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Comparison of the overall mortality among people with the primary diagnosis of stroke in patients with and without diabetes in Poland.

Porównanie ogólnej śmiertelności wśród osób z pierwotnym rozpoznaniem udaru mózgu u pacjentów z cukrzycą i bez cukrzycy w Polsce.

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Abstract

Key words: *overall mortality, stroke, diabetes mellitus*

Introduction and objective: The aim of the study was to calculate, on the basis of the database of the National Health Fund and the Central Register of Insured People, the mortality rate of the general population of Poland in 2012 among patients with primary diagnosis of stroke

Material and methods: In 2012, a total of 54,335 people, including 24,106 males and 30,227 females, died of various causes with primary diagnosis of stroke. The overall death rate of females in Poland in 2012 was 129.24 / 100,000 of the general population, and of males to 152.03 / 100,000 of the general population. One-third (33.3%) of patients who died in 2012 with a diagnosis of stroke were also diagnosed with diabetes.

Results: The overall death rate for males with no known diabetes was 92.62 / 100,000 with no known diabetes and for females 104.58 / 100,000 with no known diabetes. In contrast, the overall mortality of males with diabetes was 729.56 / 100,000 with known diabetes and 858.00 / 100,000 of female patients with known diabetes

Conclusions: Among people with known diabetes up to and including 64 years of age, the overall mortality was 14 times higher than the overall mortality in this age group, but in people without diabetes. On the other hand, the overall mortality of people with a stroke in the age group over 65 inclusive was 1.5 times higher compared to the overall mortality of people without diabetes in the same age group

Streszczenie

Słowa kluczowe: *umieralność ogólna, udar mózgowy, cukrzyca*

Wprowadzenie i cel: Celem pracy było obliczenie na podstawie bazy danych Narodowego Funduszu Zdrowia i Centralnego Wykazu Ubezpieczonych umieralności ogólnej populacji Polski w 2012 roku wśród pacjentów z pierwszoplanowym rozpoznaniem udaru mózgowego.

Materiał i metody: W 2012 roku zmarło z różnych przyczyn z rozpoznaniem pierwszoplanowym udaru mózgu łącznie 54,335 osób w tym 24,106 osób płci męskiej i 30,227 płci żeńskiej. Umieralność ogólna osób płci żeńskiej w Polsce w 2012 roku wynosiła 129.24/100,000 osób populacji ogólnej a osób płci męskiej 152.03/100,000 populacji ogólnej. Jedna trzecia (33,3%) chorych, którzy zmarli w 2012 roku z rozpoznanym udarem mózgowym, miała również rozpoznaną cukrzycę.

Wyniki: Umieralność ogólna osób płci męskiej bez znanej cukrzycy, wynosiła 92.62/100,000 osób bez znanej cukrzycy, a osób płci żeńskiej 104.58/100,000 osób bez znanej cukrzycy. Natomiast umieralność ogólna osób płci męskiej z cukrzycą wynosiła 729.56/100,000 ze znaną cukrzycą, a osób płci żeńskiej 858.00/100,000 osób ze znaną cukrzycą.

Wnioski: Wśród osób ze znaną cukrzycą w wieku do 64 roku życia włącznie, umieralność ogólna była 14-krotnie wyższa od umieralności ogólnej osób w tym przedziale wiekowym, ale u osób bez cukrzycy. Natomiast umieralność ogólna osób z przebytym udarem mózgowym w przedziale wiekowym powyżej 65 roku życia włącznie była 1,5 razy wyższa w porównaniu do umieralności ogólnej osób bez cukrzycy w tym samym przedziale wiekowym

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Introduction

Stroke occurs mainly in people over the age of 40. This is one of the most common problems of modern medicine and a cause of disability after the age of 40. This is the second cause of death in the world after ischemic heart disease [1]. In 2010, death rate due to stroke was 11.9% worldwide and the number of deaths amounted to 6.7 million [2]. Predicted number of deaths from stroke in 2030 is estimated at 7.8 million [3]. An increase in the number of cardiovascular complications is a known fact associated with type 2 diabetes [4,5]. Type 2 diabetes doubles the risk of dying from stroke [6,7]. According to the data gathered by the World Health Organization (WHO), in medium-high- and high-income countries the death rates from stroke amount to 126/100,000 and 95/100,000 inhabitants per year, respectively [8]. The 2015 and 2016 Demographic Yearbook data of the Main Statistical Office (GUS) shows that the number of deaths per 100,000 inhabitants due to cerebral vascular diseases in Poland amounted to 108/100,000 inhabitants in 2010, and to 81/100,000 inhabitants in 2014 [9,10].

