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Systematic Review

Inspiratory Muscle Training Intensity in Patients Living with Cardiovascular Diseases: A Systematic Review

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Abstract: The benefits of inspiratory muscle training (IMT) have been demonstrated in patients with cardiovascular diseases (CVD); however, the optimal training intensity is not yet fully clarified. The purpose of this study was to review the impact of IMT intensity on respiratory muscle strength, functional and exercise capacity, pulmonary function, and quality of life in patients with CVD. This systematic review was carried out according to PRISMA statement and registered in the PROSPERO database (review protocol: CRD42023442378). Randomized controlled trials were retrieved on 3 July 2023 in the following electronic databases: Web of Science, PubMed, EMBASE, and SCOPUS. Studies were included if they assessed the impact of isolated IMT on CVD patients in comparison with sham, different intensities and/or intervention groups. Eight studies were included for final analysis; IMT consistently led to significantly greater improvements in inspiratory muscle strength compared to control (CON) groups. The intensity of IMT varied in the studies based on different percentages of maximal inspiratory pressure (MIP), ranging from 25% to 60% of MIP. The time of intervention ranged from 4 to 12 weeks. Despite this variability, the studies collectively suggested that IMT is beneficial for enhancing CVD patients' conditions. However, the optimal intensity range for benefits appeared to vary, and no single intensity emerged as universally superior across all studies.

Keywords: inspiratory muscle training; cardiovascular diseases; cardiac rehabilitation; inspiratory muscle strength; functional capacity; exercise capacity

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1. Introduction

The significant rates of mortality of cardiovascular diseases (CVD) representing 32% of all global deaths in 2019 makes it a major worldwide health problem [1]. Their impact on people's health and the health care systems has sparked ongoing research into diverse approaches in order to improve cardiovascular symptoms by reducing the work of breathing, dyspnoea, muscle fatigue, and increasing exercise tolerance [2]. Among the non-pharmacological treatment strategies, inspiratory muscle training (IMT) has emerged as a non-conventional method of physical activity with potential benefits for these patients. According to Chiappa et al. (2008), IMT enhances functional capacity of patients with chronic heart failure [3]. The same authors concluded that in patients with inspiratory muscle weakness and chronic heart failure, IMT improves limb blood flow under training in these populations. Moreover, in patients with hypertension, IMT can be a complementary strategy to reduce resting heart rate, pulse pressure, systolic and diastolic blood pressures [4]. In post-stroke patients, IMT increases pulmonary function and cardiopulmonary endurance and reduces pulmonary infection incidence in this population [5]. In spite of the

fact that previous studies have reported potential IMT benefits, there is still no consensus on protocols employed in patients with CVDs.

IMT aims to improve the strength and endurance of inspiratory muscles: the diaphragm and accessory muscles [6,7]. It is known that improving respiratory muscle strength and endurance delays the respiratory muscle metaboreflex, a physiological response hyperactivated in patients with CVD, occurring during physical exercise when metabolites, for instance, lactate, adenosine and hydrogen ions, accumulate in muscles [8]. This accumulation triggers the metaboreflex that redirects the blood flow via sympathetic activation from the periphery muscles to the diaphragmatic area, thus avoiding dyspnoea due to reduction in blood supply to respiratory muscles. However, this peripheral blood flow redistribution may be responsible for the interruption of exercise as well as activities of daily living due to peripheral muscle fatigue [9,10]. Therefore, delaying the onset of this reflex might predispose individuals to a more active lifestyle and improved exercise tolerance.

While various studies have highlighted potential benefits of IMT in diverse populations, a consensus regarding the optimal intensity to effectively mitigate symptoms associated with CVD has yet to be reached. Commonly, the intensity of IMT is determined through measurements of maximal inspiratory pressure (MIP). According to Larson et al. (1988), IMT results in improvements in strength and endurance of the respiratory muscles, mainly when protocols with training loads higher than 30% of maximal inspiratory pressure (MIP) were applied [11]. Many studies [2,12,13] have described sham/control intensities at 0–15% of MIP. Despite the divergence regarding the range of low, moderate and high intensities, in our review, 20–39% is considered as low, 40–60% as moderate, and >60% as high intensity. Nevertheless, as of now, no studies have explored the optimal training intensity for IMT in patients with cardiovascular disease, despite the recommendation by Smith and Taylor (2022) [14].

A recent meta-analysis identified that patients with CVD could benefit in terms of inspiratory muscle strength, functional capacity, and quality of life when IMT is performed at intensities above 60% of MIP [15]. However, controversial results were found in another meta-analysis, suggesting that intensities between 40 and 60% of MIP could promote better outcomes for CVD patients [16]. While both meta-analyses agree on the recommended intervention duration of approximately 6 weeks, disparities regarding training intensity persist in the literature. Therefore, this systematic review aims to provide a comprehensive summary of the literature about the effects of IMT intensity on patients with CVD. This review may offer valuable guidance for the development of innovative and effective protocol/ therapeutic strategies for cardiovascular patients considering the suitable training intensity of IMT in order to maximize the benefits.

2. Materials and Methods

The systematic review was registered on Prospero (CRD42023442378). This study was conducted and reported in accordance with the PRISMA guidelines (http://www.prisma-statement.org/, accessed on 1 July 2023). The Rayyan tools were used to assist and systematize the search and data extraction (available from https://www.rayyan.ai, accessed on 3 July 2023).

