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Research Article / Araştırma Makalesi

Evaluation of Neuromuscular Functions in Hashimoto's Thyroiditis

Hashimoto Tiroiditinde Nöromusküler Fonksiyonların Değerlendirilmesi

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Abstract

Hashimoto's thyroiditis is the most prevalent autoimmune thyroid disease with an increasing incidence. Although the exact causes and pathogenesis of Hashimoto's thyroiditis are not yet fully understood, the literature indicates complex interactions of immunologic, genetic, environmental, and epigenetic factors. It generally leads to hypothyroidism which can cause neuromuscular problems including neuropathy and myopathy. Data on neuromuscular functions of Hashimoto's thyroiditis patients are relatively underreported and not up to date. The current observational study aimed to evaluate neuromuscular functions and sympathetic skin responses (SSR) in patients with Hashimoto's thyroiditis and compare them with healthy participants. In total, 50 patients (25 females, 25 males; mean age, 31.6±4.9 years; range: 25-40 years) including 33 euthyroid, 10 with subclinical hypothyroidism, and 7 with hypothyroidism were included. The control group consisted of 50 healthy individuals (25 females, 25 males; mean age: 31.5±5.1 years; range, 25-40 years). Nerve conduction studies, repetitive nerve stimulation, SSRs and F wave recordings were performed in all participants. There were significant differences in the mean SSR latency and amplitude both in the upper extremities ($p<0.001$ and $p=0.013$, respectively) and in the lower extremities ($p=0.008$ and $p=0.002$, respectively) in the comparison groups. There was a significant difference in comparison groups regarding needle electroneuromyography (EMG) tests ($p=0.012$) and 14% of the patients showed myogenic EMG findings. In addition, a significant correlation was found between EMG findings and anti-TPO levels in the Hashimoto's thyroiditis patients ($r=0.453$; $p=0.001$). No significant differences were found in the nerve conduction studies, routine EMG tests, repetitive nerve stimulations or F wave recordings between patients and control groups. Hashimoto's thyroiditis, can cause negative influences on the proper functioning of neuromuscular systems. SSR, and electrophysiological tests may be beneficial for early detection and investigation of neuromuscular abnormalities in these patients.
Keywords: Hashimoto's thyroiditis, neuromuscular problems, electromyography, autoimmune thyroid disease

Özet

Hashimoto tiroiditi, görülme sıklığı artan en sık görülen otoimmün tiroid hastalığıdır. Hashimoto tiroiditinin kesin nedenleri ve patogenezi henüz tam olarak anlaşılamamasına rağmen, literatür immünolojik, genetik, çevresel ve epigenetik faktörlerin karmaşık etkileşimlerini göstermektedir. Genellikle nöropati ve miyopati gibi nöromüsküler sorunlara neden olabilen hipotiroidizme yol açar. Hashimoto tiroiditi hastalarının nöromüsküler fonksiyonlarına ilişkin veriler nispeten az rapor edilmiştir ve güncel değildir. Bu gözlemsel çalışma Hashimoto tiroiditi olan hastalarda nöromüsküler fonksiyonları ve sempatik deri yanıtlarını (SSR) değerlendirmeyi ve sağlıklı katılımcılarla karşılaştırmayı amaçlamıştır. Çalışmaya 33 ötiroid, 10'u subklinik hipotiroidizmli, 7'si hipotiroidizmli olmak üzere toplam 50 hasta (25 kadın, 25 erkek; yaş ortalaması 31.6±4.9 yıl; dağılım: 25-40 yıl) dahil edildi. Kontrol grubu 50 sağlıklı bireyden (25 kadın, 25 erkek; yaş ortalaması: 31.5±5.1 yıl; dağılım: 25-40 yıl) oluşuyordu. Tüm katılımcılarda sinir iletim çalışmaları, tekrarlayan sinir stimülasyonu, SSRs ve F dalga kayıtları yapıldı. Karşılaştırma gruplarında hem üst ekstremitelerde (sırasıyla $p<0.001$ ve $p=0.013$) hem de alt ekstremitelerde (sırasıyla $p=0.008$ ve $p=0.002$) ortalama SSR gecikmesi ve genliğinde anlamlı farklılıklar vardı. Karşılaştırma gruplarında iğne elektronöromiyografi (EMG) testleri açısından anlamlı fark vardı ($p=0.012$) ve hastaların %14'ünde miyojenik EMG bulguları saptandı. Ayrıca Hashimoto tiroiditli hastalarda EMG bulguları ile anti-TPO düzeyleri arasında anlamlı korelasyon saptandı ($r=0.453$; $p=0.001$). Hastalar ve kontrol grupları arasında sinir iletim çalışmalarında, rutin EMG testlerinde, tekrarlayan sinir stimülasyonlarında veya F dalgası kayıtlarında anlamlı fark saptanmadı. Hashimoto tiroiditi, nöromüsküler sistemlerin düzgün çalışması üzerinde olumsuz etkilere neden olabilir. SSR ve elektrofizyolojik testler, bu hastalarda nöromüsküler anormalliklerin erken tespiti ve araştırılması için faydalı olabilir.
Anahtar Kelimeler: Hashimoto tiroiditi, nöromüsküler problemler, elektromiyografi, otoimmün tiroid hastalığı

