# LITERATURE REVIEW

# The Effects of Inspiratory Muscle Training in Lung Cancer Patients: A Scoping Review

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### ARTICLE INFO

# Article history: Received 23 July 2024 Received in revised form 12 December 2024 Accepted 13 December 2024

Available online 30 January 2025

*Keywords:* Cancer, Dyspnea, Inspiratory muscle training, Lung cancers.

Cite this as:

Kadir Y, Sabirin RM, Hasyim AA, et al. The Effects of Inspiratory Muscle Training in Lung Cancer Patients: A Scoping Review. J Respi 2025; 11: 75-82.

# ABSTRACT

**Introduction**: Lung cancer is the leading cause of cancer worldwide, with a high mortality rate. Chronic dyspnea promotes a pathologic cycle of decreased activity, which has been shown to limit exercise tolerance and deteriorate quality of life (QoL). Inspiratory muscle training (IMT) is a resistance-based exercise regimen that aims to improve the strength and endurance of the inspiratory muscles, thereby reducing respiratory symptoms. This study aimed to comprehensively review the possible beneficial effects of IMT on various aspects of lung cancer patients.

**Methods**: The PubMed, Embase, and Cochrane databases were searched from inception to 20 May 2024. All clinical trials examining the impact of IMT on lung cancer patients, utilizing either quantitative or qualitative approaches, were included. The extracted data were then descriptively presented, focusing on the main themes to provide a comprehensive literature review.

**Results:** This scoping review identified 9 unique studies comprising eight randomizedcontrolled trials and one retrospective cohort study with 460 lung cancer patients. An IMT regimen was proven to reduce sedentary behavior and significantly improve physical activity and health-related quality of life (HRQL). Furthermore, the IMT program reduced dyspnea, improving maximum inspiratory pressure (PImax) and 6-minute walking test (6MWT). It also provided the benefits of shorter postoperative stay and reduced patient distress concerning dyspnea.

**Conclusion:** Inspiratory muscle training provides several benefits, including improvements in dyspnea indexes, exercise tolerance, and overall HRQL. Further studies are required to determine the optimal IMT regimen for this special population.

### **INTRODUCTION**

Lung cancer continues to be the leading cause of cancer-related deaths worldwide.<sup>1</sup> The mortality rate from lung cancer is similar across regions, with 43% of deaths in more developed countries and 57% in less developed countries.<sup>2</sup> In Indonesia, lung cancer accounts for 12.6% of all cancer deaths, making it the top cause of cancer-related mortality.<sup>3</sup> Lung cancer accounted for 8.6% of all cancer cases in 2018, trailing only breast, cervical, and colorectal cancer.<sup>3</sup> The annual incidence is projected to nearly double from 30,023 in 2018 to 54,983 by 2040.<sup>3</sup> Survival rates for lung cancer largely depend on the disease stage and treatment approach.

The most frequently encountered symptoms of lung cancer include shortness of breath (dyspnea), cough, hemoptysis, chest pain, and weight loss.<sup>6</sup> Literature suggests that approximately 75% of patients suffer from dyspnea, and around 90% experience it in the month leading up to their death.<sup>7</sup> Dyspnea is a subjective and multifaceted experience of breathing discomfort. The understanding of "dyspnea"

Jurnal Respirasi, p-ISSN: 2407-0831; e-ISSN: 2621-8372.

Accredited No. 79/E/KPT/2023; Available at https://e-journal.unair.ac.id/JR. DOI: 10.20473/jr.v11-I.1.2025.75-82



Even with progress in understanding the genetic development of lung cancer, enhanced diagnostic precision, and improved multimodal treatments, the prognosis has not markedly improved, with the 5-year survival rate remaining stagnant at 15% for more than three decades.<sup>4,5</sup>

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has evolved significantly, leading to the professional consensus on the term "chronic breathlessness syndrome," which refers to persistent breathlessness despite optimal treatment of the underlying cause, resulting in disability.<sup>7</sup> This persistent dyspnea, combined with fatigue, establishes a harmful cycle of decreased activity, which is expected to reduce exercise tolerance and negatively affect quality of life (QoL).<sup>8</sup>

