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COMPARATIVE STUDY OF MICROCIRCULATION PARAMETERS IN THE LOWER EXTREMITIES OF PATIENTS WITH TYPE 2 DIABETES DEPENDING ON BODY WEIGHT

J.A. Nazarova
Center for the Development of Professional Qualifications of Medical Workers under the Ministry of Health of the Republic of Uzbekistan, Uzbekistan

L.Kh. Mamadinova
Andijan State Medical University, Uzbekistan

L.U. Zakirova
Andijan State Medical University, Uzbekistan

Abstract
This study focuses on the comparative analysis of microcirculation parameters in the lower extremities of patients with type 2 diabetes mellitus (T2DM), considering their body weight. Microcirculation disturbances are common in diabetic patients and are significantly influenced by obesity. The study evaluates how body weight impacts blood flow and tissue perfusion in the lower extremities. Results indicate that patients with higher body weight exhibit more pronounced microcirculation disorders, which can exacerbate complications such as diabetic foot syndrome. These findings highlight the importance of weight management in improving microvascular health in T2DM patients.

Keywords Type 2 diabetes mellitus, microcirculation, lower extremities, body weight, obesity, diabetic complications, blood flow.

INTRODUCTION

Despite advances in diagnosis and treatment, complications of diabetes mellitus (DM) remain a major concern for patients and their families. Microvascular disease can lead to blindness, renal failure, and limb amputation (1,2,3). Macrovascular complications such as myocardial infarction and stroke occur at a higher rate in patients with DM than in the general population and are the leading cause of death in patients with this disease. Both microvascular and macrovascular complications reduce patients' quality of life and ability to work, and impose significant costs on the public health and healthcare sectors (5,6,7,8).

To assess the state of arterial blood flow in the lower extremities, attending physicians mainly prescribe ultrasound of the vessels of the lower extremities, which, however, does not provide an idea of the state of the microcirculatory bed. It can be argued that the range of diagnostic capabilities for assessing disorders in the microcirculatory bed of the lower extremities is currently extremely limited. But it is the detection of early hemodynamic disorders in small vessels that will help prevent the development of severe complications. Currently, there are no specific clinical recommendations for doctors to identify hemodynamic disorders in the microcirculatory bed of the lower extremities, since the methodology of disorders in the microcirculatory bed of the lower extremities remains the subject of scientific debate. Among the existing research methods (color duplex scanning, rheolymphovasography, radionuclide lymphoscintigraphy, photon-correlation spectroscopy, etc.), laser Doppler flowmetry (LDF) has an undoubted advantage due to its ease of use, non-invasiveness of the technique, and the absence of contraindications for use. The ability to identify microcirculation disorders of the lower extremities characteristic of patients with type 2 diabetes using a simple and relatively inexpensive diagnostic method will expand the diagnostic criteria for type 2 diabetes, especially in the early stages of its development (4). All of the above became the basis for conducting research work.

Aim of the study. To study the diagnostic capabilities of laser Doppler flowmetry in the diagnosis of lower limb microcirculation disorders in type 2 diabetes.

Research material. The study was conducted at the Andijan State Medical Institute (I, II and III neurological departments) and the Regional Endocrinology Dispensary. The criteria for inclusion of patients in the study were the presence of verified type II diabetes mellitus (DM-2); disease duration of at least 5 years; age from 45 to 65 years; absence of focal brain damage according to MRI data; signing of voluntary informed consent to participate in the study. The exclusion criteria were the presence of severe or unstable concomitant somatic pathology, acute cerebrovascular accident, myocardial infarction, alcoholism, substance abuse.

A total of 110 patients diagnosed with type 2 diabetes mellitus (DM-2) were examined, 47 (42.7%) men and 63 (57.3%) women, aged 40 to 79 years, the average age of patients was 52.3+12.9 years. During the study, patients were divided into two groups.

