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Original Research Article

IMPACT OF INSPIRATORY MUSCLE TRAINING VERSUS RESISTANCE TRAINING ON VENTRICULAR DYSFUNCTION IN PATIENTS WITH DILATED CARDIOMYOPATHY: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Dilated cardiomyopathy is a common cardiac dysfunction affecting patient's functional activities. Inspiratory muscle training retains the progression of the disease and improve cardiac functions.

Objectives: To investigate the effect of inspiratory muscle training versus resistance training on left-ventricular dysfunction in patients with dilated cardiomyopathy.

Materials and Methods: Thirty male patients with ischemic dilated cardiomyopathy were randomly assigned to either the Inspiratory Muscle Training (n = 15) or Resistance Training (n = 15) Groups. The Inspiratory Muscle Training Group received supervised aerobic training plus inspiratory muscle training at 40% of the maximal inspiratory pressure for 28 min once daily 3 days a week for 16 weeks. The Resistance Training Group received aerobic training plus resistance training (50–60% of the one-repetition maximum) in three sets per session 3 days a week for 16 weeks.

Main measures: Left-ventricular end-diastolic and end-systolic diameters via echocardiography, left-ventricular ejection fraction, aerobic capacity, inspiratory muscle strength, and N-terminal prohormone of brain natriuretic peptide levels were assessed at baseline, after 16 weeks of training-based intervention, and at a 24-week follow-up.

Results: The Inspiratory Muscle Training Group exhibited significantly greater improvements in left-ventricular end-diastolic and end-systolic diameters, left-ventricular ejection fraction, aerobic capacity, respiratory muscle strength, and N-terminal prohormone of brain natriuretic peptide levels than the Resistance Training Group ($p > 0.05$). These significant gains were maintained at a 24-week follow-up.

Conclusion: Inspiratory muscle training has more significant effect in eliminating the left ventricular dysfunction than resistance training for patients with dilated cardiomyopathy.

KEY WORDS: Inspiratory muscle training, Resistance training, Dilated cardiomyopathy.

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INTRODUCTION

Dilated cardiomyopathy (DCM) is a common clinical response to prolonged diverse cardiac insults. It is a global health problem characterized by progressive depression of myocardial contractile function and ventricular dilatation

with a prevalence of up to 1 in 250 individuals [1]. DCM usually presents as a primary genetic disorder or secondary manifestation of other cardiovascular or systemic conditions [2].

Myocardial ischemia remains the most common cause of dilated cardiomyopathy, accounting for approximately half of all cases of the condition. Progressive refractory heart failure and heart transplantation are the major consequences of dilated cardiomyopathy [3]. Clinically, DCM accounts for a substantial proportion of sudden cardiac death, especially among people of working age, with an annual incidence of 2% to 3% [4].

Despite advances in clinical management, exercise therapy is still widely used as an adjuvant therapy for patients with heart failure of multiple etiologies [5].

Current evidence demonstrates that regular physical training not only improves exercise capacity and oxygen uptake in patients with heart failure, but also attenuates left-ventricular dilatation and abnormal cardiac remodeling [6]. In addition, training is associated with improved endothelial function and left-ventricular ejection fraction and reduced hospital readmissions in patients with heart failure [7] .Consistently, studies on different models of cardiac injury have indicated that exercise promotes a broad range of effects beneficial to the heart, such as the attenuation of calcium imbalance, renin–angiotensin and sympathetic nervous system activation, mitochondrial dysfunction, and oxidative stress [8,9].

In recent years, inspiratory muscle training has demonstrated a positive impact on ventilatory efficiency, respiratory muscle strength, peak oxygen consumption, and functional capacity in different types of cardiac dysfunction [10].

Inspiratory muscle training offers a solution for patients who cannot engage in conventional exercise training programs. However, the beneficial effects of inspiratory muscle training have yet to be compared with those of resistance exercise training in patients with chronic heart failure. Therefore, in this study, we compared the effects of inspiratory muscle training and resistance training on ventricular function, aerobic capacity, and respiratory muscle strength in patients with dilated cardiomyopathy.