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1. Introduction

Hashimoto's thyroiditis, also known as chronic lymphocytic thyroiditis or autoimmune thyroiditis is the most prevalent autoimmune thyroid disease with an increasing incidence. Hashimoto's thyroiditis is characterized by enhanced thyroid volume, lymphocyte infiltration of parenchyma, and the presence of specific autoantibodies against thyroid antigens, namely, thyroid peroxidase (TPO) and thyroglobulin (TG) (1, 2). Hashimoto's thyroiditis is estimated to affect about 10% of the general population, is diagnosed in females up to ten times more often than males; the frequency of disease increases with age and it can also be seen in children and even in infants (3, 4). Although the exact causes and pathogenesis of Hashimoto's thyroiditis are not yet fully understood, the literature indicates complex interactions of immunologic, genetic, environmental, and epigenetic factors. Hashimoto's thyroiditis can also coexist with various other autoimmune disorders such as type 1 diabetes, rheumatologic syndromes, celiac disease, and multiple sclerosis (4, 5). Hashimoto's thyroiditis symptoms may include weight gain, paresthesia, fatigue, constipation, muscle weakness, cramps, hair loss, infertility, and several psychological problems and it generally leads to hypothyroidism (4, 5). Among these, the role of Hashimoto's thyroiditis on the impairment of neural and muscular functions of patients is relatively underreported and not up to date, therefore, further research is required to address the issue. Neuromuscular problems including neuropathy and myopathy are common in patients with hypothyroidism with up to 80% of patients complaining of associated symptoms (6, 7). It has been reported that almost one-third of patients with hypothyroidism develop muscle weakness, myalgia, fatigue, and muscle cramps (8) and most of them may have mononeuropathy or polyneuropathy because of axonal damage or myelin involvement (9). The current study aimed to evaluate neuromuscular functions and sympathetic skin responses (SSR) in patients with Hashimoto's thyroiditis and compare them with healthy participants.

2. Material and Methods

The present observational study was conducted at Neurology Department of İzmir University of Economics Medicalpoint Hospital between January 2014 and December 2021. Patients with a diagnosis of Hashimoto's thyroiditis were included in the study. All patients were examined for systemic disorders such as diabetes mellitus, vasculitis, rheumatic disease, malignancy, and hematologic disorders and only the ones who had not any of these concurrent systemic problems were included. In total, 50 patients (25 females, 25 males; mean age, 31.6±4.9; range:25-40) including 33 euthyroid, 10 with subclinical hypothyroidism, and 7 with hypothyroidism were included in the study. The control group consisted of 50 healthy individuals (25 females, 25 males; mean age: 31.5±5.1 years; range, 25-40 years) with similar age and sex profile to the patient group and with no previous thyroid disorder any current neurological disorder. The study was approved by the Local Clinical Research Ethics Committee. All participants included in the study provided written informed consent.

Electrophysiological studies

Electrophysiological studies were conducted using the Nihon Kohden (Japan) Electromyograph measuring system (Model: MEB-9400K). All study participants underwent electroneuromyography (EMG) performed by a single physiatrist who was blind to the patient groups. Distal motor latencies and motor nerve conduction velocities were calculated using disc surface cup (Ag/AgCl) recording electrodes which were 5 mm in diameter. Sensory conduction velocity, sensory nerve action potential amplitudes, and distal sensory latencies were recorded using ring electrodes. Motor and sensory conduction recordings of ulnar nerve; motor and sensory conduction recordings of median nerve; motor conduction recordings of peroneal and tibial nerve, and sensory conduction recordings of sural nerve were performed. Needle EMG recordings were performed with the left deltoid muscles and rectus femoris muscles. Electrophysiological parameters were assessed according to the normal values of the laboratory. A minimum

ambient temperature of 25°C and distal extremity skin temperature of >32°C were conserved during all electrophysiological studies.

