

Ischaemic stroke in women and men – in-hospital prognosis

Udar niedokrwienny mózgu u kobiet i mężczyzn – rokowanie wewnątrzszpitalne

Justyna Tracz¹, Iwona Gorczyca-Głowacka^{2,3}, Marcin Wetnicki⁴, Ewa Kołodziejska⁵, Anita Rosołowska¹, Artur Mamcarz⁴, Beata Wożakowska-Kapłon^{2,3}

¹Clinic of Neurology, Swietokrzyskie Neurology Centre, Kielce, Poland
Head of the Clinic: Anita Rosołowska MD, PhD

²1st Clinic of Cardiology and Electrotherapy, Swietokrzyskie Cardiology Centre, Kielce, Poland
Head of the Clinic: Prof. Beata Wożakowska-Kapłon MD, PhD

³Collegium Medicum, University of Jan Kochanowski, Kielce, Poland
Head of the Collegium: Prof. Marianna Janion MD, PhD

⁴3rd Department of Internal Diseases and Cardiology, Warsaw Medical University, Warsaw, Poland
Head of the Department: Prof. Artur Mamcarz MD, PhD

⁵Department of Internal Diseases and Diabetology, Hospital St. Alexander, Kielce, Poland
Head of the Department: Adam Dmoch MD, PhD

Medical Studies/Studia Medyczne 2022; 38 (1): 22–30

DOI: <https://doi.org/10.5114/ms.2022.115144>

Key words: comorbidities, hospitalization, ischaemic stroke, sex differences.

Słowa kluczowe: choroby współistniejące, hospitalizacja, udar niedokrwienny, różnice płciowe.

Abstract

Introduction: Stroke is one of the most common causes of death and the leading cause of disability in the adult population worldwide. The risk of stroke increases with age in both men and women, but women have a higher rate of mortality and disability following stroke.

Aim of the research: To compare the in-hospital mortality in men and women with ischaemic stroke and to identify factors that predispose to death.

Material and methods: This retrospective, single-centre study included patients with acute ischaemic stroke hospitalized in the reference neurological centre in 2013–2014. The study population consisted of 2000 patients, of whom 50.5% were men. Data on age, sex, comorbidities, results of additional tests, and the course of hospitalization were analysed.

Results: In-hospital mortality was 15.9% and was higher in women than men (17.9% vs. 14%, $p = 0.02$). Women were older than men (77.3 vs. 69.5 years, $p < 0.001$). In women, age ≥ 75 years (OR = 2.507), chronic obstructive pulmonary disease (COPD) (OR = 2.231), and haemorrhagic transformation of the stroke site (OR = 4.77) increased the risk of in-hospital mortality. In men, a history of myocardial infarction (OR = 2.295) and a glomerular filtration rate (GFR) < 60 ml/min/1.73 m² (OR = 1.774) increased the risk of in-hospital death.

Conclusions: Better knowledge of the predictors that increase the risk of an adverse stroke may open more avenues for preventive intervention and reduce serious post-stroke complications. Further observations on potential gender differences in risk factors for adverse prognosis in acute stroke are needed to reduce in-hospital deaths.

Streszczenie

Wprowadzenie: Udar mózgu jest jedną z najczęstszych przyczyn zgonów i główną przyczyną niepełnosprawności dorosłej populacji na świecie. Ryzyko udaru wzrasta wraz z wiekiem zarówno u mężczyzn, jak i u kobiet, ale kobiety mają wyższy wskaźnik śmiertelności i niepełnosprawności po udarze.

Cel pracy: Porównanie śmiertelności wewnątrzszpitalnej u kobiet i mężczyzn z udarem niedokrwiennym mózgu oraz identyfikacja czynników predysponujących do zgonu.

Materiał i metody: Retrospektywnym, jednośrodkowym badaniem objęto pacjentów z udarem niedokrwiennym mózgu hospitalizowanych w referencyjnym ośrodku neurologicznym w latach 2013–2014. Badana populacja liczyła 2000 pacjentów, z czego 50,5% stanowili mężczyźni. Przeanalizowano dane dotyczące wieku, płci, chorób współistniejących, wyników badań dodatkowych oraz przebiegu hospitalizacji.

Wyniki: Śmiertelność wewnątrzszpitalna wyniosła 15,9% i była wyższa u kobiet niż mężczyzn (17,9% vs 14%, $p = 0,02$). Kobiety były starsze od mężczyzn (77,3 vs 69,5 roku, $p < 0,001$). U kobiet wiek ≥ 75 lat (OR = 2,507), przewlekła obturacyjna choroba płuc (POCHP) (OR = 2,231) oraz krwotoczna transformacja ogniska udarowego (OR = 4,77) zwiększały ryzyko śmiertelności wewnątrzszpitalnej. U mężczyzn przebyty zawał mięśnia sercowego (OR = 2,295) i współczynnik przesączania kłębuszkowego (GFR) < 60 ml/min/1,73 m² (OR = 1,774) zwiększały ryzyko zgonu wewnątrzszpitalnego.

