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Ischemic stroke in young adults: Gender-based differences

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Abstract

Stroke is becoming a growingly more prevalent and significant public health problem among young adults around the world. Modifiable lifestyle-related risk factors are the most common cause of stroke in young adults. The aim of this study was to perform a gender-based evaluation of risk factors, stroke subtypes, severity of stroke, level of dependency at hospital discharge, and length of hospital stay among young patients with ischemic stroke in our region. The retrospective study included patients that were diagnosed with ischemic stroke based on patient history and clinical and radiographic findings at Inonu University Medical School Neurology Department between 2015 and 2018. The patients were divided based on gender and the two groups were compared with regard to age, gender, prior stroke, risk factors, neurologic deficits at hospital admission, etiology, radiographic localization, length of hospital stay, and the levels of disability and dependency at hospital discharge were reviewed for each patient. The study included a total of 105 patients diagnosed with ischemic stroke, comprising 65 (61.9%) men and 40 (38.1%) women. Mean age was 46.02 ± 7.29 years in men and 41.18 ± 8.2 years in women and a significant difference was observed between the two groups ($p=0.002$). The incidence of diabetes mellitus (DM), myocardial infarction (MI), and smoking was significantly higher in men compared to women ($p=0.008$, $p=0.001$, and $p<0.001$, respectively), whereas the incidence of mitral stenosis was significantly higher in women compared to men ($p=0.0019$). The results indicated that modifiable lifestyle-related risk factors are the most common cause of stroke in young adults and the significance of risk factors associated with stroke in young individuals differs between genders. Future studies with larger patient populations are needed to identify further risk factors and precautions for stroke in young adults.

Keywords: Young stroke, gender differences, risk factors

Introduction

Stroke is a leading cause of disability and death worldwide [1]. Although it is traditionally a disease of elderly people, stroke is becoming a significant public health problem among young adults as well [2]. The cases of stroke in young adults account for approximately 10-12% of all stroke cases [3], and more than two million young adults will suffer a stroke every year [4]. The longer disabled life expectancy in young adults with a history of stroke compared to old-age individuals and the resultant longer durations of clinical complications result in increased socioeconomic costs [5]. On the other hand, the risk factors, prevalence, and etiology of stroke in young adults show significant differences from those of old-age individuals [3,6].

In this study, we aimed to perform a gender-based evaluation of risk factors, stroke subtypes, severity of stroke, level of dependency at hospital discharge, and length of hospital stay among young patients with ischemic stroke in our region.

Materials and Methods

Study design

The retrospective study included patients that were diagnosed with ischemic stroke based on patient history and clinical and radiographic findings at Inonu University Medical School Neurology Department between 2015 and 2018. Patient data were retrieved from a computerized hospital database (called ENLİL) which has been operant in our hospital since 2010 and allows access to all patient data recorded in all polyclinics, inpatient clinics, laboratories, and Radiology department.

Clinical evaluation

A definitive diagnosis of ischemic stroke established by radiographic examination (brain computed tomography [CT] or

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magnetic resonance imaging [MRI]) was accepted as the principal diagnostic criteria of the study even if the diagnosis had been made via patient history and clinical findings. Demographic and clinical characteristics including age, gender, prior stroke, risk factors, neurologic deficits at hospital admission, etiology, radiographic localization, length of hospital stay, and the levels of disability and dependency at hospital discharge were reviewed for each patient.

Inclusion and exclusion criteria

1. Inclusion criteria were as follows: aged 18-55 years, a history of sudden-onset ischemic stroke that lasted for at least 24 h and/or resulted in death, and detection of focal neurological deficits on neurological examination.

2. Exclusion criteria were as follows: presence of hemorrhage or absence of infarction on brain CT or MRI despite the presence of clinical features consistent with ischemic stroke.

The risk factors considered for ischemic stroke included hypertension (HT), diabetes mellitus (DM), hypercholesterolemia (HC), prior stroke, alcohol abuse, cigarette smoking, hematologic diseases, myocardial infarction (MI), coronary artery disease (CAD), cardiac spontaneous echo contrast (SEC)/thrombus, patent foramen ovale (PFO), prior coronary artery bypass surgery, congestive heart failure (CHF), atrial fibrillation (AF), and a family history of stroke. These factors were considered present in the patients that were found to have been diagnosed with any of these conditions and received treatment accordingly (e.g. antihypertensive or antidiabetic medication, coronary artery bypass surgery, coronary stent implantation) during their previous medical follow-ups and in patients that were diagnosed with any of these conditions based on clinical diagnostic tests prior to discharge from our clinic.

Depending on their neurological symptoms, the patients were classified as having total anterior circulation infarction (TACI), partial anterior circulation infarction (PACI), posterior circulation

infarction (POCI), or lacunar infarct (LACI) according to the Oxfordshire Community Stroke Project (OCSP) classification system [7].

