Respiratory muscle training in stroke patients with respiratory muscle weakness, dysphagia, and dysarthria – a prospective randomized trial

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Abstract

Objective: To examine the efficacy of combined inspiratory and expiratory respiratory muscle training (RMT) with respect to the swallowing function, pulmonary function, and dysarthria in patients with stroke.

Design: Prospective, randomized controlled trial.

Setting: Tertiary hospital.

Participants: The trial included 21 subjects (12 men, 9 women) aged 35 to 80 years presenting with 6 months' history of unilateral stroke. Respiratory muscle weakness (≥70% predicted maximal inspiratory pressure (MIP) and/or ≤70% predicted maximal expiratory pressure (MEP)), dysphagia, or dysarthria. These subjects were randomly assigned to the control (n = 10, rehabilitation) and experimental (n = 11, rehabilitation with RMT) groups.

Intervention: Inspiratory RMT starting from 30% to 60% of MIP and expiratory RMT starting from 15% to 75% of MEP for 5 days/week for 6 weeks.

Main outcome measures: MIP, MEP, pulmonary function, peak cough flow, perception of dyspnea, Fatigue Assessment Scale, Modified Rankin Scale, Brunststrom stage, Barthel index, Functional Oral Intake Scale (FOIS), and parameters of voice analysis.

Results: Significant differences were observed between both groups in terms of MIP, forced vital capacity (FVC), and forced expiratory volume per second (FEV1) of the percentage predicted. Significant difference was found with respect to the change in fatigue, shimmer percent, amplitude perturbation quotient, and voice turbulence index (VTI) according to the acoustic analysis in the RMT group. The FEV1/FVC ratio was negatively correlated with jitter percent, average relative perturbation, pitch perturbation quotient, and VTI; the maximum mid-expiratory flow (MMEF) and MMEF% were also negatively correlated with VTI. Significant differences among participants of the same group were observed while comparing the Brunnstrom stage before and after training of the affected limbs and the Barthel scale and FOIS scores in both the groups.

Conclusions: Altogether, 6-week combined inspiratory and expiratory RMT is feasible as adjuvant therapy for stroke patients to improve fatigue level, respiratory muscle strength, lung volume, dyspnea, and dysarthria.

Clinical trial registration number (Clinical Trial Identifier): NCT03491111.

Abbreviations: APQ = amplitude perturbation quotient, ERMT = expiratory respiratory muscle training, FAS = fatigue assessment scale, FEV1 = forced expiratory volume in first second, FOIS = functional oral intake scale, FVC = forced vital capacity, IPRT = inspiratory respiratory muscle training, Jtt = jitter percent, MEP = maximal expiratory pressure, MMEF = maximum mid-expiratory flow, MRS = Modified Rankin scale, PPQ = pitch perturbation quotient, RAP = relative

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The devices used are as follows: Model 4500 (Multi-Dimensional Voice) for Dimensional Voice Program, Model 5105 (KayPENTAX), Computerized Speech Lab (CSL), Dolphin Breathing Trainer (a threshold trainer), DT 11 GaleMed Corporation, DT 14 GaleMed Corporation. Product number: P009000038.

Pulmonary function tests: spirometer (Vitalograph, Serial Spirotrac, Buckingham, USA).

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1. Introduction

Stroke patients often experience respiratory muscle weakness, swallowing disturbances,[1–3] decreased peak expiratory flow, blunted reflexive cough, impaired voluntary cough,[4] impairment of the cardiorespiratory fitness,[5] and voice dysfunction in dysarthria.[6]

An 8-week inspiratory muscle training (IMT) can increase the inspiratory muscle strength and endurance in chronic stroke patients with > 90% of predicted maximal inspiratory pressure (MIP),[7] while a 6-week IMT can increase the forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), vital capacity, force expiratory flow rate 25% to 75%, and maximal voluntary ventilation in patients with unilateral stroke during the 12 months; this finding was also correlated with the exercise capacity, sensation of dyspnea, and quality of life.[8] Expiratory muscle training (EMT) can improve the MIP and peak expiratory flow rate in stroke patients[9] and improve the voice aerodynamics,[9] MEP, and swallowing ability, in acute stroke patients along with reducing vallecular residue and penetration-aspiration.[10]

Messaggi-Sartor et al reported that 3-week IMT of patients with 30% MIP and EMT of patients with 30% MEP could improve the inspiratory and expiratory muscle strength and potentially reduce the occurrence of respiratory complications at 6 months after the onset of acute stroke.[11] Furthermore, Guilien-Sola et al reported that 3-week inspiratory/expiratory muscle training could improve inspiratory and expiratory muscle strength and swallowing function.[12] However, the efficacy of combined IMT and EMT in subacute stroke patients (within 6 months) with respiratory muscle weakness, swallowing disturbance, and dysarthria has not been reported.

Respiration and swallowing require the activation of common anatomical structures. EMT can facilitate the contraction of submental muscles, elevate the hyolaryngeal complex,[12–13] pull the hyoid bone in the anterior-superior direction, and invert the epiglottis towards the pharynx during swallowing.[14–16] Dysarthria (including wet voice) and dysphagia have similar pathogenesis in stroke patients, especially those related to the laryngopharyngeal functions.[17] The acoustic change in phonation following a swallow is a high-risk indicator of fluid aspiration.[18] Moreover, the subglottal pressure initiates and maintains the vocal fold vibration that facilitates voice production.

