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PECULIARITIES OF THE FORMATION OF UNILATERAL DIABETIC TROPHIC ULCERS*

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Diabetes mellitus (DM) is one of the leading medical and social problems of increasing relevance. More than 500 million people are currently living with diabetes worldwide, and this number is predicted to rise to 643 million by 2030 and to 783 million by 2045 [1].

One of the most common and socially significant consequences of long-term and poorly controlled diabetes is the development of trophic ulcers (TU). This dangerous complication develops in every sixth patient with diabetes mellitus. Worldwide, between 19% and 34% of people with diabetes are estimated to develop foot ulcers during their lifetime. Approximately 20% of patients with TU will require lower limb amputation [2].

The rate of lower extremity amputations in individuals with diabetes ranges from 78 to 704 per 100,000 person-years, and the relative risk between patients with diabetes and those without diabetes varies between 7.4 and 41.3 [3].

The increasing incidence of diabetes mellitus and the growing number of its complications are challenging researchers and practitioners to improve the effectiveness of their treatment, which is not possible using traditional methods [4]. Current efforts to prevent and improve the effectiveness of TU treatment are aimed at identifying and eliminating new pathogenic factors of ulcer formation [2]. According to clinical practice, trophic ulcer formation occurs unilaterally. The pathways that lead to ulceration, including chronic sensorimotor neuropathy, peripheral arterial disease, diabetic osteoarthropathy, infection, and autonomic dysfunction, are well known [5]. But they have predominantly symmetrical characters. Thus, a foot-specific factor must trigger the unilateral development of destructive changes in the foot.

Uneven load and pressure on the foot can be considered the main factors of ulceration in patients with DM [6]. One of the reasons

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that may lead to leg overloading is inequality between the lower extremities' length. It is also known as leg length discrepancy (LLD) or anisomelia, which is not a rare condition [7]. In 90% of the general population, some form of leg length discrepancy was observed, with 20% exhibiting a difference greater than 0.9 cm [8]. Such factor may lead to differences in the plantar pressure distribution [9]. Healthy people are able to adapt to anisomelia due to various compensatory mechanisms of muscles, joints, and ligaments, which have been described in numerous studies [10]. However, there is currently insufficient data on the effect of LLD on the unilateral nature of trophic ulcer formation.

The aim of the study was to assess the odds and risks of unilateral plantar trophic ulcer formation in patients with diabetes mellitus based on the evaluation of the leg length discrepancy and the resulting asymmetric load distribution between the longer and shorter limbs.

MATERIALS AND METHODS

The study involved 99 diabetic patients, who were divided into 2 groups: 53 diabetic patients without trophic ulcers as a control group (group DM; 50.9% female; age [± SD] — 54.8 ± 14.4 years), and 46 patients with DM and plantar unilateral trophic ulcers (group DM + UTU; 52.2% female; age [± SD] — 64.1 ± 7.5 years). The age and gender distribution in the study groups did not differ ($p > 0.05$). According to the glycated hemoglobin (HbA1c) levels, there were no significant differences between the DM and DM+UTU groups ($p > 0.05$). The groups were also comparable in terms of body mass index ($p > 0.05$). Table 1 reflects the equal distribution of the main clinical, age, gender, and anthropometric characteristics of the patients of the comparison groups.

All the patients were treated in the Endocrinology Department of Sumy Regional Clinical Hospital and Sumy Laser Clinic. Inclusion criteria for the DM and DM + UTU groups were type 1 or type 2 diabetes mellitus, moderate/severe in the compensation stage (mean HbA1c < 7%), with a BMI ≤ 25 km/m². Patients in the group DM + UTU have diabetic foot syndrome I–II according to the E. Wagner classification [11]. The exclusion criteria were the presence of musculoskeletal disorders and decompensated comorbidities.

The distribution of patients by type of diabetes did not differ in the study groups ($p = 0.812$). Antihyperglycemic treatment in both groups included combination therapy: long-acting insulin + metformin — 15 patients (15.2%), sulfonylurea + metformin — 45 patients (45.4%), dipeptidyl peptidase 4 inhibitor + metformin — 8 patients (8.1%), metformin + sodium-glucose cotransporter 2 inhibitor — 10 patients (10.1%); monotherapy with metformin — 5 patients (5.1%) and monotherapy with insulin — 16 patients (16.1%) [12].

