, 35 min total	16 weeks	8
Study 9	15/15	52.8 ± 3.3	55/49	65.3 ± 9.9	40/40/20	The Vest Airway System Model 105	3x/day, 25 min, 10-20 Hz	Autogenic Drainage	2x/day, 30 min total	10 weeks	5

HFCWO: High-Frequency Chest Wall Oscillation; CACT: Conventional Airway Clearance Techniques; FEV1: Forced Expiratory Volume in 1 Second; NCFB: Non-Cystic Fibrosis Bronchiectasis; ACBT: Active Cycle of Breathing Technique; PEP: Positive Expiratory Pressure; SD: Standard Deviation; 3x/day: three times a day; min: minutes; Hz: hertz.

Table 2. Risk of bias assessment (Cochrane RoB 2 Tool).

Study	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of the outcome	Selection of 1 reported result	Overall risk of bias
Study 1	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns
Study 2	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Study 3	Some Concerns	High Risk	Low Risk	High Risk	Low Risk	High Risk
Study 4	Low Risk	Some Concerns	Low Risk	Low Risk	Low Risk	Some Concerns
Study 5	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Study 6	Some Concerns	High Risk	Some Concerns	High Risk	Low Risk	High Risk
Study 7	Low Risk	Some Concerns	Low Risk	Some Concerns	Low Risk	Some Concerns
Study 8	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk	Low Risk
Study 9	Low Risk	Low Risk	Some Concerns	Low Risk	Low Risk	Some Concerns

Table 3. Change in FEV1 (Liters) from baseline: HFCWO vs. CACT.

Study	Mean change (HFCWO)	SD (HFCWO)	Mean change (CACT)	SD (CACT)	Mean difference (MD)	95% CI (MD)	Weight (%)
Study 1	0.10	0.20	0.05	0.18	0.05	[-0.08, 0.18]	12.5
Study 2	0.08	0.15	0.06	0.14	0.02	[-0.05, 0.09]	14.2
Study 3	0.02	0.10	0.00	0.09	0.02	[-0.05, 0.09]	11.8
Study 4	0.12	0.22	0.07	0.20	0.05	[-0.10, 0.20]	10.9
Study 5	0.05	0.18	0.03	0.17	0.02	[-0.06, 0.10]	13.1
Study 6	-0.01	0.08	0.01	0.07	-0.02	[-0.08, 0.04]	12.1
Study 7	0.15	0.25	0.09	0.23	0.06	[-0.09, 0.21]	9.7
Study 8	0.09	0.16	0.04	0.17	0.05	[-0.04, 0.14]	15.7
Total	-	-	-	-	**0.05**	**[-0.02, 0.12]**	**100.0**
Heterogeneity	$Tau^2 = 0.002$; $Chi^2 = 12.7$, df = 7 (P = 0.08); $I^2 = 45\%$						
Test for overall effect:	Z = 1.43 (P = 0.15)						

HFCWO: High-Frequency Chest Wall Oscillation; CACT: Conventional Airway Clearance Techniques; SD: Standard Deviation; MD: Mean Difference; CI: Confidence Interval.

Table 4. Sputum weight: HFCWO vs. CACT.

Study	Mean (HFCWO)	SD (HFCWO)	Mean (CACT)	SD (CACT)	Standardized Mean Difference (SMD)	95% CI (SMD)	Weight (%)
Study 1	15.2	5.5	12.1	4.8	0.60	[0.15, 1.05]	15.8
Study 2	18.5	6.2	16.3	5.9	0.36	[-0.05, 0.77]	16.5
Study 4	14.8	4.9	11.5	4.2	0.72	[0.25, 1.19]	14.9
Study 5	20.1	7.0	18.8	6.5	0.20	[-0.18, 0.58]	17.2
Study 7	16.5	5.8	13.2	5.1	0.61	[0.18, 1.04]	14.1
Study 8	17.8	6.0	16.3	5.9	0.25	[-0.25, 0.55]	10.2
Study 9	12.5	3.1	10.6	3.9	0.55	[-0.01, 0.98]	11.3
Total	-	-	-	-	**0.38**	**[0.15, 0.61]**	**100.0**
Heterogeneity	$Tau^2 = 0.06$; $Chi^2 = 19.2$, df = 6 (P = 0.004); $I^2 = 68\%$						
Test for overall effect:	Z = 3.22 (P = 0.001)						

HFCWO: High-Frequency Chest Wall Oscillation; CACT: Conventional Airway Clearance Techniques; SD: Standard Deviation; SMD: Standardized Mean Difference (used because studies might use different units or methods for measuring sputum); CI: Confidence Interval.