Five-week EMT followed by 6 sessions of traditional voice therapy increased the subglottal pressure leading to a higher vocal intensity and increased voice dynamic range in professional voice users.[19] Meanwhile, a multi-dimensional voice program (MDVP) is suitable for voice analysis in dysarthria associated with various neurologic diseases of different severity.[6] and the MDVP Model 5105 (KayPENTAX) is reliable and advanced for speech analysis and acquisition.[19]

We hypothesized that the repetitive resistance, pressure, and force generated by threshold RMT could improve the respiratory muscle strength, swallowing function, and voice quality via sensory stimulation and motor activation of the oropharynx and respiratory muscles. RMT can also assist in the upregulation of reflex cough.[20] To our knowledge, this is the first follow-up study that investigated the feasibility and efficacy of a combined IMT and EMT with respect to pulmonary dysfunction, swallowing dysfunction, voice dysfunction due to dysarthria, and activities of daily living of subacute stroke patients.

2. Methods

2.1. Participants and setting

This prospective, single-blinded, randomized controlled study was conducted in a tertiary hospital from April 2016 to October 2018 with 47 unilateral stroke patients aged 35 to 80 years with respiratory muscle weakness, swallowing disturbance, or dysarthria for 6 months. The patients were screened by attending physicians and randomly divided into the control (conventional rehabilitation) and experimental (rehabilitation with RMT) groups by a research assistant using a random number generator algorithm. Signed informed consent from the patients or a family member was obtained, and the Institutional Review Board approved the study.

Sixteen subjects declined to participate, not meeting the inclusion criteria regarding inspiratory and expiratory muscle weakness (≥70% predicted MIP and/or ≤ predicted MEP),[20,21] In addition, patients with increased intracranial pressure, uncontrolled hypertension, uncompensated heart failure, unstable angina, recent myocardial infarction, complicated arrhythmias, pneumothorax, bullae/blebs in the preceding 3 months, severe cognitive function or infection, recurrent stroke, brain stem stroke, and aphasia were excluded.

Each patient underwent physical and neurological examination, and assessment of clinical characteristics, height, weight, body mass index, duration of stroke, Modified Rankin scale (MRS), Brunnstrom stage, hand grip of unaffected upper limb, Barthel activity of daily living index, spirometry, peak cough flow, MIP, MEP, resting heart rate, perception of dyspnea using modified Borg scale,[22] resting oxyhemoglobin saturation, fatigue assessment scale (FAS),[23] functional oral intake scale (FOIS),[24] and voice quality.[18] These parameters were recorded before and after the 6-week RMT. The technician was blinded to the group allocation.

2.2. Intervention

Patients were trained using the Dofin Breathing Trainer (DT 11 or DT 14 GaleMed Corporation), a hand-held threshold trainer with a spring-loaded valve and a colored ball that indicates whether breathing strength exceeds the set target pressure. Ten training levels were set for IMT and EMT. The DT11 has a pressure range of 5 to 39 cmH₂O during inspiration and 4 to 33 cmH₂O during expiration, while DT14 has a pressure range of 5 to 79 cmH₂O during inspiration and 4 to 82 cmH₂O during expiration.

average perturbation, $RMT = \text{respiratory muscle training}, \text{ShdB = shimmer in dB, Shim = shimmer percent, VTI = voice turbulence index.}$

**Keywords:** stroke, dysphagia, respiratory muscular training, acoustic analysis, functional performance
For IMT, the subjects were instructed to tightly seal their lips around the breathing trainer with a nose clip in a sitting position, and inhale deep and forceful breaths that were sufficient for opening the valve with a whistling sound (due to the movement of the colored ball inside the trainer). Then, they were instructed to exhale slowly and gently through the mouthpiece. The inspiratory training pressure ranged from 30% to 60% of each individual’s MIP for 6 sets of 5 repetitions. For EMT, the subjects were instructed to blow fast and forcefully which could open the valve following maximal inhalation. Expiration training pressure commenced from 15% to 75% of threshold load of an individual’s MEP for 5 sets of 5 repetitions, 1 to 2 times per day, 5 days a week for 6 weeks\(^2\), 1 to 2 minutes of rest was allowed between each set.

The training resistance was adjusted according to tolerance. We requested the patients to stop if they experienced discomfort and, in case of desaturation, the threshold load was decreased. The patients were called once a week for checking their compliance with the program and were encouraged to continue with it. A training diary was provided for them to keep a record.

In addition to RMT, both the groups underwent the regular rehabilitation, which included postural training, breathing control, improving cough technique, checking chest wall mobility, fatigue management, orofacial exercises, thermal-tactile stimulation, Mendelsohn maneuvering, effort swallowing, mobility, fatigue management, orofacial exercises, thermal-tactile stimulation, Mendelsohn maneuvering, effort swallowing, or supra-glottic maneuver among others.

### 2.3. Main outcome measurement

The primary outcome variables were: change in MIP (cmH2O) and MEP (cmH2O). For MIP, negative pressure is favorable and for MEP, positive pressure is favorable. The secondary outcome variables were the pulmonary functional parameters including FVC (liter), FVC (% prediction), FEV1 (liter), FEV1 (% of prediction), FEV1/FVC (%), maximum mid-expiratory flow (MMEF) (liter/s), MMEF%, peak cough flow (liter/s), resting heart rate, resting respiratory rate, FOIS [7-point scale, from 1 (nothing by mouth) to 7 (total oral diet with no restrictions)]\(^{[24]}\), Modified Borg scale (0.5 to 10)\(^{[22]}\), FAS (10-item, 5 levels (1: never to 5: always), score: 10 to 50)\(^{[23]}\), non-affected hand grip strength, Barthel index (0 to 100)\(^{[27]}\), MRS (5: severe disability to 0: no symptoms)\(^{[28]}\), and the variables of acoustic analysis.

