**Preventive effect of rehabilitation training therapy on** **muscle quality**

 **in patients with stroke:** **A retrospective study**

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**Abstract.**

Sarcopenia is common consequences of stroke. The purpose of this study is to explore the preventive effect of rehabilitation training therapy on sarcopenia in patients with stroke. A retrospective study was conducted on patients who have received three weeks of rehabilitation training after stroke. All patients were screened with body composition and Barthel index when admitted and after training. After rehabilitation training, body total water, muscle mass, protein content, inorganic salt content, and skeletal muscle content were increased while body fat content and body fat percentage were significantly decreased (*P*＜0.05). In addition, Barthel Index scores showed that the ability of daily living was improved after rehabilitation (*P*＜0.05). Rehabilitation training therapy may have protective effects on sarcopenia in patients with stroke.

**Background**

Sarcopenia is a group of age-related syndromes in which skeletal muscle mass and quantity decrease is associated with decreased muscle function. Sarcopenia is not only the reason for the decline of physical function and poor health status but also the performance of the decline of activity ability of the elderly [4-7].

Stroke is a leading cause of mortality and disability. The prevalence of people living with the effects of stroke has increased because of the growing and aging population [8-10]. The most common limb dysfunction after stroke is the weakness of hemiplegia of one side of the limb, which leads to the decline of the ability of daily living and serious disability, and further leads to the reduction of muscle strength and strength of patients. Sarcopenia is a common disease in the elderly, accounting for 7.5% of the diseases in the elderly [11]. The incidence of sarcopenia in the elderly over 60 years old in China is as high as 10.4%[12], at the same time, sarcopenia is highly prevalent in stroke patients admitted to the convalescent rehabilitation ward, at about 50%[13-14].

Most scholars believe that exercise therapy is an effective treatment for sarcopenia. Reasonable resistance exercise and aerobic exercise can increase the synthesis of skeletal muscle protein, increase the cross-sectional area of skeletal muscle fibers, and improve muscle mass and muscle function [15].

Rehabilitation training therapyis an effective method for functional exercise and rehabilitation of hemiplegia limbs after stroke by restoring patients' muscle strength and improving patients' ability to live by themselves [16-18]. Extensive clinical practice has proved that rehabilitation training of hemiplegic limbs has obvious and stable effects on improving patients' muscle strength and ability of daily living，restoring patients' disability state. However, there is no relevant research on prevention and improvement of rehabilitation training for patients with sarcopenia in clinical and nursing aspects. So, we evaluated the preventive effect of rehabilitation training therapy on post-stroke patients with sarcopenia in this work.

**Methods**

**Participant recruitment**

This is a retrospective study. A total of 45 patients with cerebral apoplexy, aged 33-95 years older, who were admitted to the he department of Rehabilitation medicine, Nanjing Medical University, Sir Run Run Hospital, from October 2019 to October 2020 for 3-weeks rehabilitation training were enrolled in this study. The inclusion criteria were: 1. diagnosed as stroke based on clinical presentations and CT/MRI confirmation. 2 the limb function in patients with left side or both sides hemiplegia obstacle, Brunstrom stage Ⅰ - Ⅵ；3. Stable vital signs, able to cooperate with rehabilitation training; 4. Participate in the experiment voluntarily and sign the informed consent. The exclusion criteria were: 1. history of malignant tumor;2.psychiatric disease, severe cognition impairment, and severe diseases of other systems (patients with severe circulatory system diseases, hematologic system diseases, and immunocompromised functions). ;3. Patients with severe spasm limbs, modified Ashworth evaluation class acuity Ⅱ；4. Patients with cardiac pacemakers or other metal implants;5. Patients or their family members who are unwilling to cooperate after informing the informed consent. Discontinuation Criteria：Patients who are unable to continue the rehabilitation training due to other severe acute diseases or cardiovascular and cerebrovascular events. The study was approved by the ethics committee of Nanjing Medical University, Sir Run Run Hospital (ChiCTR1900028296).

