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Carotid arterial stiffness in type 2 diabetic patients

Sztywność tętnic szyjnych u pacjentów z cukrzycą typu 2

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Abstract

Introduction. Functional carotid arterial changes expressed by arterial stiffness indices represent subclinical organ damage in subjects with type 2 diabetes mellitus (T2DM). There are still controversies to what extent diabetes *per se* influences arterial stiffness and what is the contribution of other atherosclerotic risk factors in arterial stiffness pathophysiology. The aim of the study was to assess carotid arterial stiffness in patients with uncomplicated T2DM. We examined the relationship of classical cardiovascular risk factors and haemoglobin A1 and arterial stiffness indices in diabetes.

Material and methods. The study group consisted of 168 subjects: 84 subjects with T2DM (34 M, 50 F, mean age 55.8 ± 7.9 years) and 84 healthy patients (60 M, 24 F, mean age 54.3 ± 7.0 years). From carotid arteries ultrasound — high-resolution echo-tracking (eT) arterial stiffness parameters were evaluated: β, Ep, AC, AI, PWV-β.

Results. β, Ep, AI, PWV-β were higher in patients with T2DM in the comparison with control group. In the group of T2DM in stepwise multivariate analysis of arterial stiffness indices the following models were achieved with only significant variables: $\beta = 1.8 + 0.096 \times PP + 0.07 \times age$; $R^2 = 0.166$, $Ep = 16.7 + 1.852 \times PP$; $R^2 = 0.286$, $AC = 1.9 - 0.005 \times \times SBP - 0.007 \times HR + 0.14 \times$ smoking cigarettes; $R^2 = 0.165$, $AI = 18.0 - 0.80 \times BMI + 0.40 \times age$; $R^2 = 0.147$, PWV-β = $= -0.4 + 0.77 \times SBP - 0.72 \times MAP - 0.50 \times PP + 0.03 \times HR$; $R^2 = 0.235$.

Conclusions. T2D constitutes the strong independent determinant of arterial stiffness. In patients with T2DM the independent determinants of arterial stiffness parameters were age, SBP, MBP, PP, HR, BMI and smoking cigarettes. Not only glycemic control but also a multifactorial anti-risk strategy might play an important role in the prevention of the development of vascular stiffness and subclinical target organ damage in diabetes.

Key words: arterial stiffness, diabetes mellitus, glycated haemoglobin

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Introduction

Diabetes mellitus is associated with early and accelerated atherosclerosis and an increased risk of cardiovascular morbidity and mortality [1]. Pathophysiological mechanisms underlying these associations are not completely understood. Diabetes affects the cardiovascular system through two main mechanisms: atherosis which refers to lipid deposition in the vasculature to form intimal plaques, while sclerosis refers to vessel stiffening [2].

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Arterial changes include increased intima–media thickness (IMT), smooth muscle hypertrophy, collagen accrual and cross-linking, fibrosis and inflammation [3]. These changes are aggravated by advanced glycation end-products (AGE), irreversibly glycated proteins which stimulate systemic inflammation, oxidative stress, fibrosis, extracellular matrix remodeling, tissue injury modulation and lipid deposition in the arterial wall [4]. Elevated blood glucose concentrations favour AGE formation. Thus AGE might play a significant role in arterial stiffness. Increased arterial stiffness may be an important pathway linking diabetes to increased cardiovascuar risk [5]. It is known that increased arterial stiffness predicts the development of cardiovascular disease in type 2 diabetes mellitus (T2DM) [6]. Haemoglobin A_{1c} is an AGE that serves clinically as a marker of average glycemia in patients with diabetes.

There have been studies investigating the association between the classical risk factors and arterial stiffness in diabetes mellitus. However, the role of glycated haemoglobin (HbA_{1c}) control is still unclear [7, 8]. After analyzing the largest and longest-running study of T2DM (UKPDS, United Kingdom Prospective Diabetes Study), it is still unknown whether glucose control reduces the patient's risk of cardiovascular disease (CVD) [9]. In the present study we evaluated the impact of the T2DM on arterial stiffness and the impact of the classical risk factors and HbA_{1c} on carotid arterial stiffness in diabetic patients. We examined which of them [age, sex, smoking, blood pressure, body mass index (BMI), total cholesterol level — CH, low--density lipoprotein (LDL), high-density lipoprotein (HDL)] and HbA_{1c} could act as determinants of arterial stiffness in diabetes mellitus.

