Clinical Paper

Force Generation and Muscle Activation of Knee Extensor and Flexor Muscles in Type 2 Diabetes Mellitus Patients

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is associated with decreased muscle force generation. The disturbed force generation process in T2DM could be attributed to either or both agonist and antagonist muscles activation. The present study aims to assess the effects of T2DM on the interaction of antagonist and agonist muscles in the knee joint. **Methods:** The peak torque, root mean square (RMS) of the SEMG signals, the ratio of torque/RMS, and the interaction of antagonists and agonist muscles were compared between healthy and T2DM patients. Surface ElectroMyoGraphy (SEMG) of knee flexor and extensor muscles were recorded during concentric contraction with an isokinetic dynamometer at 60°/s in 13 T2DM and 12 healthy subjects. The independent sample *t*-tests were used to compare diabetic and healthy subjects. The significance level was set at 0.05. **Results:** The antagonist/agonist interaction during maximal extension (P = 0.010) and flexion (P = 0.022) torques of the knee joint showed significantly lower activation of antagonist muscles in T2DM patients than in healthy subjects. Lower knee flexion (41.3%) and extension torques (49.1%) and RMS of agonist and antagonist muscles were observed in T2DM. The torque/RMS ratio (P > 0.05) showed no significant differences in T2DM and healthy subjects. **Conclusion:** The reduced maximal knee flexor and extensor torques in T2DM are accompanied with the decreased myoelectric activity of corresponding muscles. The related mechanism could be attributed to lower values of antagonist/agonist interaction, which may point out some neural compensatory processes to preserve the functional capacity of the neuromuscular system in T2DM.

Keywords: *Force generation, muscle activation, type 2 diabetes mellitus*

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Introduction

Type 2 diabetes mellitus (T2DM) is associated with a gradual loss of muscle strength and power.[1] Decreased muscle strength is a risk factor for functional activities and may decrease the quality of life in T2DM.[2,3] Functional capacity results from the function of neuromuscular system,[4,5] that is the force-generating capacity of muscles, the activation of muscles by the neural system, and the tuning of agonistic and antagonistic muscle activation. In people with T2DM, the functional capacity of the neuromuscular system is impaired,[6] various studies investigated impairments at different levels.[7-10]

Numerous studies reported reduced muscle strength and maximal joint torques in T2DM.[11-13] Other studies focused on impaired bioelectrical activities of agonist muscles during the maximal or submaximal joint torque generation in T2DM.[14-17] Decreased agonist activation during maximal force production in T2DM has been well demonstrated.[9,13,16] The resultant joint torques are the effect of the mechanical interaction of antagonistic and agonistic muscles. The antagonist and agonist interaction is regulated with the neural strategy of the movement.[18] The magnitude of antagonist and agonist co-contraction during force production is modified in older adults.[19] Despite the pathophysiological changes of the neuromuscular system that arise by T2DM,[6] the magnitude of bioelectrical activities of antagonistic and agonistic muscles during force production is not well documented.

To measure the co-contraction of agonistic and antagonistic muscles, the surface

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electromyographic (SEMG) of these muscles can be extracted during joint torque generation.[18] The ratio of bioelectrical activities of antagonistic-to-agonistic muscles is a measure for the antagonist/agonist interaction. The co-contraction level provides an indirect estimation of neuromuscular system capacities and characterizes the neuromuscular deficient.[20] We hypothesized that T2DM-related adaptations in the co-contraction of agonistic and antagonistic muscles play a role in the reduced joint torques observed in people with T2DM. Hence, the main goal of the present study was to assess differences in antagonist/agonist interaction of knee flexor and extensor muscles during maximal contraction between short-term T2DM patients and healthy participants.

