

# Effects of inspiratory muscle training in chronic heart failure patients: A systematic review and meta-analysis

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## Abstract

**Objective:** The aim of this study was to evaluate the effects of inspiratory muscle training (IMT) in chronic heart failure (CHF) patients.

**Design:** We searched MEDLINE, EMBASE, Cochrane Library, CINHAL, and CBMdisc to collect controlled trials on the application of inspiratory muscle training in CHF patients from the establishment of these databases to November 2016. Two reviewers independently screened literature according to the inclusion and exclusion criteria, extracted data, and assessed the quality of literature. Meta-analysis was conducted by software RevMan5.3.

**Results:** Eight studies involving 302 patients were identified. Meta-analysis indicated that IMT significantly improved  $PI_{max}$ ,  $V_E/VCO_2$  slope and dyspnea (weighted mean difference [WMD] = 16.52, 95% CI: 13.87–19.17,  $P < .01$ ; WMD = -5.78, 95% CI: -7.72 to -3.85,  $P < .01$ ; SMD = -0.95, 95% CI: -1.5 to -0.39,  $P < .01$ ), and descriptive results showed that long-term IMT ( $\geq 6$  weeks) can improve the quality of life of CHF patients, and patients in IMT group also have a significant improvement in 6-minute walking distance test (6-MWD).

**Conclusion:** IMT can improve pulmonary function, exercise tolerance, and quality of life of CHF patients and relieve the symptom of dyspnea.

## KEYWORDS

chronic heart failure, inspiratory muscle training, meta-analysis

## 1 | INTRODUCTION

Chronic heart failure (CHF) is a complex clinical syndrome that impairs ventricular filling or ejection capacity due to any structural or functional cardiac abnormality. The specific symptoms of CHF are dyspnea, fatigue, and exercise intolerance.<sup>1</sup> Heart failure patients suffer from high morbidity and mortality rates, frequent rehospitalizations, and poor quality of life.<sup>2</sup>

Inspiratory muscle weakness is prevalent and contributes to poor prognosis in 30%–50% of patients with heart failure.<sup>3</sup> Inspiratory muscle training (IMT) involves exercising the diaphragm-based muscles with inspiratory function, which can improve muscle strength and endurance, functional capacity, and ventilator response to exercise and promote the recovery of motor ability.<sup>4</sup> Some literature has studied the effect of IMT on heart failure patients, such as improving inspiratory

muscle strength, peak oxygen consumption ( $VO_2$ ), quality of life, and reduced dyspnea.<sup>5–8</sup> However, the sample sizes of original research derived from IMT have been small, and somewhat conflicting results were obtained from different studies because the manner, intensity and frequency of the IMT were slightly different. Systematic review with meta-analysis on IMT in patients with CHF have not been reported recently. Therefore, the purpose of our study is to evaluate the effects of IMT in CHF by systematic review and to provide more reliable estimates of treatment effectiveness.

## 2 | METHODS

### 2.1 | Search strategy

To gather relevant randomized controlled trials (RCTs) and non-RCTs published in English or Chinese, we searched the Cochrane Library, MEDLINE, EMBASE, CINHAL, and China Biology Medicine disc

Jing Wu and Li Kuang contributed equally to this work.

#1 heart failure [Title/Abstract]  
#2 chronic heart failure [Title/Abstract]  
#3 #1 OR #2  
#4 inspiratory muscle training [Title/Abstract]  
#5 respiratory muscle training [Title/Abstract]  
#6 muscle training [Title/Abstract]  
#7 inspiratory training [Title/Abstract]  
#8 exercise training [Title/Abstract]  
#9 #4 OR #5 OR #6 OR #7 OR #8

FIGURE 1 Search strategy in MEDLINE

(CBMdisc) from their inception to November 2016, by two authors independently. We searched the following words combined with “inspiratory muscle training,” “respiratory muscle training,” “muscle training,” “inspiratory training,” “exercise training,” “heart failure,” and “chronic heart failure.” The language was not limited. We took “MEDLINE” for example in Figure 1.

We followed the following four steps of a literature search strategy: (1) searching the systematic reviews or meta-analyses in Cochrane Library, (2) searching original articles in MEDLINE, EMBASE, CINAHL, and CBMdisc to determine the search terms, (3) using specified search terms to search the databases, and (4) retrieving the articles along with the references.

## 2.2 | Inclusions

(1) The study designs are randomized controlled trials (RCTs) and non-RCTs; (2) the CHF patients (New York Heart Association class I/II/III) were over 18 years; (3) the intervention group received IMT, for a minimum of 2 weeks, and the control group received sham IMT, education, or traditional training; (4) the main observational parameters included inspiratory muscle function (maximal static inspiratory pressure,  $PI_{max}$ ), pulmonary function ( $FEV_1$ , FVC,  $FEV_1/FVC$ ), ventilation efficiency ( $V_E/VCO_2$  slope); the secondary outcome included 6-minute walk test, dyspnea, and quality of life; and (5) follow-up time was described in the study.

