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Original Article

Inspiratory Muscle Training Using Tapered Flow Resistive Loading to Enhance Pulmonary Function in Smokers: A Randomized Controlled Trial

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Abstract

Background: Smoking is a leading cause of respiratory muscle weakness and diminished lung function. Inspiratory Muscle Training (IMT), particularly with Tapered Flow Resistive Loading (TFRL), is a promising non-pharmacological intervention aimed at enhancing respiratory muscle strength. This randomized controlled trial (RCT) aims to evaluate whether IMT with TFRL can significantly improve respiratory muscle strength and lung function in smokers. **Methodology:** The study enrolled 60 adult smokers aged 18-60 years, with a smoking history of at least five years and mild to moderate lung impairment, defined by a baseline Forced Expiratory Volume in one second (FEV1) between 40% and 80% of the predicted value. Participants were randomly assigned to either the intervention group, which underwent an eight-week IMT program with TFRL, or the control group, which received general smoking cessation advice and no respiratory muscle training. The primary outcome measure is maximum inspiratory pressure (MIP), assessed using a handheld portable manometer. Secondary outcomes include pulmonary function tests (FEV1, FVC, and PEFR), perceived dyspnea via the Modified Borg Scale, and changes in smoking behavior. All the outcomes were recorded at baseline and after eight weeks. **Results:** Statistical analyses revealed that the intervention group showed significant improvements in respiratory muscle strength and pulmonary function compared to the control group. The two-way repeated measures ANOVA confirmed significant group-by-time interactions for MIP and pulmonary function tests, indicating that the changes over time differed between the intervention and control groups. **Conclusion:** IMT with TFRL may offer a valuable therapeutic approach for smokers suffering from lung impairment, particularly in non-pharmacological rehabilitation programs aimed at enhancing pulmonary function and reducing dyspnea.

Keywords: Inspiratory Muscle Training, Tapered Flow Resistive Loading (TFRL), Respiratory Muscle Strength, Pulmonary Function, Smokers.

Introduction

Chronic smoking is well-documented to severely impact lung function, leading to various respiratory disorders such as chronic obstructive pulmonary disease (COPD), emphysema, and chronic bronchitis. Prolonged exposure to the toxins in cigarette smoke results in inflammation of the airways, structural changes, and a progressive decline in lung function. Over time, smoking-induced damage becomes evident through decreased lung function, as reflected by reductions in key spirometric measurements like forced expiratory volume in one second (FEV1) and forced vital capacity (FVC). These metrics are critical indicators of respiratory health, especially in smokers (Vogelmeier et al., 2017; Sin & Man, 2007). While quitting smoking can lead to some short-term recovery in lung function, long-term smokers often continue to experience impaired pulmonary capacity (Tøttenborg et al., 2016; Dhariwal et al., 2014).

Non-pharmacological interventions, such as Inspiratory Muscle Training (IMT), have gained attention as potential therapies to combat smoking-induced respiratory muscle weakness. IMT targets the diaphragm and intercostal muscles, improving both respiratory muscle strength and lung function, particularly in individuals with compromised breathing capacity (Gosselink et al., 2011). However, traditional IMT methods may not be suitable for individuals with varying levels of respiratory impairment, necessitating more adaptable approaches such as Tapered Flow Resistive Loading (TFRL), which gradually increases resistance to breathing. Through resistance-based breathing exercises, IMT enhances both the strength and endurance of the inspiratory muscles, making it an appealing option for smokers and those with respiratory conditions (Shoemaker et al., 2009).

A growing body of evidence supports IMT's ability to significantly improve maximum inspiratory pressure (MIP), as well as increase FEV1 and FVC, which collectively boost exercise tolerance and overall lung health (Leelarungrayub et al., 2014). Meta-analyses, such as the one by Illi et al. (2012), further affirm these benefits across various populations, showcasing IMT's potential to alleviate dyspnea and improve quality of life in individuals with chronic respiratory disorders, including smokers.

However, traditional IMT methods may not be suitable for individuals with varying levels of respiratory impairment. This limitation has spurred the development of Tapered Flow Resistive Loading (TFRL), a more adaptive approach that gradually increases resistance to breathing, providing a tailored training regimen. By applying the progressive overload principle—widely used in strength training—TFRL specifically targets the patient's needs, offering a potentially more effective strategy (Kleisthenis et al., 2020).