Table 1

Distribution of patients into groups

Groups	gender		
		n	%
Group I n=25 (19,4%)	male	14	56,0%
	female	11	44,0%
II group n=85(65,9%)	male	35	41,2%
	female	50	58,8%
Total n=110 (100,0%)	male	49	44,5%
	female	61	55,5%

The first group consisted of 25 (22.7%) patients who did not have excess body weight (BMI < 25), for this group the average BMI was 19.2 + 5.8 and the HbA1C level was 8.8 + 0.4%. The second group included 85 (77.3%) patients whose body weight was above normal (BMI> 25). In this group the average BMI was - 31.8 + 7.3, and the HbA1C level was 9.2 + 0.8% (Table 1). The control group (CG) consisted of 19 individuals (12 women and 7 men, average age 64.3 ± 7.1) with no history or objective examination of diabetes, hypertension, or other cardiovascular diseases, and no other diseases that impair cognitive functions (TBI, hypothyroidism, alcoholism, substance abuse). Individuals in the control group did not complain of decreased memory, attention, or mental performance (Table 1).

Analyzing the data of patients selected for the study, the following conclusions can be made: there were more women among the patients - the sex index was 1.4 in favor of the female sex; when analyzing the sex structure depending on age, it was noted that the percentage of men decreased with age, and women increased; there was a significant number of patients with increased body weight (BMI> 25.0) - 85 people (77.3%).

METHODS

All patients underwent a standard clinical and neurological examination (analysis of patient complaints, life history and medical history, objective examination, including study of neurological status) and somatic examination.

The initial blood flow and hemodynamic disorders in the microcirculatory bed of the lower extremities in patients were assessed using the laser Doppler flowmetry (LDF) method on a laser blood microcirculation analyzer for general practitioners LAKK-OP with 2 recording channels (manufacturer OOO NPP LAZMA PF, Russia). We analyzed microcirculation indices at rest in both lower extremities.

- The microcirculation index is the value of the average blood flow in the recording time intervals or the arithmetic mean value of the microcirculation index, measured in perfusion units (PU). A change in PM (increase or decrease) characterizes an increase or decrease in perfusion.

- The parameter RMS is the average fluctuation of perfusion relative to the average value of blood flow PM. Since perfusion registration is associated not only with rhythmic regulatory fluctuations, but also with random chaotic ones, the standard deviation is used to average the PM value. RMS reflects the average change in perfusion parameters at different registration frequencies.

3. The coefficient of variation reflects the ratio of the values of PM and SD.

4. Rhythmic components include active and passive factors of microcirculation control. Based on the ratio of predominant oscillations in the amplitude-frequency spectrum, one can draw a conclusion about the prevalence of one or another type of microcirculatory bed state.

Hell (passive factor) - respiratory wave, caused by the dynamics of venous pressure during pulmonary mechanical activity, the suction action of the “respiratory pump”. The diagnostic value of the respiratory wave lies in its connection with the venular link. However, the respiratory wave does not directly reflect the blood flow of the venous sections of the capillaries and venules, it is associated with its respiratory modulation.

Ac (passive factor) – pulse wave, this is a parameter that changes depending on the state of tone of resistive vessels.

Ae (active factor) – endothelial oscillations, caused by the functioning of the endothelium. The

diagnostic value of endothelial oscillations lies in the assessment of endothelial dysfunction by the relative change in oscillation amplitudes.

An (active factor) – neurogenic oscillations, associated with sympathetic adrenergic effects on the smooth muscles of arterioles and arteriolar sections of arteriole-venular anastomoses.

Am (active factor) – myogenic oscillations, characterize the muscle tone of blood vessels. The origin of these vasomotions is associated with local pacemakers inside smooth muscle fibers. The diagnostic value of myogenic oscillations lies in the assessment of the state of muscle tone of precapillaries, regulating the blood flow to the nutrient channel.

To ensure the accuracy and reliability of the research results, a thorough statistical analysis used both parametric and non-parametric methods. Microsoft Office Excel 2016 spreadsheets were used to collect, process, systematize and display the obtained data. For a more in-depth statistical analysis, IBM SPSS Statistics version 26 software developed by IBM Corporation was used. This software allowed for complex statistical calculations and guaranteed high accuracy of data processing.

RESULTS

The initial blood flow and hemodynamic disorders in the microcirculatory bed of the lower extremities in patients of group I were assessed in comparison with group II. When analyzing the initial blood flow and the amplitude-frequency spectrum in patients with varying degrees of severity of distal diabetic polyneuropathy depending on the presence of metabolic syndrome, we obtained the following data, presented in Table 2.

Table 2.