## 2.3 | Exclusions

(1) Animal studies and review papers were excluded; (2) participants were nonheart failure patients; (3) the study in which data were duplicated in multiple articles; and (4) the study for which we were unable retrieve as full text.

## 2.4 | Assessment of risk of bias in included studies

According to the Cochrane Collaboration's tool for assessing risk of bias for randomized controlled trials (Version 5.1.0),<sup>9</sup> the quality of studies was assessed by two authors independently, including random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. The two authors discussed any disagreements of assessment results on every study, and the third author negotiated the final result.

## 2.5 | Data extraction

Two authors extracted data by a standard data extraction form. Data included (1) general information: title of article, first author's name, year of publication, and country; (2) type of research and key elements of quality assessment; (3) general information of the participant between intervention group and control group, such as number of cases and age; and (4) the main observational parameters included inspiratory muscle function (maximal inspiratory pressure,  $PI_{max}$ ), pulmonary function ( $FEV_1$ , FVC,  $FEV_1/FVC$ ), and ventilation efficiency ( $V_E/VCO_2$  slope), and the secondary outcome included 6-minute walk test, dyspnea, quality of life, and effectiveness and safety of IMT.

## 2.6 | Statistical analysis

RevMan5.1 (Nordic Cochrane Center, Copenhagen, Denmark) was used to test the heterogeneity of included studies and conduct meta-analyses for outcome measures following IMT. The continuous data measured by the same tool were reported as weighted mean difference (WMD), while the continuous data measured by the different tool were reported as standardized mean difference (SMD). We calculated a 5% level of significance and a 95% confidence interval for all data. Besides, if the studies were homogeneous, which was analyzed by  $I^2$  statistics ( $P > .1$ ,  $I^2 < 50\%$ ), we chose a fixed-effect model, and we used a random-effect model when the studies were heterogeneous ( $P < .1$ ,  $I^2 \geq 50\%$ ). Subgroup analysis was based on heterogeneity.<sup>9</sup> When the source of heterogeneity could not be determined, we used descriptive analysis. If necessary, we tested the stability of the results by sensitivity analysis.

## 3 | RESULTS

### 3.1 | Process of studies researching

We initially included 285 studies. After the removal of duplicate, screening, and evaluation, eight studies<sup>7,8,10–15</sup> with 302 patients were finally included. Our selection procedure is shown in Figure 2.

### 3.2 | Characteristics of the included studies

Eight studies<sup>7,8,10–15</sup> were included whose outcome indicators included respiratory function and/or exercise tolerance and observation indicators included pulmonary function, 6-minute walk test, maximal inspiratory pressure ( $PI_{max}$ ), and quality of life. Five studies<sup>8,11–13,15</sup> used  $PI_{max}$