Wnioski: Lepsza wiedza na temat występowania czynników prognostycznych, które zwiększają ryzyko niepomyślnego przebiegu udaru mózgu, może otworzyć więcej możliwości interwencji zapobiegawczej i zmniejszyć poważne powikłania poudarowe. Potrzebne są dalsze obserwacje dotyczące potencjalnych różnic między płciami w czynnikach ryzyka niekorzystnego rokowania w ostrym udarze mózgu, aby zmniejszyć liczbę zgonów wewnątrzszpitalnych.

Introduction

Stroke is one of the most common causes of death in the adult population worldwide and the leading cause of disability in people aged over 45 years. It is estimated that approximately 5.5 million people die from stroke each year (accounting for ~10% of total deaths), and approximately half of the patients remain disabled [1–4]. The lifetime risk for stroke over the age of 25 years is approximately 25% among both men and women, with an 18% risk of ischaemic stroke. Increased incidence is observed in low and middle socio-demographic index countries [4]. The incidence of stroke in Poland is 175/100,000 in men and 125/100,000 in women. In the general population, men are affected more often than women [2, 3]. The risk of stroke increases with age in both men and women; however, in the elderly, a higher incidence of stroke is observed in women [2, 5, 6]. Sex also affects the clinical course of stroke and long-term prognosis, and higher percentages of mortality and disability are observed in women [1, 2, 5]. This phenomenon may be caused by the longer life span of women and more frequent incidence of stroke in old age, as well as by comorbidities predisposing to stroke, such as arterial hypertension, heart failure, atrial fibrillation (AF), and diabetes [2, 7].

Aim of research

The risk of stroke increases with age in both men and women, but women have a higher rate of mortality and disability following stroke. However, little is known about sex differences in stroke care and outcomes. The aim of the study was to compare the in-hospital mortality in men and women with ischaemic stroke and to identify factors that predispose to death.

Material and methods

Study group

This retrospective study included patients with ischaemic stroke who were subsequently hospitalized in the reference neurological centre in 2013–2014. Ischaemic stroke was diagnosed based on the clinical picture and head imaging (computed tomography or magnetic resonance imaging of the head).

The protocol of study was consistent with the Declaration of Helsinki and was approved by the Ethics Committee of Świętokrzyska Medical Chamber. All patients consented to participate in the study.

Analysed data

Data on age, sex, comorbidities, results of additional tests, and the course of hospitalization were analysed.

The extent of the stroke was assessed using computed tomography or magnetic resonance imaging. Head imaging examinations were performed on admission to the hospital and again during hospitalization.

The patency of the intracerebral arteries was assessed with a Doppler ultrasound.

All patients underwent a resting 12-lead electrocardiographic examination on admission to the hospital and on discharge from the hospital. In some patients, 24-hour electrocardiography (ECG Holter) monitoring was performed. The patients were monitored 24/7 by electrocardiography during the first day after admission to the hospital.

The neurological status of patients was assessed using the National Institutes of Health Stroke Scale (NIHSS) immediately upon admission to the hospital. The neurological deterioration was defined as an increase of ≥ 5 points.

AF was diagnosed based on the definition of the European Society of Cardiology, according to which arrhythmia can be diagnosed based on an electrocardiogram showing irregular atrial rhythm lasting longer than 30 s.

Heart failure was diagnosed according to signs and symptoms of low cardiac output based on medical charts.

Diabetes mellitus was defined as a fasting blood glucose level greater than 126 mg/dl after a minimum of 2 tests or a glucose level greater than 200 mg/dl at any time during the day.

Hypertension was diagnosed when the blood pressure (BP) was $\geq 140/90$ mm Hg in repeated tests.

Coronary heart disease was determined by a previous history of myocardial infarction and angina pectoris based on medical charts.

Study endpoint

The endpoint of the study was death during hospitalization.

Statistical analysis

The results were analysed with Statistica 13.0 software (StatSoft Inc.). The distribution of quantitative variables was assessed using the Shapiro-Wilk test. In terms of descriptive statistics, mean values, medi-

ans, minimum and maximum values, and standard deviations were presented for quantitative variables. For qualitative variables, the numbers and frequency of occurrence or modes were given, with their number and percentage share, depending on the type of data. Quantitative variables with a distribution similar to normal were compared with Student's *t*-test for unrelated variables. The correlations between these variables were tested using the Pearson correlation coefficient. Quantitative unrelated variables with a non-normal distribution were compared with the Mann-Whitney *U* test, and the correlations between these variables were tested using the Spearman correlation coefficient. The statistical significance of the differences between qualitative variables was assessed using the χ^2 test. Appropriate logistic regression models were constructed for the conditional estimation of selected random variables. For statistically significant results from the univariate and multivariate regressions, the odds ratio (OR) is presented, together with a $\pm 95\%$ confidence interval (CI) and the *p*-value. Results were considered statistically significant if $p < 0.05$.