Repetitive nerve stimulation

Repetitive nerve stimulations were recorded from the orbicularis oris muscles. Ten stimuli at 5 Hz stimulation frequency and 10 Hz stimulation frequency were applied to the facial nerve at the tragus, during rest and every minute for 4 minutes after 30 seconds exercise with maximal isometric muscle contraction of the recording muscle. A decrement of more than 10% between the first and fourth motor response was considered as positive. The decrement ratios between the first and fourth (dec1-4) motor response were calculated.

F wave recordings

F wave parameters including minimum f latency, maximum f latency, f latency chronodispersion, and f wave persistency were studied in median, ulnar, peroneal, and tibial nerves of all participants. Recording electrodes placed on the belly tendon montage, wave recording done from a relaxed muscle. The stimulating cathode was proximal to the anodal electrode to prevent anodal block

Sympathetic Skin Responses

SSRs were recorded via the active electrodes placed in the left palm and sole and the reference electrodes on the dorsum of the left hand and foot, by placing the participants in the reclining position. A two-channel recording from foot and hand as lower and upper extremities were obtained simultaneously by stimulating the contralateral median nerve at the level of the wrist. The stimulus was increased to just above the threshold level and applied not regularly to minimize habituation. Five potentials were recorded and the mean values were used for the analyses.

Statistical Analysis

Statistical analysis was performed using the PASW Statistics for Windows, Version 18.0. (SPSS Inc., Chicago, IL, USA). The descriptive statistical data were expressed as numbers and percentiles for categorical variables and as mean, standard deviation, median, and minimum-maximum (range) for numerical variables. The normal distributions of variables were tested by visual (histograms and probability graphics) and analytical (Kolmogorov-Smirnov/Shapiro-Wilk) test methods. For categorical variables, in two group comparisons, the Chi-Square test was used when appropriate. For numerical variables, in two group comparisons, the Mann-Whitney U test was used when data were not normally distributed. The Student's T-test was used when numerical variables are normally distributed. For the analysis of the correlation between needle EMG findings and free T3, free-T4, thyroid stimulating hormone (TSH), anti-thyroid peroxidase (anti-TPO), and anti-thyroglobulin (anti-TG) levels, Spearman's correlation analysis was performed for non-normally distributed variables. A p value of <0.05 was set as statistically significant.

3. Results

The study included a total of 100 participants, of whom 50 had Hashimoto's thyroiditis (33 patients with euthyroid, 10 patients with subclinical hypothyroid, and 7 patients with hypothyroid; mean age, 31.6±4.9 years) and 50 were healthy controls (mean age, 31.5±5.1 years). In the patient group, mean time since the diagnosis of hypothyroidism was 5.1±3.0 years (minimum 1 year and maximum 10 years) and of the patients, 42% were using levothyroxine, 30% have previous history of levothyroxine, and 28% were not using levothyroxine. The demographic and clinical data and the comparison of these parameters between patient and control groups are summarized in Table 1. Accordingly, there were no significant differences between patient and control groups regarding sex ($p=1.000$), age ($p=0.937$), height ($p=0.894$) and weight ($p=0.358$). Biochemistry laboratory test results regarding Hashimoto's thyroiditis namely creatine kinase levels, free T3 and T4 levels, TSH levels, anti-TPO

levels, anti-TG levels were compared between patient and control groups. There were elevated TSH levels (p=0.009), elevated anti-TPO levels (p<0.001), and elevated anti-TG levels (p<0.001) in the patient group as compared with the control group with respect to the normal laboratory range. The differences in creatine kinase levels (p=0.035), and free T3 (p=0.249) and T4 levels (p=0.354) between the patient and control group were not significant.

Facial nerve decrement ratios of the participants were compared between patient and control groups. There was no significant difference between the patient and control groups in facial nerve decrement ratios (%) between responses 1-4 for repetitive stimulations both at 5 Hz (both patient and control mean values were 5, p=0.579) and at 10 Hz (mean values were 8 and 6 for patient and control groups, respectively; p=0.097) frequencies.

F-wave recordings including minimum and maximum f-latency, f-latency chronodispersion and f-wave persistence in median, ulnar, peroneal, and tibial nerves of all participants were performed and are shown in Table 2. F wave recordings of these nerves were similar between the patient and control groups (p>0.05 for all).