Since the 1980s, non-pharmacological methods like inspiratory muscle training (IMT) have managed breathing problems. Inspiratory muscle training is a resistance-based exercise program to improve the strength and endurance of the inspiratory muscles. This enhancement helps alleviate respiratory symptoms, boost exercise capacity, and improve health-related QoL. By fortifying the inspiratory muscles, IMT decreases the effort needed for breathing, thereby reducing dyspnea.<sup>9-11</sup> Inspiratory muscle training is often performed with a threshold device that enables airflow during inspiration only after attaining a particular inspiratory pressure, which is adjusted via spring tension that corresponds with a patient's maximal inspiratory pressure. The training load is progressively increased over several initial breaths until the full load has been obtained in the subsequent breaths. This resistance is intended to mimic the length-tension balance of the inspiratory muscles, resulting in consistent training across all lung volumes.<sup>12,13</sup>

training Inspiratory muscle has gained considerable attention for its advantages in pulmonary rehabilitation, such as higher maximum inspiratory pressure, a better sense of wellness, and augmented medical status in patients with advanced cardiac conditions, pulmonary disorders, and exercise-induced breathlessness.<sup>13</sup> Additionally, a previous study showed that IMT could induce structural alterations in inspiratory muscle fibers.<sup>14</sup> Improvement of inspiratory muscle endurance and strength with IMT technique might potentially help to ameliorate dyspnea, consequently boosting activity levels and enhancing the QoL for patients with respiratory conditions, including those with lung cancer.<sup>11</sup> This study aimed to comprehensively review the potential benefits of IMT across different aspects in patients with lung cancer. To the best extent of our understanding, this represents the most recent scoping review dedicated to this topic.

# METHODS

Scoping reviews summarize existing research on a particular subject or study issue. Before conducting the literature scan and data collection, the review methodology was created by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews (PRISMA-ScR). The approach included five major steps: defining the research question (in this case, investigating scientific evidence related to the implementation of IMT in lung cancer patients), searching for suitable studies, acquiring studies, retrieving and categorizing information, and then demonstrating the findings.<sup>15,16</sup>

### Search Strategy

The topic question and search approach were developed using the PCC framework (P: Population, C: Concept, and C: Context). The PubMed, Embase, and Cochrane databases were examined independently from inception to 20 May 2024 by two reviewers. The terms "Lung Cancer," "Inspiratory Muscle Training," and "Respiratory Muscle Training" and their corresponding keywords were utilized. To ensure consistency and minimize bias, these terms and keywords were employed individually and in combination, respecting the specific database requirements. Searches employed terms combined with "AND" and "OR" connectors and were not restricted by a specific time frame. Manual searches of the references from included studies were also performed to find additional related research.

### **Eligibility Criteria**

Study inclusion and exclusion criteria were established before commencing the searches. All clinical trials investigating the effects of IMT on lung cancer patients, using either quantitative or qualitative methods, were included. Articles exploring IMT in conditions other than lung cancer were excluded, as were non-English articles and publications over ten years ago. The headings and abstracts of the acknowledged papers were arranged, and duplicates were removed. Two reviewers independently evaluated the research titles and abstracts to obtain studies of interest. Any issues about inclusion or exclusion were handled by consulting with the third reviewer.

### **Data Extraction**

To finalize the review sample, both reviewers thoroughly evaluated the papers listed according to their eligibility requirements. The reviewers extracted and qualitatively presented information such as authorship, publication year, study methods (including study design, participants, and intervention), primary results, and conclusions from the articles. Data were then descriptively analyzed, focusing on the main themes to provide a comprehensive literature review.

# RESULTS

Following searches of various databases, 98 research papers were discovered. Forty-seven identical articles were eliminated, resulting in 51 distinct works. Both reviewers reviewed the titles and abstracts of these 51 publications separately, and 36 articles were excluded because they did not fit the inclusion criteria.

The remaining 15 articles were then sought for retrieval. However, two were unable to be obtained. The entire texts of the remaining 13 publications were then examined to establish their significance to the aim fo the study. Following this full-text review, five articles were removed because they did not address IMT in lung cancer patients. The final sample of this scoping research consisted of eight studies (Figure 1).





Table 1 depicts the studies' major overview, which includes authorship, publication year, study

methodology, results, and conclusion.