Results

Characteristics of the study group

The study group of 2000 patients included 1010 (50.5%) men. The mean age was 73.4 years. The most common comorbidity in the study group was hypertension, which was found in 1538 (76.9%) patients. AF occurred in 579 (29%) patients, diabetes mellitus in 520 (26%) patients, and ischaemic heart disease in 466 (23.3%) patients. Haemorrhagic complications of the stroke site were reported in 120 (6%) patients. The functional status of patients was assessed using the NIHSS scale in 1933 patients (971 men and 961 women). Significant neurological deficit (NIHSS ≥ 5 points) on admission to the hospital was found in 1107 (57.3%) patients, and 375 (18.8%) patients had severe disability (NIHSS ≥ 15 points) (Table 1).

Comparison of the clinical characteristics of women and men

Women were older than men on admission (mean age 77.3 vs. 69.5 years, respectively, $p < 0.001$). Figure 1 presents the proportion of women and men in particular age groups. In women, arterial hypertension, AF, and heart failure were more common than in men (82.2% vs. 71.7%, $p < 0.001$; 36.2% vs. 21.9%, $p < 0.001$; 18.4% vs. 11.6%, $p < 0.001$, respectively). In men, a history of myocardial infarction and chronic obstructive pulmonary disease (COPD) (13.1% vs. 9.9%, $p = 0.044$; 7.1% vs. 3.9%, $p = 0.003$, respectively) was more frequently reported. Men were more likely to abuse alcohol (8.1% vs. 7.2%, $p = 0.476$) and smoke (10.9% vs. 9.7%, $p = 0.421$). NIHSS scores ≥ 5 points were achieved by 537 (48.6%) men and 569 (51.4%)

women ($p = 0.340$) (Table 1). In total, 170 (45.3%) men and 205 (54.7%) women had an NIHSS score ≥ 15 points, including 49 (15.5%) women and 98 (16.1%) men aged < 75 years, and 156 (24.2%) women and 72 (19.9%) men aged ≥ 74 years.

Study endpoint

During hospitalization, 318 (15.9%) patients – 141 (14%) men and 177 (17.9%) women – died ($p = 0.02$). Figure 2 shows the proportion of deaths in women and men in particular age groups.

Analysis of factors predisposing to death in women

The univariate analysis showed that the factors that increased the risk of death in women were as follows: age ≥ 75 years, arterial hypertension, COPD, glomerular filtration rate (GFR) < 60 ml/min/1.73 m², and haemorrhagic transformation of the stroke site. The multivariate analysis showed that the risk of death in women was increased by age ≥ 75 years (OR = 2.507) and COPD (OR = 2.231). The strongest predictor of death in women was haemorrhagic transformation of the stroke site (OR = 4.77). Diabetes was a factor reducing the risk of death in women (OR = 0.613) (Table 2).

Analysis of the factors predisposing to death in men

The univariate analysis showed that the history of percutaneous coronary interventions, myocardial infarction, and GFR < 60 ml/min/1.73 m² were factors increasing the risk of death in men. The multivariate analysis showed that the risk of death in men was increased by a history of myocardial infarction (OR = 2.295) and GFR < 60 ml/min/1.73 m² (OR = 1.774). Hypertension was a factor reducing the risk of death in men (OR = 0.498) (Table 3).

Discussion

In this study on patients with ischaemic stroke, the percentages of women and men were similar, but the women were older on admission compared to the men. These results are consistent with reports by other authors, as well as with the phenomenon observed in the general population for years, indicating a longer life span for women [8–10]. The in-hospital mortality in this study was relatively high and was close to 16%. Data from other studies show diverse results, and in-hospital mortality in patients with ischaemic stroke is reported as 3.3–18% [7, 8, 11–14]. Considerable discrepancies in the results arise from different treatment methods for acute stroke and different clinical characteristics of the hospitalized patients.

Syta-Krzyżanowska *et al.* [15] showed that in a group of 971 patients hospitalized due to ischaemic stroke between 2002 and 2006, the in-hospital mor-

Table 1. Clinical characteristics of the study group

Clinical characteristics	Total N = 2000	Men N = 1010	Women N = 990	P-value
Age [years]	73.36	69.5	77.3	< 0.001
Clinical characteristic, n (%):				
Hypertension	1538 (76.9)	724 (71.7)	814 (82.2)	< 0.001
Heart failure	299 (15.0)	117 (11.6)	182 (18.4)	< 0.001
Diabetes	520 (26.0)	246 (24.4)	274 (27.7)	0.101
A history of thromboembolic complications	325 (16.3)	160 (15.8)	165 (16.7)	0.653
A history of stroke	356 (17.8)	176 (17.4)	180 (18.2)	0.701
A history of TIA	49 (2.5)	27 (2.7)	22 (2.2)	0.612
Atrial fibrillation	579 (28.9)	221 (21.9)	358 (36.2)	< 0.001
Stable coronary artery disease	466 (23.3)	139 (13.8)	102 (10.3)	0.017
A history of MI	230 (11.5)	131 (13.0)	99 (10)	0.037
A history of PCI	88 (4.4)	57 (5.7)	31 (3.1)	0.006
A history of CABG	30 (1.5)	25 (2.5)	5 (0.5)	< 0.001
Atherosclerosis of the arteries of the lower extremities	91 (4.6)	52 (5.1)	39 (3.9)	0.236
Chronic pulmonary disease	111 (5.6)	72 (7.1)	39 (3.9)	0.003
Hyperthyroidism	46 (2.3)	16 (1.6)	30 (3.0)	0.045
Hypothyroidism	81 (4.0)	19 (1.9)	62 (6.3)	< 0.001
Smoking	206 (10.3)	110 (10.9)	96 (9.7)	0.421
Alcoholism	153 (7.7)	82 (8.1)	71 (7.2)	0.476
Laboratory tests:				
HGB (mean) [g/dl]	13.8	13.9	13.7	0.014
GFR (mean) [ml/min]	65.5	80.6	50.1	< 0.001
GFR < 60 ml/min, n (%)	870 (43.5)	460 (45.5)	410 (41.4)	0.067
Neurological status, n (%):				
Haemorrhagic transformation of the stroke site	120 (6.0)	63 (6.2)	57 (5.8)	1.000
NIHSS on admission \geq 5 points	1107 (57.3)	537/971 (48.6)	569/961 (51.4)	0.340

