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Inspiratory muscle training in stroke patients with congestive heart failure

A CONSORT-compliant prospective randomized single-blind controlled trial

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Abstract

Background: Cardiopulmonary function can be adversely affected after a cerebrovascular accident in patients with congestive heart failure (CHF). The aim of this study was to investigate the efficacy and feasibility of inspiratory muscle training (IMT) for stroke patients with CHF.

Methods: A prospective randomized single-blind controlled trial was conducted in a single tertiary medical center in southern Taiwan between May 2011 and July 2015. Forty-one patients were enrolled, of whom 21 completed the study (IMT group n = 11 and control group n = 10). Both groups participated in a conventional stroke rehabilitation program. Patients in the IMT group received an additional IMT program beginning with an intensity of 30% maximal inspiratory pressure (MIP), then increased by 2cmH_2O each week for 30 minutes daily for at least 5 days a week for 10 weeks. MIP, maximal expiratory pressure, spirometry, resting oxyhemoglobin saturation, modified Borg Scale, Fatigue Assessment Scale, and Barthel Index were assessed in each patient.

Results: There were significant differences from baseline in MIP ($P = 0.008$), percent predicted forced vital capacity ($P = 0.033$), forced expiratory volume in 1 second (FEV1) ($P = 0.008$), percent predicted FEV1 ($P = 0.008$), and Barthel Index ($P = 0.012$) in the IMT group, and Barthel Index ($P = 0.027$) in the control group. There were significant differences between groups in MIP (20.91 ± 19.73 vs −9.00 ± 26.01, adjusted P value = 0.023) and Barthel Index (24.55 ± 22.30 vs 7.50 ± 8.25, adjusted P value = 0.044).

Conclusion: The 10-week IMT was feasible and effective in improving inspiratory force and activities of daily living for the stroke patients with CHF.

Abbreviations: CHF = congestive heart failure, FEV1 = forced expiratory volume in 1 second, FEV1/FVC = the ratio of FEV1 to FVC, FVC = forced vital capacity, IMT = inspiratory muscle training, MEP = maximal expiratory pressure, MIP = maximal inspiratory pressure, MMEF = maximum midexpiratory flow, SpO_2 = resting oxyhemoglobin saturation.

Keywords: congestive heart failure, inspiratory muscle training, maximal expiratory pressure, maximal inspiratory pressure, pulmonary function

1. Introduction

Patients with congestive heart failure (CHF) often have generalized weakness or weakness of respiratory muscles[1,2] that can restrict ventilation (VE) and lead to the major symptoms of orthopnea, dyspnea on exertion, exercise intolerance, fatigue, or even poor activities of daily living.[3,4] Some clinical studies have reported histological and biochemical alterations of the diaphragm muscles in patients with CHF, including muscle fiber atrophy and reduced mitochondrial oxidative capacity, which can induce an increased respiratory load and systemic myopathy.[5–7] Maximal inspiratory pressure (MIP) is also an important prognostic indicator of CHF, and early diaphragmatic fatigue with a decrease in MIP has been reported to be related to limitations in VE and exercise intolerance.[8]

Stroke can affect respiratory function and contribute to desaturation because of respiratory muscle weakness. In addition, chronic weakness of the diaphragm muscles has been reported to decrease diaphragm displacement in stroke patients.[9] Another study showed significant decreases in MIP and maximal expiratory pressure (MEP) in community-dwelling

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chronic stroke survivors compared with healthy age-matched controls.[10] The symptoms of CHF can be exacerbated after an episode of stroke, resulting in avoidance of activities or exercise, thereby resulting in a vicious circle of inactivity and poor fitness.

