

## Original Article / Orijinal Makale

DOI: 10.4274/tftr.33239 Turk J Phys Med Rehab 2013;59:286-91 Türk Fiz Tıp Rehab Derg 2013;59:286-91

# **Evaluation of Muscle Strength and Fatigue Using Isokinetic Testing in Hypothyroid Patients**

Hipotiroidili Hastalarda Kas Kuvveti ve Yorgunluk Derecesinin İzokinetik Test ile Değerlendirilmesi

Mehmet Kerem UZUN, Nihal TAŞ\*, Jale MERAY\*, Mehmet ÇÖLBAY\*\*, İlhan YETKİN\*\*

Kahramanmaraş State Hospital, Physical Medicine and Rehabilitation Outpatient Clinic, Kahramanmaraş, Turkey

\*Gazi University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, Ankara, Turkey

\*\*Gazi University Faculty of Medicine, Department of Endocrinology and Metabolism, Ankara, Turkey

#### Summary

**Objective:** The present study aimed to evaluate the performance of knee muscles using an isokinetic dynamometer to determine muscle dysfunction in patients with newly diagnosed hypothyroidism, and to compare the results with that in a healthy control group.

**Materials and Methods:** Thirty patients diagnosed with subclinical hypothyroidism and 20 patients diagnosed with overt hypothyroidism, and 30 healthy volunteers were included in the study. A visual analogue scale (VAS) was used to determine the severity of fatigue. Using an isokinetic dynamometer, the peak torque values during knee flexion and extension were measured at angular velocities of 60°/s and 180°/s, and the total work were measured at the angular velocities of 180°/s.

**Results:** The mean VAS score in patients with overt hypothyroidism was significantly higher than that in those with subclinical hypothyroidism. The isokinetic peak torque values at the angular velocities of 60°/s and 180°/s for the quadriceps muscle and for the hamstring muscle was statistically significantly different in the overt and subclinical hypothyroidism groups than in the control group. The isokinetic total work at 180°/s was significantly different in the overt and subclinical hypothyroidism groups than in the control group. Although total work were higher in the subclinical hypothyroidism group, the differences were not statistically significant.

**Conclusion:** The lower muscle strength and endurance determined in overt and subclinical hypothyroid patients as compared to the controls suggest that myopathy occurs in the early stages of hypothyroidism and that it is a condition that should be evaluated at the time of diagnosis. **Key Words:** lookingtic testing hypothyroidism muscle dysfunction neak

Key Words: Isokinetic testing, hypothyroidism, muscle dysfunction, peak torque, muscle strength

#### Özet

Amaç: Çalışmamızda; hipotiroidi hastalarında kas disfonksiyonunu saptamak için diz kaslarının performansının, izokinetik dinamometre ile ölçülmesi ve sağlıklı kontrol grubu ile karşılaştırılması amaçlanmıştır.

**Gereç ve Yöntem:** Çalışmaya subklinik hipotiroidi tanılı 30, aşikar hipotiroidi tanılı 20 hasta ve 30 sağlıklı gönüllü dahil edildi. Yorgunluk şiddeti görsel ağrı skalasıyla (GAS) değerlendirildi. İzokinetik dinamometre ile 60°/sn ve 180°/sn'lik açısal hızda diz fleksiyon ve ekstansiyon pik torkları, 180°/sn'lik açısal hızda toplam iş değerleri ölçüldü.

**Bulgular:** Aşikar hipotiroidi grubundaki GAS değeri ortalaması subklinik hipotiroidi grubundan yüksek olup, fark istatistiksel olarak anlamlıydı. 60°/ sn ve 180°/sn açısal hızlarda kuadriseps ve hamstring kası izokinetik pik tork değerleri açısından aşikar ve subklinik hipotiroidi ile kontrol grubu arasında istatistiksel olarak anlamlı fark saptandı. Her iki açısal hızda subklinik hipotiroidi grubundaki pik tork değeri aşikar hipotiroidi grubundaki pik tork değerinden yüksek olmasına rağmen bu fark istatistiksel olarak anlamlı değildi. 180°/sn açısal hızda izokinetik total iş değerleri açısından aşikar ve subklinik hipotiroidi ile kontrol grubu arasındaki fark istatistiksel olarak anlamlıydı. Her iki kas için subklinik hipotiroidi grubunda total iş değeri aşikar hipotiroidi grubundaki total iş değerinden yüksek olmasına rağmen, bu fark istatistiksel olarak anlamlı değildi.