To date, there have been no comparative studies of general mortality in Poland following a primary diagnosis of stroke in people with diabetes and without known diabetes. In most cases, stroke is a consequence of atherosclerosis, the main factors of which include diabetes, hypertension, lipid disorders, and smoking.

Material and methods

The scope of health care is defined in the Polish Constitution of 1997 [11]. This basic act states that "everyone shall have the right to have his health protected" (Article 68.1) [11]. In our part, the Constitution clarifies that "equal access to health care services, financed from public funds, shall be ensured by public authorities to citizens, irrespective of their material situation" (Article 68.2) [11]. The legal dimension emphasizes that the right to health protection includes not only the right of (equal for all) access to medical care. At the same time, the Constitution imposes on the government prevention of situations when human health may be exposed to damage resulting from, inter alia, civilization diseases (diabetes is a civilization disease [12]). This is particularly important in relation to prevention against diabetes. This matter is further specified in the provisions of statutory rank. It is necessary to notice, that health care in Poland is financed by the National Health Fund (NFZ) under the Act [13] and regulations of the Minister of Health [14,15]. The provision of services is carried out through primary care, outpatient specialist care and hospital care. The organization of services is specified by the orders of the President of the NFZ [16,17]. Data of the NFZ and the Central Register of the Insured (CWU) containing patient's date of death were used to conduct epidemiological analysis. All patients with a primary diagnosis of stroke were identified in the NFZ database. The following codes of the International Classification of Diseases and Health Problems, 10th Revision (ICD-10), were used to make the selection:

- I61.0 - Intracerebral hemorrhage in hemisphere, subcortical;
- I61.1 - Intracerebral hemorrhage in hemisphere, cortical;
- I61.2 - Intracerebral in hemisphere, unspecified;
- I61.3 - Intracerebral hemorrhage in brain stem;
- I61.4 - Intracerebral hemorrhage in cerebellum;
- I61.5 - Intracerebral hemorrhage, intraventricular;
- I61.6 - Intracerebral hemorrhage, multiple localized;
- I61.8 - Other intracerebral hemorrhage;
- I61.9 - Intracerebral hemorrhage, unspecified;
- I63.0 - Cerebral infarction due to thrombosis of precerebral arteries;
- I63.1 - Cerebral infarction due to embolism of precerebral arteries;
- I63.2 - Cerebral infarction due to unspecified occlusion of stenosis of precerebral arteries;
- I63.3 - Cerebral infarction due to unspecified occlusion or stenosis of cerebral arteries;
- I63.4 - Cerebral infarction due to cerebral venous thrombosis, nonpyogenic;
- I63.5 - Other cerebral infarction;
- I63.6 - Cerebral infarction, unspecified.

A unique identifier, the Universal Electronic System for Registration of the Population (PESEL), was used to identify patients in the databases [18].

The study covered the period from 01.01.2012 to 31.12.2012. Using PESEL, we were able to identify in the CWU people who died with a primary diagnoses I61, I62, I63 or I64 as reported to the NFZ.

This combined data allowed for determination of overall mortality (from all causes) in this group of patients. In the next stage of analysis (of the same period of time), the data regarding diabetes-related services were identified in NFZ resources, where the primary diagnosis was "diabetes" with the following code extensions: E10. X – insulin-dependent diabetes, E11. X – non-insulin-dependent diabetes, E12. X – malnutrition-related diabetes, E13. X – other unspecified forms of diabetes, E14. X – undetermined diabetes, or at the same time patient filled a prescription for any drug of the groups: A10A. X (insulin), A10B. X (oral antidiabetic agents), or specialist diagnostic tests. The data was analyzed using the PQStat v. 1.6 statistical program by PQStat Software Co. Student's t test was used for comparison of independent groups. The differences were considered relevant at the 95% confidence level ($P<0.05$).

Study results

The overall mortality rates for people with a primary diagnosis of stroke (hemorrhage or cerebral infarction) were compared to the general population and, separately, to the subpopulation of people with known diabetes and subpopulation without known diabetes.