Respiratory muscle training has received considerable attention in the field of pulmonary rehabilitation.[11–15] Inspiratory muscle training (IMT), performed by generating flow with constant and specific intensity through a threshold device, has been shown to improve inspiratory muscle function, leading to better exercise capacity and endurance in patients with chronic airway limitation.[12,13]

IMT has recently been applied in both patients with stroke[16] and CHF[17] patients separately, and most of these patients had significant improvement in cardiopulmonary functions. However, there was no study about IMT in stroke patients combined with CHF. According to our clinical observations, many stroke patients combined with CHF were too weak to do exercise or perform daily activities. We supposed that IMT combined conventional regular rehabilitation program could further help these patients improve cardiopulmonary functions, thus giving rise to better exercise tolerance and performance of daily activities. The aim of this study, therefore, was to investigate the efficacy and feasibility of IMT in stroke patients with CHF.

2. Methods

2.1. Subjects

We recruited stroke patients with stable CHF from a single tertiary medical center in southern Taiwan. The inclusion criteria were stroke patients aged 20 to 85 years with the diagnosis of CHF according to the Framingham criteria, New York Heart Association functional classes[18] I to III. Computerized tomography or magnetic resonance imaging was used to confirm the diagnosis of stroke. Patients were excluded if they initially had high MIP (≥70% predicted MIP), if they could not tightly place their lips over a mouthpiece, or if air leaked during inhaling or exhaling through the threshold device, if they had a recent acute exacerbation of chronic obstructive pulmonary disease, pneumothorax or large bullae on chest radiography, long-term use of oxygen therapy, a history of recent lung surgery (within the past 12 months), or marked osteoporosis, and if they had unstable angina, decompensated CHF, or complicated arrhythmia.

The study protocol was approved by the *Institutional Review Board of Chang Gung Memorial Hospital, Kaohsiung Medical Center* (IRB number: 99-3663A3) and was registered at ClinicalTrials.gov (Clinical Trial Identifier: NCT02614001). All patients signed informed consent forms before they were included in this study.

2.2. Study design

This was a prospective randomized single-blind controlled trial evaluating the efficacy and feasibility of IMT in stroke patients with CHF. The patients were randomly assigned to either the IMT group or the control group.

2.3. Interventions

IMT was performed by an experienced respiratory therapist, using a pressure threshold device (Threshold IMT HS730, RESPIRONICS Inc., Cedar Grove, NJ). This device incorporates a flow-independent one-way valve to ensure consistent intensity (in cmH_2O). It has been shown that through training with this device, respiratory muscle strength, endurance, and exercise tolerance can be ameliorated.[19]

Figure 1. An experienced respiratory therapist instructed the patient in how to perform inspiratory muscle training by using a pressure threshold device. Arrowhead, nose clip; arrow, pressure threshold device; RT = respiratory therapist.

During the training program, the patients were instructed to place their lips around the mouthpiece in a sitting position with a nose clip (Fig. 1). The patients inhaled with enough force to open the valve and exhaled through the mouthpiece, and they continued to inhale and exhale without removing the device from their mouths. During the initial training session, the patients were encouraged to start at an intensity equal to 30% of their MIP and then to gradually increase the intensity by 2 cmH_2O/wk as far as the patients could tolerate (or 41 cmH_2O, the maximum load for this device).[20] Throughout the first training session, oxygen saturation was monitored to ensure the safety of the training. The intensity was adjusted if there was any decrease in oxygen saturation during loaded breathing. The patients were allowed to take intermittent periods of rest whenever they felt uncomfortable. If the patient could not complete the training session because of increased intensity, the training intensity of the last part of the session was maintained with the previous intensity setting. The training was immediately stopped if the patient experienced any discomfort during inspiration. All of the patients were trained for 30 min/d for at least 5 days a week for 10 weeks. The training program followed the protocol reported in our previous study in patients with bronchiectasis.[21]

Patients in both the IMT and control groups participated in a conventional stroke rehabilitation program for at least 5 days a week for 10 weeks; however, the patients in the control group did not receive any IMT. Both groups, if not admitted to hospital, were monitored by telephone twice a week until the end of the study.

