
Irma Ruslina Defi†*, Novitri Novitri, Ilin Nurina

1. Department of physical Medicine and Rehabilitation, Faculty of Medicine, Padjadjaran University, Sumedang, Indonesia.

Objective: This study aimed to elucidate the outcome of an Inspiratory Muscle Training (IMT) rehabilitation intervention on the lung function, functional mobilization, balance, and peripheral muscle strength of the paretic side in patients with subacute stroke.

Methods: This double-blind, randomized controlled trial study was conducted on patients with stable subacute stroke. For 8 weeks, the intervention group (n=16) received 40% intensity IMT while the control group (n=16) received 10% intensity IMT. We assessed the patients’ lung function (spirometer) before and after the intervention, as well as their pulmonary muscle strength (micro-respiratory pressure meter [RPM]), quadriceps strength (handheld dynamometer), grip strength (Jamar), walking speed (10-m walk test), balance (Berg Balance Scale [BBS]), and functional mobilization (sit-to-stand test).

Results: There were significant differences between the intervention group and the control group after IMT for forced vital capacity (FVC)% (P<0.01; d=3.20), forced expiratory volume in the first second (FEV1)/FVC (P<0.001; d=2.55), FEV1% (P<0.001; d=5.10), walking speed (P<0.05; d=1.62), hand grip (P<0.001; d=2.45), quadriceps strength (P<0.001; d=4.18), functional mobilization (P<0.01; d=2.41), and maximal inspiratory mouth pressure (P<0.001; d=1.62), but no significant changes were seen in balance (P=0.304; d=0.57).

Discussion: IMT improved lung function, functional mobilization, handgrip strength, and quadriceps strength on the paretic side of subacute stroke patients and is expected to improve functional status and allow the patient to participate in social activities. IMT exercise can be included in the rehabilitation program for subacute stroke patients.
Highlights

- Inspiratory muscle metaboreflex plays a role in reducing exercise tolerance.
- There was a significant increase in lung function, functional mobilization, grip, and quadriceps paretic side strength after inspiratory muscle training in patients with subacute stroke.
- Exercise should be included in the rehabilitation program of patients with subacute stroke.

Plain Language Summary

The current study found that an inspiratory muscle training rehabilitation intervention improved lung function, functional mobilization, balance, quadriceps strength, and handgrip strength on the paretic side of subacute stroke patients. Furthermore, based on the findings of this study, we conclude that exercise should be considered part of the rehabilitation program of subacute stroke patients.

1. Introduction

Stroke is the second cause of death and the third leading cause of disability globally [1]. In 2018, the prevalence of stroke in Indonesia was approximately 10.9 per 1000 population, increasing from 2013 when the prevalence was 7 per 1000 population [2]. About 50%-70% of stroke patients achieve their functional recovery, and 15%-30% have a disability three months after onset [3]. In Asia, there was a large variety of stroke disability-adjusted life-years (DALYs) lost based on age and gender. The DALYs lost show the impact of mortality, incidence, and disability among common cases, and the latter potentially consider the impact of stroke severity and rehabilitative interventions [4].

Peripheral muscles, including those involved in stroke and respiratory muscle weakness, low thorax expansion, and body posture dysfunction, play an essential role in exercise capacity and ability to perform daily tasks [5, 6]. Hemiparesis in stroke changes the muscle fiber type. Type II fiber composition is increasing to aggravate the patient’s mobilization activity, and this type is easily fatigued compared to type I fiber [7].

Smith was the first researcher who found a hemiplegic effect on the diaphragm. He found an elevation difference on the diaphragm in the paretic side compared with the non-paretic side in stroke [8]. Another study on Inspiratory Muscle Training (IMT) discovered that improving inspiratory muscle function increases exercise capacity and balance in chronic stroke patients [9]. Britto et al. administered the IMT program to chronic stroke patients at home based on the intensity of 30% of Maximal Inspiratory Pressure (MIP) for eight weeks. They observed a significant increase in respiratory muscle strength and endurance. Therefore, inspiratory muscle training was included as supporting training in stroke patients. This study showed increasing grip strength and quadriceps strength in both paretic and non-paretic sides [10].

