

Comparison of the Effects between Isokinetic and Isotonic Strength Training in Subacute Stroke Patients

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Background: The goal of the study was to compare the effects of isokinetic and isotonic strengthening program on the changes of muscle strength, functional capacity, life quality, and inflammatory cytokines in hemiparetic patients within 6 months of stroke attack. **Methods:** Thirty-one participants were randomly assigned into either isotonic training group or isokinetic training group. Both training programs were carried out 5 days a week for a total of 4 weeks. Outcome measures included the peak isometric torque of knees at 90° flexion, the peak torque of knees extension and flexion at angular velocities 60°/s and 120°/s, Short Form 36 (SF-36) Health Survey Questionnaire, Timed Up and Go test, and inflammatory cytokines including high sensitivity C-reactive protein, interleukin-6, and tumor necrosis factor- α . **Results:** Seven patients were not able to complete the training program and were excluded from our study. The results from the remaining 24 patients showed that there were more peak torque, and SF-36 items significantly improved in the isokinetic training group compared with the isotonic group. The Timed Up and Go test and interleukin-6 were improved in both groups, but tumor necrosis factor- α was improved in only the isokinetic group. There were no significant differences between the improvements of the 2 groups except the isokinetic flexion torque at 60°/s and 120°/s. **Conclusions:** Early strengthening exercise is important for subacute stroke patients, and isokinetic program, if accessible, can bring more significant benefits for them. **Key Words:** Stroke— isokinetic— isotonic— peak torque— inflammatory cytokine.

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Stroke has been one of the leading causes of mortality and handicap in the world,¹ causing tremendous health care and financial burden in the society. A past study revealed that there were 26.1% and 26.3% stroke survi-

vors remained disabled at 1 and 3 years after stroke, respectively.² Furthermore, significant correlations were noted between Barthel Index and all Short Form 36 (SF-36) domains at both time points, signifying impaired self-care ability being related to poor quality of life in poststroke patients.² In addition, the neurologic and psychosocial sequelae brought by stroke may pose huge stress on his or her spousal caregivers.³ Therefore, the impact of stroke on the patient and his family can never be overlooked by health care providers.

Nevertheless, the impact of stroke can be ameliorated by intensive and individualized poststroke rehabilitation program by restoring self-care abilities and quality of life. Muscle strengthening exercise has been a critical part of rehabilitation programs, and it was proven to improve the functional recovery after stroke.⁴⁻⁸ The benefits on balance⁹ and reducing anxiety¹⁰ have also been proven

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in the past literature. Among multiple types of strengthening exercise, isokinetic muscle strengthening by isokinetic dynamometer has been widely applied to many musculoskeletal conditions because of the exercise reproducibility, accuracy of working program setting, real-time visual and auditory biofeedback, and easy monitoring of participants performance.¹¹ Past studies revealed improved outcome after isokinetic muscle strengthening training in situations including post anterior cruciate ligament reconstruction,¹²⁻¹⁶ jumping capacity in athletes,¹⁷⁻²⁰ muscle weakness in Parkinson's disease,²¹ and even disuse atrophy of post-thermal burn patients.^{22,23} Studies^{11,24-26} using isokinetic protocols for training hemiparetic stroke patients also exist. A literature review concluded that muscle strength and walking ability can be improved after isokinetic rehabilitation programs.¹¹ However, to our knowledge, no publications demonstrated the effects of isokinetic muscle strengthening in patients within 6 months of stroke attack until now.

