gastroenterology insights

Systematic Review

The Effect of Inspiratory Muscle Training on Gastroesophageal Reflux Disease Characteristics: A Systematic Review

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Abstract: Background/Objective: Gastroesophageal reflux disease (GERD) is multifactorial and affects an increasing number of people. It is a common condition in which the stomach contents move up into the esophagus; thus, its main cause is found in the antireflux valve mechanism of the gastroesophageal junction. This consists of two sphincters, the lower oesophageal and the diaphragmatic. The disease has been related to diaphragm dysfunction, either due to the de-coordination of the diaphragms' contractility or due to decreased strength. Breathing exercises seem to have a positive effect in this population. The aim of this study was to systematically examine the effects of inspiratory muscle training (IMT) on GERD characteristics. **Methods:** We conducted a systematic review of research up to April 2024 in Scopus, PubMed, and Science Direct. We included randomized controlled trials (RCTs) and clinical trials assessing the effects of IMT on GERD characteristics. Methodological quality was assessed with the PEDro scale (Physiotherapy Evidence Database) and the Newcastle Ottawa scale (NOC). **Results:** Among the 1984 studies identified from the search, only three studies (one study with a post-COVID-19 population and two with GERD and healthy subjects) were included in this study, as they presented a fair to high methodological quality. Significant improvements in maximal inspiratory pressure ($p < 0.001$) and diaphragmatic excursion ($p < 0.001$) were revealed in one study. No significant differences between groups were mentioned for the reflux symptoms and for LES–EGJ pressure in the studies included. **Conclusions:** IMT seems to provide promising effects in strengthening the antireflux valve mechanism, as it increases MIP and diaphragmatic excursion. This systematic review established a bibliographic gap for the contribution of IMT in the antireflux valve mechanism. More evidence is needed to support the importance of IMT as a non-pharmacological intervention for GERD patients.

Keywords: inspiratory muscle training; gastroesophageal reflux disease; antireflux valve; maximum inspiratory pressure

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Academic Editor: Ludovico Abenavoli

Received: 26 December 2024
Revised: 5 February 2025
Accepted: 10 February 2025
Published: 12 February 2025

Citation: Syropoulos, S.; Moutzouri, M.; Grammatopoulou, E.; Patsaki, I. The Effect of Inspiratory Muscle Training on Gastroesophageal Reflux Disease Characteristics: A Systematic Review. *Gastroenterol. Insights* **2025**, *16*, 7. https://doi.org/10.3390/gastroent16010007

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1. Introduction

Gastroesophageal reflux disease (GERD) is a chronic disease of the upper gastrointestinal system in which gastric fluid flows into the oesophagus persistently and regularly. This leads to the appearance of oesophageal (heartburn) and extraesophageal symptoms (chronic cough, wheezing) [1]. Due to the complexity of diagnosing and managing GERD, a consensus (The Lyon Consensus 2.0) was formulated to update the criteria for diagnosing gastro-oesophageal reflux disease (GERD), focusing on the necessity of conclusive evidence from oesophageal testing to support diagnosis and management. The modern definition requires conclusive evidence of reflux-related pathology on endoscopy and/or abnormal reflux monitoring (using Lyon consensus thresholds) in the presence of compatible troublesome symptoms [2].

