SUBTYPES OF ISCHEMIC STROKE IN DIFFERENT AGE GROUPS AMONG YOUNG ADULTS

Canan Togay IŞIKAY, Deniz TUNCEL, Nermin MUTLUER,

Ankara University School of Medicine Department of Neurology, ANKARA

SUMMARY

Purpose: The studies concerning stroke in young adults usually included the patients under the age of 45 years. The aim of this study was to compare the risk factors and subtypes of stroke between two different age groups among young adults aged <45 years.
Material and Method: The files of 100 patients who were admitted with acute stroke or transient ischemic attacks (TIA) and aged 18 to 45 years were evaluated retrospectively. Patient data including stroke risk factors, clinical signs, and the results of laboratory and radiological examinations were recorded. The patients with ischemic stroke were divided into two subgroups; patients between the ages of 18-30 (Group I) and those aged over 30 years (Group II). Fisher's exact chi-square and Student t tests were used for statistical analysis.
Results: There were 56 women and 44 men. Eleven patients had hemorrhagic and 89 patients had ischemic stroke or TIA. Fifteen of patients with ischemic stroke were 18-30 years of age, and 74 patients aged over 30 years. Smoking, alcoholism and ischemic stroke due to large artery atherosclerosis or small vessel occlusion were more common in men, while ischemic stroke due to uncommon causes was detected only in women ($p<0.05$). The proportion of ischemic stroke due to cardioembolism and uncommon causes was higher in Group I, whereas stroke due to atherosclerotic vasculopathy predominated in the 31-45 year old group ($p<0.05$).
Conclusions: Our results showed that stroke causes in young adults aged over 30 years significantly differ from those in 18-30 year old patients. The 31-45 year old patients seem to have ischemic stroke due to large artery atherosclerosis and small vessel occlusion as common as the elderly.
Key Words: Stroke, young adults, etiology, risk factors

FARKLI YAŞ GRUPLARINDAKİ GENÇ ERİŞKİNLER ARASINDA İSKEMİK İNME ALT TİPLERİ

Amaç: Genç erişkinlerde inme ile ilgili çalışmalar genellikle 45 yaşın altındaki hastaları içerir. Bu çalışmanın amacı; 45 yaşın altında, iki farklı yaş grubundaki genç erişkinler arasındaki, risk faktörlerini ve inme alt tiplerini karşılaştırmaktı.
Gereç ve Yöntem: Akut inme ya da geçici iskemik atakla gelen (GİA) ve 18-45 yaşları arasında olan 100 hastanın bilgileri; geriye dönük olarak değerlendirildi. İnme risk faktörleri, klinik bulguları ve laboratuar ve radyolojik sonuçları içeren hasta bilgileri kaydedildi. İskemik inmeli hastalar iki alt tipe bölündü; 18-30 yaşları arasında olanlar (Grup I) ve 30 yaşın üzerinde olanlar (GrupII). İstatistik analiz için Fisher'ın ki-kare ve Student t testi kullanıldı.
Bulgular: Elli altı kadın ve 44 erkek vardı. On bir hasta hemorajik ve 89 hasta iskemik inme ya da GİA'tı. İskemik inmeli hastaların 15 tanesi 18-30 yaşları arasında, ve 74 tanesi 30 yaşın üzerindeydi. Sık olmayan nedenlere bağlı iskemik inme yalnızca kadınlarda bulunurken; sigara içme, alkolizm ve büyük damar aterosklerozunun ya da küçük damar tıkanıklığının neden olduğu iskemik inme, erkeklerde daha sıktı ($p<0.05$). Kardiyoembolizm ve sık olmayan nedenlere bağlı iskemik inme Grup I'de daha fazla orandaydı; halbuki aterosklerotik vasküler patolojiye bağlı inme, 31-45 yaş grubunda daha belirgindi ($p<0.05$).
Sonuç: Bizim sonuçlarımız; genç erişkinlerde inme nedenlerinin; 30 yaş üzerindekilerde, 18-30 yaşındaki hastalardan anlamlı olarak farklı olduğu göstermiştir. 31-45 yaşındaki hastalarda; büyük damar aterosklerozunun ve küçük damar tıkanıklığının neden olduğu iskemik inme, yaşlılarda ki kadar sıklıkta görülmektedir.
Anahtar Sözcükler: İnme, genç erişkinler, etiyoloji, risk faktörleri

INTRODUCTION

Stroke in the young is still a serious cause of morbidity and mortality. Recent series showed that the young adults occupy about 10% of general stroke population (1-5). However, higher proportions from 19% to 30% were reported in the developing countries (6,7).

