

The Value of Muscle Thickness of Lower Limbs in The Detection of Diabetic Peripheral Neuropathy

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Abstract:

Background: Neuropathy stands out as the highest-prevalence diabetes-related complication, impacting no less than 50% of individuals with diabetes throughout their lifespan. As the most common reason for disability due to walking difficulties, foot ulcerations, and limb loss, diabetic peripheral neuropathy is worthy of study, and early diagnosis of its signs is required.

Objectives: This study aims to aid in the identification of diabetic peripheral neuropathy by determining the muscle thickness of the lower extremities in patients with diabetes mellitus.

Methods: The study included 24 subjects with diabetic peripheral neuropathy and 25 individuals as a control group, subdivided into 10 diabetic patients without diabetic peripheral neuropathy and 15 healthy individuals. Both control and case subjects underwent peroneal and tibial motor nerve conduction studies, and high-resolution muscle ultrasounds to measure muscle thickness. The abductor hallucis muscle, extensor digitorum brevis muscle, extensor hallucis longus muscle, tibialis anterior muscle, and rectus femoris muscle were evaluated using ultrasound.

Results: Comparing the tested muscles in diabetic patients with diabetic peripheral neuropathy to the control groups, the study revealed a statistically significant decrease in the thickness of many of the muscles being tested.

Conclusions: These findings suggest that quantitative muscle ultrasound could be beneficial in identifying muscle changes associated with diabetic peripheral neuropathy. However, additional studies are necessary to verify the results in larger samples of diabetic patients.

Keywords: Diabetic Peripheral Neuropathy; Neuromuscular Ultrasound; Muscle Thickness.

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Introduction:

Diabetes (DM) is a global chronic metabolic disease. It is among Iraq's top ten causes of medical care (1). It is characterized by insulin resistance and Beta-cell dysfunction (2). On excluding other possible etiologies of peripheral neuropathy, the development of peripheral nerve dysfunction signs and symptoms in individuals with diabetes is suggestive of the presence of diabetic peripheral neuropathy (DPN). The signs and symptoms of diabetic peripheral neuropathy can be divided into two classifications: Symmetrical polyneuropathies and focal or multifocal neuropathies, both of which are distinct clinical syndromes. The pathological manifestation includes acute axonal degeneration, a form of demyelination, injury to myelinated fibers, and vasculopathy that affects the small veins and arteries within the nerve (3) Diabetic neuropathy is caused by high blood glucose and lipid levels which causes nerve damage(4). Given that diabetic neuropathy is the highest-prevalence microvascular diabetes-related complication (5), it affects at least half of all patients with diabetes at some point in their lives (6). As The most common reason for disability due to

walking difficulties, foot ulcerations, and limb loss, DPN is worthy of study, and early diagnosis of DPN signs is required. Therefore, it is critical to recognize the symptoms of DPN as soon as possible. It is the most common reason for neuropathy and non-traumatic amputations in developed countries today (7). Asymptomatic diabetic neuropathies represent around 50% of diabetic neuropathies (6). Distal symmetrical polyneuropathy is the most common type of diabetic neuropathy. It is described as a "stocking and glove" spread of symptoms, affecting the upper and lower extremities (6). The gold standard for assessing the denervation of muscles in peripheral neuropathy is the nerve conduction study (NCS). Amplitude and NCV are both commonly used in DPN lesion monitoring. CMAP amplitude is more meaningful than NCV because it better captures axonal destruction and neuropathy's impacts like sensation reduction and muscle weakness (8). However, the unpleasant quality of the electrical impulse can make NCS uncomfortable for patients. In addition, patient compliance is required to acquire accurate results during this examination (9). Musculoskeletal ultrasound (MSK US), on the other hand, is readily available and does not involve any

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sort of invasive procedure. It provides instant and dynamic information on patients (10). MSK US can identify reduced muscle thickness and cross-sectional area (CSA) which is characteristic of neuromuscular diseases. It also has the capability to detect muscular fibrosis and fat atrophy (11).