The main cause of the disease is located at the valve mechanism between the oesophagus and the stomach that acts as a barrier to reflux [3]. This antireflux barrier includes two sphincters, the lower oesophageal and an external one, known as the diaphragmatic sphincter. The two sphincters relax (shallow induced relaxation) during swallowing and the opening of the LES, and the diaphragmatic sphincter allows the swallowed bolus to be easily pushed into the stomach [4,5] and then contracts. They create pressure that is higher than the intra-abdominal pressure, preventing the reflux of gastric contents. Yet, LES and diaphragmatic sphincter distensibility are increased in reflux disease, thus leading to a greater opening of the diaphragmatic sphincter and allowing reflux to happen. A less distensible LES and diaphragmatic sphincter will result in a smaller opening, which causes a relative outflow obstruction to the bolus [5]. The diaphragmatic sphincter is also affected by the diaphragmatic excursion. Abnormal changes in intra-thoracic and intra-abdominal pressures could lead to a decreased excursion and diaphragmatic dysfunction. This weakens the barrier effect of the lower oesophageal sphincter against regurgitation [6–8]. There is also the case of transient LES relaxation (t LRESR) that accounts for small amounts of regurgitation during the day. TLESR is a physiological mechanism for the retrograde flow of stomach contents into the esophagus in cases of benching, vomiting, etc. The presence of tLESR is defined by the absence of a pharyngeal swallow signal for 4 s before to 2 s after the onset of LES relaxation. An important component of tLESR is the complete inhibition of the diaphragmatic sphincter. The normal reflux barrier is disrupted in cases of an increased frequency of transient relaxation of the lower oesophageal sphincter and the diaphragmatic sphincter. When considering that the GERD population has an increased number of tLESRs, and its effect on the diaphragmatic sphincter, we can easily understand how this could further contribute to reflux [5].

Due to regurgitation, the oesophageal epithelium is prone to the inflammatory effect of hydrochloric acid, leading to the serious injury of the mucosa. Hydrochloric acid is one of the most toxic components of the gastric fluid and is the main cause of oesophageal irritation and symptoms [9].

Currently, changes in daily life and medication present the standard treatment of GERD. Medication therapies include proton pump inhibitors and h2 blockers [10], with significant side effects. Another solution in more severe cases is surgery [10,11].

Over the past few years, the effectiveness of respiratory physiotherapy has been investigated in reducing GERD symptoms. Inspiratory muscle training might increase the lower Oesophageal sphincter (LOS) pressure, which in turn strengthens the protective mechanism of the gastroesophageal junction (GEJ) and reduces the gastric acid exposure [12]. Thus, medication use and the possibility of surgery might be reduced [13].

In recent years, IMT seems to have provided further promising results. This is a more targeted intervention for strengthening the diaphragm. Threshold trainers enable a personalized prescription of the exercise by adjusting the intensity in relation to patients' maximal inspiratory pressure (MIP). Some preliminary results showed an alleviation of GERD symptoms and an enhancement of the antireflux valve mechanism [14].

It is important to bear in mind that GERD has been found to have significant effects on respiratory function compared to healthy controls. More specifically, a GERD population with no respiratory condition has been found to present increased expiratory flow resistance and decreased MIP in relation to normal reference values [15,16]. Additionally, a significant association of lung diffusion with GERD has been found [17]. The findings suggest that the GERD population may present with a restrictive or/and obstructive airway pathology [15]. Two different mechanisms are responsible for the generation of respiratory symptoms due to GERD. The first refers to the micro-aspiration of gastric fluids into the lungs, resulting in irritation and inflammation. The second refers to bronchoconstriction caused by the stimulation of the vagal reflex from the distal esophagus due to acid reflux into the upper esophagus [18].

The aim of our work was to systematically review the published literature regarding all of the potential therapeutic effects of IMT on the GERD population.

2. Materials and Methods

The present study was conducted following the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) guidelines [19].

2.1. Search and Study Identification

A thorough search for appropriate published studies was performed by two authors (S.S. and I.P.) independently in Pubmed, Science Direct, and Scopus. The search terms used following the PICO framework were as follows:

- Population: GERD OR reflux gastroesophageal disease OR anti-reflux barrier;
- Intervention: respiratory physiotherapy OR inspiratory muscle training OR respiratory muscle training;
- Outcome: maximal inspiratory pressure OR lower esophageal sphincter.

The following search strategies were created: ("inspiratory muscle training and GERD or antireflux barrier"), ("respiratory physiotherapy and GERD or lower esophageal sphincter"), and ("respiratory muscle training and GERD or maximal inspiratory pressure"). Additionally, a search was performed by hand in all of the reference lists of the articles that were identified.

The inclusion criteria were as follows:

- Study design: randomized controlled trials (RCTs) or clinical trials;
- Study population: adults that were diagnosed with GERD;
- Intervention: IMT through a threshold device;
- Outcomes: MIP, LOS pressure, symptoms, quality of life, MIP, esophagogastric junction pressure, and diaphragmatic excursion.