MATERIALS AND METHODS

In this single-blind randomized-controlled trial, we compared the effects of inspiratory muscle training and resistance training on left-ventricular dysfunction in patients with dilated cardiomyopathy. The data were collected between 2015 and 2016 at the outpatient clinic of the Physical Medicine and Rehabilitation Department of Wadi El-Neel Hospital, Cairo, Egypt. The sample size was calculated prior to the study to provide 80% power to detect differences of 10% in maximal inspiratory pressure at a 95% confidence interval. The calculations were based on clinically meaningful differences and variability estimates used in previous studies [11,12].

Male patients aged > 45 years with ischemic dilated cardiomyopathy were recruited for the study by an independent cardiologist. The inclusion criteria were: global dilation of the left ventricle on echocardiography; New York Heart Association Class II–III disease; clinical stability without medication changes for 30 days prior to the study; a left-ventricular end-diastolic diameter > 5.5 cm; a left-ventricular end-systolic diameter > 4.5 cm; and a left-ventricular ejection fraction < 45%. The exclusion criteria were: chronic heart failure due to other causes; valvular disease requiring surgery; participation in other trials involving physical exercise; chronic obstructive pulmonary disease; recent myocardial revascularization; and disorders of the musculoskeletal system or other organs that could hinder exercise training. This study was approved by the local ethics committee and conducted in accordance with the guidelines of the Declaration of Helsinki. Patients that met the inclusion criteria were informed about the scope of the investigation and provided written informed consent before starting the corresponding intervention. This study was registered at Pan African Clinical Trial Registry (PACTR201707002364200).

Patients were randomly allocated (by a table of random numbers) to either the Inspiratory Muscle Training or Resistance Training Groups by an investigator not involved in recruitment or treatment. Participant allocation was concealed in opaque envelope that was opened

after the baseline evaluation. All assessments were performed at baseline, after 16 weeks of training, and at a 24-week follow-up by a clinical investigator blinded to group allocations.

Maximum inspiratory pressure was assessed as a parameter of inspiratory muscle strength. Measurement was performed in a sitting position using Maximum Inspiratory Pressure Meter (care fusion UK 2321td) [13]. Each pa tient was asked to expire all of the air inside their lungs through the device, and then apply the mouthpiece while the nose was clipped, inspire as rapidly and deeply as possible, and hold their breath for at least 1.5 s so that the maximum pressure could be recorded. The patients were asked to repeat the procedure three times with sufficient rest between each repeat to reach maximum performance.

Each patient underwent complete resting M-mode two-dimensional echocardiography using a Sonos ultrasound system (Hewlett-Packard, Palo Alto, CA, USA). The examination was performed in the supine left-lateral position according to the standards of the American Society of Echocardiography [14]. M-mode measurements, including left-ventricular end-diastolic and end-systolic diameters, and left-ventricular ejection fraction, were calculated from the two-dimensional images. Echocardiography data were collected by a single operator, who was blinded to the experimental design, group assignments, and interventions, at baseline, after 16 weeks, and at a 24-week follow-up.

To evaluate aerobic capacity, cardiopulmonary exercise testing was performed using an Oxycon Pro® (ER-900; Ergoline, Jaeger GmbH, Würzburg, Germany) cardiopulmonary exercise test unit with 12-channel electrocardiography on a stationary bicycle ergometer. A gas analyzer was used to measure maximum heart rate, resting heart rate, peak oxygen uptake, and ventilatory equivalent of CO2 at the anaerobic threshold at baseline, after implementation of the training program, and at a 24-week follow-up. The patients were advised to pedal at a constant speed of 50–60 revolutions per minute, with monitors attached and a tight-fitting face mask positioned over the nose and mouth to prevent air leakage, for 2–3 min without resistance. Then, the work rate was increased by 10–20 W/min by increasing the resistance of the bicycle while the patient maintained a constant pedaling rate. The optimum duration of the test was around 10 min to allow calculation of the peak oxygen uptake. The exercise test ended with a cool-down stage, in which the patient pedaled the bicycle for a brief period without resistance [15].

