

Advanced glycation end-products and arterial stiffness in patients with diabetic nephropathy and patients with chronic kidney disease without diabetes

Paweł Stróżecki¹, Robert Kurowski², Mariusz Flisiński¹, Anna Stefańska³, Grażyna Odrowąż-Sypniewska³, Jacek Manitius¹

¹ Department of Nephrology, Hypertension and Internal Medicine, Dr. Antoni Jurasz University Hospital No. 1, Nicolaus Copernicus University, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland

² Regional Centre of Pulmonology, Bydgoszcz, Poland

³ Department of Laboratory Medicine, Dr Antoni Jurasz University Hospital No. 1, Nicolaus Copernicus University, Ludwik Rydygier Collegium Medicum in Bydgoszcz, Bydgoszcz, Poland

KEY WORDS

advanced glycation end-products, arterial stiffness, chronic kidney disease, diabetes, pulse wave velocity

ABSTRACT

INTRODUCTION Formation of advanced glycation end-products (AGEs) is increased in diabetic patients. Impaired renal function also elevates AGE accumulation. Pulse wave velocity (PWV) is a measure of arterial stiffness and a prognostic parameter. An association between AGEs and arterial stiffness was observed in hemodialyzed patients.

OBJECTIVES We investigated the relationship between plasma AGE concentration and arterial stiffness in nondialyzed patients with diabetic nephropathy and those with chronic kidney disease (CKD) without diabetes.

PATIENTS AND METHODS PWV measurement was performed in 24 patients with CKD and diabetic nephropathy (DN), 36 patients with CKD and without diabetes, and 19 controls. To assess AGE concentrations, plasma fluorescence spectra were recorded.

RESULTS Patients with and without diabetes did not differ with respect to the glomerular filtration rate (33 ± 13 vs. 32 ± 14 ml/min/1.73 m², respectively). The AGE concentration was significantly higher in patients with DN compared with those without diabetes and controls (21.1 ± 6.8 vs. 12.3 ± 3.1 vs. 7.8 ± 1.2 AU/ml, respectively; $P < 0.001$). PWV was also significantly higher in patients with DN compared with those without diabetes and controls (13.7 ± 4.3 vs. 10.1 ± 2.4 vs. 8.4 ± 1.6 m/s, respectively; $P < 0.05$). A significant correlation was found between AGEs and PWV ($r = 0.39$, $P < 0.01$) in patients with CKD. In a multiple regression analysis, PWV was independently associated with age, DN, and systolic blood pressure, but not with AGEs ($R^2 = 0.45$).

CONCLUSIONS Accumulation of AGEs and arterial stiffness are increased in patients with CKD, particularly in those with DN; however, the results are not sufficient to confirm the causal role of AGE accumulation in arterial stiffening in CKD. AGEs should be considered as a potential therapeutic target in patients with CKD.

INTRODUCTION Chronic kidney disease (CKD) is a worldwide health problem of increasing incidence and prevalence, associated with high cost of therapy and poor prognosis.¹ CKD involves an increased risk of cardiovascular morbidity and mortality.^{2,3} Patients

with CKD before renal replacement therapy, those on dialysis, and those after kidney transplantation demonstrate increased arterial stiffness,⁴⁻⁸ which is a prognostic factor of mortality in hemodialyzed patients.⁹ Pulse wave velocity (PWV) is a measure of arterial stiffness

Correspondence to:
Paweł Stróżecki, MD,
Klinika Nefrologii, Nadciśnienia
Tętniczego i Chorób Wewnętrznych,
Szpital, Uniwersytecki Nr 1,
ul. M. Skłodowskiej-Curie 9,
85-094 Bydgoszcz, Poland,
phone: +48-52-585-45-51,
fax: +48-52-585-40-30,
e-mail: st_pawel@cm.umk.pl

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and a valuable prognostic parameter.^{10,11} Carotid-femoral pulse wave velocity (cfPWV) is considered to be the gold standard for measuring arterial stiffness.¹¹