**Rehabilitation training program**

after the initial functional disorder assessment and evaluation of patients by doctors, the corresponding rehabilitation training plan and schedule is formulated, which mainly includes: postural transfer training, exercise training, physical factor therapy, and occupational therapy[19].

**Postural transfer training**

During the period of bed rest, the patient should keep the hemiplegia limb in the functional position to avoid inducing the abnormal pattern of the affected limb, prevent muscle spasms and contracture, and maintain the normal muscle strength state of the limb. Patients who cannot turn over on their own shall be assisted with Bobath hand[20] to change their supine position, affected side decubitus position, and healthy side decubitus position every two hours during bed, to avoid long-term compression of one side muscle.

**Exercise** **training**

The main training methods include joint movement training, muscle strength training, balance function training, and walking training. Joint movement training raised by the therapist with side body, since the childhood by the upper shoulder, elbow, wrist, knuckles to lower limb hip, knee, ankle and toe joints in joint activities, and guide the contralateral limb in patients with the same joint activities, training for 20 minutes in the morning and afternoon, 5 days a week; Muscle strength training is the main method to enhance muscle strength. The training methods used are mainly nerve transmission impulse training, assist training, and resistance training. A type of exercise in which the entire joint is moved at a predetermined rate by matching resistance provided by an instrument, 20 minutes in the morning and afternoon, 5 days a week; Balance function training: Coma patient bedside upright bed standing training, passive trampling bed training; The awake patient first raised the head of the bed 30 degrees, maintained for 30 minutes, and then increased 10 degrees on alternate days and then trained until the patient maintained 90 degrees for more than 30 minutes, and the transition to independent sitting was assisted by one person, stand by the side of the bed with the healthy limb, repeatedly training to stand by the affected side with the help of a therapist, 20 minutes in the morning and afternoon, 5 days a week; Walking training：After evaluation the patients the ability to balance and stand, first using the parallel bars within walking training, Starting from in-place treading, repeated training, gradually assisted the patient to slowly walk to independent walking, Move the body diagonally, up and down the stairs, with the assistance of the therapist for gradual training, 20 minutes in the morning and afternoon, 5 days a week;

**Physical factor therapy**

Refers to the use of electricity, sound, light, magnetism, heat, cold water force, and other physical factors to improve the body function, improve or rebuild the body treatment methods, training methods mainly include: Bioelectrical Feedback Training(BFT)and Neuromuscular electrical stimulation therapy (NES). BFT adopts MLD B4 (Nanjing) biofeedback therapeutic instrument and NES used a Stim4 low-frequency therapy instrument [21-22]. Exercise for 20 minutes in the morning and afternoon, 5 days a week.

**Occupational therapy**

Based on the analysis of biomechanical and neurodevelopmental methods, the aim is to restore or improve the ability of self-care, learning, and work as much as possible by using targeted and selected activities. Specific training methods mainly include Upper limb intelligent feedback training, Situation simulation training, Activity of daily living (ADL) training.

The upper limb feedback rehabilitation training system (Chinese)was adopted. This device simulates the movement of human upper limbs in real-time, and can conduct video game training in one, two and three-dimensional motion space [23]. Such as catching water droplets, hammering nails, Wall-cleaning, target shooting, fruit cutting, and other multi-joint training games. Each game lasted 10 minutes, each training lasted two games, alternating between left and right hands, 20 minutes once a day, 5 days a week. After each training, the results were compared with the results of the last treatment, and the difficulty of the game was gradually adjusted.

The NT - BOX (South Korea) scene interactive training system, application of Microsoft's 3 d cameras capture the human body movement, and identify the relevant human body skeleton model, with the help of virtual skeleton model, the system can identify the key parts of the body and realize the three dimensions of space motion [24], patients through interactions with the computer, the computer virtual environment assessment or training, therapists design 3 to 5 games, each game 3 to 5 minutes, rest between each game 1 to 2 minutes, for 20 minutes Once a day, 5 days a week.

