

## Systematic review

### Impact of inspiratory muscle training on respiratory muscle function and functional capacity in patients with heart failure: a systematic review

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**Abstract:** Heart failure (HF) is one of the most prevalent diseases in the world and is characterized as a complex clinical syndrome. It is a disease that affects both the peripheral muscles and the respiratory muscles, causing damage such as reduced strength and endurance. One of the main symptoms is fatigue and exercise intolerance.

The aim of this review article is to assess whether the use of inspiratory muscle training (IMT) associated with conventional training enhances inspiratory muscle strength (P<sub>I</sub>max) and inspiratory muscle endurance (S<sub>P</sub>I<sub>max</sub>) and functional capacity in patients with HF.

**Methods:** A literature review was carried out on the use of IMT in patients, including 6 randomized clinical trials, searched in the PubMed, PEDro and Lilacs databases.

**Results:** There is evidence showing an increase in P<sub>I</sub>max and S<sub>P</sub>I<sub>max</sub> with the addition of IMT to training; in addition, an improvement in VO<sub>2</sub> peak, circulatory power and ventilatory efficiency.

**Conclusion:** The use of IMT associated with conventional training is an interesting strategy for boosting gains in strength and inspiratory muscle endurance, increasing exercise tolerance and consequently improving patients' quality of life. However, more studies are needed in order to more clearly define the selection criteria and methodology for applying IMT.

**Key words:** heart failure, inspiratory muscle training, respiratory metaborreflex, functional capacity

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#### Introduction

Heart failure (HF) is characterized as a complex clinical syndrome in which the heart is unable to pump blood to meet the metabolic demands of the tissues or does so under high filling pressures. It is one of the most prevalent diseases, with around 23 million cases worldwide and a 5-year survival rate of only 35% after diagnosis (1). This condition can occur as a result of biochemical, structural and congenital alterations, as well as being determined by extra-cardiac conditions such as systemic arterial hypertension (2). In this sense, at the beginning of the development of HF, the body recruits compensatory mechanisms to minimize the overload imposed on the myocardium, leading to cardiac remodeling, which will feed back into this condition (3, 4).

Cardio-sarcopenia is a condition that arises from the combination of two degenerative processes: sarcopenia, which is the gradual loss of skeletal muscle mass related to ageing, and cardiac dysfunction, characteristic of HF. Changes in cardiac function and structure trigger a series of negative effects on skeletal muscle, resulting in decreased strength, endurance and functional capacity.

This skeletal muscle dysfunction can, in turn, contribute to a vicious cycle, where muscle weakness resulting from HF leads to a sedentary lifestyle, further aggravating sarcopenia (5). Among the most common symptoms of HF are dyspnea, a feeling of fatigue and exercise intolerance (6). This can occur due to impaired muscle performance in both the peripheral and respiratory muscles, affecting exercise capacity and consequently reducing quality of life (4, 7).

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Factors such as hypoxia, oxidative stress, systemic inflammation and disuse are strongly related to muscle alterations, contributing to the appearance of these symptoms (3, 8).

In turn, inspiratory muscle weakness is present in 50% of patients with HF, who will show changes in variables such as maximum inspiratory pressure (MIP), which corresponds to inspiratory muscle strength, and maximum sustained inspiratory pressure (MPSI), which corresponds to inspiratory muscle endurance.

A decrease in the predicted values of these measurements is related to an increase in the sensation of dyspnea and a worsening of functional class, implying a worse prognosis (9). In this context, several studies have used inspiratory muscle training (IMT) as a form of intervention to specifically increase the strength and endurance of the inspiratory muscles and thereby improve functional capacity. This is due to the attenuation of the respiratory metaboreflex, which is a mechanism triggered by intense respiratory effort and which leads to fatigue of the peripheral muscles. In this way, there is a redistribution of flow from the peripheral muscles to the diaphragm through sympathetic vasoconstriction, exacerbating the individual's perception of effort and limiting performance in high-intensity exercise. With improved respiratory performance, this effect is minimized, leading to greater exercise tolerance and a better quality of life (10, 11).

The general aim of this article is to review the findings related to the effects of IMT in the cardiac rehabilitation of patients with HF. The specific objectives of this article include evaluating the effect of IMT on: inspiratory muscle strength and endurance, cardiopulmonary exercise test (CPET) variables, 6-minute walk test (6MWT), quality of life (QoL) and change in NYHA functional class.