Plasma N-terminal prohormone of brain natriuretic peptide levels were assessed 1 week before the initiation of training and repeated 1 day after its termination (Week 16). For this, blood samples were drawn before and after completion of the study from a peripheral vein into tubes containing ethylene diaminete traacetic acid, centrifuged immediately, and stored at -70°C for subsequent analysis. N- terminal prohormone of brain natriuretic peptide levels were measured using enzyme-linked immunosorbent assays.

Training procedure:

Patients in the Inspiratory Muscle Training and Resistance Training Groups underwent supervised individual aerobic training based on the results of cardiopulmonary exercise testing using Karvonen's method: Training heart rate = HRREST + [(HRMA - HRREST) × 55–85%]. [16].

The session began with warm-up exercises in the form of active stretching and walking for 5–10 min. A conditioning phase followed, comprising continuous aerobic exercise (cycling/walking on treadmill) for 30–40 min. Then, the patients warmed down for 5–10 min through walking and active stretching. The patients repeated this program in three sessions/week for 16 weeks.

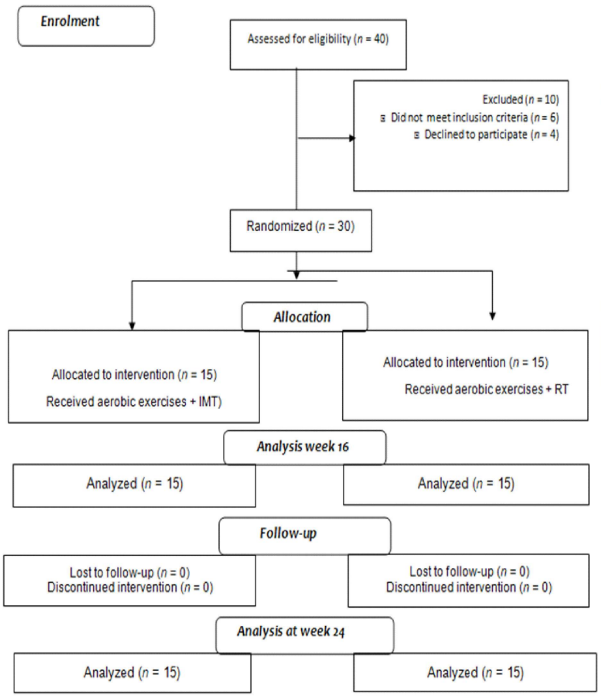
Patients in the Inspiratory Muscle Training Group participated in seven additional sets of supervised respiratory muscle training. Every set lasted 3 min with a 1-min rest period between sets. The total training time was 28 min 3 days per week for 4 months. Inspiratory load was adjusted to maintain 40% of the maximum inspiratory pressure [17].

Patients in the Resistance Training Group participated in additional resistance training with an intensity of 40–50% of the maximal weight each could lift (termed the "one-repetition maximum") for the upper limb (average weight: 2 kg)

and 50–60% for the lower limb (average weight: 3 kg). Strength was retested every tenth session to establish a new one-repetition maximum. The resistance program comprised three sets of exercises per session (each set comprising 10–12 repetitions with 1–2 minutes rest between sets) three times per week for 16 weeks.

Data analysis: Data were analyzed using SPSS Statistics version 24 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $p < 0.05$. Patients' demographic data were compared using the Student's t-test for independent samples and the Mann–Whitney U test. To analyze the effect of treatment in each group over 4 months, repeated-measures analysis of variance was used with the post-hoc Bonferroni test. The Student's t-test for dependent samples was used to compare within-group differences.

Fig. 1: Flow chart of participants through the study.



RESULTS

Forty male patients with dilated cardiomyopathy aged 52.37 ± 4.4 years were screened for eligibility. Six patients failed to meet the inclusion criteria and four patients declined to participate in the study. The remaining 30 participants were randomly assigned to the Inspiratory Muscle Training or Resistance Training Groups as shown in Fig. 1. As summarized in Table 1, there were no significant differences in baseline clinical characteristics, risk factors (diabetes, hypertension, or family history), hospitalization period, and baseline outcome measures (Week 0) between the Inspiratory Muscle Training and Resistance Training Groups ($p > 0.05$).