**Pulmonary function test:** Pulmonary function was assessed using a spirometer (Vitalograph, Serial Spirotrac, Buckingham, VA) as per the American Thoracic Society standards.\(^{[29]}\) **MIP and MEP:** MIP was measured after maximal expiration near residual volume. MEP was measured after maximal inspiration near total lung capacity while patients were sitting and wearing a nose-clip in an upright position. All pressure measurements were maintained for at least 1 second. The highest recorded value was used for calculations only when two technically satisfactory measurements were obtained.\(^{[30,31]}\)

**Voice quality analysis:** Voice quality was assessed with the Computerized Speech Lab (CSL), Model 4500 (Multi-Dimensional Voice). The participant was asked to phonate the vowel ‘a’ at their most comfortable speaking pitch and loudness for at least 3 seconds while sitting at a 30 cm distance from the microphone. The lowest pitch and highest pitch with increasing and decreasing loudness were measured.\(^{[32]}\) The parameters of voice analysis included jitter percent (Jitt), relative average perturbation (RAP), and pitch perturbation quotient (PPQ) for frequency perturbation. Amplitude was determined based on the shimmer in decibels (ShdB), shimmer percent (Shim), amplitude perturbation quotient (APQ), and peak-to-peak amplitude variation, while the noise-related parameters included noise-to-harmonic ratio and voice turbulence index (VTI).\(^{[6]}\)

### 2.4. Sample size calculation

Based on the study by Subeyaz et al.\(^{[8]}\), the mean differences of MIP between experimental group and control group before and after training were fixed at 7.87 cmH2O and 2.90 cmH2O, respectively, with standard deviation of 6.6 cmH2O and 1.9 cmH2O. After calculation, we realized that the study required at least 17 subjects in each group. While setting these conditions at a two-sided significance level at 0.05 with a statistical power of 0.80, the number of subjects in each group should be 24 under the estimation that the dropout rate was about 30%. Number of participants in the RMT group to that in the control group was set at 1:1 ratio.

### 2.5. Data analysis

Values were expressed as the mean ± standard deviation for continuous variables and number (%) for categorical variables. Linear regression analysis was used to adjust for sex, BMI, and the Brunnstrom stage of the distal part of the affected upper limb. Clinical characteristics were compared using the Mann–Whitney U test for continuous variables and the Fisher exact test for categorical variables. The Wilcoxon signed-rank test was used to examine the change in clinical data from baseline in both the groups, and the Mann-Whitney U test was applied for comparisons between the groups. The Spearman rank correlation coefficient was calculated to analyze the correlations between cardiopulmonary function parameters and clinical characteristics. All collected data were analyzed using the SPSS Statistics version 22.0 software (IBM, Armonk, NY). P value < 0.05 was considered statistically significant.

### 3. Results

A total of 47 patients were determined to be eligible initially. After exclusion of 16 patients, 31 were randomly allocated to the RMT (15 patients) and control (16 patients) groups. During training, 10 patients (32.2%) dropped out of the study, 5 from the RMT group (reasons being: they lived far away from the training venue, insisted to stay at home or in the nursing home, and had impaired vision in one eye and upper gastrointestinal bleeding) and 5 from the control group (reasons being: 4 patients did not undergo follow-up at the outpatient department and 1 patient had another disease). Finally, 21 patients completed the study (RMT group, n = 10; control group, n = 11) (Fig. 1). The Intention-To-Treat and Per Protocol analysis for all the data is shown in Tables 1 and 2.

No statistically significant difference between the groups was noted in the clinical characteristics, cardiopulmonary function, and acoustic analysis parameters (Tables 1–3), except sex (P = 0.36), height (training vs control group: 1.58 ± 0.08 vs 1.68 ± 0.08 cm, P = 0.011), body mass index (BMI) (26.0 ± 3.7 vs 21.82 ± 2.29, P = 0.011 kg/m\(^2\)) (Table 1), and Brunnstrom stage of the distal part of affected upper extremity (3.10 ± 0.75 vs 2.29 ± 2.29, P = 0.011) (Table 2).

Significant correlations were found between MIP and MEP (r = 0.632, P < 0.01); peak cough and MEP (r = 0.504, P < 0.05), FVC...
Significant differences within each group were noted for the change from baseline of the Brunnstrom stage of the affected upper and lower limbs, Barthel scale, and FOIS. However, no significant difference between the groups was observed (Table 5). Significant change from the baseline was seen in fatigue (P = .007) (Table 5), MIP (P = .008) only in the RMT group, and significant between-group differences were seen for MIP (P = .001), FVC (P = .017), and FEV1 (% predicted) (P = .047) according to the linear regression analysis adjusted for the differences already present between the groups in terms of sex, BMI, and Brunnstrom stage of the distal part of affected limb (Table 6).

Regarding voice analysis, there were significant changes among participants of the RMT group in the Shim (P = .043), APQ (P = .036), and VTI (P = .025) values (Table 7). Significant negative correlations were found between FEV1/FVC and Jitt (r = −0.574, P < .05), RAP (r = −0.574, P < .05), PPQ (r = −0.538, P < .05), and VTI (r = −0.835, P < .01). MMEF (r = −0.659, P < .05) and MMEF% (r = −0.692, P < .05) were negatively correlated with VTI (Table 8).

4. Discussion
Both RMT and control groups showed significant changes from the baseline in Brunnstrom stage of the affected limb, Barthel index, and FOIS; the stroke duration positively correlated with FVC and FEV1 (% prediction) and negatively correlated with FEV1/FVC%. These findings can be partially explained by neurologic recovery with time and the effectiveness of regular rehabilitation after stroke onset.
Values were expressed as mean (SD) for continuous variables and number (%) for categorical variables. Mann–Whitney U test for continuous variables and Fisher exact test for categorical variables. (∗P < 0.05, ∗∗P < 0.01). BMI = body mass index.

