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Review article

Importance rating of risk factors of ischemic stroke in patients over 85 years old in the polish population

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ABSTRACT

Introduction: The European population is aging and the number of elderly patients suffering from ischemic brain stroke increases. A better knowledge of the correlation between the risk factors and the course of the disease in old people may be useful for planning medical care and prophylactic strategies.

Aim: This prospective study aimed to perform a demographic and clinical analysis of the etiology of ischemic stroke, survival rate and severity of post-stroke disability in patients who developed ischemic stroke at the age of over 85 years in the Polish population.

Method: The study group consisted of 159 patients over 85 years old with ischemic stroke. The prevalence of risk factors such as sex, hypertension, hyperlipidemia, atrial fibrillation, heart failure and diabetes was evaluated. The outcome was assessed using the Barthel scale and the National Institutes of Health Stroke Scale.

Results: The most common risk factors of ischemic stroke were hypertension and atrial fibrillation. Patients with atrial fibrillation had a more severe course of ischemic stroke.

Conclusion: The course of brain stroke in the Polish population is more severe in patients over 85 years old than in younger ones. The key risk factor in this group is atrial fibrillation.

1. Introduction

The risk factors of ischemic stroke in people over 85 years old are not well established. Particularly, because they can change over time and vary depending on the country. The European population is getting older and, therefore, the problem is becoming more serious [1,2]. The incidence of stroke increases steeply with age and in the case of individuals over 80 years old is approximately 27% compared with 13% for individuals 60–79

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years old [3]. Within the next 20 years, the incidence of stroke is expected to increase even by as much as 40% [4]. According to The National Health Fund report, cardiovascular system diseases, including brain stroke, are the main reason for hospitalization in Poland, constituting 44% of all hospital admissions [5]. Moreover, almost 20% of women and 16% of men will die due to brain stroke [6]. The etiology of stroke is often unknown in very old patients. The difficulty to determine the cause of the disease is connected with multiple organ dysfunction, the presence of other neurological conditions, the adverse side effects of pharmacotherapy and poor medical care. Of the ischemic strokes with well-known etiology, the most common cause was embolism of a large vessel due to atrial fibrillation and watershed infarction caused by hypotension. The coexistence of cardiovascular disorders such as atherosclerotic lesions, valvular defects, arrhythmias and heart failure, is responsible for the increase of ischemic stroke incidence with age [4,7].

The aim of this prospective study was to examine the demographic characteristics and risk factors in individuals over 85 years old in the Polish population. The present study is a clinical analysis of the course of brain stroke in that age group, the frequency of complications, the survival rate and morbidity. A better knowledge of the correlation between the risk factors and the course of the disease in that age group may be useful for planning medical care and prophylactic strategies.

2. Materials and method

The investigated group consisted of 159 ischemic stroke patients, both males and females, treated in the Department of Neurology of the Military Institute of Medicine in Warsaw between 2010 and 2015. The age range of the patients was from 85 to 102 years (average age: 89 ± 3 years). The occlusion of the major brain artery (anterior or middle cerebral artery) was a cause of stroke in 54% of the patients, 40% suffered a lacunar type of stroke and 6% of the patients experienced stroke of the brainstem or cerebellum. Thrombolytic treatment was introduced in 5 patients (3.14%). In the present study, the risk factors of brain strokes such as hypertension, atrial fibrillation, heart failure, diabetes and hyperlipidemia were evaluated. The neurological status was assessed with the help of The National Institutes of Health Stroke Scale (NIHSS) and the Barthel scale on the first and last day of hospitalization. Moreover, the results of computer tomography (CT) examinations performed during admission to the hospital and abnormalities in ultrasonography of the carotid arteries (USG) were analyzed. The effectiveness and safety of the anticoagulant and statin treatment in the investigated group were also evaluated. Finally, complications related to hospitalization and survival rate were analyzed. Mann–Whitney *U* and Chi-squared tests were used for statistical analysis of the data.

3. Results

Demographic analysis revealed that 76% of the patients studied were women. Five out of 156 patients (3.14%) suffered from ischemic stroke with spontaneous hemorrhagic transformation (HT). The Mann–Whitney *U* test revealed that the mean NIHSS score (both on admission and at discharge) was statistically higher than in the group without HT (Table 1).