Table 1. Demographic and clinical characteristics of the 30 patients participated in this study

Characteristics	Group		Mean (SD)	p value
Age (years)	IMT		52.53 (4.6)	0.841
	RT		52.2 (4.3)	
Duration of suffering (months)	IMT		3.87 (1.1)	0.616
	RT		4.07 (0.9)	
Weight (Kg)	IMT		88 (4.8)	0.481
	RT		86.8 (4.3)	
Height (cm)	IMT		171.4 (4.7)	0.563
	RT		171.4 (5.5)	
BMI (kg/cm2)	IMT		30.11 (2.4)	0.836
	RT		29.58 (1.9)	
Hospitalization (days)	IMT		7.9(1.2)	0.1
	RT		8.6 (0.8)	
Smoking	IMT	Yes	9 (60%)	0.481
		No	6 (40%)	
	RT	Yes	7 (46.7)	
		No	8 (53.3)	
NYHA (n, %)	IMT	II	9 (60%)	0.72
		III	6 (40%)	
	RT	II	8 (53.3)	
		III	7 (46.7)	
HRMAX (bpm)	IMT		120.27 (9.5)	0.91
	RT		119.9 (8.1)	
HRREST (bpm)	IMT		69.67 (8.3)	0.95
	RT		75.47 (9.9)	

BMI: body mass index; NYHA: New York Heart Association; HRMAX: Maximum heart rate; HRREST: Resting heart rate; bpm: Beats per minute; IMT: inspiratory muscle training; RT: Resistance training; SD: standard deviation

Table 2 shows that left-ventricular end-diastolic and end-systolic diameters were significantly decreased at 16 weeks in both groups ($p > 0.05$), and were maintained at 24 weeks. Regarding between-group comparisons (Table 3), left-ventricular end-diastolic and end-systolic diameters were most improved in the Inspiratory Muscle Training Group at 16 weeks. There was no significant difference in left-ventricular end-systolic diameter between the groups at 24-weeks. Left-ventricular ejection fraction significantly increased in both groups over time compared with baseline values ($p < 0.05$). This improvement was maintained at a 24-week follow-up.

Table 2: The means (standard deviation) and p values of two-factor analysis of variance for the main outcomes achieved at the three time points for both groups.

Variables	IMT Group			RT Group			p value (Time effect)
	W0	W16	W24	W0	W16	W24	
LVEDD (cm)	6.94 (0.4)	5.62 (0.3)	5.6 (0.4)	6.86 (0.5)	6.09 (0.3)	6 (0.3)	0.001
p value (group effect)	0.023						
LVESD (cm)	5.79 (0.5)	4.8 (0.3)	4.7 (0.3)	6.12 (0.5)	5.18 (0.5)	5.07 (0.5)	0.001
p value (group effect)	0.049						
LVEF (%)	34.93 (4.7)	40.13 (3.66)	42.53 (2.6)	35.13 (3.5)	37.13 (2.4)	37.93 (1.9)	0.001
p value (group effect)	0.025						
HRREST (bpm)	74.2 (8.6)	60.8 (3.2)	59.2 (4.9)	70 (3.7)	68.2 (6.7)	65 (8.2)	0.001
p value (group effect)	0.04						
HRPEAK (bpm)	120.27 (9.5)	108.87 (7.5)	104.33 (6.5)	119.9 (8.1)	117.4 (10.2)	115.1 (11.8)	0.001
p value (group effect)	0.045						
Peak VO2 (ml/g/min)	11.6 (3.1)	16.8 (2.1)	16.9 (2.09)	10.8 (1.27)	14.6 (2.2)	15.3 (2.3)	0.001
p value (group effect)	0.034						
EqCO2 at AT (ml/min)	44.8 (3.37)	39.56 (2.4)	36.65 (4.57)	44.45 (4.31)	41.35 (4.19)	39.75 (2.73)	0.001
p value (group effect)	0.13						
PIMAX (cm H2O)	81.4 (13.7)	92.4 (11.94)	96.4 (11.18)	82.4 (8.2)	84.6 (7.1)	84.8 (6.6)	0.001
p value (group effect)	0.049						
NT-proBNP	1615.36	1543.12	-	1806.16	1741.24	-	0.001
p value (group effect)	0.11						

