Turk J Phys Med Rehab 2024;70(1):115-122
DOI: 10.5606/tftrd.2024.12502
Available online at www.turkishjournalpmr.com

Original Article

Is the isokinetic strength of nonparetic lower limb related to fatigue in stroke survivors? A cross-sectional study

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ABSTRACT

Objectives: The study aimed to investigate the correlation between nonparetic knee muscle strength and fatigue in a cohort of stroke survivors.

Patients and methods: Thirty-two stroke survivors (17 females, 15 males; median age 62 (interquartile range [IQR] 51-69), (min: 45, max: 81) years were recruited in this cross-sectional study between January 2012 and September 2012. Sociodemographic, clinical, and stroke-related parameters were recorded. All participants underwent an isokinetic measurement of the nonparetic knee flexion and extension. Functional independence measure, functional ambulation category, and Mini-Mental State Examination scores were used to evaluate the functional status, ambulation, and mental status of the patients. Anxiety, depression, and fatigue severity were measured using the Hospital Anxiety and Depression Scale and fatigue severity scale (FSS), respectively.

Results: The median duration of stroke was 3.1 (IQR: 2.5-6.5) months. Stroke survivors with reduced muscle strength were older and had lower motor and total functional independence measure scores than those with normal strength (p=0.026, p=0.034, and p=0.034, respectively). There were more patients with lower functional ambulation category scores in the group with reduced muscle strength (p=0.023). Peak torque values of knee flexors at 60°/sec and 180°/sec correlated negatively with FSS (r= −0.360, p=0.043 and r= −0.452, p=0.009, respectively). There was also a negative correlation between the work of knee extensor and flexors at 180°/sec and FSS (r= −0.398, p=0.024 and r= −0.451, p=0.010, respectively). Anxiety and depression scores were not significantly correlated with fatigue.

Conclusion: The lower strength of nonparetic knee extensor muscles was related to greater disability and worse ambulatory scores. The lower strength of knee flexor muscles and the work of both knee muscles in the nonparetic limb were related to higher fatigue levels in stroke survivors. Therefore, fatigue management and strengthening of both knee flexor and extensor muscles in the nonparetic limb is emphasized during stroke rehabilitation.

Keywords: Fatigue, muscle strength, physical function, rehabilitation, stroke.

Stroke is one of the main causes of disability in developed countries, and 40% of stroke survivors suffer from moderate disability.[1] Stroke survivors present with several clinical manifestations, such as muscle weakness, spasticity, neglect, cognitive dysfunction, and physical limitations.[1-3] Balance ability and knee extensor strength are strong predictors of walking ability in subacute stroke.[4,5] To date, the isokinetic assessment is the gold standard method for measuring muscle strength after stroke.[6]

A lower muscle peak torque and insufficient force production are demonstrated in the paretic knee extensors of stroke survivors.[5,7-9] Weakness is also observed in the nonparetic extremity[7-9] and is the strongest determinant of exercise capacity in these patients.[8] Considering the pathophysiology of stroke, impaired neural activation might lead to weakness of both sides. Quadriceps muscle strength in nonparetic extremities may be reduced by 30% in the first week after stroke.[9] Besides, immobilization is

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Received: February 09, 2023 **Accepted:** August 07, 2023 **Published online:** February 01 , 2024

Cite this article as: Ozyemisci Taskiran O, Balevi Batur E, Kaymak Karatas G, de Sire A. Is the isokinetic strength of nonparetic lower limb related to fatigue in stroke survivors? A cross-sectional study. Turk J Phys Med Rehab 2024;70(1):115-122. doi: 10.5606/tftrd.2024.12502.

an important factor for reduced muscle strength and atrophy.[10] Gerrits et al.[11] observed lower torque values in both paretic and nonparetic knee extensors using an isokinetic system in 18 poststroke patients compared to healthy controls. They also assessed muscle fatigue during torque measurement in poststroke patients and found lower fatigue resistance in the paretic knee extensors but not in the non-paretic knee compared to healthy controls.[11]

Fatigue is a common symptom in poststroke patients that interferes with ambulation and might lead to a vicious cycle resulting in functional limitations.[12,13] Moreover, the impact of fatigue on reducing mobilization might play an additional role in the development of weakness in knee muscles.[14]

To the best of our knowledge, evidence about the correlation between the nonparetic lower limb isokinetic parameters and fatigue in poststroke patients is lacking. Our hypothesis was that stroke survivors with weaker knee muscles on the nonparetic side would have higher fatigue levels. Therefore, in this cross-sectional study, we sought to investigate the correlation between nonparetic knee muscle strength and related parameters including physical and mental fatigue in a cohort of stroke survivors.