Results of evaluation of microcirculation of lower extremities in groups (Me)

LDF-gram parameter	Group I	II group	KG	Δ I-KG	Δ II-KG	Δ I-II	p≤		
				1	2	3	1--2	2--3	1--3
PM, pf.un.	9,7	10,8	12,8	-24,2%	-15,6%	-10,2%	0,005		0,05
RMS, pf.units	1,09	1,15	1,27	-14,2%	-9,4%	-5,2%	0,05		
KV	11,8	11,2	10,9	8,3%	2,8%	5,4%	0,005		0,05
Amax E	0,33	0,31	0,28	17,9%	10,7%	6,5%	0,05		
Amax H	0,35	0,38	0,41	-14,6%	-7,3%	-7,9%	0,05	0,05	0,05
Amax M	0,34	0,31	0,28	21,4%	10,7%	9,7%	0,05		0,05
Amax R	0,25	0,28	0,32	-21,9%	-12,5%	-10,7%	0,05		
Amax C	0,81	0,89	0,93	-12,9%	-4,3%	-9,0%	0,05		

When analyzing the arithmetic mean (Me) of the microcirculation index (MI) in group I, significantly lower perfusion values were found compared to group II and CG (in group I, Me CG was 24.2% lower ($p>0.005$) and compared to group II, it was 15.6% lower ($p<0.05$)) (Table 2). The standard deviation (pfd, units) was lower in group I

compared to CG and group II (Me CG was 14.2% lower in group I (p>0.05) and compared to group II, where this indicator was 9.4% lower (p>0.05)). Lower flux values obtained as a result of our work in patients in group I may be due to less intensive functioning of the mechanisms of active control of microcirculation, a decrease in cardiac and respiratory rhythms due to a smaller number of erythrocytes entering the arterioles (Table 2).

When analyzing blood flow in patients in group I, the median values for the coefficient of variation (CV) did not differ significantly from those in group II (Me in group I was 5.4% higher than Me in group II (p>0.05)).

Blood pressure (passive factor) – Amax R - respiratory wave: lower blood pressure values in patients of group I compared to the values in the control group may indicate an increase in microcirculatory pressure (Me in group I is 10.7% less than Me in group II (p>0.05)).

Ac (passive factor) – Amax C - pulse wave: significantly reduced Ac values in patients of group I, together with reduced or normal PM values, may indicate a decrease in the inflow of arterial blood into the microcirculatory bed of the lower extremities (Me of group I is 4.3% less than Me of group II (p <0.05)).

Ae (active factor) – Amax E - endothelial fluctuations: significantly elevated Ae values in patients of group I (Me in group I is 6.5% higher than Me in group II (p <0.05)) indicate the presence of endothelial dysfunction, and in patients with high-amplitude pulse rhythm – indicate dilation of small arteries and large arterioles.

An (active factor) – Amax H - neurogenic fluctuations: reduced An values in patients of group II (Me in group I is 7.9% less than Me in group II (p> 0.05)) indicate increased neurogenic tone, and are also an indicator of increased arteriolar resistance, which can be used in the diagnosis of peripheral polyneuropathy in these patients.

Am (active factor) – Amax M- myogenic fluctuations: median values did not differ significantly from those in healthy volunteers (Me in group I was 9.7% higher than Me in group II (p>0.05)).

Table 3.

Results of the evaluation of microcirculation of the lower extremities in groups depending on gender (Me)

Group I LDF-gram parameter	**men**	**women**	**KG**	**increase Δ**		**p≤**
				m/KG 1	**w/kg 2**	**1--2**
PM, pf.un.	10,2	10,0	12,9	-20,9%	-22,5%	
RMS, pf.units	1,11	1,13	1,28	-13,3%	-11,7%	
KV	11,8	11,7	10,8	9,3%	8,3%	
Amax E	0,32	0,3	0,29	10,3%	3,4%	0,05

Amax H	0,41	0,35	0,42	-2,4%	-16,7%	0,005
Amax M	0,33	0,29	0,28	17,9%	3,6%	0,05
Amax R	0,28	0,26	0,31	-9,7%	-16,1%	0,005
Amax C	0,9	0,84	0,92	-2,2%	-8,7%	0,05
II group LDF-gram parameter	**men**	**women**	**KG**	**increase Δ**		**p≤**
				m/KG 3	**w/kg 4**	**3--4**
PM, pf.un.	11,6	12,2	12,9	-10,1%	-5,4%	0,05
RMS, pf.units	1,17	1,21	1,28	-8,6%	-5,5%	
KV	10,8	11,2	10,8	0,0%	3,7%	
Amax E	0,28	0,32	0,29	-3,4%	10,3%	0,05
Amax H	0,39	0,43	0,42	-7,1%	2,4%	0,05
Amax M	0,27	0,31	0,28	-3,6%	10,7%	0,05
Amax R	0,26	0,32	0,31	-16,1%	3,2%	0,005
Amax C	0,87	0,93	0,92	-5,4%	1,1%	

We also assessed the initial blood flow and hemodynamic disorders in the microcirculatory bed of the lower extremities in patients of group I and group II depending on gender. When analyzing the initial blood flow and the amplitude-frequency spectrum in patients with varying degrees of severity in patients in subgroups, we obtained the following data, presented in Table 3.

