Inspiratory Muscle Training in Patients With Heart Failure: What Is New? Systematic Review and Meta-Analysis

Aline de Cassia Meine Azambuja, Luma Zanatta de Oliveira, Graciele Sbruzzi

Objective. The benefits of inspiratory muscle training (IMT) have already been demonstrated in patients with heart failure (HF), but the best mode of training and which patients benefit from this intervention are not clear. The purpose of this study was to review the effects of IMT on respiratory muscle strength, functional capacity, pulmonary function, quality of life, and dyspnea in patients with HF; IMT isolated or combined with another intervention (combined IMT), the presence of inspiratory muscle weakness, training load, and intervention time were considered.

Methods. The search included the databases MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Physiotherapy Evidence Database, and LILACS database through September 2019. The review included randomized studies that assessed IMT in isolation or combined with another intervention—in comparison with a control group, a placebo, or another intervention—in patients with HF. Fourteen studies were included, 13 for meta-analysis (10 for isolated IMT and 3 for combined IMT).

Results. Isolated IMT demonstrated an increase in maximal inspiratory pressure (MIP) (25.12 cm H_2O; 95% CI = 15.29 – 34.95), 6-Minute Walk Test (81.18 m; 95% CI = 9.73 – 152.63), maximum oxygen consumption (12 weeks: 3.75 mL/kg/min; 95% CI = 2.98 to 4.51), and quality of life (−20.68; 95% CI = −29.03 to −12.32). The presence of inspiratory muscle weakness, higher loads, and longer intervention times resulted in greater increases in MIP. IMT combined with another intervention demonstrated an increase only in MIP.

Conclusions. Isolated IMT resulted in an increase in inspiratory muscle strength, functional capacity, and quality of life. IMT combined with another intervention resulted only in a small increase in inspiratory strength. Isolated IMT with higher loads can be considered an adjuvant intervention, especially for those who do not adhere to conventional rehabilitation and who have respiratory muscle weakness.

Impact. A systematic review was necessary to review the effects of IMT on respiratory muscle strength, lung function, functional capacity, quality of life, and dyspnea in patients with HF. Various clinical issues important for a better training prescription were considered; these included whether the performance of the training IMT as a form of isolated training benefits patients with HF, whether the combination of IMT with another intervention has additional effects, whether any patient with HF can benefit from IMT (alone or combined with another intervention), and whether only patients who already have respiratory muscle weakness benefit. Also important was establishing which training load provides the best result and the best intervention time, so that health care can be provided more efficiently.

Lay Summary. For people with heart failure, IMT by itself, without being combined with other exercise, can improve ease of breathing, increase the amount of distance that they can walk, and improve quality of life. Inspiratory training with higher loads might be helpful for those with respiratory muscle weakness who are unable to do conventional exercise.

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Approximately 6.5 million American adults over 20 years of age were diagnosed with heart failure (HF) between 2011 and 2014.[1] This disease causes a reduction in cardiac output and blood flow to the peripheral and respiratory muscles. These changes can result in muscle dysfunction leading to fiber atrophy (mainly type I) and weakness of the peripheral and respiratory muscles, and the latter is a predictor of mortality and survival in these patients.[2,3] Thus, muscle weakness, often associated with dyspnea, can cause fatigue, reduced functional capacity, and increased exercise intolerance in these patients.[4–7] In this sense, inspiratory muscle training (IMT) may be used as an adjunct intervention to improve cardiopulmonary capacity in these individuals.[8,9] Recently, 2 systematic reviews were published on the effects of IMT in patients with HF.[10,11] Wu et al[10] included 8 studies and found that IMT improved inspiratory muscle strength (MIP), pulmonary function, exercise tolerance, and quality of life while reducing dyspnea. Sadek et al[11] included 7 studies and showed the benefit of IMT in MIP, functional capacity, and dyspnea.

However, both reviews included randomized controlled trials (RCTs) and nonrandomized studies in the same analysis, which is not the most appropriate, since these designs have distinct methodological characteristics, and the searches were performed only until 2016. Also, sensitivity analyses regarding important clinical issues for better training prescription were not performed; these encompassed the following questions: Does performing IMT as a form of isolated training benefit patients with HF? Does combining the IMT with another intervention have additional effects? Can any patient with HF benefit from IMT, either isolated or combined with another intervention, or can only patients who already have respiratory muscle weakness benefit? Which training load provides the best result, and what is the best intervention time? Therefore, this systematic review was necessary to review the effects of IMT on respiratory muscle strength, pulmonary function, functional capacity, quality of life, and dyspnea in patients with HF by considering these issues.

Methods

This systematic review was planned and conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Guideline and the Cochrane Collaboration.[12] The protocol was registered in PROSPERO (CRD42017080339).

Data Sources and Searches

The searches were carried out in the following databases: MEDLINE (PubMed), LILACS database, Physiotherapy Evidence Database, EMBASE, and Cochrane Central Register of Controlled Trials, in addition to a manual search of the references of studies already published on the subject. The search was conducted in September 2019,

and the search terms used individually or in combination included "heart failure" and "breathing exercises" as well as a specific filter for RCTs.[13] There were no restrictions regarding year and language. The complete search strategy used for PubMed is shown in Supplementary Table 1.