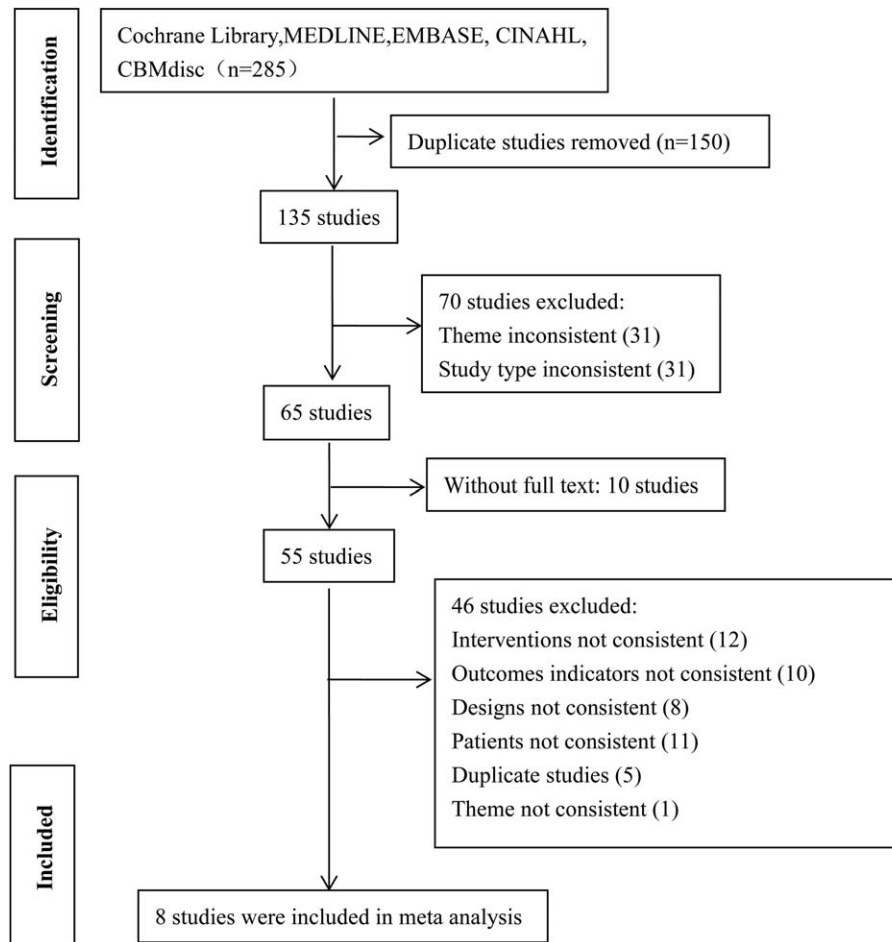


FIGURE 2 Paper screening flowchart

as outcome indicators, five studies<sup>7,8,10-12</sup> used  $V_E/VCO_2$  as slope, four studies<sup>7,10,13,14</sup> used dyspnea, four studies<sup>7,10,11,14</sup> used intervention effect of pulmonary function, and six studies<sup>7,8,11-14</sup> used quality of life.

The training time of eight studies<sup>7,8,10-15</sup> varied from 4 to 12 weeks with one study<sup>13</sup> training patients for 4 weeks, one study<sup>14</sup> for 6 weeks, one study<sup>10</sup> for 10 weeks, and five studies<sup>7,8,11,12,15</sup> for 12 weeks. Training time varied from 10 to 45 minutes; five studies<sup>7,8,11,12,14</sup>, trained patients for 30 minutes every time. These studies required patients to train 3–7 days a week, including six studies<sup>8,11-15</sup> training every day and two studies<sup>7,10</sup> three times a week.

The follow-up time of eight studies<sup>7,8,10-15</sup> varied from 4 weeks to 1 year (48 weeks). But only one study,<sup>11</sup> whose follow-up time lasted 1 year and intervention group did IMT 30 minutes/day and 7 days a week for 12 weeks, showed that IMT still could improve  $PI_{max}$  and quality of life. The follow-up of others stopped when the intervention stops.

Interventions between the intervention group and the control group are different: IMT in the intervention group and sham IMT or health education or aerobic exercise only. Five studies<sup>7,10,11,13,14</sup> used sham IMT in the control group. The main characteristics of eight studies<sup>7,8,10-15</sup> are listed in Table 1. Generally, the studies were

matched at baseline for age, NYHA class,  $PI_{max}$ , and medication use, which is presented in Table 2.

### 3.3 | Methodological quality evaluation of included studies

The quality evaluation of studies was carried out according to quality evaluation methods of the Cochrane handbook.<sup>9</sup> The overall quality of studies is good. The detailed methodological quality evaluation of included studies is presented in Table 3.

### 3.4 | Effects of interventions

#### 3.4.1 | Maximal static inspiratory pressure

Six studies<sup>7,10,12-15</sup> of the eight included studies<sup>7,8,10-15</sup> assessed maximal static inspiratory pressure ( $PI_{max}$ ). A fixed-effect model was analyzed that there was a significant improvement in  $PI_{max}$  after IMT when comparing the intervention group with the control group (WMD = 16.52, 95% CI: 13.87–19.17,  $P < .01$ ) (Figure 3). The studies were homogeneous ( $I^2 = 0\%$ ,  $P > .1$ ). In addition, forest chart structure of meta-analysis did not change when the highest weight study<sup>2</sup> was

TABLE 1 Characteristics of included studies

Author (year) country	Sample of (intervention group/control group)	Reasons for missing	Insistent time (wk)	Follow-up time	Interventions		Outcome indicators
					Intervention group	Control group	
Bosnak-Gucclu et al. (2011) <sup>14</sup> Turkey	16/14 (18/18)	Intervention group: pulmonary infection (1), moved to another city (1), control group: sudden cardiac death (1); discontinued intervention (did not want to) (3)	6	6 wk	IMT, 40% $PI_{max}$ , 30 min/d, 7 d/wk	Sham IMT, 15% $PI_{max}$ , 30 min/d, 7 d/wk	ABDCEF
Marco et al. (2013) <sup>13</sup> Spain	11/11	No missing.	4	4 wk	IMT, twice a day, 7 d/wk	Sham IMT, twice a day, 7 d/wk	BDEF
Mello et al. (2012) <sup>12</sup> Brazil	15/12 (15/15)	Reasons not mentioned.	12	12 wk	IMT, 30 min/d, 7 d/wk	No interventions.	E
Winkelmann et al. (2009) <sup>8</sup> Brazil	12/12 (19/19)	Logistic problems (9); orthopedic problems (2); death (2); hospital admission (1)	12	12 wk	IMT, 30% $PI_{max}$ , 30 min/d, 7 d/wk aerobic, 3 d/wk	Aerobic exercise, 3 d/wk	BCE
Dall'Ago et al. (2006) <sup>11</sup> Brazil	16/16 (22/22)	Intervention group: myocardial infarction (1); atrial fibrillation (1); not able to complete the training protocol (4) Control group: indication of coronary artery bypass graft surgery (2); development of symptoms at rest (3)	12	1 y	IMT, 30 min once, 7 d/wk	Sham IMT, 30 min once, 7 d/wk	ABE
Padula et al. (2009) <sup>15</sup> America	15/17 (17/17)	Bleeding secondary to oral anticoagulation (1) Reasons not mentioned.	12	12 wk	IMT, 10–20 min once, 7 d/wk	Health education	BDE
Adamopoulos et al. (2014) <sup>7</sup> Greece	21/22 (26/26)	Intervention group: pulmonary infection (1); deterioration HF/hospitalized (1); moved to another city (1); long distance travelling/finance (2) Control group: deterioration HF/hospitalized (2); long distance travelling (1); lost to follow-up (1) Reasons not mentioned.	12	12 wk	IMT, 60% $SPI_{max}$ , 30 min once, 3 times/wk, aerobic exercise, 45 min once, 3 times/wk	Sham IMT, 10% $SPI_{max}$ aerobic exercise, 45 min once, 3 times/wk	ABFEFI
Laoutaris et al. (2007) <sup>10</sup> British	15/23 (23/23)	Reasons not mentioned.	10	10 wk	IMT, 60% $SPI_{max}$ , 3 d/wk	Sham IMT, 15% $SPI_{max}$ , 3 d/wk	ABDFG