## Methods

A literature review was carried out to investigate whether combining IMT with conventional training in patients with HF had a greater impact on respiratory muscle performance and the functional capacity of these individuals. This review included articles that addressed the proposed topic between 1996 and 2022. The searches were carried out in the Pubmed, PEDro and Lilacs databases, using the descriptors: inspiratory

muscle training, exercise; and heart, failure. The initial search was carried out using articles that contained these terms in the title or abstract and were considered eligible for the review. The exclusion criteria were duplicate articles, those that were not in line with the research topic and studies that did not use IMT as a form of intervention. The remaining studies were included in the review.

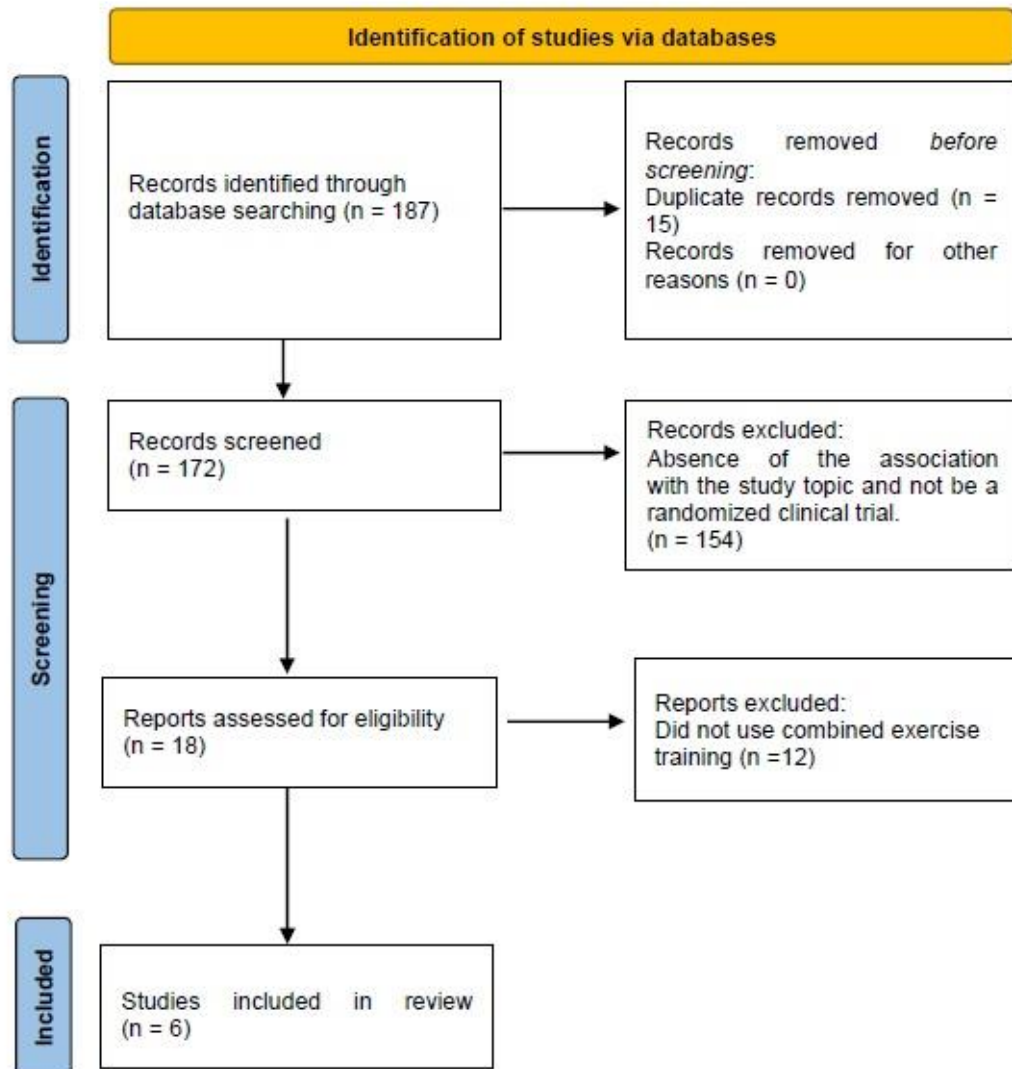
## Results

There were identified 187 possible relevant articles, with 15 being excluded as duplicates and 154 by absence of association with the study topic, remaining six studies included in the review (Fig. 1).