2.4. Outcome measures

The outcome measures were evaluated before and after the 10-week intervention by a technician blinded to the patient allocation. The primary outcome measures included MIP and MEP. MIP was measured after maximal expiration, and MEP was measured after maximal inspiration with the patient in a sitting posture wearing a nose clip. The patients were strongly urged to achieve maximal inspiration and expiration at or near residual volume and total lung capacity. Repeated measurements were made until 2 technically satisfactory measurements were recorded, with the higher value being used in the analysis.[22,23] The secondary outcome measures included the following items:

(1) *Pulmonary function*: According to the American Thoracic Society recommendations,[24] the pulmonary function tests were performed in a pulmonary function laboratory using a standard spirometer (Vitalograph, Serial Spirotrac, Buckingham, UK). The following parameters were measured: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), the ratio of FEV1 to FVC (FEV1/FVC), and maximum midexpiratory flow (MMEF). FVC, FEV1, and MMEF were also presented as percent predicted values.
(2) *Oxyhemoglobin saturation*: Resting oxyhemoglobin saturation (SpO_2) was measured using a finger pulse oximeter (FingerPrint, BCI International, WI), which is a noninvasive monitoring technique to estimate the percentage of hemoglobin saturated with oxygen.[25]
(3) *Perceived exertion*: Perceived exertion can be used to determine physical working capacity.[26] The patients were asked to rate their perceived exertion using a modified Borg Scale ranging from 0 to 10.[27] The Fatigue Assessment Scale was also used to rate perceived exertion, with scores ranging from 5 to 50.[28]
(4) *Activities of daily living:* The Barthel Index[29] can be used to evaluate activities of daily living, including feeding, transfer, personal grooming and hygiene, bathing, toileting, walking, ascending and descending stairs, and controlling bowel and bladder. The score ranges from 0 (totally dependent, needs help with every activity of daily living) to 100 (totally independent).

2.5. Sample size calculation

Sample size calculation was based on a previous study performed in stroke patients by Sutbeyaz et al.[30] The mean differences between pretraining MIP and posttraining MIP were assumed to be 7.87 and 2.90 cmH_2O in the IMT and control groups, respectively, with standard deviations of 6.6 and 1.9 cmH_2O. Applying a statistical power of 80% at a 2-sided significance level of 5%, the study required at least 34 participants. Assuming a dropout rate of 30%, the required total number of enrolled participants was 48. The sample size calculation was performed using G*Power 3.1.3 (Franz Faul, University of Kiel, Kiel, Germany).

2.6. Statistical analysis

Per-protocol analysis was conducted to evaluate the treatment effect. The baseline characteristics were presented as absolute number (percentage) or mean (standard deviation). To compare baseline characteristics between groups, the Mann–Whitney *U* test was used for continuous variables and Fisher exact test for categorical variables. The Wilcoxon signed-rank test was used to compare differences between pre- and posttraining outcomes within each group. Changes from baseline of each outcome measure between groups were compared using linear regression analysis. A 2-tailed *P* value of less than 0.05 was considered significant. All statistical analyses were performed using SPSS software version 14.0 (SPSS Inc., Chicago, IL).

3. Results

A total of 47 consecutive stroke patients combined with stable CHF were assessed for eligibility from May 2011 to July 2015. Six of these patients were excluded, 2 because they declined to participate in the study and 4 who initially had a high MIP. The remaining 41 patients were randomly assigned to receive IMT with conventional stroke rehabilitation (IMT group, n=23) or conventional stroke rehabilitation only (control group, n=18). After randomization, 3 in the IMT group and 5 in the control group did not receive the allocated intervention. Twelve patients were lost to follow-up and were also excluded from the final analysis. In total, 21 patients completed the study, with 11 in the IMT group and 10 in the control group. The reasons for not receiving the allocated interventions and being lost to follow-up are described in Fig. 2. There were no significant differences in most of the baseline characteristics between the 2 groups except for percent predicted FVC ($P=0.009$) (Table 1).