2.1. Search Strategy and Study Selection

Electronic searches were performed on 3 July 2023, in Web of Science, PubMed (via National Library of Medicine), EMBASE, and SCOPUS (Elsevier) using the following mesh terms: "breathing exercises OR inspiratory muscle training", "exercise tolerance", and "cardiovascular diseases OR heart diseases OR vascular diseases". The term "respiratory muscle training" was not included because it is already an entry term for "breathing exercises". Afterwards, combining the mesh terms between them and limiting the search to humans, language to English and French and the type to randomized controlled trials (RCT), 652 articles were retrieved from the databases. Two independent reviewers (Presse,

C. and Beaujolin, A.) screened the articles by title and abstract according to the eligibility criteria. The potentially eligible articles were screened in full text to determine inclusion. If there were some disagreements between these reviewers, a third independent reviewer (Mane, J.) was consulted.

2.2. Eligibility Criteria

The eligibility criteria were defined using the Patient/Population—Intervention—Comparison/Comparator—Outcome (PICO) format. The eligible population was adult patients suffering any type of CVD such as hypertension, stroke, coronary diseases, atrioventricular diseases, and heart diseases. Other diseases such as obesity and respiratory diseases were excluded. The intervention of interest was inspiratory muscle training (IMT) using inspiratory muscle trainers such as the POWERbreathe, Ultrabreathe, etc. Expiratory muscle training, meditation, slow breathing, IMT without devices and other types of respiratory muscle training were excluded, including IMT combined with other training types such as aerobic training. The outcomes of interest were respiratory muscle strength (MIP), respiratory endurance test (SMIP and PTHmax), exercise capacity tests (such as VO2max, ventilatory threshold, 6MWT, and CPET), and health-related quality of life questionnaire.

2.3. Data Extraction

The following information was extracted from each included study: Table 1 describes basic characteristics of studies, participants and groups (first author, year of publication, country, population (disease), groups and sample size, sex, age, and body mass index at baseline); Table 2 describes characteristics of intervention (type of device, intensity, session duration and frequency, duration of intervention, supervision, progression and follow up); and Table 3 describes main and secondary outcomes and results (respiratory muscle testing, inspiratory muscle strengthening, exercise capacity, dyspnoea, lung function and quality of life).

2.4. Quality Assessment

The methodological quality of the studies included in this systematic review was assessed using the PEDro scale that consists of 11 questions assessing their scientific rigor [12]. The questions concern the following aspects, listed in the original order: eligibility criteria, randomization of allocation, concealed allocation, follow-up, baseline comparability, blindness of the subjects, blindness of the therapists, blindness of the assessors, intention to treat analysis, between-group comparability, and measures of variability. All criteria, except the first one (eligibility criteria), receive a score of 0 or 1, corresponding to no or yes, respectively. The eligibility criterion does not receive any score, since this criterion influences external validity, but not the internal or statistical validity of the trial [17].

Therefore, a study received a maximum score of 10 points that classified the level of quality as high for a score superior to or equal to 6/10, and low for a score inferior to 6/10. The articles were classified independently by two researchers (Presse, C and Beaujolin, A). If a consensus was not reached, the third researcher (Mane, J.) would make the final decision.

2.5. Certainty of Evidence

The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach was applied in order to determine the certainty of the overall evidence. Criteria such as risk of bias, imprecision, inconsistency of results, indirectness of evidence, and publication bias can decrease the certainty of the evidence. On the other hand, certainty of evidence can be increased in situations where there are large effects, dose-response associations, or minimal residual confounding. The overall certainty of evidence was categorized into high, moderate, low, or very low [18]. The GRADE scores are described in Table 5.

3. Results

Initially, 632 relevant records were identified in the electronic databases: Web of Science, PubMed, EMBASE, and SCOPUS. We excluded 202 duplicated articles, while 180 did not meet our eligibility criteria after being scanned by title and abstract. Thus, 14 articles were left to full assessment, 5 of which included IMT combined with other interventions and 1 was in a language other than English or French. Thus, eight articles were included in this review (Figure 1). The main reasons for exclusion after analysis of full papers were (a) diseases other than CVD; (b) less than 4 weeks of intervention (to focus on long-term effect of IMT); (c) expiratory muscle training, IMT without devices, meditation, slow breathing exercises; (d) non-randomized clinical trials.

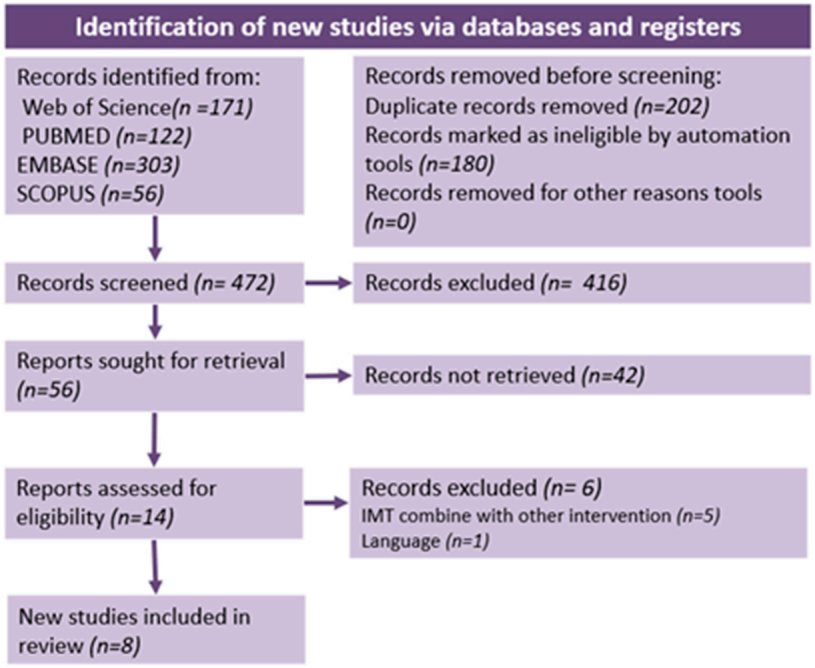

Figure 1. Flow diagram of search strategy and retrieval of articles [19].