Material and methods

The study group consisted of 84 subjects with T2DM, 34 males and 50 females, mean age 55.8 ± 7.9 years. The control group consisted of 84 age-matched healthy subjects, 24 females and 60 males. Diabetics were treated by oral hypoglicaemic agents in 74%, by statins — in 91%. All patients underwent a comprehensive clinical examination, ECG, echocardiography, vascular assessments and evaluation of biological parameters. Only patients with a normal left ventricular (LV) systolic function (EF > 55%) and without cardiomyopathy, pericardial disease or valve dysfunctions were enrolled. Patients with evidence of ischaemic heart disease [a history of angina, a history of myocardial infarction, Q waves on electrocardiography (ECG) and regional wall motion abnormalities on echocardiography] were not eligible for the study. The protocol was approved by the local research ethics committee and each subject gave informed consent.

Demographic data

General data was obtained through a structured interview. Weight and height were measured according to the standard protocol, and each patient's body mass index (BMI) was calculated.

Laboratory determinations

Total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), blood triglicerydes (TG), level of glycated hemoglobin (HbA_{1c}) were evaluated by standard techniques.

Blood pressure phenotypes

Blood pressure was measured while the patient was in the sitting position with the use of a standard sphygmomanometer on the left arm after a 5-minute rest. The first and fifth phases of Korotkoff sounds were used for systolic blood pressure (SBP) and diastolic blood pressure (DBP), respectively. The mean blood pressure (MBP) was calculated as the mean pulse pressure added to one-third of the DBP. Pulse pressure (PP) was defined as the difference between SBP and DBP.

Echocardiography

A detailed two dimensional Doppler echocardiogram (Alpha 10 Hitachi-Aloka, Japan) was recorded for all the patients. M-mode measurements of end diastolic wall thickness [of interventricular septum (IVS) and posterior wall (PW)] and cavity diameter [LV end-diastolic diameter (EDD)] were used to calculate LV mass (LVM) by the formula introduced by Devereux et al. [10] and indexed to body surface area (BSA) to obtain a LV mass index (LVMI). Left ventricular ejection fraction was assessed in each subject using the Teichholz method.

Integrated assessment of arterial structure and function

Vascular ultrasound of the right common carotid artery was performed with an Alpha 10 Hitachi-Aloka machine equipped with an integrated and automated ultrasound, Doppler and echo-tracking system. Intima media thickness (IMT) was determined according to the established standards as the distance from the leading edge of the first echogenic line to the second echogenic line, with the media-adventitia interface [11]. Images of the thickest point within 10 mm from the common carotid artery (CCA) to the carotid bulb were saved and then measured. After clear visualization of the intima-media complex of both the anterior and posterior arterial wall in its longitudinal axis with a maximal internal diameter, an echo-tracking sample was positioned at the end of the intima, with a 1 kHz sampling rate for continuous detection of carotid diameter changes. In experimental

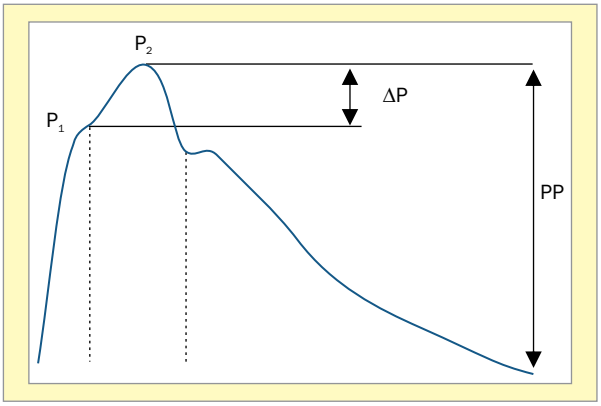

Figure 1. Augmentation index (AI) — method of calculation (source [1]); PP — pulse pressure, P1 — first systolic peak, P2 — second systolic peak, ΔP = P2 – P1

studies, diameter changes are very similar to intravascular pressure changes, which enables the automatic conversion of the carotid diameter waveform changes into arterial pressure waveforms by calibrating its peak and minimal values to systolic and diastolic brachial blood pressures [12]. The relationship of pressure-diameter is thought to be linear [12]. Three to five beats were averaged to obtain a representative waveform. The following arterial stiffness parameters were evaluated on-line [12, 13]:

β — beta stiffness index, as the ratio of the natural logarithm of systolic / diastolic blood pressure to the relative change in diameter:

$\beta = \ln (Ps/Pd/[(Ds - Dd)/Dd]$,

where: ln — the natural logarithm, Ps — systolic blood pressure, Pd — diastolic blood pressure, Ds — arterial systolic diameter, Dd — arterial diastolic diameter;

Ep — epsilon, Young modulus, pressure-strain elasticity modulus:

$Ep = (Ps - Pd)/[(Ds - Dd)/Dd]$;

AC — arterial compliance, calculated from the arterial cross area and blood pressures:

$AC = \pi(Ds \times Ds - Dd \times Dd)/[4 \times (Ps - Pd)]$;

PWV-β — one-point pulse wave velocity, calculated from the time delay between two adjacent distension waveforms from a water hammer equation with the use of β — the stiffness parameter:

$PWV\text{-}\beta = \sqrt{(\beta P/2\rho)}$,

where P — diastolic blood pressure, ρ — blood density (1050 kg/m^3).

From the parameters of wave reflection — augmentation index (AI) was calculated as:

AI = ΔP/PP, which is illustrated in Figure 1.

The blood pressure of the right arm was measured by an automated cuff sphygmomanometer with the patient being in the supine position for 10 minutes. The reproducibility of these measurements has been reported elsewhere [14]. An original example of arterial stiffness parameter examination by high resolution echo-tracking system derived from the right common carotid artery is presented in Figure 2.

Statistical analysis

Mean and standard deviations were calculated for the quantitative variables and percentages for qualitative variables. All variables were not normally distributed and therefore the differences between the groups were tested by the Mann-Whitney test for quantitative variables and by the chi-square test for the percentages of qualitative variables. Statistical significance was set at $p < 0.05$ (two-sided tests) and for multiple testing we used a statistical significance of $p < 0.01$. A multivariable logistic regression analysis was conducted considering the occurrence of arterial stiffness as a dependent variable. All the variables presenting a significant value < 0.25 at univariate analysis were included in the model. The stepwise forward method was used and odds ratios (OR) with 95% confidence interval (CI) were calculated. The model was evaluated with the Hosmer-Lemeshow test.

Results

Clinical characteristics of all patients is presented in Table 1.

All patients had normal IMT values (< 0,9 mm) and preserved LV systolic function (EF > 55%). Carotid arterial stiffness parameters like β, Ep, AI, PWV-β were higher in patients with T2DM in the comparison with control group (Table 2).

Significant linear correlations (table 3) were found between β and age ($r = 0.258$, $p = 0.001$), IMT ($r = 0.87$, $p = 0.009$), LVMI ($r = 0.177$, $p = 0.035$), SBP ($r = 0.280$, $p = 0,01$), MAP ($r = 0.227$, $p = 0.039$) and PP ($r = 0.268$, $p = 0.014$); between Ep and age ($r = 0.254$, $p = 0.002$), IMT ($r = 0.3$, $p = 0.006$), SBP ($r = 0.534$, $p < 0.001$), DBP ($r = 0.337$, $p = 0.001$), MAP (0.496, $p < 0.001$), PP ($r = 0.44$, $p < 0.001$) and HR ($r = 0.226$, $p = 0.015$); between AC and SBP ($r = -0.454$, $p < 0.001$), DBP ($r = -0.333$, $p = 0.002$), MAP ($r = -0.428$, $p < 0.001$), PP ($r = -0.366$, $p = 0.001$), heart rate (HR) ($r = -0.306$, $p = 0.005$) and smoking cigarettes ($r = 0.272$ $p = 0.013$); between AI and age ($r = 0.212$, $p = 0.011$), BMI ($r = -0.380$, $p = 0.001$) and HR ($r = -0.343$, $p = 0.003$); between PWV-β and age ($r = 0.222$, $p = 0.005$), IMT ($r = 0.293$, $p = 0.008$), SBP ($r = 0.552$, $p < 0.001$), DBP ($r = 0.467$, $p = 0.001$), MAP ($r = 0.539$, $p < 0.001$), PP ($r = 0.357$, $p = 0.001$) and HR ($r = 0.333$, $p = 0.003$). In the group with T2DM stepwise multivariate analysis (Snedecor's F distribution) of arterial stiffness indices the following models were achieved with only significant variables [age; SBP; PP; MBP; HR; smoking cigarettes, BMI):

