





Risk factors of ischaemic stroke in patients with atrial fibrillation

Czynniki ryzyka wystąpienia udaru niedokrwiennego mózgu u pacjentów z migotaniem przedsionków

Justyna Tracz¹, Iwona Gorczyca-Głowacka² , Paweł Wałek^{2,3} , Anita Rosołowska¹ ,
Beata Wożakowska-Kapton^{2,3} 

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

²Collegium Medicum, University of Jan Kochanowski, Kielce, Poland
Head of the Collegium: Prof. Marianna Janion MD, PhD

³1st Clinic of Cardiology and Electrotherapy, Swietokrzyskie Cardiology Centre, Kielce, Poland
Head of the Clinic: Prof. Beata Wożakowska-Kapton MD, PhD

Medical Studies/Studia Medyczne 2023; 39 (1): 8–13

DOI: <https://doi.org/10.5114/ms.2023.126284>

Key words: risk factors, atrial fibrillation, ischaemic stroke, CHA2DS2-VASc score.

Słowa kluczowe: czynniki ryzyka, udar niedokrwienny mózgu, migotanie przedsionków, skala CHA2DS2-VASc.

Abstract

Introduction: Atrial fibrillation (AF) is a common arrhythmia and a major risk factor for stroke. However, this risk depends on the coexistence of other factors that predispose to stroke and AF.

Aim of the research: We evaluated which of the common clinical factors were most strongly associated with stroke in patients with AF compared to patients with sinus rhythm.

Material and methods: In this retrospective, observational, single-centre study we analysed patients with acute ischaemic stroke admitted to the neurology centre between 1 January 2013 and 30 April 2015, inclusive. Patients were divided into groups with and without AF. Multivariate logistic regression analysis was used to identify predictors of stroke in the AF group.

Results: A total of 2339 ischaemic stroke patients were included in the study (mean age: 73.26 ±12.38 years, 51% male). Of these, 29.1% had AF. Patients with stroke and AF were significantly older ($p < 0.001$), were more often female ($p < 0.001$), and had higher rates of hypertension ($p < 0.001$), coronary heart disease ($p < 0.001$), and heart failure ($p < 0.001$). Multivariate logistic regression analyses identified older age (OR = 1.043, $p < 0.001$), female gender (OR = 1.389, $p = 0.001$), heart failure (OR = 2.467, $p < 0.001$), and coronary heart disease (OR = 1.618, $p < 0.001$) as independent factors that increased the risk of AF-associated stroke.

Conclusions: Patients with stroke and AF had additional risk factors coexisting with arrhythmia. The detection of other potential causes of stroke in patients with AF is important to allow modification of some of them and to establish effective treatment to improve outcomes in this group of patients

Streszczenie

Wprowadzenie: Migotanie przedsionków (MP) jest częstą arytmia i istotnym czynnikiem ryzyka wystąpienia udaru mózgu. Ryzyko to zależy jednak od współistnienia innych czynników predysponujących do wystąpienia udaru mózgu i MP.

Cel pracy: Ocena, które z powszechnie występujących czynników klinicznych najsilniej wiąże się z rozwojem udaru mózgu u pacjentów z MP w porównaniu z pacjentami z rytmem zatokowym.

Materiał i metody: W retrospektywnym, obserwacyjnym, jednośrodkowym badaniu analizowano pacjentów z ostrym udarem niedokrwiennym hospitalizowanych w ośrodku neurologicznym od 1 stycznia 2013 do 30 kwietnia 2015 roku. Pacjentów podzielono na grupę z MP i bez MP. Do identyfikacji predyktorów udaru mózgu u pacjentów z MP zastosowano wieloczynnikową analizę regresji logistycznej.

Wyniki: Do badania włączono 2339 pacjentów z udarem niedokrwiennym (średni wiek: 73,26 ±12,38 roku, 51% mężczyzn). Spośród nich 29,1% miało MP. Pacjenci z udarem i MP w porównaniu z pacjentami z udarem bez MP byli istotnie starsi ($p < 0,001$), częściej płci żeńskiej ($p < 0,001$), mieli większą częstość występowania nadciśnienia tętniczego ($p < 0,001$), choroby niedokrwiennej serca ($p < 0,001$) i niewydolności serca ($p < 0,001$). Wieloczynnikowa analiza regresji logistycznej wykazała, że starszy wiek (OR = 1,043, $p < 0,001$), płeć żeńska (OR = 1,389, $p = 0,001$), niewydolność serca (OR = 2,467, $p < 0,001$) i choroba niedokrwienna serca (OR = 1,618, $p < 0,001$) były niezależnymi czynnikami zwiększającymi ryzyko wystąpienia udaru mózgu związanego z MP.