3.1. Characteristic of Studies

Table 1 describes the characteristics of participants and groups. The total sample size was 198 participants aged from 54 to 77 years. The number of participants per group varied from 6 to 32. Three studies researched the impact of IMT on patients suffering chronic heart failure [20–22], two contained studies on heart failure with ventricular systolic dysfunction [2,13], one on heart failure with preserved ejection fraction [23], one on stroke [12] and one on pulmonary arterial hypertension [24]. Five out of the eight studies included patients suffering respiratory muscle weakness at baseline [2,12,13,20,22].

Table 1. Basic characteristics of studies.

First Author, Year	Country	Population (Disease)	Groups and Sample Size	Sex Distribution (M/F)	Age (Years), Mean ± SD *	BMI Baseline (Kg/m^2)	PEDro Total Score
Bosnak-Guclu, 2011 [2]	Turkey	HF (LVEF < 40%)	IMT (n = 16) CON (n = 14)	IMT (12/4) CON (12/2)	IMT (69.50 ± 7.96) CON (65.71 ± 10.52)	IMT (26.76 ± 4.30) CON (25.08 ± 3.17)	6/10 (High)
Dall'Ago, 2006 [20]	Brazil	CHF	IMT (n = 16) CON (n = 16)	IMT (11/5) CON (10/6)	IMT (54 ± 3) CON (58 ± 2)	IMT (27 ± 4) CON (27 ± 5)	6/10 (High)

Table 1. *Cont.*

First Author, Year	Country	Population (Disease)	Groups and Sample Size	Sex Distribution (M/F)	Age (Years), Mean ± SD *	BMI Baseline (Kg/m^2)	PEDro Total Score
Johnson, 1998 [21]	UK	CHF	IMT (n = 9) CON (n = 9)	ALL (15/3)	ALL (66.5 ± 5.6)	NR	6/10 (High)
Marco, 2013 [22]	Spain	CHF	IMT (n = 11) CON (n = 11)	IMT (7/4) CON (10/1)	IMT (68.5 ± 8.88) CON (70.1 ± 10.75)	IMT (28.4 ± 3.64) CON (26.3 ± 2.4)	9/10 (High)
Palau, 2014 [23]	Spain	HFpEF	IMT (n = 14) CON (n = 12)	IMT (7/7) CON (6/6)	IMT (68 (60–76)) CON (74 (73–77))	IMT (34.3 (28.2; 38)) CON (30 (26; 32)	7/10 (High)
Parreiras de Menezes, 2019 [12]	Brazil	Stroke	IMT (n = 19) CON (n = 19)	IMT (8/11) CON (8/11)	IMT (60 ± 14) CON (67 ± 11)	NR	6/10 (High)
Tran, 2021 [24]	Australia	PAH	IMT (n = 6) CON (n = 6)	IMT (1/5) CON (1/5)	IMT (55 ± 17) CON (66 ± 10)	IMT (22.6 ± 4.2) CON (27.7 ± 5.7)	6/10 (High)
Weiner, 1999 [13]	Israel	HF (LVEF < 40%)	IMT (n = 10) CON (n = 10)	ALL (18/2)	ALL (68 ± 6.2)	NR	6/10 (High)

*: The data are expressed as mean ± standard deviation (SD), or interquartile range when SD was not available. BMI, body mass index; CON, control group; CHF, chronic heart failure; F, female; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; IMT, inspiratory muscle training; LVEF, left ventricular ejection fraction; M, male; NR, not reported; PAH, pulmonary arterial hypertension; For age and BMI at baseline, data are expressed as mean and standard deviation.

3.2. Characteristics of Intervention

Seven out of eight studies proposed IMT protocols with intensities varying from 25 to 60% of MIP during 6 weeks to 12 weeks [2,12,13,20,21,23,24]. One study proposed a protocol with an intensity of 100% of 10 repetition maximum (RM) for 4 weeks [22]. The most common device used was the threshold inspiratory muscle training (threshold IMT). Most of the studies included did not supervise the training session or they were supervised in just one session per week. Considering the principles of training, all studies performed weekly adjustments on training intensity. All the details about interventions are shown in Table 2.

Table 2. Types of intervention.

First Author, Year	Device	Intensity	Session Duration and Frequency	Duration of Intervention	Supervised Intervention	Progression	Follow-Up
Bosnak-Guclu, 2011 [2]	Threshold IMT (Respironics, Murrysville, PA, USA)	IMT: 40% of MIP CON: 15% of MIP	ALL: 30 min per day, 7 days per week	6 weeks	1 session/week	IMT: Workload adjusted weekly to maintain 40% of the MIP CON: fixed workload	
Dall'Ago, 2006 [12]	Threshold IMT (Healthscan Products Inc., Cedar Grove, NJ, USA)	IMT: 30% of MIP CON: 0% of MIP	ALL: 30 min per day, 7 days per week	12 weeks	1 session/week	IMT: Workload adjusted weekly to maintain 30% of the MIP CON: No workload	1 year after entering the study
Johnson, 1998 [13]	Threshold IMT (Respironics, Murrysville, PA, USA)	IMT: 30% of MIP CON: 15% of MIP	ALL: 30 min per day (15 min twice daily), 7 days per week	8 weeks	None	IMT: Workload adjusted weekly to maintain 30% of the MIP CON: Fixed workload	