TIA – transient ischaemic attack, MI – myocardial infarction, PCI – percutaneous coronary intervention, CABG – coronary artery bypass, HGB – haemoglobin, GFR – glomerular filtration rate, NIHSS – National Institutes of Health Stroke Scale.

tality was 16.4%. The patients were of a similar age to those in this study.

In this study, the mortality rate of women with ischaemic stroke was higher than that of men. Similar results were shown in the study by Reeves *et al.* [7] and in two Taiwanese studies [8, 14]. However, in the Italian, Canadian, and Swedish registers, no differences were found in the in-hospital mortality between women and men [9, 10, 16]. In these registers, women were slightly older than men. In our study, women were significantly older than men, which was important for the in-hospital prognosis. A higher mortality in the

acute phase of ischaemic stroke is associated with the extent of the stroke and the severity of stroke, which has proven to be one of the most important predictors of early death in numerous studies [9, 11–14].

A NIHSS score of \geq 5 points was recorded in a similar percentage of women and men. In the Canadian, Swedish, and Qatari registers, the severity of stroke was similar between women and men [9, 16, 17]. However, with higher NIHSS values (\geq 15 points), the percentage of women increased, which may be related to the older age of the women in this group and their greater disability before the disease occurred.

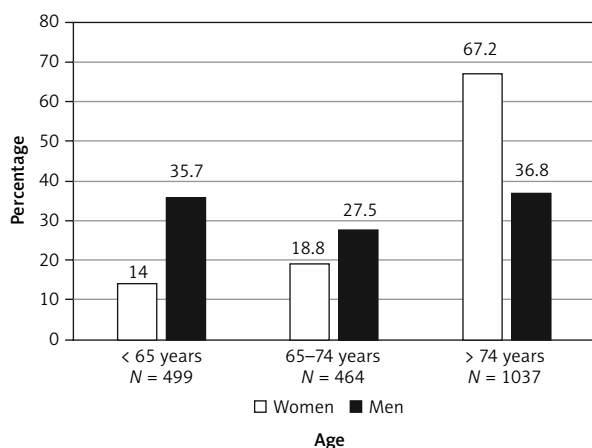


Figure 1. Percentage of women and men in particular age groups

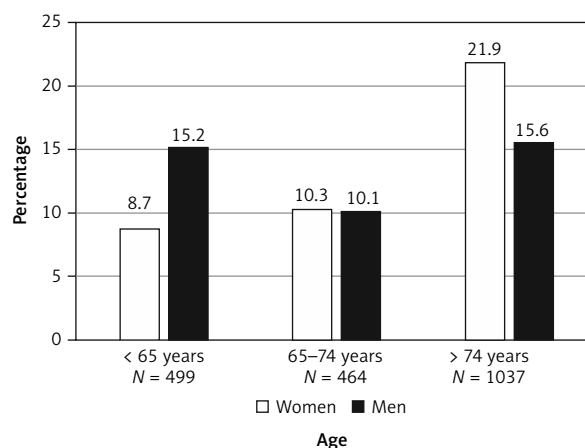


Figure 2. Percentage of death in women and men in particular age groups

Table 2. Univariate and multivariate logistic regression analysis—predictors of in-hospital mortality in women

Factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age \geq 75 years	2.655	1.756–4.013	< 0.001	2.507	1.591–3.950	< 0.001
Hypertension	1.758	1.079–2.864	0.0235	1.641	0.977–2.757	0.0608
Heart failure	0.883	0.574–1.359	0.5726			
Stable coronary artery disease	0.911	1.287–0.817	0.1523			
A history of MI	1.270	0.761–2.119	0.3606			
History of stroke/TIA	0.567	0.863–1.312	0.4899			
Atrial fibrillation	1.256	0.901–1.752	0.1788			
COPD	2.405	1.210–4.779	0.0123	2.231	1.087–4.581	0.0286
Diabetes	0.669	0.453–0.988	0.0432	0.613	0.405–0.927	0.0206
Thyroid diseases	0.885	0.582–1.347	0.5694			
GFR < 60 ml/min	1.534	1.009–2.333	0.0455	1.144	0.702–1.862	0.5879
Haemorrhagic transformation of the stroke site	4.239	2.475–7.260	< 0.001	4.770	2.714–8.385	< 0.001

OR – odds ratio, CI – confidence interval, MI – myocardial infarction, TIA – transient ischaemic attack, COPD – chronic obstructive pulmonary disease, GFR – glomerular filtration rate.