**Sonuç:** Aşikar ve subklinik hipotiroidi grubundaki hastaların kas kuvvetleri ve enduranslarının kontrol grubuna göre düşük bulunması miyopatinin hipotiroidinin erken evrelerinde ortaya çıktığını ve tanı anında değerlendirilmesi gerektiğini düşündürmektedir.

Anahtar Kelimeler: İzokinetik test, hipotiroidi, kas disfonksiyonu, pik tork, kas kuvveti

Address for Correspondence /Yazışma Adresi: Mehmet Kerem Uzun MD, Kahramanmaraş State Hospital, Physical Medicine and Rehabilitation Outpatient Clinic, Kahramanmaraş, Turkey Phone: +90 344 223 53 30 E-mail: drkeremuzun@hotmail.com

Received /Geliş Tarihi: April/Nisan 2012 Accepted/Kabul Tarihi: November/Kasım 2012

© Turkish Journal of Physical Medicine and Rehabilitation, Published by Galenos Publishing./© Türkiye Fiziksel Tıp ve Rehabilitasyon Dergisi, Galenos Yayınevi tarafından basılmıştır.

### Introduction

Neuromuscular deficits are commonly encountered findings in hypothyroid patients (1). It has been known for a long time that skeletal muscles are targets of thyroid hormone (2). Biochemical abnormalities such as a decrease in enzyme activities involved in energy production and accumulation of glycogen are observed in hypothyroid type I muscle fibers (3-5). The presence of T3 receptors on the mitochondrial membrane in skeletal muscles is indicative of a direct effect of thyroid hormones on oxidative metabolism (6). In hypothyroidism, the degree of mitochondrial damage is associated with the decreased activity of electron transport chain cytochrome complexes and key mitochondrial enzymes (7-9). In recent studies, metabolic, cardiovascular and neuromuscular alterations have also been reported in conditions in which there is no overt thyroid hormone deficiency. In these patients, it has been emphasized that a defective mitochondrial function together with an increase in lactate production during exercise is the responsible factor (10).

In their prospective study, Duyff et al. (11) reported neuromuscular symptoms in 75% of hypothyroid patients and in 67% of hyperthyroid patients and, they observed remission in these symptoms with treatment. The lack of a significant correlation between muscle weakness and biochemical severity of hypothyroidism suggests that hypothyroidism is associated with myopathy rather than functional muscle diseases (11).

In their study performed in 2009, Reuters et al. (12) reported that decreased muscle strength was frequent in patients with subclinical hypothyroidism, similar to that in patients with overt hypothyroidism, and they supported these findings by using electromyography (12).

Recently, the number of cases diagnosed with endocrine myopathies has been increasing. However, the true incidence and prevalence are unknown. While the female to male ratio is 5:1 in hypothyroid myopathy, this ratio is 1:1 in hyperthyroid myopathy. It has been reported that while the incidence of hypothyroid myopathy increases after the age of 40 years, hyperthyroid myopathy can be frequently observed between the ages of 20 and 60 years (13).

The present study aimed to evaluate the performance of knee muscles using an isokinetic dynamometer to determine muscle dysfunction in patients with newly diagnosed hypothyroidism, and to compare the results with that in a healthy control group.

#### Materials and Methods

We included 30 patients diagnosed with subclinical hypothyroidism and 20 patients diagnosed with overt hypothyroidism who were diagnosed based on laboratory findings and were attended the Endocrinology Outpatient Clinic at Gazi University Medical Faculty between July 01, 2009 and March 01, 2010. Thirty healthy volunteers without any disease comprised the control group. The inclusion criteria for the study were as follows: to be between 18 and 65 years of age, willingness to participate in the study, and having been diagnosed with subclinical and/or overt hypothyroidism. The exclusion criteria for the study were as follows: having received thyroid hormone replacement therapy within the last 1 year, presence of any other disease causing muscle weakness, presence of any contraindication to isokinetic testing (advanced osteoporosis, joint instability, fractures, joint or bone malignancy, severe peripheral vascular disease, pregnancy,

uncontrolled and symptomatic heart disease, severe restriction in joint movements), presence of any end-stage organ failure, presence of peripheral neuropathy, cerebrovascular event, having experienced any event such as head trauma leading to neurodeficits and cognitive disorders, presence of a severe pulmonary disease, and presence of a rheumatic disorder.