Advanced glycation end-products (AGEs) constitute a large group of heterogeneous molecules formed by the nonenzymatic reactions of sugar with free amino groups of proteins, peptides, and nucleic acids.¹²⁻¹⁴ Some AGEs such as pentosidine and protein cross-links are fluorescent. Several methods to measure AGE accumulation, such as enzyme-linked immunosorbent assay (ELISA), plasma or tissue fluorescence spectroscopy, and skin autofluorescence, have been developed.¹⁵⁻¹⁷ A correlation was reported between the total serum fluorescence and AGE level measured with ELISA.¹⁶ Formation of AGEs is increased in diabetic patients,^{18,19} and AGE accumulation is associated with diabetes-related complications.¹⁵ Impaired renal function also elevates AGE levels.^{14,20,21} AGEs increase vascular stiffness by inducing collagen cross-linking in the vessel wall.²² The association between AGEs and arterial stiffness was found in healthy adults,²² in hypertensive patients,²³ and in hemodialyzed patients.^{24,25} The aim of the present study was to investigate the relationship between plasma AGE concentrations and arterial stiffness in nondialyzed patients with CKD with or without diabetes.

PATIENTS AND METHODS The study was designed as a cross-sectional analysis in nondialyzed patients with CKD, stages 3–5. The protocol of the study was accepted by the local ethics committee, and informed consent was obtained from each participant. A total of 60 patients with CKD (24 with diabetic nephropathy and 36 with nondiabetic CKD) were included in the study. The control group consisted of 19 healthy individuals without kidney disease or diabetes and with normal blood pressure. The diagnostic criteria of diabetic nephropathy included proteinuria (>0.5 g/24 h) and coexisting diabetic retinopathy. Among patients with diabetic nephropathy, there were 11 patients (46%) with type 1 diabetes and 13 (54%) with type 2 diabetes. The underlying renal disease in nondiabetic patients with CKD was glomerulonephritis in 16 patients (44%), hypertensive nephropathy in 12 (33%), interstitial nephritis in 4 (11%), and other or unknown in 4 (11%). The exclusion criteria included immunosuppressive therapy and overt infection. Clinical assessment was performed in all subjects. Systolic and diastolic blood pressures (SBP and DBP, respectively) were measured in a sitting position after 10-minute rest, and pulse pressure (PP = SBP – DBP) was then calculated. Body mass, height, and body mass index (BMI) were measured. Fasting blood was collected for laboratory analyses. Patient charts were investigated to analyze antihypertensive and statin therapy. Data regarding diabetes control (glycated hemoglobin [HbA_{1c}], fasting glucose, and lipid profile) were also obtained from patient medical records.

Pulse wave velocity cfPWV was measured using a Complior® device (Artech Medical, Pantin, France). Two transducers (one positioned over the carotid artery and the other over the femoral artery) were used to measure the time delay between pulse waves. Time delay was measured on 10 successive beats, and then averaged. The distance between the carotid artery (suprasternal notch) and femoral artery was measured externally. PWV was calculated according to the following formula: PWV = distance (m) / time delay (s). PWV measurements were taken in duplicate and averaged.

Laboratory measurements Laboratory measurements were performed using an Abbott Architect ci8200 analyzer and Abbott Laboratories commercial reagents (Abbott Laboratories, Abbott Park, Illinois, United States). Additionally, high-sensitive C-reactive protein (hsCRP) was assessed using the BN™ nephelometric method (Dade Behring Inc, Deerfield, Illinois, United States). The glomerular filtration rate was estimated (eGFR) using the abbreviated Modification of Diet in Renal Disease formula (eGFR = 186 × [serum creatinine/88.4]^{-1.154} × [age]^{-0.203} × [0.742 if female] × [1.210 if African-American]). To assess the AGE concentration, plasma fluorescence spectra were recorded with Fluoroscan Ascent FL Labsystems (excitation 355 nm / emission 460 nm). AGE measurements were taken in duplicate, averaged, and expressed in arbitrary units (AU/ml). This method measures a combination of glycation and oxidation products such as pentosidine, cross-links, and others. Total serum fluorescence in humans is associated mainly with high-molecular-mass proteins, particularly albumin.¹⁶ It was also shown in patients with end-stage renal disease that 95% of serum pentosidine was linked to high-molecular-mass protein, and only 1% is in a free form.²⁶