The incidence of stroke significantly increases with age, and advanced age is a factor of poor prognosis in ischaemic stroke [6]. In the present study, age was a factor that increased the risk of death in women. Similar results were presented in the study by Ong *et al.* [8]. Kortazar-Zubizarreta *et al.* [13] showed that age was an independent risk factor for death, but only in men. However, in another Taiwanese study, age increased the risk of death in both sexes [14].

Haemorrhagic transformation of the stroke site occurred with a similar frequency in women and men, but it was a predictor of in-hospital death only in women. This result is comparable with Ong *et al.* [8]. It is possible that the more frequent occurrence of

arterial hypertension in women predisposes them to a worse prognosis after haemorrhagic transformation of the ischaemic site.

Another factor associated with a worse prognosis in women was COPD. Patients with chronic respiratory diseases have a worse prognosis after the occurrence of acute vascular events (heart attack, stroke) [18]. There are reports confirming that respiratory tract infection increases the risk of death in the early stage of ischaemic stroke [13]. In the present study, the effects of infection and of increased parameters of inflammation on the risk of death were not assessed. However, respiratory tract infections occur more frequently in patients with COPD than in the general population.

Table 3. Univariate and multivariate logistic regression analysis—predictors of death in men

Factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Age ≥ 75 years	1.233	0.858–1.772	0.2580			
Hypertension	0.588	0.852–0.405	0.0050	0.498	0.336–0.738	0.0005
Heart failure	1.053	0.609–1.821	0.8540			
Stable coronary artery disease	0.176	0.343–0.668	0.0016			
A history of PCI	1.131	2.127–3.999	0.0192			
A history of CABG	0.123	0.527–2.262	0.3891			
A history of MI	2.395	1.538–3.729	0.0001	2.295	1.424–3.699	0.0006
History of stroke/TIA	0.624	0.980–1.539	0.9291			
History of stroke	1.023	0.642–1.632	0.9223			
History of TIA	1.415	0.527–3.798	0.4913			
Atrial fibrillation	0.958	0.621–1.479	0.8463			
COPD	0.655	0.294–1.459	0.3001			
Diabetes	1.221	0.818–1.823	0.3287			
Thyroid diseases	1.292	0.747–2.234	0.3594			
GFR < 60 ml/min	1.914	1.244–2.945	0.0031	1.774	1.108–2.841	0.0168
Haemorrhagic transformation of the stroke site	1.613	0.834–3.120	0.1555			

OR – odds ratio, CI – confidence interval, PCI – percutaneous coronary intervention, CABG – coronary artery bypass, MI – myocardial infarction, TIA – transient ischaemic attack, COPD – chronic obstructive pulmonary disease, GFR – glomerular filtration rate.

Men suffer from ischaemic heart disease more often [19]. In this study, men had stable coronary artery disease and a history of myocardial infarction and coronary revascularization more frequently than women. A history of myocardial infarction significantly increased the risk of death in men. The presence of vascular disease in multiple beds, in the coronary and cerebral vessels for the men in this study, significantly worsens the prognosis compared to patients with only one vascular bed affected [19].

Another significant predictor of death in men was impaired renal function (GFR < 60 ml/min/1.73 m²). Chronic kidney disease is a recognized risk factor for thromboembolic complications, including ischaemic stroke [20, 21]. In the meta-analysis by Lee *et al.* it was shown that most patients with GFR < 60 ml/min/1.73 m² had a significantly increased risk of cardiovascular diseases, including stroke, and similarly the death rate in this group of patients was higher than in the population of patients with normal GFR [22].

Arterial hypertension is a significant risk factor for cardiovascular diseases, including stroke, in both sexes. A study by Howard *et al.* showed that normalization of blood pressure with pharmacological treatment reduces the risk of stroke, although the risk is still higher than in normotensives without pharmacological treatment [23, 24]. In the present study, in

the univariate analysis in women, hypertension was a predictor of death, but this was not confirmed by the multivariate analysis. However, in men, arterial hypertension was a factor that reduced the risk of death. It may be related to the antihypertensive treatment used. This study is retrospective and no data on the pre-hospital treatment are available. There are reports proving the influence of gender on the response to antihypertensive treatment [25, 26]. On the other hand, the Blood Pressure Lowering Treatment Trialists' Collaboration study showed that antihypertensive treatment was of equal benefit in both sexes [27]. This is inconsistent with the reports of Ong *et al.* and Akhtar *et al.*, in which arterial hypertension was associated with worse outcomes in women with ischaemic stroke [8, 17]. Kortazar-Zubizarreta *et al.* [13] and Syta-Krzyżanowska *et al.* [15] showed no effect of arterial hypertension on the prognosis in the early stage of ischaemic stroke. Although diabetes is one of the factors predisposing to stroke in both sexes, in our study it was not a significant factor of worse prognosis in men. Interestingly, diabetes has been shown to reduce the risk of death during hospitalization in women. Reports in the literature assessing the impact of diabetes mellitus on the prognosis of patients with ischaemic stroke are not consistent. In a study by Heuschmann *et al.* [11], diabetes turned out to be a significant pre-

dicator of death only in men. Ong *et al.* [8] showed that the coexistence of diabetes worsened the prognosis in men and women, but a higher percentage of severe strokes was observed only in men.