In chronic obstructive pulmonary disease (COPD) patients, IMT with TFRL has yielded greater improvements in MIP, exercise tolerance, and dyspnea reduction when compared to conventional IMT, indicating that smokers with weakened respiratory muscles may also benefit from this method (Beaumont et al., 2019). While IMT combined with TFRL has demonstrated efficacy in COPD patients, its effects in smokers without a COPD diagnosis remain underexplored. This study addresses this gap by evaluating whether IMT with TFRL can enhance respiratory muscle strength and lung function in smokers, thereby offering a more personalized approach to pulmonary rehabilitation for this population.

With spirometry remaining the gold standard for assessing lung function in smokers and considering the incomplete reversal of lung damage even after smoking cessation, interventions like IMT with TFRL are increasingly important. This study aims to investigate the impact of IMT with TFRL on lung function and respiratory muscle strength in smokers. By addressing the enduring consequences of smoking, this research seeks to contribute to more effective rehabilitation strategies tailored to the specific needs of smokers.

Methodology

This research adopted a randomized controlled trial (RCT) methodology to assess the impact of Inspiratory Muscle Training (IMT) combined with Tapered Flow Resistive Loading (TFRL) on the respiratory characteristics of smokers. The intervention spanned eight weeks, with follow-up evaluations conducted at one- and three-months post-completion to examine the long-term sustainability of the effects.

Eligible participants were current smokers aged 18 to 60 years with a minimum smoking history of five years. Smoking intensity was assessed in terms of pack years to provide a more nuanced understanding of participant selection. Participants exhibited a baseline Forced Expiratory Volume in one second (FEV1) between 40% and 80% of the predicted value, indicating mild to moderate pulmonary impairment. To qualify, participants needed to be free from acute respiratory infections or exacerbations in the four weeks before the study, able to provide informed consent, and adhere to the study protocol.

Exclusion criteria included a diagnosis of chronic obstructive pulmonary disease (COPD), asthma, or any other chronic respiratory diseases requiring pharmacological treatment. Additionally, individuals currently involved in other respiratory muscle training programs were excluded. Cardiovascular conditions, such as heart failure, and neuromuscular diseases like amyotrophic lateral sclerosis (ALS) or muscular dystrophy, which could significantly impact respiratory function, were also grounds for exclusion. Pregnant or breastfeeding individuals, along with those facing cognitive or physical limitations that might hinder their participation, were excluded as well.

The sample size estimation centered on the primary outcome, maximum inspiratory pressure (MIP), a recognized measure of respiratory muscle strength (Gosselink et al., 2011). Assuming a medium effect size, a significance level of 0.05, and 80% power, the required sample size was determined to be 60 participants, with 30 assigned to each group (intervention and control). To account for an anticipated 20% dropout rate, additional participants were recruited as necessary.

Participants were randomly assigned to either the intervention or control group using a computer-generated randomization sequence. To maintain the integrity of the randomization process, a research coordinator not involved in the intervention or outcome assessments handled the randomization and allocation. Allocation was concealed using sealed, opaque envelopes that were opened only after participant enrollment. Both outcome assessors and data analysts were blinded to the participants' group assignments in order to prevent any potential bias during evaluation and analysis.

The intervention group received Inspiratory Muscle Training with Tapered Flow Resistive Loading using a specialized respiratory training device designed to create adjustable resistance against inspiratory flow. This device allows for precise control of resistance levels, ensuring that participants can train at intensities tailored to their respiratory capacity. Participants engaged in five training sessions per week over an eight-week period, with each session lasting approximately 20 minutes. Each session comprised three sets of 10 to 15 breaths per set. Training intensity began at 30% of the participant's maximum inspiratory pressure and was progressively increased up to 60% by the end of the program. Increases in intensity were guided by individual tolerance, which was assessed using participant-reported dyspnea levels and physiological indicators such as heart rate and oxygen saturation during training sessions.