(A) Pulmonary function test: FEV<sub>1</sub>, FVC, PEF; (B)  $PI_{max}$ ; (C) 6-minute walk test; (D) dyspnea; (E) quality of life; (F) serum marker: NT-pro BNP, etc; (G) VO<sub>2</sub> peak; (H) OUES; and (I)  $SPI_{max}$ .

TABLE 2 Summary of baseline characteristics of included studies

Study	Design	Age (years)	Male (%)	BMI (kg/m <sup>2</sup> )	NYHA (%), II/III	LVEF (%)	PI <sub>max</sub> (cm H <sub>2</sub> O)	Etiology of CHF, ischemic (%)	Medication, intervention/control (%)
Bosnak-Guciu et al. <sup>14</sup>	IMT	69.5 ± 8.0	75	26.8 ± 4.3	69/31	33.4 ± 7.2	62.00 ± 33.57	87.5	BB 88/86; ACE 88/86
	Sham IMT	65.7 ± 10.5	86	25.1 ± 3.2	64/36	36.1 ± 7.6	78.64 ± 35.95	85.7	DIU 69/57; DIG 88/93
Marco et al. <sup>13</sup>	IMT	68.5 ± 8.9	64	28.4 ± 3.64	73/27	38.3 ± 16.0	55.1 ± 23.6	54.5	N/A
	Sham IMT	70.1 ± 10.8	91	26.3 ± 2.4	82/12	35.5 ± 17.5	58.1 ± 24.3	73.6	
Meilo et al. <sup>12</sup>	IMT	54.3 ± 2	60	27.4 ± 0.9	100/0	33.6 ± 2.3	56.1 ± 2.3	N/A	BB 100/100; ACE: 100/100
	Control	53.3 ± 2	42	28.8 ± 1.6	100/0	37.6 ± 1.6	56.2 ± 2.1		DIU 87/83; DIG 40/50
Winkelmann et al. <sup>8</sup>	Aerobic/IMT	54 ± 12	33	28 ± 5	N/A	39 ± 12	57 ± 12	25	BB 50/45; ACE 80/82
	Aerobic/Sham	59 ± 9	58	25 ± 4		34 ± 11	56 ± 13	8.3	DIU 80/80; DIG 40/67
Dall'Ago et al. <sup>11</sup>	IMT	54 ± 3	69	27 ± 4	N/A	39.0 ± 3.0	58.1 ± 7.1	37.5	BB 42/50; ACE 85/78
	Sham IMT	58 ± 2	63	27 ± 5		38.0 ± 3.0	60.2 ± 9.2	43.8	DIU 87/80; DIG 57/50
Padula et al. <sup>15</sup>	IMT	76	33	N/A	Overall	30.47	48.7	N/A	N/A
	Education	73	41		52/48	33.24	52.3		
Adamopoulos et al. <sup>7</sup>	Aerobic/IMT	57.8 ± 11.7	90	28.6 ± 6.7	43/57	27.7 ± 6.7	81.9 ± 21.5	ICM/DCM 48/52	BB 86/94; ACE 93/82
	Aerobic/Sham	58.3 ± 13.2	77	27.2 ± 2.9	55/45	30.1 ± 5	79.2 ± 19.4	ICM/DCM 36/64	DIU 100/82; DIG N/A
Laoutaris et al. <sup>10</sup>	IMT	53 ± 2	80	29.2 ± 2.1	67/33	28 ± 3	79.8 ± 4.7	CAD/DCM 27/73	BB 93/78; ACE 93/96
	Sham IMT	59 ± 2	87	28.6 ± 0.8	52/48	27 ± 2	80.2 ± 5	CAD/DCM 52/48	DIU 87/100; DIG 67/61

PI<sub>max</sub>, maximal static inspiratory pressure; MIP, maximal inspiratory pressure; LVEF, left ventricular ejection fraction; BB, beta-blockade; ACE, ACE-inhibitor or angiotension II receptor blocker; DIU, diuretic; DIG, digoxin; ICM, ischemic cardiomyopathy; DCM, dilated cardiomyopathy; CAD, coronary artery disease.