Wnioski: Badanie wykazało, że u pacjentów z udarem mózgu i MP występowały dodatkowe czynniki ryzyka współistniejące z arytmia. Wykrycie innych potencjalnych przyczyn udaru mózgu u pacjentów z MP jest ważne, aby umożliwić modyfikację niektórych z nich i ustalić skuteczne leczenie poprawiające wyniki w tej grupie chorych.

Medical Studies/Studia Medyczne 2023; 39/1

Introduction

Atrial fibrillation (AF) is a common cardiac arrhythmia, affecting approximately 1–1.5% of the general population [1, 2]. The most serious complication of AF is a thromboembolic event including stroke. AF is associated with a nearly fivefold increased risk of stroke [3, 4]. However, this risk may depend on the coexistence of several modifiable and non-modifiable factors that predispose to stroke and AF, such as age and vascular disease [5–7]. The occurrence of AF has been described in strokes of non-cardioembolic aetiology, such as atherosclerosis of large arteries or small vessel occlusion, and is estimated to account for 15–30% of all acute cerebrovascular events in patients with AF [5, 8]. This suggests that although AF itself is independently associated with stroke, when other risk factors are present the cause of stroke cannot be explained by arrhythmia alone [5, 9].

The most common risk factors for stroke in patients with AF are included in the CHA2DS2-VASc score (congestive heart failure, hypertension, age, diabetes mellitus, previous stroke, vascular disease, gender). This scale is used to help identify patients at low, moderate, and high risk of stroke [10, 11].

Identification of risk factors for stroke in patients with AF is important to allow modification of some of them and to establish effective treatment.

Aim of the research

The aim of the study was to assess which of the common risk factors are most strongly associated with the occurrence of stroke in patients with AF.

Material and methods

Study group

This retrospective observational single-centre study included patients with acute ischaemic stroke, who were subsequently hospitalised in the reference neurological centre between 1 January 2013 and 30 April 2015.

Ischaemic stroke was diagnosed based on clinical presentation as an episode of neurological dysfunction lasting more than 24 h and imaging studies (head computed tomography or magnetic resonance imaging).

The patients were divided into 2 groups. The experimental group consisted of patients with ischaemic stroke and AF (AF group), and the control group consisted of patients with ischaemic stroke without AF (no-AF group) (Figure 1).

AF was defined as a history of AF or AF diagnosed during the hospitalisation by electrocardiography (ECG) or 24-hour monitoring electrocardiography (Holter ECG) showing an irregular atrial rhythm lasting 30 s or longer [12].

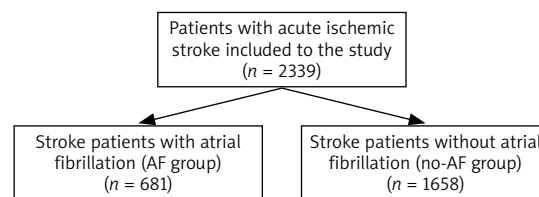


Figure 1. The flow chart of the study

We compared baseline characteristics between these 2 groups and investigated risk factors for stroke patients with AF. We analysed the common clinical factors included in the CHA2DS2-VASc scale (age, gender, hypertension, congestive heart failure, diabetes, previous stroke or TIA, vascular disease including coronary artery disease, peripheral vascular disease, and internal carotid artery (ICA) stenosis or occlusion), as well as other factors considered to be stroke risk, such as dyslipidaemia and smoking. Clinical risk factors were identified based on history and medical history according to medical records or were diagnosed during hospitalisation according to accepted criteria. Smoking was defined as current smoking of one or more cigarettes (per day). ICA stenosis $\geq 70\%$ and occlusion were assessed by Doppler ultrasound.