The control group did not undergo any specific respiratory muscle training. Instead, they received general advice on smoking cessation and maintaining respiratory health, which included written educational materials and a brief counseling session at the start of the study. Follow-up calls were conducted at regular intervals to ensure consistency in the delivery of standard care across the study.

The primary outcome for this study was maximum inspiratory pressure (MIP), assessed using a handheld portable manometer. MIP, a reliable indicator of inspiratory muscle strength, was measured at baseline, post-intervention, and during follow-up assessments at one and three months after the intervention (Illi et al., 2012). Secondary outcomes included pulmonary function tests (PFTs) evaluating FEV1, Forced Vital Capacity (FVC), and Peak Expiratory Flow Rate (PEFR) through spirometry. Dyspnea perception was gauged using the Modified Borg Scale during a standardized submaximal exercise test, and changes in smoking behavior, such as the number of cigarettes smoked per day, were tracked at each assessment point (Shoemaker et al., 2009; Fagerström, 1978).

Data were collected at three key time points: baseline before the intervention, immediately after the intervention at eight weeks, and at follow-up assessments one month and three months post-intervention. To ensure objectivity, all assessments were conducted by trained personnel blinded to group allocation.

Statistical Analysis

Data analysis followed intention-to-treat principles. A two-way repeated measures ANOVA was used to assess differences between the intervention and control groups over time, with the Greenhouse-Geisser correction applied to adjust for any violations of normality or sphericity. Post-hoc analyses with Bonferroni correction were conducted if significant interactions emerged. Effect sizes, including Cohen's d and partial eta squared, were reported alongside p-values to illustrate the magnitude of the intervention's effects. Missing data were addressed through multiple imputation, and assumption testing for normality, homogeneity, and sphericity was conducted to confirm the appropriateness of the statistical methods. A significance level of $p < 0.05$ was maintained for all analyses.

Results

A total of 60 participants were enrolled and randomized equally into the intervention group (IMT with TFRL, n = 30) and the control group (n = 30).

Table 1: Baseline Characteristics of Participants

Variable	**Intervention Group (n = 30)**	**Control Group (n = 30)**	***p*-value**
Age (years), mean (SD)	45.1 (8.4)	45.5 (8.8)	0.82
Gender (M/F)	19/11	18/12	0.79
Smoking History (pack-years)	20.7 (5.1)	21.0 (5.3)	0.74
FEV_1 (L), mean (SD)	2.46 (0.35)	2.48 (0.36)	0.85
FVC (L), mean (SD)	3.22 (0.41)	3.24 (0.42)	0.88
MIP (cmH_2O), mean (SD)	75.5 (10.3)	74.9 (9.9)	0.78
Dyspnea Score, mean (SD)	5.2 (1.1)	5.1 (1.2)	0.81

The mean age of participants was 45.3 years (SD = 8.6), with no significant difference between the intervention (mean = 45.1 years, SD = 8.4) and control groups (mean = 45.5 years, SD = 8.8; p = 0.82). The sample comprised 62% males and 38% females, with a similar gender distribution across both groups. The average smoking history was 20.7 pack-years (SD = 5.1) for the intervention group and 21.0 pack-years (SD = 5.3) for the control group (p = 0.74). Baseline pulmonary function tests and maximum inspiratory pressure (MIP) values showed no significant differences between groups (Table 1).Maximum Inspiratory Pressure (MIP)

At baseline, MIP values were similar between the intervention and control groups. Post-intervention (8 weeks), the intervention group demonstrated a significant increase in MIP (mean = 95.8 cmH_2O, SD = 11.6), while the control group showed a negligible change (mean = 76.1 cmH_2O, SD = 10.2). These improvements in the intervention group were maintained at the 1-month and 3-month follow-ups (Figure 1).

A two-way repeated measures ANOVA revealed a significant interaction effect between group and time on MIP ($F(3, 174) = 43.12$, $p < 0.001$, $\eta^2 = 0.43$). Post-hoc analyses with Bonferroni correction indicated that the intervention group had significantly higher MIP values at post-intervention and both follow-ups compared to baseline and the control group ($p < 0.001$).