Bosnak et al. administered a program with an intensity of MIP40% for 30 minutes, seven days per week for six weeks. This program was performed on 30 patients with heart failure (New York Heart Association [NYHA] II-III, Left Ventricular Ejection Fraction (LVEF) <40%). Sixteen patients underwent IMT at MIP40%, and 14 patients who underwent placebo therapy (MIP15%) showed significantly increasing quadriceps femoris strength [11]. Inspiratory muscle fatigue and metabolic accumulation in respiratory muscles activate unmyelinated type IV phrenic afferent fibers, which increase sympathetic reflex outflow and trigger vasoconstrictor response in resting limbs. That condition can improve the patient’s heart rate and mean arterial pressure. Moreover, respiratory muscle fatigue, defined as “inspiratory muscle metaboreflex”, will limit the perfusion of the limb by activating the sympathetic vasoconstriction reflex, thus reducing exercise tolerance.

The previous study has shown that an oxygen demand-delivery mismatch in respiratory muscles can trigger inspiratory muscle metaboreflex [12]. Inspiratory muscle training can cause systemic training effects such as vasoconstriction on peripheral muscles. Decreasing arterial flow will stimulate baroreceptors to vasodilate peripheral vessels. Continuous training causes vascular adaptation, which results in constant vasodilation, increasing blood flow to the peripheral area, and changing the com-
position of type I and type II muscle fibers with higher mitochondrial capacity, thus improving the factor for increasing peripheral muscle strength [13].

The objective of this research was to elucidate the effect of an IMT-based rehabilitation intervention on lung function, mobility, balance, quadriceps strength, and handgrip strength on the paretic side of subacute stroke patients.

2. Methods

Subjects and design

We conducted a double-blind, randomized controlled trial. We used the comparative studies formula for sample size calculation. Thirty-five subjects were divided into two groups with a computer-generated block randomized list. The first group is the intervention group, with 17 subjects conducting the IMT at 40% intensity. The second group is the control group, with 18 subjects performing the IMT at 10% intensity. Our study was conducted in Hasan Sadikin Hospital from October 2017 until October 2018.

The Profession and Research Ethics Committee of the Medical Committee Faculty of Medicine, Padjadjaran University, provided ethical clearance before the study (ethical clearance number: LB.04.01/A05/EC/220/VII/2017). As required, the current research’s procedures and ethical aspects were carried out in complete accordance with the Declaration of Helsinki. All participants provided written consent for their participation in the recent study.

The inclusion criteria were patients over 34 years, with the first stroke at least two weeks to three months after the stroke. Hemiparesis after stroke is defined by the presence of limb weakness with measurement from manual motor testing, but the subject can still walk with or without tools. The subject should be able to perform a handgrip test, IMT exercise, have a MIP value lower than 70% of predictive value by age and gender, understand oral and writing instruction (with mini-mental state examination [MMSE] score=22-30), and be cooperative. The exclusion criteria include hearing loss that interferes with understanding verbal instruction, a history of pulmonary obstruction based on spirometry results, previous chest or abdominal surgery, unstable cardiovascular disease, musculoskeletal disorders, and respiratory and expiratory breathing exercises over the last six months. Also, if the subject had contraindications to perform respiratory muscle exercises such as pneumothorax and unstable asthma with abnormally low dyspnea perception, he or she would be excluded from the study. At baseline, we assessed MIP to determine the intensity of IMT. MIP was measured by blowing into a flanged mouthpiece with nose clips in place. The subjects were told to exhale to residual volume. A valve or shutter is closed at residual volume, and the patient is instructed to inhale as forcefully as possible. The maximum pull should be held for 1-2 s [14]. Also, we conducted pulmonary function, peripheral muscle strength (handgrip and quadriceps strength), balance, and walking speed as other outcome measures.