$\beta = 1.8 + 0.096 \times PP + 0.07 \times age$; $R^2 = 0.166$,

$Ep = 16.7 + 1.852 \times PP$; $R^2 = 0.286$,

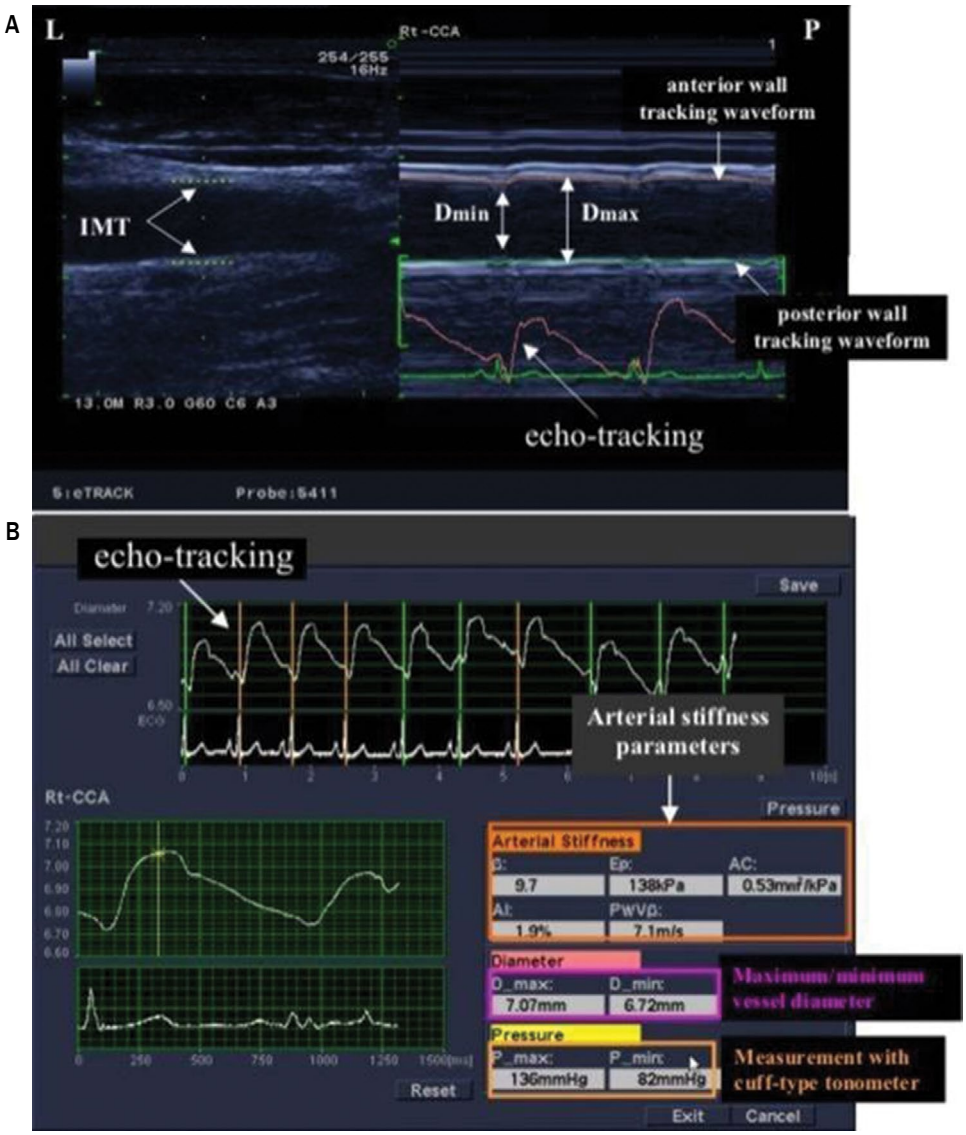

Figure 2A, B. Left (L): B-mode visualisation of right common carotid artery. Right (P): echo-tracking computed curve of dynamic diameter carotid artery. Lower: arterial stiffness parameters: β — beta; Ep — epsilon; AC — arterial compliance; PWV-β — one-point pulse wave velocity; AI — augmentation index

AC = 1.9 – 0.005 × SBP – 0.007 × HR + 0.14 × smoking cigarettes; $R^2 = 0.165$,

AI = 18.0 – 0.80 × BMI + 0.40 × age; $R^2 = 0.147$,

PWV-β = –0.4 + 0.77 × SBP – 0.72 × MAP – 0.50 × PP + 0.03 × HR; $R^2 = 0.235$.