Materials and Methods

Thirteen T2DM patients (mean ± standard deviation [SD]: age 55.0 ± 6.5 years, weight 79.4 ± 11.5 kg, height 167.0 ± 8.0 cm, body mass index 28.3 ± 3.3 kg/m², duration of T2DM 6.8 ± 2.1 years, and 58% men) and 12 nondiabetic healthy, well-matched subjects (mean ± SD: age 50.4 ± 6.4 years, weight 77.3 ± 8.7 kg, height 166.0 ± 8.0 cm, body mass index 27.8 ± 1.7 kg/m², and 58% men) participated in this study. T2DM was clinically diagnosed by an endocrinologist. All patients suffered from T2DM for 4 to 10 years. All patients used oral medications to control diabetes. The T2DM subjects had fasting blood sugar (FBS) between 110 and 150 mg/dl and 2 h after taking 75-g glucose, the oral glucose tolerance test (OGTT) was more than 200 mg/dl. The glycated hemoglobin (HbA1c) was between 7% and 9%.

The well-matched control group had FBS <100 mg/dl, OGTT <130 mg/dl, and HbA1c <5.7%. The Michigan Questionnaire Score, to examine peripheral neuropathy, ranged between 4 and 7 scores for both control and T2DM groups. None of the subjects suffered from central or peripheral neurological or orthopedic diseases, retinopathy, foot ulcers, renal failure, hepatic, respiratory, or cardiovascular diseases. There was no history of regular or professional exercise during the last 6 months. There was no history of drug and alcohol addiction and smoking. If autonomic neuropathy symptoms emerged during tests, participants were excluded from the study. All testing protocols were approved by Tarbiat Modares University ethics committee. All volunteers filled out an informed consent form before participation in the study.

Peak torque evaluation

The knee flexor and extensor concentric peak torques of the dominant leg were evaluated by an isokinetic dynamometer (HUMAC NORM 2009). All participants were asked to flex and extend their knee joint over a range from 0° flexion to 90° of knee flexion (full extension of the knee joint represented 0°). The velocity of isokinetic concentric contraction was adjusted at 60°/s. The tests were performed at the seated position with 90° flexion of hip and knee joints and the ankle was placed at the neutral position. The axis of rotation of the isokinetic dynamometer was aligned with the frontal axis of the knee. The ankle pad was placed above the lateral malleolus. To produce the maximal effort during tests, visual and verbal feedback were given to encourage to generate maximal knee extensor and flexor contraction. The test protocol included five isokinetic concentric contractions with 6 s hold and 120 s rest between each repetition to prevent fatigue. The normalized maximum values of knee extensor and flexor peak torques to weight were considered the test values.

Surface electromyography evaluation

A bipolar multichannel SEMG amplifier (Bayamed Co.www.bayamed.com 2016) was used to record the SEMG activity. SEMG activities of knee flexor muscles including biceps femoris (BF) and medial hamstring (MH) and knee extensor muscles including vastus lateralis (VL), vastus medialis oblique (VMO), and rectus femoris (RF) were recorded during maximal concentric contraction of knee flexor and extensor muscles. Before attaching the SEMG electrodes, the skin was shaved and abraded with alcohol. Pairs of disposable Ag-Ag/Cl electrodes (20 mm inter-electrode distance) were positioned according to Surface Electromyography for the NonInvasive Assessment of Muscles recommendation. The ground electrode was attached to the lateral malleolus of the other leg.

Raw SEMG signals were recorded at a sampling frequency of 1000 Hz during maximal isokinetic concentric contraction. A bandpass filter with low and high cutoff frequencies of 20 and 500 Hz was used. The SEMG signals and isokinetic dynamometer were temporally synchronized with a digital switch and LabVIEW software.[21] The root mean square (RMS) value of the SEMG signals of knee flexor and extensor muscles during isokinetic concentric contraction was calculated and considered the amplitude indicator. The maximal RMS value of five repetitions was considered SEMG output. The RMS values were normalized to isometric maximal voluntary contraction values.[22]