Several studies have shown that the risk factors and etiology of stroke in young adults differ from those in the elderly. In the young, cardioembolism and nonatherosclerotic causes are relatively important causes of ischemic stroke as compared to atherosclerotic vasculopathy and small artery occlusion (1,8-10). The importance of vascular risk factors and atherosclerosis increases with advancing age (1,4,11). In young women; valvular heart diseases, migraine, pregnancy

Yazışma Adresi: Deniz Tuncel MD Birlik Mahallesi 5. Cadde No: 27/3 06100 Ankara/Turkey Phone: +90 312 495 85 57 Fax: +90 312 310 63 71 E-mail: tuncedeniz@hotmail.com
Geliş Tarihi: 03.12.2003 **Kabul Tarihi:** 10.03.2004

Received: 03.12.2003 **Accepted:** 10.03.2004

and oral contraceptive use play important role in the development of stroke (1,12,13). Etiology of stroke cannot be clarified in almost one third of patients aged <45 years, although they are examined thoroughly by laboratory and radiological imaging methods (4,14).

Most of the studies concerning stroke in young adults included the patients aged 18 to 45 years, but did not attempt to categorize these patients in different age groups. In this study, we aimed to assess the risk factors and subtypes of stroke in different age groups among young adults.

MATERIAL AND METHODS

Medical records of 100 consecutive patients who were under the age of 45 years and admitted to our clinic with the diagnosis of acute stroke or TIA were reviewed retrospectively. Patients with venous infarctions, subarachnoid hemorrhage, and cerebral hematoma due to trauma were excluded. The patient data, including medical history, risk factors for stroke, neurological findings, and the results of radiological and laboratory examinations were recorded. Ischemic stroke subtypes were determined according to the TOAST (Trials of Org 10172 in Acute Stroke Treatment) criteria as follows: 1-Large artery atherosclerosis, 2-Small vessel disease, 3-Cardioembolism, 4-Uncommon causes, 5-Undetermined etiology (cryptogenic).

The patients with ischemic stroke were divided into two groups. Group I included the patients aged ≤30 years, while Group II was consisted of those with the age over 30 years. These two subgroups were compared in terms of risk factors and subtypes of stroke. Statistical analysis was made by Student t test for numerical variables and Fisher's exact chi-square test for nominal variables, and p values <0.05 were considered significant.

RESULTS

The mean age±SD of patients was 37.4±7.8 with a range between 18-45 years. There were 56 women with a mean age ±SD of 36.0±8.1 and 44 men with a mean age±SD of 38.2±6.8 years. Eleven patients had hemorrhagic and 89 patients had ischemic stroke or TIA. Fifteen of patients with ischemic stroke were 18-30 years of age (Group I), and 74 patients aged over 30 years (Group II). Two genders were equally present in Group II, while Group I was consisted of four men (26.7%) and eleven women (73.3%).

Smoking and chronic alcoholism were more frequent among men than women (p<0.001 and p<0.05), while other risk factors did not show significant difference between two genders. Three men in Group II had peripheral artery diseases. The prevalence of smoking was higher in Group II, while pregnancy/postpartum period and mechanic valve were found more frequent in Group I (p<0.05). The risk factors for ischemic stroke in two genders and age groups were shown in Table 1.

Ischemic stroke due to large artery atherosclerosis and small vessel occlusion predominated in men, while cardioembolic stroke was significantly more frequent among women (p<0.005). Uncommon causes of ischemic stroke were not found in males, while this subtype of stroke affected almost one third of women. None of the patients in Group I had ischemic stroke or TIA due to large artery atherosclerosis or small vessel occlusion (Table 2). Cardioembolism and uncommon causes occupied a relatively large proportion of stroke subtypes in Group I compared to Group II (p<0.005). Uncommon causes of ischemic stroke were shown in Table 3. Other possible causes of ischemic stroke were excluded in these cases.