Discussion

Cardiovascular diseases constitute the main cause of death in diabetes. Increased arterial stiffness is one of the key mechanisms of augmented cardiovascular risk in T2DM patients.

Hyperglycemia in T2DM stimulates the formation of advanced glycation end products (AGEs). The AGEs cross-links within the vascular wall further exacerbate vascular stiffness and large artery atherosclerosis [3]. The mechanisms by which high levels of glycaemia might lead to arteriopathy might become clear through recent studies. Accumulated AGE products have been known to be related to glycation and preferential oxidation of LDL and further uptake by macrophages to create foam cells [15] and finally glycaemia increases atherosclerosis [16]. The atherosclerotic process consists of two different aspects: atherosis (structural process) and sclerosis (functional process).

Table 1. Clinical characteristics of patients

Variable	Control group (C) N = 84	Diabetes (D) N = 84	K vs. D p
Age [years old]: $\bar{x}$ ± SD	54.3 ± 7.0	55.8 ± 7.9	0,086[a]
Sex:			< 0.001[b]
• females [%]	24 (28.6%)	50 (59.5%)	
• males [%]	60 (71.4%)	34 (40.5%)	
Body mass index (BMI) [kg/m^2]: $\bar{x}$ ± SD	25.9 ± 3.8	30.3 ± 4.7	< 0.001[b]
Heart rate (HR) [min^{-1}]: $\bar{x}$ ± SD	71 ± 11	72 ± 9	0.290[c]
Systolic blood pressure (SBP) [mm Hg]: $\bar{x}$ ± SD	128 ± 14	136 ± 18	0.003[c]
Diastolic blood pressure (DBP) [mm Hg]: $\bar{x}$ ± SD	77 ± 9	75 ± 9	0.120[c]
Pulse pressure (PP) [mm Hg]: $\bar{x}$ ± SD	52 ± 9	61 ± 14	< 0.001[c]
Total cholesterol [mg/dL]: $\bar{x}$ ± SD	230 ± 37	198 ± 39	< 0.001[d]
Low-density lipoproteins (LDL) [mg/dL]: $\bar{x}$ ± SD	146 ± 29	116 ± 34	< 0.001[d]
High-density lipoproteins (HDL) [mg/dL]: $\bar{x}$ ± SD	59 ± 18	49 ± 12	0.003[a]
Triglycerides (TG) [mg/dL]: $\bar{x}$ ± SD	127 ± 98	161 ± 82	0.001[a]
Glucose [mg/dL]: $\bar{x}$ ± SD	98 ± 15	147 ± 62	< 0.001[c]
Cigarette smoking: yes	40 (47.6%)	18 (21.4%)	< 0.001[b]
Creatinine [mg/dL]: $\bar{x}$ ± SD	0.83 ± 0.15	0.87 ± 0.19	0.544[c]
C-reactive protein (CRP) [mg/L]: $\bar{x}$ ± SD	1.61 ± 1.27	1.62 ± 1.59	0.985[c]
Ejection fraction (EF) [%]: $\bar{x}$ ± SD	69.5 ± 8.4	69.2 ± 7.0	0.811[c]
Left ventricular mass (LVM) [g]: $\bar{x}$ ± SD	154 ± 50	222 ± 60	< 0.001[c]
Intima media complex (IMT) [mm]: $\bar{x}$ ± SD	0.54 ± 0.15	0.67 ± 0.15	< 0.001[a]

[a]The Mann-Whitney U test; [b]Pearson's chi-squared test; [c]Student's *t*-test; [d]Fisher exact test; SD — standard deviation

Table 2. Carotid arterial stiffness indices in control and diabetes group

Variable	Control group (C) N = 84	Diabetes (D) N = 84	K vs. D p
β [–]: $\bar{x}$ ± SD	7.59 ± 2.53	10.04 ± 3.15	< 0.001[a]
Ep [kPa] : $\bar{x}$ ± SD	104.9 ± 41.1	137.2 ± 50.6	< 0.001[a]
AC [mm^2/kPa] : $\bar{x}$ ± SD	0.66 ± 0.23	0.70 ± 0.26	0.332[a]
AI [%]: $\bar{x}$ ± SD	20.01 ± 12.80	16.78 ± 13.34	0.035[a]
PWV-β [m/s]: $\bar{x}$ ± SD	6.1 ± 1.1	6.8 ± 1.2	< 0.001[b]