Torque to root mean square Ratio

The proportion of the produced force to the amplitude of SEMG signals could be an estimation of neuromuscular system efficiency.[23] The torque-to-RMS ratio of knee extensor muscles (Torque/RMS_{EXT}) is calculated by dividing the isotonic extension peak torque (PT_{EXT}) by the mean of the RMS of knee extensor muscles. The torque-to-RMS ratio of knee flexor muscles (Torque/ RMS_{EXT}) is obtained from deviation of the isotonic flexion peak torque (PT_{EXT}) by the mean of the RMS of knee flexor muscles.

$$Torque/RMS_{EXT} = PT_{EXT}/\overline{x}\, RMS_{VL+VMO+RF} \quad (1)$$

$$Torque/RMS_{FLEX} = PT_{FLEX}/\bar{x}\,RMS_{BF+MH} \quad (2)$$

Where PT is peak torque, $\bar{x}\ RMS_{VL+VMO+RF}$ is the mean of the RMS of VL, VMO, and RF muscles, $\bar{x}\ RMS_{BF+MH}$ is the mean of the RMS of BF and MH muscles.

Antagonist-to-agonist interaction

Antagonist-to-agonist interaction (AAI) is the ratio of the amplitude of SEMG activity of the antagonist muscles to the agonist muscles during force production.[24] AAI_{EXT} is calculated by the ratio of the mean of the RMS of knee flexor muscles to the mean of the RMS of knee extensor muscles. Furthermore, the ratio of the mean of RMS of knee flexor muscles to the mean of the RMS of knee extensor muscles represents the AAI_{FLEX}.

$$AAI_{EXT} = \bar{x}\,(RMS_{BF} + RMS_{MH})/\bar{x}\,(RMS_{VL} + RMS_{VMO} + RMS_{RF}) \quad (3)$$

$$AAI_{FLEX} = \bar{x}\,(RMS_{VL} + RMS_{VMO} + RMS_{RF})/\bar{x}\,(RMS_{BF} + RMS_{MH}) \quad (4)$$

Where $\bar{x}\,(RMS_{BF} + RMS_{MH})$ represents the mean of the RMS of BF and MH muscles, $\bar{x}\,(RMS_{VL} + RMS_{RF})$ is the mean of the RMS of VL, VMO, and RF muscles.

Data analysis

We performed independent sample *t*-tests to compare the demographics and peak joint torques and neuromuscular variables between diabetic and healthy subjects. The significance level was set at 0.05.

Results

Knee extension peak torque (49.1%) and knee flexion peak torques (41.3%) in T2DM subjects were significantly lower than in healthy subjects. RMS of agonist muscles including VL (P = 0.040), vastus medialis oblicus (VMO) (P = 0.009), BF (P = 0.035), and MH (P = 0.001) in participants with T2DM was significantly lower than those in healthy subjects; RMS of RF did not differ significantly between both groups of participants [Table 1 and Figure 1a]. The RMS of antagonist muscles including VL (P = 0.005), vastus medialis (P = 0.001), RF (P = 0.014), BF (P = 0.001), and MH (P = 0.001) during knee flexion and extension was significantly lower in T2DM than healthy subjects [Table 1 and Figure 1b]. The torque/RMS ratio of knee extensor and flexor muscles in T2DM and healthy subjects showed no significant differences [Table 1]. The antagonist/agonist interactions during maximal knee extension (P = 0.010) and knee flexion (P = 0.022) in T2DM participants were significantly lower than in healthy subjects.

Discussion

The results showed that the maximal knee extension and flexion torques and the RMS of the knee flexor and extensor muscles in T2DM were significantly lower than in healthy participants. In line with the current study results, previous studies showed that T2DM patients have lower values of knee flexor and extensor peak torques.[12] Hatef *et al*. showed that lower RMS of agonist muscles is correlated with reduced peak torque in T2DM.[14] The present study results showed that the bioelectrical activity of all knee flexor and extensor muscles in T2DM is less than in healthy subjects except for the activation of the RF. The RF is a biartricular, small, and pinnate muscle which may represent different patterns of electromyography activity.[25] Figure 1a and b show the contribution of agonist and antagonist muscles activity during knee extension and flexion torques. The antagonist muscles activation showed lower RMS in T2DM than in healthy subjects, and no specific pattern of changes between muscles was observed. The results suggest that possibly no discriminate of muscles specific adaptations in T2DM patients occurred.