Patients and Methods:

Patients: This case-control study was conducted during the period between October 1, 2022, and February 26, 2023. A sample of 24 middle age Iraqi patients (of both genders) who are diagnosed with type 2 diabetes mellitus with an age range from 40 to 65 years, were selected for the study. They have experienced pain, paresthesia, and/or weakness in the hands and feet, particularly their lower limbs. A full history was taken from the patients, and they underwent clinical examination and nerve conduction study (NCS). Patients who had abnormal NCS findings were included in the study as patients with DPN. Body mass index (BMI) was calculated by the formula (kg/m^2) where (kg) is the weight in kilograms which was measured by an electronic scale and (m^2) is the height in square meters, measured by a measuring tape. HbA1c was measured using high-performance liquid chromatography (HPLC). Those patients were selected from the EMG unit in Ghazi Al-Hariri Hospital in Baghdad. They were compared to a control group of 25 individuals which is further subdivided into 15 healthy subjects and 10 diabetics without DPN. Patients with neuropathy caused by endocrine/metabolic triggers (chronic renal impairment, liver dysfunction, hypothyroidism), autoimmune medical conditions (SLE, RA, Sjogren syndrome), drugs (amiodarone, isoniazid, chemotherapy), tumors (direct tumor infiltration, leukemia, lymphoma), or intake of alcohol were excluded from the study. After explaining the purpose of the study to each participant, verbal consent was gained. The ethical committee of the College of Medicine/ University of Baghdad gave its approval of the research.

Methods: NCS was done for the motor nerves (peroneal and tibial) using the Natus, model 2019 EMG devise. Transverse US images of the abductor hallucis (AH) muscle which has its nerve supply from the tibial nerve, the peroneal-innervated extensor digitorum brevis (EDB), extensor hallucis longus (EHL), and tibialis anterior (TA) muscles, and the femoral-innervated rectus femoris (RF) muscle were acquired to measure muscle thickness (T) in (mm). The US was conducted with the individual in a relaxed supine position with the ankle at neutral (0°). The probe was positioned on the foot medially midpoint between the heel and the ball of the foot for AH measurement. EDB measurement was done on the dorsal side of the foot over the muscle belly 2-3 fingerbreadths distal to the lateral malleolus. For EHL the probe was located 4-5 fingerbreadths above the

ankle, just lateral to the TA tendon, the muscle is palpable by extending the big toe. TA thickness was measured by placing the probe on the muscle belly just lateral to the tibial crest, two-thirds the distance from the ankle towards the knee. For the RF muscle, the probe was positioned on the anterior thigh, at the midpoint between the hip and the knee. Figures (1) and (2) are US images captured during the US examination under this study. They show the difference in the thickness of EDB muscle between a healthy subject and a diabetic patient with DPN. The US examination was performed on the same day as the nerve conduction study using HD11XE Philips 2009 and a linear probe with a frequency range of 10-12 MHz.



Figure (1): showing EDB muscle thickness in a healthy individual.



Figure (2): showing EDB muscle thickness in a patient with DPN.

Statistical Analysis:

Data management was done using the statistical package for social sciences SPSS (version 25). The mean, standard deviation, and range were used to describe numerical data. Categorical variables, data were summarized using frequencies and relative frequencies (percentages). Comparisons between groups were done using the one-way ANOVA test for normally distributed quantitative variables, with (p -value ≤ 0.05) being considered statistically significant and (p -value < 0.001) highly significant.

Results:

Tables (1) and (2) present the baseline demographic information of the study population. The results indicate that there were no significant differences in age, weight, height, or body mass index (BMI)

Parameter - Mean±SD (Range)	DM With DPN	DM Without DPN	Healthy Controls	p-value
AGE (years)	52.1±1.63 (40-65)	48.1±2.25 (42-61)	48.5±1.79 (40-60)	0.226
WEIGHT (kg)	79.1±15.0 (50-125)	81.7±10.1 (63-93)	80.3±10.7 (59-98)	0.865
HEIGHT(m)	1.7±0.09 (1.50-1.85)	1.7±0.10 (1.51-1.85)	1.7±0.08 (1.50-1.81)	0.444
BMI (kg/m ²)	27.8±4.88 (16.9-45.2)	27.6±1.71 (22.7-30.1)	28.9±3.23 (24.1-37.3)	0.670
DM DURATIO N (years)	10.3±6.59 (3-20)	4.6±1.07 (3-6)	--	0.001*
HbA1c (%)	9.9±2.24 (6.5-14.1)	6.2±0.82 (4.9-7.5)	--	0.005*

between the study groups, with a p-value greater than 0.05.