Stroke is the result of ischemia and reperfusion injury, causing brain tissue damage due to apoptotic and necrotic cell death. Inflammatory response is activated at acute stage of stroke, leading to increased inflammatory cytokine level in plasma including interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- α), and lipoprotein(a). After series of rehabilitation program, the level of lipoprotein(a) can be decreased significantly.²⁷ Another study revealed significantly increased levels of Toll-like receptor-4 expression in rats that underwent middle cerebral artery occlusion. However, it was attenuated after treadmill running exercise training.²⁸ Because exercise after stroke has been proven to decrease the inflammatory cytokines in plasma, we are interested in whether different kinds of exercise, such as isokinetic and isotonic exercise in our study program, can influence the expression level of inflammatory cytokines. Overall, our study was the first one in the literature, which is designed to compare the effects of isokinetic and isotonic training on the muscle strength of the hemiparetic knee, walking performance, life quality, and inflammatory cytokine changes in patients within 6 months of stroke attack, and our result can provide valuable suggestions to health care providers regarding strengthening programs selection in subacute stroke patients.

Methods

Participants

The study was randomized controlled in design, which was registered and approved by the Institutional Review Board of Taichung Veterans General Hospital in Taiwan. Patients within 6 months of stroke attack were randomly assigned into 2 training groups: (1) isokinetic muscle strengthening group and (2) isotonic muscle strengthening group. The inclusion criteria were as follows:

(1) unilateral hemiparesis resulted from stroke within 6 months of attack and (2) capable of finishing the "Timed Up and Go test" (stand up from a chair, walk for 3 m, turn back to the original chair, and then, sat down without other's help throughout the whole process). The exclusion criteria included: (1) being overweight (body mass index >30); (2) lesions at lower limbs such as bony fracture that affect gait performance; (3) history of diabetic polyneuropathy; (4) history of cardiopulmonary diseases that posed higher risk during strenuous exercise; (5) impaired cognition that cannot obey isokinetic assessment and strengthening; and (6) had any infectious diseases that cause elevated plasma inflammatory cytokine level during the study period. Informed consents were obtained from each patient, and inclusion/exclusion criteria were checked before starting assessment and training programs.

Outcome Measures

Before the beginning of the 4 weeks of muscle strengthening program, outcome measures were assessed for each participant as following: (1) the peak torque of isometric flexion and extension of bilateral knees at 90° of flexion; (2) the peak torque of isokinetic flexion and extension of bilateral knees at angular velocity 60°/second and 120°/second, the previously mentioned 2 parameters were measured by Biodex dynamometer; (3) SF-36 subdomain scores including physical functioning, role limitations due to physical health, pain, general health condition, energy/fatigue, social functioning, role limitations due to emotional problems, emotional well-being, and total SF-36 score; (4) the Timed Up and Go test: stand up from a chair, walk for 3 m, turn back to the original seat, and then sit down. Participants can use assistive devices, which they used to walk with; and (5) the plasma level of inflammatory cytokines including high sensitivity C-reactive protein, IL-6, and TNF- α . The previously mentioned outcome measures were assessed before and after the 4 weeks of strengthening training program.

Intervention

Participants in both groups received the same program for poststroke rehabilitation, including electrical stimulation at the hemiparetic limbs, gait training, trunk balance training, stretching exercise, and task-orientated functional training for activity of daily life. The only difference between the 2 groups lied in the muscle strengthening program.

Experimental Group

The program of the experimental group consisted of 3 sets of isokinetic strengthening exercise. Each set included 5 times of isokinetic knee concentric flexion/concentric extension and 5 times of knee eccentric

extension/eccentric flexion at 60°/second. During the training period, we encouraged the participant to do his best continuously by oral commands. Furthermore, the peak torque graph on the monitor of Biodex dynamometer was shown to the participant as a kind of visual biofeedback to ensure his best performance. The program was performed 3 sets per day, 5 days per week, and continued for a total of 4 weeks.

Control Group

The program of the control group was composed of 3 sets of isotonic strengthening programs. The isotonic resistance was set at 60% of the maximal isometric flexion and extension peak torque at 90° flexion of bilateral knees. One set of isotonic strengthening exercise included 10 repetitions of isotonic knee flexion and extension. The training schedule was the same as the isokinetic training group, which being 3 sets per day, 5 days per week, and a total of 4 weeks.