The exclusion criteria were as follows:

- Article published in a language other than English;
- Availability of full text;
- Reviews, technical notes, case reports, letters to editors, encyclopedias, and scientific chapters.

Two authors independently screened the titles and abstracts for the relevant studies and the same individuals assessed the full texts of all eligible studies. Potential disagreements were discussed and resolved by the adjudication of a third author.

2.2. Methodological Quality

The quality of the included RCT studies was evaluated by the Physiotherapy Evidence Database (PEDro) scale, a valid and reliable tool [19]. Total scores from 6 to 10 referred to high quality, a score of 4–5 was considered to be fair quality, and $\leq$3 reflected a poor quality. The grading of each study was carried out separately by two physical therapists with knowledge in the study of scientific research. Different ratings and unclear issues were discussed, and disagreements were resolved by the adjudication of a third author [19].

The quality of the prospective studies was evaluated by the Newcastle Ottawa scale (NOS) [20]. The NOS contains eight items grouped under three components: selection, comparability, and outcome. For each item, a series of response options is provided. A star system is used to allow for a semi-quantitative assessment of study quality, such that the highest quality studies are awarded a maximum of one star for each item, except for the item related to comparability that allows for the assignment of two stars. The NOS score ranges from zero to nine stars [20]. Good quality refers to 3 or 4 stars for the selection component, 1 or 2 stars for the comparability, and 2 or 3 stars for the outcome component. Fair quality is 2 stars for the selection component, 1 or 2 stars for the comparability component, and 2 or 3 stars for the outcome component. Poor quality is 0–1 star for the selection component or 0 stars in comparability or 0–1 star in outcome [20].

3. Results

3.1. Identification of Studies

A total of 1984 studies were identified from the search. From these, 17 were removed before screening as they were duplicates; 354 via automation tools as they were reviews, conference papers, chapters, etc.; and 14 as they were non-English studies. Then, 1599 studies were screened based on their titles and abstracts. Having excluded studies with different populations and other types of interventions, we assessed the full text of five studies. Three studies investigating the role of IMT through a threshold device for the GERD population were included in this review. A detailed flowchart is presented in Figure 1.