No.Author (year)	) Study Design	Study Participants	Study Intervention	Results	Conclusion
1. Ha, et al. (2023) <sup>9</sup>	Pilot randomized trial	28 lung cancer patients	12-week telemedicine- based IMT and walking vs general exercise	Significant improvement in HRQL (SES: -1.03 to -1.30), increased moderate- vigorous intensity physical activity (SES: 1.08), and reduced sedentary behavior (SES: 0.94)	Telemedicine-based IMT combined with walking was practical, suitable, and secure among patients who had undergone curative therapy, with the potential of interrupting the "dyspnea-inactivity" cycle
2. Sakai, <i>et al.</i> (2023) <sup>8</sup>	Retrospective cohort	71 lung cancer patients	2-week IMT and exercise therapy vs. exercise therapy only	Significant changes in PImax, with values increasing from $33.2\pm7.2$ cmH <sub>2</sub> O at baseline to $40.3\pm8.4$ cmH <sub>2</sub> O at week 1 and further to $42.2\pm8.4$ cmH <sub>2</sub> O at week 2 (p<0.01). Dyspnea at rest decreased notably, from $2.3\pm0.9$ mBS at baseline to $1.4\pm0.9$ mBS at week 1 and $1.3\pm1.0$ mBS at week 2 (p<0.01). Similarly, dyspnea at exertion was significantly reduced, from $3.8\pm0.8$ mBS at baseline to $2.9\pm1.0$ mBS at week 1 and further to $2.6\pm0.9$ mBS at week 2 (p<0.01).	IMT is effective and has a considerable tenacity rate in those who experience breathlessness and cannot conduct intense physical treatment
3. Liu, <i>et al.</i> (2021) <sup>17</sup>	Randomized controlled trial	63 lung cancer patients undergoing VATS	6-week IMT and aerobic exercise vs. standard perioperative pulmonary rehabilitation program	Significant improvement in PImax at week 6 (difference: $22.7+2.1 \text{ cmH}_2\text{O}$ , p=0.018), PEmax at week 2 (difference: $20\pm3.9 \text{ cmH}_2\text{O}$ , p=0.015), and week 12 (difference: $22.5+15.1$ , p=0.012), significant improvement of lung expansion volume at week 2 (difference: $377\pm191$ , p=0.02) and week 12 (difference: $685\pm291$ , p<0.001), improvement of 6MWT at week 2 (difference: $80\pm4\text{m}$ , p=0.002), week 6 (difference: $59\pm10\text{m}$ , p=0.007) and week 12 (difference: $42\pm7\text{m}$ , p=0.036)	The combined use of IMT and aerobic exercise for 6 weeks enhanced the strength of respiratory muscles and exercise endurance starting at two weeks after VATS
Messagi- 4. Sartor, <i>et al.</i> (2019) <sup>18</sup>	Randomized controlled trial	37 NSCLC patients after tumor resection	8-week aerobic exercise and IEMT vs. standard physical activity	Substantial improvement in VO <sub>2</sub> peak (2.13 mL/Kg/min), PImax (18.96 cm $H_2O$ ), and PEmax (18.58 cm $H_2O$ )	Eight-week fitness regimen involving aerobic activity along with IMT enhanced exercise tolerance and breathing muscle endurance following lung resection
5. $\frac{\text{Brocki, et al.}}{(2018)^{19}}$	Randomized controlled trial	68 lung cancer patients undergoing lung resection	2-week postoperative IMT vs. standard physiotherapy	Less sedentary activity 2 weeks after surgery (sedentary 6%, light activity 56%, moderate activity 38%) as opposed to control group (sedentary 22%, light activity 66%, moderate activity 12%; $p = 0.006$ )	In high-risk individuals, IMT tends to avert a reduction in physical activity.
6. Lai, <i>et al</i> . (2017) <sup>20</sup>	Randomized controlled trial	60 lung cancer patients undergoing lobectomy	1-week preoperative IMT and aerobic endurance training vs. standard pulmonary rehabilitation	Significant differences were observed in the following measures: 6MWD (difference: 19.2 m, p=0.029), PEF (difference: 18.0 L/min, p<0.001), postoperative LoS (3.5 days, p=0.010), and total hospital stay (3.7 days, p=0.012)	Intensive lung rehabilitation program (IMT plus endurance exercise) preoperatively could be an effective rehabilitation approach for elderly patients planning for surgery, with beneficial physical and psychological consequences
7. Brocki, <i>et al.</i> $(2016)^{21}$	Randomized controlled trial	68 lung cancer patients undergoing lung resection	2-week IMT postoperatively vs. regular physical therapy	Significant improvement in SpO <sub>2</sub> levels (day 3 postoperative: $93.8\pm3.4$ , day 4 postoperative: $93.5\pm3.5$ , p=0.02)	Compared to regular physical therapy alone, two weeks of IMT improved oxygenation in susceptible patients recovering from surgery
8. Molassiotis, <i>et al.</i> (2015) <sup>11</sup>	Feasibility randomized trial	46 lung cancer patients	12-week IMT sessions vs. standard care	Statistical differences were observed in several areas: difficulties with dyspnea $(p=0.03)$ , ability to manage dyspnea $(p=0.01)$ , contentment from dyspnea control $(p=0.001)$ , exhaustion $(p=0.005)$ , mental performance $(p=0.011)$ , proficiency in managing dyspnea $(p=0.015)$ , and depression $(p=0.028)$	IMT is practical and beneficial in individuals with lung cancer