ADL training:The therapist instruct patients to use healthy hands to drive hemiplegic hands or with tools to eat, undress, take a bath, dress, urinate, go to the toilet, transfer bed and chair, walk, up and down stairs and other basic daily activities [25]. Therapists encourage patients to be independent, or compensate with tools, in order to reduce the number of home care, improve the patient's initiative, and improve the patient's ability to care for themselves.

**Outcome assessments**

Basic information including gender, age，whether suffering from high blood pressure, diabetes, and other basic diseases before onset, whether has the health behavior such as smoking drinking，ADL level, stroke type, lesion location, lower limb paralysis (Brunnstrom recovery stage) , serum albumin level and c-reactive protein, urea, uric acid, creatinine, serum transaminase, bilirubin，and other biochemical indicators were obtained on admission to the ward. Modified Barthel Index scoring scale was used for ADL level [27]. Any adverse events were recorded throughout the intervention period. The primary outcome measure was the changes in body composition before and after rehabilitation training. Bio-impedance analysis (InBody S10) was used to assess body composition before and after the intervention.

The secondary outcome measures were the changes of ADL before and after training. The Modified Barthel Index score measures the independence in performing the ADL. The Modified Barthel Index assesses patients，ADL based on 10 categories, including passing urine, food intake, and transfer, activity, dressing, and bathing. Each category is scored using varying weights (5, 10, or 15) for a total scale ranging 0~100 (100 = normal ADL; 61-100 = mild functional defect; 41- 60= moderate functional defect; 0-40 = severe functional defect). Lower scores represent significant deficits and greater dependence of patients. Patients with a score of 100 are considered independent in performing the ADL[28].

**Statistical analysis**

All analyses were conducted using SPSS.26 (Statistical Product and Service Solutions)software. Use Office Excel (Excel 2010, Microsoft, Washington, D.C.) for preliminary data entry. Measurement data were expressed as mean ± standard deviation, and enumeration data were expressed as a rate (%). The descriptive analysis method was used to analyze the general data of patients, and comparisons between two groups were assessed with a t-test was used to analyze the changes of human index components before and after comprehensive rehabilitation training. The change of ADL scores before and after comprehensive rehabilitation training was analyzed by rank-sum test, *P*＜0.05 represents a statistically significant difference.

**Results**

**Subjects**

A total of 45 patients  (32 females, 13 males) were collected in this study, with an average age of 56.5±14.5 years. The baseline demographic and clinical characteristics of the patients are shown in Table 1.

**Table1** Baseline demographic and clinical characteristics

|  |  |
| --- | --- |
| Baseline Characteristics |  |
| age（years）Sex, Male/Female, n (%) | 56.5±14.532/13 (71.1/28.9) |
| height（cm） | 167.1±9.2 |
| weight（Kg） | 64.6±11.4 |
| BMI（Kg/m2） | 22.9±2.8 |
| Stroke classification |
| Cerebral hemorrhage | 23 |
| Cerebral infarction | 22 |
| Lesion location |
| Left | 16 |
| Right | 13 |
| On both sides | 11 |
| The brain stem | 3 |
| Risk factors |
| Smoking | 8 |
| Drink | 6 |
| hypertension | 33 |
| diabetes | 19 |
| Laboratory indicators  |
| K+ (mmol/L) | 4.06±0.36 |
| Na+ (mmol/L) | 140.82±3.60 |
| Cl- (mmol/L) | 102.17±4.44 |
| Ga2+ (mmol/L) | 2.24±0.10 |
| Mg2+ (mmol/L) | 0.82±0.07 |
| HCO3- (mmol/L) | 25.93±2.22 |
| BUN (umol/L) | 5.04±1.78 |
| UA (umol/L) | 273.33±81.38 |
| Cr (umol/L) | 61.38±31.45 |
| ALT (U/L) | 26.83±28.88 |
| AST (U/L) | 20.23±15.98 |
| ALP (U/L) | 76.28±28.33 |
| GGT (U/L) | 34.61±31.20 |
| TBL (umol/L) | 9.32±4.02 |
| DBL(umol/L) | 3.83±2.04 |
| IBL(umol/L) | 5.43±2.46 |
| TP（g/L） | 68.33±6.20 |
| ALB (g/L) | 40.53±4.57 |
| TG (mmol/L) | 1.55±0.86 |
| HDL (mmol/L) | 0.93±0.24 |
| LDL (mmol/L) | 2.30±0.82 |
| WBC（10^9/L） | 6.10±2.25 |
| Hb（g/L） | 127.69±18.56 |
| PLT（10^9/L） | 216.96±107.42 |
| CRP（mg/L） | 10.4±5.17 |