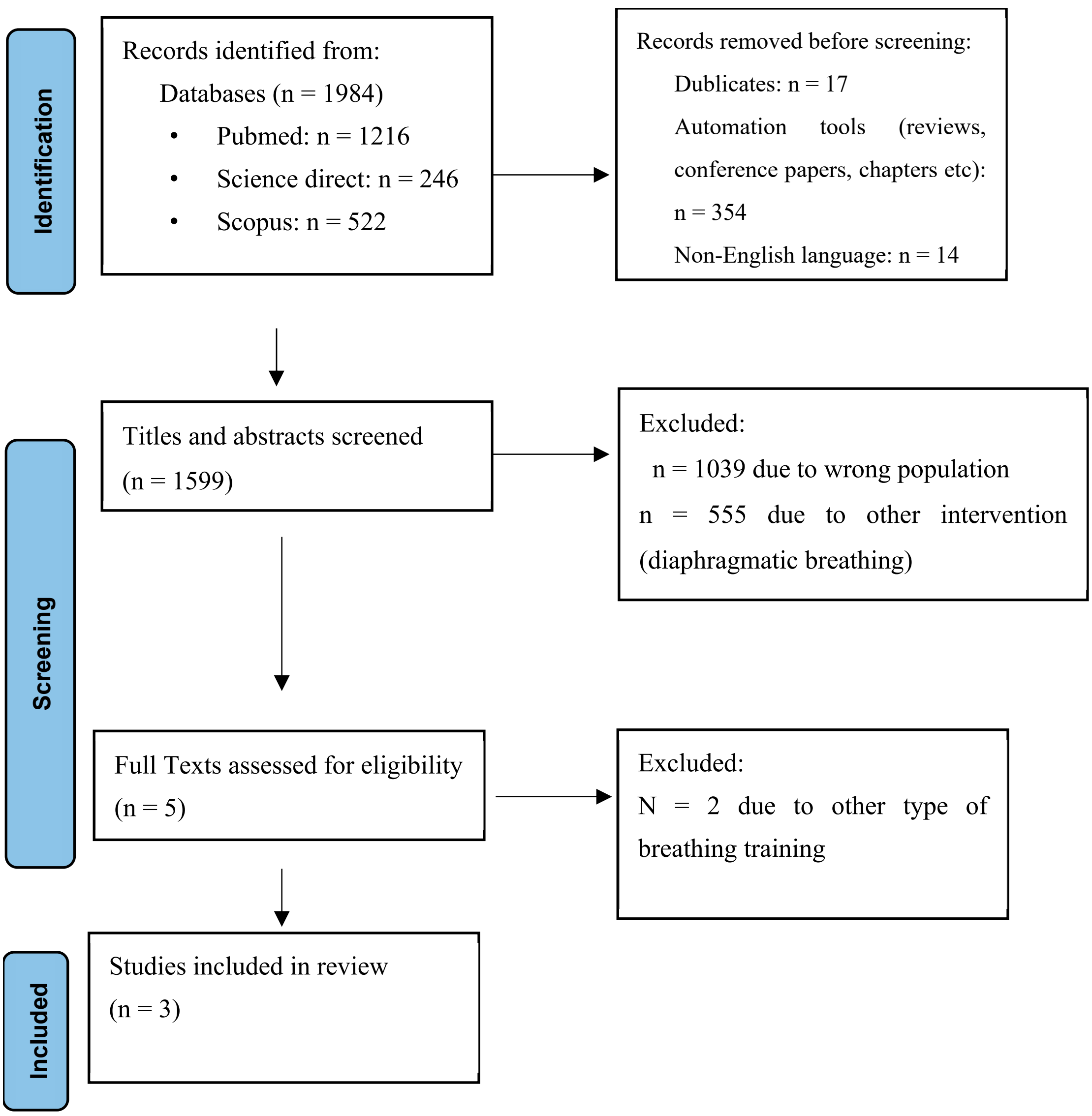

Figure 1. PRISMA flow chart of the studies identified and included in the systematic review.

3.2. Quality of Studies

According to the rating criteria of the PEDro scale, two studies [21,22] showed a high methodological quality with an average rating of 6.5 (Table 1).

Table 1. Rating of included studies according to PEDro scale.

	Criteria of PEDro Scale										
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Overall Rating**
Chaves et al. [21]	x			x			x	x	x	x	6/10
Widjanantie et al. [22]	x	x	x	x	x		x	x	x	x	9/10

According to the NOS, the third study [23] showed a fair methodological quality (5 stars: 2 stars in the selection component, 1 star in the comparability component, and 2 stars in the outcomes component).

3.3. Description of Studies

3.3.1. Population

The total number of participants in this systematic review was 98 people (Table 2). A total of ninety-one participants had GERD and seven were healthy. In the study by Chaves et al. [21], 29 people were diagnosed with GERD according to clinical endoscopic criteria and pH metric findings. An oesophageal manometry test was performed and demonstrated hypotensive LES values between 5 and 10 mmHg. In the study by Souza et al. [23], nine participants were diagnosed with GERD: eight of grade A, and one of grade B, according to the Los Angeles classification. The authors also included three participants with nonerosive reflux disease (NERD) diagnosed by oesophageal pH monitoring. In the study by Widjanantie et al. [22], there were 50 participants with gastrointestinal symptoms (GERDQ score $\geq$ 8) after a moderate COVID-19 infection (within six months).

Table 2. Features of the selected studies.