The present study was designed as a prospective controlled study. The study was approved by the Local Ethics Committee of Gazi University Faculty of Medicine. After all patients were informed verbally and in writing about the aim of the study, possible adverse effects, and possible problems that would be encountered, all patients signed the informed consent form. Data including gender, age, body weight, height, and dominant extremity were recorded. Musculoskeletal and neurological examinations were performed.

The severity of fatigue was assessed using a 100-mm visual analogue scale (VAS), ranging from 0 mm (no fatigue) to 100 mm (extreme fatigue). The body mass index (BMI) [weight (kg)/height (m<sup>2</sup>)] was calculated for patients in whom the body weights and heights were measured.

The laboratory values were obtained from the analyses performed during the diagnostic process [thyroid stimulating hormone (TSH; normal range: 0.55-4.78 µIU/mL; free triiodothyronine (FT3); normal range: 2.30-4.20 pg/mL); free thyroxine (FT4; normal range: 0.89-1.76 ng/dL).

The patients were informed prior to the isokinetic testing about the procedure, concentric and eccentric movements, and the sensations that the patients would feel during the procedure. It was also explained to the patients that the test speed of dynamometer was pre-adjusted and that the resistance would change proportional to the force applied by the patient. It was demonstrated to the patients how they should push and pull the arm of the device, and it was explained that they should exert maximum effort during pushing and pulling. The joint was placed in the most appropriate position for ideal testing. The backrest angle of the chair of the dynamometer was adjusted to 85° and the patient was seated. The rotational axis of the dynamometer shaft was aligned with the rotational axis of the knee joint (lateral femoral condyle). The knee adaptor of the dynamometer was attached to the extremity, in which the measurements were performed, 3 cm proximal to the dorsal surface of the foot. For stabilization, the belts were fastened across the pelvis, chest and the other knee joint.

#### Test Protocol

Speed, duration and number of repetitions

Firstly, four warm-up trials were performed at the angular velocity of 60°/s. Following a resting period of one minute, five repeated tests were performed in order to measure the peak torque values during knee flexion and extension.

Following a resting period of one minute, four repeated warm-up trials at the angular velocity of 180°/s were performed. Then, following a resting period of one minute, 20 repeated tests were carried out in order to measure the peak torque values and total work performed during knee flexion and extension.

#### Verbal Encouragement

It has been demonstrated that verbal encouragement has positive effects on the test results. Thus, verbal encouragement was given to all patients and the individuals in the control group.

#### **Statistical Analysis**

Data were transferred into electronic database and were analyzed using the statistical program for social sciences (SPSS, Inc., Chicago, IL, USA) version 16.0. Data were expressed as mean±standard deviation (SD), median (interquartile range) and percentages (%). A p value of <0.05 was considered statistically significant.

The Kolmogorov-Smirnov test was used to test the normality of data distribution. The chi-square test was used for comparison of the dichotomous variables (gender) between the three groups (overt hypothyroidism group, subclinical hypothyroidism group, and control group). The Kruskal-Wallis variance analysis was used to compare the non-normally distributed continuous variables (age, VAS score, TSH levels) in the three groups. The Mann-Whitney U test was used to identify the group that caused the significant difference. The analysis of variance (ANOVA) test was used to compare normally distributed continuous variables (height, weight, FT3, FT4, the knee extensor peak torque at the angular velocities of 60°/s and 180°/s, the knee flexor peak torque at the angular velocities of 60°/s and 180°/s, the total work during knee flexion and extension at angular velocity of 180°/s) between the three groups. The Tukey test was used to identify the group that caused the significant difference.

#### Results

Demographic characteristics of the patients with newly diagnosed hypothyroidism (overt hypothyroidism and subclinical hypothyroidism) admitted to the Endocrinology Outpatient Clinic at Gazi University and of healthy volunteers are presented in Table 1. The education level in the patient groups was: 2% illiterate (1), 40% elementary school (20), 32% high school (16) and 26% university graduate (13) and in the control group 40% elementary school (12), 33% high school (10) and 27% university graduate (8).

