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PROGNOSIS AND RISK FACTORS FOR GERIATRIC STROKE PATIENTS IN EACH DECADE

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Abstract

Introduction: We aimed to compare the demographic characteristics, stroke localizations, stroke risk factors, and prognoses of geriatric stroke patients in different age groups.

Materials and Methods: Geriatric patients who had a neurological consultation following an acute ischemic stroke were evaluated in the study. Patients were divided into age groups of 65–69, 70–79, 80–89, and 90 years and older. The demographic findings, the diseases of the patients, pre-stroke antiaggregant or anticoagulant treatment, previous history of cerebrovascular disease, presence of atrial fibrillation, laboratory data, imaging reports from initial presentation, Echocardiography and Carotid-Vertebral Doppler Ultrasonography results were recorded. Neurological deficits were evaluated using the National Institutes of Health Stroke Scale and the Modified Rankin Score.

Results: The study evaluated 298 patients (161 females, 137 males). Significant differences were found in all four age groups in terms of the presence of diabetes mellitus. In relation to infarct localization, there were no significant differences between the four age groups. Previous antiaggregant or anticoagulant treatments were similar in all age groups. There were significant differences between the groups in terms of the presence of atrial fibrillation at presentation. In the 90 years and over age group, the values for the National Institutes of Health Stroke Scale and Modified Rankin Score were significantly higher.

Conclusion: The incidence of stroke can be reduced by the regular evaluation of elderly individuals for modifiable risk factors and their management. In elderly individuals who had ischemic strokes, we recommend to comprehensive cardiac assessment, including procedures like a 24-hour Holter monitor and transesophageal echocardiography for cardioembolic origins.

Keywords: Stroke; Geriatric; Risk factors; Prognosis.

INTRODUCTION

Stroke is the second leading cause of death worldwide, and its global prevalence is increasing with the aging of the population (1). The proportion of populations that comprise the elderly is increasing throughout the world, particularly in developed countries. Ischemic stroke may occur at any age, but most patients are elderly. Age is the most important unmodifiable risk factor for all types of stroke. In people aged 65 or older (the geriatric age group), the prevalence of stroke varies from 46–71 per 1,000 people (2). Studies report that 75–89% of all strokes occur in people over the age of 65 (3). Changes that occur in the brain with advancing age result in older people being affected more severely by stroke. Symptoms of aging can be observed in cerebral vessels (4).

It is common knowledge that the incidence of stroke rises with age. However, when geriatric patients are evaluated independently, our information –especially regarding the impact of age on prognosis– is quite limited (5). In addition, there are large gaps in the information on the prevention and treatment of stroke in the elderly (1).

The present study aims to compare the demographic characteristics, stroke localizations, stroke risk factors, and prognoses of geriatric stroke patients in different age groups.

MATERIALS AND METHODS

All consecutive patients who presented to the emergency service of Ankara Bilkent City Hospital –which serves as the stroke reference center in Ankara Turkey– with suddenly developing focal or global cerebral dysfunction signs and symptoms between January 1, 2020, and December 31, 2020, and who, after neurological consultation, were diagnosed with acute ischemic stroke and admitted to the neurology ward or intensive care unit, were evaluated in the present study.

Patients under the age of 65, those who had an intraparenchymal hematoma, a transient ischemic attack (TIA), head trauma, or cerebral venous thrombosis, and those patients found to have COVID-19 at presentation were excluded from the study.

Overall, 298 patients were eligible for the study. Neurologists had kept medical records for these patients until their discharge, and these records were evaluated in detail for the study.

The geriatric patients included in the study were divided into age groups of 65–69, 70–79, 80–89, and 90 and older. The age and sex of the patients were recorded and, if present, their diseases prior to the stroke (hypertension, diabetes mellitus, hyperlipidemia), any pre-stroke antiaggregant or anticoagulant treatment, whether valve replacement had been carried out, any previous history of cerebrovascular disease, the presence of atrial fibrillation in their electrocardiography (ECG), laboratory data for stroke on initial presentation, and imaging reports during the presentation (CT and MRI) were also recorded. The infarct areas detected by the neuroimaging investigations were classified into lacunar (LACI), posterior (POCI), total anterior (TACI), and partial anterior (PACI) circulation infarcts, after hemorrhage had been ruled out (6, 7). For the quantitative measurement of neurological deficits associated with stroke at both admission and discharge, the National Institutes of Health Stroke Scale (NIHSS) (8) (1–4 mild, 5–15 moderate, 16–20 moderate to severe, and 21–42 very severe) scores were recorded, and for an assessment of the degree of functional neurological disability developing after the stroke, the admission and discharge Modified Rankin Score (mRS) (9) (1 and 2 independent, 3 and over dependent) were recorded.