The statistics of the general population/subpopulation of people with known diabetes and without known diabetes used for analysis are as follows:

1. According to the GUS data, the total population of Poland in 2012 was 38,533,789 people, including 18,651,441 males and 19,882,348 females [19].
2. A total of 2,227,453 people with known diabetes, including 975,364 males and 1,252,089 females, were identified in the Polish population analyzed between January 1 and December 31, 2012.
3. The overall population of people without known diabetes in Poland in 2012 amounted to 36,305,336 people, including 17,676,077 males and 18,630,259 females [19,20].

Table I compiles patients with a primary diagnosis of stroke who died between 01.01.2012 and 31.12.2012, depending on gender and the diagnosis of diabetes.

	Males	Females	Total
Patients with known diabetes	7735	10743	18478
Patients without known diabetes	16371	19484	35855
Total	24106	30227	54335

Table I *A compilation of the number of deaths with primary diagnosis of stroke, among patients who died between 01.01.2012 and 31.12.2012 from various causes divided according to sex and diagnosis of diabetes.*

About 1/3 of patients who died with a primary diagnosis of stroke in Poland were also diagnosed with diabetes.

Table II presents the mean ages of stroke patients who died between 01.01.2012 and 31.12.2012 depending on sex and presence of diabetes as per the NFZ database.

	Mean age in males (± SD) in years	Mean age in females (± SD) in years
Patients with diabetes	72.45 ± 12.00	79.67 ± 10.57
Patients without known diabetes	74.44 ± 10.92	80.03 ± 8.51

Table II *Mean age (with standard deviations) of patients with primary diagnosis of stroke, who died between 01.01.2012 and 31.12.2012 depending on gender and presence of diabetes.*

In both subpopulations, i.e. people with known diabetes and without diabetes, females were significantly older (P<0.001) compared to males. Males with known diabetes were significantly younger than males without known diabetes (P<0.001). Females with known diabetes were significantly younger compared to females without diabetes (P=0.0013).

Table III presents the overall mortality rates between 01.01.2012 and 31.12.2012 in Poland in patients from general population, who had a diagnosis of stroke, depending on sex as per NFZ and CWU databases per 100,000 inhabitants.

Males	129.21/100 000
Females	152.03/100 000
Total, both sexes	144.00/100 000

Table III *Overall mortality of patients with a leading diagnosis of stroke in 2012 in the general population in Poland per 100,000 general population depending on sex.*

Overall mortality in females was significantly higher compared to the overall male mortality rate (P<0.001).

Table IV presents the overall mortality rates in 2012 in people with primary diagnosis of stroke in Poland depending on sex in the subpopulation of patients without diabetes per 100,000 people without diabetes.

Males	92.62/100,000
Females	104.58/100,000
Total, both sexes	98.76/100,000

Table IV *Overall mortality of patients with a primary diagnosis of stroke in 2012, in Poland, in a subpopulation of patients with known diabetes per 100,000 people without known diabetes, depending on sex.*

Overall mortality in non-diabetic females was higher compared to males without diabetes (P<0.001).

Table V compares the overall mortality rates among patients with a primary diagnosis of stroke in a subpopulation of people with known diabetes per 100,000 people, depending on sex.

Males	729.56/100,000
Females	858.00/100,000
Total, both sexes	829.56/100,000

Table V *Overall mortality among patients with primary diagnosis of stroke in 2012, in Poland, in a subpopulation of patients with known diabetes per 100,000 people with known diabetes, depending on sex.*

Overall mortality among females with diabetes and history of stroke was significantly higher compared to males with diabetes and history of stroke (P<0.001). Overall mortality among females with diabetes and history stroke was significantly higher than the overall mortality in a female subpopulation without diabetes (P<0.001). Overall mortality of males with known diabetes and history of stroke was significantly higher than the overall mortality of males without known diabetes (P<0.001). Overall mortality among the subpopulation of patients with diabetes, both male and female, was over 8 times higher than the overall mortality of people without known diabetes.

Table VI shows the proportion of deaths among patients with primary diagnosis of stroke in a subpopulation with and without diabetes depending on sex and age range, i.e. 64 years of age, inclusive, and over 65 years, inclusive, in Poland, in 2012.

	People with diabetes		People without known diabetes	
Age range	**Male**	**Female**	**Male**	**Female**
Up to and including 64 years	18.63	7.16	27.23	10.08
Age of 65 years or more	84.87	92.84	72.77	89.92

Table VI *Proportion of deaths among patients with primary diagnosis of stroke depending on sex, age range, and the diagnosis of diabetes in Poland, in 2012.*

In both subpopulations, i.e. with and without diabetes, the death rate was higher in the age group over 65 years.