[a]The Mann-Whitney U test; [b]Student's *t*-test; β — beta stiffness index; SD — standard deviation; Ep — epsilon; AC — arterial compliance; AI — augmentation index; PWV-β — one-point pulse wave velocity

IMT reflects structural changes and arterial stiffness indices are functional markers [17]. There are many methods to assess systemic and regional arterial stiffness, such as applanation tonometry and mechanotransduction with the evaluation of 'gold standard' carotid-femoral pulse wave velocity [5, 6, 14, 18]. Echo-tracking systems, especially new high resolution ones, may provide easy-to-measure local arterial stiffness parameters in the detection of early functional arterial changes that precede vascular structural remodelling. European Society of Cardiology (ESC) experts recommend local arterial stiffness measurements for pathophysiologic studies [19]. Echo-tracking of carotid arteries has been shown as a convenient method to measure arterial stiffness parameters [13, 18, 20]. In the present study, similarly to Avgeropoulou et al. [21] the mean values of arterial stiffness parameters like β, Ep, AI, PWV-β were significantly higher in diabetic patients comparing to control subjects . In patients with diabetes mellitus the independent determinants of carotid arterial stiffness parameters were age (of β stiffness, AI), systolic blood pressure (of AC,

Table 3. Linear regression correlation coefficients of carotid arterial stiffness indices in type 2 diabetic group

Variable	β	Ep	AC	AI	PWV-β
Age [years]	**r = +0.258***	**r = +0.254***	r = –0.119	**r = +0.212***	**r = +0.222***
	p = 0.001	**p = 0.002**	NS	**p = 0.011**	p = 0.005
Duartion of type 2 diabetes [years]	r = +0.200	r = +0.233	r = –0.234	r = +0.019	r = +0.242
	NS	NS	NS	NS	NS
HbA_{1c} [mmol/mol]	r = +0.054	r = +0.075	r = +0.021	r = –0.131	r = +0.058
	NS	NS	NS	NS	NS
Total cholesterol [mmol/L]	r = –0.067	r = –0.066	r = +0.101	r = +0.060	r = –0.048
	NS	NS	NS	NS	NS
IMT [mm]	r = +0.287	r = +0.300	r = +0.063	r = –0.224	r = +0.293
	p = 0.009	p = 0.006	NS	NS	p = 0.008
LDL-cholesterol [mmol/L]	r = –0.138	r = –0.133	r = +0.166	r = +0.071	r = –0.135
	NS	NS	NS	NS	NS
HDL-cholesterol [mmol/L]	r = +0.163	r = +0.126	r = –0.159	r = +0.167	r = +0.131
	NS	NS	NS	NS	NS
Triglycerides [mmol/L]	r = –0.077	r = –0.010	r = +0.001	r = –0.198	r = +0.040
	NS	NS	NS	NS	NS
BMI [kg/m^2]	r = –0.042	r = +0.034	r = –0.013	**r = –0.380***	r = +0.025
	NS	NS	NS	**p = 0.001**	NS
LVMI [g/m^2]	**r = 0.177***	r = +0.009	r = –0.051	r = +0.066	r = +0.006
	p = 0.035	NS	NS	NS	NS
SBP [mm Hg]	r = 0.280*	r = +0.534*	**r = –0.454***	r = –0.070	**r = +0.522***
	p = 0.010	p < 0.001	**p < 0.001**	NS	**p < 0.001**
DBP [mm Hg]	r = + 0.142	r = +0.377*	r = –0.333*	r = –0.051	r = +0.467*
	NS	p = 0.001	p = 0.002	NS	p = 0.001
MAP [mm Hg]	r = 0.227*	r = + 0.496*	r = –0.428*	r = –0.062	r = +0.539*
	p = 0.039	p < 0.001	p < 0.001	NS	p < 0.001
PP [mm Hg]	**r = 0.268***	**r = +0.440***	**r = –0.366***	r = – 0.058	**r = +0.357***
	p = 0.014	**p < 0.001**	**p = 0.001**	NS	**p = 0.001**
HR [min^{-1}]	r = +0.207	r = +0.266*	r = –0.306*	r = –0.343*	r = + 0.333*
	NS	p = 0.015	p = 0.005	p = 0.003	p = 0.003
Cigarette smoking (1 — yes, 0 — no)	r = –0.129	r = –0.148	**r = +0.272***	r = +0.074	r = –0.144
	NS	NS	**p = 0.013**	NS	NS