SSR and motor and sensory functions of median nerve were measured in all participants and the results are demonstrated in Table 3. According to the collected data, there were significant differences in the mean SSR latency and amplitude both in the upper extremities (p<0.001 and p=0.013, respectively) and in the lower extremities (p=0.008 and p=0.002, respectively) in the comparison groups. For both upper and lower extremities, mean SSR latency was higher and mean SSR amplitude was lower in the patient group than those of the control group. There was no significant difference between the patient and control groups in motor latency (p=0.942), motor distal amplitude (p=0.874), and motor velocity (p=0.485) values of the median nerve. In addition, no significant difference was found between the patient and control groups in the sensory data of the median nerve recorded for both thumb (p=0.208, p=0.684, p=0.402 for latency, amplitude and velocity values, respectively) and index fingers (p=0.296, p=0.496, p=0.289 for latency, amplitude and velocity values, respectively).

Motor and sensory functions of the ulnar nerve were tested in all participants and the findings are shown in Table 4. There was no significant difference between the patient and control groups in ring finger median-ulnar sensory latency difference (p=0.447), motor distal latency (p=0.772), motor amplitude of below sulcus segment (p=0.981), motor amplitude of above sulcus segment (p=0.970), motor velocity of below sulcus segment (p=0.740), motor velocity of above sulcus segment (p=0.539), and sensory data (p=0.972, p=0.959, p=0.505 as latency, amplitude, and velocity, respectively) of the ulnar nerve.

Nerve conduction studies of peroneal, tibial, and sural nerves were performed in all participants and the results are shown in Table 5. There was no significant difference between the patient and control groups in distal motor latency (p=0.948), and motor amplitude (p=0.992; p=0.961) and motor velocity (p=0.883; p=0.581) in the caput fibula 2 cm distal and 9 cm proximal of the peroneal nerve, respectively. Similarly, no significant difference was found between the patient and control groups in motor latency (p=0.830), motor amplitude (p=0.841) and motor velocity (p=0.567) parameters of the tibial nerve, and in sensory latency (p=0.749), sensory amplitude (p=0.646), and sensory velocity (p=0.890) parameters of the sural nerve. There was no significant difference between the patient and control groups in routine EMG tests (p=0.242), whereas there was a significant difference in comparison groups regarding needle EMG tests (p=0.012) and 7% of the patients showed myogenic EMG findings. Further, the correlation analysis between the needle EMG findings and free T3; free-T4; TSH; anti-TPO, and anti-TG levels was performed in the patients with Hashimoto's thyroiditis (Table 6) and a significant correlation was found between EMG findings and anti-TPO levels (r=0.453; p=0.001). No significant correlation was found for the following parameters: free T3, free-T4, TSH, and anti-TG levels.

Table 1. Demographic and clinical data of the patient and control groups

	Patients **N=50**	Controls **N=50**	p
Sex, n (%)			
Female	25 (50.0)	25 (50.0)	1.000*
Male	25 (50.0)	25 (50.0)	
Age, years, Mean±SD	31.6 ± 4.9	31.5 ± 5.1	0.937**
Height, cm, Mean±SD	165.3 ± 3.8	165.2 ± 3.6	0.894**
Weight, kg Mean±SD	65.1 ± 4.7	64.2 ± 4.8	0.358**
Euthyroid, n (%)	33 (66.0)	50 (100.0)	N/A
Subclinical hypothyroidism, n (%)	10 (20.0)	-	N/A
Hypothyroidism, n (%)	7 (14.0)	-	N/A
Creatine kinase level, u/L (29-168), Mean (min-max)	125 (49-1588)	102.5 (39-167)	0.035***
Free T3, pg/mL (1.5-4.6), Mean (min-max)	1.9 (1.1-4.5)	2.7 (1.5-4.5)	0.249***
Free T4, ng/dL (0.7-1.7), Mean (min-max)	1.3 (0.2-1.7)	1.3 (0.7-1.7)	0.354***
TSH, miu/mL (0.35-4.94), Mean (min-max)	4.305 (0.68-11.2)	3.515 (0.68-4.94)	0.009***
Anti-TPO, iu/mL (0-5.6), Mean (min-max)	258.75 (4.3-1349)	3.4 (0.3-5.3)	<0.001***
Anti-TG, iu/mL (0-4.11), Mean (min-max)	78.55 (1.8-283.9)	3.1 (0.9-4.1)	<0.001***