### Table 1. Summary of the studies assessed in the scoping review

6MWD: 6-minute walking distance; 6MWT: 6-minute walking test; HRQL: health-related quality of life; IEMT: inspiratory-expiratory muscle training; IMT: inspiratory muscle training; LoS: length of stay; mBS: modified Borg scale; NSCLC: non-small cell lung cancer; PEF: peak expiratory flow; PEmax: maximum expiratory pressure; PImax: maximum inspiratory pressure; SES: standardized sife effect; SpO<sub>2</sub>: oxygen saturation, VATS: videoassisted thoracoscopic surgery; VO<sub>2</sub> peak: peak oxygen uptake

Of the eight articles included in the analysis, seven were a randomized controlled trial, and one was a retrospective cohort study. This scoping review comprised 441 lung cancer patients as the study cohort. The latest randomized trial by Ha, et al. (2023) noted that a 12-week inspiratory muscle training significantly enhanced health-related quality of life (HRQL), accompanied by improvement of moderate to vigorous intensity activity levels and reduced sedentary habits.9 The authors stated that IMT is a practical, suitable, and secure method to disrupt lung cancer patients' "dyspneainactivity" spiral.9 This result was in line with a previous study by Brocki, et al. (2018), which demonstrated a sedentary activity reduction of two weeks postoperatively in lung cancer patients undergoing lung resection.19

Three studies by Sakai, et al. (2023), Liu, et al. (2021), and Messagi-Sartor, et al. (2019) found a significant improvement in maximum inspiratory pressure (PImax) with a 2-week, 6-week, and 8-week IMT regimen, respectively.<sup>8,17,18</sup> Moreover, using a modified Borg scale as the measuring instrument, Sakai, et al. (2023) demonstrated a significant reduction of dyspnea at rest and exertion.<sup>8</sup> They found that IMT was particularly useful for lung cancer patients who could not tolerate vigorous physical rehabilitation.<sup>8</sup> Liu, et al. (2021) further demonstrated an improvement in maximum expiratory pressure (PEmax), lung expansion capacity, and 6-minute walking test (6MWT) as early as the second-week post-VATS.<sup>17</sup> The same result was also described by Lai, et al. (2017), who found a significantly longer 6-minute walking distance (6MWD) in patients undergoing lobectomy.<sup>20</sup> Huge beneficial effects of reduced postoperative and total hospital stay in these patients accompanied this positive result.

# DISCUSSION

In this scoping review, we found that IMT offers several benefits for lung cancer patients, primarily by alleviating dyspnea symptoms associated with the disease. These findings are pivotal for reducing breathlessness and enhancing health-associated QoL in this population. Dyspnea is a critical patient-centered symptom that significantly affects HRQL in those with lung cancer. A high burden of dyspnea can diminish functional exercise capacity and worsen survival rates. Dyspnea intensifies following lung cancer surgery due to a 10-15% decrease in lung function. Over half of those with lung cancer who have survived develop clinically significant dyspnea.<sup>22,23</sup>

Lung cancer survivors often experience worsening dyspnea after curative therapy, which can continue for a considerable time, irrespective of the treatment approach. This condition can arise due to excised or injured lung tissue, harmed or detached nerve filaments, and heightened stimulation of peripheral receptors. Changes in the wall of the thoracic cage, breathing muscles, and respiratory tract can lead to neuromechanical dissociation and increased central 'corollary discharge'.<sup>24,25</sup> Patients found the effort required to breathe to be particularly distressing, and this was accompanied by other symptoms such as fatigue, anxiety, loss of appetite, and a decline in the overall sense of well-being and QoL.<sup>7</sup>

Inspiratory muscle training was previously granted as a promising therapy for people with impaired respiratory muscles. A study of the effects of IMT on inspiratory muscle durability, exercise tolerance, dyspnea, and QoL in adults with COPD found that IMT regimen significantly enhanced outcomes in inspiratory muscle strength (PImax), endurance, physical activity capability, peak activity rate, and dyspnea.<sup>26</sup> A different study discovered that a minimalintensity workout regimen ameliorated pulmonary function, especially vital capacity, in stable COPD patients with PImax levels below 60 cmH<sub>2</sub>O.<sup>27</sup> Inspiratory muscle training has also been shown to drastically enhance PImax, dyspnea, Borg scale ratings, respiratory muscle endurance, incremental load pressure, exercise capacity, and health-associated QoL in COPD patients.<sup>27</sup>