TABLE 3 Evaluation of included studies' quality

Included studies	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Attrition bias	Selective reporting	Other bias
Bosnak-Guclu et al. <sup>14</sup>	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Marco et al. <sup>13</sup>	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Mello et al. <sup>12</sup>	Not mentioned	Low risk	High risk	Low risk	High risk	Low risk	High risk
Winkelmann et al. <sup>8</sup>	Not mentioned	Not mentioned	High risk	Low risk	Low risk	Low risk	Low risk
Dall'Ago et al. <sup>11</sup>	High risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Padula et al. <sup>15</sup>	Low risk	High risk	High risk	Low risk	Low risk	Low risk	Low risk
Adamopoulos et al. <sup>7</sup>	High risk	Not mentioned	Low risk	Low risk	Low risk	Low risk	Low risk
Laoutaris et al. <sup>10</sup>	High risk	High risk	Low risk	Low risk	High risk	Low risk	Low risk

deleted by sensitivity analysis (WMD = 18.96, 95% CI: 14.84–23.07,  $P < .01$ ) (Figure 4).

### 3.4.2 | Ventilation efficiency ( $V_E/VCO_2$ slope)

Five studies<sup>7,8,10–12</sup> reported  $V_E/VCO_2$  slope ( $n = 164$ ), two<sup>7,8</sup> of which required patients to do IMT with aerobic exercise in the intervention group and aerobic exercise in the control group. Other three studies<sup>10–12</sup> required patients to do only IMT in the intervention group, and sham-IMT or nonintervention in the control group. Therefore, clinical heterogeneity was analyzed as subgroups. Figure 5 shows that IMT could significantly improve ventilation efficiency ( $V_E/VCO_2$  slope) in CHF patients (WMD =  $-6.62$ , 95% CI:  $-7.53$  to  $-5.72$ ,  $P < .01$ ). In the second subgroup, there was homogeneity in the studies ( $I^2 = 0\%$ ,  $P = .43$ ) and there was no significant difference between the intervention group and the control group (WMD =  $-1.33$ , 95% CI:  $-4.45$  to  $1.79$ ,  $P > .01$ ) (Figure 5).

### 3.4.3 | Dyspnea

Four studies<sup>7,10,13,14</sup> reported the effect of IMT on dyspnea in CHF patients ( $n = 133$ ). Two studies<sup>7,10</sup> assessed dyspnea at the end of the walk by the Borg scale, and two other studies<sup>11,13</sup> assessed dyspnea severity by the Modified Medical Research Council (MMRC) dyspnea scale. Therefore, statistical heterogeneity can be explained in the studies ( $I^2 = 56\%$ ,  $P < .1$ ). Figure 6 shows that IMT could significantly improve dyspnea perception in the CHF patients by a random-effect model (SMD =  $-0.95$ , 95% CI:  $-1.51$  to  $-0.39$ ,  $P < .01$ ).

### 3.4.4 | Pulmonary function

Four studies<sup>7,10,11,14</sup> involved FEV<sub>1</sub> and FVC. One study<sup>11</sup> indicated that patients in the IMT group and sham IMT groups showed no significant improvement in FEV<sub>1</sub> and FVC. Three studies<sup>7,10,14</sup> were excluded in the meta-analysis because of great heterogeneity of interventions although they all involved FEV<sub>1</sub>, FVC, as well as FEV<sub>1</sub>/FVC. One study<sup>10</sup> showed a significant improvement in FVC in the intervention group with high-intensity IMT after 10 weeks ( $P < .05$ ) and FEV<sub>1</sub>/FVC in the control group with low-intensity IMT after 10 weeks ( $P < .05$ ). One study<sup>14</sup> showed a significant improvement in FEV<sub>1</sub> and FVC in the intervention group with IMT after 6 weeks and FEV<sub>1</sub>/FVC in the intervention group with IMT compared to control group with sham IMT ( $P < .05$ ). One study<sup>7</sup> did not show any significant improvement in three outcomes after 12 weeks.