*SD: Standard deviation; N/A: Not applicable; *Chi-Square test; **Student's T-test. ***Mann Whitney U test. T3: triiodothyronine; T4: thyroxine; TSH: thyroid stimulating hormone; anti-TPO: anti-thyroid peroxidase; anti-TG: anti-thyroglobulin.*

Table 2. F-wave recordings of median, ulnar, peroneal and tibial nerves in patient and control groups

	Patients **N=50**	Controls **N=50**	p*
Median nerve minimum f latency, ms, upper limit 26-28	25 (21.3-30.1)	24.1 (21.3-27.9)	0.052
Median nerve maximum f latency, ms, upper limit 30-34	28,8 (24.1-36.1)	27.5 (24.1-31.1)	0.058
Median nerve f latency chronodispersion, ms, should be <4 ms	3.35 (2-7)	3.1 (2-4)	0.132
Median nerve f wave persistency, should be >50%	65 (43-81)	68 (50-81)	0.474
Ulnar nerve minimum f latency, ms, upper limit 27-29	27.65 (23.8-31.1)	26.9 (23.8-28.9)	0.082
Ulnar nerve maximum f latency, ms, upper limit 31-33	30.9 (26.9-35.4)	30.6 (26.9-32.9)	0.069
Ulnar nerve f latency chronodispersion, ms, should be maximum 4 ms	3.5 (2-5.9)	3.5 (2-4.1)	0.152
Ulnar nerve f wave persistence, should be >50%	62 (50-81)	68 (50-81)	0.543
Peroneal nerve minimum f latency, ms, upper limit 46-52	49.6 (43.9-54.8)	49.1 (45.5-51.8)	0.103
Peroneal nerve maximum f latency, ms, upper limit 52-58	54.85 (49.7-60.1)	54.2 (49.9-56.9)	0.066
Peroneal nerve f latency chronodispersion, ms, should be maximum 6 ms	5.3 (3-8.7)	5 (3-6.3)	0.062
Peroneal nerve f wave persistence, %	62 (37-81)	68 (50-81)	0.498
Tibial nerve minimum f latency, ms, should be maximum 45-53	50.2 (45.5-55.5)	49.9 (45.5-52.5)	0.209
Tibial nerve maximum f latency, ms, should be maximum 51-59	54.9 (49.9-61.7)	54.9 (49.9-58.9)	0.204
Tibial nerve f latency chronodispersion (ms), should be maximum 6 ms	5.25 (4-7,4)	5.2 (4-6.4)	0.340
Tibial nerve f wave persistence, %	62 (43-81)	68 (50-81)	0.480

*ms: milliseconds; *Mann Whitney U test; The descriptive statistical data are shown as median (minimum-maximum).*

Table 3. Sympathetic skin responses, and motor and sensory conduction recordings of median nerve in patient and control groups

	Patients **N=50**	Controls **N=50**	p*
Upper extremities sympathetic skin response (5 responses) mean latency, s (1.46±0.04)	1.495 (1.18-2.5)	1.39 (1.18-1.55)	<0.001
Upper extremities sympathetic skin response (5 responses) mean amplitude, mV (2.5±0.3)	2.025 (1.5-3.1)	2.2 (1.5-3.1)	0.013
Lower extremities sympathetic skin response (5 responses) mean latency, s (1.4±0.07)	1.5 (1.15-2.2)	1.415 (1.22-1.59)	0.008
Lower extremities sympathetic skin response (5 responses) mean amplitude, mV (1.6±0.2)	1.3 (0.8-2.5)	1.6 (1.1-2.5)	0.002
Median nerve motor latency, ms	3.61 (3.1-3.95)	3.61 (3.1-3.95)	0.942
Median nerve motor distal amplitude, mV	18.7 (12.1-25.1)	18.7 (12.2-25.1)	0.874
Median nerve motor velocity, m/s	54.4 (50.1-61.3)	55.6 (50.1-61.3)	0.485
Median nerve sensory latency, ms, thumb	3.2 (2.7-4.5)	3.1 (2.7-3.5)	0.208
Median nerve sensory amplitude, mV, thumb	20.5 (10.5-29.1)	20.7 (16.8-29.1)	0.684
Median nerve sensory velocity, m/s, thumb	52.9 (38.9-60.1)	53.55 (50.2-60.1)	0.402
Median nerve sensory latency, ms, index finger	3.25 (2.7-4.3)	3.2 (2.7-3.4)	0.296
Median nerve sensory amplitude, mV, index finger	19.4 (11.9-29.1)	20.15 (14.7-29.1)	0.496
Median nerve sensory velocity, m/s, index finger	53.4 (39.4-59.8)	53.5 (50.7-59.8)	0.289