The dominant extremity was the left extremity in one patient in the overt hypothyroidism group and in one participant in the healthy control group, and the dominant extremity was the right extremity in the remaining participants in the three groups. A significant difference was found between the patients with overt hypothyroidism and those with subclinical hypothyroidism in terms of VAS scores [median VAS scores: 50.0 (range: 30.0-63.8) vs. 30.0 (20.0-50.0); p=0.028].

There was a significant difference between the three groups in terms of TSH levels [median TSH levels:  $30.5 \mu$ IU/mL (range,  $12.5-128.9 \mu$ IU/mL),  $6.2 \mu$ IU/mL (range,  $5.8-7.6 \mu$ IU/mL),  $1.8 \mu$ IU/mL (range,  $1.3-2.8 \mu$ IU/mL), respectively; p<0.001]. The TSH levels in patients with overt hypothyroidism were significantly higher than that in patients with subclinical hypothyroidism and that in controls. However, TSH levels in controls were significantly lower than that in patients both in the overt and subclinical hypothyroidism groups.

A statistically significant difference was determined between the three groups in terms of FT3 levels (mean FT3 levels:  $2.33\pm0.78$  pg/mL,  $2.99\pm0.42$  pg/mL,  $2.80\pm0.47$ pg/mL, respectively; p<0.001). In paired comparisons, the overt hypothyroidism group was found to be the group that caused the significant difference (p=0.01 for the overt hypothyroidism group vs. the control group; p<0.001 for the overt hypothyroidism group vs. subclinical hypothyroidism group; p=0.39 for the subclinical hypothyroidism group vs. the control group).

There was a significant difference between the three groups in terms of FT4 levels (mean FT4 levels:  $0.56\pm0.18$  ng/dL,  $0.94\pm0.17$  ng/dL,  $1.09\pm0.15$  ng/dL, respectively; p<0.001). Paired comparisons revealed that there was a significant difference between the overt hypothyroidism group and the control group (p<0.001), between the overt hypothyroidism group and the subclinical hypothyroidism group (p<0.001), and between the subclinical hypothyroidism group and the control group (p<0.05). The TSH, FT3 and FT4 levels in the patient and control groups are presented in Table 2.

The measurements performed using the isokinetic dynamometer in the patient and control groups revealed a significant difference between the overt hypothyroidism and control groups and between the subclinical hypothyroidism and control groups in terms of isokinetic peak torque values of quadriceps muscle at angular velocities of  $60^{\circ}/s$  and  $180^{\circ}/s$  (p=0.007 and p=0.01, respectively for  $60^{\circ}/s$ ; p=0.015

Table 1. Demographic characteristics of the patient and control groups.										
Groups	Ν	Gender (M/F)	Age (Mean±SD)	Height (Mean±SD)	Weight (Mean±SD)	BMI (Mean±SD)				
Overt hypothyroidism	20	2/18	37.95±12.26	163.60±6.33	71.05±12.18	26.71±5.29				
Subclinical hypothyroidism	30	3/27	40.80±11.99	161.97±6.47	68.53±11.40	26.14±4.21				
Control	30	3/27	39.30±10.54	164.00±6.99	67.37±12.49	24.99 ±4.04				
р		>0.05	>0.05	>0.05	>0.05	>0.05				

M: Male, F: Female, BMI: Body Mass Index, SD: Standard Deviation.

Table 2. Thyroid stimulating hormone, free triiodothyronine and free thyroxine levels of the patient and control groups.								
Groups	TSH (μIU/mL) (Mean±SD)	FT3 (pg/mL) (Mean±SD)	FT4 (ng/dL) (Mean±SD)					
Overt hypothyroidism	67.65±80.36	2.33±0.78	0.56±0.18					
Subclinical hypothyroidism	8.29±5.77	2.99±0.42	0.94±0.17					
Control	2.02±0.93	2.80±0.47	1.09±0.15					
р	<0.001	<0.001	<0.001					

TSH: Thyroid Stimulating Hormone, FT3: Free Triiodothyronine, FT4: Free Thyroxine, SD: Standard Deviation.

