

Concomitant diseases and selected cardiovascular complications in hospitalised patients with hypertension and diabetes

Choroby współistniejące i wybrane powikłania sercowo-naczyniowe u hospitalizowanych chorych z nadciśnieniem tętniczym i cukrzycą

Alicja Stępień-Wałek¹, Iwona Gorczyca-Michta¹, Ewa Tomasiak², Maciej Kluk¹, Łukasz Dobaj¹, Barbara Sosnowska-Pasiarska¹, Katarzyna Dziubek¹, Paweł Salwa¹, Kamil Michta³, Beata Wożakowska-Kapłon^{1, 2}

¹First Department of Cardiology, Świętokrzyskie Cardiology Centre, Kielce, Poland

²Faculty of Health Sciences, Jan Kochanowski University, Kielce, Poland

³Department of Cardiac Surgery, Świętokrzyskie Cardiology Centre, Kielce, Poland

Abstract

Introduction. Patients with type 2 diabetes and hypertension are at a significantly increased risk of cardiovascular mortality, including due to myocardial infarction, and often suffer from other diseases and cardiovascular complications.

Material and methods. We studied 2513 hospitalised patients with hypertension who were divided into two groups: with diabetes (DM+, n = 637) and without diabetes DM–, n = 1876). The two groups were compared in regard to age, gender, and selected concomitant diseases and cardiovascular complications.

Results. Mean age was 70 ± 9.7 years in the DM+ group vs. 68 ± 11.0 years in the DM– group (p = 0.0001), with 51.2% women in the DM+ group compared to 43.4% women in the DM– group (p = 0.0004). The following conditions were more frequent in the DM+ group compared to the DM– group: heart failure (43.8% vs. 35.5%, p = 0.0001), atrial fibrillation (34.8% vs. 24.7%, p = 0.03), stroke (6.6% vs. 4.4%, p = 0.03), hypertriglyceridaemia (153 ± 72.1 vs. 37.1 ± 74.4 mg/dL, p = 0.0004), low HDL cholesterol level (43.4 ± 14.6 vs. 46.9 ± 19.7 mg/dL, p = 0.0002), and reduced glomerular filtration rate (51.42 ± 19.82 vs. 56.94 ± 16.08 mL/min/1.73 m² (p = 0.0001). No differences were found in regard to the rates of stable coronary artery disease (33.7% vs. 29.3%, p = NS) and left ventricular hypertrophy (34.8% vs. 30.7%, p = NS).

Conclusions

1. Diabetes was significantly more common among hypertensive women compared to hypertensive men. Patients with diabetes were significantly older.
2. Macroangiopathic complications (previous myocardial infarction or stroke) and concomitant diseases (atrial fibrillation, heart failure, nephropathy) were significantly more frequent in patients with diabetes.
3. Stable coronary artery disease and left ventricular hypertrophy occurred at a similar rate in patients with or without diabetes.
4. Atherogenic dyslipidaemia was more frequent among patients with diabetes.

Key words: diabetes, hypertension, myocardial infarction, heart failure, left ventricular hypertrophy

(Folia Cardiologica 2014; 9, 1: 10–16)

Introduction

Type 2 diabetes is a major cardiovascular risk factor. In the European Society of Cardiology guidelines, diabetes was considered a coronary heart disease risk equivalent, indicating a very high cardiovascular risk in these patients [1]. Multiple studies show that the risk of myocardial infarction and cardiovascular mortality among diabetes patients without established coronary heart disease is similar to the risk among non-diabetic patients after a myocardial infarction. It has been estimated that in diabetic patients, coronary heart disease manifests on average 15 years earlier than in non-diabetic subjects [2].

Compared to patients without diabetes, diabetic patients are usually older, with a higher proportion of women and higher rates of obesity, hypertension, previous myocardial infarction, heart failure, and previous revascularisation procedures [3].

The rate of hypertension accompanying type 2 diabetes is increased up to three-fold compared to the general population [1]. Concomitant occurrence of hypertension and diabetes, with its complex underlying pathogenetic mechanisms, is associated with a significantly increased risk of cardiovascular mortality, including due to myocardial infarction [4].

Material and methods

We retrospectively analysed 2513 patients with hypertension hospitalised in a cardiology department in 2009–2010. The study group (DM+) included 637 patients with hypertension and concomitant diabetes (25.3% of the overall study population), and the control group (DM-) included 1876 with hypertension and no concomitant diabetes (74.7%). The proportion of men among all patients was 54.6% ($n = 1372$), and 22.6% of them had diabetes, and for women these figures were 45.4% ($n = 1140$) and 28.6%, respectively. The two groups were compared in regard to the rates of selected concomitant diseases and cardiovascular complications.