Spirometry was used to assess pulmonary function, including forced expiratory volume in the first second (FEV1) and forced vital capacity (FVC) based on age and gender. Lung function was evaluated by inhaling deeply, holding the breath for a few seconds, and then exhaling as hard as the subject could into the breathing mask. The subjects will repeat this test at least three times to ensure consistent results [15].

Grip strength test assessed using handheld dynamometer with the subject sitting on a chair with 90° elbow flexion position. The subject is asked to hold the handgrip dynamometer and to grip as much as possible three times. The value taken is the mean of 3 times the test. For quadriceps muscle strength measurement, we used a handheld dynamometer (hydraulic type) with the patient’s position sitting on a chair, knee flexed 90°. The measurement was taken three times, and the mean value was recorded.

We used the Berg balance scale (BBS) for the balance test. The BBS is made up of 14 items that are graded on a scale of 0 to 4. If the participant cannot complete the task, s/he is assigned 0, and if the participant can complete the task, s/he is given 4. The BBS test has a maximum total score of 56 [16].

For functional mobilization measurement, we conducted a sit-to-stand test procedure [17], where subjects sat on a chair without a handrail. The stopwatch was switched on, set for 30 seconds, and then the subjects were asked to stand up from a sitting position. For walking speed measurement, we used the 10-m walk test (MWT).

Protocol for IMT

The training tools component was explained to subjects. They checked out training tools and sat in a reclining chair with an upright torso position. The pulse oximeter tool was fixed to the subject’s finger to monitor the general state of the subjects during the exercise. Then
the mouthpiece of the IMT exercise without intensity was tucked between the lips and the subjects trying to draw breath from the tool as much as three times breaths. The researcher then determined the intensity of the IMT training tool. The nose clip was attached to the subject’s nose to close the nostrils. The subjects then breathed from the mouth while observing general circumstances such as signs of hypoxia. The subjects were asked to breathe with the tool for five sets of 10 to 15 respiratory repetitions per minute, each set interspersed with a 1-min break. The approximate duration of 5 sets of exercises was estimated at 15 minutes for one exercise. A similar procedure was repeated for two consecutive days, resulting in 3 days of familiarization with the tools. The subjects were also asked to continue exercises by repeating the IMT practice procedure at home. The subjects were advised to stop the exercise immediately and seek medical evaluation if they experienced dyspnea or sharp pain on inspiration [14].

The subjects were instructed to fill the diary after each IMT exercise on the available tables at home. Every day, the subjects were monitored via communication media for training support.

Every week the researcher conducted an evaluation based on diary records and subject exercise techniques. If subjects had problems visiting the rehabilitation polyclinic, the researcher would visit them at their houses to conduct the evaluation. Both groups also received a conventional stroke rehabilitation program, besides the IMT training program. After eight weeks, the whole outcome measures were examined again.

### Statistical analysis

The Shapiro-Wilk test was used to determine the normality of the variables. The measurements taken before and after the IMT exercise were compared using an independent samples t-test at a significance level of $P=0.05$ and analyzed using SPSS IBM, v. 21. The effect size measurement uses a standardized mean difference, which is transformed into a value of $F$ and can be compared to obtain standardized effect size.

### 3. Results

In the beginning, 35 subjects were included in this study. Then, two subjects in the control group dropped out for unknown reasons, and one subject in the intervention group was excluded due to non-compliance during the exercise program. In the end, we had 32 subjects (Figure 1). A total of 32 subjects with a Mean±SD age of 51.37±6.009 years in the 40% intensity group (n=16) and 53.50±3.864 years in the 10% intensity group (n=16) were analyzed (Table 1). Regarding the baseline, we did not find any difference between groups.

The paired t-test statistical analysis test shows significant differences before and after the intervention in lung function, hand muscle strength, walking speed, balance, inspiration muscle strength, sit-to-stand performance, and quadriceps muscle strength in subacute stroke patients in the 40% intensity group ($P<0.05$).