CHA2DS2-VASc score was calculated for all patients without consideration of a current stroke event. One point was assigned each for age 65–75 years, hypertension, diabetes, history of heart failure, female sex, and vascular disease, and 2 points were assigned each for stroke/transient ischaemic attack (TIA) or history of thromboembolic disease and age ≥ 75 years. Low thromboembolic risk patients were classified as having a score of 0, intermediate thromboembolic risk patients as having a score of 1, and high thromboembolic risk patients as having score ≥ 2 [10].

Stroke severity was evaluated in accordance with the National Institutes of Health Stroke Scale (NIHSS) at admission.

The protocol of study was consistent with the Declaration of Helsinki and was approved by the Ethics Committee of Swietokrzyska Medical Chamber (3/2021-VIII).

Statistical analysis

Analyses were performed using IBM SPSS Statistics 28. The aim of the analyses was to find determinants of stroke incidence in patients with AF, including the following risk factors: heart failure, hypertension, diabetes mellitus, stroke/TIA, ischaemic heart disease, dyslipidaemia, peripheral artery disease, smoking, and carotid artery stenosis $> 70\%$. In addition, the factors of age, gender, NIHSS score at admission, and CHA2DS2-VASc score were controlled. A comparison of the results of each parameter was presented and compared between the AF and no-AF

Table 1. Baseline characteristic of the study group

Parameter	All (n = 2339)	AF (n = 681)	No AF (n = 1658)	P-value
Age [years]	73.26 ±12.38	78.47 ±9.54	71.11 ±12.78	< 0.001
Age, n (%):				
< 65	590 (25.2)	69 (10.1)	521 (31.4)	< 0.001
65–74	548 (23.4)	140 (20.6)	408 (24.6)	0.036
> 74	1199 (51.3)	471 (69.2)	728 (43.9)	< 0.001
Gender, n (%):				
Male	1194 (51)	265 (38.9)	928 (56.0)	
Female	1145 (49)	416 (61.1)	729 (44.0)	< 0.001
Comorbidity, n (%):				
Heart failure	317 (13.6)	173 (25.4)	144 (8.7)	< 0.001
Hypertension	1806 (77.2)	556 (81.6)	1250 (75.4)	0.001
Diabetes mellitus	618 (26.4)	188 (27.6)	430 (25.9)	0.405
Previous stroke/TIA	472 (20.2)	153 (22.5)	319 (19.2)	0.077
Coronary heart disease	782 (33.4)	321 (47.1)	461 (27.8)	< 0.001
Hyperlipidaemia	354 (15.1)	90 (13.2)	264 (15.9)	0.097
Peripheral arterial disease	98 (4.2)	30 (4.4)	68 (4.1)	0.739
Smoking	266 (11.4)	78 (11.5)	188 (11.3)	0.937
ICA stenosis/occlusion	246 (10.5)	76 (12.6)	209 (14.0)	0.411
NIHSS score, mean (SD)	8.0 ±7.20	7.91 ±6.77	8.03 ±7.37	0.641
CHA2DS2-VASc score, mean (SD)	3.45 ±1.81	4.20 ±1.60	3.14 ±1.80	< 0.001

AF – atrial fibrillation, ICA – internal carotid artery, TIA – transient ischaemic attack, NIHSS – National Institutes of Health Stroke Scale.

groups. Quantitative variables were compared using the Mann-Whitney *U* test, bicategorical qualitative variables using Fisher's exact test, and multicategorical variables using the χ^2 test. Risk factors that were statistically significant were entered twice into univariate and multivariate logistic regression models to calculate the odds ratio (OR) of independent risk factors for stroke patients with AF, with 95% confidence intervals of the true result. A threshold of $\alpha = 0.05$ ($p < 0.05$) was considered to indicate statistical significance.

Results

Characteristics of the study group

A total of 2339 patients with acute ischaemic stroke were included. The mean age was 73.26 ±12.38 years, and 51% of the patients were male. The AF group comprised 29.1% of the patients and the control no-AF group comprised 70.9% of the patients.

The most common risk factors in the study group were hypertension (77.2%), coronary heart disease (33.4%), diabetes mellitus (26.4%), previous stroke/TIA (20.2%), dyslipidaemia (15.1%), and heart failure (13.6%). The mean NIHSS score at admission was

8.0 ±7.2. The mean CHA2DS2-VASc score was 3.45 ±1.81. The baseline characteristics of the patients are shown in Table 1.