Statistical analysis A statistical analysis was performed using the Statistica 7.0 PL software (StatSoft Inc., Tulsa, Oklahoma, United States). Data were presented as mean ± standard deviation. Distribution of variables was analyzed using the Shapiro–Wilk test. The statistical analysis was performed using the *t* test. If a variable was not normally distributed, the Mann–Whitney test was used. Qualitative data were compared with the χ^2 test. A linear correlation between variables was analyzed. A multiple linear regression analysis with PWV as a dependent variable was also performed. A *P* value of less than 0.05 was considered statistically significant.

RESULTS Clinical characteristics of the study groups are presented in TABLE 1. The study groups did not differ with respect to age and sex. SBP was significantly higher in nondiabetic and diabetic patients compared with controls. Nondiabetic and diabetic patients did not differ with respect to the serum creatinine concentration and

TABLE 1 Clinical and laboratory characteristics of the study groups

	Controls (n = 19)	Nondiabetic CKD (n = 36)	Diabetic CKD (n = 24)
age, y	46 ± 13	51 ± 15	53 ± 14
male sex	11 (58)	21 (58)	14 (58)
SBP, mmHg	125 ± 10	137 ± 21 ^a	148 ± 24 ^b
DBP, mmHg	79 ± 6	84 ± 10 ^a	80 ± 10
PP, mmHg	46 ± 6	54 ± 15 ^a	69 ± 19 ^{b,c}
BMI, kg/m ²	24.4 ± 2.9	26.1 ± 4.9	26.9 ± 4.4 ^a
creatinine, μmol/l	95.5 ± 12.4	203.3 ± 74.2 ^b	212.2 ± 88.2 ^b
eGFR, ml/min/1.73 m ²	81 ± 15	33 ± 13 ^b	32 ± 14 ^b
hsCRP, mg/l	1.1 ± 1.2	4.2 ± 6.6 ^a	3.3 ± 7.9
AGEs, AU/ml	7.8 ± 1.2	12.3 ± 3.1 ^b	21.1 ± 6.8 ^{b,d}
PWV, m/s	8.4 ± 1.6	10.1 ± 2.4 ^a	13.7 ± 4.3 ^{b,d}
fasting glucose, mmol/l	5.1 ± 0.6	5.1 ± 0.6	7.4 ± 2.5 ^{b,d}
HbA _{1c} , %	–	–	7.5 ± 0.7
total cholesterol, mmol/l	4.7 ± 0.9	5.9 ± 1.5 ^a	5.1 ± 0.9 ^c
LDL cholesterol, mmol/l	2.8 ± 0.9	3.9 ± 1.4 ^b	3.1 ± 1.0 ^c
HDL cholesterol, mmol/l	1.4 ± 0.4	1.3 ± 0.4	1.4 ± 0.3
triglycerides, mmol/l	1.5 ± 1.2	2.3 ± 1.1 ^a	1.5 ± 0.5 ^c
number of antihypertensive drugs	–	3 ± 1	4 ± 1 ^c
patients treated with ACEI or ARB	–	27 (75)	21 (88)
patients treated with statin	–	13 (36)	14 (58)

Data are presented as mean ± standard deviation or number (percentage).

a $P < 0.05$ vs. controls, **b** $P < 0.001$ vs. controls, **c** $P < 0.05$ vs. nondiabetic, **d** $P < 0.001$ vs. nondiabetic