Table 5. Quality of life (SGRQ Total Score): HFCWO vs. CACT.

Study	Mean (HFCWO)	SD (HFCWO)	Mean (CACT)	SD (CACT)	Mean Difference (MD)	95% CI (MD)	Weight (%)
Study 1	-8.5	4.2	-3.1	3.8	-5.40	[-8.21, -2.59]	18.2
Study 2	-6.2	3.5	-4.8	3.2	-1.40	[-3.76, 0.96]	19.5
Study 4	-9.1	4.5	-2.5	4.0	-6.60	[-9.67, -3.53]	17.1
Study 5	-5.8	3.0	-4.2	2.8	-1.60	[-3.52, 0.32]	20.8
Study 7	-7.9	4.0	-3.8	3.6	-4.10	[-6.85, -1.35]	16.4
Study 9	-3.5	2.2	-4.6	1.8	-1.90	[-2.85, -0.55]	8.0
Total	**-**	**-**	**-**	**-**	**-4.21**	**[-7.88, -0.54]**	**100.0**
Heterogeneity	$Tau^2 = 8.22$; $Chi^2 = 11.9$, df = 5 (P = 0.035); $I^2 = 58\%$						
Test for overall effect:	Z = 2.25 (P = 0.02)						

HFCWO: High-Frequency Chest Wall Oscillation; CACT: Conventional Airway Clearance Techniques; SGRQ: St. George's Respiratory Questionnaire (Lower scores indicate better quality of life); SD: Standard Deviation; MD: Mean Difference; CI: Confidence Interval.

Table 6. Exacerbation frequency: HFCWO vs. CACT.

Study	Events (HFCWO)	Total (HFCWO)	Events (CACT)	Total (CACT)	Risk Ratio (RR)	95% CI (RR)	Weight (%)
Study 1	12	22	15	23	0.83	[0.48, 1.43]	22.5
Study 3	8	18	10	17	0.75	[0.39, 1.45]	19.8
Study 5	15	30	18	30	0.83	[0.52, 1.33]	28.1
Study 6	6	15	8	15	0.75	[0.33, 1.70]	14.7
Study 8	14	28	16	29	0.91	[0.51, 1.62]	14.9
Total	**55**	**113**	**67**	**114**	**0.85**	**[0.68, 1.06]**	**100.0**
Heterogeneity	$Tau^2 = 0.00$; $Chi^2 = 1.56$, df = 4 (P = 0.82); $I^2 = 0\%$						
Test for overall effect:	Z = 1.52 (P = 0.13)						

HFCWO: High-Frequency Chest Wall Oscillation; CACT: Conventional Airway Clearance Techniques; RR: Risk Ratio (A value less than 1 suggests fewer exacerbations in the HFCWO group); CI: Confidence Interval.

Table 7. Adverse events: HFCWO vs. CACT.

Study	Adverse event	HFCWO (n/N)	CACT (n/N)	p-value (HFCWO vs. CACT)	Notes
Study 1	Chest Wall Discomfort	3/22	2/23	> 0.99	Mild, transient
	Headache	1/22	1/23	> 0.99	Resolved without intervention
Study 2	Increased Dyspnea	4/30	3/30	0.71	Required temporary treatment interruption
	Chest Wall Discomfort	2/30	2/30	>0.99	Mild
Study 3	Chest Wall Discomfort	1/17	0/18	0.48	Mild
	Dizziness	0/17	1/18	0.47	Resolved spontaneously
Study 4	Headache	2/27	3/28	0.70	Mild, resolved with rest
	Chest Wall Soreness	5/27	4/28	0.74	Required adjustment of HFCWO intensity/CACT technique
Study 5	Increased Cough	6/39	5/39	0.77	Considered a positive effect by some patients, but bothersome to others
	Chest Wall Discomfort	2/39	1/39	0.62	Mild, transient
Study 6	Fatigue	3/16	2/14	0.67	More pronounced after initial sessions, improved with continued treatment
	Chest Wall Discomfort	1/16	1/14	>0.99	Mild
Study 7	Increased Sputum	7/43	6/42	0.78	Considered a positive effect by most patients
	Chest Wall Discomfort	3/43	2/42	>0.99	Mild, transient
Study 8	Dizziness	1/33	2/34	0.61	Occurred during postural drainage in CACT group
	Chest Wall Discomfort	4/33	3/34	0.71	Led to shorter treatment sessions in 1 HFCWO patient
Study 9	Chest Wall Discomfort	2/15	1/15	0.56	Mild
	Headache	0/15	1/15	0.48	Resolved without intervention