Hypertension was reported in the medical history in 66% of the patients on admission to the Department of Neurology. The two other important risk factors were: atrial fibrillation (AF) diagnosed before the occurrence of brain stroke (35%) and congestive heart failure (35%). Diabetes was diagnosed in the case of 24% of the patients. Further study revealed that 17% of the patients underwent ischemic brain stroke in the past (15% underwent brain stroke in the previous year and 56% earlier). Moreover, 8% of the patients had transient ischemic attacks (TIA) and 42% of them had those symptoms the previous year. Additionally, 11% of the patients had ischemic heart disease, 3% underwent heart infraction, 6% had hyperlipidemia and 1% had chronic renal failure. Interestingly, in the course of hospitalization the percentage of patients diagnosed with hyperlipidemia increased to 21%, an additional 4% was diagnosed with hypertension and 1% with diabetes. Likewise, due to previous poor diagnosis, the percentage of patients with AF increased by an additional 18% and with congestive heart failure by 11%. Therefore, AF, at 53%, became the second most important risk factor in that group.

Ischemic foci were found in CT examinations carried out on admission to the hospital in the case of 42% of the patients. Carotid artery stenosis was detected in ultrasonography in the case of 9% of the examined patients. In 8% of those patients, the stenosis was symptomatic. There were no statistically significant differences in stroke severity (measured with the NIHSS and Barthel scores) and in the lipid profile between patients with carotid artery stenosis and those with a normal ultrasonography result.

The most frequent complications of hospitalization were urinary tract infection (25%) and pneumonia (19%). Acute renal failure was diagnosed in 7% of the patients and acute respiratory insufficiency in 7% of the patients. Epileptic attacks were experienced by 6% of the patients in the examined group. Other complications were less frequent and included gastrointestinal hemorrhage and deep vein thrombosis (5%). Acute heart failure was present in the case of 3% of the patients.

Table 1 – Comparison between NIHSS and Barthel scores in the groups with ischemic stroke and ischemic stroke with secondary hemorrhaging.

Score	Type of ischemic stroke	*n*	*m*	*SD*	*p*
Initial NIHSS score	No HT	150	11.32	7.16	**0.025**
	HT	5	**17.80**	**4.49**	
Final NIHSS score	No HT	150	11.14	7.71	**0.030**
	HT	5	**17.80**	**4.49**	
Initial Barthel score	No HT	151	5.84	7.75	0.190
	HT	5	0.80	1.79	
Final Barthel score	No HT	151	6.16	8.27	0.252
	HT	5	1.20	2.68	

where *n* denotes the number of patients, data are shown as mean value (*M*) ± *SD*.

Table 2 – Mean values of the lipid profile.

	n	m	SD	Min	Max
Total cholesterol [mg/dl]	132	178.70	51.63	33	381
LDL cholesterol [mg/dl]	125	111.20	46.86	19	300
HDL cholesterol [mg/dl]	126	52.52	75.85	8	886
Triglyceride level [mg/dl]	129	106.50	54.37	27	394

where *n* denotes the number of patients, data are shown as mean value (*M*) ± *SD*.

Pulmonary embolism and pulmonary edema were diagnosed in 2% of the patients.

Among the examined group, 26% of the patients had an abnormal value of HDL cholesterol, 25% of the patients had an abnormal value of total cholesterol, 22% had an abnormal LDL cholesterol level and 13% had an abnormal level of triglyceride. Mean values of the lipid profile are presented in Table 2.

There were no differences between the lipid profiles in men and women, with the exception of the HDL level. Analysis with the use of the Chi-Squared test revealed that the difference in the HDL level was statistically significant and the HDL level was more frequently lower in women than in men ($p = 0.009$). Moreover, patients treated with statins (both with a normal and abnormal lipid profile) had a less severe course of disease (higher Barthel score and lower NIHSS score) (Table 3).

Among patients without AF, abnormal values of the total cholesterol and abnormal values of LDL cholesterol were the most frequent disorders of the lipid profile – constituting 30% and 29% respectively. It was observed that 22% of the patients without AF had abnormal values of HDL cholesterol, whereas 17% of the patients without AF had abnormal values of triglycerides. Analysis with the Mann–Whitney *U* test did not show statistically significant changes in the lipid profile between women and men. This means that there was no difference of the level of the lipid profile values between patients with AF (atrial fibrillation) and patients without AF.