Data are expressed as means (standard deviation) LVEDD: left-ventricular end-diastolic diameter; LVESD: left-ventricular end-systolic diameter; LVEF: left-ventricular ejection friction; HRPEAK: maximum heart rate; HRREST: resting heart rate; bpm: beats per minute; peak VO2: peak oxygen consumption; EqCO2 at AT: ventilatory equivalent of CO2 at the anaerobic threshold; PIMAX: maximum inspiratory pressure; NT-proBNP: N-terminal prohormone of brain natriuretic peptide; IMT: inspiratory muscle training; RT: resistance training; W: Week.

Table 3: Comparing the effects of inspiratory muscle training and resistance training on left-ventricular function between and within groups.

Differences within groups				Differences between groups (95% CI)		
IMT Group		**RT Group**		**W0**	**W16**	**W24**
W0–16	**W0–24**	**W0–16**	**W0–24**	**IMT–RT**	**IMT–RT**	**IMT – RT**
−5.2‡ (2)	−7.6‡ (3.5)	−2.1‡ (3.3)	−2.8‡ (3.3)	2 (−2.9–3.3)	−3.1* (−5.3–−0.66)	−4.6* (−6.3–−2.8)
1.31‡ (0.5)	1.34‡ (0.57)	0.77‡ (0.52)	0.86‡ (0.33)	−0.07 (−0.42–0.27)	0.37* (0.01–0.73)	0.4* (0.11–0.68)
1.04‡ (0.5)	1‡ (0.58)	0.93 (0.48)	1.04‡ (0.5)	0.32 (−0.09–0.75)	0.34* (−0.01–0.7)	0.28 (−0.4–0.6)

Data are expressed as mean (standard deviation)/mean differences (95% confidence intervals) LVEF%: left-ventricular ejection fraction; LVEDD: left-ventricular end-diastolic diameter; LVESD: left-ventricular end-systolic diameter volume; IMT: inspiratory muscle training; RT: Resistance training; CI: confidence interval; W: Week.
‡significant within group; * significant between groups

The mean cardiopulmonary testing results showed that there was a significant improvement in all cardiopulmonary test results over time ($p > 0.05$). Peak oxygen uptake and ventilatory equivalent of CO^2 at the anaerobic threshold were more significantly improved in the Inspiratory Muscle Training Group at 16 weeks. This effect was maintained at a 24-week follow-up (Fig. 2,3).

Maximum inspiratory pressure significantly improved in both groups over time compared with baseline measurements. At 16 weeks, patients

in the Inspiratory Muscle Training Group showed a more significant improvement in maximum inspiratory pressure than those in the Resistance Training Group. This significant improvement was only maintained in the Inspiratory Muscle Training Group at a 24-week follow-up. Both groups were comparable at baseline. At the end of training (Week 16), there were no statistically significant changes in N-terminal prohormone of brain natriuretic peptide levels between or within the groups (Fig.4).

Fig. 2: Mean value of peak oxygen consumption achieved by IMT and RT at baseline, 16W and 24W follow up; a significant within group; b significant between groups.

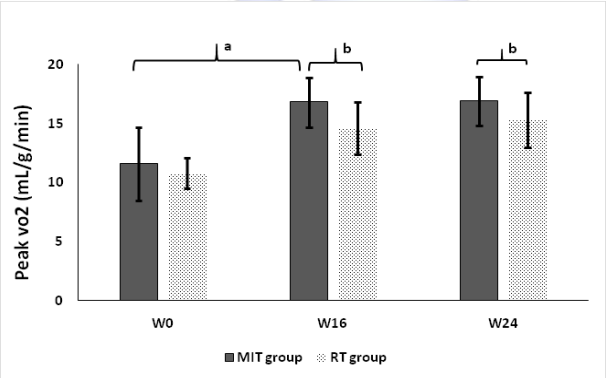


Fig. 3: Mean value of ventilatory equivalent of CO2 at anaerobic threshold achieved by IMT and RT at baseline, 16W and 24W follow up; a significant within group; b significant between groups.