PATIENTS AND METHODS

In this cross-sectional study, 65 stroke survivors who were consecutively admitted to the Physical Medicine and Rehabilitation Department of the Gazi University Faculty of Medicine between January 2012 and September 2012 were assessed for eligibility. After the evaluation, 32 patients (17 females, 15 males; median age 62 (interquartile range [IQR] 51-69), (min: 45, max: 81) years were included in the study. The flowchart is provided in Figure 1. The inclusion criteria were as follows: surviving a stroke; age ≥18 years; ability to understand and speak the Turkish language; ability to follow three-step commands; no contraindication for isokinetic assessments. The exclusion criteria were as follows: uncontrolled heart, pulmonary, renal, or thyroid disease, cancer, rheumatological disease, or other neurological disorders that may cause fatigue; severe cognitive or communication deficits preventing the completion of the questionnaires; systemic, musculoskeletal, or psychiatric disorders preventing isokinetic measurements. This study was performed in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[15]

Outcome measures

The following sociodemographic and clinical data were assessed: age, sex, educational and employment status, body mass index, type and duration of stroke, functional ambulation category (FAC),[16] functional independence measure (FIM), Mini-Mental State Examination, Hospital Anxiety and Depression Scale, and Brunnstrom stages.

All participants underwent an isokinetic measurement of the nonparetic knee flexion and extension via the Cybex 770 Norm (Lumex Inc., Ronkonkoma, NY, USA) dynamometer, following the protocols described in previous studies.[17-19] Each patient was seated with their trunk, pelvis, and thigh stabilized via straps; hip and knee joints were in 90° flexion initially. The mechanical axis of the dynamometer was aligned with the imaginary transverse line at the level of the femoral epicondyles. The lever arm was adjusted according to the leg length of the patient and secured with a strap proximal to the ankle joint. The weight of the tested leg was measured before the test, and the effect of gravity was adjusted by the dynamometer. Full extension of the knee was considered the anatomic zero position. Before the test, the subject-specific range of knee motion was measured by the dynamometer. The test started

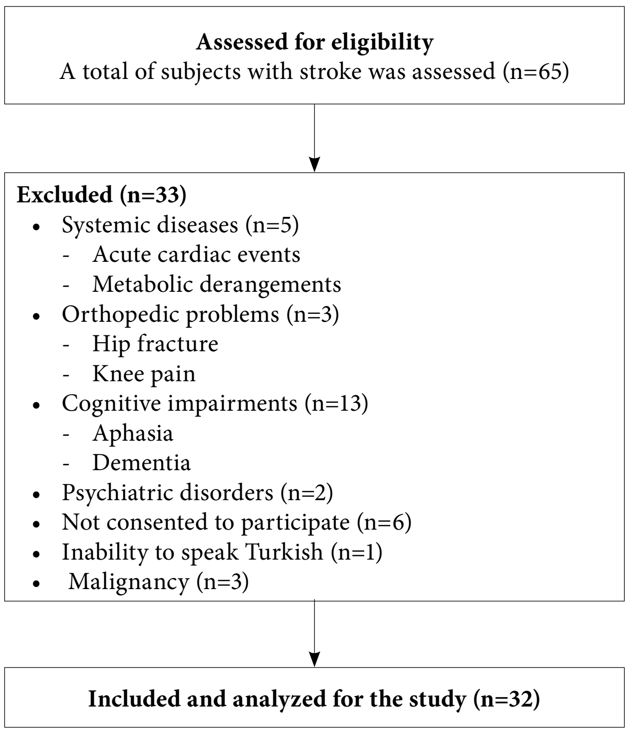

Figure 1. Flowchart of the study participants.

with knees fully flexed, and the first movement was extension (Figure 2).

Concentric knee flexion and extension were evaluated at 60°/sec and 180°/sec angular velocities. Before testing at each angular velocity, the patients were instructed about the test, and for familiarization, four submaximal contractions were performed. Following the practice contractions, a rest period of 10 sec was allowed before test trials. For strength measurements at 60°/sec angular velocity, patients were asked to perform five repetitions of knee flexion and extension with the maximum possible force. Following a rest period of 20 sec, strength measurements at 180°/sec angular velocity were recorded while the patients were asked to perform 20 repetitions of flexion and extension as fast as possible. Measurements were performed by the same investigator, and standard verbal encouragement was used. Weight-adjusted peak torque values were recorded in foot-pounds (FtLbs) and put into analysis. Total knee extension and flexion works (J) performed during the entire range of motion of each repetition were computed using the device's software.