#### Uzun et al. Muscle Strength in Hypothyroidism

Table 3. Peak torque values of quadriceps and hamstring muscle at angular velocities of 60°/s and 180°/s and total work at the angular velocity of 180°/s in the patient and the control groups.									
Groups	Quadriceps PT (Nm) at 60°/s (Mean±SD)	Quadriceps PT (Nm) at 180°/s (Mean±SD)	Hamstring PT (Nm) at 60°/s (Mean±SD)	Hamstring PT (Nm) at 180°/s (Mean±SD)	Quadriceps TW (joule) at 180°/s (Mean±SD)	Hamstring TW (joule) at 180°/s (Mean±SD)			
Overt hypothyroidism	77.40±37.53	34.80±18.57	35.10±11.89	16.70±8.89	807.35±405.64	313.25±170.89			
Subclinical hypothyroidism	81.90±39.70	37.07±19.96	36.07±19.20	17.50±11.36	861.50±445.46	321.10±212.55			
Control	111.67±37.15	42.15±42.15	53.37±23.45	28.47±16.61	1286.43±101.95	623.10±407.07			
р	0.003	0.002	0.001	0.002	0.001	<0.001			
PT. Book Terroup New Newton meter TWA Tatal Work, SD: Standard Dovision									

PT: Peak Torque, Nm: Newton-meter, TW: Total Work, SD: Standard Deviation.

and p=0.019, respectively for  $180^{\circ}/s$ ). Although the peak torque values at both angular velocities in the subclinical hypothyroidism group were higher than that in the overt hypothyroidism group, this difference was not statistically significant (p=0.913 for  $60^{\circ}/s$ ; p=0.926 for  $180^{\circ}/s$ ). The peak torque values of the quadriceps muscle at the angular velocities of  $60^{\circ}/s$  and  $180^{\circ}/s$  are presented in Table 3.

A statistically significant difference was determined between the overt hypothyroidism and control groups and between the subclinical hypothyroidism and control groups in terms of isokinetic peak torque values of the hamstring muscle at angular velocities of 60°/s and 180°/s (p=0.005 and p=0.003, respectively for 60°/s; p=0.007 and p=0.005, respectively for 180°/s). Although the peak torque values at both angular velocities in the subclinical hypothyroidism group were higher than that in the overt hypothyroidism group, this difference was not statistically significant (p=0.984 for 60°/s; p=0.976 for 180°/s). The peak torque values of hamstring muscle at the angular velocities of 60°/s and 180°/s are shown in Table 3.

The total work performed by the quadriceps and hamstring muscles at the angular velocity of 180°/s in the patient and control groups is presented in Table 3.

Statistically significant differences were found between the overt hypothyroidism and control groups and between the subclinical hypothyroidism and control groups in terms of isokinetic total work of the quadriceps and hamstring muscles at the angular velocity of  $180^{\circ}/s$  (p=0.003 and p=0.003, respectively for the quadriceps muscle; p=0.001 and p<0.001, respectively for the hamstring muscle). Although the total work performed by the quadriceps and hamstring muscles in the subclinical hypothyroidism group was higher than that in the overt hypothyroidism group, this difference was not statistically significant (quadriceps: p=0.920 and p=0.995, respectively).

#### Discussion

Decreased muscle strength is a frequent finding in overt hypothyroidism (11,14), however, there are considerably less data available concerning subclinical hypothyroidism. Some researchers have emphasized that muscle dysfunction and neuromuscular symptoms are frequently observed with electromyography (11,12,15,16). In the present study, we determined a statistically significant difference between the subclinical hypothyroidism and control groups in terms of muscle strength and endurance, similar to that between the overt hypothyroidism and control groups. It is known that parameters such as age, gender, height, weight, and dominant extremity affect isokinetic dynamometer measurements (17-20). In this study, there was no statistically significant difference among the over hypothyroidism, subclinical hypothyroidism and control groups in terms of age, gender, height, weight, BMI and dominant extremity.

In the present study, severity of fatigue was evaluated using the VAS in the three groups. The mean VAS scores were found to be 49.25 mm, 34.33 mm, and 0 in the patients with overt hypothyroidism, in those with subclinical hypothyroidism, and in the controls, respectively. Determination of a statistically significant difference between the overt hypothyroidism and subclinical hypothyroidism groups in terms of VAS scores suggests a correlation between the severity of thyroid function disorder and fatigue. In their study, Evans et al. (21) evaluated the endocrine causes of fatigue and stated that thyroid dysfunction was frequently observed among the causes of this condition.