Comparison of the clinical characteristics and risk factors of AF and no-AF patients with ischaemic stroke

Patients with stroke and AF were significantly older than no-AF stroke patients (median age: 78.5 vs. 71.1 years, respectively, $p < 0.001$) and were more often female (61.1%, $p < 0.001$). Hypertension, coronary heart disease and heart failure were significantly more frequent in the AF group than in the no-AF group (81.6% vs. 75.4%, $p < 0.001$; 47.1% vs. 27.8%, $p < 0.001$; 25.4% vs. 8.7%, $p < 0.001$, respectively). There were no significant differences in history of stroke/TIA, diabetes mellitus, dyslipidaemia, and smoking between patients with AF and those without AF.

Patients with IS and coexisting AF had significantly higher CHA2DS2-VASc scores (mean: 4.20 ±1.60). The percentage of patients with several CHA2DS2-VASc risk factors increased in the presence of AF (Figure 2). The NIHSS score at admission was similar in the AF and no-AF group (mean: 7.91 ±6.77 vs. 8.03 ±7.37; $p = 0.641$).

Analysis of factors predisposing to ischaemic stroke in patients with AF

Based on univariate and multivariate logistic regression analyses to determine the risk of stroke according to the presence of AF compared to those without AF, several major risk factors were identified (Table 2). In the group of patients with stroke and AF in univariate logistic regression analysis, risk factors of stroke were female sex (OR = 1.998, $p < 0.001$), older age (OR = 1.057, $p < 0.001$), heart failure (OR = 3.581, $p < 0.001$), coronary heart disease (OR = 2.315, $p < 0.001$), and hypertension (OR = 1.452, $p = 0.001$). In multivariate logistic regression analysis, which included all the above variables, the independent risk factors for stroke were female sex (OR = 1.389, $p = 0.001$), older age (OR = 1.043, $p < 0.001$), heart failure (OR = 2.467, $p < 0.001$), and coronary heart disease (OR = 1.618, $p < 0.001$).

Discussion

AF is a recognised independent factor for thromboembolic stroke. Despite this significant association, several other risk factors for stroke in AF have been reported. The most common risk factors for both AF and stroke are advanced age and cardiovascular diseases, such as hypertension, diabetes mellitus, heart failure, hyperlipidaemia, and smoking [6, 13–15].

In our study we found that in patients with AF, age, female sex, and vascular diseases such as heart failure and coronary heart disease were the strongest independent risk factors for stroke. Interestingly, hypertension increased the risk of stroke in the AF group in the univariate analysis, but this effect was not statistically significant after adjusting for other predictors.

Advanced age is a strong, independent, non-modifiable predictor of ischaemic stroke and AF. The prevalence of stroke and AF increases progressively in the elderly. It is assumed that the incidence of cerebrovascular events doubles for each decade after the age of 55 years. Moreover, other clinical risk factors for stroke, such as hypertension, heart failure, and dia-

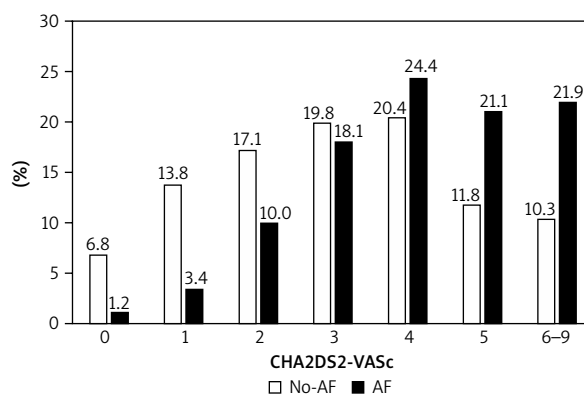


Figure 2. Distribution of CHA2DS2-VASc score in stroke patients in the AF group and no-AF group

betes, are also closely correlated with age, increasing the stroke incidence in AF patients [16, 17].

Female gender has been identified as a risk modifier rather than a risk factor for stroke in atrial fibrillation. The association of higher incidence of stroke in women is mainly related to advanced age and higher prevalence of comorbidities [18–20].