Table 2

Functional and pulmonary baselines of patients in the training and control groups.

| Intention to treat analysis | Per protocol analysis |
|-----------------------------|-----------------------|
| Total (n = 31) | Training (n = 15) | Control (n = 16) | P value | Total (n = 21) | Training (n = 10) | Control (n = 11) | P value |
| Brunstrom stage | | | | | | | |
| Upper extremity | | | | | | | |
| Proximal part | 2.77 (1.06) | 3.13 (1.30) | 2.44 (1.63) | .066 | 2.81 (0.98) | 3.10 (1.20) | 2.55 (0.68) | .304 |
| Distal part | 2.65 (1.05) | 3.13 (1.19) | 2.19 (1.66) | .010* | 2.62 (0.97) | 3.10 (0.99) | 2.18 (0.75) | .021* |
| Lower extremity | 3.29 (0.90) | 3.60 (0.99) | 3.00 (0.73) | .003** | 3.14 (0.85) | 3.40 (0.97) | 2.91 (0.70) | .204 |
| Barthel index | 27.26 (18.97) | 27.33 (18.98) | 27.19 (19.58) | .983 | 26.43 (16.29) | 25.00 (15.09) | 27.73 (17.94) | .859 |
| FOIS | 4.00 (2.48) | 4.40 (2.50) | 3.63 (2.47) | .393 | 4.29 (2.43) | 4.30 (2.45) | 4.27 (2.53) | .884 |
| MRS | 4.26 (0.78) | 4.33 (0.90) | 4.19 (0.60) | .608 | 4.33 (0.60) | 4.50 (0.71) | 4.18 (0.60) | .212 |
| Hand grip of unaffected side (kg) | 24.70 (10.03) | 22.51 (10.16) | 26.75 (9.77) | .246 | 22.56 (9.47) | 19.90 (10.09) | 24.97 (8.61) | .217 |
| FAS | 23.90 (6.40) | 24.87 (6.08) | 23.00 (7.66) | .427 | 24.19 (6.37) | 24.30 (5.70) | 24.09 (6.81) | .915 |
| Resting heart rate | 84.70 (14.56) | 79.89 (14.31) | 88.88 (14.02) | .093 | 84.15 (13.35) | 80.00 (10.79) | 87.55 (14.75) | .287 |
| Peak cough | 257.24 (108.89) | 246.15 (102.99) | 266.25 (115.98) | .630 | 271.05 (103.92) | 268.75 (112.31) | 272.73 (102.97) | .901 |
| SpO2 at rest (%) | 97.45 (1.26) | 97.80 (1.32) | 97.13 (1.15) | .139 | 97.38 (1.16) | 97.50 (1.18) | 97.27 (1.19) | .715 |
| Borg scale | 0.50 (0.43) | 0.63 (0.52) | 0.38 (0.29) | .094 | 0.55 (0.44) | 0.65 (0.58) | 0.45 (0.27) | .466 |
| MIP (cm H2O) | 47.29 (20.67) | 38.40 (16.16) | 55.63 (32.04) | .089 | 44.57 (22.29) | 35.60 (17.33) | 52.73 (23.70) | .081 |
| MEP (cm H2O) | 50.45 (18.28) | 45.60 (16.36) | 55.00 (19.32) | .154 | 49.71 (18.21) | 44.40 (17.07) | 54.55 (18.64) | .157 |
| Pulmonary function test | | | | | | | |
| FVC (liter) | 2.23 (0.84) | 2.01 (0.76) | 2.47 (0.89) | .142 | 2.03 (0.69) | 1.83 (0.64) | 2.26 (0.71) | .327 |
| FVC (% predicted) | 67.42 (21.12) | 70.85 (24.53) | 63.75 (16.88) | .375 | 68.11 (20.31) | 74.22 (24.99) | 61.31 (11.23) | .270 |
| FEV1 (liter) | 1.90 (0.73) | 1.69 (0.59) | 2.13 (0.83) | .108 | 1.76 (0.61) | 1.58 (0.54) | 1.96 (0.66) | .288 |
| FEV1 (% predicted) | 71.88 (21.34) | 74.77 (24.47) | 68.79 (17.79) | .461 | 73.05 (20.68) | 79.08 (25.90) | 66.36 (10.57) | .391 |
| FEV1/FVC (%) | 86.60 (8.59) | 86.83 (9.93) | 86.67 (9.55) | .968 | 86.82 (9.80) | 87.11 (9.79) | 86.40 (10.63) | .775 |
| MMEF (liter/sec) | 2.50 (1.29) | 2.31 (1.10) | 2.69 (1.49) | .436 | 2.23 (1.00) | 1.98 (0.71) | 2.51 (1.23) | .165 |
| MMEF (%) | 74.60 (29.88) | 70.11 (21.87) | 79.10 (36.51) | .438 | 72.93 (28.88) | 71.10 (26.81) | 74.77 (32.35) | .691 |

Mann–Whitney U Test (∗P < 0.05, ∗∗P < 0.01). FAS = fatigue assessment scale. FEV1 = forced expiratory volume in first second. FOIS = Functional oral intake scale. FVC = forced vital capacity (expressed in liters) and in % of theoretical value. MEP = maximal expiratory pressure. MIP = maximal inspiratory pressure. MMEF = maximum mid-expiratory flow. MRS = modified Rankin scale. SpO2 = oxygen saturation by pulse oximetry.