Table 2. *Cont.*

First Author, Year	Device	Intensity	Session Duration and Frequency	Duration of Intervention	Supervised Intervention	Progression	Follow-Up
Marco, 2013 [14]	Respiratory trainer (Orygen-Dual valve, Girona, Spain)	IMT: Adjusted based on 100% of their 10 RM CON: 10 cm H2O	ALL: 5 sets × 10 reps, twice a day, 7 days per week	4 weeks	1 session/week	IMT: Workloads adjusted weekly according to 10 RM CON: Workload increased weekly of 2.5 cmH2O	
Palau, 2014 [15]	Threshold IMT (Respironics, Respironics, Murrysville, PA, USA)	IMT: 25–30% of MIP CON: Usual care	IMT: 40 min per day (20 min twice daily), 7 days per week	12 weeks	None	IMT: Workload adjusted weekly to be within the training threshold range	Baseline Weekly +Diary card
Parreiras de Menezes, 2019 [9]	Respiratory trainer (Orygen-Dual valve, Girona, Spain)	IMT: 50% of MIP CON: 0% of MIP	ALL: 40 min per day (20 min twice daily), 7 days per week	8 weeks	None	IMT: Workloads adjusted weekly to maintain 50% of MIP CON: Fixed workload	Baseline 8-week (end of intervention) 12-week +Diary
Tran, 2021 [16]	Electronic KHP2 respiratory muscle training (POWERbreathe International Ltd. Warwickshire, UK)	IMT: 2 × 30 breaths at 30–40% of MIP CON: Usual care	IMT: 5 days per week	8 weeks	1 session/week. Compliance to unsupervised sessions monitored through KHP2 device data extraction	IMT: Training intensity adjusted weekly to be within the training threshold range	Training data were extracted from the POWERbreathe to monitor compliance
Weiner, 1999 [10]	Threshold IMT (Healthscan, Cedar Grove, NJ, USA)	IMT: 15% of MIP the first week, increased incrementally, 5% each session, to reach 60% at the end of the 1st month. Then continued for the next two months at 60% of MIP. CON: 0% of MIP	ALL: 30 min per day, 6 days per week	12 weeks	All sessions	IMT: Training intensity adjusted every week to the new MIP achieved.	Baseline MIP weekly 3-month

%, per cent; 10 RM, ten maximum repetitions; cmH2O, centimetre of water; CON, control group; CR, cardiac rehabilitation; IMT, inspiratory muscle training; MIP, maximal inspiratory pressure.

3.3. Primary Outcomes Results

All protocols exhibited significant improvements of inspiratory muscle strength. Exercise capacity (EC) was assessed using a 6 min walk test (6MWT), a 12 min walk test (12MWT), cardiopulmonary exercise testing (CPET), a treadmill stress test (modified Bruce protocol) and a corridor walk test. The walk distance significantly improved after IMT at 60% of MIP in the 12MWT [13], and after IMT at 25–40% of MIP [2,20,23,24], except at 50% in the 6MWT [12]. EC, assessed by VO2 max, exhibited significant enhancement solely after 12 weeks of IMT at 25–30% of MIP [23], while no significant improvements were observed after 8 weeks of IMT at 30–40% [24] and after 12 weeks of IMT at 60% [13]. The time of the treadmill stress test and the corridor test showed no change for IMT at 30% of MIP [21].

Inspiratory muscle endurance demonstrated significant improvement at 30%, 50%, and 60% of MIP, in conjunction with 100% of 10 RM [12,13,20,22].

Overall, treatment groups undergoing IMT displayed significant enhancements in inspiratory muscle strength, endurance, and functional capacity compared to control groups. Notably, significant improvement in EC was observed only after 12 weeks of IMT at 25–30% of MIP [23].

3.4. Secondary Outcome Results

Secondary outcomes and their results are described in Table 3. Only the included studies proposing protocols longer than 12 weeks showed significantly greater improvement in quality-of-life questionnaires (in the SF-36 and MLHF) compared to control group [20,23]. Even though Bosnak-Guclu et al. (2011) proposed a protocol lasting 6 weeks, they reported significant reduction in the Montgomery Âsberg depression rating scale with an IMT at 40% [2]. Six studies [2,12,13,20–22] assessed perceived dyspnoea with four studies [2,12,13,22] assessing the impact of dyspnoea on daily activities using the dyspnoea index decribed by Mahler and Harver, MMRC, and MRC dyspnoea scales, while two studies [20,21] used the Borg scale during the walking tests. Four out of the six studies reported greater reduction in dyspnoea, all of them had a protocol with an intensity higher than 30% or an intervention period longer than 8 weeks [2,12,13,20]. When reported, the results of lung function diverged between the studies: some showed improvement in both groups [2], others with greater improvement compared to shame [12,20], and others without significant improvement at all [21,22]. Details on primary and secondary outcomes are described in Table 3.

Table 3. Outcomes and results.

Intensity	First Author, Year	Main Outcomes	Results	Secondary Outcomes	Results
Low (25–30% MIP)	Palau, 2014 [15]	Inspiratory muscle strength: MIP Exercise capacity: 6MWT (distance, HRrest, HRmax), CPET (VO2 peak, VO2AT, VE/VCO2 slope, METs, RER)	The IMT group showed significantly greater improvement in MIP, VO2 peak, VO2 AT, VE/VCO2 slope, METs, 6MWD compared to the CON group.	QoL: the MLHF questionnaire	The IMT group showed significantly greater improvement of QoL compared to the CON group.
Low (30% MIP)	Dall'Ago, 2006 [12]	Inspiratory muscle strength: MIP Inspiratory muscle endurance: Pthmax Exercise capacity: CPET (VO2max, blood pressure, VE peak, maximal circulatory power), 6MWT (distance + dyspnoea Borg scale)	The IMT group showed significantly greater improvement in MIP, Pthmax, VE peak, VO2peak, maximal circulatory power, and 6MWD compared to the CON group.	Dyspnoea: the Borg scale QoL: the MLHF Questionnaire Lung function: FVC, FEV1	The IMT group showed significantly greater improvement in dyspnoea and QoL compared to the CON group. No significant improvement in lung function in any of the groups.
Low (30% MIP)	Johnson, 1998 [13]	Inspiratory muscle strength: MIP Exercise capacity: treadmill stress test (modified Bruce protocol), Corridor walk test (time)	IMT showed significantly greater improvement in MIP compared to the CON group. No significant improvement in treadmill test time, corridor walk test time in both groups.	Dyspnoea: the Borg scale (during activity) QoL: disease-specific questionnaire	No significant improvement in dyspnoea and QoL scores in both groups.