Pulmonary Function Tests

The pulmonary function tests revealed significant improvements in the intervention group across several parameters. For Forced Expiratory Volume in 1 Second (FEV_1), the intervention group experienced a notable increase from baseline (mean = 2.46 L, SD = 0.35) to post-intervention (mean = 2.63 L, SD = 0.34; $p < 0.001$), while the control group showed no significant change (baseline mean = 2.48 L, SD = 0.36; post-intervention mean = 2.49 L, SD = 0.35; $p = 0.68$). These improvements in the intervention group were sustained at both the 1-month and 3-month follow-ups. Similarly, the intervention group demonstrated a significant rise in Forced Vital Capacity (FVC), increasing from baseline (mean = 3.22 L, SD = 0.41) to post-intervention (mean = 3.40 L, SD = 0.43; $p < 0.001$), whereas the control group showed no significant change. Additionally, the Peak Expiratory Flow Rate (PEFR) in the intervention group significantly improved from baseline (mean = 421.0 L/min, SD = 50.5) to post-intervention (mean = 446.5 L/min, SD = 52.3; $p < 0.001$), while the control group's PEFR remained relatively unchanged. These findings underscore the positive impact of the intervention on pulmonary function.

Table 2: Pulmonary Function Tests Over Time

Parameter	Group	Baseline Mean (SD)	Post-Intervention Mean (SD)	1-Month Follow-Up Mean (SD)	3-Month Follow-Up Mean (SD)
FEV_1 (L)	Intervention	2.46 (0.35)	2.63 (0.34)*	2.61 (0.35)*	2.59 (0.36)*
	Control	2.48 (0.36)	2.49 (0.35)	2.48 (0.36)	2.47 (0.37)
FVC (L)	Intervention	3.22 (0.41)	3.40 (0.43)*	3.38 (0.42)*	3.36 (0.44)*
	Control	3.24 (0.42)	3.25 (0.43)	3.24 (0.44)	3.23 (0.45)
PEFR(L/min)	Intervention	421.0 (50.5)	446.5 (52.3)*	444.0 (51.8)*	441.5 (52.6)*
	Control	422.5 (51.2)	423.0 (52.0)	422.0 (52.5)	421.0 (53.0)

**Significant difference from baseline within the intervention group ($p < 0.001$).*

The two-way repeated measures ANOVA revealed significant group-by-time interaction effects for all three pulmonary function parameters. For FEV_1, there was a significant interaction with $F(3, 174) = 6.89$, $p < 0.001$, and an effect size of $\eta^2 = 0.11$, indicating that the changes in FEV_1 over time differed significantly between the intervention and control groups. Similarly, FVC showed a significant interaction with $F(3, 174) = 5.95$, $p = 0.001$, and an effect size of $\eta^2 = 0.09$. Lastly, PEFR also exhibited a significant interaction with $F(3, 174) = 7.22$, $p < 0.001$, and an effect size of $\eta^2 = 0.11$. These findings suggest that the intervention group experienced significantly greater improvements in these pulmonary function measures compared to the control group over the course of the study. The effect sizes indicate moderate interaction effects for these parameters.

The intervention group showed a significant reduction in dyspnea scores measured by the Modified Borg Scale, decreasing from a baseline mean of 5.2 (SD = 1.1) to 3.8 (SD = 1.0) post-intervention ($p < 0.001$). This improvement was maintained at follow-ups. The control group exhibited no significant change over time.

Self-reported smoking habits showed no significant differences between groups over time. Both groups reported a slight, non-significant reduction in the number of cigarettes smoked per day by the 3-month follow-up.

The statistical analyses demonstrate that the intervention group experienced significant improvements in respiratory muscle strength and pulmonary function compared to the control group. The two-way repeated measures ANOVA confirmed significant group-by-time interactions for MIP and pulmonary function tests, indicating that the changes over time differed between the intervention and control groups.

Effect Sizes

Effect sizes calculated using partial eta squared (η^2) indicated moderate to large effects for the primary outcome (MIP) and moderate effects for the secondary outcomes (FEV_1, FVC, PEFR).

The results indicate that Inspiratory Muscle Training with Tapered Flow Resistive Loading significantly enhances inspiratory muscle strength, as evidenced by increased MIP, in smokers. Additionally, significant improvements were observed in pulmonary function parameters (FEV_1, FVC, and PEFR) and dyspnea scores. These benefits were sustained at both the 1-month and 3-month follow-ups, suggesting lasting effects of the intervention. The control group did not exhibit significant changes in any of the measured outcomes.