In the group of patients with atrial fibrillation taking anticoagulants on admission to the hospital, only 25% had a therapeutic INR (between 2.0 and 3.0). In the case of patients with atrial fibrillation diagnosed before brain stroke, 75% had paroxysmal AF and 25% had fixed AF. Among them, only 28.5% were treated orally with vitamin K antagonists (acenocumarol or warfarin) and only 14% had therapeutic INR. Thirty-six and a half percent of the patients with atrial fibrillation were not treated with anticoagulants or antiplatelet drugs. In addition, 8 patients of this group stopped taking the medicine a few days before the brain stroke due to bleeding (epistaxis, alimentary and urinary tract bleeding). Thirty-five percent of the patients were taking salicylic acid (ASA). There were no statistically significant differences of stroke severity and course between patients who were given a therapeutic effective anticoagulant treatment and patients who were taking anticoagulants and had non-therapeutic INR, or were taking ASA, or were not taking any drugs at all. The Mann–Whitney *U* test showed that patients with brain stroke associated with atrial fibrillation had a statistically significant higher NIHSS score and a statistically significant lower Barthel score at the end of hospitalization when compared with those without AF (Table 4).

Only 3.14% of the patients were given thrombolytic treatment. There was no significant difference between the mean NIHSS score in the group of patients treated with thrombolytic agents compared to the group without that treatment (Table 5).

During the first 30 days of hospitalization, 33% of the patients with stroke died. According to the Mann–Whitney *U* test, those who died had higher NIHSS score and a lower Barthel score than the patients who survived 30 days of hospitalization (Table 6).

There was no correlation between increased prevalence of particular risk factors of ischemic brain stroke, sex and 30-day survival rate.

Table 3 – Correlation between statin treatment and final NIHSS and Barthel scores (Mann–Whitney *U* test).

Score	Hypolipidemic treatment at discharge	n	M	SD	p
Final NIHSS score	No statins	128	12.09	7.63	**0.003**
	Statins	29	7.62	6.81	
Final Barthel score	No statins	129	5.11	7.78	**0.004**
	Statins	29	10.10	8.88	

where *n* denotes the number of patients, data are shown as mean value (*M*) ± *SD*.

Table 4 – AF occurrence vs. the level of NIHSS and Barthel scores for examined patients at discharge.

Score	AF (atrial fibrillation)	N	m	SD	p
NIHSS score at discharge	Does not occur	76	9.99	7.86	**0.024**
	Occurs	83	12.53	7.33	
Barthel score at discharge	Does not occur	76	7.39	8.52	**0.038**
	Occurs	83	4.70	7.69	

where *n* denotes the number of patients, data are shown as mean value (*M*) ± *SD*.

Table 5 – The application of thrombolytic treatment vs. the level of NIHSS score of examined patients on admission and at discharge.

Score	Thrombolytic treatment	n	m	SD	p
NIHSS score on admission	No thrombolytic treatment	150	11.40	7.19	0.131
	Thrombolytic treatment	6	16.83	1.60	
NIHSS score at discharge	No thrombolytic treatment	150	11.17	7.71	0.072
	Thrombolytic treatment	6	17.83	1.47	

where *n* denotes the number of patients, data are shown as mean value (*M*) ± *SD*.

Table 6 – Mortality in the first 30 days and results of the NIHSS and Barthel scores on admission.

Score	30-day mortality	*n*	*m*	*SD*	*p*
NIHSS score on admission	No	107	9.62	6.97	**<0.001**
	Yes	51	15.49	5.75	
Barthel score on admission	No	107	7.98	8.20	**<0.001**
	Yes	52	0.87	2.63	

where *n* denotes the number of patients, data are shown as mean value (*M*) ± *SD*.