Table 3. *Cont.*

Intensity	First Author, Year	Main Outcomes	Results	Secondary Outcomes	Results
Low/Moderate (30–40% MIP)	Tran, 2021 [16]	Inspiratory muscle strength: MIP Exercise capacity: CPET on ergometer (resting VO2, VO2 peak, resting SpO2, SpO2 peak, peak HR, O2 pulse, VE/VCO2, OUES, peak RER), 6MWT (mean change in distance)	The IMT group showed significantly greater improvement in MIP compared to the CON group. Significant improvement in 6MWD in the IMT group, with no significant improvement observed in the CON group. No significant differences In peak VO2 between groups.	Lung function: FVC, FEV1	No significant improvement in lung function in any of the groups.
Moderate (40% MIP)	Bosnak-Guclu, 2011 [2]	Inspiratory muscle strength: MIP Exercise capacity: 6MWT (distance + % predicted distance + HRmax%)	The IMT group showed significantly greater improvements in MIP and 6MWD compared to the CON group.	QoL: Turkish version of the SF-36, Fatigue Severity Scale, Montgomery Âsberg Depression Rating Scale Dyspnoea: MMRC dyspnoea scale + Borg scale (during activity) Lung function: FEV1, FVC, PEF	Significant decreases in depression and dyspnoea in the IMT group compared to CON group. Improvements in lung function, QoL and fatigue perception are significant but similar in both groups.
Moderate (50% MIP)	Parreiras de Menezes, 2019 [9]	Inspiratory muscle strength: MIP Inspiratory muscle endurance: number of breaths Exercise capacity: 6MWT (distance)	The IMT group showed significantly greater improvement in MIP and inspiratory endurance compared to the CON group. No significant difference in 6MWD between groups.	Dyspnoea: the MRC scale	The IMT group showed significantly greater improvement in dyspnoea compared to the CON group.
High (100% of 10 RM)	Marco, 2013 [14]	Inspiratory muscle strength: MIP Inspiratory muscle endurance: 10 RM	The IMT group showed significantly greater improvement in MIP and 10 RM compared to the CON group.	Dyspnoea: the MMRC dyspnoea scale QoL: the MLHF questionnaire, SF-36	No significant differences between groups.
High (60% MIP)	Weiner, 1999 [10]	Inspiratory muscle strength: MIP Inspiratory muscle endurance: PmPeak Exercise capacity: 12MWT (distance), exercise tolerance test (VO2max + RR)	Significant improvement in MIP, inspiratory muscle endurance, twelve-minute distance walk in the IMT group, with no significant improvement observed in the CON group. No significant changes in VO2max in both groups.	Lung function: FVC, FEV1 Dyspnoea: dyspnoea index described by Mahler and Harver	Significant improvement in dyspnoea and minimal but significant increase in FVC in the IMT group compared with the CON group. No significant improvement in FEV1 in any of the groups.

6MWD, six-minute walk distance; 6MWT, six-minute walk test; 12MWT, twelve-minute walk test; CON, control group; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; HR, heart rate; HRmax, maximum heart rate; IMT, inspiratory muscle training; METs, metabolic equivalents; MIP, maximal inspiratory pressure; MLHFq, the Minnesota living with heart failure questionnaire; MMRC, modified medical research council; MRC, medical research council; NYHA, New York heart association; OUES, oxygen uptake efficiency slope; PEF, peak expiratory flow; PmPeak, peak pressure; Pthmax, respiratory muscle endurance pressure; QoL, quality of life; RER, respiratory exchange ratio; RM, repetition maximum; RR, respiratory rate; SF-36, short-form 36 health-related quality of life; SpO2, peripheral capillary oxygen saturation; VC, vital capacity; VCO2, carbon dioxide production; VE, minute ventilation; VE/VCO2, minute ventilation/carbon dioxide production; VO2, oxygen uptake, VO2 AT, oxygen uptake at anaerobic threshold; VO2 peak, peak exercise pulmonary oxygen uptake.

3.5. Quality Assessment

Eight studies were included for final analysis and presented an average score of 6.5 ranging from 6 to 9 in the PEDro scale, which is considered to be indicative of high methodological quality. It should be highlighted that in all the studies, therapists were not blinded when administering the IMT. On the other hand, four studies blinded the assessors who measured at least one key outcome. All studies [2,13,20–24], except one [12], had groups with similar important prognostic indicators at baseline and all studies reported at least one primary outcome the results of between-group statistical comparisons. Full details of the PEDro scale scores are reported in Table 4.

Table 4. PEDro scale.