The diagnosis of hypertension was based on history (including a history of antihypertensive drug use) and physical examination findings – the mean of at least two blood pressure measurements on at least two days of hospital stay ≥ 140 mm Hg for systolic blood pressure and/or ≥ 90 mm Hg for diastolic blood pressure. The diagnosis of diabetes was based on three complementary criteria: fasting blood glucose level > 125 mg/dL (two measurements on two consecutive days of hospital stay), random blood glucose level ≥ 200 mg/dL with clinical signs of hyperglycaemia, and a positive oral glucose tolerance test (blood glucose level 2 hours after oral administration of 75 g of glucose ≥ 200 mg/dL). Heart failure was diagnosed based on typical symptoms and signs. Ischaemic heart disease was

diagnosed based on a history of typical symptoms and/or previous myocardial infarction. Dyslipidaemia was defined as the following lipid levels: total cholesterol ≥ 190 mg/dL, low-density lipoprotein (LDL) cholesterol ≥ 115 mg/dL, high-density lipoprotein (HDL) cholesterol ≤ 40 mg/dL, and triglycerides ≥ 150 mg/dL, or a history of lipid-lowering drug use. Left ventricular ejection fraction was evaluated by echocardiography using the Simpson method or by visual assessment, and left ventricular hypertrophy was defined as interventricular septum thickness of ≥ 12 mm. Atrial fibrillation was diagnosed based on a history of arrhythmia and/or electrocardiographic findings. Renal dysfunction was evaluated based on glomerular filtration rate as estimated using the Modification of Diet in Renal Disease (MDRD) formula.

Statistical analysis was performed using a licensed copy of the STATISTICA 10 package. For each variable, the arithmetic mean with standard deviation was calculated. Normal distribution of the variables was evaluated using the Shapiro-Wilk test. Significance of differences in the mean values of normally distributed variables was evaluated using the Student *t* test for unpaired samples, and the Mann-Whitney U test was used for non-normally distributed variables. For these comparisons, $p < 0.05$ was considered statistically significant.

Results

The mean age was 70 ± 9.7 years in the DM+ group compared to 68 ± 11.0 years in the DM- group, a statistically significant difference ($p = 0.0001$). The proportion of women was 51.2% (326/637) in the DM+ group compared to 43.4% (814/1876) in the DM- group, again a statistically significant difference ($p = 0.0004$). Diabetes was significantly more frequent among women compared to men (326/1140 [28.6%] vs. 310/1372 [22.6%] patients, respectively, $p = 0.001$). Insulin therapy was used in 138 patients in the DM+ group (21.7%), and the remaining patients ($n = 497$, 78.0%) received oral hypoglycaemic agents.

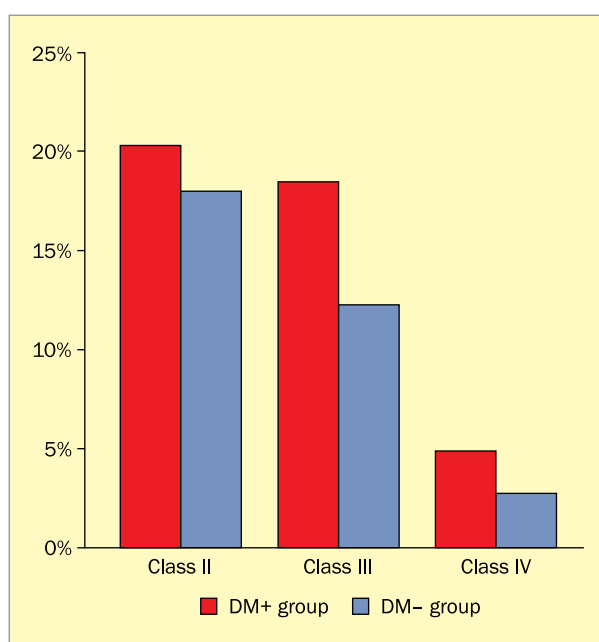
Previous myocardial infarction was reported in 78 patients (12.3%) in the DM+ group compared to 155 patients (8.3%) in the DM- group ($p = 0.002$). The rate of stable coronary artery disease did not differ between the groups (214/637 [33.7%] vs. 550/1876 [29.3%] patients, respectively, $p = \text{NS}$).

Heart failure was significantly more common in the DM+ group (278 patients [43.8%] compared to 667 patients [35.5%] in the DM- group, $p = 0.0001$) (Table 1). When we analysed the severity of heart failure in the DM+ and DM- groups as assessed using the New York Heart Association (NYHA) classification, 129 (20.3%) vs. 337 (18.0%) patients were in NYHA class II, respectively, 118 (18.5%) vs. 277 (12.3%) patients were in NYHA class III, and 31 (4.9%) vs. 53 (2.8%) patients were in NYHA class