*SSR: Sympathetic skin response; ms: milliseconds; mV: millivolt; *Mann Whitney U test; The descriptive statistical data are shown as median (minimum-maximum).*

Table 4. Motor and sensory conduction recordings of ulnar nerve in patient and control groups

	Patients **N=50**	Controls **N=50**	p*
Ring finger median ulnar sensory latency difference (>0.3 is pathological)	0.2 (0.1-0.5)	0.2 (0.1-0.3)	0.447
Ulnar nerve motor distal latency, ms	3.1 (2.8-3.6)	3.1 (2.8-3.6)	0.772
Ulnar nerve motor amplitude, mV, below sulcus segment (5 cm distal)	19.45 (12.3-27.8)	19.4 (14.3-27.8)	0.981
Ulnar nerve motor amplitude, mV, above sulcus segment (5 cm proximal)	19.9 (14.1-27.5)	19.9 (15.1-26.8)	0.970
Ulnar nerve motor velocity, m/s, below sulcus segment	57.5 (50.3-62.5)	57.5 (50.3-62.5)	0.740
Ulnar nerve motor velocity, m/s, above sulcus segment	65.1 (57.1-69.9)	65.7 (57.1-69.9)	0.539
Ulnar nerve sensory latency, ms	3.2 (2.7-3.8)	3.2 (2.7-3.8)	0.972
Ulnar nerve sensory amplitude, mV	20.7 (14.9-30.3)	20.5 (14.9-30.3)	0.959
Ulnar nerve sensory velocity, m/s	57.35 (50.1-67.4)	58.2 (51.6-67.4)	0.505

*ms: milliseconds; mV: millivolt; *Mann Whitney U test; The descriptive statistical data are shown as median (minimum-maximum).*

Table 5. Motor conduction recordings of peroneal and tibial nerve, and sensory conduction recordings of sural nerve in patient and control groups

	Patients	Controls	p*
Peroneal nerve distal motor latency, ms	4.63 (3.8-5.2)	4.5 (3.9-5.2)	0.948
Peroneal nerve motor amplitude, mV, caput fibula 2 cm distal	9.85 (4.7-15.2)	9.9 (6.7-15.2)	0.992
Peroneal nerve motor velocity, m/s, caput fibula 2 cm distal	49.25 (45.4-55.4)	49.3 (45.4-55.4)	0.833
Peroneal nerve motor amplitude, mV, caput fibula 9 cm proximal	11.3 (5.3-17.3)	11.3 (7.3-17.3)	0.961
Peroneal nerve motor velocity, m/s, caput fibula 9 cm proximal	58.1 (54.1-62.4)	58.1 (54.3-62.4)	0.581
Tibial nerve motor latency, ms	4.7 (3.7-5.2)	4.7 (3.7-5.2)	0.830
Tibial nerve motor amplitude, mV	10.9 (7.6-18.4)	11.05 (7.6-18.4)	0.841
Tibial nerve motor velocity, m/s	49.7 (43.9-55.1)	50 (45.9-55.1)	0.567
Sural nerve sensory latency, ms	4.15 (3.1-4.9)	4.1 (2.9-4.8)	0.749
Sural nerve sensory amplitude, mV	18.6 (11.3-25.3)	18.6 (11.3-25.3)	0.646
Sural nerve sensory velocity, m/s	49.65 (42.8-57.2)	49.65 (44.3-57.2)	0.890

*ms: milliseconds; mV: millivolt; *Mann Whitney U test; The descriptive statistical data are shown as median (minimum-maximum).*

Table 6. Results of the correlation analysis between the needle electroneuromyography (EMG) findings and biochemistry laboratory test results in the patients with Hashimoto's thyroiditis

		Free T3	Free T4	TSH	anti-TPO	anti-TG
Needle EMG	**r**	0.054	0.048	-0.016	0.453	0.202
	p*	0.708	0.740	0.912	**0.001**	0.160

**Spearman's correlation analysis. TSH: thyroid stimulating hormone; anti-TPO: anti-thyroid peroxidase; anti-TG: anti-thyroglobulin.*