First Author, Year	PEDro Ratings												Quality of Evidence
	1	2	3	4	5	6	7	8	9	10	11	Total	
Bosnak-Guclu, 2011 [2]	Yes	✔	✗	✔	✔	✗	✔	✗	✗	✔	✔	6	High
Dall'Ago, 2006 [20]	Yes	✔	✔	✔	✗	✗	✔	✗	✗	✔	✔	6	High
Johnson, 1998 [21]	No	✔	✗	✔	✔	✗	✗	✔	✗	✔	✔	6	High
Marco, 2013 [22]	Yes	✔	✔	✔	✔	✗	✔	✔	✔	✔	✔	9	High
Palau, 2014 [23]	Yes	✔	✗	✔	✗	✗	✔	✔	✔	✔	✔	7	High
Parreiras de Menezes, 2019 [12]	Yes	✔	✔	✗	✔	✗	✗	✗	✔	✔	✔	6	High
Tran, 2021 [24]	Yes	✔	✗	✔	✗	✗	✗	✔	✔	✔	✔	6	High
Weiner, 1999 [13]	Yes	✔	✗	✔	✗	✗	✗	✔	✔	✔	✔	6	High

✔: yes, ✗ : no. Description of PEDro categories: 1 = "eligibility criteria were specified" [25]; 2 = "subjects were randomly allocated to groups" [25]; 3 = "allocation was concealed" [25]; 4 = "groups were similar at baseline regarding the most important prognostic indicators" [25]; 5 = "blinding of all subjects" [25]; 6 = "blinding of all therapist who administered the therapy" [25]; 7 = "blinding of all assessors who measured at least 1 key outcome" [25]; 8 = "measures of 1 key outcome were obtained from 85% of subjects initially allocated to groups" [25]; 9 = "all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome were analyzed by "intention to treat" [25]; 10 = "the results of between-group statistical comparisons are reported for at least 1 key outcome" [25]; 11 = "the study provides both point measures and measures of variability for at least 1 key outcome" [25].

3.6. Certainty of Evidence

Table 5 describes the certainty of evidence of included studies based on GRADE classification. Evidence was categorized into the following four levels as follows: (1) high quality; further research is very unlikely to change our confidence in the estimation of the effect. All five domains were also met; (2) moderate quality; further research is likely to have an important impact on our confidence and might change the estimate of the effect. One of the five domains was not met; (3) low quality; further research is very likely to have an important impact on our confidence and is likely to change the estimate of effect. Two of the five domains were not met; and (4) very low quality, any estimate of effect is very uncertain. Three of the five domains were not met.

Table 5. GRADE analysis to assess the overall quality of evidence.

Number of Studies (Design)	Comparison	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention (n)	Comparator (n)	Certainty
MIP									
3 RCTs [2,21,22]	IMT vs SHAM IMT	Not serious	Serious [a]	Not serious	Serious [d]	None	36	34	⊕⊕◯◯ Low
5 RCTs [12,13,20,23,24]	IMT vs no intervention	Not serious	Not serious	Not serious	Serious [d]	None	65	63	⊕⊕⊕◯ Moderate

Table 5. *Cont.*

Number of Studies (Design)	Comparison	Risk of Bias	Inconsistency	Indirectness	Imprecision	Other Considerations	Intervention (n)	Comparator (n)	Certainty
Walking distance									
4 RCTs [12,20,23,24]	IMT vs no intervention	Not serious	Serious [b]	Not serious	Very serious [d,e]	None	55	53	⊕◯◯◯ Very low
1 RCT [2]	IMT vs SHAM IMT	Not serious	Not serious	Not serious	Serious [d]	None	16	14	⊕⊕⊕◯ Moderate
VO2 peak									
3 RCTs [20,23,24]	IMT vs no intervention	Not serious	Serious [c]	Not serious	Serious [d,f]	None	36	34	⊕⊕◯◯ Low

Explanations: a. Marco et al. [22] used a different outcome for intensity (100% of 10 RM) from that used by Bosnak-Guclu et al. [2] and Johnson et al. [21] (% of MIP). However, their conclusions showed consistency. b. One [12] over four studies did not show significant improvement of 6 MWD. c. One [24] over three studies did not show significant improvement of the VO2peak after IMT. d. Less than 300 participants. e. Three studies showed wide CI95% [12,23,24] while only one study presented a narrow CI95% [20]. f. One study [24] over three [20,23,24] showed wide CI95%. ⊕⊕⊕⊕: Represents high certainty in the evidence; ⊕⊕⊕◯: Indicates moderate certainty in the evidence; ⊕⊕◯◯: Reflects low certainty in the evidence; ⊕◯◯◯: Denotes very low certainty in the evidence.

4. Discussion

The present systematic review aimed to assess the impact of IMT intensity on cardiovascular patients especially on inspiratory muscle strength, endurance, and exercise capacity. After the analysis of eight randomized controlled clinical trials, we found that IMT demonstrated significant improvement in inspiratory muscle strength and endurance in IMT groups of all studies while noting different degrees of improvement, from one article to another. Exercise capacity, assessed through different outcomes, was enhanced in some studies but not in others. Substantial differences between the studies including the training protocol, duration of training session and duration of intervention could explain the heterogeneity of study results. The discussion of these results is addressed individually for each primary and secondary outcome analyzed.

4.1. Primary Outcomes

4.1.1. Inspiratory Muscle Strength

All studies demonstrated significant improvements in MIP in IMT groups compared to CON groups. The better results (+115%) at the end of the intervention compared to baseline measurements were observed after 12 weeks of training at 30% of MIP for a total duration of 42 h [20] followed by +90% after 12 weeks of training at 25–30% for a total duration of 56 h [23]. Significant improvements could also be observed in two studies [2,12] with, respectively, +56.66% of progression after 40% of MIP during 6 weeks for a total duration of 21 h and +62% of progression after 50% of MIP during 8 weeks for a total duration of 37.33 h. Progress was more moderate for the other four studies [13,21,22,24]: +25.4% of progression after 30% of MIP during 8 weeks for a total duration of 28 h [21], +36.77% of MIP with a progressive approach starting at 15% and gradually increasing to 60% of MIP over 4 weeks, maintaining 60% for the next 8 weeks, with a total training duration of 36 h [13], +15.3% after 30 to 40% of MIP for 8 weeks [24]. Finally, Marco, which used a different approach by implementing an intensity of 100% of 10 RM over 4 weeks, showed +26.22% of progression [22].