To answer the question of whether any changes in joint torques are proportional to muscular activation, the ratio of torque/RMS of the agonist muscles was calculated. The proportion of maximal torque to the amplitude of muscular bioelectric activity provides an indirect estimation of neuromuscular system efficiency.[26] Decreased neuromuscular efficiency is attributed to neural and muscular degenerative changes in T2DM.[6] The results showed no significant changes in the torque/RMS ratio of knee extensor and flexor muscles between T2DM and healthy subjects. Preserved torque/RMS ratio in T2DM could be attributed to the absence of neuropathy symptoms and/or short duration of suffering from T2DM in the present study and/or intervention of neural compensatory mechanisms[10] such as agonist/antagonist co-contraction.[27]

Inability to generate maximal torque is attributed to agonist muscles deactivation.[28] In addition, the interaction of agonist and antagonist muscles may interfere in the resultant torque.[29] The primary outcome of the present study showed that the antagonist/agonist interactions of knee flexion and extension in T2DM were lower than in healthy subjects. Indicating that in T2DM, the antagonists to a lesser extent counteract the effect of the agonistic muscles. Figure 2 illustrates that the reduced antagonist/agonist interaction of knee flexor and extensor muscles in T2DM results from a decreased agonist activation and an even more decreased antagonist activation. Billot *et al*. (2014) indicated that a higher decline of antagonists muscles activation is necessary to maintaining maximal torque.[20] Błażkiewicz *et al*. showed that activation of antagonist muscles in the ankle joint during the maximal effort of agonist muscles is decreased in T2DM patients. They indicated that the central nervous system may modulate the antagonist/agonist

Table 1: Knee extension and flexion peak torques, root mean square of agonist muscles, root mean square of antagonist muscles, ratio of torque/root mean square of knee extensor and flexor muscles, antagonist/agonist interaction of knee extension and flexion

Variables (units)	Mean±SD		Exact *P*
	Healthy control group	T2DM group	
PT_{EXT} (%)	283.58±41.55	144.31±9.87	0.000
PT_{FLEX} (%)	196.42±52.21	115.31±27.17	0.000
RMS of agonis muscles (a.u.)			
VMO	99.18±27.29	82.32±19.88	0.040
VL	99.12±28.02	80.02±26.49	0.009
RF	96.24±31.48	92.15±23.42	0.521
MH	96.04±32.12	76.54±35.66	0.035
BF	99.15±18.29	78.58±32.62	0.001
RMS of antagonist muscles (a.u.)			
VMO	48.75±12.50	35.18±10.85	0.001
VL	50.82±15.93	32.44±12.63	0.005
RF	47.70±20.15	28.08±14.37	0.014
MH	48.75±14.36	24.52±8.85	0.001
BF	45.64±18.52	23.36±9.05	0.001
Torque/RMS extension (%)	0.73±0.21	0.64±0.18	0.072
Torque/RMS flexion (%)	0.71±0.15	0.66±0.28	0.239
Antagonist/agonist interaction of knee extension (a.u.)	0.42±0.19	0.26±0.12	0.010
Antagonist/agonist interaction of knee flexion (a.u.)	0.38±0.13	0.25±0.09	0.022

RMS – Root mean square; VMO – Vastus medialis oblique; VL – Vastus lateralis; RF – Rectus femoris; MH – Medial hamstring; BF – Biceps femoris; SD – Standard deviation; PT_{EXT} – Extension peak torque; PT_{FLEX} – Flexion peak torque