The results recorded at the beginning and end of the 10-week training program are summarized in Table 2. There were significant differences from baseline in MIP ($P=0.008$), percent predicted FVC ($P=0.033$), FEV1 ($P=0.008$), percent predicted FEV1 ($P=0.008$), and Barthel Index ($P=0.012$) in the IMT group, and in Barthel Index ($P=0.027$) in the control group. There were no significant changes from baseline in SpO_2, modified Borg Scale, Fatigue Assessment Scale, FVC, FEV1/FVC, or MMEF in either group. In addition, there were significant differences from baseline between groups in MIP (20.91 ± 19.73 vs -9.00 ± 26.01, adjusted *P* value=0.023) and Barthel Index (24.55 ± 22.30 vs 7.50 ± 8.25, adjusted *P* value=0.044) after adjusting for baseline percent predicted FVC in linear regression analysis.

4. Discussion

In this study, we analyzed 21 stroke patients with stable CHF who underwent IMT or not for 10 weeks. Comparing the 11 patients in the IMT group to the 10 patients in the control group, there were no significant differences in most of the baseline characteristics except for percent predicted FVC. MIP, percent predicted FVC, FEV1, percent predicted FEV1, and Barthel Index significantly improved compared to the pretraining status in the IMT group, while only Barthel Index significantly improved compared to the pretraining status in the control group. Moreover, there were significant differences from baseline between the 2 groups in MIP and Barthel Index after adjusting for baseline percent predicted FVC using linear regression analysis.

IMT has been shown to significantly improve peak oxygen consumption, VE/carbon dioxide production slope, quality of life, respiratory muscle strength, exertional dyspnea, exercise capacity, and blood flow in the extremities during exercise and rest in heart failure patients.[4,31–35] IMT has also been shown to improve FEV1, FVC, vital capacity, MMEF, maximum voluntary VE, and peak oxygen consumption in patients with subacute stroke[30] and to have a short-term effect on inspiratory strength and endurance in chronic stroke patients.[36] One systematic review including 9 randomized controlled trials compared IMT versus control interventions in CHF patients.[17] Although the patients with normal inspiratory muscle strength had improvements in exercise performance after IMT, those with inspiratory muscle weakness had greater improvements in maximal and submaximal exercise capacity.[17] Stroke can be viewed as a cause of inspiratory muscle weakness due to peripheral and central etiologies. In the peripheral etiology, respiratory muscle weakness of the affected side, instability of the chest, and an inactive lifestyle can lead to bilateral inspiratory muscle weakness.[10,37–39] In the central etiology, abnormal magnetic evoked potentials, cortical latency, central conduction time of the