### 3.4.5 | Quality of life

Six studies<sup>7,8,11–14</sup> involved quality of life. Because of unified measuring tools as well as heterogeneity between different control groups, quality of life was analyzed in the descriptive analysis. One study<sup>8</sup> showed the control group with aerobic exercise and the invention group with IMT and aerobic exercise both improved quality of life after 12 weeks. One study<sup>7</sup> showed the control group with aerobic exercise did not improve the quality of life and the invention group with IMT and aerobic exercise improved quality of life after 12 weeks. One study<sup>11</sup> showed the intervention group with IMT and the control group with sham IMT both improved quality of life significantly after 12 weeks and the

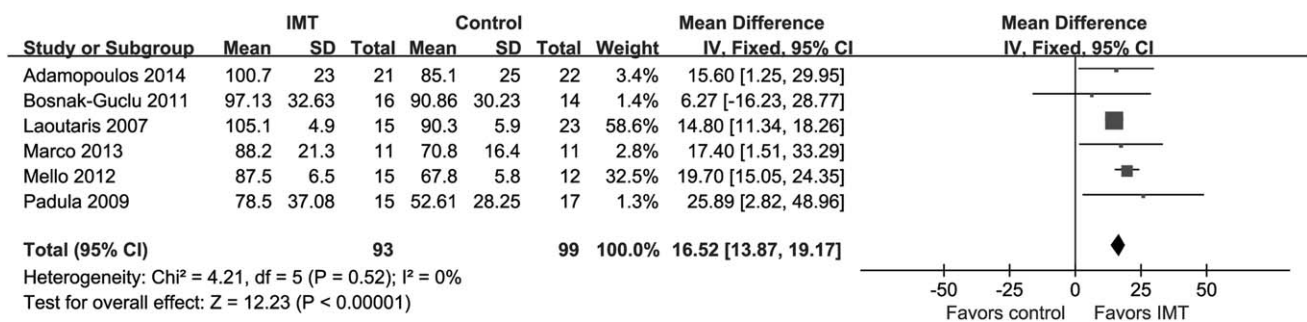


FIGURE 3 Mean difference in  $P_{I_{max}}$ , IMT vs control

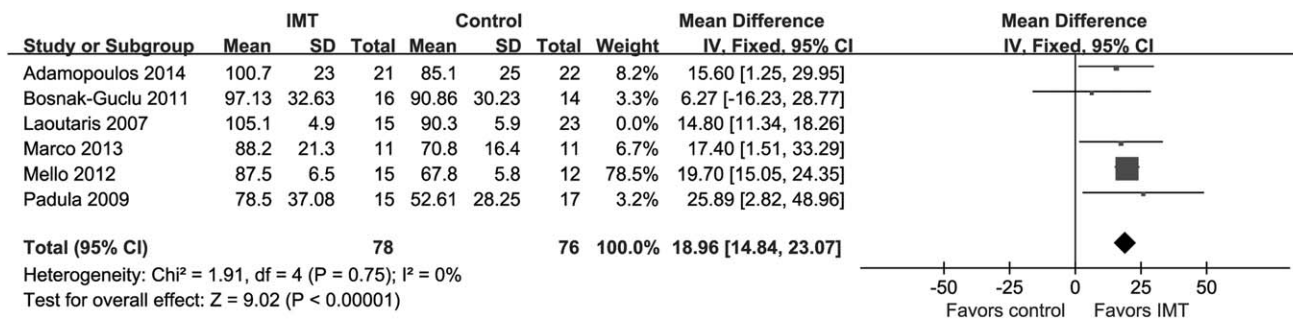


FIGURE 4 Sensitivity analysis in  $\text{PI}_{\text{max}}$ , IMT vs control

intervention group showed greater improvement than the control group ( $P < .001$ ). One study<sup>12</sup> showed the intervention group with IMT improved quality of life and the control group did not improve quality of life after 12 weeks. One study<sup>13</sup> used MLHFQ and SF-36 showing no significant improvement between two groups nor each group after 4 weeks training.

### 3.4.6 | Six-minute walk test

Because of greater clinical heterogeneity, the 6-minute walk test was included in the descriptive-analysis by comparing four studies<sup>8,10,11,14</sup> that involved this outcome. Patients with IMT in two studies<sup>13,14</sup> showed a significant improvement in 6-minute walk test compared to control groups without IMT ( $P < .05$ ). One study<sup>10</sup> indicated patients with high-intensity IMT showed a significant improvement in 6-minute walk test compared to low-intensity IMT, but one study<sup>8</sup> showed a significant improvement in two groups both requiring patients to do aerobic exercise, in which the intervention group required patients to do IMT and aerobic exercise.

## 4 | DISCUSSION

To some extent, our finding is that IMT is effective in CHF patients, based on the quality of the included studies. Seven studies (87.5%)

mentioned to conduct a randomized, controlled trial, and only one study (12.5%) describes the specific methods of randomization and the implementation process. Four studies (50%) described allocation concealment. Three studies (37.5%) did not specifically described blinding. Four studies (50%) reported the reason of missions. All studies compared the baseline data of the patients between experimental group and the control group by Student's *t* test ( $P > .05$ ).

Our meta-analyses suggested  $\text{PI}_{\text{max}}$ ,  $V_E/V\text{CO}_2$  slope, dyspnea perception are both significantly improved after IMT. IMT involves exercising the diaphragm-based muscles with inspiratory function, so the patient's maximum static inspiratory pressure ( $\text{PI}_{\text{max}}$ ) was improved by improving the inspiratory muscle strength. The CHF patients in the control group of three studies<sup>7,10,14</sup> received the lower loads sham-IMT at 10%–15% of individual sustained maximal static inspiratory pressure ( $\text{SPI}_{\text{max}}$ ) or maximum inspiratory pressure (MIP), and the results also showed the corresponding improvement of  $\text{PI}_{\text{max}}$  in the control group, but the intervention group performed with better results when the patients received IMT at 40%–60% of individual  $\text{SPI}_{\text{max}}$  or MIP. Yet to our knowledge, whether the increase in  $\text{PI}_{\text{max}}$  can change the symptoms or quality of life of patients with CHF is still unknown.