Table 1. Rates of selected comorbidities and complications in the DM+ and DM- groups

| Parameter | DM+ group (n = 637) | DM- group (n = 1876) | p |
|--|-------------------------|--------------------------|--------|
| Age (years) | 70 ± 9.7 | 68 ± 11.4 | 0.0001 |
| Gender (women/men) | 326 (51.3%)/309 (48.7%) | 813 (43.4%)/1063 (56.7%) | 0.0004 |
| Previous myocardial infarction | 78 (12.3%) | 155 (8.3%) | 0.002 |
| Ischaemic heart disease | 214 (33.7%) | 550 (29.3%) | NS |
| Heart failure | 278 (43.8%) | 667 (35.5%) | 0.0001 |
| Atrial fibrillation | 221 (34.8%) | 464 (24.7%) | 0.03 |
| Previous stroke | 42 (6.6%) | 84 (4.4%) | 0.03 |
| Total cholesterol [mg/dL] | 170 ± 71.5 | 179 ± 49.0 | 0.0002 |
| LDL cholesterol [mg/dL] | 101 ± 44.5 | 107.9 ± 42.9 | 0.001 |
| HDL cholesterol [mg/dL] | 43.4 ± 14.6 | 46.9 ± 19.7 | 0.0002 |
| Triglycerides [mg/dL] | 153 ± 72.4 | 137.1 ± 74.4 | 0.0004 |
| eGFR [mL/min/1.73 m ²] | 51.42 ± 19.82 | 56.94 ± 16.08 | 0.0001 |
| Blood glucose [mg/dL] | 150 ± 66.83 | 100 ± 39.3 | 0.0001 |
| Left ventricular ejection fraction (%) | 46 ± 13 | 50 ± 16 | 0.0001 |
| Left ventricular hypertrophy [mm] | 221 (34.8%) | 577 (30.7%) | NS |

DM – diabetes mellitus; NS – not significant

**Figure 1.** Heart failure severity in the DM+ and DM- groups as assessed using the New York Heart Association classification; DM – diabetes mellitus

IV (Figure 1). Left ventricular ejection fraction was significantly lower in the DM+ group compared to the DM- group (46% ± 13% vs. 50% ± 16%, $p = 0.0001$). The rate of left ventricular hypertrophy did not differ between the DM+ and DM- groups (221 [34.8%] vs. 577 [30.7%] patients, respectively, $p = NS$).

Atrial fibrillation was significantly more frequent in the DM+ group compared to the DM- group (221 [34.8%] vs. 464 [24.7%] patients, respectively, $p = 0.03$), as was previous stroke (42 [6.6%] vs. 84 [4.4%] patients, respectively, $p = 0.03$).

Compared to the DM- group, dyslipidaemia was significantly more frequent in the DM+ group, including hypertriglyceridaemia (153 ± 72.1 mg/dL vs. 37.1 ± 74.4 mg/dL, respectively, $p = 0.0004$) and low HDL cholesterol level (43.4 ± 14.6 mg/dL vs. 46.9 ± 19.7 mg/dL, $p = 0.0002$) (Figure 2).

Glomerular filtration rate estimated using the MDRD formula was significantly lower in the DM+ group compared to the DM- group (51.42 ± 19.82 vs. 56.94 ± 16.08 mL/min/1.73 m², respectively, $p = 0.0001$).

A summary of these findings is shown in Table 1.

Discussion

In our study, diabetes was present in 24.5% of hospitalised patients, significantly more frequently among women compared to men. The proportion of women was higher among diabetic patients than among those with normal glucose tolerance (51% vs. 43%, respectively).

The mean age was 70 years in the diabetic group compared to 68 years in the non-diabetic group. It has been noted that the prevalence of diabetes increases with age until about 70-75 years of age and then decreases, likely due to premature mortality related to diabetes complications [5]. Based on a 7-year follow-up study by Haffner et al. who showed that the incidence of myocardial infarction among patients with diabetes was similar to that among non-diabetic patients after myocardial infarction [6],