In a study by Duyff et al. (11), in which neuromuscular findings were evaluated in patients with thyroid dysfunction, muscle weakness was evaluated using the manual muscle testing (MMT) in hypothyroid and hyperthyroid patients, and decreased muscle strength was determined in 37.5% of the hypothyroid patients and in 62% of the hyperthyroid patients. They also evaluated muscle weakness using a hand-held dynamometer and determined muscle weakness in at least one muscle group in 58% of the hypothyroid patients and in 81% of the hyperthyroid patients (11). In this study, we assessed muscle strength and endurance using an isokinetic dynamometer in patients with overt hypothyroidism, in those with subclinical hypothyroidism and in controls. In the isokinetic dynamometer measurements, we found a significant difference between the patient groups and the control group in all parameters (peak torque values of the guadriceps and hamstring muscles at the angular velocity of 60°/s, peak torgue values of the guadriceps and hamstring muscles at the angular velocity of 180°/s, and the total work). These findings suggest that muscle dysfunction may occur in all patients diagnosed with hypothyroidism. In this study, no statistically significant difference was determined between the patients with overt and subclinical hypothyroidism in any of the parameters. However, the mean values of all parameters (peak torque values of the quadriceps and hamstring muscles at the angular velocity of 60°/s, peak torque values of the quadriceps and hamstring muscles at the angular velocity of 180°/s, and the total work values) in the overt hypothyroidism group were lower than that in the subclinical hypothyroidism group, which suggests a correlation between severity of thyroid function disorder and loss of muscle strength and endurance.

In their study, Reuters et al. (12) compared patients with subclinical hypothyroidism with healthy controls and evaluated neuromuscular symptoms, muscle strength and exercise capacity; they questioned the neuromuscular symptoms, tested muscle strength for neck, shoulder, arm and hip muscle groups using MMT, and evaluated guadriceps muscle strength using a dynamometer and inspiratory muscle strength using a manuvacuometer. They reported that neuromuscular complaints were observed more frequently in the patient group than in the control group and that the muscle strength evaluated by MMT was lower in the patient group (12). They observed no difference in quadriceps strength between the patient and control groups (12). In contrast to these results, we determined a significant difference in quadriceps muscle strength in the overt hypothyroidism group and in the subclinical hypothyroidism group as compared to that in the control group. Quadriceps muscle strength was measured using a dynamometer both in the study by Reuters et al. (12) and in this study. However, it was measured isokinetically in this study, whereas isometric contraction was measured in the study by Reuters et al. (12). Thus, we consider that the difference between the results of the study by Reuters et al. (12) and that of our study may be originated from measurements of different contraction types. Furthermore, Reuters et al. (12) reported that the changes in muscle strength evaluated by MMT were more frequent in those with neuromuscular complaints and that this rate was determined to be 30.8% in the subclinical hypothyroidism group. Duyff et al. (11) reported this rate to be 37.5% in patients with overt hypothyroidism. Although Reuters et al. (12) did not determine a significant difference between the guadriceps and inspiratory muscles and reported that there was a decrease in the quadriceps and inspiratory muscle strengths in those with neuromuscular symptoms and MMT changes. As a result, they concluded that MMT and neuromuscular complaints were subjective methods in evaluating muscle strength, however, they emphasized that it could be used as a valuable indicator in the assessment of neuromuscular dysfunction (12). In some studies, the use of the dynamometer has been reported to be more sensitive than MMT in the measurement of muscle strength, for clinical followup and in the evaluation of treatment efficacy (11,22,23).

In another study by Monzani et al. (24), the clinical and biochemical features of muscle dysfunction were evaluated in patients with subclinical hypothyroidism and an exercise program (aerobic dynamic exercises) was applied to the patients. This protocol is based on the recruitment sequence of the slow and fast motor units according to the involvement of aerobic mechanisms at the beginning, and then, the involvement of anaerobic mechanisms as the level of contraction increases (24-26). They measured serum lactate and pyruvate levels before and after exercise in order to demonstrate the changes in energy metabolism of muscles (24). In hypothyroidism, biochemical abnormalities such as accumulation of glycogen and decreased enzyme activity have been previously described in type I muscle fibers in energy production (4,5,24). The rapid decrease in energy reserves in the hypothyroid muscle has been explained by the decrease in mitochondrial activity. Monzani et al. (24) aimed to evaluate the possible role of defective