All study participants gave informed consent for participation in the study in accordance with the WMA Declaration of Helsinki — Ethical Principles for Medical Research Involving Human Subjects, 2013. The study protocol was approved by the Ethics Committee of the Sumy State University.

Table 1

The main clinical characteristics of the comparison groups

Indicator	DM (n = 53)	DM + UTU (n = 46)	p
Age, years ± SD, (Min-Max)	54.8 ± 14.4 (25–82)	64.1 ± 7.5 (45–76)	0.053
Sex, men / female, (%)	49.1 / 50.9	47.8 / 52.2	0.151
Type of DM, 1 / 2, (%)	17.0 / 83.0	15.2 / 84.8	0.812
HbA1c, %	6.8 ± 0.5	6.9 ± 0.3	0.835
BMI, kg/m²	24.5 ± 0.5	24.0 ± 0.7	0.735

Notes:
DM — diabetes mellitus;
p — the statistical significance of differences between DM and DM + UTU groups;
categorical variables were compared using the $\chi 2$ test, quantitative variables — using the t-test.

To measure lower limb length, we used a device consisting of a platform with a 1 m rail set at a 45° angle to the longer side. One end of the rail was fixed in the middle of the longer side of the platform, while the other end held a tripod for a mobile phone equipped with a "virtual ruler" application. The platform was positioned against a vertical wall, with the patient standing upright, ensuring that the back of the head, shoulder blades, buttocks, and heels touched the wall. The knees were bent, and the feet, without shoes, were placed on opposite sides of a separating strip. We palpated the anterosuperior iliac spine and marked this point as the proximal landmark on both sides. The distal landmark was marked at the point of maximum increase of the outer bone of the tibia. The mobile device was then fixed on the tripod (Fig. 1).

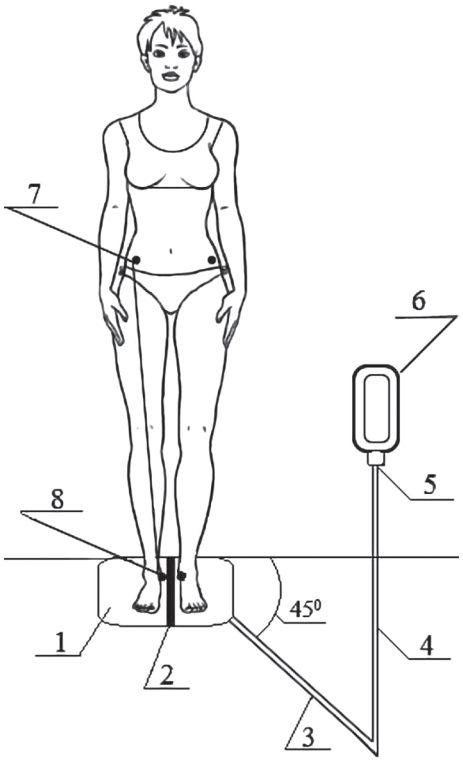

Fig. 1. Lower limb length measuring device.
Description:
1 — platform, 2 — dividing line,
3 — 1 m rail set at a 45° angle
to the longer side of the platform, 4 — tripod,
5 — device for attaching a mobile device,
6 — mobile phone, 7 — proximal landmark,
8 — distal landmark.

The measure application was used to focus on the proximal landmark. The device was moved through the distal landmark to the point where it intersected with the horizontal plane (floor), capturing the second measurement point. The digital length between the two points was displayed on the screen, and a photo was taken to document the measurement for further calculations. This process was repeated for the other limb, and the difference between the two leg lengths was calculated. Three measurements were taken for each limb, and the arithmetic mean was calculated for analysis [13].