In our study, AF did not increase the risk of in-hospital mortality. Patients with stroke and AF had additional risk factors associated with arrhythmia [28], and therefore AF was expected to increase in-hospital mortality in stroke patients.

Our result contrasts with what other studies have shown in both sexes [11, 12, 14] or only in women [8, 13]. Similarly to our study, the study by Andersen *et al.* also did not show that AF increased mortality in the acute phase of stroke (within 7 days). However, they did find such a correlation during a 30-day follow-up of patients after stroke [12]. Our study concerned patients staying in hospital for an average of 9 days from the onset of stroke. It is possible that AF would impact prognosis over a longer period. Another study [29] in the elderly population also did not show that AF was a significant predictor of mortality in people with stroke. The analysis by Marzona *et al.* [30] found no difference in mortality between men and women with AF, despite an increased risk of stroke in women, especially those over 65 years of age. However, there was a correlation between the risk of death from cardiovascular disease in women with AF and not receiving oral anticoagulant therapy. In the study by Senoo *et al.* [31], no significant differences were found in the frequency of strokes and mortality between women and men despite the use of anticoagulation. There were also no differences between age groups. The discrepancy in the results may be related to different inclusion criteria for patients in studies assessing the impact of AF on the occurrence of stroke and its consequences, such as comorbidities that, together with AF, worsen the prognosis of stroke, the assessment of patients in different age groups, and the use of anticoagulation therapy.

Our results show that men and women with ischaemic stroke have a different clinical profile and prognosis.

The main limitations of our study result from its retrospective nature. The lack of data on the treatment of patients before admission to the hospital, including data on anticoagulation, antihypertensive, and lipid-lowering treatment, makes it impossible to assess its impact on the prognosis of patients. Moreover, additional tests, such as echocardiography, 24-hour electrocardiographic monitoring, and lipid profile, were not performed in all patients. The impact of thrombolytic therapy on the prognosis of patients has not been evaluated. In the years covered by this analysis, people aged over 80 years, who constituted a significant part of the study group, were disqualified from thrombolytic treatment according to the adopted criteria.

However, our results indicate that there are factors that worsen stroke prognosis according to gender. Further observations on potential gender differences in risk factors for adverse prognosis in acute stroke are needed to reduce in-hospital deaths.

Conclusions

In this study in-hospital mortality in patients with ischaemic stroke was higher in women. In women, previous haemorrhagic stroke, age ≥ 75 years, and COPD increased the risk of in-hospital mortality. In men, a history of myocardial infarction and GFR < 60 ml/min/1.73 m² increased the risk of in-hospital death.

Certain comorbidities may increase the risk of an adverse stroke course. Potential gender differences in risk factors for an unfavourable prognosis in acute stroke should be considered in order to reduce the number of hospital deaths.

Better knowledge of the predictors that increase the risk of an adverse stroke may open more avenues for preventive intervention and reduce serious post-stroke complications.

Acknowledgments

Language and formatting assistance was provided by Proper Medical Writing, Warsaw, Poland.

Conflict of interest

The authors declare no conflict of interest.

References

- Girijala RL, Sohrabji F, Bush RL. Sex differences in stroke: review of current knowledge and evidence. *Vasc Med* 2017; 22: 135-145.
- Stróżyńska E, Ryglewicz D. Czynniki ryzyka udaru mózgu u kobiet. *Pol Prz Neurol* 2013; 9: 135-140.
- Czarnecka D, Zabojszcz M. Nadciśnienie tętnicze a udar mózgu. *Choroby Serca i Naczyń* 2004; 1: 19-25.
- GBD 2016 Lifetime Risk of Stroke Collaborators. Feigin VL, Nguyen G, Cercy K, Johnson CO, Alam T, Parmar PG, Abajobir AA, Abate KH, Abd-Allah F, Abejie AN, Abyu GY, Ademi Z, Agarwal G, Ahmed MB, Akinyemi RO, Al-Raddadi R, Aminde LN, Amlie-Lefond C, Ansari H, Asayesh H, Asgedom SW, Atey TM, Ayele HT, Banach M, Banerjee A, Barac A, Barker-Collo SL, Bärnighausen T, Barregard L, Basu S, Bedi N, Behzadifar M, Béjot Y, Bennett DA, Benseñor IM, Berhe DF, Boneya DJ, Brainin M, Campos-Nonato IR, Caso V, Castañeda-Orjuela CA, Rivas JC, Catalá-López F, Christensen H, Criqui MH, Damasceno A, Dandona L, Dandona R, Davletov K, de Courten B, deVeber G, Dokova K, Edessa D, Endres M, Faraon EJA, Farvid MS, Fischer F, Foreman K, Forouzanfar MH, Gall SL, Gebrehiwot TT, Geleijnse JM, Gillum RF, Giroud M, Goulart AC, Gupta R, Gupta R, Hachinski V, Hamadeh RR, Hankey GJ, Hareri HA, Havmoeller R, Hay SI, Hegazy MI, Hibstu DT, James SL, Jeemon P, John D, Jonas JB, Józwiak J, Kalani R, Kandel A, Kasaeian A, Kengne AP, Khader YS, Khan AR, Khang YH, Khubchandani J, Kim D, Kim YJ, Kivima-