Significant changes in MIP, MEP, and fatigue level from baseline were observed only in the RMT group. However, the linear regression analysis, adjusted for between-group differences in sex, BMI, and Brunstrom stage of the affected limb, demonstrated significant between-group differences in the change from baseline in mean MIP, FVC, and FEV1 (% predicted).
Table 3
Data of Multi-Dimensional Voice report in the training and control groups.

|                  | Unit         | Training          | Non-training       | T-Test P value between training and non-training |
|------------------|--------------|-------------------|--------------------|-----------------------------------------------|
| Jitter Percent   | %            | 2.59 (1.56)       | 2.40 (2.81)        | .973                                          |
| Shimmer in dB    | dB           | 0.92 (0.62)       | 0.61 (0.55)        | .435                                          |
| Shimmer Percent  | %            | 10.06 (7.18)      | 6.41 (5.45)        | .378                                          |
| Relative Average | %            | 1.52 (0.93)       | 3.99 (1.84)        | .934                                          |
| Pitch Perturbation Quotient (PPQ) | % | 1.54 (1.05) | 1.50 (1.84) | .967 |
| Amplitude Perturbation Quotient (APQ) | % | 7.62 (5.80) | 5.19 (4.07) | .499 |
| Peak-to-peak Amplitude Variation (vAm) | % | 23.32 (6.18) | 23.21 (6.94) | .763 |
| Voice Turbulence Index (VTI) | % | 0.27 (0.70) | 0.23 (0.16) | .696 |

Mann-Whitney U Test. (*P < .05, **P < .01).

Table 4
Relationships between cardiopulmonary function and clinical characteristics.

| Predictors | MIP (cmH2O) | MEP (cmH2O) | FVC (litre) | FVC (%predicted) | FEV1 (litre) | FEV1 (%predicted) | FEV1/FVC (%) | MMFE | MMFE (%) |
|------------|-------------|-------------|-------------|------------------|--------------|-------------------|---------------|------|---------|
| Age        | -.270       | -.052       | -.538*      | -.301            | -.590**      | -.384             | -.206         | -.584** | -.292    |
| Stroke Duration (months) | -.044 | .104 | .438 | .594** | .256 | .458* | -.456** | -.219 | -.162   |
| Barthel index | .250 | .165 | -.001 | .030 | -.176 | -.152 | -.179 | -.233 | -.353   |
| FOIS       | -.158       | .077        | -.084       | .142             | -.019        | .140              | -.082         | -.067  | .000     |
| MRS        | -.245       | -.088       | -.229       | -.360            | -.173        | -.374             | -.107         | -.200  | -.286    |
| FAS        | -.314       | -.422       | -.115       | .156             | -.276        | -.116             | -.272         | -.362  | -.348    |
| Borg Scale | -.216       | -.505**      | -.437       | -.128            | -.274        | .023              | .245          | -.142  | .024     |
| Resting heart rate | .336 | -.060       | .047        | -.038            | .328         | .251              | .411          | .457   | .528*    |
| Peak cough flow | .358 | .504*       | .781***     | .196             | .739**       | .214              | .043          | .466   | .213     |
| MP         | 1.000       | .832**       | .348        | .091             | .407         | .255              | .200          | .386   | .277     |
| MEP        | .832**      | 1.500       | .419        | .000             | .346         | .038              | -.043         | .246   | .130     |

Spearman correlation (*P < .05, **P < .01).
FAI = fatigue assessment scale, FOIS = functional oral intake scale, MEP = maximal expiratory pressure, MP = maximal inspiratory pressure, MRS = modified Rankin scale, SpO2 = oxyhemoglobin saturation by pulse oximetry.

Table 5
Clinical data before and after the 6-week study in the training and control groups.

|                     | Baseline Mean (SD) | Post 6-week Mean (SD) | Change from baseline Mean (SD) | P value for change from baseline | P for change between groups | P for change between groups (linear regression) |
|---------------------|--------------------|-----------------------|-------------------------------|---------------------------------|-----------------------------|---------------------------------------------|
| Clinical data       |                    |                       |                               |                                 |                             |                                             |
| Brunstrom stage     |                    |                       |                               |                                 |                             |                                             |
| Upper extremity     |                    |                       |                               |                                 |                             |                                             |
| Proximal part       | 3.10 (1.29)        | 3.80 (1.23)           | 0.70 (0.83)                   | .038*                           | .878                        | .252                                        |
| Control             | 2.55 (0.69)        | 3.09 (0.70)           | 0.55 (0.68)                   | .034*                           |                             |                                             |
| Distal part         | 3.10 (0.99)        | 3.90 (1.20)           | 0.80 (0.79)                   | .023*                           | .878                        | .118                                        |
| Control             | 2.18 (0.73)        | 2.91 (0.70)           | 0.73 (0.65)                   | .011*                           |                             |                                             |
| Lower extremity     | 3.40 (0.97)        | 4.30 (0.82)           | 0.90 (0.99)                   | .024*                           | .537                        | .198                                        |
| Control             | 2.91 (0.70)        | 3.91 (0.30)           | 1.00 (0.63)                   | .005*                           |                             |                                             |
| Barthel index       | 25.00 (15.09)      | 41.00 (14.87)         | 16.00 (19.41)                 | .049*                           | .831                        | .628                                        |
| FOIS                | 27.73 (17.84)      | 43.18 (19.01)         | 15.45 (18.90)                 | .026*                           |                             |                                             |
| Training            | 4.30 (2.45)        | 6.50 (0.85)           | 2.20 (2.20)                   | .027*                           | .971                        | .586                                        |
| Control             | 4.27 (2.53)        | 6.45 (0.93)           | 2.18 (2.44)                   | .020*                           |                             |                                             |
| MRS                 | 4.50 (0.71)        | 4.20 (0.42)           | -.30 (0.95)                   | .317                            | .612                        | .145                                        |
| Hand grip of unaffected side | 4.18 (0.68) | 4.00 (1.78) | -.18 (0.87 | .480 | |
| Training            | 19.90 (10.09)      | 20.30 (8.78)          | 0.40 (4.20)                   | .514                            | .359                        | .347                                        |
| Control             | 24.97 (8.61)       | 26.30 (6.74)          | 1.33 (4.94)                   | .050                            |                             |                                             |
| FAS                 | 24.30 (5.70)       | 18.20 (3.46)          | -.61 (3.96)                   | .007**                          | .215                        | .495                                        |
| Control             | 24.09 (7.20)       | 26.64 (4.92)          | -.34 (6.31)                   | .093                            |                             |                                             |