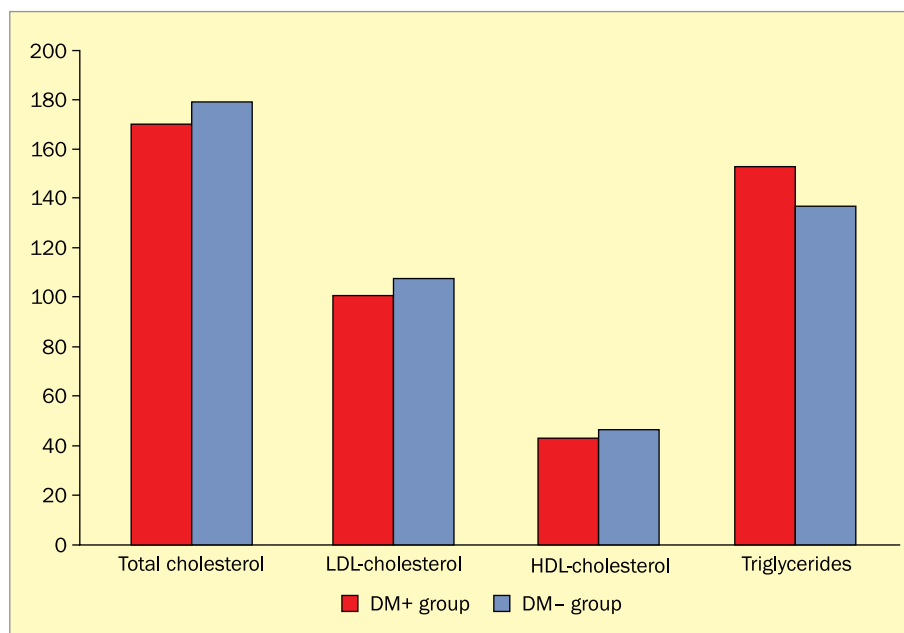


Figure 2. Lipid profile in the DM+ and DM- groups; DM – diabetes mellitus; LDL – low-density lipoprotein; HDL – high-density lipoprotein

diabetes was considered a coronary heart disease risk equivalent [7].

Multiple studies showed that cardiovascular disease in diabetic patients is significantly more frequent and occurs much earlier compared to patients without diabetes. In the Framingham Heart Study population, the rate of cardiovascular disease was increased 2-fold in diabetic men and 3-fold in diabetic women [8]. One study showed that on average, the presence of diabetes was associated with a 15-fold increase in cardiovascular risk [2]. In addition, cardiovascular complications often precede the diagnosis of diabetes. In the study by Kowalska et al. among men with stable ischaemic heart disease with no prior diagnosis of diabetes, in whom coronary atherosclerotic lesions were confirmed by angiography, abnormal glucose tolerance was identified by oral glucose tolerance test in more than 50% of patients (including type 2 diabetes in 16% of patients, and impaired glucose tolerance in 36% of patients) [9]. An increased rate of myocardial infarction in patients with diabetes was confirmed by Haffner et al. who showed that during a 7-year follow-up, the risk of myocardial infarction in diabetic patients was significantly increased in patients with a history of myocardial infarction compared to those with no previous infarction (45% vs. 20.2%), while these rates in non-diabetic patients were 18.8% vs. 3.5%, respectively ($p < 0.001$) [6]. Also in the Framingham Heart Study, recurrent myocardial infarction in diabetic patients was found to occur more frequently and earlier, particularly among women [10]. In our study, previous myocardial infarction was noted in 12% of diabetic patients compared to 8% of

patients without diabetes. Stable ischaemic heart disease was noted in 34% vs. 29% of these patients, respectively, with no significant differences between the two groups.

In our study, the rate of atrial fibrillation was higher among patients with diabetes (221/637, 34.8%) compared to those without diabetes (464/1876, 24.7%). In previously published reports, diabetes was found in 7.6–13% of patients with atrial fibrillation. Nichols et al. reported that atrial fibrillation was significantly more frequent in patients with established diabetes compared to those without diabetes [11]. Much data on the coexistence of atrial fibrillation and diabetes were provided by the Atherosclerosis Risk in Communities (ARIC) study. Compared to patients without diabetes, the risk of incident atrial fibrillation was increased by 1/3 in patients with diabetes. A significant association was shown between fasting blood glucose and glycated haemoglobin levels in diabetic patients and the occurrence of atrial fibrillation. Diabetes was identified as an independent risk factor for atrial fibrillation in some, but not all studies [12]. Thus, identification of atrial fibrillation has not been a priority in patients with diabetes due to more frequent occurrence of asymptomatic arrhythmia. In addition, the European Society of Cardiology recommends looking for atrial fibrillation by taking pulse, and recording an electrocardiogram whenever irregular heart rate is identified, in all patients aged ≥ 65 years seen by primary care physicians [13]. Presence of diabetes is associated with worse outcomes of atrial fibrillation due to an increased risk of all-cause mortality, increased cardiovascular mortality, and an increased risk of heart failure and particularly

ischaemic stroke. In our study, stroke was more frequent in the diabetic compared to the non-diabetic group, as diabetes is a risk factor for thromboembolic complications in this patient population.