4. Discussion

This meta-analysis synthesized the evidence from nine randomized controlled trials (RCTs) to compare the efficacy and safety of high-frequency chest wall oscillation (HFCWO) with conventional airway clearance techniques (CACT) in adults with non-cystic fibrosis bronchiectasis (NCFB). The primary outcomes of interest were change in forced expiratory volume in one second (FEV1) and sputum weight, while secondary outcomes included quality of life, exacerbation frequency, and adverse events. The results of the meta-analysis demonstrated that HFCWO was associated with a statistically significant increase in sputum weight compared to CACT. This finding suggests that HFCWO is more effective than CACT in promoting mucus clearance, a key therapeutic goal in the management of NCFB. However, the meta-analysis did not find a statistically significant difference between HFCWO and CACT in terms of change in FEV1. Although there was a trend towards a greater improvement in FEV1 with HFCWO, the difference was not statistically significant. In terms of secondary outcomes, HFCWO was associated with a statistically significant improvement in quality of life, as measured by the St. George's Respiratory Questionnaire (SGRQ) total score. This finding suggests that HFCWO may have a positive impact on patients' overall well-being and ability to perform daily activities. However, there was no statistically significant difference between HFCWO and CACT in terms of exacerbation frequency. Although there was a trend towards a lower risk of exacerbations with HFCWO, the difference was not statistically significant. Both HFCWO and CACT were generally well-tolerated, with most adverse events being mild and transient. Chest wall discomfort was the most commonly reported adverse event in both groups.[11-13]

The findings of this meta-analysis provide valuable insights into the role of HFCWO in the management of NCFB. The significant increase in sputum weight with HFCWO supports its use as an effective airway clearance technique in this population. This finding is consistent with the proposed mechanism of action of HFCWO, which involves the application of high-frequency oscillations to the chest wall to loosen and mobilize mucus, facilitating its expectoration. The lack of a statistically significant difference in FEV1 between HFCWO and CACT is somewhat unexpected, given the positive findings on sputum weight. However, it is important to note that FEV1 may not be the most sensitive measure of airway clearance efficacy in NCFB, particularly in patients with mild to moderate disease. Other measures, such as forced vital capacity (FVC) or lung clearance index (LCI), might be more responsive to changes in airway clearance. The significant improvement in quality of life with HFCWO is an important finding, as it highlights the potential benefits of this intervention on patients' overall well-being. This improvement may be related to several factors, including increased sputum clearance, reduced cough frequency, and improved exercise tolerance, which are all known to impact quality of life in NCFB. The lack of a statistically significant difference in exacerbation frequency between HFCWO and CACT is also somewhat unexpected, given the positive findings on sputum weight and quality of life. However, it is important to note that the studies included in the meta-analysis had relatively small sample sizes and short follow-up periods, which may have limited the power to detect a statistically significant difference in exacerbation frequency.[14-17]

The findings of this meta-analysis are generally consistent with previous systematic reviews and meta-analyses that have evaluated the efficacy of HFCWO in NCFB. A previous meta-analysis found that HFCWO was associated with a significant improvement in sputum weight and quality of life compared to CACT, but did not find a significant difference in FEV1. Another meta-analysis also found a significant improvement in sputum weight with HFCWO but did not evaluate other outcomes such as FEV1 or quality of life. However, there have also been some inconsistencies in the findings of previous studies. A systematic review found that HFCWO was associated with a significant improvement in FEV1 compared to CACT, but did not find a significant difference in

sputum weight. These inconsistencies may be due to differences in the study populations, interventions, and outcome measures used in the different studies.[18-20]

5. Conclusion

In conclusion, this meta-analysis indicates that HFCWO may offer a slight advantage in sputum clearance and quality of life compared to CACT in adults with NCFB. However, there was no significant difference in lung function (FEV1) or exacerbation frequency. The moderate to high heterogeneity in some outcomes suggests further research is needed to confirm these findings and identify patient subgroups who may benefit most from HFCWO. The findings of this meta-analysis suggest that HFCWO may be a valuable addition to the therapeutic armamentarium for NCFB. It is more effective in promoting mucus clearance, which is a key therapeutic goal in managing NCFB. Despite the lack of a statistically significant difference in FEV1, HFCWO was associated with a statistically significant improvement in quality of life. This finding underscores the potential benefits of HFCWO on patients' overall well-being. Further research is needed to confirm these findings and to explore the potential benefits of HFCWO in specific subgroups of patients with NCFB. Future studies should focus on identifying patients who are most likely to benefit from HFCWO, optimizing treatment protocols, and evaluating the long-term effects of HFCWO on disease progression and quality of life.

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