Data Analysis

Predictive Analytics SoftWare (PASW version 18.0, Chicago, IL) was used for statistical analysis in our study. We performed chi-square test and Mann–Whitney *U* test to determine the difference of basic characteristics between the experimental and control groups. The Wilcoxon signed-rank test was then used to examine the statistical significance of improvement after 4 weeks of strengthening training program in both groups. Finally, Mann–Whitney *U* test was done to determine if there was significant difference in the degree of improvement between the 2 groups. *P* less than .05 was considered statistically significant in our study.

Results

A total of 31 participants entered our study. Seven of them were not able to complete the 4 weeks of training program and were excluded from our study. One quitted because he felt the training program was too exhausting. Two of them were excluded because of the upper respiratory tract infection, and 4 of them were excluded because of their personal reasons resulting in incomplete training programs. The baseline characteristics of the remaining 24 patients were shown in Table 1. No significant differences in participants' age, gender, hemiparetic side, etiology, lesion location, and duration from the stroke onset were noted between the experimental and control groups.

After 4 weeks of isotonic strengthening training, significant improvements were noted in parameters including the isometric flexion peak torque and the isokinetic flexion peak torque at 120°/second of the nonparetic side of knee, physical functioning in SF-36, Timed Up and Go test, and IL-6 plasma level. The result was shown in Table 2.

Table 1. Baseline characteristics of the participants of our study

Baseline Characteristics	Isotonic group	Isokinetic group	<i>P</i> value
Age, y, mean ± SD	67.1 ± 11.9	64.7 ± 13.5	.713*
≥65	8	6	.68
<65	4	6	
Gender			
Male	6	7	1
Female	6	5	
Hemiparetic side			
Right	6	6	1
Left	6	6	
Etiology			
Ischemic stroke	3	1	.829
Hemorrhagic stroke	2	2	
Lacunar infarction	7	9	
Lesion location			
Lobar	3	2	.641
Basal ganglia	4	7	
Thalamus	4	3	
Pons	1	0	
Duration from the onset, mo	3.16 ± 1.59	3.24 ± 1.36	.795*

Abbreviation: SD, standard deviation.

*Mann–Whitney *U* test; chi-square test for all other *P* values.

Comparing with the isotonic strengthening group, there were more parameters that showed statistically significant improvement in the isokinetic strengthening group. The data were shown in Table 3. All the parameters regarding knee strength improved significantly after 4 weeks of isokinetic training. Furthermore, the score of physical functioning, physical subdomain, and total SF-36 also showed significant improvements. The result of Timed Up and Go and plasma level of IL-6 and TNF- α also improved significantly.

Despite much more items showed significant improvement in the isokinetic training group comparing with the isotonic training group, there were no significant differences in the degree of improvement between the 2 groups. As shown in Table 4, only the peak torque of isokinetic flexion at 60°/second and 120°/second at hemiparetic knee showed statistically significant difference between them (*P* < .05).

Discussion

This is the first randomized controlled study evaluating the influence of the mode of muscle strengthening training in walking performance, quality of life, and inflammatory cytokines reduction in stroke patients within 6 months of onset. The benefits of resistance muscle training in stroke patients without spasticity aggravation

Table 2. Comparison of parameters between before and after isotonic strengthening program for 4 weeks