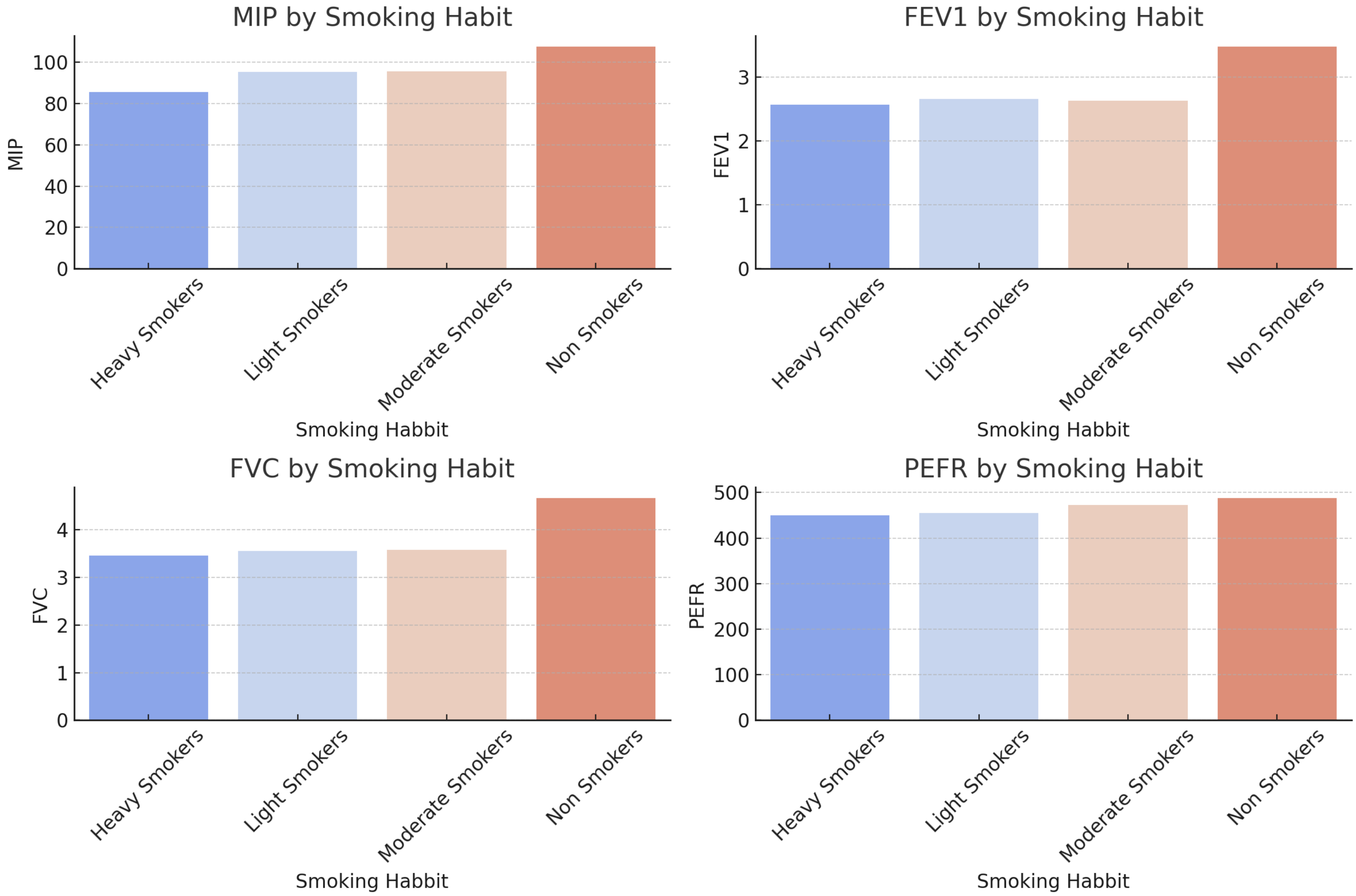

Figure 1: Respiratory Health Metrics By Smoking Habit.