Continuous pulmonary inflammation caused by several cytokines in COPD promotes a protumor microenvironment, which contributes to lung cancer. Reduced mucociliary clearance may also allow carcinogens to linger in the lungs for an extended time. Furthermore, the COPD lung microbiome differs from healthy people's, potentially promoting inflammatory that contribute responses to lung cancer pathogenesis.<sup>28,29</sup> As COPD patients are more inclined to develop lung cancer, it is possible that IMT could benefit individuals with lung cancer. Several studies have indicated that it is uncertain how the progression of COPD affects lung cancer vulnerability, the possibility that similar primary factors drive both diseases, or if it is a mix of these factors.<sup>30,31</sup> Furthermore, the majority of individuals with lung cancer additionally suffer from COPD, as the two conditions are primarily attributable to cigarette use. As a result, a multitude of the manifestations of lung cancer parallel those of COPD. 30,31

Individuals with COPD and lung cancer exhibit elevated airflow restriction, air accumulation, and lung hyperventilation, putting their respiratory muscles under constant strain. Ventilation becomes shallower and faster, causing symptoms including shortness of breath and decreased exercise capacity. As a result, patients may limit their everyday activities, which can exacerbate their dyspnea and lower their exercise tolerance as well as their QoL.<sup>11</sup> Improving inspiratory muscle function can assist in preserving the balance between the inspiratory muscles' ability to facilitate breathing and the inspiratory burdens imposed on them, potentially reducing these symptoms.<sup>32</sup>

Breathing muscle performance has successfully been enhanced within the first few days following surgery with preoperative IMT at 30-60% PImax for at least two weeks before the procedure, eliminating the likelihood of postoperative pulmonary issues by 50%.<sup>33</sup> Following pulmonary dissection, the dynamic efficacy of the breathing muscles, particularly the diaphragm, might be hindered due to pleural adhesions and temporary chest wall deformation. Similarly, removing lung sections might impede ventilatory performance postoperatively, particularly among high-risk patients.<sup>34</sup> The premise behind IMT in this situation is that conditioning with greater inspiratory resistance may aid in postoperative lung expansion, preserve the integrity of the distal airways, and consequently strengthen diaphragm movement. This could lead to stronger expiratory efforts for secretion clearance, contributing to a quicker restoration of lung function.<sup>21</sup>

Inspiratory muscle training is a safe procedure that might induce only short-term adverse effects. According to Souza, et al. (2014), 13% of participants in the intervention group reported respiratory distress during the sessions.<sup>35</sup> However, this adverse effect ceased during the training protocol.<sup>35</sup> Nausea after training sessions was also reported, although this adverse effect ceased after the first month of the training protocol.<sup>35</sup> They explained that since all volunteers had a low initial PImax, respiratory distress during the sessions was caused by the higher effort to open the inspiratory valve of the training device.<sup>35</sup> Nausea following training may be due to the use of the mouthpiece, which generates a mouth-breathing pattern correlated to hyperventilation during IMT. Other reported side effects of IMT include paradoxical breathing, desaturation, hemodynamic instability, and supraventricular tachycardia.36

It is important to acknowledge the limitations of this scoping review. The topic is still nascent in this field of research, as just eight studies were identified in the three sources reviewed. Several limitations were noted in these papers, including small sample sizes and inadequate evaluation of other parameters (such as cancer stage, treatment regimen, and comorbidities) that could impact study outcomes. Additionally, the search was restricted to English-language publications, potentially omitting relevant studies and introducing bias into the findings. Regardless of its restrictions, this scoping study provided a solid framework for further research. We highlighted the need for more robust studies to provide accordant scientific evidence and potentially establish standardized recommendations regarding the use of IMT for individuals with lung cancer.

### SUMMARY

Lung cancer is among the most prevalent type of cancer globally, with a high fatality rate. Chronic dyspnea in lung cancer patients reduces exercise tolerance and overall QoL. Inspiratory muscle training, a resistance exercise regimen, has increased inspiratory muscle strength and endurance. It provides several benefits, including improvements in dyspnea indexes, tolerance for physical activity, and overall healthassociated QoL. Additional research is needed to identify this population's most effective IMT regimen.

### Acknowledgments

None declared.

### **Conflict of Interest**

The authors declared there is no conflict of interest.

### Funding

None declared.

### **Authors' Contributions**

Conceptualizing, designing: YK, SS. Collecting data, and interpreting results: YK, RMS, AAH. Preparing manuscript and revising: YK, RMS, AAH, RMI, SS. All authors contributed and approved the final version of the manuscript.

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