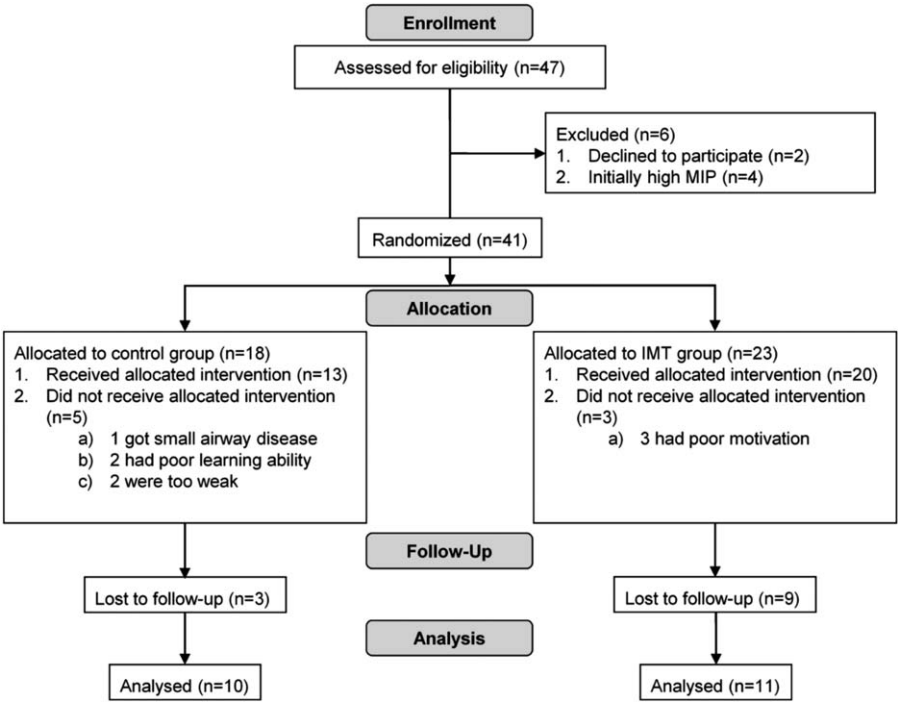

Figure 2. Flow diagram of participants through the study.

Table 1

Baseline characteristics of the patients in the inspiratory muscle training and control groups.

	Control (n=10)	IMT (n=11)	Total (n=21)	*P*
Gender				1.000
Female	6 (60.0)	7 (63.6)	13 (61.9)	
Male	4 (40.0)	4 (36.4)	8 (38.1)	
Age, y	67.50 (10.35)	63.73 (14.64)	65.52 (12.61)	0.459
Body height, m	1.57 (0.05)	1.58 (0.09)	1.58 (0.07)	0.915
Body weight, kg	60.91 (8.75)	62.18 (12.76)	61.58 (10.78)	0.724
BMI, kg/m^2	24.70 (3.82)	24.94 (5.34)	24.83 (4.56)	0.778
Time since stroke onset, d	58.30 (58.27)	71.00 (49.92)	64.95 (53.07)	0.481
Paretic side				
Right	3 (30.0)	5 (45.5)	8 (38.1)	0.659
Left	7 (70.0)	6 (54.5)	13 (61.9)	
Lesion type				
Ischemic	9 (90.0)	8 (72.7)	17 (81.0)	0.586
Hemorrhagic	1 (10.0)	3 (27.3)	4 (19.0)	
Barthel Index	23.50 (16.34)	35.00 (21.10)	29.52 (19.42)	0.166
Baseline cardiopulmonary function				
NYHA class				1.000
II	7 (70.0)	7 (63.6)	14 (66.7)	
III	3 (30.0)	4 (36.4)	7 (33.3)	
EF	61.00 (12.43)	60.55 (14.29)	60.76 (13.10)	0.805
SpO_2	97.90 (1.10)	97.09 (2.98)	97.48 (2.27)	0.774
Modified Borg Scale	1.10 (0.32)	1.45 (0.52)	1.29 (0.46)	0.080
MIP, cmH_2O	44.00 (20.66)	33.64 (15.67)	38.57 (18.52)	0.237
MEP, cmH_2O	50.00 (17.00)	56.36 (36.41)	53.33 (28.34)	0.746
FVC, L	1.72 (0.55)	2.14 (0.88)	1.94 (0.76)	0.139
FVC (% predicted)	63.35 (12.04)	77.64 (19.26)	70.83 (17.44)	0.009‡
FEV1, L	1.43 (0.30)	1.76 (0.74)	1.60 (0.59)	0.139
FEV1 (% predicted)	72.14 (14.37)	83.49 (21.12)	78.09 (18.70)	0.078
FEV1/FVC (%)	86.30 (12.91)	83.75 (11.96)	84.97 (12.18)	0.526
MMEF (%)	72.33 (23.05)	76.59 (31.56)	74.56 (27.24)	0.778

Values are expressed as mean (SD) or number (%). BMI = body mass index, EF = ejection fraction, FEV1 = forced expiratory volume in 1 second (expressed in liters and in % of theoretical value), FVC = forced vital capacity (expressed in liters and in % of theoretical value), IMT = inspiratory muscle training, MEP = maximal expiratory pressure, MIP = maximal inspiratory pressure, MMEF = maximum midexpiratory flow (expressed in % of theoretical value), NYHA = New York Heart Association, SD = standard deviation, SpO_2 = resting oxyhemoglobin saturation by pulse oximetry.