Congestive heart failure is also a thromboembolic risk factor for AF and for stroke. AF and heart failure often coexist, with a frequency of 10% to 50%, and together they tend to have worse outcomes. The strong correlation between the 2 diseases is associated with a higher risk of stroke severity and mortality [21, 22].

Vascular disease (myocardial infarction, peripheral arterial disease) and AF are closely related. Coronary heart disease is the most common vascular disease that is associated with an increased risk of ischaemic stroke in AF patients. The presence of coronary artery disease in patients with AF increases the risk of recurrent arrhythmic episodes and is associated with a higher risk of mortality [23].

The other stroke risk factors that were analysed in this study were not found to be significantly more strongly associated with concomitant AF. Hypertension is the biggest single risk factor for stroke, increasing its incidence by 2–3-fold. Although hypertension

Table 2. Analysis of risk factors of ischaemic stroke in patients with AF compared with patients without AF

Risk factors	Univariable logistic regression models			Multivariable logistic regression model*		
	OR	CI	P-value	OR	CI	P-value
Age	1.057	1.048–1.067	< 0.001	1.043	1.033–1.053	< 0.001
Heart failure	3.581	2.808–4.565	< 0.001	2.467	1.909–3.190	< 0.001
Hypertension	1.452	1.161–1.816	0.001	1.016	0.797–1.296	0.898
Coronary heart disease	2.315	1.924–2.785	< 0.001	1.618	1.323–1.977	< 0.001
Female sex	1.998	1.666–2.397	< 0.001	1.389	1.136–1.698	0.001

*Total adjusted model; independent variables: age (quantitative variable), heart failure hypertension, ischaemic heart disease, gender (F/M). Dependent variable: AF (1) vs. no AF (0). AF – atrial fibrillation, OR – odds ratio.

is also associated with a 1.7-fold increased risk of AF, it was not a predictor of stroke in patients with AF in our analysis [6, 24, 25].

We also found no significant differences between patients with and without AF in other risk factors in the aetiology of atherosclerotic ischaemic stroke, such as diabetes mellitus, dyslipidaemia, smoking, and carotid artery. They are often associated with other risk factors that increase the incidence of stroke. For example, diabetes often coexists with hypertension and dyslipidaemia [26, 27]. Dyslipidaemia is an important risk factor for stroke but also a significant risk for coronary artery disease, although the association with AF is less clear [14, 28]. Smoking is an independent and modifiable risk factor for stroke and other vascular diseases, such as coronary artery disease and peripheral artery disease [29]. However, it is possible that our results were influenced by other factors that were not measured or analysed in this study.

The most common risk factors for stroke in patients with AF were summarized in the CHA2DS2-VASc score. Several reports have found that most of these factors were independent predictors of stroke in patients with AF [30–32], which is also similar to our study. Therefore, it is not surprising that our patients with AF had a high CHA2DS2-VASc score. Stratification of stroke risk using this scale can help identify patients at “low risk” (CHA2DS2-VASc score = 0 in men, or 1 in women), who do not require antithrombotic therapy, and patients in whom oral anticoagulation should be considered (CHA2DS2-VASc \geq 1 in men and \geq 2 in women) [33]. Recently, it has been suggested that an increase in CHA2DS2-VASc score not only predicts stroke in patients with AF, but is also associated with prognosis after stroke [34].

Our study shows that in patients with AF, ischaemic stroke is not necessarily the result of cardioembolism. Other factors, such as vascular disease, which may increase the risk of stroke, may also be factors in the development of AF. Identification of other potential causes of stroke in patients with AF is important, as is monitoring stroke patients with other risk factors to detect asymptomatic AF that may be unrecognised. These findings have important implications for secondary stroke prevention.

Limitations

There are several limitations of our study. This was a single-centre, retrospective study, so there exist potential unidentified confounders. The incidence of AF may have been underestimated because of asymptomatic AF episodes. We evaluated only the most common clinical risk factors of stroke. Further prospective studies with evaluation of a larger population and consideration of other risk factors of stroke are needed.

Conclusions

Patients with stroke and AF had additional risk factors coexisting with arrhythmia. In our study, independent risk factors for stroke in the AF group were female gender, older age, heart failure, and coronary artery disease. The detection of other potential causes of stroke in patients with AF is important to allow modification of some of them and to establish effective treatment to improve outcomes in this group of patients.