During IMT, resistance is added to breathing, making the inspiratory muscles work harder [26]. This leads to the recruitment of a greater number of muscle fibers within the inspiratory muscles [26]. This recruitment, along with regular training, can induce hypertrophy—increasing the size and strength of these muscle fibers. Respiratory muscle strength is known as a positive prognosis factor for HF patients [27,28]. In fact, these patients present muscular atrophy and/or decreased number of cross-bridges, resulting in respiratory muscle weakness [29]. Therefore, IMT allows an improved respiratory muscle function, consequently, this leads to a delay of the metaboreflex. Moreover, improving cardiac autonomic control can impact the stroke volume and cardiac output, thereby

enhancing exercise tolerance and positively influencing the prognosis of patients with HF [27,28,30].

The studies reporting better results [20,23] are the longest ones with low intensity: 12 weeks of intervention with 25–30% of MIP, suggesting that a long duration of intervention of a minimum of 12 weeks combined with a low intensity (30%) is more beneficial than shorter duration of intervention combined with high or moderate intensity (more than 40%). Thus, a long intervention duration of at least twelve weeks associated with a low intensity of 25–30% can avoid excessive muscular fatigue and incite a gradual adaptation of the inspiratory muscles allowing a progressive and lasting development of their strength and endurance [20]. Moreover, the study which obtained the best results [20] highlights that one year after intervention, the MIP was partly preserved. However, it should be noted that in this study, all the patients presented inspiratory muscle weakness at baseline, which increased the margin for progression of these patients. In patients with COPD, IMT improvement in MIP was reported during the first 3 months (32%), followed by smaller increases (~6%) for the four subsequent 3 months of IMT, indicating the existence of a "plateau", even in the presence of training progression [31].

4.1.2. Inspiratory Muscle Endurance

Out of the eight studies, four assessed inspiratory muscle endurance, and all of them resulted in significant improvement of endurance [12,13,20,22]. This can be explained by the improvement of muscle fiber recruitment, increased mitochondrial function of energy production, optimized coordination, and reduction in fatigue-inducing metabolites through the metaboreflex [32]. IMT is a type of resistance exercise that provides resistance during inspiration to strengthen inspiratory muscles [33]. This type of exercise can increase respiratory capacity and intrinsic function of skeletal muscle mitochondria. While the physiological mechanisms are not completely elucidated, strengthening the inspiratory musculature can lead to improved exercise capacity, predisposing individuals to a more active lifestyle. Consequently, higher levels of physical activity are linked to mitochondrial biogenesis and efficiency, which is crucial for energy production, and its increased function contributes to better endurance [34]. Training promotes better coordination between the respiratory muscles, optimizing their function [35]. As the muscles become more efficient in generating force and sustaining contractions, inspiratory muscle endurance improves. The metaboreflex, activated during IMT, plays a role in reducing fatigue by improving blood flow and helping clear metabolites like lactate and hydrogen ions that can contribute to muscle fatigue [36]. The gains in inspiratory muscle endurance were reached when patients trained between 30% and 60% of MIP [12,13,20] or when they achieved 100% of their 10 RM [22]. This improvement in inspiratory muscle endurance has implications for overall exercise capacity, potentially leading to a more active lifestyle by increasing the ability to sustain prolonged inspiratory efforts. Additionally, patients with CVDs often exhibit alterations in the composition of respiratory muscle fibers due to reduced oxidative capacity, consequently reducing exercise capacity [37].

4.1.3. Exercise Capacity

Exercise capacity was assessed in seven of eight studies, involving various walking tests, with the 6MWT being the most used. In five studies [2,13,20,23,24], significant improvements were reported in the average walking distance for the IMT groups compared to the CON groups: from +24.5 meters [24] representing a progression of 4.69% to +101 meters [20] (+19%) in reference to baseline. In fact, while exercising, there is an increase in blood flow and onset of muscle fatigue due to accumulation of metabolites [38]. This triggers the metaboreflex which can explain the improvement of exercise capacity [38]. Two studies [12,21] failed to demonstrate significant improvement in walking distance after IMT. The absence of improvement in Parreiras et al.'s study [12] may be attributed to its focus on a post-stroke population unlike the other included studies. Following a stroke, the severity of participants' motor impairments such as muscle weakness, loss of

balance and compromised motor coordination could impact performance on the walk test and overshadow positive effects of IMT on exercise capacity when assessed through a walk test [39]. Four studies [13,20,23,24] also evaluated exercise capacity by measuring the VO2 peak: Dall'Ago et al. [20] and Palau et al. [23] found positive effects of IMT on mean VO2 peak with +4 and +2.9 mL/min/kg, respectively, in IMT groups in reference to baseline in patients with chronic HF with ventricular systolic dysfunction and HF with preserved ejection fraction, respectively. However, Tran et al. [24] and Weiner et al. [13] did not note significant change in the mean VO2 peak in either group. The two studies [20,23] that showed the efficiency of IMT on the VO2 peak had a training protocol with a low MIP intensity between 25% and 30% with 12 weeks of protocol while the two other studies [13,24] only worked at the targeted MIP intensity for 8 weeks. These results confirm the previous hypothesis suggesting that interventions lasting at least 12 weeks seem more beneficial than the MIP intensity regarding the improvement of the walking distance and the VO2 peak for patients living with HF or PAH.