Table VII shows the overall mortality rate for people without diabetes vs. those with known diabetes, who died from various causes, with a primary diagnosis of stroke, depending on age range (up to 64 years and over 65 years) per 100,000 population.

	People without known diabetes	People with known diabetes
Up to and including 64 years	19.89	295.64
Over 65 years	734.49	1098.87

Table VII *Overall mortality of a subpopulation of patients without known diabetes and with known diabetes and a primary diagnosis of stroke, depending on the age range per 100,000 each subpopulation.*

The overall mortality rate in patients of both sexes with diabetes per 100,000 people in diabetic subpopulation below 64 years of age was significantly higher compared to the overall mortality rate in people of both sexes without diabetes below 64 years of age per 100,000 people in diabetic subpopulation (P<0.001). These rates were 14 times higher in the group of people with a diagnosis of diabetes. The overall mortality rates in people of both sexes with known diabetes per 100,000 people with known diabetes mellitus aged over 65 were significantly higher compared to the overall mortality rate of the non-diabetic subpopulation over the age of 65 (P<0.001). The overall mortality rate in the subpopulation of patients with known diabetes over the age of 65 was 1.5 times higher than the mortality rate in people without diabetes in the same age range.

Discussion

Average survival of diabetics aged 55-64 years was 8 years shorter and 4 years shorter in individuals aged 65-74 compared to non-diabetics [21, 22]. People with diabetes are 2.14 times more likely to die than those without diabetes [23]. Tuomilehto et al. believe that stroke is on average 1.5-3 times more likely to be the cause of death in people with diabetes compared to those without the disease [24]. Many authors believe that diabetes is one of the most significant risk factors for ischemic stroke in both women and men, women being at a greater risk. In our study we demonstrated indexes of overall mortality due to cerebral stroke or other extracerebral causes. A patient with diabetes manifests also with many other disorders, such as hypertension, heart disease, lung disease. About half of patients with stroke die from comorbid disorders [25].

More than one third of patients after cerebral stroke are diagnosed with diabetes and elevated blood glucose in the initial phase of stroke is observed in 2/3 of patients [26,27]. Among those who died in Poland in 2012 with the primary diagnosis of stroke, more than one third of patients had a diagnosis of diabetes. In diabetics, atherosclerosis appears more frequently, involves both large and small arteries, lesions are more advanced and it corresponds to vascular changes seen in people 10 years older without diabetes [28]. Our observations show that the average age of patients with diabetes mellitus and primary diagnosis of stroke was significantly lower than the average age of patients without diabetes and stroke, both in male and female populations. and stroke, both in male and female populations. According to the data by the World Health Organization (WHO), most deaths take place in countries with moderately high or high incomes. In middle-income countries, the mortality rate was 126.0/100,000 general population in 2010, and in high-income countries, mortality due to stroke amounted to 95.0/100,000 general population [8]. In Poland, the stroke death was 93.3/100,000 inhabitants in 2010 [2]. During the

same period, mortality from stroke in Italy amounted to 40.4/100,000 general population. In the Netherlands it was 32.5/100,000 general population, in the UK 38.3/100,000, in Germany 32.6/100,000, in the Czech Republic 81.8/100,000, in Romania 159.0/100,000, and in Hungary 88.0/100,000 general population [2]. Our studies do not assess the mortality rate of stroke alone, but overall mortality, i.e. from all other causes. Overall mortality for both sexes in Poland in 2012 amounted to 141.0/100,000 general population. Overall mortality among females was 152.0/100,000 general population and was significantly higher than the overall mortality rate among males, which amounted to 129.24/100,000 male population ($P<0.001$). It should be taken into account that about 1/2 of all deaths were from extracerebral causes [25]. Overall mortality in people with diabetes and stroke was 8 times higher in both sexes compared to overall mortality in individuals without diabetes. Thus, in non-diabetics, the average overall mortality rate was 98.76/100,000 population without diabetes and the average overall mortality among people with known diabetes was 829.56/100,000 people with diabetes.