Statistical analysis was carried out using the SPSS 27.0 software package (USA). Quantitative variables were presented as mean ± standard deviation for normally distributed data and percentage values. The normality of quantitative data was evaluated using the Shapiro-Wilk test. Student t-test was conducted to compare the quantitative variables of the two groups. Pearson's chi-squared ($\chi 2$) test of independence was used to analyze the categorial variables of the two groups and data distribution. All p-values less than 0.05 were considered statistically significant. For qualitative data, odds ratio (OR) and relative risk (RR) were calculated.

RESULTS AND THEIR DISCUSSION

To characterize the prevalence of anisomelia in the study groups, the leg length discrepancy was categorized into the following ranges: less than 0.5 cm; 0.5 to 1.5 cm; and more than 1.5 cm. The mean limb length difference measurement of less than 0.5 cm was considered statistically and clinically insignificant due to technical and anthropometric measurement errors.

The average leg length discrepancy between the right and left extremities in the group DM was 0.98 ± 0.88 cm. In the group DM + UTU, the average leg length discrepancy was 0.92 ± 0.68 cm ($p_{DM - DM + UTU} > 0.05$).

Among the 53 patients of the group DM, 69.6% had a discrepancy between the two limbs, and only in 30.4% the differences were not found. A mild difference of 0.5 to 1.5 cm was observed in 52.2%, and 17.4% had LLD greater than 1.5 cm.

There was no difference in leg length in 28.3% of patients in group DM + UTU. A mild difference, equal to 0.5–1.5 cm, was found in

Table 2

Leg length discrepancy in study groups

Indicator	DM (n = 53)	DM + UTU (n = 46)	p
Average LLD ± SD, cm	0.98 ± 0.88	0.92 ± 0.68	0.157
Δl < 0.5 (%); (n)	30.4% (16)	28.3% (13)	0.835 (χ^2 = 0.36)
Δl = 0.5–1.5 (%); (n)	52.2% (28)	50.0% (23)	
Δl > 1.5 (%); (n)	17.4% (9)	21.7% (10)	

Notes:
Δl — the value of the difference between the lengths of the lower extremities;
p — the statistical significance of differences.
Student t-test was used to compare mean values, frequency distribution was compared using Pearson's chi-squared (χ2) test.

50.0%, and greater than 1.5 cm was present in 21.7%.

There was no statistically significant difference between the mean LLD values of the DM and DM + UTU groups (p = 0.157). So, the distribution of patients with different degrees of anisomelia did not differ between the two groups (χ^2 = 0.36; p = 0.835). The results of the comparison of the two groups are shown in Table 2.

Trophic ulcer localization and the presence of LLD were analyzed in the DM+UTU group. Trophic ulcer development occurred in 12 people with equal limb lengths (26.1%). Among 34 patients with trophic ulcers (73.9%) who had anisomelia, plantar ulcer formation was observed on the shorter limb in 30 patients (65.2%) and on the longer limb in 4 patients (8.7%) (Fig. 2).

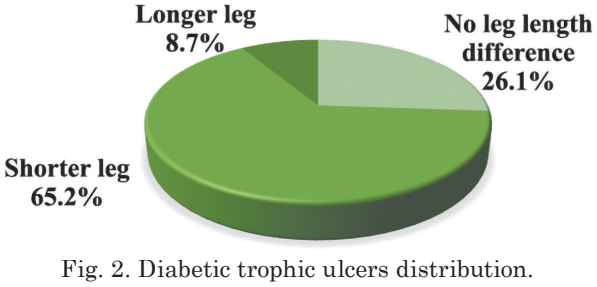

Fig. 2. Diabetic trophic ulcers distribution.

The risk of the development of trophic plantar ulcer on the shorter leg was analyzed using OR and RR calculations. The odds ratio was 3.57 (95% CI, 1.14–11.18), indicating that the patient had significantly higher odds of developing a trophic ulcer on the shorter leg (p = 0.025). Additionally, the relative risk for ulcer development on the shorter leg was 1.89 (95% CI, 1.04–3.43), indicating that the risk of occurrence of a trophic ulcer was higher in persons with the shorter leg compared to those without such factor.