Eligibility Criteria

The RCTs that evaluated the effects of IMT (isolated or in combination with another intervention-conventional rehabilitation or exercise) were compared with control groups, placebo, or another intervention in the treatment of patients with HF in both decompensation and outpatient care. The following outcomes were considered: respiratory muscle strength, pulmonary function, functional capacity (assessed by distance walked in the 6-Minute Walk Test [6MWT] and maximum oxygen consumption [Vo_2peak]), quality of life (assessed with the Minnesota Living With Heart Failure Questionnaire), and dyspnea.

Study Selection

The titles and abstracts of all identified articles were independently assessed by 2 reviewers (A.C.M.A. and L.Z.O.) in duplicate. All abstracts that failed to provide sufficient information on the inclusion and exclusion criteria were selected for evaluation of the full text and were included according to the eligibility criteria. Disagreements among the reviewers were resolved by consensus.

Data Extraction

The data were extracted through a standardized form created by the authors themselves containing information regarding the methodological characteristics of the studies, participants, interventions, and outcomes. Disagreements were also resolved by consensus. The main outcome was respiratory muscle strength (through MIP and maximal expiratory pressure). Secondary outcomes were pulmonary function (through forced vital capacity [FVC] and forced expiratory volume in the first second [FEV_1]), functional capacity (assessed with the 6MWT and Vo_2peak [in mL/kg/min]), quality of life (assessed with the Minnesota Living With Heart Failure Questionnaire, where lower scores should be interpreted as higher quality of life), and dyspnea (assessed with the Borg Scale).

Quality Assessment

The risk of bias assessment was performed by 2 independent reviewers (A.C.M.A. and L.Z.O.) using the items established by the Cochrane Collaboration tool:[12] generation of randomization sequence, concealment of allocation, masking of patients and therapists, masking of outcome assessors, description of losses and exclusions, and intention-to-treat analysis. Studies without a clear

description of these items were considered unclear or uninformed.

The level of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[12] For each outcome, the quality of the evidence was based on 5 factors: risk of bias, inconsistency, indirect evidence, imprecision, and potential for publication bias, resulting in 4 levels of evidence quality: high, moderate, low, and very low. The evaluation was performed on https://gradepro.org.

Data Synthesis and Analysis

The meta-analysis was performed using the random effects model, and the measures of effect were calculated by the difference between the means and the SD of the difference between the means. A 95% CI was considered significant. The statistical heterogeneity of the treatment effect in all studies was evaluated by the inconsistency test (I^2), in which values between 25% and 50% were considered as indicating moderate and high heterogeneity, respectively. Sensitivity analyses were performed considering the following characteristics: IMT isolated or combined with another intervention, inclusion of patients with or without inspiratory muscle weakness (MIP < 70% of the predicted value),[14] load used in the IMT, and intervention time. All analyses were performed using Review Manager 5.3 software (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

Role of the Funding Source

This study was funded in part by the Coordenação de Aperfeiçoamento de Pessoal de Nivel Superior. The funder played no role in the design, conduct, and reporting of this study.

Results

Description of the Studies

The search strategy resulted in 1746 articles, of which 35 studies were considered relevant for detailed analysis; 14 of these studies met the eligibility criteria and were included in the systematic review (n = 374), and 13 of these studies were included in the meta-analysis (n = 342) (Fig. 1). Stein et al[15] provided the results of MIP expressed in different ways, therefore not allowing this study to be included in the meta-analysis.

Ten studies performed isolated IMT and compared it with control groups.[14–23] Of these studies, 7 included individuals with inspiratory muscle weakness.[7,14,18,20–23] Regarding the load, 6 studies used loads of up to 30% of MIP,[14,17,18,20,22,23] 1 study used loads of up to 40% of MIP,[12] 2 studies used loads of 60% to 90% of MIP,[19,22] and 1 study[18] used 100% for 10 maximal repetitions. Regarding the intervention time, 3 studies performed the training for a period of 4 to

6 weeks,[16,18,20] 2 studies performed it for 8 weeks,[16,19] and 5 studies performed it for 12 weeks[14,20,22–24] (Tab. 1).

Four studies performed IMT combined with another intervention, 2 of which were combined with aerobic training,[25,26] 1 with peripheral resistance training,[26] and 1 with neuromuscular electrical stimulation.[27] Of the 4 studies, only 1 included patients with muscle weakness.[26] Regarding load, 3 studies used loads of up to 30% of MIP,[26–28] and 1 study used a load of 60% of MIP.[25] Regarding the intervention time, 3 were performed for 12 weeks[25,26,28] and 1 was performed for 8 weeks[27] (Tab. 1). In addition, all studies included outpatients care.

Risk of Bias

Of the studies included, 35.7% presented random sequence generation, 14.3% reported concealment of the allocation, 21.4% had masking of patients and used the intention-to-treat principle for statistical analysis, and none of the studies reported masking of therapists, presenting a high risk of bias for these characteristics. Moreover, 42.9% were masked by the evaluators of the outcomes (moderate risk of bias), and 78.6% described losses in follow-up and exclusion, characterizing a low risk of bias Supplementary Table 2.