Diabetic patients are characterized by an increased incidence of heart failure. This is largely related to the development of atherosclerosis related to diabetes, but diabetic cardiomyopathy resulting from impaired cardiomyocyte metabolism also plays a role [14]. Diabetes impairs both systolic and diastolic function of the left ventricle due to myocardial fibrosis and ischemia. A relation between diabetes and heart failure was first identified in the Framingham Heart study [15]. In the overall study population (aged 45–74 years), diabetes was associated with a 2-fold increased risk of heart failure in men and a 5-fold increased risk in women, and in younger subjects (< 65 years) this risk was increased as much as 8-fold in women and 4-fold in men compared to subjects without diabetes [15]. The rate of heart failure among diabetic patients is up to 22%, and the incidence has been estimated at 0.4–13% per year [16]. On the other hand, the rate of diabetes among patients with heart failure is 20–30%, and thus it is much increased compared to the general population [17]. In our study, the rate of heart failure in hospitalised patients with diabetes and hypertension was 43.8% (278/637) compared to 35.5% (667/2876) among those without diabetes. Left ventricular ejection fraction was also significantly lower in patients with diabetes (46% vs. 50%, respectively; $p = 0.0001$). Risk factors for heart failure in diabetes include symptomatic coronary artery disease, age, female gender, obesity, hypertension, long duration of diabetes, hyperglycaemia, and microangiopathy. The incidence of heart failure is twice increased among diabetic patients with a history of coronary artery disease compared to those without coronary artery disease. Only one third of heart failure cases develop in subjects without previously established coronary artery disease [16].

The prevalence of left ventricular hypertrophy in diabetic patients is increased independently from the occurrence of the major cause of hypertrophy, i.e. arterial hypertension. In the Strong Heart Study, left ventricular hypertrophy was identified in 19% of diabetic patients without concomitant hypertension and in 38% of patients with diabetes and hypertension [18]. In our study, left ventricular hypertrophy was present in 35% of patients with diabetes and hypertension compared to 31% of patients without diabetes. Diabetes, hypertension, and obesity are all independent risk factors for left ventricular hypertrophy [19].

The atherogenic dyslipidaemia of diabetes, characterised by elevated triglycerides, low HDL cholesterol level, and increased levels of small dense LDL, apolipoprotein B, and very low-density lipoproteins (VLDL), initiates and

promotes progression of atherosclerosis, leading to an increase in cardiovascular risk [20]. Elevated triglyceride level is the major lipid abnormality in diabetes. In addition, triglyceride-rich lipoproteins are elevated, both originating from the small intestine (chylomicrons) and endogenously synthesized (VLDL), leading to increased and prolonged postprandial hyperlipaemia. This results in an increased exposure of the vessel wall to the atherogenic effect of these lipoproteins. In our study group with hypertension and diabetes, a significantly higher triglyceride level was found compared to the study group, along with a significantly lower HDL cholesterol level, which confirmed the presence of an atherogenic lipid profile in patients with diabetes. At the same time, we found significantly lower levels of total cholesterol and LDL cholesterol compared to the control group, which is consistent with the literature data indicating that no significant hypercholesterolemia is usually present in patients with diabetes [20]. This was also likely related to appropriate lipid-lowering treatment in those patients with diabetes and hypertension. An elevated total cholesterol level may result from poorly controlled diabetes. LDL cholesterol level was only slightly elevated, thus not reflecting the actual cardiovascular risk related to dyslipidaemia that accompanies diabetes [20]. Although LDL cholesterol level is not significantly increased, each LDL particle carries a larger load of apolipoprotein B in diabetic than in non-diabetic patients.

Nephropathy is also an important factor affecting cardiovascular risk in patients with diabetes and hypertension. At the time when type 2 diabetes is diagnosed, microalbuminuria is present in 19% of patients, and overt proteinuria in 5% of patients. Diabetic nephropathy is associated with an increased mortality risk and increased rates of cardiovascular complications [21]. In our study, mean glomerular filtration rate was significantly lower in diabetic than in non-diabetic patients.

Study limitations

The major limitation of our study was a sample size disproportion between the groups with or without diabetes, with a much larger control group without diabetes. Our findings indicate, however, a strong predilection for cardiovascular complications among those fewer patients with diabetes. It is even more important due to the fact that the overall study population was quite large (more than 2500 subjects), increasing the statistical power of our results. Another limitation was the fact that we performed a single-centre, retrospective analysis of the prevalence of selected conditions depending on the presence of diabetes, without a prospective attempt to follow-up progression of these disturbances in relation to diabetes duration and control.

Conclusions

1. Diabetes was significantly more common among hypertensive women compared to hypertensive men. Patients with diabetes were significantly older than those without diabetes.
2. Macroangiopathic complications including previous myocardial infarction and stroke and concomitant diseases such as atrial fibrillation, heart failure, and nephropathy were significantly more frequent in hypertensive patients with diabetes than in those without concomitant diabetes.
3. Stable coronary artery disease and left ventricular hypertrophy occurred at a similar rate in patients with or without diabetes.
4. Atherogenic dyslipidaemia, defined as hypertriglyceridemia and low HDL cholesterol level, was more frequent among hypertensive patients with diabetes.

Conflict of interest

None declared.

Streszczenie

Wstęp. Chorych na cukrzycę typu 2 z nadciśnieniem tętniczym cechuje istotnie podwyższone ryzyko zgonu z przyczyn sercowo-naczyniowych, w tym zawału serca, oraz często zapadają na inne choroby i powikłania sercowo-naczyniowe.