4.2. Secondary Outcomes

4.2.1. Dyspnoea

Six studies [2,12,13,20–22] assessed perceived dyspnoea during daily activities or walking tests. Marco et al. [22] failed to demonstrate significant improvement in perceived dyspnoea in the IMT group in contrast with the three other studies [2,12,13] that highlighted a significant improvement in IMT groups. This lack of improvement in the study could be linked to the duration of the intervention: 4 weeks [22] compared to 6 to 12 weeks for the three other studies [2,12,13]. These disparate results suggest that the duration of the intervention may play a crucial role in the effectiveness of IMT on dyspnoea. Gradually increasing workloads over weeks could promote progressive physiological adaptations and allow for participants to gradually develop their exercise tolerance so improve symptoms associated with exercise such as dyspnoea [20]. Two studies [20,21] used the Borg scale to assess the perception of breathlessness during walking tests. Dall'Ago et al. [20] showed a significant improvement in dyspnoea perception during activity in the IMT group after 12 weeks of intervention in contrast with Johnson et al. [21] after 8 weeks of intervention. It can be observed that the latter already showed a lack of exercise capacity improvement in their IMT group [21]. The authors suggest that the results could be due to the low intensity which could not be sufficient to overload the respiratory muscles [21]. Nonetheless, Dall'Ago et al. [20] achieved noteworthy outcomes at a comparable intensity, despite the durations of the intervention differing. This supports the assumption that the duration of intervention plays a significant role in the relief of dyspnoea compared to the intensity of IMT.

4.2.2. Quality of Life

Two [20,23] out of five studies assessing quality of life showed significant improvement, supported by Sbruzzi et al. [40] and Wu et al. [16]. This can be explained by the long period of intervention and delayed metaboreflex activation, improving exercise capacity and therefore self-reported outcomes related to mobility and daily life activity [41]. The only study assessing the effect of IMT on depression specifically shows a significant decrease in symptoms. As cardiovascular patients are more exposed to depression than the general population, the impact on IMT on this symptom should be deeply explored [42].

4.2.3. Lung Function

Four [2,13,20,24] out of eight studies assessed lung function, with only one study [13] showing a small but significant improvement in FVC in the IMT group compared to the CON group. None of the studies reported significant improvement in FEV1 in the IMT group compared to the CON group [2,13,20,24]. These results are expected, as IMT is designed to improve respiratory muscles strength, not lung volume considering the specificity principle. A review with meta-analysis by HajGhanbari et al., based on 21 research studies,

similarly to our review, found no significant improvement in lung function parameters among athletes undergoing respiratory muscle training [43]. Moreover, the patients in the eight studies [2,12,13,20–24] did not present a marked reduction in lung function parameters at baseline, thereby limiting the potential improvement margin from the start to the end of IMT.

4.3. Comparison with the Literature

Sadek et al. support our conclusion that long durations of IMT (12 weeks) show better results in HF patients than shorter interventions, notably quality of life and dyspnoea [44]. However, two meta-analyses suggest that higher intensities (60% MIP) increase the effectiveness of IMT on HF patients [15,44]. Menezes et al. [45] confirm the effectiveness of IMT on inspiratory muscle strength and endurance in stroke patients. Their results confirm that the duration of the intervention seems more important than the intensity, as their RCT with the longest duration (8 weeks) displayed better improvement than the shortest (1–4 weeks) [45]. IMT has also shown good effectiveness regarding the reduction in respiratory complications due to stroke [5,45] However, it has not yet shown impact on quality of life and needs to be explored more [5,45,46]. While the intensity of IMT does not seem to be as important as the duration in the first 12 weeks of IMT for stroke and HF patients, the meta-analysis conducted by Zheng et al. [4] suggested that low-intensity IMT is more effective on hypertension than moderate and high intensities. However, its effect on quality of life remains uncertain [47,48].

4.4. Methodological Quality of Studies

The eight included studies [2,12,13,20–24] showed high methodological quality presented an average of 6.5 in the PEDro scale (Table 4) reflecting the rigorous research methods that were conducted. This has the effect of reducing the risks of bias or confounding factors and improving internal validity, making the results and conclusions of studies trustworthy. Thus, it makes our review strong from a methodological point of view. For future studies, therapists who administrated therapy should be blinded to reduce bias.

4.5. Limitations

This study was limited by studies mainly involving HF patients; therefore, extrapolation of our results to all CVD needs to be taken with caution; no studies assessed the effect of IMT with intensity higher than 60% of MIP. The wide duration ranges of interventions (4–12 weeks) can affect the intensity training effect.

4.6. Future Perspective

As a future perspective, some gaps should be filled. Firstly, the effect of IMT on depression could be assessed more deeply as it is a high prognosis factor for CVD. Secondly, intensities higher than 60% are only explored in recreational athletes [49] but not in CVD. Therefore, RCTs assessing the effects of high intensity of IMT (i.e., >60% MIP) in CVD could be proposed. Lastly, the time of intervention longer than 12 weeks and its long-term effect should be explored more.

5. Conclusions

In conclusion, this review indicates that IMT intensities ranging from 25 to 60% of MIP have a positive impact on CVD patients in terms of inspiratory muscle strength, endurance, exercise capacity, and quality of life. However, the effects of higher intensities (more than 60%) of MIP on CVD patients should be explored for future studies. Additionally, the results of this review suggest that the duration of intervention is also a crucial component that might have an important impact on outcomes of interest for these patients. In terms of duration, protocols involving at least 12 weeks of training seem more beneficial than shorter interventions in terms of dyspnoea and quality of life.

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