Outcome measures	Before training	After training	P value
Isometric extension torque (lesion side)	44.7 ± 24.1	54.5 ± 26.2	.071
Isometric flexion torque (lesion side)	21.5 ± 18.8	26.6 ± 23.2	.071
Isokinetic extension torque at 60°/s (lesion side)	32.1 ± 20.4	39.9 ± 21.3	.695
Isokinetic flexion torque at 60°/s (lesion side)	18.2 ± 9.9	23.0 ± 13.1	.182
Isokinetic extension torque at 120°/s (lesion side)	25.9 ± 18.9	32.3 ± 12.0	.158
Isokinetic flexion torque at 120°/s (lesion side)	18.9 ± 10.6	22.1 ± 10.8	.084
Isometric extension torque (sound side)	66.5 ± 30.4	75.0 ± 30.1	.099
Isometric flexion torque (sound side)	33.4 ± 17.8	37.2 ± 18.1	.012*
Isokinetic extension torque at 60°/s (sound side)	52.8 ± 23.5	54.9 ± 21.2	.594
Isokinetic flexion torque at 60°/s (sound side)	32.3 ± 13.7	34.9 ± 11.9	.17
Isokinetic extension torque at 120°/s (sound side)	41.2 ± 18.5	47.5 ± 21.9	.071
Isokinetic flexion torque at 120°/s (sound side)	31.3 ± 13.7	34.7 ± 12.7	.034*
Physical functioning	27.9 ± 19.2	41.7 ± 21.6	.003*
Role limitation due to physical health	8.3 ± 28.9	5.2 ± 14.6	.655
Pain	59.6 ± 24.7	58.9 ± 27.1	.959
General health	41.3 ± 10.5	41.7 ± 14.7	.952
Physical subdomain	34.3 ± 13.7	41.7 ± 21.6	.326
Energy/fatigue	46.7 ± 7.5	48.8 ± 10.7	.377
Social functioning	41.8 ± 13.4	38.5 ± 18.0	.111
Role limitation due to emotional problems	5.6 ± 19.2	5.2 ± 14.6	.066
Emotional well-being	50.7 ± 15.6	55.3 ± 11.8	.083
Mental subdomain	36.2 ± 10.9	40.5 ± 12.7	.053
Total SF-36 score	35.2 ± 9.6	38.7 ± 10.3	.064
Timed Up and Go	22.9 ± 10.7	17.9 ± 8.8	.019*
hsCRP	.6 ± .3	.4 ± .2	.06
IL-6	7.6 ± 1.9	4.7 ± 3.8	.023*
TNF- α	.8 ± .4	.7 ± .5	.53

Abbreviations: IL, interleukin; SF-36, Short Form 36; TNF, tumor necrosis factor; hsCRP, high sensitivity C-reactive protein.

* $P < .05$.

have been mentioned by previous studies.^{26,29,30} From the results of our study, the improvements in walking performance, life quality, and inflammatory cytokine reduction after both kinds of strengthening programs were revealed. Although the isotonic group provided strength and life quality improvement in fewer items, there were nearly no statistically significant differences in the change of improvement between the 2 groups. Kim et al²⁵ also discovered improvements in lower limbs strength and walking speed in both the isokinetic and control training groups. It is worth noticing that Kim et al used only passive range of motion as the training protocol in their control group, and the change of improvements still cannot achieve significant difference. The control group of our study used isotonic strengthening program, but also got similar result as the study by Kim et al. It is probably because the short training period could not differentiate the difference between the 2 groups. One study revealed that 3 weeks of isokinetic training could not acquire significant improvement in hip muscle strength, gait speed, stairs climbing speed, and performance in Timed Up and Go test, but 6 weeks

of training could.³¹ Furthermore, the small sample size may also contribute to it.

In our study, significant improvement in Timed Up and Go test was noted in both the experimental and control group. The result is contradictory to the study by Sharp and Brouwer,²⁶ which revealed improvement in neither Timed Up and Go test nor stairs climbing ability after 6 weeks of isokinetic training. There may be 2 reasons to explain the difference. First, study by Sharp and Brouwer recruited chronic stroke patients beyond 6 months of onset, whereas our study focused on subacute stroke patients within 6 months. The recovery of limbs function may be faster in those subacute stage of stroke patients recruited in our study under the training of isokinetic dynamometer. Second, the training program in the study by Sharp and Brouwer consisted of isokinetic training 3 days/week for 6 weeks, whereas our study provided more concentrated training protocol within 4 weeks. The higher frequency of training may also contribute to the better improvement in Timed Up and Go test. In our study, the difference between the 2 groups was not statistically different. It is probably