Study	Study Design	Population	Intervention	Comparison	Outcomes	Results
Chaves et al. [21]	Clinical trial	n = 20 (intervention group) n = 9 (sham group)	IMT (30%Pimax) 40 inspirations, 7 days/week (twice a day, morning–evening) for 8 weeks.	IMT (constant 7 cm H_2O)	MIP, MEP, LES	MIP ns MEP ns LES ns
Souza et al. [23]	Clinical trial Pre–post study	n = 12 (intervention group) n = 7 healthy volunteers (comparison group)	IMT (30% Pimax). 10 series of 15 inspirations, 5 days/week (once daily) for 8 weeks.	-	Heartburn–regurtitation (scores), average EGJp, tLESR	(Before and after IMT) heartburn $p = 0.003$, regurgitation ($p = 0.008$), average EGJp ($p < 0.01$), tLESR ($p = 0.032$, $p = 0.034$)
Widjanantie et al. [22]	RCT	n = 25 (intervention group) n = 25 (control group)	Modified diaphragmatic training (IMT 60% MIP) 5 days per week (once daily) for 4 weeks.	Conventional diaphragmatic training	MIP, GERDQ score, diaphragmatic excursion	MIP ($p < 0.05$), diaphragmatic excursion (RDE, LDE) (both $p < 0.001$) GERDQ score ($p < 0.001$-fourth week)

RCT: Randomized Control Trial, IMT: Inspiratory Muscle Training, MIP: Maximal Inspiratory Pressure, MEP: Maximal Expiratory Pressure, EGJp: esophagogastric junction pressure, t-LESR: transient lower esophageal sphincter relaxation, Total GER proximal progression: difference between the number of proximal refluxes and nonprogressing refluxes. RDE: right diaphragmatic excursion, LDE: left diaphragmatic excursion, ns: non-significant.

3.3.2. Interventions

Chaves et al. [21] used a training program that consisted of 40 maximum inspirations from the residual volume through a pressure threshold device, conducted twice a day (morning and evening) for 7 days a week across a period of eight weeks. The inspiratory load for the progressive training group was always set at 30% of the participants' MIP, while for the sham group, it was constantly 7 cmH_2O, the minimum allowed for the device. MIP was measured every 15 days for all participants.

Souza et al. [23] implemented an IMT program with a threshold device, which was performed daily over a period of 2 months. Each IMT session consisted of 10 series of 15 inspirations (lasting about 30 min). The initial resistance was set at 30% of the maximal inspiratory pressure (MIP) and was increased, as long as was tolerated, by 5% every 5 days. As a comparison group, the authors included seven healthy volunteers who participated only in the assessments.

Widjanantie et al. [22] applied a four-week modified diaphragmatic training program which was performed once daily, for 5 days per week. The training consisted of diaphragmatic breathing combined with IMT at 60% of the participants' MIP, as measured every week. The control group was instructed to perform diaphragmatic breathing.

3.3.3. Effects of Intervention

Maximal Inspiratory and Expiratory Pressure (MIP-MEP)

Of the selected studies, only two [21,22] assessed MIP-MEP before and after IMT. Specifically, in the study by Widjanantie et al. [22], significant differences in MIP were found between the intervention and control groups (mean $\pm$ SD: 74.8 $\pm$ 20.33 vs. 68.68 $\pm$ 21.25, $p < 0.05$). In the study by Chaves et al. [21], there were no significant differences in MIP.

GERD Symptoms

Two of the included studies examined the effects of IMT on reflux symptoms [22,23]. No significant differences between groups were mentioned in the studies included. In the study by Widjanantie et al. [22], the differences between groups reached statistical significance for the GERDQ scores only during the fourth week of the application of IMT (mean $\pm$ SD: 1.84 $\pm$ 2.17 vs. 3.32 $\pm$ 1.49, $p = 0.015$), but not earlier.

Lower Esophageal Sphincter (LES)–Esophagogastric Junction (EGJ) Pressures

Two of the included studies [21,23] assessed the effects of IMT on LES–EGJ pressures. No significant differences between groups were mentioned.

Diaphragmatic Excursion

Only one study examined the effects of IMT on diaphragmatic excursion [22]. In the study by Widjanantie et al. [22], significant differences in the diaphragmatic excursion were found between groups ($p < 0.001$). The mean right diaphragmatic excursion (RDE) after the end of week 4 was significantly different ($p < 0.001$) between the intervention (6.84 $\pm$ 0.92 cm) and the control group (5.57 $\pm$ 0.95 cm). The mean left diaphragmatic excursion (LDE) was 6.48 $\pm$ 0.78 cm in the intervention group vs. 5.33 $\pm$ 0.90 cm in the control group ($p < 0.001$).