Abbreviations: ACEI – angiotensin converting enzyme inhibitor, AGEs – advanced glycation end-products, ARB – angiotensin receptor blocker, BMI – body mass index, CKD – chronic kidney disease, DBP – diastolic blood pressure, eGFR – estimated glomerular filtration rate, HDL – high-density lipoprotein, hsCRP – high-sensitive C-reactive protein, LDL – low-density lipoprotein, PP – pulse pressure, PWV – pulse wave velocity, SBP – systolic blood pressure

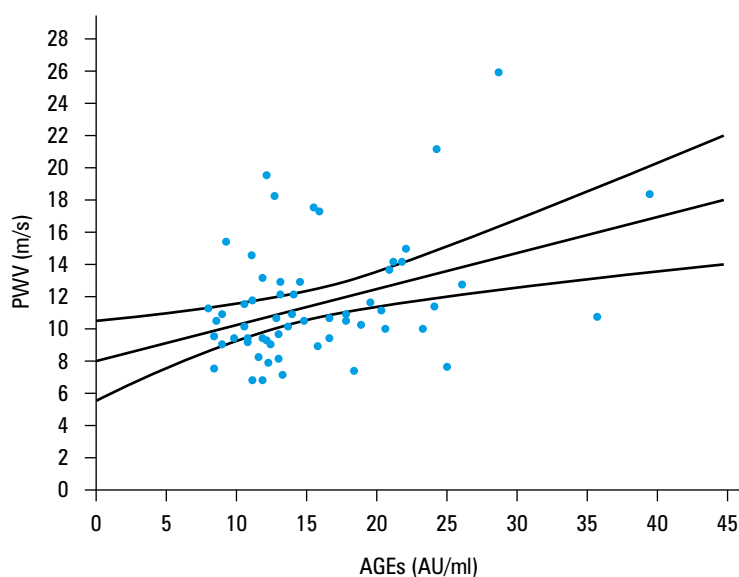


FIGURE Correlation between plasma levels of advanced glycation end-products (AGEs) and pulse wave velocity (PWV) in patients with chronic kidney disease

eGFR. The number of antihypertensive drugs was higher in diabetic than in nondiabetic patients.

A significant correlation was observed between AGEs and PWV in the whole study population ($r = 0.49$, $P < 0.001$, $n = 79$) as well as in CKD patients ($r = 0.39$, $P < 0.01$, $n = 60$) (FIGURE). In CKD patients, a significant correlation was also found between PWV and age ($r = 0.41$, $P = 0.001$), SBP

($r = 0.49$, $P < 0.001$), and PP ($r = 0.63$, $P < 0.001$). In this group, the AGE concentration was significantly and positively correlated with PP ($r = 0.28$, $P < 0.05$) and negatively with eGFR ($r = -0.43$, $P < 0.01$). We did not observe any correlations between hsCRP and PWV ($r = 0.06$, nonsignificant [NS]) or hsCRP and AGEs ($r = -0.15$, NS). A model of a multiple linear regression analysis with PWV as a dependent variable and age, SBP, diabetic nephropathy, and AGEs as independent variables was designed. As SBP was interrelated with PP ($r = 0.91$, $P < 0.001$), only SBP was included in the model. The results of the multiple regression analysis are shown in TABLE 2.

In the CKD group without diabetes, we observed a significant positive correlation between PWV and age ($r = 0.57$, $P < 0.001$), BMI ($r = 0.34$, $P < 0.05$), PP ($r = 0.52$, $P < 0.01$), number of antihypertensive medications ($r = 0.46$, $P < 0.01$), and hsCRP levels ($r = 0.39$, $P < 0.05$). The AGE concentration was negatively correlated with eGFR ($r = -0.53$, $P < 0.01$). In the CKD group with diabetes, we observed a negative correlation between AGEs and eGFR ($r = -0.58$, $P < 0.01$) and a significant positive correlation between PWV and SBP ($r = 0.53$, $P < 0.01$) and PP ($r = 0.58$, $P < 0.01$).