**Change in body composition at 3 weeks**

Table 2 shows the body composition values at baseline, 3 weeks and change from baseline.. The results showed that the body component analysis index of 45 patients had obvious changes after the rehabilitation training. The total body moisture, muscle mass, protein content, inorganic salt content, and skeletal muscle content were significantly increased after rehabilitation training, while the body fat content and body fat percentage were significantly decreased (P＜0.05). In the analysis of muscle balance of limbs and trunk, the muscle content of limbs and trunk increased after intervention, including right upper limb (2.02±0.55 *VS* 2.20±0.69), left upper limb (2.00±0.56 *VS* 2.23±0.88), trunk (18.37±3.39 *VS* 19.33±4.22), right lower limb (8.96±2.14 *VS* 9.60±2.12), left lower limb (8.77±2.05 *VS* 9.60±2.12). *P*≤0.05., the water level analysis results of limbs and trunk showed that the water content of limbs and trunk was significantly improved after the rehabilitation training

Skeletal muscle index (SMI) is one of the important diagnostic indicators in the diagnosis of sarcopenia. As shown in Table 2, SMI was significantly increased after training (P=0.009), which proved that rehabilitation training therapy had a significant improvement effect on muscle loss and decline in stroke patients. Thus effectively prevent the occurrence of sarcopenia after stroke.

In addition, the body composition report also measured the internal and external cellular water content, basal metabolic rate, abdominal circumference, visceral fat area, bone mineral content, body cell volume, upper arm circumference, and other indicators in human body composition as research items.

**Table 2** Analysis of changes in human body composition before and after rehabilitation training

|  |  |  |  |
| --- | --- | --- | --- |
|  | Before the intervention | After the intervention | P-value |
| **Body composition** |
| Total Body Water (L) | 35.23±7.37 | 36.97±7.09 | **0.003** |
| Protein (kg) | 9.22±2.00 | 9.67±2.12 | **0.042** |
| Soft Lean Mass (kg) | 45.02±9.47 | 47.35±9.10 | **0.002** |
| Skeletal Muscle (kg) | 25.8±6.05 | 27.25±5.64 | **0.013** |
| body fat mass (kg) | 16.94±7.63 | 14.2±5.79 | **0.002** |
| Percentage of body fat mass (%) | 25.63±10.11 | 22.07±8.35 | **0.003** |
| **Segmental lean analysis** |
| Right Arm (kg) | 2.02±0.55 | 2.18±0.67 | **0.017** |
| Left Arm (kg) | 2±0.56 | 2.23±0.88 | **0.019** |
| Trunk (kg) | 18.37±3.39 | 19.33±4.22 | **0.020** |
| Right Leg (kg) | 8.96±2.14 | 9.6±2.12 | **0.018** |
| Left Leg (kg) | 8.77±2.05 | 9.31±2.03 | **0.018** |
| **Segmental water  analysis** |
| Right Arm (L) | 1.58±0.42 | 1.71±0.53 | **0.036** |
| Left Arm (L) | 1.56±0.44 | 1.73±0.66 | **0.019** |
| Trunk (L) | 14.35±2.63 | 15.09±3.28 | **0.022** |
| Right Leg (L) | 7.03±1.66 | 7.49±1.62 | **0.030** |
| Left Leg (L) | 6.88±1.62 | 7.31±1.56 | **0.015** |
| Other indicators  |
| Intracellular cell Water (L) | 21.34±4.61 | 22.59±4.44 | **0.002** |
| Extracellular Water (L) | 13.89±2.82 | 14.39±2.77 | **0.016** |
| basal metabolic rate (kcal) | 1404.8±2119.9 | 1457.5±209.9 | **0.002** |
| Waist circumference (cm) | 72.26±8.77 | 69.38±7.14 | **0.007** |
| visceral fat area (cm2) | 61.68±30.57 | 56.19±23.69 | 0.060 |
| bone mineral content (kg) | 2.86±0.71 | 3±0.74 | **0.046** |
| amount of body cells (kg) | 30.57±6.61 | 32.57±6.36 | **0.002** |
| Upper arm circumference (cm) | 26.96±2.88 | 27.83±5.48 | 0.223 |
| SMI (kg/m2) | 9.14±1.60 | 9.69±1.47 | 0.009 |