As we all known,  $V_E/V\text{CO}_2$  slope, peak  $\text{VO}_2$  and ventilator threshold were reliable predictors of prognosis in CHF patients.<sup>16</sup> When the intervention group only received IMT, the result was significantly

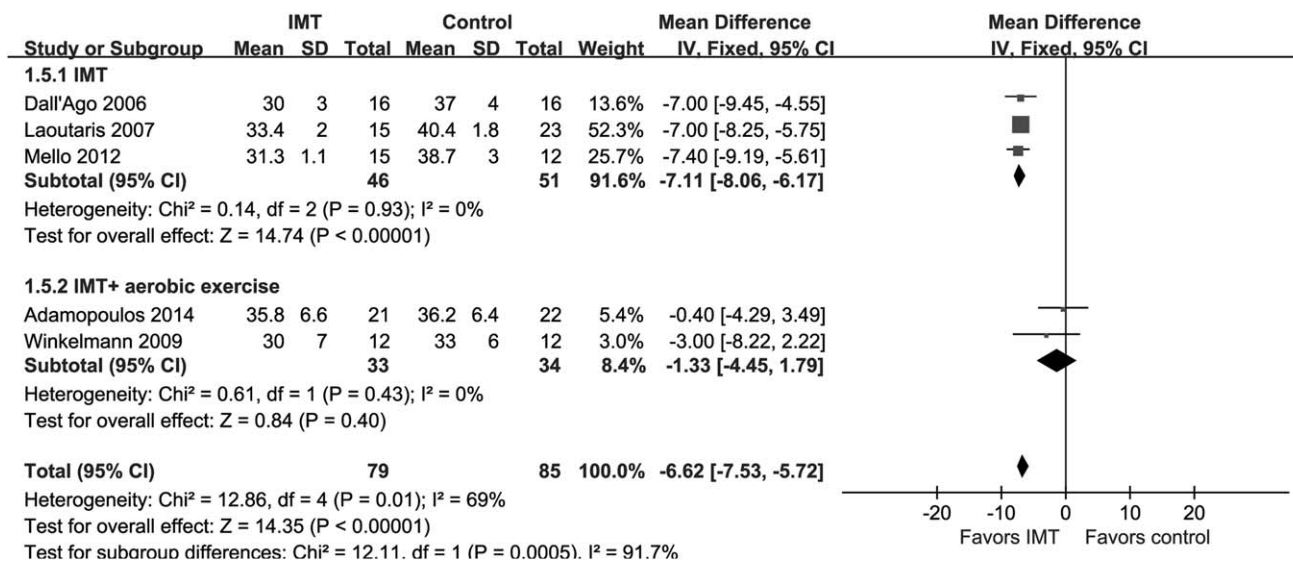


FIGURE 5 Mean difference in  $V_E/V\text{CO}_2$  slope, IMT vs control

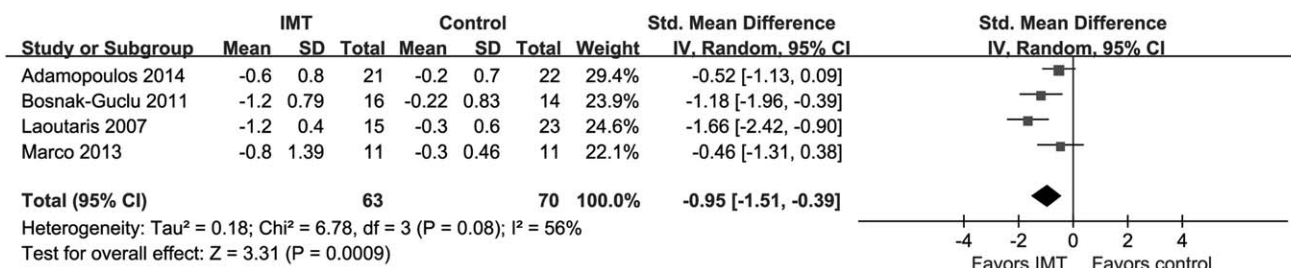


FIGURE 6 Mean difference in dyspnea, IMT vs control

improved (reduced) compared to the control group. While the intervention group received IMT with aerobic exercise and the control group received aerobic exercise, there seemed to be no significant difference in the effect of IMT. The mechanism may be that IMT training can improve the sympathetic and parasympathetic modulation of the cardiovascular system, and improve skeletal muscle perfusion, thereby improving the respiratory function during exercise in CHF patients.<sup>17,18</sup> Additionally, aerobic exercise could affect the small diaphragm group and the ventilation function of the patients was not severely impaired at baseline.