A statistically significant (p<0.05) difference was found between diabetic patients with DPN and those without DPN in the duration of diabetes mellitus and the HbA1c levels. Both parameters were higher in those with DPN than those without.

Table (2): Comparison of muscle thickness in the three study groups

Muscle Thickness (mm) Mean±SD (Range)	DM With DPN	DM Without DPN	Healthy Controls	P-value
Abductor hallucis	1.11±0.194 (0.75-1.60)	1.15±0.179 (0.80-1.40)	1.29±0.208 (1.08-1.69)	0.020*
Extensor digitorum brevis	0.57±0.150 (0.30-0.85)	0.67±0.102 (0.532-0.82)	0.78±0.150 (0.56-0.99)	<0.001*
Extensor hallucis longus	1.54±0.336 (1.11-2.20)	1.59±0.272 (1.18-1.91)	1.77±0.127 (1.55-2.01)	0.045*
Tibialis anterior	2.89±0.325 (2.20-3.49)	2.77±0.305 (2.35-3.21)	2.83±0.281 (2.28-3.12)	0.551
Rectus femoris	1.34±0.402 (0.58-1.99)	1.64±0.535 (1.17-2.87)	1.58±0.241 (1.20-1.97)	0.075

Discussion:

In this study, muscle thickness was reduced significantly in many muscles (AH, EDB, and EHL) when compared to the control groups. While (TA and RF) had a non-significant difference in their thickness. These results agree with previous studies (8) (12) (13). The pattern of muscle atrophy in this study reflects the length-dependent neuropathic involvement in diabetic peripheral neuropathy. This is similar to the results of a study conducted by Kadhim et al (14) where the thickness of muscles distally (TA and AHB) was significantly less in patients with DPN than in the control groups, but a non-significant difference was found in the proximal (biceps femoris muscle). This study was conducted on 73 patients (44 males and 29 females) diagnosed with DPN, matched to 73 subjects as the control group.

A small amount of functioning muscle fibers could be seen by ultrasound in individuals with very low CMAP amplitude (below 1 mV) and even in subjects without a recordable amplitude. This might result from a few scattered muscle fibers being embedded in fatty and fibrous tissue. NCS amplitude may underestimate the quantity of contractile mass in extensively wasted muscles, whereas ultrasound might overestimate muscle size. Future US-guided positioning of needle electrodes in the rest of the functioning muscle fibers, enabling precise

Table (1): Comparison of study parameters between the case and control groups

Table (2): Distribution of the study groups by gender

Gender	DM With DPN		DM Without DPN		Healthy Controls	
	Number	%	Number	%	Number	%
Males	19	79.2	7	70	11	73.3
Females	5	20.8	3	30	4	26.7
Total	24	100.0	10	100.0	15	100.0

Muscle thickness was assessed for five muscles in the lower extremities: Extensor digitorum brevis, abductor hallucis, extensor hallucis longus, tibialis anterior, and rectus femoris. The results for the three groups are displayed in Table (3). Statistically significant differences in muscle thickness between the three groups were detected with P-values<0.05 for the first three muscles, while the other two showed non-significant differences.

recordings of the neurophysiological response, could reduce that. DPN patients exhibited higher HbA1c and longer DM duration, confirming previous studies. Long-term diabetes and inadequate glycaemic management increase glycosylation end products, metabolic derangements, endothelial damage, and oxidative products(15). The current study had a few weaknesses. First, there weren't enough subjects overall, so the effects of age and gender on muscle thickness were not looked at because the number of people in the sample was not large enough for statistical analysis. Since we only had one US examiner, we were unable to evaluate the inter-rater reliability of the quantitative US, which requires two operators to administer US exams for each individual on the same day. Therefore, applying the findings to all DPN patients is not suitable. To better understand the therapeutic relevance and applicability of this technique, additional research with a larger sample size and examination by two US examiners is required.