The comparison between CKD patients with type 1 and type 2 diabetes was also performed and the results are presented in TABLE 3. PWV and

TABLE 2 Results of a multiple linear regression analysis with pulse wave velocity as a dependent variable in patients with chronic kidney disease

	β	β standard error	<i>P</i> value
age	0.28	0.11	0.01
diabetic nephropathy (1 vs. 0)	0.29	0.14	0.04
SBP	0.30	0.11	0.01
AGEs	0.14	0.13	0.30

$R = 0.67$, $R^2 = 0.45$, adjusted $R^2 = 0.41$, $F = 11.4$, $P < 0.0001$

Abbreviations: see [TABLE 1](#)

TABLE 3 Comparison of type 1 and type 2 diabetic patients with chronic kidney disease

	Type 1 diabetes CKD (n = 11)	Type 2 diabetes CKD (n = 13)	<i>P</i> value
age, y	41 ± 8	64 ± 8	<0.001
duration of diabetes, y	25 ± 9	17 ± 8	<0.05
male sex	6 (58)	8 (62)	NS
SBP, mmHg	135 ± 22	159 ± 22	<0.02
DBP, mmHg	79 ± 8	80 ± 11	NS
PP, mmHg	56 ± 17	80 ± 11	<0.01
BMI, kg/m ²	23.8 ± 2.4	29.5 ± 3.9	<0.001
creatinine, μmol/l	218.3 ± 97.2	206.9 ± 70.7	NS
eGFR, ml/min/1.73 m ²	35 ± 18	30 ± 11	NS
hsCRP, mg/l	5.0 ± 11.4	1.8 ± 1.2	NS
AGEs, AU/ml	20.2 ± 6.9	21.8 ± 6.9	NS
PWV, m/s	12.4 ± 4.2	14.8 ± 4.3	NS
fasting glucose, mmol/l	8.0 ± 2.9	6.9 ± 2.2	NS
HbA _{1c} , %	7.8 ± 0.7	7.4 ± 0.7	NS
total cholesterol, mmol/l	5.5 ± 1.0	4.8 ± 0.7	NS
LDL cholesterol, mmol/l	3.3 ± 1.2	2.9 ± 0.8	NS
HDL cholesterol, mmol/l	1.4 ± 0.5	1.3 ± 0.2	NS
triglycerides, mmol/l	1.7 ± 0.7	1.4 ± 0.3	NS
number of antihypertensive drugs	4 ± 1	4 ± 1	NS
patients treated with ACEI or ARB	10 (91)	11 (85)	NS
patients treated with statin	8 (73)	6 (46)	NS

Data are presented as mean ± standard deviation or number (percentage).

Abbreviations: NS – nonsignificant, others – see [TABLE 1](#)

AGE concentrations did not differ significantly between CKD patients with type 1 and type 2 diabetes, despite significant differences in age, BMI, SBP, and PP. In diabetic patients, there was no correlation between diabetes duration and AGE levels ($r = 0.22$, NS) or between diabetes duration and PWV ($r = 0.18$, NS). There was no correlation between the AGE concentration and HbA_{1c} ($r = -0.19$, NS).

DISCUSSION Predialysis patients with CKD are characterized by elevated arterial stiffness with a stepwise increase in PWV with progression of CKD.⁵⁻⁷ Several factors associated with increased arterial stiffness, such as age, male sex, hypertension, diabetes, and waist circumference, were identified in this population.^{6,7,27} In the study by Wang et al.,⁷ blood pressure and eGFR, but not diabetes, were independently associated with

arterial stiffening in CKD.⁷ On the other hand, Kimoto et al.²⁷ revealed that PWV was elevated in patients with type 2 diabetes without CKD when compared with controls, and it further increased with the advanced stages of diabetic CKD.²⁷ An increase in PWV was greater in the central elastic arteries than in limb arterial segments.²⁷ In an earlier study, it was shown that the serum AGE concentration and tissue AGE content are elevated in patients with diabetes, and they are particularly high in diabetic patients with end-stage renal disease.²⁰ There have been no studies investigating the relationship between AGEs and arterial stiffness in nondialyzed CKD patients.