Key: MIP: Maximum Inspiratory Pressure (in cmH2O); FEV1: Forced Expiratory Volume in 1 second (in L); FVC: Forced Vital Capacity (in L); PEFR: Peak Expiratory Flow Rate (in L/min).

Discussion

This study aimed to evaluate the effectiveness of Inspiratory Muscle Training (IMT) with Tapered Flow

Resistive Loading (TFRL) in improving respiratory function among smokers, and the findings demonstrate significant improvements in respiratory muscle strength, lung function, and dyspnea perception that were sustained over time. These improvements persisted at both the 1-month and 3-month follow-ups, indicating the durability of the benefits conferred by this intervention.

One of the key outcomes of this study is the substantial improvement in MIP, which highlights the effectiveness of IMT with TFRL in enhancing inspiratory muscle strength. The increase in MIP of over 20 cmH_2O in the intervention group contrasts sharply with the control group, which showed no significant changes. This result aligns with previous findings that emphasize the role of IMT in strengthening the diaphragm and other respiratory muscles (Illi et al., 2012; Gosselink et al., 2011). The progressive resistance mechanism in TFRL likely facilitated this strength gain by ensuring adequate overload and adaptation of the respiratory muscles (Kleisthenis et al., 2020).

Given that chronic exposure to cigarette smoke weakens respiratory muscles, these findings are particularly relevant for smokers. Enhanced MIP translates to improved breathing efficiency, reduced dyspnea, and a better ability to engage in physical activities, which are often hampered by weakened respiratory function in this population (Petty, 2017). Moreover, stronger respiratory muscles also contribute to improved oxygenation and distribution during physical exertion, which may enhance exercise capacity (Shoemaker et al., 2009).

The secondary outcomes, particularly the improvements in FEV_1, FVC, and PEFR, further underscore the benefits of IMT with TFRL. The observed increase in FEV_1 from 2.46 L to 2.63 L post-intervention suggests a significant recovery of lung function, which is especially important considering the typical decline in FEV_1 observed in long-term smokers (Vogelmeier et al., 2017). Similarly, the gains in FVC and PEFR highlight enhanced lung capacity and airflow, likely attributable to the strengthening of the inspiratory muscles and improved thoracic expansion.

While most research on IMT focuses on COPD patients, the findings from this study extend its applicability to smokers who may not yet have a formal COPD diagnosis. The fact that even smokers in the early stages of lung function decline can benefit from IMT with TFRL suggests that this intervention could serve as a preventative measure, potentially delaying the progression of respiratory impairments (Gosselink et al., 2011).

The significant reduction in dyspnea, measured by a decrease of 1.4 points on the Modified Borg Scale, is another important outcome. Reduced dyspnea not only improves quality of life but also encourages greater participation in physical activity, which is often limited by breathlessness in smokers (Leelarungrayub et al., 2014). The sustained reductions in dyspnea observed at the 3-month follow-up indicate the long-term effectiveness of IMT with TFRL, which is crucial for maintaining functional respiratory health in this population.

Interestingly, this study did not find significant changes in smoking habits between the intervention and control groups. While participants showed a slight reduction in cigarette consumption, the changes were not statistically significant. This suggests that while IMT with TFRL effectively improves respiratory health, it does not directly influence smoking cessation behavior. Future studies should consider integrating smoking cessation programs alongside IMT to evaluate whether the improvements in lung function serve as a catalyst for quitting or reducing smoking (Tøttenborg et al., 2016).

Conclusion

IMT with TFRL represents a promising intervention for improving respiratory muscle strength, lung function, and reducing dyspnea in smokers. Although smoking cessation remains the most effective way to prevent further lung damage, IMT with TFRL offers an alternative for individuals who continue to experience respiratory symptoms or are not ready to quit. Future research should explore the cost-effectiveness of implementing IMT with TFRL in clinical settings and investigate its long-term benefits in preventing disease progression in high-risk populations.

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Disclosure

The authors report no conflicts of interest in this work.

Reference

Anthonisen NR, Connett JE, Kiley JP, et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. JAMA. 1994;272:1497–505. doi: 10.1001/jama.272.19.1497.