Conclusions:

Patients diagnosed with DPN had noticeably less muscle mass compared to the control groups. The fact that the US can detect existing muscles in patients who have low or unrecordable amplitude suggests that this method, which we investigated, may provide additional information when dealing with patients

who have advanced neuropathy and severe muscle wasting. Ultrasound of the neuromuscular system can be used in combination with NCS as a screening method for DPN because it is less expensive, does not pose any health risks, and is easier to access.

Authors declaration:

There is no conflict of interest.

We hereby confirm that all figures and tables included in the manuscript are mine/ours. In addition, the figures and images, which are not mine/ours, have been given permission for republication attached to the manuscript. -Authors signed on ethical consideration's approval-ethical clearance: The project was approved by the local ethical committee at Al-Shaheed Ghazi Al-Hariri Hospital, Medical City, per code number (87.4.6.2022).

Author contributions:

Study conception & design: (Abdulnasir H. Ameer). Literature search: (Abdulnasir H. Ameer). Data acquisition: (Abdulnasir H. Ameer). Data analysis & interpretation: (Sally H. Abdulkareem & Abdulnasir H. Ameer). Manuscript preparation: (Sally H. Abdulkareem & Abdulnasir H. Ameer). Manuscript editing & review: (Sally H. Abdulkareem & Abdulnasir H. Ameer).

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قيمة سمك العضلات للأطراف السفلية في الكشف عن الاعتلال العصبي المحيطي السكري.

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الخلاصة:

خلفية البحث: يبرز الاعتلال العصبي باعتباره من أكثر المضاعفات المرتبطة بمرض السكري انتشاراً، حيث يؤثر على ما لا يقل عن 50% من الأفراد المصابين بداء السكري طوال حياتهم، باعتباره السبب الأكثر شيوعاً للإعاقة بسبب صعوبات المشي، وتقرحات القدم، وفقدان الأطراف، فإن الاعتلال العصبي المحيطي السكري يستحق الدراسة، وإن التشخيص المبكر لأعراضه مهم.

الاهداف: تهدف الدراسة إلى المساعدة في تحديد الاعتلال العصبي المحيطي السكري من خلال تحديد سمك العضلات في الأطراف السفلية لدى المرضى المصابين بهذا المرض.

المرضى والمنهجية: شملت الدراسة 24 مريضاً يعانون من الاعتلال العصبي المحيطي السكري و 25 متطوعاً غير مصابين بالمرض، والذين تم تقسيمهم إلى مجموعتين: 10 أفراد مصابين بمرض السكري لكن غير مصابين بالاعتلال العصبي المحيطي و 15 فرداً سليماً. خضع كل من هؤلاء الأشخاص لفحص الاعصاب الحركية الشظوية والقصبية لكلا الأرجل والموجات فوق الصوتية لخمسة عضلات لقياس سمك العضلات. تم قياس سمك العضلة المبعدة لابهام القدم، العضلة الباسطة الفصيرة لأصابع القدم، عضلة الطويلة المثنية لابهام القدم، العضلة الظنبوبية الأمامية، والعضلة الفخذية المستقيمة على كلا الجانبين باستخدام الموجات فوق الصوتية.

النتائج: كشفت الدراسة عن انخفاض معتد به إحصائياً في سمك العديد من العضلات التي يتم اختبارها عند المرضى المصابين بالاعتلال العصبي المحيطي عند مقارنتها بمجموعة الأشخاص غير المصابين به.

الاستنتاجات: تشير هذه النتائج إلى احتمال أن تكون الموجات فوق الصوتية الكمية للعضلات مفيدة في تحديد التغيرات العضلية المرتبطة بالاعتلال العصبي المحيطي السكري. من الضروري إجراء دراسات إضافية للتحقق من النتائج في عينات أكبر من مرضى السكري.

مفتاح الكلمات: الموجات فوق الصوتية العصبية العضلية، سمك العضلات، الاعتلال العصبي المحيطي السكري.