Fatigue was measured using the fatigue severity scale (FSS)[20] and the fatigue impact scale (FIS).[21] Both scales are valid and reliable to measure fatigue in stroke patients. The FSS consists of nine items, each scored using a Likert-type scale ranging from 1 (strongly disagree) to 7 (strongly agree). The total score is the sum of these items divided by the number of items. A score ≥4 indicates fatigue, and high scores indicate high levels of fatigue. The FIS consists of 40 items: physical (10 items), cognitive (10 items), and psychosocial (20 items) impact of fatigue on the patient. Each item is scored using a Likert-type scale ranging from 0 (no issues) to 4 (extreme issues), and the maximum FIS score is 160.

Figure 2. A stroke survivor performing the isokinetic strength test of the nonparetic knee.

Statistical analysis

The sample size analysis was conducted using G*Power version 3.1 software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany). A priori sample size of 30 participants was estimated based on a previous study for a 0.94 effect size at the 0.05 alpha level with a power of 0.80.[14]

Statistical analysis was performed using IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Descriptive statistics were provided using median and interquartile range (IQR) or percentages. Participants were divided into two groups according to knee extension peak torque values at 60°/sec: survivors with reduced and normal isokinetic knee extensor strength. Cut-off values for knee extension strength for males and females were regarded as 94.5 Nm (70 FtLbs) and 62.3 Nm (46 FtLbs), respectively, which were shown to predict slow gait speed in older adults.[22] The chi-square test or Fisher exact test was used as appropriate to examine the differences between categorical variables of the groups. The Mann-Whitney U test was run to assess the difference between the continuous variables of the two groups. Spearman correlation coefficients were computed to analyze the relationship between peak torque values and all other parameters, including fatigue scores since the distribution of variables was non-homogenous. The statistical relationship between age and muscle strength and fatigue was tested using analyses of covariance. A p-value <0.05 was considered statistically significant.

RESULTS

The median duration of stroke was 3.1 (IQR: 2.5-6.5) months. The etiology of stroke was ischemic in 26 (81%) subjects and hemorrhagic in six (19%) subjects. The dominant hemisphere was affected in 14 (44%) patients. There was only one (3%) recurrent stroke. The median Mini-Mental State Examination score was 26 (IQR: 23.5-28.5). The median FIM total score was 89 (IQR: 75-112). Functional ambulation category grades were ≤3 in 16 patients. The median body mass index was 28.65 kg/m^2 (IQR: 24.54-31.22 kg/m^2).

TABLE 1
Median peak torque values of nonparetic knee flexion and extension at 60°/sec and 180°/sec angular velocities

	Participants (n=32)		
Variables	Median	IQR	Min-Max
Peak torque at 60°/sec			
Extension (FtLbs)	75	56	21-152
Flexion (FtLbs)	33	29	1-101
Peak torque at 180°/sec			
Extension (FtLbs)	38	26	12-69
Flexion (FtLbs)	20	18	6-48
Extension work (Joule)	778	651	179-1651
Flexion work (Joule)	245	324	6-1046

IQR: Interquartile range; PT: Peak torque; FtLbs: Foot-pounds.

Peak torque values of nonparetic knee flexion and extension are depicted in Table 1. Eleven (34%) patients had reduced knee extensors at 60°/sec. Stroke survivors with reduced muscle strength were older and had lower FIM motor and FIM total scores than those with normal strength. There were more patients with lower FAC scores in the group with reduced muscle strength. There were no statistically significant differences between the two groups regarding sex, systemic diseases, type, duration, and side of stroke, Brunnstrom stages, anxiety, depression, or fatigue scores compared to isokinetic data (Tables 2, 3).

When the patients were divided into two groups according to FAC grades (grades ≤3 and ≥4 in 16 and 16 patients, respectively). Age, body mass index, stroke duration, fatigue scores, depression, and anxiety scores were similar. Patients' knee flexor strength at 60°/sec and knee extensor work at 180°/sec were significantly higher in FAC grade ≥4 group (p=0.021 and p=0.043, respectively). Similarly, motor and total FIM scores were significantly higher in FAC grade ≥4 group (p<0.001).

Almost all peak torque and work values were correlated with age and motor subscores, cognitive subscores, and total scores of FIM, although the highest correlation coefficients were observed with the 60°/sec peak torque values (Table 4). Peak torque values were not correlated with FAC, except for knee flexors at 60°/sec (r=0.359, p=0.048). Flexion peak torque and work at 180°/sec were the two isokinetic parameters that had the highest correlation with FSS.