Materiały i metody. Analizą objęto 2513 hospitalizowanych chorych z nadciśnieniem tętniczym, których podzielono na dwie grupy: z cukrzycą (DM+) – 637 chorych i bez cukrzycy (DM-) – 1876 chorych. Grupy porównano pod względem wieku, płci oraz współwystępowania wybranych chorób i powikłań sercowo-naczyniowych.

Wyniki. Średnia wieku w grupie DM+ wynosiła $70 \pm 9,7$ roku, a w grupie DM- $68 \pm 11,0$ lat ($p = 0,0001$). W grupie DM+ kobiety stanowiły 51,2%, natomiast w grupie DM- 43,4% ($p = 0,0004$). W grupie DM+ częściej niż w grupie DM- występowały: niewydolność serca (43,8 v. 35,5%; $p = 0,0001$), migotanie przedsionków (34,8 v. 24,7%; $p = 0,03$), udar mózgu (6,6 v. 4,4%; $p = 0,03$), hipertriglicerydemia ($153 \pm 72,1$ mg/dl v. $37,1 \pm 74,4$ mg/dl; $p = 0,0004$), obniżone stężenie cholesterolu frakcji HDL ($43,4 \pm 14,6$ mg/dl v. $46,9 \pm 19,7$ mg/dl; $p = 0,0002$), obniżony wskaźnik filtracji kłębuszkowej ($51,42 \pm 19,82$ v. $56,94 \pm 16,08$ ml/min/1,73 m²; $p = 0,0001$). Nie wykazano różnic w zakresie współwystępowania stabilnej choroby wieńcowej (33,7 v. 29,3%; $p = \text{NS}$) i przerostu lewej komory (34,8 v. 30,7%, $p = \text{NS}$).

Wnioski

1. Cukrzyca występowała istotnie częściej u kobiet niż u mężczyzn z nadciśnieniem tętniczym. Chorzy na cukrzycę byli istotnie starsi.
2. Powikłania makroangiopatyczne (przebyty zawał serca i udar mózgu) i choroby towarzyszące (migotanie przedsionków, niewydolność serca, nefropatia) występowały istotnie częściej u chorych na cukrzycę.
3. Stabilna choroba wieńcowa i przerost mięśnia sercowego występowały z podobną częstością u chorych na cukrzycę i u osób bez cukrzycy.
4. Aterogenna dyslipidemia częściej występowała w populacji chorych na cukrzycę.

Słowa kluczowe: cukrzyca, nadciśnienie tętnicze, zawał serca, niewydolność serca, przerost mięśnia sercowego

(Folia Cardiologica 2014; 9, 1: 10–16)

References

1. Ryden L., Grant P., Anker S. et al. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). Eur. Heart J. 2013; 34: 3035–3087.
2. Booth G., Kapral M., Fung K., Tu J. Relation between age and cardiovascular disease in men and women with diabetes compared with non-diabetic people: a population-based retrospective cohort study. Lancet 2006; 368: 29–36.
3. Franklin K., Goldberg R., Spencer F. et al. GRACE Investigators. Implications of diabetes in patients with acute coronary syndromes. The Global Registry of Acute Coronary Events. Arch. Intern. Med. 2004; 164: 1457–1463.
4. Gaciong Z., Lewandowski J. Leczenie nadciśnienia tętniczego u pacjenta z cukrzycą. Terapia 2010; 4: 52–57.
5. Buchta P., Frycz-Kurek A., Poloński L. Wyniki leczenia ostrych zespołów wieńcowych u chorych w podeszłym wieku. Choroby Serca i Naczyń 2009; 6: 123–130.
6. Haffner S., Lehto S., Rönnemaa T. et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects

- with and without prior myocardial infarction. *N. Engl. J. Med.* 1998; 339: 229–234.
7. Tatoń J., Czech A., Krzemińska-Pakuła M. et al. Rekomendacje prewencji, diagnostyki i leczenia chorób układu sercowo-naczyniowego u osób z cukrzycą. *Przegląd Kardiodiabetologiczny* 2008; 3: 85–206.
 8. Kannel W., McGee D. Diabetes and cardiovascular risk factors: the Framingham study. *Circulation* 1979; 59: 8–13.
 9. Kowalska I., Prokop J., Bachórzewska-Gajewska H. et al. Disturbances of glucose metabolism in men referred for coronary arteriography. Postload glycemia as predictor for coronary atherosclerosis. *Diabetes Care* 2001; 24: 897–901.
 10. Lewczuk A., Hirnle T., Sobkowicz B. et al. Choroba wieńcowa i zawał serca u pacjenta z zaburzeniami gospodarki węglowodanowej. *Przegl. Kardiodiabetol.* 2008; 3: 285–295.
 11. Nichols G., Reinier K., Chugh S. Independent contribution of diabetes to increased prevalence and incidence of atrial fibrillation. *Diabetes Care* 2009; 32: 1851–1856.
 12. Huxley R., Lopez F., Folsom A. et al. Absolute and attributable risks of atrial fibrillation in relation to optimal and borderline risk factors. *Circulation* 2011; 123: 1501–1508.
 13. Camm J., Lip G., De Caterina R. et al. Wytyczne ESC dotyczące postępowania w migotaniu przedsionków na 2012 rok. *Kardiol. Pol.* 2012; 70: 197–234.
 14. Fein S., Sonnenblick E. Diabetic cardiomyopathy. *Cardiovasc. Dis.* 1985; 27: 255–270.
 15. Kannel W., Hjortland M., Castelli W. Role of diabetes in congestive heart failure: the Framingham study. *Am. J. Cardiol.* 1974; 34: 29–34.
 16. Bertoni A., Hundley W., Massing W. i wsp. Heart failure prevalence, incidence and mortality in the elderly with diabetes. *Diabetes Care* 2004; 27:699–703.
 17. Betoni A., Tsai A., Kasper E. et al. Diabetes and idiopathic cardiomyopathy. A nationwide case-control study. *Diabetes Care* 2003; 26: 2791–2795.
 18. Bella J., Devereux R., Roman M. et al. Separate and joint effects of systemic hypertension and diabetes mellitus on left ventricular structure and function in American Indians (the Strong Heart Study). *Am. J. Cardiol.* 2001; 87: 1260–1265.
 19. Kuperstein R., Hanly P., Niroumand M. et al. Importance of age and obesity on the relations between diabetes and left ventricular mass. *J. Am. Coll. Cardiol.* 2001; 37: 1957–1962.
 20. Rubiec-Niemirska A., Czech A. Dyslipidemia cukrzycowa – znaczenie kliniczne i leczenie. *Przew. Lek.* 2009; 2: 61–67.
 21. Bakris G., Weir M., Shanifar S. et al. Effects of blood pressure level on progression of diabetic nephropathy: results from the RENAAL study. *Arch. Intern. Med.* 2003; 163: 1555–1565.

Komentarz

Makronaczyniowe powikłania cukrzycy – wyzwanie „multidyscyplinarne”, ważne informacje praktyczne



Przedstawiony Państwu artykuł dotyczy bardzo ważnego z praktycznego punktu widzenia zagadnienia – charakterystyki klinicznej pacjentów chorujących na cukrzycę, hospitalizowanych na oddziale kardiologicznym w porównaniu z pacjentami bez cukrzycy. Ponadto u wszystkich osób z analizowanej grupy występowało nadciśnienie tętnicze.

Badanie ma charakter analizy retrospektywnej; jest oparte na dużej populacji (2513 osób, w tym 637 chorych na cukrzycę). Jego wyniki są zgodne z wcześniej publikowanymi danymi z piśmiennictwa: chorzy na cukrzycę w większym odsetku przeżyli zawał serca, częściej występowały u nich cechy niewydolności krążenia, niższa była u nich frakcja wyrzutowa, częściej występowały zaburzenia rytmu serca pod postacią migotania przedsionków. Częstsze były także zaburzenia lipidogramu pod postacią hipertriglicydemii i obniżonego stężenia cholesterolu frakcji HDL oraz niższy był wskaźnik filtracji kłębuszkowej (GFR, *glomerular filtration rate*).

Problem ryzyka powikłań sercowo-naczyniowych jest kluczowy z punktu widzenia terapii cukrzycy. Powikłania makronaczyniowe są główną przyczyną nadumieralności pacjentów z cukrzycą typu 2; dane z piśmiennictwa na ten temat są szeroko cytowane w omawianej pracy. W tym kontekście chciałbym zwrócić uwagę Czytelnika na praktyczne znaczenie wyników uzyskanych przez autorów komentowanego artykułu, potwierdzających niekorzystne trendy chorobowości sercowo-naczyniowej u chorych na cukrzycę w populacji polskiej.

Zgodnie z wytycznymi Polskiego Towarzystwa Diabetologicznego (PTD) cele glikemiczne leczenia cukrzycy, intensywność terapii, powinny zależeć właśnie między innymi od obecności powikłań makronaczyniowych [1]. O ile celem lecze-

nia u większości pacjentów będzie uzyskanie wartości hemoglobiny glikowanej (HbA_{1c}) poniżej 7% (< 53 mmol/mol), to u znacznej części chorych, których dotyczyło omawiane badanie (pacjenci w wieku > 70 lat z wieloletnią cukrzycą i współistniejącymi istotnymi powikłaniami o charakterze makroangiopatii, takimi jak **przebyty zawał serca i/lub udar mózgu**), celem terapii będzie uzyskanie odsetka HbA_{1c} poniżej 8% (64 mmol/mol). Taka wartość HbA_{1c} oznacza średnie glikemie na poziomie **183 mg/dL** (95-proc. przedział ufności [CI, *confidence interval*]: 147–217), czyli **10,2 mmol/l** (95% CI: 8,1–12,1 mmol/l). Zbyt intensywne leczenie glikemii w tej grupie chorych, szczególnie narażenie na hipoglikemie, może stanowić dla nich duże zagrożenie [2]. Zatem w przypadku znacznego odsetka pacjentów hospitalizowanych na oddziałach kardiologicznych za zadowalające należy uznać osiągnięcie stosunkowo liberalnych celów leczenia.