† $P<0.05$.

‡ $P<0.01$.

Table 2

Data analysis before and after the 10-week study in the inspiratory muscle training and control groups.

	Baseline mean (SD)	Posttreatment mean (SD)	Change from baseline mean (SD)	*P* for change from baseline	*P** for change between groups
MIP, cmH_2O					
Control	44.00 (20.66)	35.00 (15.09)	−9.00 (26.01)	0.292	0.023†
IMT	33.64 (15.67)	54.55 (25.83)	20.91 (19.73)	0.008‡	
MEP, cmH_2O					
Control	49.00 (17.29)	41.00 (20.79)	−8.00 (14.76)	0.084	0.167
IMT	56.36 (36.41)	66.36 (35.85)	10.00 (15.49)	0.058	
FVC, L					
Control	1.72 (0.55)	1.67 (0.47)	−0.05 (0.29)	0.507	0.056
IMT	2.14 (0.88)	2.30 (1.01)	0.16 (0.29)	0.050	
FVC (% predicted)					
Control	63.35 (12.04)	64.77 (12.24)	1.42 (12.17)	0.959	0.075
IMT	77.64 (19.26)	82.58 (15.61)	4.95 (6.75)	0.033†	
FEV1, L					
Control	1.43 (0.30)	1.45 (0.35)	0.02 (0.23)	0.859	0.193
IMT	1.76 (0.74)	1.98 (0.84)	0.22 (0.28)	0.008‡	
FEV1 (% predicted)					
Control	72.14 (14.37)	73.22 (19.91)	1.08 (11.90)	0.953	0.117
IMT	83.49 (21.12)	95.96 (23.99)	12.47 (13.52)	0.008‡	
FVC/FEV1 (%)					
Control	86.30 (12.91)	87.75 (6.73)	1.45 (11.17)	0.646	0.638
IMT	83.75 (11.96)	86.77 (4.21)	3.02 (8.80)	0.182	
MMEF (%)					
Control	72.33 (23.05)	71.52 (15.02)	−0.81 (19.48)	0.959	0.461
IMT	76.59 (31.56)	83.13 (16.91)	6.54 (21.00)	0.091	
SpO_2					
Control	97.90 (1.10)	97.30 (1.70)	−0.60 (1.78)	0.305	0.247
IMT	97.09 (2.98)	98.18 (1.33)	1.09 (3.08)	0.368	
Modified Borg Scale					
Control	1.10 (0.32)	1.00 (0.00)	−0.10 (0.32)	0.317	0.773
IMT	1.45 (0.52)	1.55 (0.82)	0.09 (0.70)	0.655	
FAS					
Control	29.30 (7.42)	27.60 (8.04)	−1.70 (9.64)	0.475	0.198
IMT	29.73 (8.53)	26.73 (7.50)	−3.00 (6.88)	0.218	
Barthel Index					
Control	23.50 (16.34)	31.00 (19.12)	7.50 (8.25)	0.027†	0.044†
IMT	35.00 (21.10)	59.55 (18.09)	24.55 (22.30)	0.012†	

FAS = Fatigue Assessment Scale, FEV1 = forced expiratory volume in 1 second (expressed in liters and in % of theoretical value), FVC = forced vital capacity (expressed in liters and in % of theoretical value), IMT = inspiratory muscle training, MEP = maximal expiratory pressure, MIP = maximal inspiratory pressure, MMEF = maximum mid-expiratory flow (expressed in % of theoretical value), SD = standard deviation, SpO_2 = resting oxyhemoglobin saturation by pulse oximetry.

* Adjusted for FVC (% predicted) using linear regression analysis.

† $P < 0.05$.