According to the contemporary database, asymmetrical length of the legs is not a rare phenomenon, but it is important to analyze what exact discrepancy value can influence a person's health. The difference between the length of the legs < 2.0 cm is considered insignificant in the general population worldwide [14]. However, a leg length discrepancy of even 0.5–1.5 cm leads to uneven vertical plantar pressure during walking, with the shorter leg typically experiencing higher pressure compared to the longer one [8].

In physiological conditions, inequality in leg length is usually associated with compensatory changes in the gait and musculoskeletal adaptation [15]. However, an insignificant asymmetry that does not manifest itself in some people can become a trigger for the development of serious complications of various diseases under certain conditions [10]. In patients with diabetes compensatory capabilities for LLD are significantly reduced due to diabetic neuropathy, angiopathy, and musculoskeletal disorders, resulting in decreased sensitivity, blood supply insufficiency, and impairment of the ability to adapt to such changes [16]. The difference in the length of the lower extremities affects the uneven distribution of the load on the feet, which, combined with the above pathological processes, becomes one of the main risk factors for the development of trophic ulcers [6].

Anisomelia causes a displacement of the body mass axis and an asymmetric distribution of weight load on the lower extremities [7]. The unequal length of the extremities creates exces-

sive pressure on the forefoot, and, especially, on the first pinned finger and thumb of the shorter limb. This leads to excessive supination and plantar flexion during stance, as well as early heel lift. Meanwhile, the longer limb is forced to compensate by pronation, increased dorsiflexion at the end of the stance phase, and a delayed peak in dorsiflexion [16].

Peripheral diabetic neuropathy impairs the ability to effectively adjust their gait in response to leg length discrepancy [16]. Diabetic neuropathy damages sensory, motor, and autonomic nerves, followed by impairing sensation, muscle control, and local blood flow in the feet. Sensory neuropathy leads to a loss of protective sensation, increasing the risk of unnoticed tissue damage. Autonomic neuropathy impairs circulation, causing blood to drain away from tissues, which delays healing and increases the risk of infection. Permanent excessive pressure on the foot in the case of LLD, especially during walking, further complicates wound healing [17].

Our study confirms the above-mentioned influence of lower leg discrepancy on the pathogenesis of plantar trophic ulcers in patients with diabetes mellitus. The odds and relative risks of the development of UTU on the shorter leg were significantly increased ($p = 0.025$). These findings suggest that overloading of a shorter leg is a major risk factor for the development of unilateral plantar trophic ulcers. Measuring the length of the lower limbs may be an essential diagnostic method for early determining of anisomelia and the subsequent necessary equalization of leg length [7]. Understanding LLD's influence on the unilaterally trophic ulcer formation has a significant impact on developing a risk stratification system, management, and treatment protocols for patients with diabetic foot syndrome. Only pathogenetically based prevention and treatment for patients with a high risk of ulceration could reduce the occurrence of TU and amputations.

The study has several limitations. The limited number of participants is an indication that the results should be interpreted with caution in terms of wider generalizations. Further multicenter studies of a cohort of patients with diabetes are needed. Conducting a larger-scale study similar to this one can lead to the establishment of better diabetic foot management and risk stratification systems.

CONCLUSIONS

Results of our study have demonstrated that diabetic patients with anisomelia have significantly higher odds and risks of trophic ulcer formation at the shorter leg. These findings confirm a strong relationship between the presence of a leg length discrepancy with an asymmetric redistribution of the load on the shorter leg. It suggests that even small differences in limb length should be carefully considered when assessing diabetic patients, as it may be an important factor in the prevention and management of trophic ulcers.

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Background. An estimated 19–34% of people with diabetes develop foot ulcers during their lifetime, with around 20% requiring lower limb amputation. Diabetic trophic ulcers are typically unilateral, suggesting a foot-specific factor triggering the destructive changes in the foot. **The aim of the study** was to assess the odds and risks of unilateral trophic ulcer formation in diabetic patients based on the evaluation of the leg length discrepancy and the resulting asymmetric load distribution between the longer and shorter limbs.

