Study protocol

Effect of inspiratory muscle training on respiratory function, diaphragm thickness, balance control, exercise capacity and quality of life in people after stroke: a randomized controlled trial

Background of the study

Neuromuscular and balance impairment are major dysfunctions associated with people after stroke, affecting their exercise capacity and quality of life. Further, respiratory functions are often affected in the acute post-stroke period and possibly leading to long term diaphragmatic dysfunction. The thickness of the diaphragm muscle on the stroke-affected side was reported to be only 50% of that in age- and gender-matched healthy adults. The diaphragm muscle, while being the principal muscle for inspiration, also works synergistically with the pelvic floor, abdominal and back muscles contributing to trunk/core stability. Therefore, weakness of respiratory muscles including the diaphragm, may be an important contributing factor to balance impairments in people after stroke.

Inspiratory muscle training (IMT) is a common intervention used to improve the strength of the diaphragm. The reported training intensity adopted in an IMT program varied from 30% to 80% maximum inspiratory pressure (MIP), however the optimal training intensity associated with maximal recruitment of the diaphragm muscles in patients after a stroke has not been established. Our previous study showed that inspiratory load intensity at 50% MIP elicits the highest diaphragm contraction in a stroke population. There is therefore a need to ascertain whether adopting 50%MIP as the training intensity for an IMT program induces a significant positive effect on inspiratory function and balance control, thereby increasing exercise capacity and quality of life in individuals after stroke.

A traditional IMT program is typically conducted with the patient sitting on a stable surface (e.g., chair). As balance in patients with stroke is often impaired, challenging the dual role of the diaphragm both as a respiratory muscle as well as core-muscle stabilizer by requesting the

patient to undertake the IMT protocol on an unstable surface may further stimulate recruitment of the diaphragm muscles, promote synergistic activation of the diaphragm and other trunk muscles, and augment a positive effect on balance training.

This study is designed to explore the effects of a 4-week protocol of IMT on respiratory function, diaphragm thickness, balance control, exercise capacity, and quality of life in people after stroke. To ascertain the effect of IMT on the relationship between diaphragm muscle contraction and activation of other trunk muscles, this study also explores whether any effect of the 4-week IMT protocol on balance control is associated with changes in the anticipatory posture adjustments (APAs) time – the onset time of postural muscles during a required task (e.g., the rapid shoulder flexion test). The postural muscles including the erector spinae, rectus abdominis, external oblique, and internal oblique/ transversus abdominis.

Methods

Ethical approval

Ethical approval was granted by the Research Ethics Committee of Hong Kong Metropolitan University (ethics approval number: HE-OT2023/13) and Shenzhen Second People's Hospital (ethics approval number: 2023-274-01PJ).

Sample Size Calculation

The sample size calculation was performed using one-way ANOVA (ANOVA) in G*Power 3.1.9.7. No similar studies with three groups were available for reference in sample size estimation, the sample size was calculated based on our pilot data. The primary outcome was the among-group difference in diaphragmatic thickness during maximum contraction of the hemiplegic side, with the calculated effect size being 0.39. Considering an alpha error probability of 0.05 and a power of 0.80, the estimated sample size is 23 participants per group. To account for a potential 20% attrition rate, an additional 20% was added, resulting in a final required sample size of at least 28 participants per group (total n = 84).

The sample size will be recalculated and updated after half of the planned number of subjects completed the 4-week intervention training.

Participants

Inclusion criteria for people after stroke:

(1) Age ⩾ 40 years and < 80 years; (2) breathing spontaneously; (3) clinically diagnosed with ischemic and/or haemorrhagic stroke; (4) duration of stroke from onset falls within 1 month to 12 months after diagnosis; (5) no thoracic or abdominal surgery within the last 6 months; (6) able to understand and follow verbal instructions; (7) no facial palsy, or mild facial palsy without limitation of labial occlusion; (8) able to maintain a resting sitting posture without feet support for at least 30 seconds; (9) no cognitive impairment (Montreal Cognitive Assessment (MoCA) score ⩾ 26); (10) able to independently walk at least 10 meters with or without an assistive device.