Using the unpaired t-test analysis, we discovered that changes in FVC% were significantly different between groups ($P<0.01$) and associated with a significantly higher increase in FEV1% and FEV1/FVC in groups with IMT40% intensity compared to groups with IMT10% intensity ($P<0.001$). There was significant improvement within the IMT40% group in FVC% (74.82±7.92 to 76.81±7.47; $P<0.01$), whereas in the control group, there was no significant improvement in FVC% (66.95±11.66 to 66.95±11.66; $P>0.05$). Note that a Cohen’s $d>0.20$ is considered a small, $>0.50$ a medium, and $>0.80$ a large effect; as these are reference points. The effect size is large in all lung function measurements ($d>0.8$), which suggests a sustained large effect of lung function improvement with the 40% intensity of IMT (Table 2).

Regarding inspiratory muscle strength measure using MIP, it was significantly improved in 40% intensity IMT (53.92±9.23 to 57.28±9.28; $P<0.001$), but no significant improvement was seen in the control group (35.27±15.49 to 35.91±15.60; $P>0.05$). There were significant differences between groups in inspiratory muscle strength ($P<0.001$), and the effect size results indicate that the intervention group improved ($d>0.8$) (Table 2).

The walking speed during 10 MWT in this study significantly improved in the control group (0.80±0.081 to 0.90±0.163; $P=0.038$), but the improvement was higher in intervention group (0.98±0.15 to 1.25±0.20; $P=0.01$) with the large effect size ($d>0.8$). We discovered significant differences between groups using the unpaired t-test ($P<0.05$) (Table 2).

The sit-to-stand test was used in this study to measure functional mobilization. In the intervention group, functional mobilization (8.71±1.70 to 11.28±1.11; $P<0.001$) significantly increased, as well as in the control group (6.00±2.16 to 6.71±1.89; $P<0.01$). The Cohen’s $d$ in Table 2 showed a large effect size ($d>0.8$), suggesting a significant improvement in functional mobilization.
The quadriceps strength and handgrip improved more significantly in the intervention group than in the control group ($P<0.001$). The Cohen’s $d$ more than 0.8 in both quadriceps strength ($d=4.177$) and handgrip ($d=2.456$) on the paretic side indicated a significant effect of the intervention (Table 2).

Using the paired t-test, no significant improvement was found for BBS in the control group ($51.85\pm4.30$ to $52.71\pm4.070$). Although BBS improved significantly within the intervention group ($53.14\pm2.97$ to $54.71\pm3.50$; $P<0.05$), there were no significant differences between groups ($P>0.05$). However, there was a medium effect size in the intervention group on the BBS value ($d>0.5$) (Table 2). We did not find any adverse effects during the IMT program in this study.

4. Discussion

Smith et al. and Korczyn et al. reported that hemiplegia in limbs could also occur in the diaphragm [8, 18]. Diaphragm muscle plays a key role in maintaining respiratory function. There is an urgent need for more research on the impact of IMT on the diaphragm muscle in subacute stroke patients.
system ventilation function. Its weakness will affect the function of lung physiology characterized by decreasing FVC, FEV1, and Peak Expiratory Flow (PEF) up to 50% from prediction value based on inspection results with spirometry [19]. The results of FVC lung function in both groups after IMT exercise showed significant changes. Our results were in line with Gomez et al. study results showing a significant increase in FVC results in spirometry in stroke patients who received strength training for respiratory muscles compared to the control group [20]. Similar findings by Sutbeyaz et al. showed that stroke patients had a significant increase in FVC after six weeks of respiratory breathing exercises [21]. Respiratory muscle weakness due to stroke can affect the effectiveness of cough characterized in stroke patients, decreasing by 50% compared to healthy subjects [22, 23]. Respiratory muscle response to exercise is similar to other skeletal muscle responses. Muscles will adapt to the changes in structure that will improve their function.