4. Discussion

In the present study, it was found that there was a significant difference in SSRs between the patient and control groups. For both upper and lower extremities, the mean SSR latencies were prolonged, and the mean SSR amplitudes were decreased in the patient group than those of the healthy control group implying the impairment of the sympathetic system function in the patients compared to the controls. Consistently with the current study, in a previous research, Merello et al. (10) reported that patients with autoimmune hypothyroidism showed sudomotor dysfunctions revealed by the abnormal SSR results likely be resulted from a destructed autoimmune reaction. On the other hand, there are some other studies found contrary results regarding SSR measurements. Gautam et al. (11) and Ümit Yemişci et al. (7) found no significant alterations in SSRs between hypothyroid patients and healthy controls in their research. SSR is one of the most frequently used non-invasive techniques for the evaluation of sympathetic fibers dysfunction in neuropathies and sympathetic system disorders in other diseases. It is simple, fast, and easy to apply; however, it has its methodical limitations similar to other electrophysiological procedures (12, 13). In addition to these limitations, variations in the characteristics of the patient groups, sample size, and the stages of the disease may result in controversial SSR measurements. Nevertheless, the literature lacks adequate data in terms of SSR in immunologically mediated disorders which suggest the need for further investigations of SSR in Hashimoto's thyroiditis to have more comparable and insightful clinical data (14). Although SSR alone cannot be used as a diagnostic tool for autonomic dysfunction, it may be utilized in combination with some other methods such as cardiovascular reflexes for the evaluation of autonomic nervous system functions and before the therapeutic interventions, as suggested previously (7, 10).

Apart from SSR measurements, various electrophysiological tests including repetitive stimulations of facial nerve; F-wave recordings of the median, ulnar, peroneal, and tibial nerves; motor and sensory conduction recordings of the median and ulnar nerve; motor conduction recordings of the peroneal and tibial nerve, and sensory conduction recordings of the sural nerve were performed to investigate any abnormalities in the patients with Hashimoto's thyroiditis. In all of these detailed tests, no significant differences were found in the electrophysiological parameters between patients and control groups. In a previous study, Ozata et al. (9) studied the distal latency, nerve conduction velocity, and F responses in the median and peroneal nerves, and they recorded sensory nerve conduction

velocities and sensory potential amplitudes in the sural and median nerves. As consistent with the current study, they could not find any significant difference in the electrophysiological data between patients with subclinical hypothyroidism and controls and they speculated that the results may be associated with the early stage of the disease in these patients. In another study, oppose to these results, researchers measured some extent of electromyographic variations, even in the early stages of subclinical hypothyroidism where they found motor parameters were more affected in the longer nerves and a higher proportion as compared to the sensory nerves and the progression of thyroid insufficiency was correlated with the decline of the motor and sensory amplitudes in all of the studied nerves (15). In two other studies, the hypothyroidism patients displayed a significant tendency of nerve conduction slowness as compared with controls (16, 17). Khedr et al. (18) recorded electrophysiological measurements showing that half of the hypothyroid patients had peripheral nervous system involvement, and a few of them had axonal neuropathy (9%) and myopathy (9%). Similarly, in the current study, 7 of the patients with Hashimoto's thyroiditis (14%) showed myogenic EMG findings. Furthermore, a significant correlation was found between EMG findings and anti-TPO levels in the patients, which supports the association between Hashimoto's thyroiditis and neuromuscular disorders. In addition, despite no statistical significance between the groups, early phase carpal tunnel syndrome was observed in three patients (6% of the patients). It revealed the importance of performing electrophysiological tests in hypothyroid patients, even in the very early stage of disease to detect the nervous system involvement. Eslamian et al. (8) measured similar electrophysiological abnormalities in patients with untreated spontaneous hypothyroidism and suggested early treatment to slow down the progression rate of the neuromuscular complications or minimize their formation.

As expected, there were elevated TSH levels, anti-TPO, and anti-TG levels in the patient group than those in the control group as the indicators of Hashimoto's thyroiditis and may have possible effects on the functioning of the neuromuscular system and thus on the recordings. The differences in creatine kinase levels and free T3 and T4 levels between the patient and control group were not significant and they may not interfere with the test results.

The homogeneity of the comparison groups in the current study was high with no significant difference according to the demographic features. Further, patients with no concurrent disease were recruited in the study which otherwise may interfere recorded neuromuscular data. This matching data between patient and control groups and specific selection of the patients enhances the reliability of the data comparison and the strength of the study. On the other hand, coexisting systemic disorder free selection of the study participants restricted the population of the study and low number of participants in both groups may be insufficient to record and address all of the neuromuscular effects of Hashimoto's thyroiditis.