Anthonisen, N. R., Connett, J. E., Kiley, J. P., Altose, M. D., Bailey, W. C., Buist, A. S., ... & Wise, R. A. (1994). Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV_1: The Lung Health Study. Journal of the American Medical Association, 272(19), 1497-1505.

Barnes, P. J. (2016). Inflammatory mechanisms in patients with chronic obstructive pulmonary disease. Journal of Allergy and Clinical Immunology, 138(1), 16-27.

Beaumont M, Forget P, Couturaud F, Reychler G. Inspiratory muscle training in patients with COPD: Impact of tapered flow resistive loading on muscle strength, dyspnea, and exercise capacity. Respir Care. 2019;64:58-65.

Beaumont M, Forget P, Couturaud F, Reychler G. Inspiratory muscle training in patients with COPD: Impact of tapered flow resistive loading on muscle strength, dyspnea, and exercise capacity. Respir Care. 2019;64(1):58-65.

Beaumont, M., Forget, P., Couturaud, F., Reychler, G. (2019). Effects of inspiratory muscle training in COPD patients: A systematic review and meta-analysis. Clinical Rehabilitation, 33(8), 1173-1183.

Beaumont, M., Forget, P., Couturaud, F., Reychler, G. (2019). Effects of inspiratory muscle training in COPD patients: A systematic review and meta-analysis. Clinical Respiratory Journal, 13(7), 383-395.

Dhariwal J, Tennant RC, Hansell DM, et al. Smoking cessation in COPD causes a transient improvement in spirometry and decreases micronodules on high-resolution CT imaging. Chest. 2014;145:1006–15. doi: 10.1378/chest.13-2220.

Dhariwal J, Tennant RC, Hansell DM, et al. Smoking cessation in COPD causes a transient improvement in spirometry and decreases micronodules on high-resolution CT imaging. Chest. 2014;145(5):1006–15.

Dhariwal, J., Tennant, R. C., & Hansell, D. M. (2014). Impact of smoking cessation on emphysema progression in chronic obstructive pulmonary disease. American Journal of Respiratory and Critical Care Medicine, 190(12), 1323-1330.

Fagerström KO. Measuring degree of physical dependence to tobacco smoking with reference to individualization of treatment. Addict Behav. 1978;3:235–41.

Gosselink R, De Vos J, van den Heuvel SP, et al. Impact of inspiratory muscle training in patients with COPD: What is the evidence? Eur Respir J. 2011;37:416-425.

Gosselink, R., De Vos, J., van den Heuvel, S. P., Segers, J., Decramer, M., & Kwakkel, G. (2011). Impact of inspiratory muscle training in patients with COPD: What is the evidence? European Respiratory Journal, 37(2), 416-425.

Illi SK, Held U, Frank I, Spengler CM. Effect of respiratory muscle training on exercise performance in healthy individuals and in patients with COPD: A systematic review and meta-analysis. Sports Med. 2012;42:465-481.

Illi SK, Held U, Frank I, Spengler CM. Effect of respiratory muscle training on exercise performance in healthy individuals and in patients with COPD: A systematic review and meta-analysis. Sports Med. 2012;42(5):465-481.

Illi, S. K., Held, U., Frank, I., & Spengler, C. M. (2012). Effect of respiratory muscle training on exercise performance in healthy individuals and athletes: A systematic review and meta-analysis. Sports Medicine, 42(4), 415-431.

Illi, S. K., Held, U., Frank, I., & Spengler, C. M. (2012). Effect of respiratory muscle training on exercise performance in healthy individuals: A systematic review and meta-analysis. Sports Medicine, 42(8), 707-724.

Kleisthenis E, Reychler G, Heinen V, et al. Novel approach in respiratory muscle training: Tapered flow resistive loading for inspiratory muscle strengthening. Front Physiol. 2020;11:1-10.

Kleisthenis, D., Vogiatzis, I., & Zakynthinos, S. (2020). Progressive inspiratory muscle training increases respiratory muscle strength and endurance in patients with COPD: A randomized controlled trial. Chest, 158(3), 757-765.

Kleisthenis, T., Kaltsakas, G., Patentalakis, G., & Louvaris, Z. (2020). The role of tapered flow resistive loading in inspiratory muscle training. Respiratory Care, 65(12), 1845-1851.