The main finding of our study is that the AGE level is elevated in CKD patients, particularly in those with diabetic nephropathy. cFPWV is also elevated in these patients, with significantly higher values in patients with diabetic nephropathy.

A significant positive correlation was also found between AGE concentrations and PWV, but lost its significance in a multiple linear regression analysis. The association between AGEs and arterial structure and function was found in several previous studies. Semba et al.²² revealed an association between an AGE, namely, serum carboxymethyllysine, and PWV in relatively healthy community-dwelling adults.²² In another study,²⁸ in subjects with normal glucose and serum creatinine levels, an association between carboxymethyllysine and an increased carotid artery diameter, but not with PWV, was observed. In hypertensive patients, both AGE levels and PWV were significantly higher than in the normotensive control group.²³ In this study, the plasma AGE concentration was independently associated with PWV.

Januszewski et al.²⁹ investigated the relationship between ocular and skin autofluorescence (a measure of tissue AGE accumulation) and arterial function in type 1 diabetic patients. In their study, lens, corneal, and skin autofluorescence were increased, and small artery elasticity was reduced in type 1 diabetic compared with nondiabetic subjects. Small and large artery elasticity was inversely correlated with lens, corneal, and skin autofluorescence. A significant positive correlation between tissue AGEs and C-reactive protein (CRP) was also found in this population.²⁹ Moreover, a significant positive correlation between serum pentosidine (a well-defined AGE) and both PWV and carotid artery intima-media thickness was found in patients with type 2 diabetes.³⁰

The association between AGEs and arterial stiffness was confirmed in hemodialyzed patients.^{24,25} Zhou et al.²⁵ revealed that serum pentosidine was independently associated with reduced arterial distensibility. The comparison of diabetic and nondiabetic patients on hemodialysis showed no significant difference in serum pentosidine levels, but distensibility coefficient was significantly lower in diabetic patients.²⁵ In another study,²⁴ in Japanese patients with end-stage renal disease, a relationship between skin autofluorescence and PWV was found.²⁴ It should be emphasized that skin autofluorescence was identified as a prognostic factor of cardiac mortality in diabetic patients.³¹ Moreover, it has been recently shown that AGE accumulation in hemodialyzed patients is associated with an increased risk of cardiovascular events and mortality.³²⁻³⁴

Numerous clinical and experimental studies confirmed a pathophysiological link between AGEs and cardiovascular complications.^{13,14,35} AGEs constitute a large group of heterogeneous molecules formed by the non-enzymatic reactions of sugar with free amino groups of proteins, peptides, and nucleic acids.^{13,14,35} The formation of AGEs is increased in the blood and tissues of diabetic subjects as a result of hyperglycemia.¹⁸ AGEs can also be formed independently of hyperglycemia, as a result of increased oxidative stress.^{13,36} Another source of AGEs is diet, particularly Western diet, where

foods are processed in high temperature.¹² In patients with CKD, AGEs accumulate as a consequence of decreased excretion and increased production, resulting from oxidative and carbonyl stress.¹⁴ It is suggested that AGE levels could represent accumulated oxidative stress during the progression of CKD.³³ AGE accumulation positively correlates with the duration of CKD²¹ and negatively with glomerular filtration rate.¹⁴ In our study, a significant negative correlation between AGEs and eGFR in CKD patients was also observed.

AGEs can cause tissue damage by protein cross-linking. Glycation of long-lived extracellular matrix proteins such as collagen and elastin leads to cross-linking of protein fibers. AGE-linked extracellular matrix is stiffer and less susceptible to enzymatic turnover.^{13,14,35} Thus, accumulation of AGEs is considered a pathogenic factor of increased arterial stiffness. It was also shown that AGEs upregulate CRP synthesis by human hepatocytes through stimulation of monocyte interleukin 6 and interleukin 1 β production.³⁷ In hemodialyzed patients, the tissue level of AGEs was an independent determinant of the hsCRP level.³⁸ In our study, there was no relationship between plasma AGE levels and hsCRP. However, a significant correlation between hsCRP and PWV in nondiabetic CKD patients, but not in nondiabetic CKD patients, might suggest that the pathophysiology of arterial stiffening differs between these two patient groups.