Effects of Interventions

Maximal inspiratory pressure. Of the 13 studies eligible for the meta-analysis, only 12 studies were included in the analysis of the effects of IMT on MIP (n = 374).[14,16–23,25–28] The study by Palau et al[28] was excluded from this analysis because it presented only baseline values for MIP; it was therefore impossible to calculate the mean difference.

Nine studies evaluated isolated IMT, showing an increase of 25.12 cm H_2O in MIP (95% CI = 15.29 – 34.95) compared with the control group.[14,16–23] Because of the high heterogeneity, 3 sensitivity analyses were performed: (1) analysis only of studies that included individuals with inspiratory muscle weakness,[18,20–23] in which it was possible to observe an even greater increase in MIP of 31.89 cm H_2O (95% CI = 18.04 – 45.74) in relation to patients without inspiratory muscle weakness[16,17,19] who had an increase of 14.47 cm H_2O (95% CI = 6.54 – 22.40); (2) analysis of the training load, in which studies that used a load of up to 40% of MIP had an increase of 24.62 cm H_2O (95% CI = 11.82 – 37.41),[14,16,17,19–22] and studies that used loads of 60% to 90% of MIP had an increase of 31.69 cm H_2O (95% CI = 4.68 – 58.71);[21,23] and (3) analysis of the intervention time, in which studies performed for 6 to 8 weeks demonstrated an increase of 21.83 cm H_2O (95% CI = 7.89 – 35.77),[16,20,22,23] and studies with 12 weeks of intervention had a greater increase, reaching 32.40 cm H_2O (95% CI = 13.79 – 51.00)[14,20,22,23] (Fig. 2). On the basis of the GRADE approach, the level of evidence for this result was considered to be very low (Tab. 2).
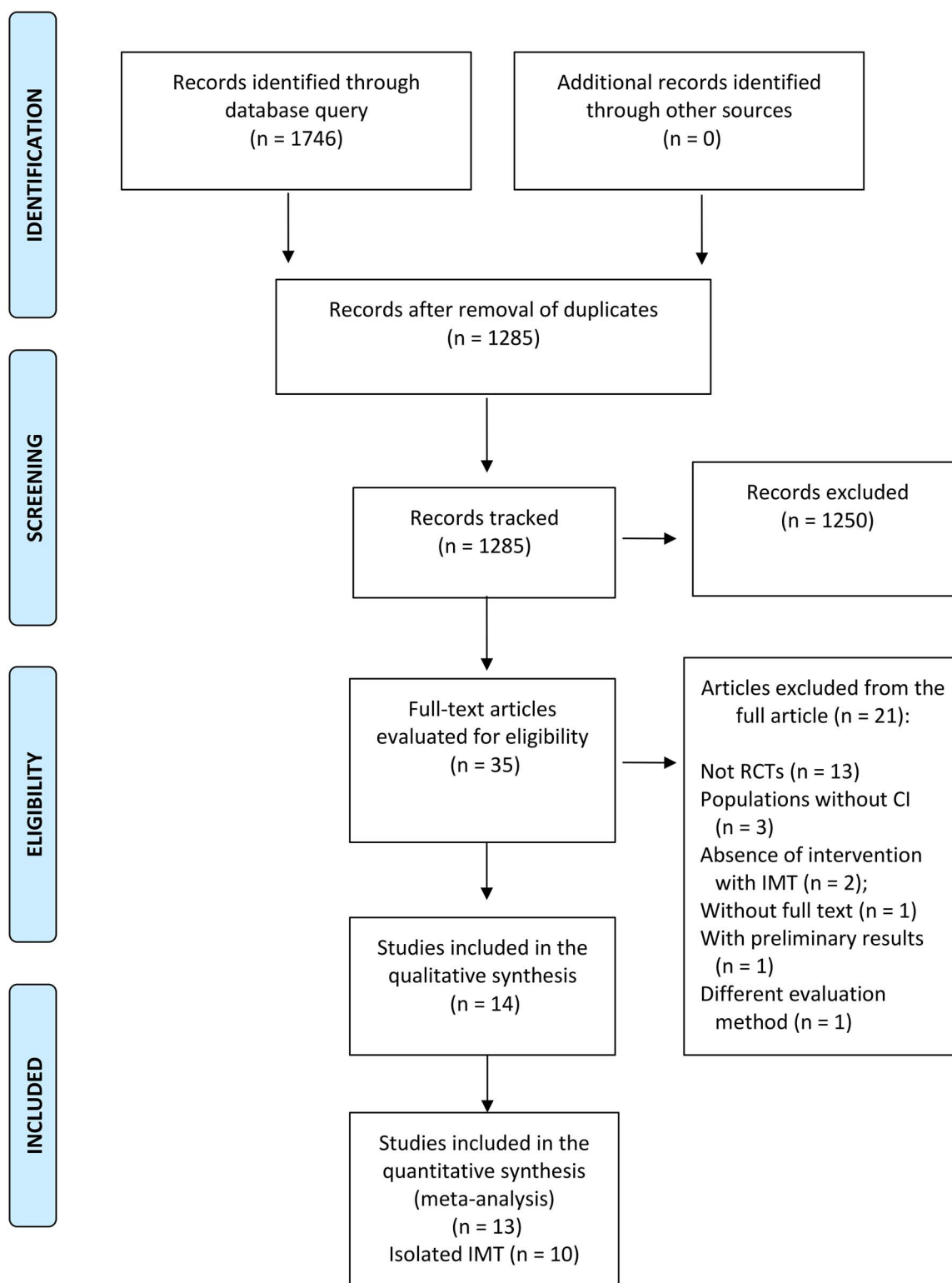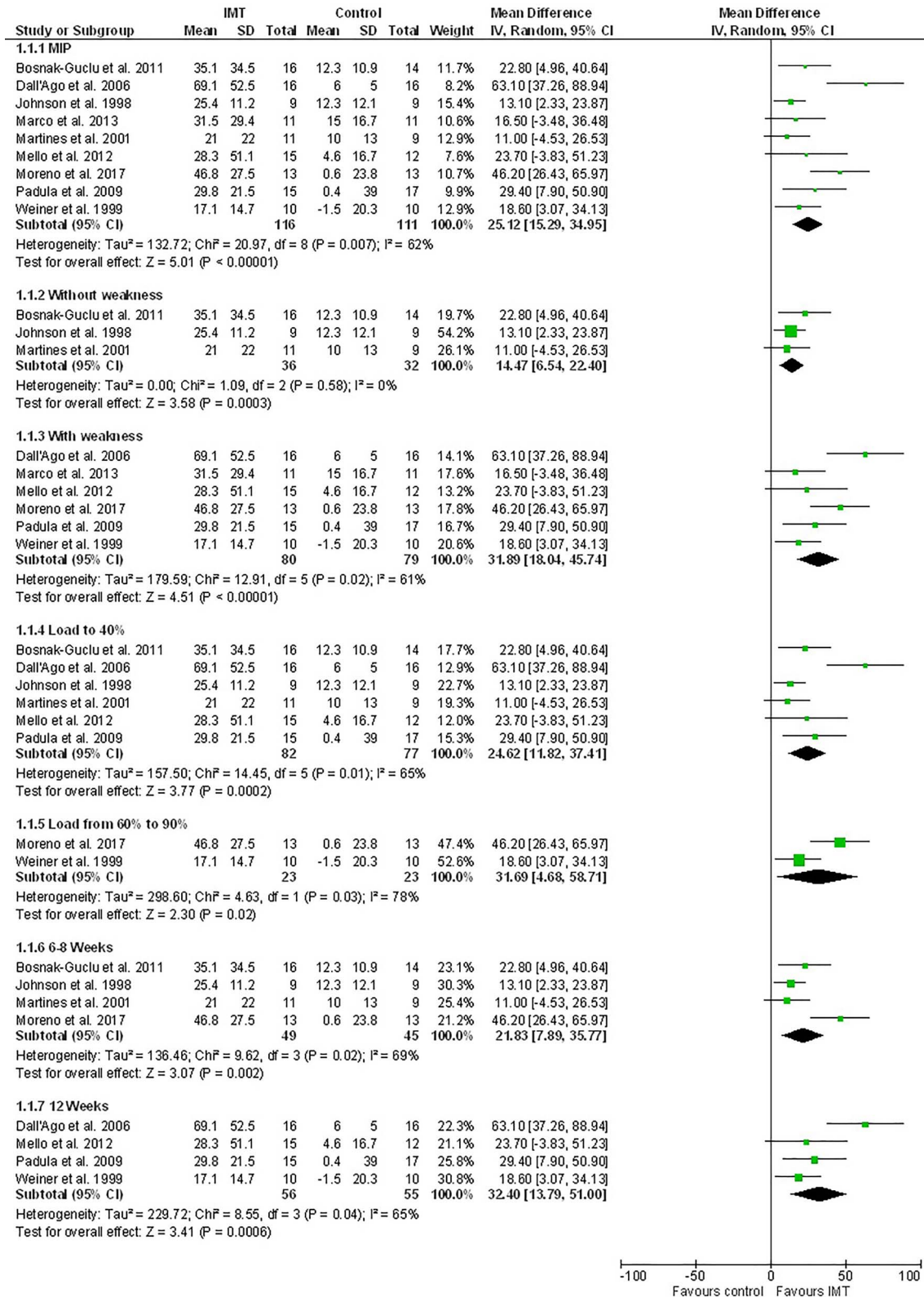
Figure 1.
PRISMA flow diagram.