Echocardiography and Carotid-Vertebral Doppler Ultrasonography (USG) results on admission for stroke were also recorded. According to the Doppler USG findings, patients were

divided into four groups: no stenosis, intima-media thickening, asymptomatic stenosis (under 70%), and symptomatic stenosis (70–99%). Whether the occlusion in the carotid artery was complete was also noted.

Statistical Analysis

The data were analyzed using the IBM SPSS 22 program. In the analysis, $p < 0.05$ was accepted as statistically significant. Descriptive statistics of categorical variables included percentage frequency values (%), and the descriptive statistics of numerical variables included min, max, mean, and standard deviations. The patients were divided into four age groups: 65–69, 70–79, 80–89, and 90+. Statistical interpretations of numerical fields for these age groups were examined with the Kruskal-Wallis independent samples test. The Kruskal-Wallis test was used because the sample size was more than 2. Pearson's chi square method was used for the relationship between age groups and categorical variables. The Ethics Committee of Ankara City Hospital granted approval for this retrospective data analysis with approval number E1-21-1483.

RESULTS

The distribution according to age groups of the 298 (161 female, 137 male) patients included in the study is illustrated in Table 1.

The previous presence of hypertension (HT) and a diabetes mellitus (DM) diagnosis are considered established risk factors for stroke. In the present study, no significant difference was found between the four age groups in terms of the presence of HT ($p = 0.986$). However, a significant difference was found between the groups in terms of the presence of DM (25 patients in the 65–69 age group, 58 patients in the 70–79 age group, 28 patients in the 80–89 age group, and two patients in the 90 and older age group) ($p = 0.028$)*.

Blood lipid profile and glycosylated hemoglobin (HbA1c) values, also considered stroke risk factors, are demonstrated in Table 2. It was observed that as age increased, HbA1c and triglyceride (TG) values decreased.

No significant differences were found between patients in the four geriatric age groups with respect to antiaggregant or anticoagulant treatment received prior to the stroke (acetylsalicylic acid, clopidogrel, warfarin, new-generation oral anticoagulants, and combined treatments).

No significant differences were found between patients in the four geriatric age groups regarding valve replacement history or a previous history of cerebrovascular disease ($p = 0.278$ and $p = 0.434$), respectively.

However, a significant difference was found between the four age groups in terms of the presence of atrial fibrillation (AF) on presentation. According to the ECG investigation ($p = 0.029$), in the age range 70–89, AF was present in 56 patients overall (28 patients between 70 and 79, and 28

Table 1. Distribution of patients according to age group

Gender	Age Groups				Totals
	65–69	70–79	80–89	90 and older	
Female	26	68	55	12	161
Male	30	65	40	2	137
Total	56	133	95	14	298

Pearson's chi-squared test was used.
($p = 0.046$)

Table 2. Blood lipid profiles and HbA1c values for the groups

	Age Groups			
	65–69	**70–79**	**80–89**	**90 and Older**
Low density lipoprotein (LDL) mg/dL	115,4	110,1	111,1	97,4
High density lipoprotein (HDL) mg/dL	38,9	40,8	40,3	46,3
Triglycerides (TG)* mg/dL	**147,3**	**135,6**	**123,2**	**99,1**
Hemoglobin A1c (HbA1c) ** **(%)**	**7,83**	7,11	**6,64**	6,46

Kruskal–Wallis test was used.
* p = 0.002
** p = 0.002

Table 3. Comparison of age groups according to admission and discharge stroke severity scores

		Age groups				Totals
		65-69	**70-79**	**80-89**	**90+**	
Admission NIHSS*	No symptom	5	9	4	**1**	19
	Mild	27	66	47	**3**	143
	Moderate	21	51	37	**7**	116
	Moderate–severe	2	6	3	**2**	13
	Very severe	1	1	4	**1**	7
Discharge NIHSS**	No symptom	4	19	7	**1**	31
	Mild	34	74	50	**3**	161
	Moderate	15	33	34	**8**	90
	Moderate–severe	2	4	1	**1**	8
	Very severe	1	3	3	**1**	8
Admission mRS***	Independent	27	65	39	4	135
	Dependent	29	68	56	10	163
Discharge mRS******	Independent	36	75	38	**4**	153
	Dependent	16	52	48	**7**	123
	Died	4	6	9	**3**	22
Totals		56	133	95	14	298

NIHSS: National Institutes of Health Stroke Scale; mRS: Modified Rankin Score
Monte Carlo chi-square test was used.
* p = 0.024 (statistically significant)
** p = 0.029 (statistically significant)
*** p = 0.075 (statistically not significant)
**** p = 0.000 (statistically significant)

patients between 80 and 89), in eight patients between the ages of 65 and 69, and in four patients aged 90 or older.