Regarding age as a confounding factor, univariate analysis of covariance showed that fatigue and muscle strength were not related to the participant's age (F(33,14)=0.93, p=0.688; F(33,14)=1.52, p=0.2, respectively).

TABLE 2
Comparison of continuous variables between participants with normal and reduced knee extensor strength at 60°/sec

	Reduced strength (n=11)		Normal strength (n=21)		
Variables	Median	IQR	Median	IQR	*p*
Age (year)	69	16	60	14	0.026
Duration of stroke (month)	3.8	4.9	3.1	1.7	0.798
MMSE	26.0	5.5	26.5	5.5	1.000
HAD-Anxiety	9	8	8	7	0.266
HAD-Depression	8	6	7	6	0.454
FIM					
FIM-motor	44	20	67	34	**0.034**
FIM-cognitive	30	5	35	0	1.000
FIM-total	74	23	102	34	**0.034**
FSS	5.3	1.2	4.9	3.5	1.000
FIS					
FIS-cognitive	14	14	13	17	1.000
FIS-physical	21	17	13	10	1.000
FIS-psychological	30	33	43	36	0.795
FIS-total	67	59	78	62	0.795

IQR: Interquartile range; MMSE: Mini-Mental State Examination; HAD: Hospital Anxiety and Depression Scale; FIM: Functional Independence Measure; FSS: Fatigue severity scale; FIS: Fatigue impact scale.

TABLE 3
Comparison of dichotomous variables between participants with normal and reduced knee extensor strength at 60°/sec

	Reduced strength (n=11)		Normal strength (n=21)		
Variables	n	%	n	%	*p*
Sex					0.712
Man	6	54	12	57	
Woman	5	46	9	43	
Marital status					0.667
Married	8	73	17	81	
Not married	3	27	4	19	
Employment status					0.272
Employed	0	0	4	19	
Unemployed	11	100	17	81	
Education years					1.000
8 years	8	73	14	67	
>8 years	3	27	7	33	
Stroke side					1.000
Dominant	5	46	9	43	
Non-dominant	6	54	12	57	
Etiology					0.637
Ischemic	10	91	16	76	
Hemorrhagic	1	9	5	24	
Brunnstrom, lower extremity					0.076
3	7	64	6	29	
≥4	4	36	15	71	
Brunnstrom, upper extremity					1.000
3	6	55	12	57	
≥4	5	45	9	43	
Brunnstrom, hand					1.000
3	6	55	12	57	
≥4	5	45	9	43	
FAC					**0.023**
3	9	82	7	33	
≥4	2	18	14	67	
Presence of systemic disease					
Diabetes mellitus	6	55	7	33	0.283
COPD	2	18	3	14	1.000
HT	11	100	17	81	0.272
HPL	3	27	10	48	0.450

FAC: Functional ambulation scale; COPD: Chronic obstructive pulmonary disease; HT: Hypertension; HPL: Hyperlipidemia.

DISCUSSION

This cross-sectional study demonstrated that peak torque values of nonparetic knee extensor muscles, particularly at 60°/sec velocity, significantly correlated with disability in a cohort of stroke survivors. The study also showed that both knee flexor and extensor works were negatively correlated with fatigue severity.

A negative correlation between the work performance of knee muscles and FSS may reveal the association between physical fatigue and muscle endurance. As work is a velocity-dependent parameter and high velocity is related to endurance,[23] the work capacity of knee muscles in these patients might be decreased in accordance with fatigue.

Lower rates of corticospinal tract excitability have been hypothesized as a possible mechanism underpinning central fatigue in poststroke patients, also affecting the nonparetic extremity.[24] Compensatory mechanism is another explanation, as the nonparetic limb is activated to compensate for the impaired motor function of the paretic limb, requiring greater energy, which might play a role in the reduction of

TABLE 4
Correlations between the isokinetic measurements and FIM, age, and fatigue

	Age	FIM total	FIM motor	FIM cognitive	FSS
Extension PT, 60°/sec					
r	-0.498	0.671	0.621	0.643	-0.207
p	0.004	<0.001	<0.001	<0.001	0.256
Flexion PT, 60°/sec					
r	-0.427	0.607	0.528	0.666	-0.360
p	0.015	<0.001	0.002	<0.001	0.043
Extension PT, 180°/sec					
r	-0.387	0.476	0.472	0.393	-0.169
p	0.029	0.007	0.007	0.029	0.356
Flexion PT, 180°/sec					
r	-0.464	0.397	0.335	0.426	-0.452
p	0.007	0.027	0.066	0.017	0.009
Extension work, 180°/sec					
r	-0.489	0.476	0.467	0.369	-0.398
p	0.004	0.007	0.008	0.041	0.024
Flexion work, 180°/sec					
r	-0.533	0.327	0.234	0.423	-0.451
p	0.002	0.072	0.205	0.018	0.010