The etiological subtypes of stroke were classified according to the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) classification into the following categories: (i) large artery atherosclerosis, (ii) cardioembolism, (iii) small vessel occlusion, (iv) ischemic stroke associated with other factors, and (v) idiopathic ischemic stroke [8].

The severity of presenting neurologic deficits was assessed using the National Institutes of Health Stroke Scale (NIHSS) [9]. The levels of disability and dependency at discharge were evaluated using the modified Rankin Scale (mRS) [10]. The patients were divided based on gender and the two groups were compared with regard to age, clinical syndrome, etiological subtype, risk factors, NIHSS score, mRS score, and length of hospital stay.

Statistical analysis

Data were analyzed using SPSS 15 for Windows (SPSS Inc. Co, Chicago, IL, USA). The two groups were compared using t-test. Nonparametric data were compared using Fisher's exact chi-square. Descriptives were expressed as mean and standard deviation (SD). A p value of <0.05 was considered significant.

Results

The study included a total of 105 patients diagnosed with ischemic stroke, comprising 65 (61.9%) men and 40 (38.1%) women.

Demographic and clinical characteristics

Mean age was 46.02 ± 7.29 years in men and 41.18 ± 8.2 years in women and a significant difference was observed between the two groups ($p=0.002$). However, no significant difference was found with regard to clinical syndrome, etiological subtype, NIHSS score, mRS score, and length of hospital stay (Table 1).

Table 1. Demographic and clinical characteristic

		Women n=40 (%)	Men n=65 (%)	p
Age (years)		41.2 ± 8.2	46.0 ± 7.2	0.002*
Clinical	LACI	7 (17.5)	11 (16.9)	0.729
	syndrome	17 (42.5)	25 (38.5)	
	POCI	7 (8.8)	16 (14.2)	
	TACI	6 (15)	9 (15)	
Stroke Etiology (according to TOAST)	Large artery atherosclerosis	6 (15)	13 (20)	0.699
	Cardioembolism	10 (25)	20 (30.8)	0.815
	Small vessel occlusion	3 (7.5)	5 (7.7)	0.996
	Other factors	11 (27.5)	12 (18.5)	0.546
	Idiopathic	11 (27.5)	13 (20)	0.374
NIHSS Score		5.75 ± 6.02	6.69 ± 5.8	0.431
Modified Rankin Score		2.18 ± 2.02	2.45 ± 2.09	0.516
Hospital stay (days)		15.28 ± 19.7	14.82 ± 16.6	0.899

LACI: lacunar infarct, PACI: partial anterior circulation infarction, POCI: posterior circulation infarction, TACI: total anterior circulation infarction, TOAST: Trial of ORG 10172 in Acute Stroke Treatment, NIHSS: National Institutes of Health Stroke Scale

Risk factors

The incidence of DM, MI, and smoking was significantly higher in men compared to women, whereas the incidence of mitral stenosis was significantly higher in women compared to men ($p < 0.05$ for both). Nevertheless, no significant difference was found with regard to the incidence of HC, hereditary thrombophilia, PFO, CHF, cardiac SEC/thrombus, AF, alcohol abuse, and prior stroke ($p > 0.05$) (Table 2).

Table 2. Risk factors

	Women n=40 (%)	Men n=65 (%)	P
Hypertension	10 (25)	24 (36.9)	0.146
Diabetes Mellitus	5 (12.5)	21 (32.3)	0.018*
Smoking	7 (17.5)	43 (66)	<0.001*
Alcohol abuse	1 (2.5)	7 (58)	0.118
Hypercholesterolemia	12 (30)	26 (40)	0.205
Hematologic Gene Mutation	14 (35)	15 (23.1)	0.275
Patent Foramen Ovale	0(0)	1(1.5)	0.619
Mitral Stenosis	4 (36)	0 (0)	0.019*
Myocardial Infarction	0 (0)	7 (10.8)	0.001*
Cardiac SEC/Thrombus	1 (2.5)	5 (7.7)	0.257
Congestive Heart Failure	4 (10)	12 (18.5)	0.187
Atrial Fibrilasyon	6 (15)	4 (6.2)	0.125
Prior stroke	4 (10)	5 (7.7)	0.381
Family history of stroke	2 (5)	8 (12.3)	0.187

SEC: spontaneous echo contrast

Discussion

Recent epidemiological studies have shown a significant increase in the global incidence of first-ever stroke, stroke, and stroke-related mortality and in disability-adjusted life-years (DALYs) in adults aged 20-64 years as a result of increased prevalence of metabolic disorders associated with poor lifestyle practices [4,11]. Additionally, the incidence of ischemic stroke in deaths associated with DALY loss and stroke has been shown to increase by 1.4-1.8 times over the last 25 years [12].