Figure 2.
Maximal inspiratory pressure for inspiratory muscle training (IMT) versus control group. 1.1.1 = IMT for all studies; 1.1.2 = studies without inspiratory muscle weakness; 1.1.3 = studies with inspiratory muscle weakness; 1.1.4 = studies with load of up to 40%; 1.1.5 = studies with loads of 60%–90%; 1.1.6 = studies conducted for 6–8 weeks; 1.1.7 = studies conducted for 12 weeks.

Table 1.
Characteristics of Studies[a]

IMT	Study (y)	Methods		Characteristics of Patients	Age, y, Mean (SD)	
		Intervention Group (No. of Patients)	Control Group (No. of Patients)		Intervention Group	Control Group
Isolated	Bosnak-Guclu et al,[16] 2011	IMT, 40% load; 30 min/d, 7 times/wk (16)	IMT, placebo, 15% load; 30 min/d, 7 times/wk (14)	Functional class: NYHA II or III Stable outpatients	69.5 (8)	65.7 (10.5)
	Dall'Ago et al,[14] 2006	IMT, 30% load (16)	IMT without inspiratory load (16)	Outpatient individuals	58 (2)	54 (3)
	Johnson et al,[17] 1998	IMT, 30% load (9)	IMT, placebo, 15% load (9)	NYHA II or III Stable individuals	70 (4.6)	63.4 (4.5)
	Marco et al,[18] 2013	Inspiratory pressure that allowed 10 consecutive maximal repetitions (11)	IMT, placebo, 10% load (11)	NYHA II or III Stable individuals	68.5 (8.88)	70.1 (10.8)
	Martinez et al,[19] 2001	IMT, 30% load (11)	IMT, minimum load of 10% (9)	NYHA II or III Stable individuals	60 (14)	57 (13)
	Mello et al,[20] 2012	IMT, 30% load (15)	IMT, no load (12)	NYHA II	54.3 (2)	53.3 (2)
	Moreno et al,[21] 2017	IMT, 60% load (13)	No training (13)	NYHA II or III	61 (14)	60 (13)
	Padula et al,[22] 2009	IMT, 30% load (15)	Standard education protocol (17)	NYHA II or III Stable individuals	76 (28)	73 (47)
	Stein et al,[15] 2009	IMT, 30% load (16)	IMT, no load (16)		NR	NR
	Weiner et al,[23] 1999	IMT, 15% load (10)	IMT, placebo (10)	NYHA II or III	66.2 (4.6)	63.8 (4.0)
Combined with another intervention	Adamopoulos et al,[25] 2014	IMT, 60% load + aerobic training (21)	IMT, placebo, 10% load + aerobic training (22)	NYHA II or III	57.8 (11.7)	58.3 (13.2)
	Kawauchi et al,[27] 2017	IMT, 30% load for moderate intensity and 15% load for low intensity + peripheral resistance training (13)	Control (9)	NYHA II or III	56 (7)	56 (7)
	Winkelmann et al,[26] 2009	IMT, 30% load + aerobic exercise training (12)	Aerobic exercise training (12)	Stable individuals	54 (12)	59 (9)
	Palau et al,[28] 2018	IMT, 25–30% load +NMES in bilateral quadriceps, 400 μs and 10–50 Hz (13)	IMT, 25–30% load (13)	NYHA III or IV	73 (10)	75 (10)

[a]IMT = inspiratory muscle training; NMES = neuromuscular electrical stimulation; NR = not reported; NYHA = New York Heart Association.

Three studies that assessed IMT combined with another intervention were evaluated.[23,24] It was observed that MIP increased by 11.08 cm H_2O (95% CI = 2.14 – 20.01) in relation to the control group. When considering only the 2 studies that included individuals without inspiratory muscle weakness[25,27] for the sensitivity analysis, the increase in MIP was 17.36 cm H_2O (95% CI = 1.77 – 32.96). Most studies also used training loads of 30%. When analyzing only these studies,[26,27] a nonsignificant increase of 13.05 cm H_2O (95% CI = −3.40 – 29.51) was observed. Finally, 2 studies performed IMT for 12 weeks and obtained a nonsignificant increase of 9.23 cm H_2O (95% CI = −0.21 – 18.67)[25,26] (Fig. 3). On the basis of the GRADE approach, the level of evidence for this result was considered low (Tab. 2).

Table 2.
Quality of Evidence[a]

IMT	Measure of Result	No, of Studies	Risk of Bias	Inconsistency	Indirectness	Imprecision	Absolute Mean Difference (95% CI)	Quality of Evidence
Isolated	Maximal inspiratory pressure	9	Serious[b]	Very serious[c]	Not serious	Not serious	25.12 (15.29–34.95)	Very low
	6-Min Walk Test	3	Serious[b]	Serious[c]	Not serious	Very serious[e]	81.18 (9.73–152.63)	Very low
	Vo$_2$peak	5	Serious[b]	Very serious[c]	Not serious	Not serious	2.21 (0.1–4.51)	Very low
	Quality of life	2	Very serious[b]	Serious[d]	Not serious	Serious[e]	20.68 (29.03–12.32)	Very low
	Dyspnea	2	Serious[b]	Very serious[c]	Not serious	Not serious	1.11 (2.97–0.75)	Very low
Combined with another intervention	Maximal inspiratory pressure	3	Serious[b]	Not serious	Not serious	Serious[c]	11.08 (2.14–20.01)	Low
	Maximal expiratory pressure	2	Serious[b]	Not serious	Not serious	Serious[c]	18.24 (5.73–42.22)	Low
	6-Min Walk Test	2	Serious[b]	Not serious	Not serious	Very serious[c]	42.5 (17.91–102.92)	Very low
	Vo$_2$peak	3	Serious[b]	Not serious	Not serious	Not serious	0 (0.32–0.31)	Moderate

[a] IMT = inspiratory muscle training; Vo$_2$peak = maximum oxygen consumption.
[b] Methodological limitation.
[c] High heterogeneity.
[d] Moderate heterogeneity.
[e] Large CI.