Powikłania naczyniowe są również ważne dla wyboru leku hipoglikemizującego. Niewydolność krążenia będzie przeciwwskazaniem do leczenia pioglitazonem [3], ostrożnie należy stosować saksagliptynę [4]. Po wykluczeniu przeciwwskazań terapią z wyboru u większości pacjentów z cukrzycą typu 2 i podwyższonym ryzykiem sercowo-naczyniowym pozostaje metformina [5]. Ogólnie bezpieczne wydają się też w tym przypadku leki działające w oparciu o oś inkretynową [4, 6]. Niewydolność nerek, z kolei, może wymagać odstawienia większości pochodnych sulfonylomocznika, zmniejszenia dawki bądź odstawienia metforminy; bezpieczne będą w tym przypadku tiazolidinediony bądź niektóre inhibitory dipeptydylopeptydazy IV (DPP-IV), takie jak linagliptyna [1, 5].

Jeżeli chodzi o hipertriglicerydemię u pacjentów z cukrzycą, to pamiętajmy o tym, że w zdecydowanej większości przypadków jest to zjawisko wtórne do hiperglikemii – normalizacja glikemii prowadzi do obniżenia hipertriglicerydemii. W leczeniu hipertriglicerydemii ważne jest także zmniejszenie nadwagi, ograniczenie spożycia alkoholu, zmniejszenie spożycia mono- i dwusacharydów (redukcja spożycia fruktozy), ograniczenie spożycia tłuszczów nasyconych, włączenie do diety tłuszczów jednonienasyconych, redukcja spożycia węglowodanów [1]. Dlatego niezmiernie rzadko powinniśmy u chorych na cukrzycę sięgać po celowaną na triglicerydy farmakoterapię (fibrat) w monoterapii. U wszystkich chorych na cukrzycę i obciążonych podwyższonym ryzykiem sercowo-naczyniowym istnieją wskazania do leczenia statynami; dopiero wówczas sięgamy po terapię skojarzoną z fibratem, gdy nie osiągamy zakładanych celów lipemicznych w monoterapii statyną [1]. Zgodnie z zaleceniami PTD u chorych na cukrzycę ze współistniejącą hipertriglicerydemią większą lub równą 2 mmol/l (≥ 177 mg/dl), utrzymującą się po osiągnięciu docelowego stężenia cholesterolu frakcji LDL za pomocą statyn, należy rozważyć zwiększenie dawki statyn, aby obniżyć stężenie cholesterolu nie-HDL, który stanowi wtórny cel leczenia. W uzasadnionych przypadkach należy rozważyć leczenie skojarzone z fibratem lub pochodnymi kwasu nikotynowego [1].

dr hab. n. med. Tomasz Klupa, prof. UJ

Pracownia Zaawansowanych Technologii Diabetologicznych Katedry Chorób Metabolicznych
Collegium Medicum Uniwersytetu Jagiellońskiego w Krakowie

Piśmiennictwo

1. Zalecenia kliniczne dotyczące postępowania u chorych na cukrzycę 2013. Stanowisko Polskiego Towarzystwa Diabetologicznego. *Diabetol. Klin.* 2013; 2 (supl. A): A3–A52.
2. Miller M.E., Williamson J.D., Gerstein H.C. i wsp.; for the ACCORD Investigators. Effects of randomization to intensive glucose control on adverse events, cardiovascular disease and mortality in older versus younger adults in the ACCORD trial. *Diabetes Care* 2013 Oct 29 [złożone do druku].
3. Kung J., Henry R.R. Thiazolidinedione safety. *Expert Opin. Drug Saf.* 2012; 11: 565–579.
4. Scirica B.M., Bhatt D.L., Braunwald E. i wsp.; SAVOR-TIMI 53 Steering Committee and Investigators. Saxagliptin and cardiovascular outcomes in patients with type 2 diabetes mellitus. *N. Engl. J. Med.* 2013; 369: 1317–1326.
5. Bell D.S., Patil H.R., O'Keefe J.H. Divergent effects of various diabetes drugs on cardiovascular prognosis. *Rev. Cardiovasc. Med.* 2013; 14: e107–e122.
6. White W.B., Cannon C.P., Heller S.R. i wsp.; EXAMINE Investigators. Alogliptin after acute coronary syndrome in patients with type 2 diabetes. *N. Engl. J. Med.* 2013; 369: 1327–1335.