Table 1: Risk factors for ischemic stroke in two genders and age groups

Risk factors (%)	Group I	Group II	Women	Men	Total
Hypertension	13.3	38.4	29.8	39	34
Diabetes	6.7	11	10,6	9,8	10,2
Hyperlipidemia	13,3	35,6	31,9	31,7	31,8
Smoking	20	54,2	27,7	72,5	48,3
Alcoholism	-	6,8	-	12,2	5,7
Family history	-		19,2	10,6 22	15,9
Migraine	6,7	-	2,1	-	1,1
Pregnancy	28,6	1,6	10,6	-	6,5
OC use	-	7,9	10,6	-	6,5
Mechanic valve	26,7	8,6	17	5,3	11,8

OC: oral contraceptive

Table 2: Distribution of ischemic stroke subtypes in two groups and genders

	Group I (%)	Group 2 (%)	Women (%)	Men (%)	Total
LAA+SVD	-	48.6	27.1	56.1	40.4
CE	40	21.6	31.3	17.1	24.7
UC	40	10.8	29.2	-	15.7
Cryptogenic	20	18.9	12.5	26.8	19.1

LAA: Large artery atherosclerosis, SVD: Small vessel disease, CE: Cardioembolism, UC: Uncommon causes

Table 3: Uncommon causes of ischemic stroke

Uncommon causes	Patients (n)
Pregnancy/postpartum	5
Oral contraceptive use	4
Migraine	1
Essential thrombocytosis	1
Sneddon syndrome	1
Fibromuscular dysplasia	1
Moyamoya disease	1

The most common localization of infarctions showed by cranial CT or MRI was partial or total anterior circulation (47 patients), followed by posterior circulation (19 patients), and multiple infarctions (12 patients). Bilateral carotid duplex ultrasound was performed in all patients with the diagnosis of TIA or ischemic stroke. High-grade stenosis (>70%) or occlusion of ICA was observed in 11% of these patients.

Transthoracic echocardiography (TTE) was performed in 62 of 89 patients with the diagnosis of TIA or ischemic stroke. Twenty six studies showed abnormal findings, including valve diseases (17 patients), left atrium dilatation (6 patients), hypokinetic or akinetic ventricular segment (6 patients), mitral valve prolopsus (2 patients), mitral annulus calcification (2 patients) and left ventricular aneurysm (1 patient). Ten patients had undergone heart valve replacement. Transeosophageal echocardiography (TEE) was performed in 14 patients. TEE showed intracardiac thrombus in 5 patients and interatrial septum aneurysm in one patient. None of these studies revealed patent foramen ovale. The patients shown to have intracardiac thrombus by TEE had mitral stenosis, left atrium dilatation or akinetic ventricular segment in TTE examinations.

Cerebral angiography was performed in 27 patients, and significant stenosis or occlusion of intracranial or extracranial cerebral arteries were observed in 10 patients. Two angiographies showed Moyamoya disease and fibromuscular dysplasia. One of the patients with cerebral hematoma had arteriovenous malformation in the cerebral angiography.

There were eleven patients with cerebral hematoma (three men, eight women). Two patients had cerebral hematoma due to thrombocytopenia associated with idiopathic thrombocytopenic purpura, one patient was on warfarin with therapeutic level of INR, and one patient was shown to have arteriovenous malformation in the cerebral angiography. Six patients were over 30 years of age and had untreated hypertension.

DISCUSSION

The incidence of large artery atherosclerosis and small vessel occlusion has been reported between 7-30% for ischemic stroke patients under the age of 50 years (15). We found a higher frequency for these subtypes of stroke (40.4%) in our patient population, which might be explained with the high proportion of patients aged 30-45 years (84%).

As in previous studies, in our series women predominated among patients aged ≤30 years, mainly because of the more frequent presence of nonatherogenic risk factors, such as oral contraceptive use, pregnancy, and rheumatic heart disease (4,12,13). Early atherothrombotic disease appeared to predominate among patients aged over 30 years, thus making this group more similar to the general population.

In this study, none of the patients with age ≤30 (Group I) had ischemic stroke or TIA due to large artery atherosclerosis or small vessel occlusion. Similar results were also obtained by other authors (1). Kwon et al reported that all the patients having atherosclerotic stroke were aged above 35 years, and most of them were men (1). There is an agreement on the role of atherosclerosis in men over the age of 35 years (8). The absence of stroke due to large artery atherosclerosis or small vessel occlusion in Group I may also be related with higher proportion of females in this group. Vascular risk factors, such as smoking and chronic alcoholism were less frequent among women compared to men.