Maximal expiratory pressure. Two studies that compared IMT combined with another intervention with control groups evaluated maximal expiratory pressure and obtained a nonsignificant increase of 18.24 cm H$_2$O (95% CI = −5.73 to 42.22).[26,27] Only 1 study that compared isolated IMT with the control group evaluated maximal expiratory pressure, and it was not possible to perform a meta-analysis of maximal expiratory pressure (Supplementary Fig. 1).[16] On the basis of the GRADE approach, the level of evidence for this result was considered low (Tab. 2).

Functional capacity: 6MWT. Three studies evaluated isolated IMT and used a training load of up to 40% of MIP.[14,16,19] When analyzing these studies, an increase of 81.18 m in the 6MWT (95% CI = 9.73 – 152.63) was observed. Because of the moderate heterogeneity, a sensitivity analysis was performed based on the study of Dall'Ago et al,[14] which included individuals with inspiratory muscle weakness. Thus, heterogeneity was reduced to 0%, but there was no significant difference in outcome (29.01 m; 95% CI = −58.26 to 116.27) (Fig. 4). On the basis of the GRADE approach, the level of evidence for this result was considered to be very low (Tab. 2).

Two studies performed combined IMT and used loads of 30%.[26,27] When observing these studies, there was a nonsignificant increase of 42.50 m in the 6MWT (95% CI = −17.91 to 102.92) compared with the control group (Supplementary Fig. 2). On the basis of the GRADE approach, the level of evidence for this result was considered to be very low (Tab. 2).

Functional capacity: Vo$_2$peak. In relation to Vo$_2$peak, 5 studies that performed isolated IMT versus control evaluated this outcome, but there was no significant difference between groups (2.21 mL/kg/min; 95% CI = −0.10 to 4.51).[14,18–20,23] A sensitivity analysis that only assessed the studies that included individuals with inspiratory muscle weakness found no significant difference (2.41 mL/kg/min; 95% CI = −0.03 to 4.86).[15,19,23] A significant increase in this outcome (3.75 mL/kg/min; 95% CI = 2.98 – 4.51) was observed only in the studies that performed training for 12 weeks (Supplementary Fig. 3).[14,20] On the basis of the GRADE approach, the level of evidence for this result was considered to be very low (Tab. 2).