Exclusion criteria for people after stroke:
(1) acute myocardial infarction or acute heart failure; (2) acute pain in any part of the body; (3) with respiratory illness or positive clinical signs of impaired respiratory function (such as shortness of breath, hypoxemia, chronic cough and sputum retention); (4) with chronic cardiovascular dysfunction; (5)Trunk Impairment Scale (TIS) score ⩾ 20; (6) patient with a nasal feeding tube, tracheal tube and/or any condition that prevents the measurement or the implementation of the study procedure.

Procedure

Intervention

Patients meeting the inclusion criteria will be randomized into three groups (Group A, Group B, and Group C). Group allocation will be performed with block, stratified randomization and maintained in different sealed opaque envelopes by a physiotherapist who is not involved in this study. Group A (sham IMT- stable group) will receive sham IMT (training intensity at 10% MIP) on a flat stable surface. Group B (IMT-stable group) will receive IMT (training intensity at 50% MIP) with training to be conducted in sitting on a flat stable surface. Group C (IMT-unstable group) will receive IMT similar to Group B but on an unstable surface. All three groups will also receive conventional treatment (see below).

The conventional treatment

Participants in all groups will receive a standardised conventional rehabilitation protocol. It includes limb range of motion, muscle tone reduction, strengthening and endurance of limb muscles, transfer skills, task-directed movements, general gait training, and activities of daily living training. This standardised protocol will be implemented for 60 minutes per session, 5

days per week, for 4 weeks.

IMT intervention

All participants will receive IMT thrice daily (morning, afternoon, and evening). Each session will consist of 5 sets (10 breaths per set) of pre-determined intensity, with one-minute rest intervals between sets. The total duration will be around 15 minutes per session. Training will be conducted 5 days per week for 4 weeks.

Group A (sham IMT- stable group) will receive sham IMT (training intensity at 10% MIP) on a flat stable surface.

Group B (IMT-stable group) will receive IMT (training intensity at 50% MIP) with training to be conducted in sitting on a flat stable surface. Adjustment of training load will be made according to any change in the MIP from the weekly reassessment.

Group C (IMT-unstable group), patients will perform IMT similar to Group B, but with IMT conducted while sitting on progressively staged unstable surfaces. The stages are as follows:

Stage 1: Sitting on a soft pad with both feet supported on the ground.
Stage 2: Sitting on a soft pad with each foot supported by separate pads.
Stage 3: Sitting on a soft pad with both feet supported by a single pad.
Stage 4: Sitting on a soft pad with no foot support.

All patients will begin at Stage 1. At the end of each week, they will be evaluated to determine their readiness for progression. If the patient could maintain an upright sitting posture in the subsequent stage while simultaneously breathing at the target inspiratory load, they will enter the next stage. Otherwise, they will remain at their current stage for an additional week of training before being re-evaluated.

All participants are blinded to the group allocation but informed that they will receive an IMT with a different inspiratory load. Data collection and assessment will be performed by another physiotherapist, who is blinded to the group assignment and not involved in the delivery of interventions to any participants.

Outcome Measurements

The primary outcome is the change of diaphragm thickness, and the secondary outcomes are a) respiratory function [measured by spirometry including MIP, forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1)]; b) balance control – reflected by multiple assessment tools including a force plate to measure changes in the center of pressure (COP) during various tasks performed in a sitting position; the Trunk Impairment Scale (TIS); the Timed Up-and-Go test (TUG); and the Falls Efficacy Scale–International (FES-I). c)Exercise capacity will be reflected by the distance covered in the 6-minute walk test (6MWT). d) QOL measured with Stroke Impact Scale 3.0 (SIS)). e) Activation activities of the included trunk muscles will be measured by surface electromyography (sEMG) during the sitting balance test; f) The anticipatory postural adjustment (APA) time of trunk muscles will be recorded and measured during the rapid shoulder flexion test using sEMG.