Considering the interventions presented by the studies (Table 1), only one study did not perform aerobic training (AT) as an intervention associated with IMT. One study performed the aerobic interval training (AIT) modality in aerobic training and the others used moderate continuous training. 3 of the 6 studies used resistance training associated with IMT.

## Effect of IMT on inspiratory muscle strength and endurance

In all the studies, P<sub>lmax</sub> measurements were taken pre- and post-intervention, and two studies did not assess S<sub>P</sub>l<sub>max</sub>. In the study by Winkelmann et al. (12), P<sub>lmax</sub> increased significantly (110% compared to 72%) when compared to the control group, which only performed AT. Similarly, in all the other studies there was an improvement in P<sub>lmax</sub>, both in the group that used IMT and in the groups that used AT and/or resistance training (RT). However, the most significant improvement occurred in the groups that used combined training. In addition, S<sub>P</sub>l<sub>max</sub>, which corresponds to inspiratory muscle endurance, was assessed in 4 studies (13-15, 17), and only showed a significant increase in the groups that underwent combined training. In the study by Kawauchi et al. (16), the low-intensity training group and the moderate-intensity training group both increased P<sub>lmax</sub>, but the greatest increase was in the moderate-intensity group and occurred more quickly than in the low-intensity group. Another point worth highlighting in this study is that the patients in the control group who did not undergo any type of intervention had an 8% reduction in P<sub>lmax</sub>.



**Figure 1. Identification of studies via databases**

### **Cardiopulmonary Exercise Test Variables**

In the study by Winkelmann et al. (12), interesting responses were seen in terms of the variables derived from the CPET. With the inclusion of CMT associated with aerobic training in the intervention group, significant improvements were seen in VO<sub>2</sub> peak, circulatory power, O<sub>2</sub> recovery kinetics and ventilatory efficiency (VE/VCO<sub>2</sub> slope). The 2013 study by Lautaris

et al. (13) corroborates the findings of the study by Winkelmann et al. (12). There was a significant improvement in VO<sub>2</sub> peak; exercise time; ventilatory threshold and reduction in VE/VCO<sub>2</sub> slope in the ARIS group (Aerobic Training (AT) + Resistance Training (RT) + IMT). The aerobic training group had a significant increase in VO<sub>2</sub> peak, exercise time and ventilatory threshold. Circulatory power improved significantly in both groups.