mitochondrial oxidative metabolism in patients with subclinical hypothyroidism. It is known that excessive lactate production is an indicator of functional mitochondrial impairment in vivo. Monzani et al. (24) also aimed to contribute to this result by evaluating blood lactate levels in patients with subclinical hypothyroidism after exercise. They reported that pre-exercise lactate and pyruvate levels were normal in both the control and subclinical hypothyroidism groups, however, an increase in only lactate levels was determined in the subclinical hypothyroidism group, and no statistically significant difference was found (24). It was reported that the presence of muscle symptoms in subclinical hypothyroidism could be a possible indicator of mitochondrial oxidative dysfunction, as in overt hypothyroidism (24). The results of the study by Monzani et al. (24) in which the biochemical features of muscle dysfunction were determined to be similar in subclinical hypothyroidism and overt hypothyroidism, support the clinical findings of muscle dysfunction determined in the present study.

In a study by Duyff et al. (11), while the rate of clinical improvement in the neuromuscular findings in hyperthyroid patients after a one-year treatment was found to be 87%, it was found to be 67% in hypothyroid patients. While atrophy and an increase in the number of internal nuclei have been observed in type II muscle fibers, the pathological changes in hypothyroid patients have been explained by the observation of an increase in core-like structures in type I muscle fibers (11,27). In the same study by Duyff et al. (11), no significant correlation was observed between biochemical severity of hypothyroidism and the level of muscle weakness, and this finding was interpreted as indicating that hypothyroidism was associated with myopathy rather than functional muscle diseases. In the present study, although there was a correlation between biochemical severity of hypothyroidism and muscle weakness, no statistically significant difference was determined.

The basis of the isokinetic contraction mechanism is as follows: both type I and type II muscle fibers can be maximally stimulated at low angular velocities (e.g. 60°/s), and as the velocity increases (e.g. 180°/s), the number of muscle groups that are stimulated decrease gradually; thus, first the slowly contracting type I muscle fibers, and then the faster type IIA muscle fibers return to their passive state. Only the type IIB muscle fibers remain to be stimulated till the end of the isokinetic contraction. Accordingly, the observation of the decrease in the isokinetic test parameters at low and high angular velocities in overt and subclinical hypothyroid ism appears to be secondary to changes in hypothyroid type I and type II muscle fibers, as emphasized in previous studies (17).

In conclusion, although it has been known for a long time that hypothyroidism leads to myopathy, to our knowledge, there are no controlled studies in the literature evaluating muscle strength and endurance using an isokinetic dynamometer in the comparison of overt hypothyroidism and subclinical hypothyroidism. In this study, the lower muscle strength and endurance determined in the overt hypothyroidism and subclinical hypothyroidism groups as compared to the control group and the lack of difference between subclinical hypothyroid and overt hypothyroid patients lead us to think that myopathy occurs at the early stages of hypothyroidism and that it should be evaluated at the time of diagnosis. A limitation of this study is that the number of patients and controls was relatively small. Furthermore, our study demonstrated that isokinetic dynamometer could be a sensitive and useful tool for evaluating muscle dysfunction in hypothyroid patients. However, further controlled studies evaluating muscle strength and endurance before and after treatment using an isokinetic dynamometer in overt and subclinical hypothyroidism are required.

#### **Conflict of Interest**

Authors reported no conflicts of interest.