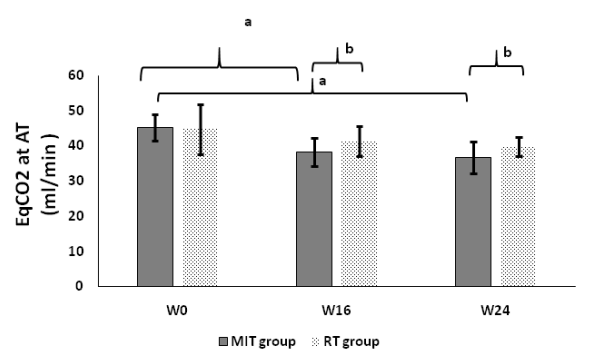
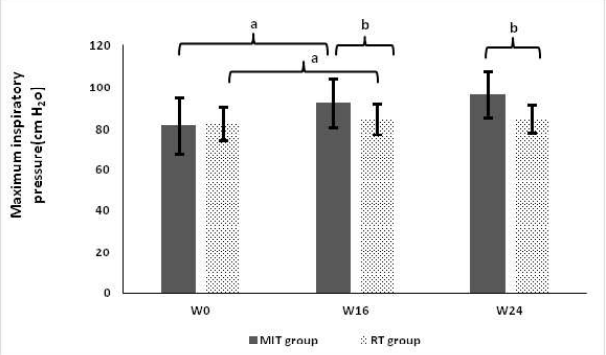


Fig. 4: Mean value of maximum inspiratory pressure achieved by IMT and RT at baseline, 16W and 24W follow up; a significant within group; b significant between groups.



DISCUSSION

In this study, we compared the effects of inspiratory muscle training and resistance training in patients with dilated cardiomyopathy. Our results demonstrate that 16 weeks of supervised inspiratory muscle training induced a significantly greater improvement in left-ventricular function, aerobic capacity, and inspiratory muscle strength than resistance training. Our study also shows the long-term effect of training through 24-week follow-up measurements. We found that that the improvements persisted at 24 weeks at a similar magnitude in the Inspiratory Muscle Training Group. To our knowledge, this is the first randomized-controlled study to compare the effects of inspiratory muscle training and resistance training in patients with dilated cardiomyopathy.

Dilated cardiomyopathy is typified by enlargement of the ventricular chamber, thinning of the ventricular wall, and impaired contraction of the left ventricle or both ventricles [18]. During the compensatory phase of declining heart function, the heart undergoes pathologic remodeling [19]. Clinically, cardiac remodeling manifests as changes in the size, shape, and pumping function of the heart as a result of increased hemodynamic load and neurohormonal stress [20]. As a compensatory mechanism for reduced cardiac output, the heart attempts to enlarge its chambers. However, although these compensatory mechanisms initially increase cardiac output, they ultimately lead to increased myocardial wall pressure, reduced cardiac function, and the development or worsening of heart failure [21]. Exercise capacity in patients with heart failure is believed to be limited by respiratory muscle function and/or abnormal ventilatory responses to exercise [22]. Consequently, strategies to enhance respiratory muscle function have gained considerable attention in recent years.

Previous research has demonstrated that abnormalities of both skeletal muscle and vasomotor tone characteristic in cardiac patients can be reversed with exercise. Regular training can improve the volume density of mitochondria and cytochrome c oxidase-positive mitochondria, with an attendant increase in the expression of

oxidative metabolic enzymes. A return to Type-I oxidative fibers (from Type-II) is evident on muscle biopsy. Peak exercise leg blood flow and leg arterio–venous oxygen difference increase after training. A decrease in leg venous lactate levels seems to be inversely related to changes in mitochondrial volume density and unrelated to leg blood flow [23].