**Table 1. Characteristics of clinical trials and their training protocols**

Study	Subjects characteristics	Training protocol	Main outcomes
Winkelmann et al. (11) 2009	Total sample n = 38 NYHA: N/A (1) AT: n= 19, final n = 12 M/W: 7/5 Age: 59(9) yrs FEV1: 34(11)% PImax: 56 (13) cmH <sub>2</sub> O (2) AT + IMT: n= 19, final n= 12 M/W: 4/8 Age: 54(12) yrs FEV1: 39(12)% PImax: 57 (12) cmH <sub>2</sub> O	Duration: 12 weeks - 3x a week. AT: 1st week 20 minutes, adding 5 minutes each week. Totaling 45 min at the end.  AT + IMT: IMT 7 times a week for 30 minutes. 30% of PImax, readjusted weekly.	Significant improvement in PImax, peak VO <sub>2</sub> and circulatory power in the AT + IMT group. There was also a significant decrease in the VE/VCO <sub>2</sub> slope and ventilatory oscillations in the combined group. There were similar improvements in QoL in both groups.
Lautaris et al. (12) 2013	Sample: n= 27 (1) ARIS: n = 13 M/W: 10/3 Age: 57.1(11) yrs FEV1: 27.8 (8)% NYHA (II/III): 6/7 PImax: 75.3( 11) cmH <sub>2</sub> O  (2) AT: n = 14 M/W: 12/2 Age: 58.6 (8) yrs FEV1 (%): 30.6 (5.4) NYHA (II/III): 8/6 PImax: 79(9.1) cmH <sub>2</sub> O	Duration: 12 weeks - 3x a week. (1) ARIS: AT: 70%-80% of HRmax. Initial 20 minutes and 1 min increase each session until reaching 30 minutes.  (2) AT: 70-80% HR max. Initial 20 minutes and increased by at least 1 min each session. Totaling up to 45 minutes at the end. RT: 15 minutes Quadriceps – 3x12 repetitions at 50% of the 1RM, recalculated every 2 weeks. MMSS exercises – 1 and 2 kg dumbbell (4x12 repetitions) IMT: 60% SMIP - 15 minutes 60% of SPImax.	Significant increase in SPImax, peak VO <sub>2</sub> , exercise time, ventilatory threshold and reduction in VE/VCO <sub>2</sub> slope in the ARIS group.  The AT group significantly improved peak VO <sub>2</sub> , exercise time and ventilatory threshold.  Circulatory power improved in both groups.  QoL and NYHA functional class improved only in the ARIS group.
Adamopoulos et al. (13) 2014	Sample: n= 43 (1) AT/IMT: n = 21 M/W: 19/2 Age: 57.8 (11.7) yrs FEV1: 27.7 (6.7)% NYHA (II/III): 9/12 PImax: 81.9 (21.5) cmH <sub>2</sub> O  (2) AT/SHAM: n= 22 M/W: 17/5 Age: 58.3(13.2)yrs FEV1: 30.1(5)% NYHA (II/III): 12/10 PImax: 79.1(9.4) cmH <sub>2</sub> O	Duration: 12 weeks – 3x a week. AT: 45 min at 70-80% HR max for both groups. IMT protocol for both groups. Level 1: 60s of rest between sets. Level 2: 45s of rest. Level 3: 30s of rest. Level 4: 15s of rest. Level 5: 10s of rest. Level 6: 5s rest.  AT/IMT: 60% of SPImax in the group, readjusted every week. AT/SHAM: 10% of SPImax in the group, readjusted every week. 30 minutes - 3x a week.	Significant improvement in SPImax, exercise time, respiratory exchange ratio , ventilation and QoL in the AT/IMT group.  No significant difference in circulatory power, VE/VCO <sub>2</sub> slope and ventilatory threshold. VO <sub>2</sub> peak improved in both groups. NYHA functional class improved in both groups.