SMI: Skeletal muscle index

After rehabilitation training, ICW, ECW, BMR, bone mineral content, somatic cell number，and other body components are significantly improved (*P*＜0.05), at the same time visceral fat area also decreased significantly(*P*＜0.05). The results also showed that there was no statistically significant difference in the changes around the upper arm, suggesting that rehabilitation training did not  improve it significantly .

**Comparison of ADL before and after intervention**

Table 3 shows that according to Barthel Index score, 13 patients had mild dysfunction, 6 patients had moderate dysfunction, and 25 patients had severe dysfunction. After the intervention, the numbers were reduced to 22, 6, and 17. The results of rank-sum test showed that the daily living ability of the patients was significantly improved after the rehabilitation training, and the difference was statistically significant (*P*＜0.05). This result also confirms the positive preventive effect of rehabilitation training therapy on improving the dysfunction caused by muscle loss in stroke patients.

**Table 3** Comparison of ADL before and after intervention

|  |  |  |  |
| --- | --- | --- | --- |
| group | ADL score grading | Z |  P-value |
| N | severe functional defect | moderate functional defect | mild functional defect |
| Before the intervention | 45 | 25 | 6 | 13 | 2.033 | 0.042 |
| After the intervention | 45 | 17 | 6 | 22 |
| Difference |  | 8 | 0 | -11 |

ADL: the activities of daily living

**Discussion**

Stroke is considered to be one of the major disabling diseases in the world. Patients with stroke are accompanied by severe muscle mass loss, resulting in serious dysfunction and affecting quality of life. Muscle is the main organ for functional activities of human body. Studies have shown that the number of movement units in hemiplegic limbs can be observed 4 hours after stroke, and muscle strength can be detected one week after stroke, and muscle volume can be decreased by 20%-24% [29-30].Studies have shown that decreased limb muscle mass after stroke is associated with multiple mechanisms, including muscle disuse atrophy due to reduced limb movement, dysphagia leading to malnutrition, sympathetic hyperactivation and stress inflammatory response, and denervation of motor neuron loss [31].

After stroke, low intensity exercise results in muscle atrophy and significant decrease in muscle mass [32]. Dysphagia is the main complication of stroke, dysphagia patients lack of protein and other nutrients intake caused by muscle mass reduction [33]. The stress response of acute cerebral apoplexy causes the hyperexcitation of sympathetic nerves throughout the body, Consequent immunosuppression, inflammation, and catabolic activation induce tissue degradation and muscle loss [34-36]. In addition, stroke accelerates denervation, and the loss of motor neurons is an important factor in the decline of skeletal muscle mass [37].