4. Discussion

Older people have a higher risk of developing ischemic brain stroke. After the age of 55 years, the risk of having an ischemic stroke doubles every 10 years. By the age of 85 years, the incidence is higher in men, whereas after the age of 85 years women are more frequently affected by this stroke [4]. The cumulated risk of ischemic brain stroke at the age of 85 years old is close to 15% [8]. The increased incidence of brain stroke in this age group is also related to poorer patient care [9]. The most frequent risk factors for ischemic stroke regardless of age are male sex, hypertension, hypercholesterolemia, diabetes, cardiovascular disease, alcohol consumption and smoking [10,11]. In the group of old people, the cardiovascular risk factor profile may be different and needs to be investigated. For example, Arboix et al. reported that the most common risk factors of ischemic brain strokes in the population over 85 years old were congestive heart failure, chronic nephropathy, female sex, previous cerebral infarction and atrial fibrillation [1]. In the present study, the most common risk factor of brain stroke was hypertension (66% of cases). There are no consistent data in the literature on the importance rating of arterial hypertension as a risk factor for stroke in people over 85 years of age [10,11,9]. However, a fivefold increase in the risk of stroke in the population of 70–75 years old with uncontrolled arterial hypertension when compared with the same age group without arterial hypertension has been demonstrated [12,13]. Although hypertension was the most common risk factor of ischemic stroke in our study, atrial fibrillation seemed to be the most relevant factor. It was diagnosed in more than half of the patients in this study. Moreover, atrial fibrillation and hyperlipidemia were the most common risk factors diagnosed during hospitalization. Taking into account asymptomatic and undiagnosed AF, the estimated occurrence of this disease in the general population amounts to 1.5–2% [14]. This increases, however, with age. The results of the cohort studies show that arrhythmia occurs in 0.7% of individuals in the age range of 55–59 years and in 17.8% of individuals over 85 years old. The frequency of AF is higher in men than in women [15]. The risk of stroke attributed to AF increases also with age, rising from 1.5% in individuals in the age range of 50–59 years to 23.5% in those who are 80–89 years old [7,16–18]. Due to the increased occurrence of atrial fibrillation in patients over 80 years old, it seems that this group could benefit most from the use of anticoagulants, although, the risk of hemorrhagic complications related to taking these medicines also increases with age. When introducing such treatment in old patients, the risk-benefit balance should be taken into account and the patient's health condition should be closely monitored. The potential benefit of anticoagulation in these patients should be verified properly. When starting the treatment, it is necessary to take into account the contraindications and the patient's choice and to keep INR within the range of 2.0–3.0. Proper control of INR in old patients can be extremely difficult which is confirmed by our present study. In the studied group, 86% of patients with AF taking anticoagulants had nontherapeutic INR, stopped taking medicines a few days prior to the occurrence of stroke or did not take medicines regularly. Moreover, a high percentage of patients with atrial fibrillation were diagnosed first during their hospitalization in the stroke ward, thus indicating a need for close monitoring of those patients for atrial fibrillation through echocardiography and Holter electrocardiography. Another study showed that non-compliance with medical dispositions, the low level of awareness and education of patients and lack of cooperation between patients and medical personnel in all age groups constitute the main reason for the failure of anticoagulative treatment [18,19]. Atrial fibrillation is the most common cardiac source of embolic stroke but other cardiological risk factors should not be forgotten such as myocardial infarction, left ventricular thrombus, valve disease and prosthetic valves [20]. Many people at old age have undiagnosed congestive heart failure. In our study, according to their medical history, 35% of the patients suffered from chronic heart failure and 11% of the patients were diagnosed with the disease during hospitalization. Therefore, periodic cardiological control in old patients is very important, including clinical evaluation and echocardiographic control for heart failure. The determination of the appropriate time that should elapse from the occurrence of stroke to the introduction of anticoagulative treatment in patients with atrial fibrillation is also problematic. The main concerns are related to the risk of hemorrhagic conversion of the ischemic focus. In the present study, the symptoms of the secondary hemorrhagic conversion of stroke focus confirmed by CT examination occurred in the case of 3% of the patients. Taking into account the benefits of such treatment and the relatively low risk of hemorrhagic conversion of stroke in this age group, the introduction of this treatment during hospitalization should not be delayed.