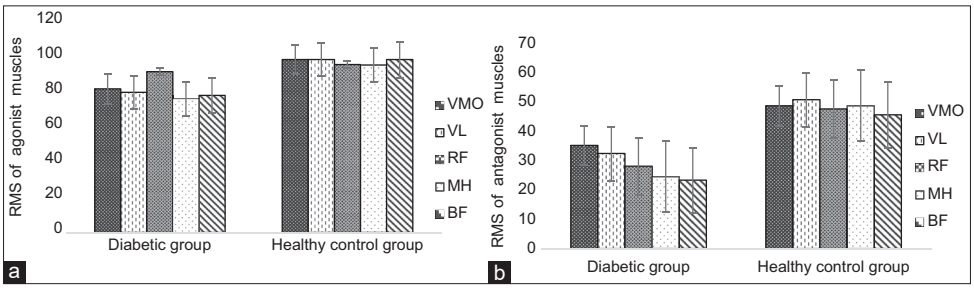

Figure 1: (a) RMS (a.u.) of knee extensor and flexor agonist muscles in healthy and T2DM, (b) RMS (a.u.) of knee extensor and flexor antagonist muscles in healthy and T2DM. VMO – Vastus medialis oblique; VL – Vastus lateralis; RF – Rectus femoris; MH – Medial hamstring; BF – Biceps femoris; RMS – Root mean square; T2DM – Type 2 Diabetes Mellitus

co-activation in T2DM patients to increase the ability of maximal force-generating.[27]

In contrast to the present study results, Petrofsky *et al*. and Kwon *et al*. showed higher agonist and antagonist co-contraction in the knee and ankle joints in diabetic patients during gait.[30,31] Required joint stability is responsible for increased agonist–antagonist co-contraction in T2DM during gait. This inconsistency with our results could be related to differences of the task properties and severity of force production. The magnitude of antagonist activation is dependent on the force level, accuracy, and velocity of movements.[32] Gait is a balance-challenging task, which requires joint stabilization. To facilitate stability and accuracy in gait, high co-activation of antagonist and agonist muscles is required.[33] Whereas the T2DM participants in the present study were assessed in a stable position which intended to achieve maximal force. We suppose antagonist muscle deactivation may occur to indemnify the decreased agonist muscle activation to reach the required maximal force in T2DM patients.

The muscle force generation could be affected by peripheral and central components of movement.[20,34] The peripheral components including sarcopenia, decreased muscle membrane excitability, and impaired contractile materials may lead to decrease resultant torque. The central control of movements including motor learning, synchronization, and antagonist/agonist interaction could modify the capacity of the entire activation of muscles. The antagonist/agonist interaction provides an indirect estimation of motor control strategies.[35] The antagonist activity during torque generating is preliminary controlled by the neural mechanism of movement.[36] Changed antagonist/agonist interaction in T2DM may modulate the efficacy of force production in these patients.[30] Hence, the

Table 2: Characteristics of similar previous studies

Authors (year)	Subjects (*n*)	Ages (years)	Methods	Results
IJzerman (2012)[12]	98 T2DM with DPN 39 T2DM with DPN 19 Healthy subjects	<50	Isometric and isokinetic lower limb muscle strength	Reduced muscle strength
Hatef (2016)[14]	30 T2DM 20 Healthy subjects	25-70	Isokinetic and EMG activity of knee flexor and extensor muscles	Reduced muscle strength
Blazkiewicz (2015)[27]	20 T2DM patients 20 Healthy subjects	50-68	Maximal isometric ankle plantarflexion and dorsiflexion	The agonist/antagonist muscle force ratio were significantly different for the healthy and the people with diabetes
Petrofsky (2005)[30]	25 Healthy subjects 15 T2DM patients 10 T1DM patients	40-70	Lower extremity EMG activity and joint moments during gait	Diabetic patients showed more agonist antagonist co-contraction of muscles activity during
Kwon (2003)[31]	9T2DM patients 9 Healthy subjects	35-79	Lower extremity EMG activity and joint moments during gait	Diabetic subjects showed more co-contractions of agonist and antagonist muscles at the ankle and knee joints during stance phase