‡ $P < 0.01$.

affected hemisphere, and no bilateral motor representation of each hemidiaphragm can result in respiratory dysfunction.[9,38] Another systematic review including 3 randomized controlled trials and 3 cross-sectional studies compared IMT with a control intervention in stroke patients, and the results showed that the stroke patients had improvement in MIP after the IMT program.[16]

In the present study, we included stroke patients who also had stable CHF, and all of the patients had inspiratory muscle weakness (inspiratory muscle strength less than 70% predicted MIP). We hypothesized that these patients would have a greater improvement in MIP compared to those with normal inspiratory muscle strength based on the results of a previous study.[17] In addition, we assumed that patients with respiratory muscle weakness, dyspnea, or dyspnea on exertion would have a greater motivation to receive IMT training. Furthermore, IMT has been suggested to be an alternative modality to treat CHF patients with more severe deconditioning.[40] These factors formed the rationale for the selection of these patients for the IMT program. The initial intensity of the IMT was 30% MIP, which was then increased weekly to achieve a target MIP at the patient's maximum load. The training intensity, frequency, and duration were similar to those used in other trials (5–6 d/wk for 6–12 weeks).[4,14,16,17,35,42]

It was difficult to recruit a sufficient number of patients for our IMT program, possibly because stroke patients with CHF were more likely to die or have morbidity than stroke patients without CHF,[41] a general lack of awareness of the IMT and pulmonary rehabilitation programs, and poor motivation. Boredom with IMT may also have discouraged the patients from training. No adverse events were noted throughout the whole IMT program.

4.1. Limitations

There are several limitations to this study. First, there was a significant difference in percent predicted FVC between the

groups at the beginning of the study. Although there were no significant differences in other baseline characteristics between the 2 groups, some discrepancies still existed. Therefore, we compared differences in the change from baseline of each outcome between groups using linear regression analysis with adjustments for baseline percent predicted FVC. Second, the sample size was small. Although we calculated the sample size with an estimated dropout rate of 30%, there was still considerable loss after randomization. Third, data on the 6-minute walk distance, an important cardiopulmonary index, were not reported because the walking distance could be biased by the functional status of stroke patients. Fourth, there is currently no consensus or recommendations about the training protocol of IMT programs in stroke patients with CHF. Our training program was based on the protocol of our previous study in patients with bronchiectasis,[21] and the training intensity, frequency, and duration seemed to be adequate to show the clinical effectiveness after the IMT, even the statistical power was low because of small sample size. Fifth, we did not use sham IMT intervention in the control group, which might cause performance bias. Despite sham intervention was used in some trials on IMT for CHF patients,[42–44] we did not use sham intervention in the present study because the patients could possibly differentiate the sham intervention from the true IMT intervention. In fact, blinding is generally regarded as being difficult to carry out in trials assessing nonpharmacological treatments.[45] Future studies should address how to deal with this methodological challenge. Finally, the follow-up duration in previous IMT trials ranged from 4 to 12 weeks,[16,17] and no long-term follow-up results have been published. Further studies with larger sample size and longer duration are warranted to investigate the long-term efficacy among these patients.

4.2. Future research

As discussed, it was difficult to recruit eligible subjects for this study, and only half of those recruited were able to continuously perform or tolerate the training programs (either IMT plus conventional stroke rehabilitation or conventional stroke rehabilitation only) and complete the whole training course. This may be explained by the relatively weak study population and poor compliance. It is well known that stroke patients with CHF have poorer fitness and more complications, which often deters the patients from training. In addition, over 30% of the patients in our study complained of fatigue and boredom during the training program, which consequently led to poor compliance. Therefore, appropriate selection of participants and methods to improve compliance (such as virtual reality for stroke rehabilitation) should be considered in future studies.

5. Conclusion

In addition to conventional stroke rehabilitation, our results suggest that stroke patients with stable CHF can benefit from a 10-week IMT with regard to inspiratory strength and activities of daily living.

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