FIM: Functional Independence Measure; FSS: Fatigue severity scale; PT: Peak torque.

muscle endurance.[25] The compensatory activation of the nonparetic limb often results in a longer duration of contraction, which might lead to decrease in muscle activity and eventually to fatigue.[26] The proportion of type 2 fibers in the rectus femoris muscle and hence its susceptibility to muscle fatigue is high. The amplitude in the rectus femoris of the nonparetic side, as well as the paretic side, increased over time during the single-support phase of a 20-min walk. This amplitude rise might be a result of increased recruitment of motor units for compensation for the reduced force of contraction.[26]

The downward spiral of physical inactivity, physical deconditioning, and subsequent avoidance of physically demanding activities might also contribute to muscle weakness in stroke. Harmsen et al.[14] reported that knee muscle weakness was more pronounced in survivors of subarachnoid hemorrhage with few or no neuromotor lesions. The authors attributed weakness to physical inactivity rather than neurological impairment. They found that patients with greater fatigue levels had lower flexor and extensor muscle strength at 60°/sec velocity.[14]

The results of our study also demonstrated a correlation between FSS scores and knee flexor strength of the intact side at both velocities but not with knee extensor strength. We suggest that it might be related to the predominance of the gait and mobility training in the rehabilitation programs that might lead to the main focus on extensor muscles. The greater involvement of knee extensors during rehabilitation and daily activities might activate neuroplasticity and some changes in the muscle fibers, making the extensors gain greater strength than that of flexors. Another explanation might be related to the stroke survivors being in the relatively acute-subacute period, which is different from other studies with longer duration of stroke.[11,24,25,27,28] In the earlier periods, stroke-related impairments and complications might have a greater impact on functioning than fatigue.

The negative correlation between knee flexor strength at both velocities and FSS scores in our findings might be explained by the relatively less representation of flexor strengthening exercises in rehabilitation programs and the resulting increase in susceptibility of knee flexor muscles to fatigue. The reduction in muscle mass and the cross-sectional area of muscle fibers and the increase in fatty infiltration of skeletal muscles that result from physical deconditioning developing between three weeks and six months after stroke in both paretic and nonparetic extremities may also contribute to this process.[29-31]

An electromyographic study investigating the contribution of nonparetic muscle activities during walking found that hamstring activity was increased during early stance. The authors explained that the increased hamstring activity might be compensation for reduced propulsion of the paretic extremity since hamstring activation enhances extension of the nonparetic leg and forward acceleration of the trunk.[32] This novel compensatory pattern of increased activation might be an explanation for the negative correlation between knee flexors and FSS scores.

A distinct quality of our study is that we assessed the strength of the nonparetic limb, which enabled the inclusion of stroke patients with lower ambulation capacity or lower muscle strength in the paretic limb who could not perform isolated knee extension and flexion with the paretic limb.

This study has some limitations. First, there is a potential selection bias since patients who were not able to perform isokinetic assessment were excluded. This could underestimate the relationship between muscle strength and fatigue. Moreover, we measured perceived fatigue and not performance fatigue. A physical and cognitive performance test evaluating fatigue would provide additional information about the objective impact of fatigue.

In conclusion, the findings of the present study suggest that the lower strength of nonparetic knee extensor muscles is significantly correlated with disability and worse ambulatory scores. Lower strength of knee flexors muscles and work of knee muscles in the nonparetic limb were related to higher fatigue severity in stroke survivors. Therefore, fatigue management and strengthening of both knee flexors and extensor muscles in the nonparetic limb, as well as the paretic limb, might help in the complex rehabilitative framework of stroke survivors.

Acknowledgements: The authors would like to thank to Mustafa Cengiz, MD for the support to this study.

Ethics Committee Approval: The study protocol was approved by the Gazi University Faculty of Medicine Local Ethics Committee (date: 01.06.2009, no: 304). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Study conceptualization and design: O.O.T., G.K.K.; Data acquisition: O.O.T., E.B.B., G.K.K.; Data analysis and interpretation: O.O.T., A.S.; Literature research: E.B.B., G.K.K.; Writing first draft: O.O.T., E.B.B., G.K.K.; Revision first draft: A.S.; Submission: E.B.B.; Supervision: O.O.T., A.S.; Revision and approval of the final draft by all the authors.

Conflict of Interest: The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding: The authors received no financial support for the research and/or authorship of this article.

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