- ki M, Kokubo Y, Kolte D, Kopec JA, Kosen S, Kravchenko M, Krishnamurthi R, Kumar GA, Lafranconi A, Lavados PM, Legesse Y, Li Y, Liang X, Lo WD, Lorkowski S, Lotufo PA, Loy CT, Mackay MT, Abd El Razek HM, Mahdavi M, Majeed A, Malekzadeh R, Malta DC, Mamun AA, Mantovani LG, Martins SCO, Mate KK, Mazidi M, Mehta S, Meier T, Melaku YA, Mendoza W, Mensah GA, Meretoja A, Mezgebe HB, Miazgowski T, Miller TR, Ibrahim NM, Mohammed S, Mokdad AH, Moosazadeh M, Moran AE, Musa KI, Negoi RI, Nguyen M, Nguyen QL, Nguyen TH, Tran TT, Nguyen TT, Anggraini Ningrum DN, Norrving B, Noubiap JJ, O'Donnell MJ, Olagunju AT, Onuma OK, Owolabi MO, Parsaeian M, Patton GC, Piradov M, Pletcher MA, Pourmalek F, Prakash V, Qorbani M, Rahaman M, Rahman MA, Rai RK, Ranta A, Rawaf D, Rawaf S, Renzaho AM, Robinson SR, Sahathevan R, Sahebkar A, Salomon JA, Santalucia P, Santos IS, Sartorius B, Schutte AE, Sepanlou SG, Shafieesabet A, Shaikh MA, Shamsizadeh M, Sheth KN, Sisay M, Shin MJ, Shiue I, Silva DAS, Sobngwi E, Soljak M, Sorensen RJD, Sposato LA, Stranges S, Suliankatchi RA, Tabarés-Seisdedos R, Tanne D, Nguyen CT, Thakur JS, Thrift AG, Tirschwell DL, Topor-Madry R, Tran BX, Nguyen LT, Truelsen T, Tsilimparis N, Tyrovolas S, Ukwaja KN, Uthman OA, Varakin Y, Vasankari T, Venketasubramanian N, Vlassov VV, Wang W, Werdecker A, Wolfe CDA, Xu G, Yano Y, Yonemoto N, Yu C, Zaidi Z, El Sayed Zaki M, Zhou M, Ziaiean B, Zipkin B, Vos T, Naghavi M, Murray CJL, Roth GA. Global, Regional, and Country-Specific Lifetime Risks of Stroke, 1990 and 2016. *N Engl J Med* 2018; 379: 2429-2437.
5. Persky RW, Turtzo LC, McCullough LD. Stroke in women: disparities and outcomes. *Curr Cardiol Rep* 2010; 12: 6-13.
 6. Petrea RE, Beiser AS, Seshadri S, Kelly-Hayes M, Kase CS, Wolf PA. Gender differences in stroke incidence and post-stroke disability in the Framingham heart study. *Stroke* 2009; 40: 1032-1037.
 7. Reeves MJ, Bushnell CD, Howard G, Gargano JW, Duncan PW, Lynch G, Khatiwoda A, Lisabeth L. Sex differences in stroke: epidemiology, clinical presentation, medical care, and outcomes. *Lancet Neurol* 2008; 7: 915-926.
 8. Ong CT, Wong YS, Sung SF, Wu CS, Hsu YC, Su YH, Hung LC. Sex-related differences in the risk factors for in-hospital mortality and outcomes of ischemic stroke patients in rural areas of Taiwan. *PLoS One* 2017; 12: e0185361.
 9. Kapral MK, Fang J, Hill MD, Silver F, Richards J, Jaigobin C, Cheung AM. Sex differences in stroke care and outcomes: results from the Registry of the Canadian Stroke Network. *Stroke* 2005; 36: 809-814.
 10. Santalucia P, Pezzella FR, Sessa M, Monaco S, Torgano G, Anticoli S, Zanolli E, Maimone Baronello M, Paciaroni M, Caso V. Sex differences in clinical presentation, severity and outcome of stroke: results from a hospital-based registry. *Eur J Intern Med* 2013; 24: 167-171.
 11. Heuschmann PU, Kolominsky-Rabas PL, Misselwitz B, Hermanek P, Carsten Leffmann C, RWC Janzen, Rother J, Buecker-Nott HJ, Berger K. Predictors of in-hospital mortality and attributable risks of death after ischemic stroke: the German Stroke Registers Study Group. *Arch Intern Med* 2004; 164: 1761-1768.
 12. Andersen KK, Andersen ZJ, Olsen TS. Predictors of early and late case-fatality in a nationwide Danish study of 26,818 patients with first-ever ischemic stroke. *Stroke* 2011; 42: 2806-2812.
 13. Kortazar-Zubizarreta I, Pinedo-Brochado A, Azkune-Calle I, Aguirre-Larracochea U, Gomez-Beldarrain M, Garcia-Monco JC. Predictors of in-hospital mortality after ischemic stroke: a prospective, single-center study. *Health Sci Rep* 2019; 2: e110.
 14. Ong CT, Wong YS, Wu CS, Su YH. Atrial fibrillation is a predictor of in-hospital mortality in ischemic stroke patients. *Ther Clin Risk Manag* 2016; 12: 1057-1064.