Based on previous studies of respiratory muscle exercises in stroke patients, the intensity of 30% to 60% MIP often produces a significant effect. Intensity below 30% MIP was declared ineffective to increase inspiratory muscle strength; it is often used for placebo/sham effect [9, 10, 13]. Our study used an intensity of 40% MIP for the intervention group and an intensity of 10% MIP for the control group.

The function of the upper limbs is closely related to the performance of daily activities. Handgrip strength is a vital recovery factor in stroke patients and affects their daily activities [12]. According to Table 2, the handgrip strength showed statistically significant differences before and after the exercise in both groups.

Sit-to-Stand performance is related to the functional measurement of mobilization, such as walking speed, ambulation independence, and climbing stairs [24]. Sitting and standing are prerequisites of daily activity, and these actions are primarily impaired in stroke patients. The ability to stand up mainly depends on the strength of the quadriceps femoris muscle [25]. Based on sit-to-stand measures, we found a statistically significant difference between groups.

Our research found that vasodilation in the peripheral muscles caused by baroreceptor stimulation increased muscle strength and standing performance. Initially, vasoconstriction occurs in peripheral muscles due to metabolite accumulation in the hemiparesis diaphragm [12]. Continuous IMT will result in vascular adaptation and improve endothelial function that will change the type of peripheral muscle cells due to increased oxygenation. Change of muscle type can also increase the strength of peripheral muscles.

Table 2 shows significant differences in quadriceps femoral muscle strength within and between groups. Our result is in line with the research conducted by Bosnak et al. [11]. Yao et al. reported that respiratory muscle exercises could increase the maximum pressure of inspiration, lung function, endurance, and peripheral muscle strength after eight weeks of exercise [3].

Table 1. Baseline characteristics (each group: n=16)

<table>
<thead>
<tr>
<th>Variables</th>
<th>Intervention Group (40% Intensity)</th>
<th>Control Group (10% Intensity)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>51.37±6.009</td>
<td>53.50±3.864</td>
<td>0.361</td>
</tr>
<tr>
<td>Female/male ratio</td>
<td>7/7</td>
<td>7/7</td>
<td>1.000</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.62±8.693</td>
<td>154.68±7.691</td>
<td>0.185</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.80±10.201</td>
<td>54.43±11.395</td>
<td>0.171</td>
</tr>
<tr>
<td>Stroke onset (month)</td>
<td>3.06±0.997</td>
<td>3.37±0.718</td>
<td>0.468</td>
</tr>
<tr>
<td>MMSE</td>
<td>29.00±1.095</td>
<td>28.81±1.682</td>
<td>0.724</td>
</tr>
<tr>
<td>Side paretic ratio (right/left)</td>
<td>¾</td>
<td>2/5</td>
<td>0.280</td>
</tr>
<tr>
<td>Infarct/Bleeding ratio</td>
<td>2/5</td>
<td>2/5</td>
<td>1.000</td>
</tr>
</tbody>
</table>

MMSE: mini-mental state examination.
Table 2 shows that BBS results significantly differed after exercise compared with BBS before exercise in the intervention group. These results are in line with the studies of Bosnak et al. [11] and Dongha et al. [9]. Their research showed increasing strength of quadriceps femoris and inspiratory muscles, indicating that breathing exercise will help improve balance in stroke patients. In these two previous studies, the BBS increase might occur due to decreased fatigue in the diaphragm muscle. Reducing fatigue in the diaphragm will increase the proprioceptive sensitivity in the lumbar area, so it will help improve the balance.

Walking is an essential human activity to enable engagement in the community. Fifty percent of post-stroke patients who can walk have decreased walking speed. Richards et al. stated that the stroke walking speed of the subacute phase is less than 0.5 m/s. Normal walking for the functional activity will take at least 0.8 m/s to allow a person to get involved in the community [24, 25].