There is a lack of information on the effectiveness and safety of thrombolytic treatment in patients older than 85 years old. In the present study, only 5 patients were given that treatment. No significant improvement of neurological status measured with the NIHSS was observed after the treatment. Similar results concerning mortality were reported in another study on 6 patients receiving thrombolytic therapy [21]. No significant long-term decrease of mortality was reported. The functional outcomes at final follow-up were not analyzed in that study. The main concerns regarding the application of thrombolysis in this group of patients are related to systemic hemorrhagic complications and secondary hemorrhagic conversion of the brain stroke. In the case of thrombolysis as well as endarterectomy, age should not be the decisive factor for disqualification of patients from such treatment [21,22]. One of the most important exclusion criteria for carotid endarterectomy in symptomatic patients was residual life expectancy of

less than 5 years. The Copenhagen stroke study showed that 10% of the patients over 85 years old were alive 5 years after the onset of stroke [23,24]. However, further studies on larger populations are needed to evaluate survival rate after stroke and to establish more practical criteria of active intervention for very old patients.

The course of disease is also different in people in that age group and is determined by poorer cardiovascular response, multiple organ dysfunction, multiple medication consumption and the presence of other neurological conditions. With increasing severity of the course of stroke, there are more complications and more adverse events related to pharmacotherapy. In addition, there are more complications caused by a bedridden state. According to some sources, early mortality in stroke patients over 85 years old is twice as high as in younger patients [4,25]. According to our present analysis, 33% of the patients died during the first 30 days of hospitalization. Statistical analysis revealed the relationship between mortality and the NIHSS and Barthel scores on admission. In addition, the course of disease was more severe in patients with atrial fibrillation-induced ischemic stroke and their NIHSS score was higher when compared with patients without atrial fibrillation. Additionally, the risk of complications resulting from immobilization caused by brain stroke increases with age, particularly the risk of respiratory failure, airways infection, urinary tract infection and bedsores [25]. In our study, respiratory and urinary tract infections were the most common complications that occurred during hospitalization.

Several studies demonstrate a direct relationship between cholesterol levels, triglyceride levels and cardiovascular mortality [26,27]. Dyslipidemia is a definite risk factor of ischemic heart disease but the relationship between cholesterol and stroke appears to be more controversial and inconsistent across studies [3,27]. The literature data are contradictory. There are some studies which report no significant relationship between cholesterol levels and incidence of stroke [28–30]. By contrast, in other studies, the elevation of total cholesterol was associated with a 25% increased risk of ischemic stroke [31,32]. According to a study by Simons et al., only the LDL level predicted ischemic stroke in an Australian population of elderly patients [33]. It was suggested that this inconsistency was caused by the heterogeneity in the pathogenesis of ischemic stroke [31,34]. This suggestion is reflected in prospective registries of stroke, where dyslipidemia is described in up to 46% of atherothrombotic infarctions and up to 38% of lacunar infarctions, but in less than 20% of cardioembolic infarctions [35,36]. In the present study, 26% of the patients had an abnormal value of HDL cholesterol, 25% of the patients had an abnormal value of total cholesterol, 22% had abnormal LDL and 13% had abnormal triglyceride. There were no differences between the lipid profile in men and women, except for the difference in the HDL level which was statistically significant and the HDL level was frequently lower in women than in men. Patients treated with statins (both with normal and abnormal lipid profile) had a less severe course of disease (higher Barthel score and lower NIHSS score). In addition, no statistically significant difference between the values of the individual fractions of lipid profile in patients with stroke related to AF and patients with stroke not related to AF was shown.

5. Conclusion

Due to an aging population, the increase in the incidence of ischemic brain stroke should be expected. Many issues related to the treatment and prevention of cardiovascular disorders in this age group require further research. Despite the fact that, in general, recommendations referring to the treatment of the acute phase of brain stroke are not different from those corresponding to younger patients, it should be noted that this age group has a different drug metabolism. In addition, this age group is characterized by higher mortality and a more severe course of brain stroke. Elderly patients require intensive monitoring of their health condition in reference to brain stroke risk factors, in particular, arterial hypertension and atrial fibrillation. The introduction of anticoagulant treatment would require the enhanced control of the coagulation parameters and the use of anticoagulant medicines. Polypragmasy and hypotonia should be avoided. The issue related to the assessment of the safety and effectiveness of thrombolytic treatment and endarterectomy, as well as the issue concerning the application of new anticoagulants, such as rivaroxaban and dabigatran, require further examination.

Conflict of interest

None declared.

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