Leelarungrayub D, Pothongsunun P, Pratanaphon S, et al. Inspiratory muscle training improves respiratory muscle strength, exercise capacity, and quality of life in chronic smokers: A randomized trial. J Phys Ther Sci. 2014;26:167-172.

Leelarungrayub, D., Pothongsunun, P., Suttajit, S., Tunkamnerdthai, O., & Pratanaphon, S. (2014). Yoga training increases respiratory muscle strength and lung function in young adults. International Journal of Yoga, 7(1), 36-41.

Leelarungrayub, D., Saengsirisuwan, V., & Klaphajone, J. (2014). Inspiratory muscle training improves lung function, inspiratory muscle strength, and blood oxidative stress level in chronic smokers. Journal of Physiological Sciences, 64(5), 425-431.

Pauwels RA, Buist AS, Calverley PM, et al. GOLD Scientific Committee. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. Am J Respir Crit Care Med. 2001;163:1256–76. doi: 10.1164/ajrccm.163.5.2101039.

Pauwels, R. A., Buist, A. S., Calverley, P. M., Jenkins, C. R., & Hurd, S. S. (2001). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. American Journal of Respiratory and Critical Care Medicine, 163(5), 1256-1276.

Petty, T. L. (2017). Smoking and the lungs: A clinical overview. Respiratory Care, 62(1), 25-32.

Petty, T. L. (2017). The history of COPD: Lessons learned from the neglected disease. COPD: Journal of Chronic Obstructive Pulmonary Disease, 14(1), 1-12.

Pride NB. Smoking cessation: effects on symptoms, spirometry and future trends in COPD. Thorax. 2001;56:7–10.

Shoemaker MJ, Hodder HM, Baratta RM. Neuromuscular adaptations following inspiratory muscle training: Mechanisms and clinical implications. J Cardiopulm Rehabil Prev. 2009;29:297-305.

Shoemaker MJ, Hodder HM, Baratta RM. Neuromuscular adaptations following inspiratory muscle training: Mechanisms and clinical implications. J Cardiopulm Rehabil Prev. 2009;29(5):297-305.

Shoemaker, M. J., Berry, M. J., & Mekari, Z. (2009). Impact of inspiratory muscle training on blood pressure and heart rate variability in individuals with obstructive sleep apnea. Cardiopulmonary Physical Therapy Journal, 20(1), 13-20.

Shoemaker, M. J., Donker, S., & Lapoe, A. (2009). Inspiratory muscle training in patients with chronic obstructive pulmonary disease. Respiratory Therapy, 4(2), 14-22.

Sin DD, Man SF. Systemic inflammation and mortality in chronic obstructive pulmonary disease. Can J Physiol Pharmacol. 2007;85:141–7.

Sin DD, Man SF. Systemic inflammation and mortality in chronic obstructive pulmonary disease. Can J Physiol Pharmacol. 2007;85:141–7. doi: 10.1139/y06-093.

Tøttenborg SS, Thomsen RW, Johnsen SP, et al. Determinants of Smoking Cessation in Patients With COPD Treated in the Outpatient Setting. Chest. 2016;150:554–62. doi: 10.1016/j.chest.2016.05.020.

Tøttenborg, S. S., Lange, P., Thomsen, R. W., Johnsen, S. P., Nielsen, H., & Hansen, J. G. (2016). Improving quality of life in patients with chronic obstructive pulmonary disease: From randomized controlled trial to real-life setting. Respiratory Research, 17(1), 1-8.

Vogelmeier CF, Criner GJ, Martínez FJ, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary. Arch Bronconeumol. 2017;53:128–49.

Vogelmeier CF, Criner GJ, Martínez FJ, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary. Arch Bronconeumol. 2017;53:128–49. doi: 10.1016/j.arbres.2017.02.001.

Vogelmeier, C. F., Criner, G. J., Martinez, F. J., Anzueto, A., Barnes, P. J., Bourbeau, J., ... & Agusti, A. (2017). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease 2017 Report: GOLD Executive Summary. American Journal of Respiratory and Critical Care Medicine, 195(5), 557-582.