**Table 1. Characteristics of clinical trials and their training protocols (continued)**

Study	Subjects characteristics	Training protocol	Main outcomes
Kawauchi et al. (14) 2017	<p>Sample: n= 35</p> <p>(1) Control group: n= 9 M/W: 5/4 Age: 56(7) yrs FEV1: 29(7)% NYHA (II/III): 5/4 PImax: 74 (24) cmH<sub>2</sub>O</p> <p>(2) Low intensity training: n= 13 M/W: 6/7 Age: 54(10) yrs FEV1: 30(6)%; NYHA (II/III): 6/7 PImax: 72 (20) H<sub>2</sub>O</p> <p>(3) Moderate intensity training: n= 13 M/W: 8/5 Age: 56(7) yrs FEV1: 28 (5)% ; NYHA (II/III): 5/8 PImax: 70(14) cmH<sub>2</sub>O</p>	<p>Duration: 8 weeks – 7x a week, supervised every 15 days by a physiotherapist.</p> <p>Loads were readjusted every 15 days for RT and IMT.</p> <p>IMT lasted 30 minutes for both groups.</p> <p>(1) Control group: no intervention</p> <p>(2) Low intensity group: IMT at 15% of PImax, reassessed every 15 days. RT with 0.5 kg.</p> <p>(3) Moderate intensity group: 30% of PImax. RT with 50% of the 1RM.</p>	<p>PImax increased significantly and faster in the moderate-intensity group.</p> <p>In the control group there was an 8% reduction in PImax.</p> <p>Both groups improved the 6MWT covered distance and QoL.</p> <p>Significant improvement in NYHA functional class in the moderate intensity group.</p>
Sadek et al. (15) 2020	<p>Sample: n= 40 patients</p> <p>(1) Control group: n= 10 M/W: 5/5 Age: 52.6 (11.2) yrs PImax: 35.8(10.5) mmHg</p> <p>(2) AIT: n= 10 M/W: 5/5 Age: 51.6(13.8) PImax : 34.4(11.4) mmHg</p> <p>(3) IMT: n= 10 M/W: 5/5 Age: 52.5(13.7) yrs PImax: 36.4 (14.3) mmHg</p> <p>(4) AIT/IMT: n= 10 M/W: 5/5 Age: 51.8 (8.3) yrs PImax: 33.5 (13.1) mmHg</p>	<p>Duration: 12 weeks of training – 3x a week.</p> <p>AIT: AT 4 min at 60% to 90% HRmax   2 minutes at 50% HR max for 30 minutes.</p> <p>IMT: 20 minutes 3x a week. 60% PImax, adjusted every 2 weeks.</p>	<p>Significant increase in SPImax, distance covered in the 6MWT and QoL in the AIT/IMT group.</p>
Lautaris et al. (16) 2021	<p>Sample: n= 74 patients</p> <p>(1) AT: n= 18 Age: 64.8 (60.4–69.1) yrs M/W: 16/2 NYHA (II/III): 11/7 LVEF: 26.8 (24.7–28.8)% PImax: 83.1 (75.3–90.8) cmH<sub>2</sub>O</p> <p>(2) AT/RT: n= 17 Age: 67.5 (64–70.9) yrs M/W: 16/1 NYHA (II/III): 10/7 LVEF: 29.6 (27.2–32.1)% PImax: 79.8 (70.3–89.4) cmH<sub>2</sub>O</p> <p>(3) AT/IMT: n= 20 Age: 68.1 (65.2–71) yrs M/W: 20/0 NYHA (II/III): 11/9 LVEF: 28.8 (25.1–32.5)% PImax: 85.6 (75.6–95.5) cmH<sub>2</sub>O</p> <p>(4) ARIS: n= 19 Age: 63.9 (59.8–68) yrs M/W: 17/2 NYHA (II/III): 9/10 LVEF: 28.3 (25.9–30.7)% PImax: 82.6 (73.9–91.3) cmH<sub>2</sub>O</p>	<p>Duration: 12 weeks of training – 3x a week.</p> <p>AT group: 30 min treadmill or cycle ergometer at 60-80% of HR max.</p> <p>30 min of calisthenics exercises.</p> <p>AT/IMT group: 30 min of aerobic activity + IMT at 60% of SPImax / PImax for 30 min.</p> <p>AT/RT group: 30 minutes of aerobic activity + 30 minutes of resistance training at 50% of the 1 RM (3x12-15 repetitions).</p> <p>ARIS group: 30 min aerobic + 10 min RT with 50% 1RM (3x12-15 repetitions) + 20 min IMT with 60% SPImax / PImax.</p>	<p>Significant increase in PImax in ARIS and SPImax in ARIS and AT/IMT groups.</p> <p>There was a trend towards an increase in peak VO<sub>2</sub> in ARIS group.</p> <p>Circulatory power and CPET performance time were higher in the ARIS group.</p> <p>Significant improvement in QoL in the ARIS group.</p> <p>NYHA functional class tended to increase when compared to AT.</p> <p>AT/IMT obtained a significant improvement in QoL and NYHA functional class when compared to AT.</p>

Data are presented as mean (SD), median (range) and numbers

6MWT - 6-minute walk test, AIT - aerobic interval training, ARIS - combined AT/RT/IMT, AT - aerobic training, IMT - inspiratory muscle training, LVEF - left ventricular ejection fraction, M- man, PImax - maximum inspiratory pressure, QoL - quality of life, RM - maximum repetition, RT - resistance training, SPImax - maximum sustained inspiratory pressure, W-woman, years- yrs



In another study, Lautaris et al. conducted an intervention program with 4 groups: ARIS, who performed IMT associated with aerobic and resistance training; AT + IMT, performed inspiratory muscle training associated with aerobic training; AT + RT, performed aerobic and resistance training; AT who performed only aerobic training. As a result, VO<sub>2</sub> peak showed no significant difference between the groups, but the ARIS group tended to increase. In addition, circulatory power and CPET time were higher in the ARIS group when compared to the other groups. Parameters such as ventilatory efficiency, VE/VCO<sub>2</sub> slope and O<sub>2</sub> recovery kinetics did not have significant differences between the groups (17).

The study by Adamopoulos et al. (14) found no significant differences in circulatory power, ventilatory threshold and VE/VCO<sub>2</sub> slope, like the other studies. VO<sub>2</sub> peak improved in both groups and the intervention group achieved a significant improvement in exercise time, respiratory exchange ratio and ventilation. The studies by Kawauchi et al. (15) and Sadek et al. (16) did not perform CPET.

#### **6 minute walk test**

In the study by Kawauchi et al. (15), the distance in the 6MWT improved significantly in the low- and moderate-intensity intervention group when compared to the control group. The ARIS group in the most recent study by Lautaris et al. (17) showed significant results for the distance covered in the 6MWT.