*p < 0.05 considered significant; β — beta stiffness index; Ep — epsilon; AC — arterial compliance; AI — augmentation index; PWV-β — one-point pulse wave velocity; HbA_{1c} — glycated haemoglobin; IMT — intima-media complex; LDL; HDL; BMI — body mass index; LVMI — left ventricular mass index; SBP — systolic blood pressure; DBP — diastolic blood pressure; MAP — mean blood pressure; PP — pulse pressure; HR —heart rate

PWV-β), mean blood pressure (of PWV-β), pulse pressure (of β stiffness, Ep, PWV-β), heart rate (of AC, PWV-β), body mass index (AI) and smoking cigarettes (AC) but not HbA_{1c}.

There are still controversies to what extent diabetes *per se* influences arterial stiffness and what is the contribution of other atherosclerotic risk factors into arterial stiffness pathophysiology in diabetes. Some authors have indicated the main role of hypertension and age in arterial stiffness increase in diabetic patient [22]. Based on the meta-analysis of 77 studies with 26,970 patients included Cecelja et al. [23] documented diabetes as the independent determinant of arterial stiffness in about half of the studies while age and hypertension — in 90% of them. It has been suggested that co-existing hypertension may

mask the independent influence of diabetes on arterial stiffness. Our data are consistent with the studies in which age and blood pressure were the main determinants of arterial stiffness [24]. Tanakouchi et al. [25] showed that age and systolic blood pressure were significantly correlated with PWV in patients with non-insulin-dependent diabetes mellitus. Also Takahara [26] proved that age and systolic blood pressure had a significant impact on PWV in type 2 diabetes subjects. Age exposes the aortic wall to degenerative phenomena such as collagen accumulation, fragmentation of elastic fibers and calcification of the media responsible for the increase in aortic rigidity [27]. Long-standing arterial pulsation in the central artery has a direct effect on the structural matrix proteins, collagen and elastin in the arterial wall, disrupting muscular attachments and causing elastin fibers to fatigue and fracture [28]. This would explain why age and blood pressure are the major determinants of arterial stiffness [29].

Several studies also reported an independent association between HR and arterial stiffness [24]. The underlying mechanism is still unknown. Those studies indicated that the rate of elastin fractures depends on the number of stress cycles, that is, the number of heartbeats experienced which may explain the relationship between HR and arterial stiffness [25]. Consistently with our data, some studies reported that BMI was associated with arterial stiffness measured by baPWV [24]. In our study, we observed no significant association between HbA_{1c} levels and arterial stiffness indices in patients with T2DM. These data are consistent with Taniwaki et al. [30], who showed that HbA_{1c} was not an independent risk factor for arterial stiffness parameters (baPWV) in diabetic subjects. Kumeda et al. [31] also reported that in hemodialysis patients HbA_{1c} was not correlated with baPWV. Seong-Woo Choi et al. [7] showed that HbA_{1c} was not associated with baPWV in Korean T2DM patients. The exact reasons for these results are unknown. The first reason might be that arterial stiffness is strongly related to the ageing process [32] so that the ageing effect might have been so great that the effects of hyperglycemia may be covered. The second reason might be that almost all patients have been treated by statins which have a potential confounding effect on the association between hyperglycemia and arterial stiffness. Also, the usefulness of HbA_{1c} in T2DM has been questioned for more than 15 years [33]. Abnormal glycaemia may lead to the development of atherosclerosis in diabetes after many years of the disease. The results of the study by Larsen et al. [34], who had observed the metabolic control in patients with type 1 diabetes for 18 years, revealed the relationship between the mean values of HbA_{1c} and the progression of atherosclerotic changes in carotid and coronary arteries. As HbA_{1c} reflects the mean values of glycaemia for 3 months preceding the evaluation, it might not be an ideal parameter for the long follow-up of glycemic status. Standl i Ceriello [35] proved that sudden and acute glycemic changes as well as postprandial glycaemia are the most toxic factors for endothelium. Also HbA_{1c} does not express glycemic alterations and low serum glucose levels, which are known as factors modifying endothelium function. Postprandial glycaemia and glycemic spikes are thought to be a more predictive independent risk factor for cardiovascular diseases in T2DM than HbA_{1c} level [36, 37].