All outcomes will be measured at the baseline and after 4 weeks of intervention. To explore the prolonged effect of the program on functional improvement, the TIS, TUG, FES-I and SIS 3.0 will be repeated again at 12 weeks after intervention.

Demographic data

Demographic data of each participant, including age, gender, height, weight, and body mass index (BMI), will be collected for all participants. Additionally, information regarding stroke type (cerebral infarction, intracerebral haemorrhage), duration from the first onset of stroke, medical history (hypertension, diabetes mellitus, lipidemia, kidney disease), drinking and smoking history will also be recorded. The National Institutes of Health Stroke Scale (NIHSS), Modified Rivermead Mobility Index (MRMI), Modified Rankin Scale (mRS), and Barthel Index (BI) will be retrieved from the patient's medical records.

Diaphragmatic thickness

The diaphragmatic thickness of both the left and right diaphragms will be measured by an ultrasound machine (Mindray M9, Shenzhen, China), undertaken by an experienced and trained physiotherapist.

Spirometric lung function

Forced Vital Capacity and Forced Expiratory Volume in one second will be measured using a

spirometer (XEEK, X1, China). MIP will be measured using another spirometer (POWER Breathe, KH2, UK). All lung function tests will be conducted following the recommendations proposed by the American Thoracic Society guidelines.

Balance control function

Factors relating to balance control function of people after stroke will be assessed through the following five measurements:

(1) Changes of center of pressure (COP) during the performance of various tasks in sitting positions.

COP will be measured using a force plate (Sensor Medica, Guidonia Montecelio, Roma, Italy). Surface electromyography (sEMG) (Noraxon USA, Inc., Scottsdale, AZ, USA) will also be used to simultaneously measure the bilateral muscle contraction of the erector spinae, rectus abdominis, external oblique muscle, internal oblique muscle, and transversus abdominis muscles.

(2) Trunk impairment scale (TIS)

The TIS will be used to measure static sitting balance, dynamic sitting balance, and trunk coordination. The total TIS score ranges from 0 to 23 points, with a higher score indicating better trunk function.

(3) Timed Up-and-Go Test (TUG).

TUG will be used to measure the time that a participant needs to stand up from a standard armchair, walk a short distance of about 3 meters, turn around, walk back to the chair, and sit down again.

(4) Falls Efficacy Scale–International scale (FESI).

This scale will be used to explore whether the confidence of the patient in maintaining balance control is modified by the IMT intervention.

Exercise capacity

The exercise capacity of patients will be assessed by the distance covered in the 6-Minute Walk Test (6MWT).

Quality of life

The Chinese version of the Stroke Impact Scale 3.0 (SIS) will be used to measure the quality of life.

The anticipatory posture adjustment (APA) time of trunk muscles

APA time of each trunk muscle refers to the adjustments made by the trunk in preparation for an upcoming movement or external perturbation. Rapid shoulder flexion will be used as external perturbation in this study. These trunk muscle adjustments typically occur before the voluntary (shoulder) movement itself and are essential for maintaining balance and stability. To measure the APA time of each involved trunk muscle, participants will be asked to perform rapid shoulder flexions in both the standing and sitting positions on the force plate. sEMG will be used to measure the onset activation time of the deltoid, erector spinae, rectus abdominis, external oblique muscle, internal oblique muscle, and transversus abdominis contraction. The difference between the onset time of deltoid muscle and each above mentioned trunk muscle will represent the APA time for each of the trunk muscle.

Data analysis

All data will be analyzed using the IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp).

Repeated-measures ANOVA will be performed to compare the changes of lung function, diaphragmatic function, balance function, exercise capacity, and quality of life, respectively among the three groups.

Receiver operating characteristic (ROC) curve analyses will be used to determine the MCID of changes in diaphragmatic thickness.

Repeated-measures ANOVA will be performed to compare the changes of the contraction of trunk muscles, and APA time of trunk muscles, respectively among the three groups.