As mentioned, patients were separated into the following infarct localization groups according to the neuroimaging findings at the emergency service: LACI, POCI, TACI, and PACI circulatory infarcts. No significant difference was found between the four age groups in relation to infarct localization ($p = 0.544$).

The NIHSS and mRS values for all patients at both presentation and discharge and their statistical analyses are presented in Table 3. Admission–discharge NIHSS and discharge mRS values were significantly higher in the 90 and over age group than in the other age groups.

No significant differences were found between the four geriatric age groups in relation to stenosis as detected by carotid-vertebral Doppler ultrasonography or in relation to the presence of thrombus, as shown in the echocardiography ($p = 0.565$ and $p = 0.201$, respectively).

DISCUSSION

Stroke is one of the major causes of morbidity and mortality in the geriatric age group. The main factor increasing the prevalence of stroke is age. However, there are large gaps in the available information regarding the prevention and prognosis of strokes occurring in old and very old individuals (1). In our country, the prevalence of ischemic stroke has increased by 115% in the last 30 years. This increase is particularly evident over the age of 70. Likewise, the mortality rate tends to increase with age, regardless of gender (10). In United States the age distribution of the general population is shifting upwards and the average age at first stroke is expected to increase accordingly. In the year 2010, strokes affecting individuals over the age of 85 constituted 23% of all stroke cases in the United States. However, projections indicate that by the year 2050, this proportion is expected to rise to 34%, signifying that more than half of all stroke incidents will occur after the age of 75 (11). The determination and elimination of risk factors for stroke, particularly in geriatric age groups, is of primary importance in both developed and developing countries, so that the incidence and mortality of stroke, and the high costs associated with it, can be reduced. The aim of the present study was to compare the risk factors and prognosis of four different age groups (separated by decades) in geriatric patients 65 years of age and older.

The significant difference found between the different age groups in terms of sex distribution may be attributed to the markedly higher number of women in the 90 and older age groups (12 females, two males). As is known, average life expectancy is higher in women than in men (12, 13). Moreover, stroke can occur at a younger age in women than in men (3). It was assumed that the significant difference in sex distribution was associated with these facts.

While the effectiveness of hypertension treatment in lowering the risk of stroke has been demonstrated, the timeline at which this reduction in stroke occurrence becomes evident remains less certain. Conversely, the adverse effects associated with hypertension treatment, such as orthostatic hypotension, syncope, falls, and electrolyte imbalances, seem to manifest shortly after the commencement of treatment (14). Due to the addition of other risk factors with increasing age, the presence of HT is a less significant risk factor for older patients than for younger ones. Studies have established that HT loses its significance as a risk factor, particularly over the age of 90 (15). Similarly, in the present study, no significant difference was found between the four geriatric age groups in terms of the presence of HT. HT was detected at similar rates in all age groups, indicating that HT no longer influences the risk of stroke with advanced age.

The mean ages of the patients included in the studies Action to Control Cardiovascular Risk in Diabetes (ACCORD), Action in Diabetes and Vascular Disease Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE), and the Veterans Affairs Diabetes Trial (VADT), which are the three largest studies to have investigated the relationship between DM and cardiovascular diseases, were 62, 66, and 60, respectively (15). All three studies recommended that other risk factors (such as HT, dyslipidemia, smoking, sedentary lifestyle, etc.) should be considered in addition to DM to decrease microvascular risk (16). In another study, 11,140 type 2 DM patients over the age of 55 were followed for five years to evaluate the development of microvascular and macrovascular risks. Their mean age was 66 ± 6. In this study, no significant differences were found between the group whose blood sugar levels were intensively reduced and the group whose blood pressure (BP) was not reduced intensively in terms of the development of major macrovascular events (17). There is no evidence to indicate that an intensive blood glucose level reduction decreases the risk of stroke (16). However, elderly patients are seldom included in studies such as the aforementioned. Among elderly or frail patients with a higher risk of hyperglycemia or a shorter life expectancy, according to American Diabetes Association (ADA) guidelines, a higher glycemic target is recommended (18). Patients who experienced ischemic stroke faced an elevated risk of stroke recurrence within one year in association with prolonged diabetes duration (≥8 years), as opposed to cases of shorter-term diabetes duration (19). In the present study, of the four age groups, the DM rate was relatively lower in the 90 and over age group (two of 12 patients). This difference may be attributed to the fact that the number of patients was relatively lower than in the other groups and that this group refers at a lower rate to routine hospital controls or outpatient clinics.