Materials and methods. The study involved 53 diabetic patients without plantar ulcers and 46 with unilateral plantar trophic ulcers, comparable in age, gender, and body mass index. A device with a tripod for a mobile phone, equipped with a «virtual ruler» app, was used to measure leg length. Data analysis was performed using SPSS 27.0 software.

Results. There was no statistically significant difference in mean leg length discrepancy between the two studied groups ($p = 0.157$). The distribution of patients with different degrees of anisomelia was also similar between groups ($\chi^2 = 0.36$; $p = 0.835$). Among 34 patients with trophic ulcers (73.9%) who had anisomelia, plantar ulcer formation was observed on the shorter limb in 30 patients (65.2%) and on the longer limb in 4 patients (8.7%). The odds ratio was 3.57 (95% CI, 1.14–11.18), indicating that the patient with the shorter leg had significantly higher odds of developing a trophic ulcer ($p = 0.025$). The relative risk for ulcer development on the shorter leg was 1.89 (95% CI, 1.04–3.43), indicating that the risk of occurrence of a trophic ulcer was higher in persons with the shorter leg compared to those without such factor.

Conclusions. Diabetic patients with anisomelia have significantly higher odds and risks of trophic ulcer formation at the shorter leg. This suggests that asymmetric load distribution plays a crucial role in unilateral trophic ulcer development.

Keywords: diabetes mellitus, anisomelia, trophic ulcer, leg length discrepancy.

ОСОБЛИВОСТІ ФОРМУВАННЯ УНІЛАТЕРАЛЬНИХ ДІАБЕТИЧНИХ ТРОФІЧНИХ ВИРАЗОК

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Приблизно 19–34% людей, хворих на цукровий діабет, протягом життя зіштовхуються з формуванням плантарних виразок і близько 20% з них потребують ампутації нижньої кінцівки. Діабетичні трофічні виразки зазвичай виникають унілатерально, що свідчить про можливе існування певного чинника, який призводить до деструктивних змін лише на одній зі стоп.

Мета дослідження — оцінити ймовірність та ризики формування однобічних трофічних виразок у пацієнтів із діабетом на основі оцінки різниці в довжині ніг та асиметричного розподілу навантаження між довшою та коротшою кінцівками.

Матеріали та методи. У дослідженні взяли участь 53 пацієнти з діабетом без підошовних виразок та 46 пацієнтів з односторонніми плантарними трофічними виразками, співставні за віком, статтю та індексом маси тіла. Для вимірювання довжини ніг використовували пристрій зі штативом для мобільного телефону, обладнаного додатком «віртуальна лінійка». Статистичний аналіз проводили за допомогою програмного забезпечення SPSS 27.0.

Результати. Не було виявлено статистично значущої відмінності середніх значень різниці довжини ніг між двома досліджуваними групами ($p = 0{,}157$). Розподіл пацієнтів з різними ступенями анізомелії також не відрізнявся між групами ($\chi^2 = 0{,}36$; $p = 0{,}835$). Серед 34 пацієнтів із трофічними виразками (73,9%), які мали анізомелію, формування виразок на коротшій кінцівці спостерігалося у 30 пацієнтів (65,2%), на довшій — у 4 пацієнтів (8,7%). Відношення шансів становило 3,57 (95% ДІ, 1,14–11,18), що вказує на те, що у пацієнта з наявною коротшою кінцівкою вірогідно вищі шанси на розвиток трофічної виразки ($p = 0{,}025$). Відносний ризик розвитку виразки на короткій нозі становив 1,89 (95% ДІ, 1,04–3,43), що вказує на те, що ризик виникнення трофічної виразки був вищим у людей з коротшою ногою порівняно з тими, хто не мав такого фактору.

Висновки. Пацієнти з цукровим діабетом та анізомелією мають значно вищі шанси та ризики формування трофічних виразок на коротшій кінцівці. Це свідчить про те, що асиметричний розподіл навантаження відіграє ключову роль у розвитку односторонніх трофічних дефектів.

Ключові слова: цукровий діабет, анізомелія, трофічна виразка, різниця довжини ніг.