When analyzing the arithmetic mean value of the microcirculation index (MI) in group I, lower perfusion values were found in men compared to women and the CG ($p<0.05$).

RMS (pfd, units) was lower in men (group I) compared to the CG and women (group I) (Me men (group I) by 13.3% less Me CG and Me women (group I) by 11.7% less Me CG ($p>0.05$ reliability not revealed), Lower flux values obtained as a result of our work in male patients (group I) may be due to less intensive functioning of the mechanisms of active control of microcirculation, a decrease in cardiac and respiratory rhythms due to a smaller number of erythrocytes entering the arterioles (Table 3).

When analyzing blood flow in male patients (group I), the median values for the coefficient of variation (CV) did not differ significantly from those of women (group I) (Me of men (group I) was 9.3% higher than Me of CG and Me of women (group I) was 8.3% higher than Me of KG, no significance was found).

Blood pressure (passive factor) – Amax R - respiratory wave: lower blood pressure values in patients of group I compared to the values in the control group may indicate an increase in microcirculatory pressure (Me in men (group I) is 9.7% lower than Me in the control group and Me in women (group I) is 16.1% lower than Me in the control group, ($p> 0.005$)).

Ac (passive factor) – Amax C - pulse wave: significantly reduced Ac values in male patients of group I together with reduced or normal PM values may indicate a decrease in the inflow of arterial blood into the microcirculatory bed of the lower extremities (Me in men (group I) is 2.2% less than Me KG and Me in women (group I) is 8.7% less than Me KG, (p>0.05)).

Ae (active factor) – Amax E - endothelial fluctuations: reliably elevated Ae values in male patients (group I) (Me in males (group I) is 10.3% higher than Me in CG and Me in females (group I) is 3.4% higher than Me in CG, (p> 0.05)). indicate the presence of endothelial dysfunction, and in patients with high-amplitude pulse rhythm – indicate dilation of small arteries and large arterioles.

An (active factor) – Amax H - neurogenic fluctuations: reduced An values in patients in group I (Me men (group I) by 2.4% less than Me CG and Me women (group I) by 16.7% less than Me CG, (p> 0.05)) indicate increased neurogenic tone, and are also an indicator of increased arteriolar resistance, which can be used in the diagnosis of peripheral polyneuropathy in these patients.

Am (active factor) – Amax M- myogenic fluctuations: the median values did not differ significantly from the values in healthy volunteers (Me in men (group I) was 17.9% higher than Me KG and Me in women (group I) was 3.6% higher than Me CG, (p>0.05)).

In Group II, we observed similar changes in the microcirculation balance, which were more pronounced in male patients, less pronounced compared to Group I (Table 3).

The obtained results, presented in Tables 2 and 3, allowed us to determine the specific features of microcirculation for patients with type 2 diabetes depending on the presence of metabolic syndrome (MS).

Patients with type 2 diabetes in comorbidity with MS in the anamnesis are characterized by reduced perfusion indices, pulse and respiratory waves up to 30%, high microcirculatory pressure, signs of dilation of small arteries and large arterioles, more pronounced changes were in male patients in this group.

CONCLUSION

Based on the identified changes in microcirculation in patients with type 2 diabetes in comorbidity with MS, negative dynamics of pathological processes in the microcirculatory bed of the lower extremities due to endothelial dysfunction were established.

It should be noted that in patients with type 2 diabetes in comorbidity with MS, the severity of microcirculation correlates with the level of glycemia, the glycated hemoglobin index, male gender, the pain syndrome score according to the PainDetect scale, and with the scale indicators (objective manifestations of diabetic distal neuropathy in patients). In this regard, by assessing the microcirculation of the upper and lower extremities using the LDF method, it is possible to assess the severity of distal polyneuropathy.

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