Even though the current study results did not establish any significant difference in the electrophysiological data of the patient and healthy samples with the exception of SSRs data, it seems that electrophysiological studies may be useful as a tool in the case of early detection of neuromuscular issues in particular individuals with Hashimoto's thyroiditis.

In conclusion, it is well known that thyroid hormones are the main regulators of human metabolism and they are involved in many processes and biological activities of the neuromuscular systems. Hashimoto's thyroiditis, which results from impaired or abnormal thyroid hormones, can cause negative influences on the proper functioning of these systems. SSR and electrophysiological tests may be beneficial for early detection and investigation of neuromuscular abnormalities in patients with Hashimoto's thyroiditis.

REFERENCES

1. Ralli M, Angeletti D, Fiore M, et al. Hashimoto's thyroiditis: An update on pathogenic mechanisms, diagnostic protocols, therapeutic strategies, and potential malignant transformation. *Autoimmun Rev*. 2020;19:102649.
2. Zaletel K, Gaberšček S. Hashimoto's thyroiditis: From genes to the disease. *Curr Genomics*. 2011;12:576-588.
3. Rydzewska M, Jaromin M, Pasierowska IE, et al. Role of the T and B lymphocytes in pathogenesis of autoimmune thyroid diseases. *Thyroid Res.* 2018;11:2.
4. Kust D, Matesa N. The impact of familial predisposition on the development of Hashimoto's thyroiditis. *Acta Clin Belg*. 2020;75:104-108.
5. Ahmed R, Al-Shaikh S, Akhtar M. Hashimoto thyroiditis: a century later. *Adv Anat Pathol*. 2012;19:181-186.
6. 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;68:750-755.
7. Ümit Yemişci O, Özen S, Öztürk Şişman T, Anıl C, Saraçgil Coşar SN. Sympathetic skin responses and electromyographic reaction times in chronic autoimmune thyroiditis: An overlooked electrodiagnostic study. *Turk J Phys Med Rehab.* 2022;68:100-106.
8. Eslamian F, Bahrami A, Aghamohammadzadeh N, Niafar M, Salekzamani Y, Behkamrad K. Electrophysiologic changes in patients with untreated primary hypothyroidism. *J Clin Neurophysiol*. 2011;28:323-328.
9. Ozata M, Ozkardes A, Corakci A, Gundogan MA. Subclinical hypothyroidism does not lead to alterations either in peripheral nerves or in brainstem auditory evoked potentials (BAEPs). *Thyroid*. 1995;5:201-205.
10. Merello M, Nogues M, Leiguarda R, López Saubidet C, Florin A. Abnormal sympathetic skin response in patients with autoimmune vitiligo and primary autoimmune hypothyroidism. *J Neurol*. 1993;240:72-74.
11. Gautam S, Tandon OP, Awashi R, Sekhri T, Sircar SS. Correlation of autonomic indices with thyroid status. *Indian J Physiol Pharmacol*. 2003;47:164-170.
12. Kucera P, Goldenberg Z, Kurca E. Sympathetic skin response: review of the method and its clinical use. *Bratisl Lek Listy*. 2004;105:108-116.
13. Vetrugno R, Liguori R, Cortelli P, Montagna P. Sympathetic skin response: basic mechanisms and clinical applications. *Clin Auton Res*. 2003;13:256-270.
14. Bir LS, Aktan S. Sympathetic skin response in psoriasis and vitiligo. *J Auton Nerv Syst*. 1999;77:68-71 [published correction J Auton Nerv Syst 2000;80:114].
15. Misiunas A, Niepomniszcze H, Ravera B, Faraj G, Faure E. Peripheral neuropathy in subclinical hypothyroidism. *Thyroid*. 1995;5:283-286.
16. Cruz MW, Tendrich M, Vaisman M, Novis SA. Electroneuromyography and neuromuscular findings in 16 primary hypothyroidism patients. *Arq Neuropsiquiatr*. 1996;54:12-18.
17. Nemni R, Bottacchi E, Fazio R, et al. Polyneuropathy in hypothyroidism: clinical, electrophysiological and morphological findings in four cases. *J Neurol Neurosurg Psychiatry*. 1987;50:1454-1460.
18. Khedr EM, El Toony LF, Tarkhan MN, Abdella G. Peripheral and central nervous system alterations in hypothyroidism: electrophysiological findings. *Neuropsychobiology*. 2000;41:88-94.