We did not observe significant correlations of carotid arterial stiffness indices and cholesterol levels. It is worth noting that almost all diabetic subjects in our study were treated with statins. The results of studies on the influence of statins on arterial stiffness are controversial [38, 39]. The lack of the association between carotid arterial stiffness and lipids in intriguing while taking into consideration documented relationship of cfPWV and atherosclerotic plaques [40, 41]. This may be explained by the lack of the impact of classical risk factors on the early stages of atherosclerotic process [42].

Limitations of the study

The study population was relatively small, only Caucasian and well-educated, which limits the generalisability of our findings . Blood pressure values used to calculate carotid eT arterial stiffness indices were measured over the brachial artery, which tends to overestimate carotid pressures due to central to peripheral blood pressure amplification. This is especially important in young subjects, but may have less relevance due to the mean age of our study patients, which was 57 ± 10.4 years. However, studies have shown a significant correlation between central and brachial blood pressure measurements [43] and many epidemiological studies use brachial artery blood pressure to estimate carotid artery stiffness.

Conclusions

In patients with T2DM, the independent determinants of carotid arterial stiffness parameters were age, systolic blood pressure, mean blood pressure, pulse pressure, heart rate, body mass index and smoking cigarettes but not HbA_{1c}. Not only glycemic control but also multifactorial anti-risk strategy (antihypertensive therapy, change of lifestyle) might play an important role in preventing the development of vascular stiffness and subclinical target organ damage in diabetes.

Statement of human and animal rights

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 [5].

Statement of informed consent

Informed consent was obtained from all patients for being included in the study.

Conflict of interest

The authors declare no conflict of interest.

Streszczenie

Wstęp. Zmiany czynnościowe tętnic szyjnych, które są wyrażone jako wskaźniki sztywności, są marekrem subklinicznego uszkodzenia narządowego u chorych na cukrzycę typu 2 (T2DM). Istnieją kontrowersje co do tego, w jakim stopniu cukrzyca *per se*, a w jakim stopniu inne czynniki ryzyka miażdżycy wpływają na sztywność naczyń. Celem pracy była ocena sztywności tętnic szyjnych u pacjentów z niepowikłaną T2DM. Autorzy zbadali zależność między klasycznymi czynnikami ryzyka sercowo-naczyniowego i wartością hemoglobiny A1 a sztywnością tętnic w cukrzycy.

Materiał i metody. Badaną grupę stanowiło 168 chorych, w tym 84 pacjentów z T2DM (34 M, 50 K, średnia wieku 55,8 ± 7,9 roku) oraz 84 zdrowe osoby stanowiące grupę kontrolną (60 M, 24 K, średnia wieku 54,3 ± 7,0 roku). Metodą *echo-tracking* (Ep) oceniono sztywność tętnic szyjnych za pomocą następujących parametrów: β, Ep, AC, AI, PWV-β.

Wyniki. U chorych z T2DM wartości wskaźników sztywności tętnic szyjnych (β, Ep, AC, AI, PWV-β) były istotnie wyższe niż u osób z grupy kontrolnej. W grupie z T2DM w analizie regresji wielokrotnej uzyskano natępuące istotne modele parametrów sztywności: $\beta = 1{,}8 + 0{,}096 \times PP + 0{,}07 \times age$; $R^2 = 0{,}166$, $Ep = 16{,}7 + 1{,}852 \times PP$; $R^2 = 0{,}286$, $AC = 1{,}9 - 0{,}005 \times SBP - 0{,}007 \times HR + 0{,}14 \times$ liczba papierosów, $R^2 = 0{,}165$, $AI = 18{,}0 - 0{,}80 \times BMI + 0{,}40 \times$ a wiek; $R^2 = 0{,}147$, PWV-$\beta = -0{,}4 + 0{,}77 \times SBP - 0{,}72 \times MAP - 0{,}50 \times PP + 0{,}03 \times HR$; $R^2 = 0{,}235$

Wnioski. Cukrzyca typu 2 jest silnym niezależnym czynnikiem sztywności tętnic. U pacjentów z T2DM niezależnymi determinanatmi parametrów sztywności tętnic były wiek, SBP, MBP, PP, HR, BMI oraz palenie papierosów. Nie tylko kontrola glikemii, ale także wieloczynnikowa strategia prewencyjna może odgrywać istotną rolę w zapobieganiu rozwojowi sztywności naczyń oraz subklinicznym uszkodzeniom narządowym w cukrzycy.

Słowa kluczowe: sztwyność naczyń, cukrzyca. hemoglobina glikowana

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