4. Discussion

This is the first systematic review that has comprehensively investigated and summarized the effects of IMT on the GERD population. Primarily, from the studies included in this systematic review, we noticed a significant increase in MIP [22]. This is further reinforced by the significant increase in the diaphragmatic excursion noted by Widjanantie et al. [22]. In the same study, the authors found a significant reduction in the GERDQ score that assesses GERD symptoms. As EGJ is surrounded by muscle segments of the diaphragm, the strengthening of the diaphragmatic sphincter could have effectively managed and reduced the symptoms associated with reflux [3,23].

These positive effects were evident in the COVID-19 population, where the impact of the infection on the functionality of the respiratory system is well documented. COVID-19 is known to cause systemic inflammation leading to respiratory muscle weakness and dysfunction [24]. Additionally, we should note that COVID-19 has been associated with phrenic nerve paralysis which innervates the diaphragm [25]. Diaphragmatic dysfunction can compromise the LES, thereby weakening the barrier against gastric content reflux [22]. This is something that we should bear in mind when assessing populations that have a compromised respiratory system. Since the crural diaphragm is an inspiratory striated muscle, its tone normally depends on the following two factors: the basic viscoelastic properties of the soft tissues associated with the muscle and its degree of activation muscle contractility [26]. IMT is a training program that targets the strengthening of the diaphragm. Thus, IMT could alter these two factors by increasing the diaphragm muscle tone and strength. Some studies have shown a significant positive correlation between diaphragmatic breathing mobility (best excursion), measured by diaphragmic ultrasound, and inspiratory muscle strength (MIP, SNIP) as well as lung function (FVC, FEV1) in healthy subjects [27]. Furthermore, the diaphragmatic excursion has been clinically recognized as a crucial marker in recognizing patients with inspiratory weakness [28]. Lerolle et al. [29] studied patients requiring prolonged mechanical ventilation after cardiac surgery and discovered that a diaphragmatic excursion lower than 25 mm during diaphragmatic breathing was associated with a reduced Gilbert index. This index indicates severe diaphragmatic dysfunction and is calculated through the different gastric pressures produced at different points of breathing. Additionally, in another study involving intubated patients, diaphragmatic displacement was significantly correlated with transdiaphragmatic pressure—Pdi and oesophageal pressure—Pes [30]. Besides the effect of IMT on the diaphragm as a muscle, we should also consider its effect on the autonomous nervous system, whose neural pathways mediate the function of LES [31]. Inspiratory muscle training has positive responses in the autonomic nervous system modulation in chronic diseases such chronic heart failure [32]. Studies have shown that IMT promotes the increase in the respiratory metaboreflex activation threshold, and that changes in the respiratory pattern encourage baroreflex activity [31].

Two studies [21,23] evaluated the impact of IMT on the low esophageal sphincter and esophagogastric junction (LES–EGJ) pressure. Chaves et al. [21] reported no significant effect on LES pressure. Souza et al. [23] found an improvement in EGJ and transient lower esophageal relaxation (tLESR) following training, which led to a significant reduction in GERD symptoms. The authors have commented on the role of the autonomous system on smooth muscle tone and t LER. Given that IMT is a training intervention, it may enhance autonomic nervous system function and potentially benefit both EGJ and tLER. However, it is important to note that we could not draw definite conclusions due to methodological issues, such as the sample size [21] and homogeneity of the groups (GERD–Healthy) [23]. Healthy volunteers were recruited to underline the deficits that the GERD population presented.