In the literature, the relationship between cholesterol levels and the risk of stroke is controversial. In the Framingham cohort, no significant relationship was found between cholesterol levels and the incidence of stroke (20). In a study investigating the relationship between age and dyslipidemia in 2,074 ischemic stroke patients either under or over the age of 65, it was reported that in patients over 65, namely the geriatric group, total cholesterol, TG, and LDL levels were lower than those in the non-geriatric group (21). In that study, total cholesterol, TG, and LDL levels were found to be significantly higher in ischemic stroke patients between the ages of 50–59 and 60–69 than in those aged 80 and older. In the non-geriatric group, a more severe and common disturbance was found in the lipid levels. Similarly, in the comparison of the four age groups in the present study, it was established that as age increased, TG and LDL levels decreased, with the decrease in TG levels being statistically significant ($p = 0.002$). It was assumed that this difference might be due to decreased intake through diet as age increases.

For stroke prevention, recommendations based on clinical studies support the utilization of acetylsalicylic acid, clopidogrel, and combined antiaggregant treatments (22). However, there is limited evidence of the benefit/risk ratio of the prophylactic administration of combination treatments, especially in very old individuals. In a study by Arnett et al., entitled ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease, the initiation of routine, low-dose acetylsalicylic acid (75–100 mg) for the prevention of atherosclerotic cardiac diseases in individuals over the age of 70 was not recommended, since it increases the risk of bleeding (17, 18). Exploration into novel antiplatelet treatments like clopidogrel, ticagrelor, or prasugrel has not been conducted within the context of primary prevention, and thus, they should not be immediately regarded as substitutes for acetylsalicylic acid in this particular role (23). In

present study there was no significant differences between patients in the four geriatric age groups with respect to antiaggregant or anticoagulant treatment received prior to the stroke.

AF is the most common cardiac arrhythmia and a major risk factor for ischemic stroke. From the literature, it can be seen that AF prevalence increases two-fold with each decade of increase in age, reaching a rate as high as 9% in the age range of 80–89. In the Framingham study, the risk of stroke associated with atrial fibrillation was found to be 1.5% between the ages of 50 and 59, while it was 23.5% between the ages of 80 and 89 (24, 25, 26, 27). In the present study, and consistent with the literature, the prevalence of AF was found to be significantly higher in the age groups 70–79 and 80–89. In addition, of the 228 ischemic stroke patients between the ages of 70–89, 56 were established as having AF through an ECG at presentation. However, in this age group, only 25 patients were on anticoagulants (seven on warfarin, 18 on new-generation oral anticoagulants). The role of anticoagulant therapy in prophylactic management of stroke in patients with AF has been demonstrated in many studies. However, the present study indicated that prophylactic treatment for AF patients had not been administered to an adequate degree.

The most important study aimed at determining the etiology of stroke all over the world reported that over half of all stroke types occurred in individuals over the age of 75 (2). Studies have shown that, particularly in patients aged 80 and older, the risk profile for ischemic stroke is different from that of younger patients (25). As in other countries, the results obtained in the present study suggest that routine cardiac examination and ECG investigation in this age group, with changes to risk factors and proper anticoagulation measures in patients with AF, may lead to a marked drop in the incidence of stroke. In the present study of 228 ischemic stroke cases between the ages of 70 and 89, 15 died and 100 were discharged with dependency. In light of this, it is our suggestion that the addition of an ECG and Holter investigation to a control examination—even if the patient does not have a previous history of any cerebrovascular event—may be beneficial for decreasing the morbidity and mortality associated with ischemic stroke in this population.

In most studies on ischemic stroke, the very old group (age over 90) was generally excluded. These patients were included in our study. Both discharge NIHSS and discharge mRS were higher in patients over 90 years of age. Our study supports the need to be more careful when deciding on acute treatment (intravenous and intra-arterial) and secondary prophylaxis in patients aged > 90 years who applied in the acute period.

The main limitations of the present study are associated with its retrospective nature in a single center. Because we were unable to obtain all body mass index (BMI) and smoking figures accurately, we could not incorporate these factors into the study, and patient follow-up was carried out only until discharge. Information on dementia and malnutrition, which could affect discharge NIHSS and mRS scores, was missing. There was no left atrial dilatation information on transthoracic echocardiography, which is frequently associated with atrial fibrillation. In terms of long-term mortality, mRS information at day 90 was not noted.

CONCLUSIONS

The incidence of stroke, which increases markedly with age, and the morbidity, mortality, and high financial burden associated with it may be reduced by the regular evaluation of elderly individuals for modifiable risk factors (especially the ECG) and their management. When an etiologic cause cannot be found in elderly ischemic stroke patients, a detailed cardiac examination (such as 24-hour Holter, transesophageal echocardiography) should be performed.

Further studies with larger patient series are required to determine the changes in risk with interventions on modifiable risk factors and to follow patients for a longer period of time.

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