Wilcoxon Signed-Ranks Test, Mann-Whitney U Test. (*P < .05, **P < .01).
FAI = fatigue assessment scale, FOIS = functional oral intake scale, MRS = modified Rankin scale.
Furthermore, a significant mean change from baseline of MEP was found only in the RMT group. The mean MEP positively correlated with FVC and FEV1; MEP also negatively correlated with the Borg scale. These findings indicate that the 6-week combined RMT could improve the respiratory muscle strength patients.

Clinically, the discoordination between inhaling and exhaling should be resolved at the beginning of RMT and the active inspiratory volume needs to be enough for forceful expiration or cough flow. This explains why a significant between-group difference was seen only in MIP and not in MEP or peak cough as a 6-week program may be too short to achieve a significant effect on expiratory muscle force. This finding was consistent with results of a systemic review, which showed that RMT shows greater improvement in MIP, but has no effect on MEP in patients with various neurologic disorders.[32] Further, 5-week EMT for ischemic stroke patients increases the average expiratory muscle force. This finding was consistent with results of a systemic review, which showed that RMT shows greater improvement in MIP, but has no effect on MEP in patients with various neurologic disorders.[32] Furthermore, a 4-week RMT by using threshold resistance device in acute stroke patients significantly improved the mean MIP by 14 cmH2O, MEP by 15 cmH2O, and the peak expiratory flow rate (74 L/min) of all three groups, regardless of the allocation of expiratory, inspiratory, or sham training; but no between-group differences was noted.[33] Similarly, our study showed no significant between-group difference in MEP and peak cough flow. Furthermore, our study also revealed no difference between both groups in terms of MRS, hand grip strength, and FOIS.

### Table 6

Data changes in cardiopulmonary function before and after the 6-week study in the training and control groups.

|                          | Baseline | Post 6-week | Change from baseline | P value for change from Baseline | P for change between groups | P for change between groups (linear regression) |
|--------------------------|----------|-------------|----------------------|----------------------------------|----------------------------|---------------------------------------------|
| Resting heart rate       |          |             |                      |                                  |                            |                                            |
| Training                 | 83.00 (9.88) | 82.43 (13.70) | 0.57 (10.49)        | 1.000                           | .171                       | .676                                        |
| Control                  | 88.90 (14.81) | 79.70 (15.41) | 9.20 (19.67)        | .074                            |                            |                                            |
| Peak cough               |          |             |                      |                                  |                            |                                            |
| Training                 | 278.57 (17.53) | 305.71 (102.45) | 27.14 (54.69)       | .236                            | .845                       | .570                                        |
| Control                  | 290.00 (90.19) | 337.00 (83.14) | 47.00 (85.38)       | .123                            |                            |                                            |
| SpO2_Rest (%)           |          |             |                      |                                  |                            |                                            |
| Training                 | 97.50 (1.18) | 97.50 (1.65) | 0.00 (1.94)         | 1.000                           | .500                       | .836                                        |
| Control                  | 97.27 (1.19) | 97.82 (0.87) | 0.55 (0.95)         | .084                            |                            |                                            |
| Borg scale               |          |             |                      |                                  |                            |                                            |
| Training                 | 0.65 (0.58) | 0.70 (0.75) | 0.05 (0.55)         | .783                            | .114                       | .317                                        |
| Control                  | 0.46 (0.27) | 0.23 (0.26) | 0.23 (0.26)         | .025                            |                            |                                            |
| MIP (cm H2O)            |          |             |                      |                                  |                            |                                            |
| Training                 | 35.60 (17.33) | 81.50 (41.64) | 45.90 (29.31)       | .005**                          | .008**                     | .001**                                      |
| Control                  | 52.73 (23.70) | 58.18 (24.42) | 5.45 (20.18)        | .366                            |                            |                                            |
| MEP (cm H2O)            |          |             |                      |                                  |                            |                                            |
| Training                 | 44.40 (17.07) | 71.00 (26.44) | 26.60 (26.92)       | .017*                           | .227                       | .256                                        |
| Control                  | 54.55 (18.64) | 68.18 (16.01) | 13.64 (24.61)       | .093                            |                            |                                            |
| FVC (liter)             |          |             |                      |                                  |                            |                                            |
| Training                 | 1.98 (0.58) | 2.21 (0.91) | 0.24 (0.47)         | .575                            | .793                       | .017**                                      |
| Control                  | 2.33 (0.73) | 2.50 (0.77) | 0.18 (0.25)         | .093                            |                            |                                            |
| FVC (% pred)            |          |             |                      |                                  |                            |                                            |
| Training                 | 79.93 (24.61) | 81.55 (21.36) | 1.63 (17.61)        | .889                            | .529                       | .105                                        |
| Control                  | 63.26 (10.24) | 68.40 (0.77) | 5.14 (50)           | .069                            |                            |                                            |
| FEV1 (liter)            |          |             |                      |                                  |                            |                                            |
| Training                 | 1.66 (0.85) | 1.73 (0.47) | 0.07 (0.79)         | .944                            | .753                       | .569                                        |
| Control                  | 2.00 (0.69) | 1.97 (0.74) | 0.03 (0.25)         | .889                            |                            |                                            |
| FEV1 (% pred)           |          |             |                      |                                  |                            |                                            |
| Training                 | 85.49 (25.06) | 87.20 (20.25) | 1.71 (16.79)        | 1.000                           | 1.000                      | .047**                                      |
| Control                  | 67.86 (10.21) | 67.55 (15.37) | 0.31 (10.59)        | .889                            |                            |                                            |
| FVC/FEV1 (%)            |          |             |                      |                                  |                            |                                            |
| Training                 | 88.46 (7.37) | 88.40 (7.74) | 0.06 (4.45)         | .889                            | .345                       | .995                                        |
| Control                  | 85.42 (10.82) | 80.94 (16.73) | 4.48 (8.55)         | .161                            |                            |                                            |
| MMEF (liter/s)          |          |             |                      |                                  |                            |                                            |
| Training                 | 2.14 (0.59) | 2.25 (0.64) | 0.11 (0.43)         | .327                            | .270                       | .076                                        |
| Control                  | 2.48 (1.31) | 2.35 (1.86) | 0.13 (0.96)         | .674                            |                            |                                            |
| MMEF (%)                |          |             |                      |                                  |                            |                                            |
| Training                 | 77.00 (21.53) | 81.54 (16.33) | 4.54 (18.01)        | .263                            | .294                       | .082                                        |
| Control                  | 74.09 (54.51) | 71.71 (54.39) | 2.38 (31.69)        | .674                            |                            |                                            |