In previous studies, breathing exercises were found to have a beneficial role in strengthening the valve mechanisms, highlighting the essential function of the diaphragm [14,33,34]. Yet, it is important to differentiate breathing exercises from a training program for the inspiratory muscles. To effectively enhance the crural diaphragm tension, a strengthening program, following the principles of training such as progression, specificity, and reversibility, may be more appropriate [35]. Besides the three studies that have been included in the systematic review, similar findings have been presented in two conference papers

(Table 3). Fonseca et al. [36] enrolled 20 participants, while Souza et al. [37] studied 17 reflux esophagitis patients with heartburn. Fonseca et al. [36] reported a significant increase in MIP and a significant reduction in symptoms like throat cleaning and heartburn. Similarly, Souza et al. [37] observed a significant increase in EGJ pressure and contractility. The positive effect noted by both Widjanantie et al. [22] and Fonseca et al. [36] regarding MIP may be attributed to the implementation of higher loads (50–60%) of MIP. It is likely that these authors sought to explore whether such an approach would be more effective in targeting muscle strengthening.

Table 3. Studies from conference abstracts.

Article	Study Design	Population	Intervention	Comparison	Outcomes	Results
Fonseca et al. [36]	RCT	n = 10 (intervention group) n = 10 (control group)	IMT (50%mip) 3 times a week, (once daily) for a total of 8 weeks.	No intervention	MIP, heartburn, throat cleaning, basal LES pressure	MIP (p = 0.02); heartburn (p = 0.007); throat cleaning (p = 0.016); basal LES pressure (p = 0.03).
Souza et al. [37]	Pre–post study	n = 17	IMT	-	IDL, Max EGJ, CI	IDL (p = 0.008); MaxEGJ (p = 0.008); CI (p = 0.03).

IMT: Inspiratory Muscle Training, MIP: Maximal Inspiratory Pressure, IDL: inspiratory diaphragm lowering, Max EGJ: maximal esophagogastric junction pressure, CI: esophagogastric junction contractility integral.

GERD poses a significant challenge for modern society, with an increasing number of people experiencing it every day. Regurgitation and its symptoms can lead to reduced work productivity, the limitation of daily activities, and a reduced quality of life [38]. Furthermore, GERD may lead to an increased risk of repeated hospitalizations, thus increasing the risk for the further deterioration of one's health. Additionally, the GERD population is at an elevated risk of developing mental illness [39]. The ongoing need for medication also places a significant burden on the public health system [38,40]. The present systematic review focused on inspiratory muscle training in patients with GERD, suggesting that this intervention may yield promising outcomes. Yet, there is a need for RCTs with an improved methodological design to evaluate the various proposed outcome measures. Additionally, looking into the revolution of IMT and the presence of new electronic devices that provide a different kind of loading, such as tapered flow resistance, one could think that there is still a lot to be investigated. The ability of electronic IMT devices to measure a dynamic property of inspiratory pressure could provide valuable insights. The maximum dynamic inspiratory pressure (S index) has been validated in the general population [41,42]. This measurement is believed to create a greater recruitment of the inspiratory muscles compared to a maximal static inspiratory effort (MIP), as it is a more functional maneuver [42]. Unlike MIP, dynamic assessment allows for the measurement of inspiratory muscle output in total lung volume. This finding suggests that it may be a more appropriate method for measuring inspiratory muscle strength than the isometric estimates of peak inspiratory pressure [41]. There are studies on different muscle groups showing that static assessments are unable to predict functional muscle capacity [43,44]. However, they have a strong correlation and good agreement with each other, indicating that both can reliably assess inspiratory muscle strength [41,42].

Moreover, it is crucial to explore the co-existence of gastroesophageal reflux disease (GERD) with other respiratory conditions, and the effectiveness of inspiratory muscle training (IMT), considering that IMT plays a vital role in pulmonary rehabilitation [45].

The present systematic review had a few limitations, such as the small number of studies included, the variance of the populations, and the outcomes examined. In addition, there were methodological issues, such as the calculation of the sample size and the absence of a control group.

5. Conclusions

The present systematic review established a bibliographic gap in the contribution of IMT to the antireflux valve mechanism. More evidence is needed to support the importance of IMT as a non-pharmacological intervention for GERD patients.

Author Contributions: I.P. and S.S. conceptualized and designed the research; I.P. and performed the research; S.S. and M.M. analyzed the data; I.P. and S.S. wrote the paper; and M.M. and E.G. revised the paper. All authors have contributed equally to the manuscript. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Conflicts of Interest: The authors declare no conflicts of interest.

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