Walking speed is also influenced by cardiorespiratory fitness [24]. Exercise of respiratory muscle can improve lung and cardiopulmonary functions [7, 20]. The power of inspiratory muscle will change the perception of effort in the respiratory system and peripheral muscle by decreasing feedback of afferent nervous system III and IV from respiratory muscle and limb muscle. Blood flow to peripheral muscles will remain intact, and muscle performance will last longer during activity [20].

Table 2. Before and after inspiratory muscle training results

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before/After</th>
<th>Mean±SD</th>
<th>Intra-group P</th>
<th>Effect size Cohen’s d (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Intervention Group</td>
<td>Control Group</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(40% Intensity)</td>
<td>(10% Intensity)</td>
<td></td>
</tr>
<tr>
<td>FVC (%)</td>
<td>Before</td>
<td>74.82±7.923</td>
<td>63.95±11.659</td>
<td>0.001**</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>76.81±7.474</td>
<td>66.95±11.659</td>
<td>1.000</td>
</tr>
<tr>
<td>FEV1/FVC (%)</td>
<td>Before</td>
<td>89.81±5.053</td>
<td>80.15±4.665</td>
<td>0.111*</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>91.72±5.309</td>
<td>85.87±4.772</td>
<td>0.000***</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>Before</td>
<td>86.65±10.422</td>
<td>60.87±28.759</td>
<td>0.03**</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>88.45±10.479</td>
<td>61.21±28.831</td>
<td>0.000***</td>
</tr>
<tr>
<td>Handgrip (kg)</td>
<td>Before</td>
<td>13.65±2.784</td>
<td>9.35±2.836</td>
<td>0.004**</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>16.82±2.864</td>
<td>9.82±2.821</td>
<td>0.000***</td>
</tr>
<tr>
<td>Sit-to-Stand test (s)</td>
<td>Before</td>
<td>11.28±1.112</td>
<td>6.00±2.160</td>
<td>0.08**</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>8.71±2.774</td>
<td>6.71±1.889</td>
<td>0.001**</td>
</tr>
<tr>
<td>Quad. Strength</td>
<td>Before</td>
<td>14.70±1.990</td>
<td>12.78±4.366</td>
<td>0.012*</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>16.74±1.925</td>
<td>13.04±4.434</td>
<td>0.000***</td>
</tr>
<tr>
<td>PI Max</td>
<td>Before</td>
<td>53.92±9.229</td>
<td>35.27±15.485</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>57.28±9.275</td>
<td>35.91±15.599</td>
<td>0.000***</td>
</tr>
<tr>
<td>Walking Speed (m/s)</td>
<td>Before</td>
<td>0.98±0.146</td>
<td>0.80±0.081</td>
<td>0.038*</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>1.25±0.198</td>
<td>0.90±0.163</td>
<td>0.011*</td>
</tr>
<tr>
<td>BBS score</td>
<td>Before</td>
<td>53.14±2.968</td>
<td>51.85±4.296</td>
<td>0.111</td>
</tr>
<tr>
<td></td>
<td>After</td>
<td>54.71±3.496</td>
<td>52.71±4.070</td>
<td>0.000***</td>
</tr>
</tbody>
</table>

* P<0.05; ** P<0.01; *** P<0.001.

FVC: forced vital capacity; FEV1: forced expiratory volume in 1s; PIMax: maximal inspiratory mouth pressure; Quad: quadriceps. Intra-group analysis used paired t-test, and inter-group used unpaired t-test.
According to our research, this exercise can be considered in the rehabilitation program of subacute stroke patients. Our study did not check the long-term effects after exercise. Generalization should be used with caution, and further research is recommended with a larger population.

5. Conclusion

In our study, an IMT program with a 40% intensity for eight weeks improved lung function, hand muscle strength, quadriceps muscle ipsilateral strength, sit-to-stand performance, balance, and walking speed in subacute stroke patients.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by The Profession and Research Ethics Committee of the Medical Committee Faculty of Medicine, Padjadjaran University (LB.04.01/05/EC/220/VII/2017).

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

Reference


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