#### References

- Bastron JA. Neuropathy in diseases of the thyroid and pituitary glands. In: Dyck PJ, Thomas PK, Lambert EH, Bunge RP, editors. Peripheral neuropathy. Saunders, Philadelphia; 1984. p. 1833-46.
- Argov Z, Renshaw PF, Boden B, Winkokur A, Bank WJ. Effects of thyroid hormones on skeletal muscle bioenergetics. In vivo phosphorus-31 magnetic resonance spectroscopy study of humans and rats. J Clin Invest 1988;81:1695-701.
- Chu DT, Shikama H, Khatra BS, Exton JH. Effects of altered thyroid status on beta-adrenergic actions on skeletal muscle glycogen metabolism. J Biol Chem 1985;260:9994-10000.
- 4. Leijendekker WJ, van Hardeveld C, Kassenaar AA. Coupled diminished energy turnover and phosphorylase a formation in contracting hypothyroid rat muscle. Metabolism 1985;34:437-41.
- Khaleeli AA, Gohil K, McPhail G, Round JM, Edwards RH. Muscle morphology and metabolism in hypothyroid myopathy: effects of treatment. J Clin Pathol 1983;36:519-26.
- Sterling K, Lazarus JH, Milch PO, Sakurada T, Brenner MA. Mitochondrial thyroid hormone receptor: localization and physiological significance. Science 1978;201:1126-9.
- Ianuzzo CD, Chen V, O'Brien P, Keens TG. Effect of experimental dysthyroidism on the enzymatic character of the diaphragm. J Appl Physiol Respir Environ Exerc Physiol 1984;56:117-21.
- Ianuzzo D, Patel P, Chen V, O'Brien P, Williams C. Thyroidal trophic influence on skeletal muscle myosin. Nature 1977;270:74-6.
- 9. Janssen JW, van Hardeveld C, Kassenaar AA. Evidence for a different response of red and white skeletal muscle of the rat in different thyroid states. Acta Endocrinol (Copenh) 1978;87:768-75.
- 10. Caraccio N, Natali A, Sironi A, Baldi S, Frascerra S, Dardano A, et al. Muscle metabolism and exercise tolerance in subclinical hypothyroidism: a controlled trial of levothyroxine. J Clin Endocrinol Metab 2005;90:4057-62.
- 11. Duyff RF, Van den Bosch J, Laman DM, van Loon BJ, Linssen WH. Neuromuscular findings in thyroid dysfunction: a prospective clinical and electrodiagnostic study. J Neurol Neurosurg Psychiatry 2000;68:750-5.

- Reuters VS, Teixeira Pde F, Vigário PS, Almeida CP, Buescu A, Ferreira MM, et al. Functional capacity and muscular abnormalities in subclinical hypothyroidism. Am J Med Sci 2009;338:259-63.
- 13. Horak HA, Pourmand R. Endocrine myopathies. Neurol Clin 2000;18:203-13.
- 14. Rao SN, Katiyar BC, Nair KR, Misra S. Neuromuscular status in hypothyroidism. Acta Neurol Scand 1980;61:167-77.
- Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC. L-Thyroxine therapy in subclinical hypothyroidism. A double-blind, placebocontrolled trial. Ann Intern Med 1984;101:18-24.
- Cakir M, Samanci N, Balci N, Balci MK. Musculoskeletal manifestations in patients with thyroid disease. Clin Endocrinol (Oxf) 2003;59:162-7.
- 17. Brown LE. Isokinetics in human performance. The United States of America: Champaing; 2000.
- Kallman DA, Plato CC, Tobin JD. The role of muscle loss in the agerelated decline of grip strength: cross-sectional and longitudinal perspectives. J Gerontol 1990;45:82-8.
- Larsson L, Grimby G, Karlsson J. Muscle strength and speed of movement in relation to age and muscle morphology. J Appl Physiol Respir Environ Exerc Physiol 1979;46:451-6.
- Lindle RS, Metter EJ, Lynch NA, Fleg JL, Fozard JL, Tobin J, et al. Age and gender comparisons of muscle strength in 654 women and men aged 20-93 yr. J Appl Physiol (1985) 1997;83:1581-7.
- 21. Evans KM, Flanagan DE, Wilkin TJ. Chronic fatigue: is it endocrinology? Clin Med 2009;9:34-8.
- Bohannon RW. Manual muscle test scores and dynamometer test scores of knee extension strength. Arch Phys Med Rehabil 1986;67:390-2.
- 23. van der Ploeg RJ, Oosterhuis HJ, Reuvekamp J. Measuring muscle strength. J Neurol 1984;231:200-3.
- 24. Monzani F, Caraccio N, Siciliano G, Manca L, Murri L, Ferrannini E. Clinical and biochemical features of muscle dysfunction in subclinical hypothyroidism. J Clin Endocrinol Metab 1997;82:3315-8.
- Wasserman K, Whipp BJ, Koyl SN, Beaver WL. Anaerobic Anaerobic threshold and respiratory gas exchange during exercise. J Appl Physiol 1973;35:236-43.
- Milner-Brown HS, Stein RB, Yemm R. The orderly recruitment of human motor units during voluntary isometric contractions. J Physiol 1973;230:359-70.
- 27. Ono S, Inouye K, Mannen T. Myopathology of hypothyroid myopathy. Some new observations. J Neurol Sci 1987;77:237-48.