Conflict of interest

The authors declare no conflict of interest.

References

1. Chen LY, Shen WK. Epidemiology of atrial fibrillation: a current perspective. *Heart Rhythm* 2007; 4 (3 Suppl): S1-S6.
2. Hannon N, Sheehan O, Kelly L, Marnane M, Merwick A, Moore A, Kyne L, Duggan J, Moroney J, McCormack PM, Daly L, Fitz-Simon N, Harris D, Horgan G, Williams EB, Furie KL, Kelly PJ. Stroke associated with atrial fibrillation-incidence and early outcomes in the north Dublin population stroke study. *Cerebrovasc Dis* 2010; 29: 43-49.
3. Abu-Assi E, Otero-Raviña F, Allut Vidal G, Coutado Méndez A, Vaamonde Mosquera L, Sánchez Loureiro M, Canela Villar MC, Fernández Villaverde JM, Maestro Saavedra FJ, González-Juanatey JR; Grupo Barbanza researchers. Comparison of the reliability and validity of four contemporary risk stratification schemes to predict thromboembolism in non-anticoagulated patients with atrial fibrillation. *Int J Cardiol* 2013; 166: 205-209.
4. Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; 22: 983-988.
5. Kamel H, Okin PM, Elkind MS, Iadecola C. Atrial fibrillation and mechanisms of stroke: time for a new model. *Stroke* 2016; 47: 895-900.
6. Fohtung RB, Rich MW. Identification of patients at risk of stroke from atrial fibrillation. *US Cardiol Rev* 2016; 10: 60-64.
7. Benjamin EJ, Levy D, Vaziri SM, D’Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. *JAMA* 1994; 271: 840-844.
8. Tsioufis C. Ischaemic stroke in atrial fibrillation patients: don’t put the blame always on heart. *Hellenic J Cardiol* 2020; 61: 208-209.
9. Christiansen CB, Gerds TA, Olesen JB, Kristensen SL, Lamberts M, Lip GY, Gislason GH, Køber L, Torp-Pedersen C. Atrial fibrillation and risk of stroke: a nationwide cohort study. *Europace* 2016; 18: 1689-1697.
10. Alshehri AM. Stroke in atrial fibrillation: review of risk stratification and preventive therapy. *J Family Community Med* 2019; 26: 92-97.
11. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, Boriani G, Castella M, Dan GA, Dila-veris PE, Fauchier L, Filippatos G, Kalman JM, La Meir M, Lane DA, Lebeau JP, Lettino M, Lip GYH, Pinto FJ, Tho-