It is widely known that stroke is more common in men than in women and the association between stroke and gender shows age-related differences. Additionally, stroke has been shown to be more prevalent in women aged 35-44 years and ≥ 85 years than in men of the same ages [13]. In our study, most of the patients were men aged less than 55 years.

Recent studies have indicated that poor lifestyle practices, in addition to commonly known stroke-related risk factors, play a key role in the development of stroke in young adults [14-16]. In our study, smoking was revealed as the most prevalent risk factor in men and was also found to be a significant risk factor for men compared to women.

Literature indicates that smokers have two-to-four-fold increased risk of stroke compared to nonsmokers or individuals who had quit smoking more than 10 years prior [17]. Moreover, the risk of

stroke increases with the amount of smoking (15). On the other hand, passive smoking is also a major risk factor for stroke and adult passive smokers have a 30% higher risk of stroke compared to non-exposed adults [18]. Meaningfully, the risk of stroke increases with the dose of exposure to passive smoking [19]. The chemical substances in tobacco smoke increase the production of reactive oxygen species (ROS) that cause endothelial dysfunction and inflammation, thereby accelerating atherosclerosis. Moreover, cigarette smoking increases platelet aggregation and also leads to elevated hematocrit and carboxyhemoglobin levels and to decreased high-density lipoprotein (HDL) levels via fibrinogen synthesis [17]. In our study, cigarette smoking was found to be a significant risk factor particularly for men, as consistent with the literature.

In a Tunisian study, Kefi et al. also found cigarette smoking as the most prevalent risk factor in their patients, although they performed no gender-based analysis [20]. In a Korean study, Kwon et al. evaluated young adults with stroke and also found that cigarette smoking was the most important risk factor among the patients. The authors also noted that the prevalence of smoking was significantly higher in men compared to women [21]. In a study conducted in a Greek population, Spengos et al. also reported that cigarette smoking was the most prevalent and the most important risk factor and also was more prevalent in men compared to women [22]. In a German study, Aigner et al. evaluated young adults with stroke and indicated that cigarette smoking was a more prevalent risk factor in men compared to women and was a more important risk factor in adults aged 45-55 years compared to individuals in younger age groups [23]. A previous case-control study by O'Donnell et al. found that cigarette smoking was more prevalent in young adults with stroke compared to old-age individuals (16). Aigner et al., in contrast to O'Donnell et al., did not compare young adults (18-55 years) with old adults (≥ 55 years) in terms of stroke risk, although they compared the subgroups of the young-adult group with each other [23].

In our study, the incidence of MI was significantly higher in men compared to women. The reported significant risk factors associated with ischemic stroke include a history of acute MI within the last four weeks and rarely seen cardiac diseases such as dilated cardiomyopathy, rheumatic valve disease, PFO, and mitral stenosis [24]. Putaala et al. evaluated a large cohort of 1,008 young patients with stroke and, in a similar way to our study, found a significantly higher incidence of MI in men compared to women [25]. Spengos et al. reported similar findings in a Greek population [22], whereas a Polish study by Lasek-Bal et al., unlike our study, found that the incidence of MI was significantly higher in women than in men [26].

In our patients, the incidence of mitral stenosis was significantly higher in women compared to men. Nevertheless, we found no study in the literature that performed a gender-based analysis for the incidence of mitral stenosis in young patients with stroke.

The incidence of DM in our patients was significantly higher in men compared to women. Numerous studies have indicated that the presence of DM and prediabetes increases the risk of ischemic stroke by 1.4-6 times. DM is an early-onset and fast-progressing disease triggering early atherosclerosis and leads to a significant

increase in the risk of stroke in individuals aged less than 65 years as well [27]. In a similar way to our study, the studies by Spengos et al. [22], Aigner et al. [23], and Putaala et al. [25] reported that the incidence of DM was significantly higher in young men with stroke compared to women [22]. In contrast, Lasek-Bal et al. found that the incidence of DM was significantly higher in young women with stroke compared to men [26].

Conclusion

Both the present study and numerous studies around the world indicated that modifiable lifestyle-related risk factors are the most common cause of stroke in young adults. The disability in young adults, who are in their productive ages, leads to more serious outcomes compared to that of old-age individuals. Accordingly, identification of novel risk factors in addition to the known modifiable lifestyle-related risk factors and investigation of gender-based differences with regard to these risk factors are of paramount importance both for primary and secondary protection in atherothrombotic diseases. Meaningfully, these investigations are also highly important for the prevention of stroke in the Turkish population as well, which is dominated by individuals aged 18-55 years. Future studies with larger patient populations are needed to identify further risk factors and precautions for stroke in young adults.

Competing interests

The authors declare that they have no competing interest.

Financial Disclosure

There are no financial supports.

Ethical approval

This study was approved by the Institutional Ethics Committee and conducted in compliance with the ethical principles according to the Declaration of Helsinki.

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