 15. Syta-Krzyżanowska A, Choraży M, Karpowicz B, Drozdowski W. Ocena wpływu czynników ryzyka chorób sercowo-naczyniowych na śmiertelność w udarze mózgu. *Aktual Neurol* 2013; 13: 62-67.
 16. Dahl S, Hjalmarsson C, Andersson B. Sex differences in risk factors, treatment, and prognosis in acute stroke. *Womens Health (Lond)* 2020; 16: 1745506520952039.
 17. Akhtar N, Kate M, Kamran S, Singh R, Bhutta Z, Saqqr M, Elzouki AN, Babu B, Bourke P, Morgan D, Joseph S, Jose N, Francis R, Imam Y, Amir N, Own A, Shuaib A. Sex-specific differences in short-term and long-term outcomes in acute stroke patients from Qatar. *Eur Neurol* 2020; 83: 154-161.
 18. Passowicz-Muszyńska E, Gostkowska-Malec A, Jankowska R, Piesiak P. Przewlekła obturacyjna choroba płuc a choroby układu sercowo-naczyniowego. *Pneumonol Alergol Pol* 2010; 78: 28-32.
 19. Soler EP, Ruiz VC. Epidemiology and risk factors of cerebral ischemia and ischemic heart diseases: similarities and differences. *Curr Cardiol Rev* 2010; 6: 138-149.
 20. Chou CC, Lien LM, Chen WH, Wu MS, Lin SM, Chiu HC, Chiou HY, Bai CH. Adults with late stage 3 chronic kidney disease are at high risk for prevalent silent brain infarction: a population-based study. *Stroke* 2011; 42: 2120-2125.
 21. Kapłon-Cieślicka A, Budnik M, Gawałko M, Peller M, Gorczyca I, Michalska A, Babiarz A, Bodys A, Uliński R, Żochowski M, Scisło P, Kochanowski J, Filipiak KJ, Opoliski G. Atrial fibrillation type and renal dysfunction as important predictors of left atrial thrombus. *Heart* 2019; 105: 1310-1315.
 22. Lee M, Saver JL, Chang KH, Liao HW, Chang SC, Ovbigele B. Low glomerular filtration rate and risk of stroke: meta-analysis. *BMJ* 2010; 341: c4249.
 23. Olszanecka A, Czarnecka D. Nadciśnienie tętnicze u kobiet. *Kardiologia po Dyplomie* 2013; 12: 14-22.
 24. Howard VJ, Lackland DT, McVay J, Meschia JF, Muntner P, Oparil S, Rightmyer M, Taylor HA. Is blood pressure control for stroke prevention the correct goal? The lost opportunity of preventing hypertension. *Stroke* 2015; 46: 1595-1600.
 25. Rydberg DM, Mejyr S, Loikas D, Schenck-Gustafsson K, von Euler M, Malmström RE. Sex differences in spontaneous reports on adverse drug events for common anti-hypertensive drugs. *Eur J Clin Pharmacol* 2018; 74: 1165-1173.
 26. Szczepaniak-Chicheł L, Tykarski A. Gender-related differences in the management of arterial hypertension in women. *Arterial Hyperten* 2009; 13: 349-361.
 27. Blood Pressure Lowering Treatment Trialists' Collaboration. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively

- designed overviews of randomized trials. *Arch Intern Med* 2005; 165: 1410-1419.
28. Wańkowicz P, Nowacki P, Gołąb-Janowska M. Risk factors for ischemic stroke in patients with non-valvular atrial fibrillation and therapeutic international normalized ratio range. *Arch Med Sci* 2019; 15: 1217-1222.
 29. Friedman PJ. Atrial fibrillation after stroke in the elderly. *Stroke* 1991; 22: 209-214.
 30. Marzona I, Proietti M, Farcomeni A, Romiti GF, Romanazzi I, Raparelli V, Basili S, Lip GYH, Nobili A, Roncaglioni MC. Sex differences in stroke and major adverse clinical events in patients with atrial fibrillation: a systematic review and meta-analysis of 993,600 patients. *Int J Cardiol* 2018; 269: 182-191.
 31. Senoo K, Lip GY. Female sex, time in therapeutic range, and clinical outcomes in atrial fibrillation patients taking warfarin. *Stroke* 2016; 47: 1665-1668.

Address for correspondence:

Justyna Tracz

Clinic of Neurology

Swietokrzyskie Neurology Centre

Kielce, Poland

Phone: +48 604955161

Fax: +48 41 3671542

E-mail: justyna_t@o2.pl