EMG – Electromyography, T2DM – Type 2 diabetes mellitus, DPN – Diabetic peripheral neuropathy

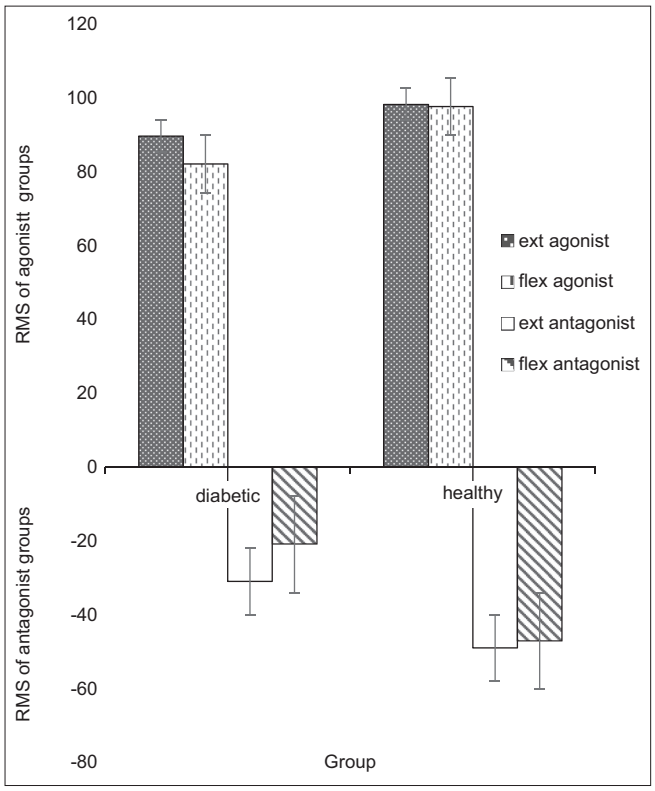

Figure 2: The mean ± SD of knee antagonist and agonist extensor and flexor muscles activation in diabetic and healthy subjects. SD – Standard deviation

reduced antagonist/agonist interaction may preserve the optimal function of the modified neuromuscular system in T2DM.[37]

The specification, methods, and results of similar previous studies are inserted in Table 2. The different results could be attributed to subject characteristics and methods differences, therefore, to generalize the present study results, the conditions of the experiment or the specifications of the subjects should be considered. The limitations of SEMG signals recording, processing, and analyzing may interfere with the results.[38] In addition, the biomechanical factor during knee flexion/extension movement including joint angle, gravity effect, muscle length, and momentum of arm may lead to misestimating of findings. To minimize the limitations effects, we normalized the SEMG signals, aligned the dynamometer axis with the axis of rotation of the knee joint, and normalized maximal torques to body weight. On the other hand, this study is one of few studies that investigate the mechanism of force production in T2DM patients. According to previous studies, the mechanism of muscle force generation in diabetic patients is defined by muscle strength and electromyography activities separately.[9,12,14] However, the analysis of the force generation mechanism often combines the EMG activity and kinesiology method.[39] The present study innovated an interaction method of bioelectrical muscle activity during muscle force production to estimate the force generation mechanism and muscle activation among T2DM patients.

Conclusion

T2DM patients have decreased resultant torque, lower antagonist/agonist interaction, decreased myoelectric activity of agonist muscle, and higher decreased of antagonist muscles activation. The modified antagonist/agonist interaction in T2DM patients may happen to compensate for insufficient activation of agonist muscles to preserve maximal force generation. The antagonist muscles deactivation may allow T2DM patients to increase their net joint torque to some extent. Although this study provided a preliminary insight into the co-contraction of antagonist and agonist muscles in T2DM, further study is required to explore the exact source of rescued muscle force in T2DM.

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Conflicts of interest

There are no conflicts of interest.

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