Diabetic patients with CKD are characterized by higher prevalence and incidence of cardiovascular events compared with nondiabetic patients with CKD.³⁹ Cardiovascular complications of diabetes are considered to be multifactorial with growing evidence of the important pathophysiological role of advanced glycation.^{15,18,19} Accumulation of AGEs was observed in diabetic patients with normal kidney function and in diabetic patients with CKD.²⁰ Skin autofluorescence was higher in diabetic than in nondiabetic patients on hemodialysis, and a similar relationship was found in patients on peritoneal dialysis.²¹ The measurement of AGE accumulation is also considered to be a useful method for assessing metabolic control over a longer period of time than that reflected by HbA_{1c} levels.^{15,40} Several studies revealed a significant positive correlation between AGEs and HbA_{1c},^{15,40} but other did not report such a relationship.⁴¹ The lack of correlation between AGEs and HbA_{1c} in our study may arise from the fact that HbA_{1c} was not assessed from the same blood sample but taken from patient medical records.

AGEs are considered a novel marker of unfavorable prognosis in diabetes. In patients with type 1 diabetes, higher baseline plasma AGE levels were associated with incident cardiovascular events as well as all-cause mortality during 12-year follow-up, independently of traditional cardiovascular risk factors.⁴² What is more, PP is an independent predictor of cardiovascular

complications in type 1 diabetic patients.⁴³ This phenomenon might be at least partly explained by the effect of AGE accumulation on arterial stiffness.⁴⁴ It was shown in patients with type 1 diabetes that age-related changes in PP, which reflects arterial stiffening, occur 15 to 20 years earlier than in healthy subjects.⁴⁵ In our study, PWV values were significantly higher in diabetic subjects, with no significant difference between type 1 and type 2 diabetes, even though type 2 diabetic patients were much older than type 1 diabetic patients. It is in agreement with the earlier findings of early age-related rise in PP in subjects with diabetic nephropathy, which was considered to be an index of accelerated arterial aging in type 1 diabetic patients.⁴⁵ It should also be noted that in type 1 diabetic patients with end-stage renal disease, increased arterial stiffness was not reversed even by simultaneous kidney-pancreas transplantation.⁴⁶ Thus, alterations in the arterial wall resulting from long-lasting glucotoxicity and CKD may be irreversible.

Our study has several limitations related mainly to a small number of subjects. The causal relationship between the AGE concentration and arterial stiffness cannot be established owing to the cross-sectional design of the study. Another limitation is related to the fact that serum AGE concentrations may not correspond to tissue AGE accumulation.²⁵ The lack of the relationship between AGEs and PWV in the multiple regression analysis in our study did not exclude the pathogenic effect of AGE accumulation on arterial stiffening, but may suggest that this effect was small. An adjusted R^2 of 0.41 in our multiple regression model suggests that other variables that were not included in our analysis, such as smoking status or autonomic neuropathy, account for arterial stiffening in CKD patients before dialysis.

In conclusion, AGE accumulation and arterial stiffness are increased in CKD, particularly in patients with diabetic nephropathy; however, the results are not sufficient to confirm the causal role of AGE accumulation in arterial stiffening. AGEs should be considered as a potential therapeutic target in patients with CKD.