Table 3. Comparison of parameters between before and after isokinetic strengthening program for 4 weeks

Outcome measures	Before training	After training	P value
Isometric extension torque (lesion side)	73.0 ± 44.2	85.5 ± 47.2	.031*
Isometric flexion torque (lesion side)	21.2 ± 14.7	30.4 ± 20.2	.007*
Isokinetic extension torque at 60°/s (lesion side)	50.6 ± 34.8	66.7 ± 35.0	.006*
Isokinetic flexion torque at 60°/s (lesion side)	25.6 ± 17.7	37.7 ± 17.5	.002*
Isokinetic extension torque at 120°/s (lesion side)	36.0 ± 24.3	49.6 ± 27.8	.003*
Isokinetic flexion torque at 120°/s (lesion side)	24.1 ± 13.7	33.6 ± 16.6	.004*
Isometric extension torque (sound side)	101.3 ± 48.9	118.4 ± 47.4	.019*
Isometric flexion torque (sound side)	44.1 ± 21.4	53.6 ± 24.6	.005*
Isokinetic extension torque at 60°/s (sound side)	86.2 ± 45.4	97.2 ± 40.5	.011*
Isokinetic flexion torque at 60°/s (sound side)	46.1 ± 25.1	61.2 ± 26.7	.023*
Isokinetic extension torque at 120°/s (sound side)	61.6 ± 34.5	71.0 ± 35.3	.023*
Isokinetic flexion torque at 120°/s (sound side)	40.8 ± 21.6	47.2 ± 19.8	.008*
Physical functioning	33.8 ± 26.3	51.7 ± 24.6	.004*
Role limitation due to physical health	0 ± 0	8.3 ± 16.3	.102
Pain	64.9 ± 22.5	65.5 ± 20.8	.678
General health	50.4 ± 17.9	46.7 ± 17.4	.217
Physical subdomain	37.3 ± 12.6	43.2 ± 12.5	.037*
Energy/fatigue	46.7 ± 20.9	53.8 ± 21.7	.153
Social functioning	48.5 ± 15.7	49.6 ± 12.1	.886
Role limitation due to emotional problems	27.8 ± 44.6	36.1 ± 43.7	.18
Emotional well-being	57.7 ± 17.3	57.6 ± 18.2	.878
Mental subdomain	45.2 ± 20.2	49.3 ± 20.2	.136
Total SF-36 score	41.2 ± 13.9	46.3 ± 14.5	.041*
Timed Up and Go	23.1 ± 11.5	14.3 ± 6.5	.01*
hsCRP	.8 ± .2	.5 ± .2	.019
IL-6	5.7 ± 3.7	2.3 ± 1.6	.002*
TNF- α	1.3 ± .9	.6 ± .5	.003*

Abbreviations: hsCRP, high sensitivity C-reactive protein; IL, interleukin; SF-36, Short Form 36; TNF, tumor necrosis factor.

* $P < .05$.

because that the Timed Up and Go test challenges many aspects of body functions, including muscle strength, power, endurance, balance, proprioception, coordination, and so forth. The trivial difference in strength gain between the 2 groups may be a relatively small factor contributing to the overall performance in Timed Up and Go test.

In our study, both the experimental and the control groups showed improved physical functioning in SF-36 scoring. The isokinetic group further brought improvement in the physical subdomain and total SF-36 scores. The result is different from study by Kim et al, which showed no significant SF-36 improvement in both the isokinetic and the control group.²⁵ The reason may also lie in the different study subjects' selection and the more concentrated training protocol in our study. Subacute stroke survivors with more intensive isokinetic training programs felt better in their physical functioning compared with chronic stroke patients with less intensive training protocol.