- mas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL; ESC Scientific Document Group. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. *Eur Heart J* 2021; 42: 373-498.
12. Camm AJ, Kirchhof P, Lip GY, Schotten U, Savelieva I, Ernst S, Van Gelder IC, Al-Attar N, Hindricks G, Prendergast B, Heidbuchel H, Alfieri O, Angelini A, Atar D, Colonna P, De Caterina R, De Sutter J, Goette A, Gorenek B, Heldal M, Hohloser SH, Kolh P, Le Heuzey JY, Ponikowski P, Rutten FH; ESC Committee for Practice Guidelines. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace* 2010; 12: 1360-1420.
 13. Brunner KJ, Bunch TJ, Mullin CM, May HT, Bair TL, Elliot DW, Anderson JL, Mahapatra S. Clinical predictors of risk for atrial fibrillation: implications for diagnosis and monitoring. *Mayo Clin Proc* 2014; 89: 1498-1505.
 14. Hankey GJ. Potential new risk factors for ischaemic stroke: what is their potential? *Stroke* 2006; 37: 2181-8.
 15. Janion-Sadowska A, Turek Ł, Dudek A, Andrychowski J, Sadowski M. Atrial fibrillation and atrial flutter – the state of the art. Part 1. *Medical Studies* 2021; 37: 151-161.
 16. Soto-Cámara R, González-Bernal JJ, González-Santos J, Aguilar-Parra, J.M, Trigueros R, López-Liria R. Age-related risk factors at the first stroke event. *J Clin Med* 2020; 9: 2233.
 17. Frost L, Johnsen SP. Age and risk of stroke in Asians with atrial fibrillation. *Stroke* 2018; 49: 1809-1810.
 18. Nielsen PB, Skjøth F, Overvad TF, Larsen TB, Lip GYH. Female sex is a risk modifier rather than a risk factor for stroke in atrial fibrillation: should we use a CHA2DS2-VASc score rather than CHA2DS2-VASc? *Circulation* 2018; 137: 832-840.
 19. Mikkelsen AP, Lindhardsen J, Lip GY, Gislason GH, Torp-Pedersen C, Olesen JB. Female sex as a risk factor for stroke in atrial fibrillation: a nationwide cohort study. *J Thromb Haemost* 2012; 10: 1745-1751.
 20. 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.
 21. Kang SH, Kim J, Park JJ, Oh IY, Yoon CH, Kim HJ, Kim K, Choi DJ. Risk of stroke in congestive heart failure with and without atrial fibrillation. *Int J Cardiol* 2017; 248: 182-187.
 22. Bordignon S, Chiara Corti M, Bilato C. Atrial fibrillation associated with heart failure, stroke and mortality. *J Atr Fibrillation* 2012; 5: 467.
 23. Shahid F, Pastori D, Violi F, Lip GYH. Prognostic and therapeutic implications of vascular disease in patients with atrial fibrillation. *Pharmacol Res* 2018; 132: 149-159.
 24. Murakami N, Tanno M, Kokubu N, Nishida J, Nagano N, Ohnishi H, Akasaka H, Miki T, Tsuchihashi K, Miura T. Distinct risk factors of atrial fibrillation in patients with and without coronary artery disease: a cross-sectional analysis of the BOREAS-CAG Registry data. *Open Heart* 2017; 4: e000573.
 25. Dzeshka MS, Shantsila A, Shantsila E, Lip GYH. Atrial Fibrillation and Hypertension. *Hypertension* 2017; 70: 854-861.
 26. Tun NN, Arunagirinathan G, Munshi SK, Pappachan JM. Diabetes mellitus and stroke: a clinical update. *World J Diabetes* 2017; 8: 235-248.
 27. Chen R, Ovbiagele B, Feng W. Diabetes and stroke: epidemiology, pathophysiology, pharmaceuticals and outcomes. *Am J Med Sci* 2016; 351: 380-386.
 28. Li F, Du X, He L, Jiang C, Xia S, Ma C, Dong J. Relationship between serum lipid levels and ischaemic stroke in patients with atrial fibrillation: a nested case-control study based on the China Atrial Fibrillation Registry. *BMC Cardiovasc Disord* 2021; 21: 424.
 29. Pan B, Jin X, Jun L, Qiu S, Zheng Q, Pan M. The relationship between smoking and stroke: a meta-analysis. *Medicine* 2019; 98: e14872.
 30. Stroke Risk in Atrial Fibrillation Working Group. Independent predictors of stroke in patients with atrial fibrillation: a systematic review. *Neurology* 2007; 69: 546-554.
 31. Risk factors for stroke and efficacy of antithrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Arch Intern Med* 1994; 154: 1449-1457.
 32. Wańkiewicz P, Nowacki P, Gołąb-Janowska M. Atrial fibrillation risk factors in patients with ischaemic stroke. *Arch Med Sci* 2019; 17: 19-24.
 33. Savino JA 3rd, Halperin JL. Should patients with atrial fibrillation and 1 stroke risk factor (CHA2DS2-VASc Score 1 in Men, 2 in Women) be anticoagulated? The CHA2DS2-VASc 1 conundrum: decision making at the lower end of the risk spectrum. *Circulation* 2016; 133: 1504-1511.
 34. Nam KW, Kim CK, Yu S, Chung JW, Bang OY, Kim GM, Jung JM, Song TJ, Kim YJ, Kim BJ, Heo SH, Park KY, Kim JM, Park JH, Choi JC, Park MS, Kim JT, Choi KH, Hwang YH, Oh K, Seo WK. Pre-admission CHADS2 and CHA2DS2-VASc scores on early neurological worsening. *Cerebrovasc Dis* 2021; 50: 288-295.

Address for correspondence:

Justyna Tracz
Clinic of Neurology
Swietokrzyskie Neurology Center
Kielce, Poland
Phone: +48 604955161
Fax: +48 41 3671542
E-mail: justyna_t@o2.pl