Hsieh et al. [24] reported that exercise training improves oxygen use and oxidative capacity through increased activity of oxidative enzymes and increased mitochondrial content. These changes enhance peak oxygen uptake and lactate threshold, and delay the onset of anaerobic metabolism after training. Moreover, regular training can increase the proportion of Type-I fibers, which derive energy mainly from aerobic metabolism. There is a positive correlation between peak oxygen uptake and mitochondrial volume density [25].

The significant increase in peak oxygen uptake in both groups may be attributable to improved central adaptations (increased left-ventricular ejection fraction and reduced left-ventricular end-diastolic and end-systolic diameters), because there was a significant proportional correlation between relative changes in left-ventricular ejection fraction and peak oxygen uptake along with peripheral adaptations (improved cardiac output redistribution, enhanced endothelial function, and increased capacity of muscles to extract oxygen owing to an increase in the density of capillaries, equating to more time for oxygen diffusion, and facilitated by an increased number of mitochondria) [26].

The significant difference in aerobic capacity and echocardiographic changes in both groups in our study may be attributable to the attenuation of left-ventricular remodeling and improvement of respiratory muscle strength as a result of inspiratory muscle training.

There is growing evidence that inspiratory muscle training improves ventilatory efficiency, lowers ventilatory oscillations during incremental exercise, and attenuates the metaboreflex in inspiratory muscles [27] .Inspiratory muscle training may delay the development of diaphragmatic fatigue in patients with heart failure, preventing the recruitment of accessory respiratory muscles, increasing ventilatory efficiency, reducing the blood flow required by the respiratory muscles during exercise, and improving the perfusion of the peripheral muscles, thereby decreasing workload on the heart [28].

Passino et al. Suggested that the anti-remodeling effect of exercise training may be due to a reduction in vasoconstrictive hormones, homodynamic loading, or resting plasma angiotensin II, aldosterone, vasopressin, atrial natriuretic peptide, brain natriuretic peptide, and catecholamine levels. Training is also associated with improved sympathovagal balance coupled with a decline in vasoconstrictive neurohormones, which may reduce vascular load, thereby attenuating left-ventricular remodeling. Thus, aerobic training is an inexpensive and effective nondrug, nondevice, nonsurgical intervention that reverses ventricular remodeling and improves peak oxygen uptake in clinically stable patients with heart failure [29].

Haykowsky et al. reported that aerobic exercise training reverses ventricular remodeling in clinically stable individuals with heart failure. Long-term moderate exercise training has been shown to induce reverse remodeling in patients with stable chronic heart failure, and this was associated with significant increases in work capacity and peak oxygen uptake. In this high-risk group, only stable patients with New York Heart Association Class-II and -III heart failure lacking complex arrhythmias should be referred for exercise training [26].

Moreover, Piepoli et al. suggested that regular exercise training is closely associated with the attenuation of left-ventricular dilation and improvements in left-ventricular ejection fraction, left-ventricular end-diastolic and end-systolic volumes, maximal heart rate, systolic blood pressure, and cardiac output. In addition, physical training has attracted attention for its beneficial effects on neurohumoral, inflammatory, metabolic, and central hemodynamic responses and endothelial, skeletal muscle, and cardiovascular functions in patients with chronic heart failure. [30]. Improvements in left-ventricular ejection fraction and left-ventricular end-systolic diameter were evident in both groups, not only confirming the safety of our program, but also suggesting the benefits for cardiac structure and function. Our findings are encouraging

and consistent with those of previous studies, which have shown a similar attenuation of remodeling mainly attributed to a decrease in peripheral vascular resistance following aerobic exercise [31].

The results of this study are in agreement with those of previous studies that compared inspiratory muscle training with other modes of training These studies reported that the addition of inspiratory muscle training to aerobic training [13,28] or combined aerobic and resistance training [32] resulted in significant improvements in respiratory muscle strength, functional capacity, and cardiorespiratory responses to exercise in patients with chronic heart failure and inspiratory muscle weakness. [13,28,32] However, our findings are contradicted by those of Weiner et al. [33], who failed to achieve a significant improvement in peak exercise oxygen consumption following 3 months of specific inspiratory muscle training, and Adamop-oulos et al., who reported that the addition of inspiratory muscle training to aerobic training gained an additional improvement in respiratory muscle function without significant changes in cardiopulmonary exercise testing [13]. Possible explanations for these discrepancies in our study include small sample size, absence of a control group, different training procedures, short-term observations.