The pathogenesis of sarcopenia is complex, which may be related to the decrease of the patient's physical activity, decreased protein synthesis ability, decreased mitochondrial function in intracellular, enhanced protein decomposition reaction in intracellular and other reasons [38-39], among which the most important cause is the decrease of body activity. This is also one of the reasons for the occurrence of limb dysfunction complicated with sarcopenia after stroke. Researchers will try a variety of methods to prevent and cure sarcopenia, including drug therapy and nutritional support, but none of them have achieved significant effects and have certain side effects [40-41]. Stroke is characterized by high morbidity, high mortality, and high disability rate globally [42], which seriously affects the quality of life of patients and has become an important public health problem threatening human health.

Rehabilitation training therapy on muscle disease prevention and improve the effect is not clear, most studies have shown that exercise therapy is effective for sarcopenia prevention [43-44]. Based on the existing rehabilitation training system and scientific management of rehabilitation medicine, this study retrospectively studied the rehabilitation training of stroke patients, aiming to explore the treatment and prevention methods of  sarcopenia, and to provide research basis and academic reference for the effective prevention of post-stroke patients with sarcopenia.

Rehabilitation training aim on limb dysfunction after stroke patients, there is rare rehabilitation exercise training method was applied to treatment for sarcopenia, the results show that the rehabilitation therapy for improving body muscle mass such as the human body composition and the patient's daily activity ability is valuable. Our research mainly evaluated the effect of rehabilitation therapy for body muscle mass in sports training, total body water, protein, inorganic salt, body fat content, skeletal muscle, limbs and trunk muscles, and moisture analysis, basal metabolic rate, visceral fat area, bone mineral content, amount of body cells of human body composition indexes, the aim is to further explore the treatment of sarcopenia, since whether rehabilitation training therapy is an effective treatment has not been previously reported in the literature.

Exercise therapy has been shown to reduce the risk of sarcopenia, however, these findings mainly based on the research of relatively healthy people [45], for itself the subgroup of patients with limb dysfunction such as this study of the midbrain legacy limb dysfunction after stroke patients and common studying Alzheimer's patients with severe dysfunction is not clear, so we study for the training of rehabilitation therapy in improving itself has the advantages of low limb dysfunction for sarcopenia with muscle content amount, distribution of the muscles of the limbs and trunk, the amount of nutrients such as protein, inorganic salt, and daily life activities ability effectively provides new evidence.

The limitation of our study is First of all, due to the limitation of hospitalization time and economic factors, patients generally cannot stay in hospital for a long time. Therefore, our rehabilitation training cycle is generally 21 days for one hospitalization cycle. R. Wang et al. reported that short-term exercise has a significant effect on the treatment of sarcopenia in elderly inpatients aged 80 years and above. Even within a short period of two weeks, exercise can effectively improve the daily activity ability of elderly inpatients with sarcopenia recently [46]. Secondly, this study did not refer to and compare some important related factors, such as the rehabilitation training period of patients, the beginning and end time of training, nutritional supply, and the measurement positions of different patients were different. Third, its relatively small sample size, and did not randomly assign participants, selection bias, and single-center study design might limit the generalizability of the results, and lack of a control group. Fourth, as with other clinical trials of rehabilitation training, generalizations of studies may be limited because individual rehabilitation training programs often need to be tailored to their individual circumstances, and there is no guarantee that the training program will be consistent for every patient.

**Conclusions**

The results of our study indicate that rehabilitation training therapy has a positive effect on the prevention of muscle loss and limb function decline after a common stroke.

Rehabilitation training therapy can improve the muscle content and skeletal muscle quality of stroke patients, improve the ability of daily living, and prevent the symptoms of sarcopenia in stroke patients and the occurrence of sarcopenia after stroke effectively . It also has positive therapeutic effects on sarcopenia. Whether rehabilitation training therapy can be popularized and applied to the prevention and treatment of sarcopenia patients caused by other different reasons is the focus and direction of further research in the future. It is also hoped that the conclusions of this study can be popularized and applied to the clinical treatment of sarcopenia.

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