Sadek et al. (16) also observed a significant improvement in the combined group (HIIT + TMI) when compared to the control group. And in their study, Winkelmann et al. (12), unlike the other studies, found that both groups showed improvements in the distance covered in the 6MWT.

#### **NYHA rating and quality of life**

The study by Winkelmann et al. (12) saw similar improvements in both groups. The study by Lautaris et al. (13) showed that QoL and NYHA functional class improved only in the intervention group, which underwent combined training.

Two studies found that QoL improved more in the combined training group, but NYHA improved in both

training groups (14,16). Kawauchi et al (15), in turn, obtained improved QoL in all their groups, but the moderate intensity training group significantly improved functional class and NYHA symptoms.

Finally, the most recent study by Lautaris et al. (17) showed a more significant increase in QoL in the ARIS group. NYHA class tended to improve in the ARIS group when compared to AT alone. The AT + IMT group also achieved significant improvements in QoL and NYHA when compared to AT alone.

#### **Discussion**

Inspiratory muscle training has been widely studied as a form of intervention in patients with HF, with the aim of improving their functional capacity and QoL by increasing the strength and endurance of the inspiratory muscles. Most of the studies included in this review showed that patients who underwent IMT associated with conventional training showed a significant increase in inspiratory muscle performance. These results suggest that the use of IMT is beneficial for patients with HF, attenuating the respiratory metaboreflex, improving peripheral blood flow and increasing exercise tolerance (17, 18).

The study by Meyer et al. (7) highlights that inspiratory muscle strength is an important predictor of prognosis in HF and that a reduction in P<sub>Imax</sub> is related to increased mortality in these patients. When analyzing the study by Kawauchi et al. (15), we observed that patients in the control group, who did not use IMT as an intervention, reduced their P<sub>Imax</sub> by 8%. These results raise the hypothesis of whether only patients with reduced P<sub>Imax</sub> should be eligible for IMT or whether all HF patients should use this resource to prevent respiratory function decline and thus reduce mortality. On the other hand, studies such as those by Winkelmann et al.(12) and Sadek et al. (16), recruited patients with P<sub>Imax</sub> lower than predicted for their age, categorizing inspiratory muscle weakness and showed that there was a significant improvement in P<sub>Imax</sub> in the groups that used IMT as an intervention force. This raises the hypothesis that the patients who benefit most from IMT in terms of gaining inspiratory muscle strength are those with inspiratory muscle weakness.

However, other studies have also shown that even patients without inspiratory muscle weakness can benefit from IMT. More in-depth research into this issue is therefore needed in order to define more effectively which patients meet the selection criteria for IMT.

Another relevant study for reducing mortality in HF patients is HF-ACTION (18). This study showed that a 6% increase in maximum oxygen consumption (VO<sub>2</sub> peak) was associated with a 5% reduction in all-cause mortality and hospitalization rates. Most of the studies selected for this review showed a significant increase in VO<sub>2</sub> peak in the combined and conventional training groups. Several studies suggest (19-21) that the most significant improvement in VO<sub>2</sub> peak occurred in patients with reduced P<sub>lmax</sub>, which raises the hypothesis that the most effective indication for IMT would be for these patients.

Although there is promising evidence of the benefits of IMT in HF patients, more studies are needed in order to clarify the best way to prescribe it, the ideal duration of treatment and whether all HF patients would benefit from using IMT as a form of intervention.

### Study limitations

The heterogeneity of the included studies in terms of methodology, intervention and outcomes made it difficult to directly compare the results. In addition, most of the studies had a small sample size and limited duration, making it difficult to assess significant effects. In addition, the lack of standardization in IMT protocols and assessment measures may also have introduced bias into the results.

In terms of future prospects, it is important to carry out well-designed studies, with larger samples and longer follow-up periods, in order to provide more robust evidence on the benefits of IMT in HF patients. These issues are important for directing the clinical application of IMT and optimizing outcomes for HF patients.

### Conclusion

According to the studies analyzed, we can conclude that the use of IMT associated with other conventional training modalities in HF patients is beneficial for increasing not only inspiratory muscle strength, but also inspiratory muscle endurance. As well as exercise tolerance time, distance covered in the 6MWT,

ventilatory efficiency and circulatory power. As for quality of life and NYHA classification, the results are still controversial, but exercise alone showed a significant improvement in these parameters.

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