The combination of resistance and aerobic training in the Resistance Training Group had beneficial effects, as reported by Mampuya, who stated that exercise protocols should include not only endurance training, but also resistance training, because the improvement in muscle strength enhance patients' performance of activities of daily living and may be more effective than aerobic training alone at reversing peripheral metabolic limitations and skeletal muscle myopathy and increasing overall functional capacity[34].

The findings of this study show great consistency with those of Bouchla et al. who studied the effect of the addition of strength training to aerobic interval training on muscle strength and body composition in patients with chronic heart failure. They found a significant improvement in peak oxygen uptake in patients who participated in the combined training compared with patients who participated in aerobic interval training alone. Also, they concluded that adaptations other than hypertrophy, such as muscle fiber-type alterations and/or neuromuscular adjustments, may account for their results [35].

Mehani et al. studied changes in diastolic dysfunction following endurance training and showed that regular training leads to an increase in left-ventricular stroke volume at rest and during exercise and a small but significant decrease in left-ventricular end-diastolic diameter and left-ventricular function. There was a correlation between improved endothelium-dependent vasodilatation of the skeletal muscle vasculature and reduction of total peripheral resistance during exercise. Therefore, training is associated with a reduction in afterload that can improve ejection fraction [36].

The findings of this study are also supported by those of Laoutaris et al., who studied the benefits of a combined exercise program including aerobic, resistance, and inspiratory muscle training. The program consisted of bicycle exercise at 70–80% of the maximum heart rate, quadriceps resistance training at 50% of the one-repetition maximum, upper-limb exercises using dumbbells weighing 1–2 kg, and inspiratory muscle training at 30% of the maximal inspiratory pressure compared with aerobic exercise alone in the Control Group. They found additional and significant improvements in the Study Group in cardiopulmonary function, quadriceps strength and endurance, maximum inspiratory pressure, and dyspnea compared with the Control Group [37].

Because aerobic exercise is the cornerstone of any rehabilitation program for heart failure, we added aerobic exercise in both training groups, and did not assess the impact of inspiratory muscle training alone because we did not want to withhold aerobic exercise from our patients. Our results show an improvement in serum N-terminal prohormone of brain natriuretic peptide levels in both groups after training without significant differences within or between the groups. One possible reason for this is the moderate functional status of our participants. These results are broadly consistent with those of Laoutaris et al., who concluded that improvements in dyspnea and exercise tolerance after

inspiratory muscle training were not associated with changes in N-terminal prohormone of brain natriuretic peptide expression in patients with mild-to-moderate chronic heart failure[38].

According to the American Thoracic Society/ European Respiratory Society, a maximal inspiratory pressure < 80 cm H2O indicates inspiratory muscle weakness. In this study, none of our participants had inspiratory muscle weakness, so our results may be inapplicable to patients with dilated cardiomyopathy and inspiratory muscle weakness. However, they clearly reveal the efficacy of inspiratory muscle training at reversing the remodeling process associated with heart failure. The long-term follow-up is a strength of our study. The limitations of our study include its relatively small sample size, our failure to measure peripheral muscle strength (hindering its inclusion in in meta-analyses), and also the lack of follow-up assessment of N-terminal prohormone of brain natriuretic peptide levels, because this neural hormone may be significantly changed after regular long-term training.

CONCLUSION

Based on the outcome of our investigation, it is possible to conclude that inspiratory muscle training for 16 weeks at 40% of the maximum inspiratory pressure improved left-ventricular function, aerobic capacity, and respiratory muscle strength significantly more than resistance training. These findings provide impetus for the incorporation of inspiratory muscle training into cardiac rehabilitation programs for patients with dilated cardiomyopathy.

Clinical Message: Sixteen weeks of supervised inspiratory muscle training caused significant improvements in respiratory muscle strength, left-ventricular function and diameter, and aerobic capacity in patients with dilated cardiomyopathy.

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