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Produkty zaawansowanej glikacji i sztywność tętnic u pacjentów z nefropatią cukrzycową oraz pacjentów z przewlekłą chorobą nerek bez cukrzycy

Paweł Stróżecki¹, Robert Kurowski², Mariusz Flisiński¹, Anna Stefańska³,
Grażyna Odrowąż-Sypniewska³, Jacek Manitius¹

- 1 Klinika Nefrologii, Nadciśnienia Tętniczego i Chorób Wewnętrznych, Szpital Uniwersytecki Nr 1 im. dr. A. Jurasza w Bydgoszczy, Uniwersytet Mikołaja Kopernika w Toruniu, Collegium Medicum im. Ludwika Rydygiera, Bydgoszcz
- 2 Kujawsko-Pomorskie Centrum Pulmonologii, Bydgoszcz
- 3 Zakład Diagnostyki Laboratoryjnej, Szpital Uniwersytecki Nr 1 im. dr. A. Jurasza w Bydgoszczy, Uniwersytet Mikołaja Kopernika w Toruniu, Collegium Medicum im. Ludwika Rydygiera, Bydgoszcz

SŁOWA KLUCZOWE

cukrzyca, prędkość fali tętna, produkty zaawansowanej glikacji, przewlekła choroba nerek, sztywność tętnic

STRESZCZENIE

WPROWADZENIE Powstawanie produktów zaawansowanej glikacji (*advanced glycation end-products* – AGEs) jest zwiększone u pacjentów z cukrzycą. Upośledzona czynność nerek również zwiększa kumulację AGEs. Prędkość fali tętna (*pulse wave velocity* – PWV) jest miernikiem sztywności tętnic oraz wskaźnikiem rokowniczym. Związek między AGEs i sztywnością tętnic wykazano u pacjentów hemodializowanych.

CELE Oceniano związek między osoczymym stężeniem AGEs i sztywnością tętnic u niedializowanych pacjentów z nefropatią cukrzycową oraz pacjentów z przewlekłą chorobą nerek (*chronic kidney disease* – CKD) bez cukrzycy.

PACJENCI I METODY Pomiar PWV przeprowadzono u 24 pacjentów z nefropatią cukrzycową (*diabetic nephropathy* – DN) 36 pacjentów z CKD bez cukrzycy oraz 19 osób zdrowych. Aby ocenić stężenie AGEs mierzono widma fluorescencji osocza.

WYNIKI Pacjenci z DN i CKD bez cukrzycy nie różnili się wielkością filtracji kłębuszkowej (33 ± 13 vs 32 ± 14 ml/min/1,73 m²). Stężenie AGE było większe u pacjentów z DN niż u pacjentów bez cukrzycy i w grupie kontrolnej ($21,1 \pm 6,8$ vs $12,3 \pm 3,1$ vs $7,8 \pm 1,2$ AU/ml; $p < 0,001$). PWV było również większe w grupie z DN w porównaniu z grupą bez cukrzycy i grupą kontrolną ($13,7 \pm 4,3$ vs $10,1 \pm 2,4$ vs $8,4 \pm 1,6$ m/s; $p < 0,05$). U pacjentów z CKD wykazano znamienne dodatnią korelację między stężeniem AGEs i PWV ($r = 0,39$; $p < 0,01$). W analizie regresji wielokrotnej PWV było niezależnie związane z wiekiem, nefropatią cukrzycową oraz ciśnieniem tętniczym skurczowym, ale nie z AGEs ($R^2 = 0,45$).

WNIOSKI Akumulacja AGEs i sztywność tętnic są zwiększone u pacjentów z CKD, a zwłaszcza u pacjentów z DN, jednak wyniki badania nie pozwalają na potwierdzenie przyczynowej roli AGEs w zwiększeniu sztywności tętnic w CKD. AGEs powinny być brane pod uwagę jako potencjalny cel terapeutyczny u pacjentów z CKD.

Adres do korespondencji:
dr med. Paweł Stróżecki, Klinika Nefrologii, Nadciśnienia Tętniczego i Chorób Wewnętrznych, Szpital Uniwersytecki Nr 1 im. dr. A. Jurasza, ul. M. Skłodowskiej-Curie 9, 85-094 Bydgoszcz, tel.: 52-585-45-51, fax: 52-585-40-30, e-mail: st_pawel@cm.umk.pl
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