Our study demonstrated reduced IL-6 plasma level in both groups, and the isokinetic group further showed decreased TNF- α after 4 weeks of training. Past articles

mentioned the outcome prognostic ability of IL-6 in stroke patients,^{32,33} and 1 study also revealed the role of TNF- α in the mechanisms of early stroke-induced inflammation and a predictive value of outcome of stroke.³⁴ Despite the importance of IL-6 and TNF- α in stroke related inflammation, 1 past study did not discover significant reduction of IL-6 and TNF- α level in stroke patients undergoing rehabilitation,²⁷ which is different from our study result. The reason behind this phenomenon deserves further study to clarify.

Conclusion

Our study revealed the benefit of early strengthening exercise in poststroke patients compared with previous studies. Although the isotonic exercise showed less significant improvement in muscle strength, both modes of strengthening programs brought considerable benefits in complex motor function such as Timed Up and Go test and self-perceived quality of life regarding physical functioning. From the result of our work, we suggest early strengthening intervention as a necessary part of poststroke rehabilitation program. Isokinetic training, if

Table 4. Comparison of the improvement between the isotonic and the isokinetic strengthening program for 4 weeks

Outcome measures	Isotonic	Isokinetic	P value
Isometric extension torque (lesion side)	9.8 ± 17.6	12.5 ± 18.9	.41
Isometric flexion torque (lesion side)	5.1 ± 8.1	9.1 ± 13.6	.799
Isokinetic extension torque at 60°/s (lesion side)	7.8 ± 21.2	16.1 ± 16.1	.114
Isokinetic flexion torque at 60°/s (lesion side)	4.9 ± 9.5	12.1 ± 7.5	.039*
Isokinetic extension torque at 120°/s (lesion side)	6.3 ± 12.4	13.6 ± 10.9	.078
Isokinetic flexion torque at 120°/s (lesion side)	3.2 ± 5.5	9.5 ± 7.6	.017*
Isometric extension torque (sound side)	8.6 ± 14.2	17.2 ± 22.3	.114
Isometric flexion torque (sound side)	3.8 ± 4.9	9.5 ± 8.6	.06
Isokinetic extension torque at 60°/s (sound side)	2.7 ± 6.2	15.1 ± 27.6	.052
Isokinetic flexion torque at 60°/s (sound side)	2.7 ± 6.2	15.1 ± 27.6	.052
Isokinetic extension torque at 120°/s (sound side)	6.3 ± 10.9	9.4 ± 15.6	1
Isokinetic flexion torque at 120°/s (sound side)	3.4 ± 4.4	6.3 ± 7.9	.443
Physical functioning	13.8 ± 9.8	17.9 ± 10.3	.266
Role limitation due to physical health	−3.1 ± 15.2	8.3 ± 16.3	.319
Pain	−.7 ± 17.0	.5 ± 25.3	.59
General health	.4 ± 12.1	−3.8 ± 10.7	.319
Physical subdomain	2.6 ± 9.0	5.9 ± 8.1	.443
Energy/fatigue	2.1 ± 8.4	7.1 ± 19.6	.219
Social functioning	−3.3 ± 10.9	1.1 ± 15.6	.478
Role limitation due to emotional problems	13.9 ± 22.3	8.4 ± 20.8	.551
Emotional well-being	4.7 ± 8.5	−.1 ± 21.1	.242
Mental subdomain	4.3 ± 4.8	4.1 ± 16.0	.63
Total SF-36 score	3.5 ± 4.7	5.0 ± 11.1	.671
Timed Up and Go	−5.1 ± 5.5	−5.1 ± 5.5	.799
hsCRP	−.2 ± .3	−.2 ± .3	.671
IL-6	−2.9 ± 3.6	−3.3 ± 2.5	.977
TNF-α	−.1 ± 0.7	−.7 ± 0.9	.266

Abbreviations: IL, interleukin; SF-36, Short Form 36; TNF, tumor necrosis factor; hsCRP, high sensitivity C-reactive protein.

* $P < .05$.

feasible, can benefit this group of patients more in muscle strength performance.

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Supplementary Data

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