Marco et al.<sup>13</sup> found that the IMT improved the dyspnea perception in CHF patients, but did not achieve the desired effect of the intervention; the reason may be that the modified Medical Research Council (MMRC) dyspnea scale is less sensitive to CHF patients. In the future, researchers need to consider carefully which scale to use to assess quality of life in CHF patients. The patients have a poor quality of life with severe dyspnea symptom, and we will discuss the effect of IMT in combination with changes in quality of life.

FEV<sub>1</sub>/FVC is always used to evaluate pulmonary ventilation function.<sup>19</sup> Three studies<sup>7,10,14</sup> that discussed FEV<sub>1</sub>, FVC, and FEV<sub>1</sub>/FVC in eight studies did not involve enough patients and use different interventions which led to clinical heterogeneity. Only one study<sup>14</sup> showed a significant improvement in FEV<sub>1</sub>, FVC, and FEV<sub>1</sub>/FVC in the intervention group and the control group. However, baseline pulmonary function of included patients in this study is lower than those in other studies which may lead to great differences in FEV<sub>1</sub>, FVC, and FEV<sub>1</sub>/FVC.

IMT (≥6 weeks) can significantly improve quality of life in CHF patients. The MLHFQ, which has been most commonly used in the quality of life in heart failure patients, includes two dimensions consisting of 21 items.<sup>20</sup> Each item is divided into six levels. The SF-36, which is a self-administered tool, contains eight dimensions, including 36 items. Six studies<sup>7,8,11-14</sup> showed a significant improvement in quality of life. One study<sup>13</sup> showed no significant improvement between the intervention group and control group after 4 weeks. It is likely that time was too short so that no difference appeared. Although one study<sup>8</sup> showed quality of life in both groups improved significantly, it did not exclude the effect of aerobic exercise in two groups. More research is still needed to confirm the impact of different training time on the quality of life of CHF patients.

Six-minute walk test, which is aimed at exercise tolerance, can reflect patients' function status as one indicator to predict patients'

survival.<sup>21</sup> One study<sup>8</sup> required patients in both groups to conduct aerobic exercise showed 6-minute walk test in both groups improved significantly, but aerobic exercise could also affect the 6-minute walk test in patients, which was not explained in this study. Four studies<sup>8,10,11,14</sup> used 6-minute walk test as one outcome indicator, and three studies<sup>10,11,14</sup> showed a significant improvement in 6-minute walk test in the intervention group. In conclusion, IMT can improve the results of CHF patients' 6-minute walk test.

As to whether there is a relationship between follow-up time and outcome, eight studies<sup>7,8,10-15</sup> did not explain it in details, which only reported their follow-up time and patients' corresponding outcome separately. One study<sup>14</sup> whose follow-up time was 6 weeks showed that IMT could improve pulmonary function, P<sub>I<sub>max</sub></sub>, and quality of life. Four studies<sup>7,8,12,13</sup> whose follow-up time was 12 weeks showed that IMT had positive effect on quality of life, and two studies<sup>7,8</sup> of these four studies<sup>7,8,12,13</sup> showed IMT had positive effect on P<sub>I<sub>max</sub></sub>. However, one study<sup>15</sup> held the opinion that improvement in the quality of life remained questionable because of uncompleted secondary aims and small sample size. One study<sup>13</sup> whose follow-up time was 4 weeks and one study<sup>10</sup> whose follow-up time was 10 weeks showed that IMT could improve P<sub>I<sub>max</sub></sub>, but only one study<sup>11</sup> showed that the effects of IMT on P<sub>I<sub>max</sub></sub> and quality of life are consistent and are partially maintained after 1 year of follow-up. So we still need more studies to explore the long time effect of IMT and best follow-up time.

## 5 | LIMITATION

No convincing conclusions can be drawn by analyzing only eight included studies. We will still continue to increase the number of included studies by searching new studies to improve our conclusions' reliability in the future. Some of the included studies did not explain how to perform allocation concealment or involve allocation concealment, which may lead to selective bias. In addition, SF-36 has a difference with MLHFQ in measured aspects such as psychological, physiological, and social aspects so that the studies cannot be included in meta-analysis.

## 6 | CONCLUSION

IMT training can improve exercise tolerance in patients with CHF as well as the symptom of dyspnea. Also, it is difficult to change the life quality in the short term, so our study recommends that the medical



staff implement IMT training (6 weeks) to change the patients' conditions and improve the quality of life of patients with CHF step by step. Randomized controlled trials for IMT training in patients with CHF are few in the development country. More original studies are still needed to determine how long the most appropriate follow-up time is for IMT training in CHF patients.

## CONFLICT OF INTEREST

There is no conflict of interest.

## AUTHOR CONTRIBUTIONS

*Study design:* Wu, Kuang, Fu

*Data collection and analysis:* Wu, Kuang, Fu

*Manuscript preparation:* Wu, Kuang

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