Wilcoxon Signed-Ranks Test, Mann-Whitney U Test. Adjusted for sex, BMI and Brunntrom stage of distal part of affected upper limb by using linear regression analysis. (*P<.05, **P<.01).

FEV1 = forced expiratory volume in first second, FVC = forced vital capacity (expressed in liters and in % of theoretical value), MEP = maximal expiratory pressure, MIP = maximal inspiratory pressure, MMEF = maximum mid-expiratory flow, SpO2 = oxyhemoglobin saturation by pulse oximetry.
Table 7
Data of Multi-Dimensional Voice report before and after the 6-week study in the training and non-training groups.

|                          | Baseline Mean (SD) | Post 6-week Mean (SD) | Change from baseline Mean (SD) | P value for change from Baseline | P for change between groups |
|--------------------------|--------------------|-----------------------|-------------------------------|---------------------------------|-----------------------------|
| Jitter Percent (Jitt)    | Training 2.59 (1.56) | 2.30 (1.63)           | −0.29 (0.61)                  | 0.296                           | 0.101                       |
|                          | Non-training 2.40 (2.81) | 1.65 (2.22)           | −0.75 (1.04)                  | 0.104                           |                             |
| Shimmer in dB (Shdb)     | Training 0.92 (0.62)  | 0.79 (0.65)           | −0.13 (0.14)                  | 0.075                           | 0.101                       |
|                          | Non-training 0.61 (0.55) | 0.48 (0.32)           | −0.14 (0.42)                  | 0.427                           |                             |
| Shimmer Percent (Shim)   | Training 10.06 (7.18) | 8.46 (6.65)           | −1.60 (1.45)                  | 0.043*                          | 0.116                       |
|                          | Non-training 6.41 (5.45) | 5.10 (3.23)           | −1.31 (4.37)                  | 0.458                           |                             |
| Relative Average Perturbation (RAP) | Training 1.52 (0.93) | 1.38 (0.97)           | −0.14 (0.33)                  | 0.332                           | 0.087                       |
|                          | Non-training 1.39 (1.64) | 0.93 (1.28)           | −0.46 (0.60)                  | 0.091                           |                             |
| Pitch Perturbation Quotient (PPQ) | Training 1.54 (1.05) | 1.53 (1.17)           | −0.01 (0.27)                  | 0.974                           | 0.272                       |
|                          | Non-training 1.50 (1.84) | 0.99 (1.45)           | −0.51 (0.72)                  | 0.109                           |                             |
| Amplitude Perturbation Quotient (APQ) | Training 7.62 (5.80) | 6.55 (5.50)           | −1.07 (0.92)                  | 0.036*                          | 0.087                       |
|                          | Non-training 5.19 (4.07) | 3.96 (2.11)           | −1.23 (3.35)                  | 0.368                           |                             |
| Peak-to-peak Amplitude Variation (vAm) | Training 23.32 (6.18) | 21.74 (7.51)          | −1.58 (7.68)                  | 0.636                           | 0.133                       |
|                          | Non-training 23.21 (9.94) | 19.97 (7.67)          | −3.24 (5.11)                  | 0.145                           |                             |
| Noise to Harmonic Ratio (NHR) | Training 0.27 (0.70)  | 0.22 (0.11)           | −0.05 (0.06)                  | 0.126                           | 0.116                       |
|                          | Non-training 0.23 (0.16) | 0.17 (0.58)           | −0.06 (0.12)                  | 0.238                           |                             |
| Voice Turbulence Index (VTI) | Training 0.09 (0.31)  | 0.07 (0.16)           | −0.02 (0.08)                  | 0.025*                          | 0.100                       |
|                          | Non-training 0.11 (0.09) | 0.07 (0.04)           | −0.04 (0.06)                  | 0.274                           |                             |

Wilcoxon Signed-Ranks Test, Mann-Whitney U Test. ∗P < .05.