The 3 studies that performed combined IMT versus control for 12 weeks evaluated Vo$_2$peak but did not
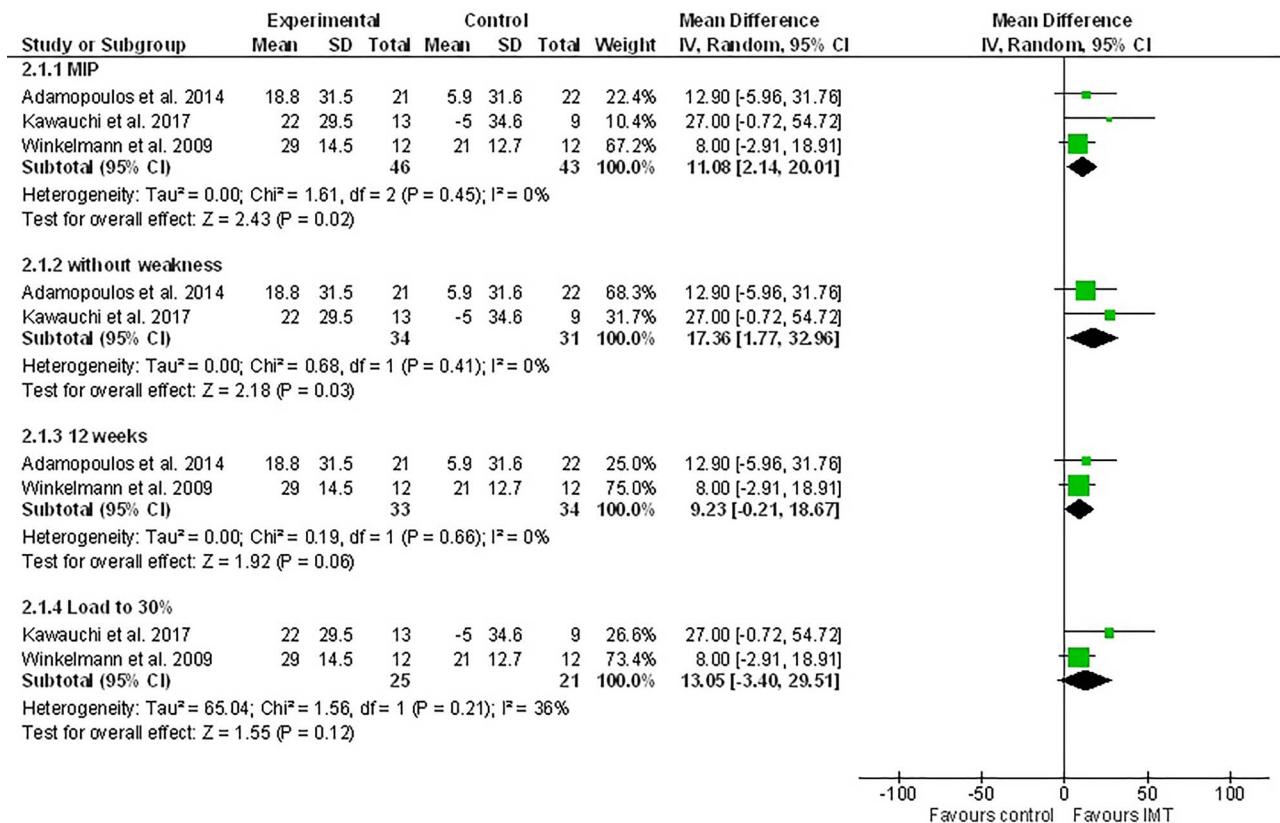
Figure 3.
Maximal inspiratory pressure for combined inspiratory muscle training (IMT) versus control group. 2.1.1 = IMT for all studies; 2.1.2 = studies without inspiratory muscle weakness; 2.1.3 = studies conducted for 12 weeks; 2.1.4 = studies with load of up to 30%.
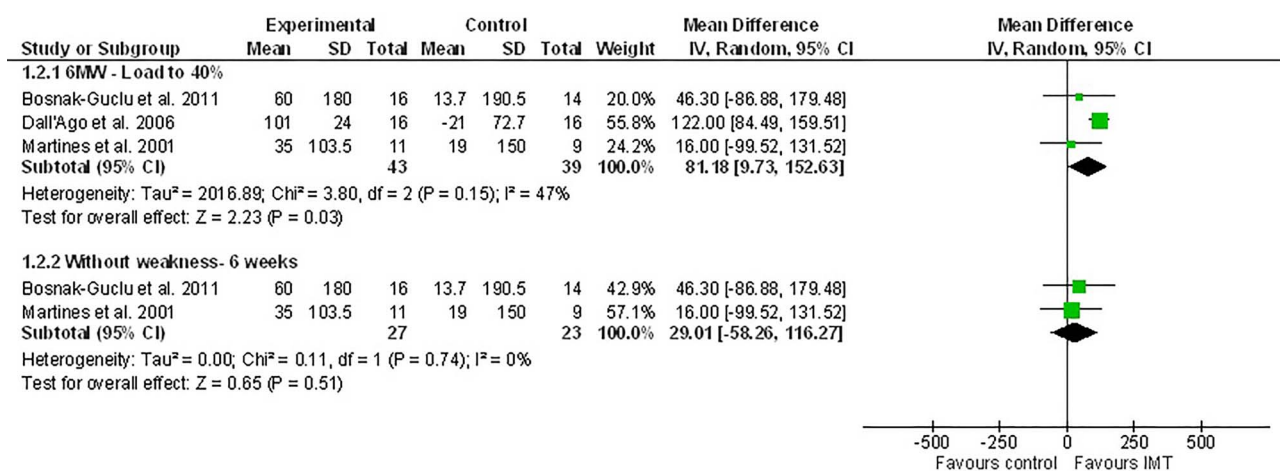

Figure 4.
Distance walked in the 6-Minute-Walk Test for inspiratory muscle training (IMT) versus control group. 1.2.1 = distance walked in the 6-Minute-Walk Test for all studies; 1.2.2 = distance walked in the 6-Minute-Walk Test for studies conducted with patients who were given IMT and had no inspiratory muscle weakness for 6 weeks.

observe an increase (−0.00 mL/kg/min; 95% CI = −0.32 to 0.31),[25,26,28] and the same result was found when analyzing only the 2 studies that used loads of up to 30% (Supplementary Fig. 4).[26,28] On the basis of the GRADE approach, the level of evidence for this result was considered moderate (Tab. 2).

Quality of life.   Two studies performed isolated IMT. A decrease in MLHQF score of −20.68 (95% CI = −29.03 to −12.32) was observed, indicating improvement in quality of life.[14,20] Both studies included individuals with inspiratory muscle weakness and performed the intervention for 12 weeks (Supplementary Fig. 5). On the basis of the GRADE approach, the level of evidence for this result was considered to be very low (Tab. 2).

Four studies performed combined IMT versus control, with no significant difference in this outcome (−5.04; 95% CI = −11.78 to 1.70).[24–27] The same behavior was observed in the sensitivity analyses in relation to the use of loads of 30% (−1.07; 95% CI = −13.01 to 10.86)[26–28] and the intervention time for 12 weeks (−4.89; 95% CI = −11.88 to 2.10 l)[23,24,26] (Supplementary Fig. 6). On the basis of the GRADE approach, the level of evidence for this result was considered moderate (Tab. 2).

Dyspnea.   Two studies performed isolated IMT versus control and assessed dyspnea, but no significant reduction was observed in this outcome (−1.11; 95% CI = −.97 to 0.75) (Supplementary Fig. 7).[14,16] On the basis of the GRADE approach, the level of evidence for this result was considered to be very low (Tab. 2).

Only 1 study that performed combined IMT versus control assessed dyspnea.[26] The authors found a significant reduction of dyspnea in the intervention group compared with the control group.

Pulmonary function.   It was not possible to perform a meta-analysis for any variables related to pulmonary function because of the lack of data or units of measurement.