Vascular microangiopathy, which affects small arteries and capillaries, is a specific complication of diabetes mellitus [29]. In patients with diabetes and associated severe coagulation disorders [21] as well as vasculopathy, we also observe changes resulting from microangiopathy, which can present as lacunar stroke or subcortical atherosclerotic encephalopathy [30]. Lacunar focal lesions are more common in diabetics than in people without diabetes. It was observed that the risk of stroke increases 3-fold in people with symptoms of diabetes and kidney disease, which is related to the development of microangiopathy in cerebral vessels as well as advanced atherosclerosis of the large vessels [31].

The risk of death from cerebral vascular disease in people with diabetes is high, especially at a young age. In a population under 55, it is more than 10 times higher in people with diabetes compared to people without the disease [28,32]. In our studies, the overall mortality in people below and including the age of 64, with diabetes and stroke amounted to 295.64/100,000 patients, while the total mortality in people of the same age group, after stroke, but without diabetes was 14 times lower and amounted to 19.89/100,000 patients. However, overall mortality among patients with diabetes and history of stroke above the age of 65 was 1098.87/100,000 and was 1.5 times higher than mortality in patients without known diabetes aged above 65 years, which amounted to 743.49/100,000 patients. Factors, such as increased blood viscosity, decreased erythrocyte elasticity, propensity of red blood cells to formation of microangiopathy, coagulation disorders and fibrinolysis may also affect the increased overall mortality in people with history of stroke and diabetes. Some authors suggest that type 2 diabetes is sometimes considered an equivalent of cerebral stroke risk [35,36]. High overall mortality in the subpopulation of patients with known diabetes and cerebral stroke among young age groups compared to the overall mortality in the subpopulation of people without diabetes and history of stroke can explain the higher incidence of stroke in diabetic individuals. In the group of young adults with diabetes, the incidence of stroke may be 10 times higher compared to the incidence among the elderly without diabetes [37]. Other authors reported that young, white men with diabetes are 20 times more likely to have stroke than those of a similar age group, but without diabetes. They also found that the incidence of stroke in young African women with diabetes was 3 times lower compared to the incidence of stroke of African women without known diabetes [38]. Diabetes, as a risk factor for stroke, affects both the course of the acute phase, treatment, complications and distant sequelae of the disease observed in those patients. Diabetes is usually complicated by other diseases involving the heart, lower limbs, kidneys and eyes, which develop as a consequence of macroangiopathy, as well as nephropathy, retinopathy and neuropathy. Our research was based on reliable data from the National Health Fund and involved the entire population of Poland in 2012. These studies had some limitations, which are presented below. Our studies were retrospective, and the data did not allow accurate determination of precise location and the extent of stroke. It was not possible to assess the type of diabetes and the extent of metabolic control, or whether there were other vascular complications of diabetes, if there was coexistent hypertension, hyperlipidemia, or obesity. Despite these limitations, the results indicate the need to reduce the overall mortality among people with stroke, particularly in diabetics, as their mortality rates are several times higher than those of people without diabetes. High mortality rate in the general population indicates the need for control of sugar metabolism, prevention of complications, treatment of hypertension and lipid disorders, but also for antiplatelet and anticoagulant therapy. Precise determination of the mechanisms of stroke in diabetic patients remains difficult. In diabetics, ischemic stroke is common and often affects small vessels. Moreover, type 2 diabetes doubles the risk of the second stroke [6,7,39]. Stroke in diabetic patients poses a huge challenge; it is one of the main causes of disability in the modern world. Stroke is not only a serious medical complication, but also a social and economic challenge. Decrease in mortality due to stroke has been noted in many Western European countries as a result of implementation of preventive measures. In Poland, overall mortality among people without diabetes, with diabetes, and with chronic stroke disease is higher than in the Western European countries.

Conclusions

The following conclusions are based on the analysis of complete data NFZ and CRU databases:

1. Among deaths from all causes with a primary diagnosis of stroke, diabetes was confirmed in more than 1/3 of patients.
2. Mean age of patients with diabetes mellitus was lower than mean age of patients without diabetes, who died of all causes with a leading diagnosis of stroke.
3. Overall mortality rate in people with diabetes and stroke was 8 times higher than the mortality rate in people without diabetes and history of stroke.
4. Overall mortality in people with diabetes and stroke in the age group 64 or less was 14 times higher compared to the mortality rate in people in a similar age group without diabetes and with history of stroke.
5. Overall mortality among people with diabetes and stroke aged 65 more was 1.5 times higher than in people without diabetes and with stroke in a similar age range.

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