Table 8
Data of Multi-Dimensional Voice report before and after the 6-week study in the training and non-training groups.

|                          | Baseline Mean (SD) | Post 6-week Mean (SD) | Change from baseline Mean (SD) | P value for change from Baseline | P for change |
|--------------------------|--------------------|-----------------------|-------------------------------|---------------------------------|-------------|
| Jitter Percent (Jitt)    | Training 2.59 (1.56) | 2.30 (1.63)           | −0.29 (0.61)                  | 0.298                           | .101        |
|                          | Non-training 2.40 (2.81) | 1.65 (2.22)           | −0.75 (1.04)                  | 0.104                           |             |
| Shimmer in dB (Shdb)     | Training 0.92 (0.62)  | 0.79 (0.65)           | −0.13 (0.14)                  | 0.075                           | 0.101       |
|                          | Non-training 0.61 (0.55) | 0.48 (0.32)           | −0.14 (0.42)                  | 0.427                           |             |
| Shimmer Percent (Shim)   | Training 10.06 (7.18) | 8.46 (6.65)           | −1.60 (1.45)                  | 0.043*                          | 0.116       |
|                          | Non-training 6.41 (5.45) | 5.10 (3.23)           | −1.31 (4.37)                  | 0.458                           |             |
| Relative Average Perturbation (RAP) | Training 1.52 (0.93) | 1.38 (0.97)           | −0.14 (0.32)                  | 0.332                           | 0.087       |
|                          | Non-training 1.39 (1.64) | 0.93 (1.28)           | −0.46 (0.60)                  | 0.091                           |             |
| Pitch Perturbation Quotient (PPQ) | Training 1.54 (1.05) | 1.53 (1.17)           | −0.01 (0.27)                  | 0.974                           | 0.272       |
|                          | Non-training 1.50 (1.84) | 0.99 (1.45)           | −0.51 (0.72)                  | 0.109                           |             |
| Amplitude Perturbation Quotient (APQ) | Training 7.62 (5.80) | 6.55 (5.50)           | −1.07 (0.92)                  | 0.036*                          | 0.087       |
|                          | Non-training 5.19 (4.07) | 3.96 (2.11)           | −1.23 (3.35)                  | 0.368                           |             |
| Peak-to-peak Amplitude Variation (vAm) | Training 23.32 (6.18) | 21.74 (7.51)          | −1.58 (7.68)                  | 0.636                           | 0.133       |
|                          | Non-training 23.21 (9.94) | 19.97 (7.67)          | −3.24 (5.11)                  | 0.145                           |             |
| Noise to Harmonic Ratio (NHR) | Training 0.27 (0.70)  | 0.22 (0.11)           | −0.05 (0.06)                  | 0.126                           | 0.116       |
|                          | Non-training 0.23 (0.16) | 0.17 (0.58)           | −0.06 (0.12)                  | 0.238                           |             |
| Voice Turbulence Index (VTI) | Training 0.09 (0.31)  | 0.07 (0.16)           | −0.02 (0.08)                  | 0.025*                          | 0.100       |
|                          | Non-training 0.11 (0.09) | 0.07 (0.04)           | −0.04 (0.06)                  | 0.274                           |             |

Wilcoxon Signed-Ranks Test, Mann-Whitney U Test. ∗P < .05.
which may be attributed to the heterogeneity in neurological lesion characteristics and existence of multiple comorbidities including congestive heart failure, atrial fibrillation, hypertension, and diabetes mellitus. Most of our participants’ brain lesions were located in the middle cerebral artery territory. Moreover, quite a few participants had borderline cardiomegaly or congestive heart.

The physical activity level in stroke patients is usually limited by fatigue and dyspnea. Some patients were too fatigued to attend the program at the time of eligibility screening. However, our RMT group patients showed a significant change from baseline of FAS in contrast to that in the control group.

For stroke patients, the perception of dyspnea is low and blunted, which is due to their dissociation between respiratory effort and dyspnea. This can explain the similar Borg scale scores of both groups.

Regarding voice signals, Shim and ShdB are associated with hoarse and breathy voices; APQ and PPQ indicate the inability of the cords to support a periodic vibration. Hoarse and breathy voices usually have increased APQ, PPQ, or RAP. Moreover, the subglottal pressure initiates and maintains the vocal fold vibration and voice production. Wingate et al reported that 5-week EMT followed by 6 sessions of traditional voice therapy could increase subglottal pressure, which increased the vocal intensity, frequency, and duration of training program. Moreover, the subglottal pressure initiates and maintains the vocal fold vibration and voice production. Wingate et al reported that 5-week EMT followed by 6 sessions of traditional voice therapy could increase subglottal pressure, which increased the vocal intensity, frequency, and duration of training program.

No adverse event was reported throughout the program, except in one subject with transient facial muscle soreness, which subsided within 2 to 3 days. Similar to previous studies, the results proved that RMT could be feasible as adjunct therapy in stroke patients with respiratory muscle weakness, dysphagia, and dysarthria. However, the 6-week combined RMT was considered not long enough to demonstrate efficacy for expiratory muscle strength, swallowing, functional activity, and dysarthria and designing an intervention strategy based on the intensity, frequency, and duration of training program remains a challenge.

Study limitations: This study is limited by the small number of patients recruited. It took us two to three years to recruit the participants and those with apraxia, aphasia, and loose teeth, and those who could not hold a breath or perform a spirometry test were excluded. This study is also limited by the marked degree of drop-out rate (33.3% in RMT and 31.3% in control group). Moreover, the long-term effects and maintenance of RMT were not evaluated.

5. Conclusions:

Altogether, RMT significantly improved the respiratory muscle strength, FVC, FEV1, and fatigue in stroke patients with respiratory muscle weakness. In addition, the improvement in post-stroke dysphagia and dysarthria was also enhanced through RMT. The 6-week combined inspiratory and expiratory RMT is thus feasible as adjuvant therapy in stroke patients.

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