Four studies evaluated pulmonary function through the FEV_1/FVC outcome.[16,21,23,25,27] Of these, 2[16,21] performed isolated IMT and the meta-analysis was not performed, since 1 of the studies[20] did not present postintervention values, making it impossible to analyze a single study.[16] The study by Bosnak et al[16] presented a reduction in FEV_1/FVC ratio in the intervention group and increase in the control group after 6 weeks of intervention.

The other 2 studies that evaluated this outcome performed combined IMT.[25,27] The study by Adamopoulos et al[25] found no significant improvement after 12 weeks of

intervention, and neither did the study by Kawauchi et al[27] after 8 weeks of intervention.

FEV_1 and FVC were assessed by 3 studies.[16,23,25] Two performed isolated IMT.[16,23] The studies by Bosnak et al[16] and Weiner et al[23] found no significant difference in the increase in FEV_1 and FVC compared with the intervention and control groups. One study performed combined IMT and obtained a reduction in FEV_1 and FVC in the intervention group (IMT plus aerobic training) and an increase in the control group (aerobic training).[26]

Discussion
The results from our pooled analyses indicate that isolated IMT resulted in an increase in inspiratory muscle strength, functional capacity, and quality of life, and this increase was higher in studies that included patients with respiratory muscle weakness who used training loads higher than 60% and who had longer intervention times. However, the IMT, when performed in combination with another intervention, demonstrated only a small increase in respiratory muscle strength.

As noted in this study, the improvement in inspiratory muscle strength promoted by isolated IMT may aid in the application of the improved functional capacity, as the respiratory muscle fatigue and dyspnea presented by these patients are associated with a low functional capacity.[29,30]

Still, the use of IMT with progressive inspiratory loads attenuates the respiratory muscle metaboreflex in patients with heart failure. The attenuation of the respiratory muscle metaboreflex subsequently improves perfusion to limb muscles during exercise by preventing the redistribution of blood flow to the inspiratory muscles.[31,32] Furthermore, IMT can attenuate peripheral chemoreflex response and improve cardiac function, which is directly combined to a reduction in sympathetic excitation in patients with HF, improving systemic vasodilation and peripheral muscle perfusion while increasing ventilatory efficiency and, subsequently, functional capacity.[33]

It was also observed in the studies performed by Sbruzzi et al[34] and Wu et al[10] that isolated IMT improves the quality of life of patients with HF, as measured with the Minnesota Living With Heart Failure Questionnaire. This improvement may be related to the benefits of IMT in cardiovascular and respiratory response and reduced perception of dyspnea,[14] especially in individuals with inspiratory muscle weakness, since respiratory muscle strength may be an independent predictor of prognosis in patients with HF.[2]

Dyspnea was not significantly modified after intervention with isolated IMT in this review. Some factors may explain this result: the 2 studies included used low IMT loads (loads <60% of MIP), and 1 of the studies performed the

training for a period of only 6 weeks.[12,13] In the study by Bosnak-Guclu et al,[16] both groups presented improvement in dyspnea following isolated IMT and concluded that higher workloads are necessary for their improvement.

When analyzing the IMT combined with another intervention compared with only performing another intervention, a small increase was observed, with no additional results in the other evaluated outcomes. Adamopoulos et al[25] justify the lack of improvement in functional capacity with the addition of IMT to another intervention by the small diaphragmatic muscle training added to aerobic exercise and/or baseline functional status because the patients included had no serious impairment.

Strengths and Limitations

Our study presents a few strengths, such as a specific research question, comprehensive bibliographic search, explicit eligibility criteria, and meta-analysis. In addition, we evaluated some specific and important clinical questions regarding this type of intervention and for this type of population, which may directly interfere with the results found: IMT isolated or combined with another intervention; presence of inspiratory muscle weakness; training load; and intervention time. As limitations, we found that most RCTs were at high risk of bias, and the level of evidence for most outcomes was low or very low. This means that any estimate of effect is very uncertain, and it is very likely that new research will have an impact on the confidence to estimate the effect.[35]

Comparisons With Other Reviews

This review differs from the recent reviews published in 2018 by Wu et al[10] and Sadek et al,[11] since the authors carried out the search only until the year 2016, included both RCTs and nonrandomized clinical trials, and did not perform all sensitivity analyzes observing the mentioned clinical issues cited above. Furthermore, Plentz et al[9] and Sbruzzi et al[34] performed sensitivity analyses regarding the intervention time and the presence of respiratory muscle weakness. However, they excluded articles that associated IMT with another intervention and did not perform analyses in relation to the training load. Thus, this review addresses more complex and relevant issues for clinical practice.

Isolated IMT resulted in an increase in inspiratory muscle strength, functional capacity, and quality of life, and this increase was higher in studies that included patients with respiratory muscle weakness who used training loads higher than 60% and who had longer intervention times. The IMT, when performed in combination with another intervention, demonstrated only a small increase in respiratory muscle strength. So isolated IMT can be considered as an adjuvant intervention in patients with

HF, especially for patients who do not adhere to conventional rehabilitation.

Author Contributions

Concept/idea/research design: A.C.M. Azambuja, L.Z. de Oliveira, G. Sbruzzi
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Fund procurement: A.C.M. Azambuja
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