In previous series, the proportion of cardioembolism ranged from 8% to 32.7% (1,13,14). The highest proportion of cardioembolic stroke was reported in the Nothern Sweden Study. The authors stated that the high incidence of cardioembolism mainly resulted from using advanced cardiac evaluation methods including TEE (14). Since TEE was performed in a small number of our patients, patent foramen ovale and right to left atrial shunt might have been under-recognized in this group. In our study, rheumatic heart disease was the major determinant of cardioembolic stroke and was more prevalent among women. In contrary to previous studies, cardioembolic stroke was significantly more prevalent among patients with

age ≤30 (8,14).

Uncommon causes of ischemic stroke, such as migraine, fibromuscular dysplasia, essential thrombocytosis, Moyamoya disease, and Sneddon syndrome were observed only in women and especially among patients ≤30 years of age. We have not seen any patients with ischemic or hemorrhagic stroke associated with illegal drug use; a finding consistent with low incidence of illegal drug use in this country.

As further hematological tests, including homocysteine, antiphospholipid antibodies and activated protein C resistance, and cerebral angiography were not performed in all patients, uncommon causes, such as hypercoagulopathy, arterial dissection, and other nonatherosclerotic vasculopathies might have been undetermined in our study group. Arterial dissection has been reported as a relatively common cause for ischemic stroke among young adults (>%10) (1,13,14). The importance of the deficiency of protein C, protein S or antithrombin III and activated protein C resistance in arterial stroke is still controversial (14). The etiology of stroke in young adults remains unknown in almost one third of the cases, despite extensive diagnostic investigations (4,14).

The patients with intracerebral hematoma comprised %11 of our study population. Marini et al reported that the prevalence of intracranial hemorrhage among young adults was high (42.7%) compared to the elderly population (15.7%) (8). The low rate of intracerebral hematoma in this series was explained by exclusion of cases with subarachnoid hemorrhage and cerebral hematoma due to trauma.

Although there are several studies concerning stroke subtypes and risk factors in the young, there are only a few studies comparing different age groups among young stroke patients (1,4,11). When the causes of stroke in the young are broken down by age, atherosclerosis becomes increasingly prominent from the 15-30 year age group (2%) to the 31-45 year group (30-35%). This increase was more remarkable in our study group; since none of the patients in the 18-30 year old group had stroke due to atherosclerotic vasculopathy, while 48.6% of patients in the 31-45 year old group suffered that kind of stroke. Therefore, we propose that stroke patients younger than 31 years of age should be evaluated separately from those aged >30 years.

KAYNAKLAR

1. Kwon SU, Kim JS, Lee JH, Lee MC. Ischemic stroke in Korean young adults. Acta Neurol Scand 2000; 101: 19-24.
2. Bogousslavsky J, Pierre P. Ischemic stroke in patients under age 45. Neurol Clin 1992; 10: 113-124.
3. Neto JIS, Santos AC, Fabio SR, Sakamoto AC. Cerebral infarction in patients aged 15 to 40 years. Stroke 1996; 27: 2016-2019.
4. Carolei A, Marini C, Ferranti E, Frontoni M, Prencipe M, Fieschi C, and the National Research Council Study Group. A prospective study of cerebral ischemia in the young. Stroke 1993; 24:362-367.
5. Nencini P, Inzitari D, Baruffi MC, Fratiglioni L, Gagliardi R et al. Incidence of stroke in young adults in Florence, Italy. Stroke 1988; 19: 977-981.
6. Radhakrishan K, Ashok PP, Sridharan R, Mousa ME. Stroke in the young: incidence and pattern in Benghazi, Libya. Acta Neurol Scand 1986; 73: 434-438.
7. Kittner SJ, McCarter RJ, Sherwin RW, Sloan MA, Stern BJ et al. Black-white differences in stroke risk among young adults. Stroke 1993; 24: 113-115.
8. Chant H, McCollum C. Stroke in young adults: The role of paradoxical embolism. Thromb Haemost 2001; 85: 22-29.
9. Marini C, Totaro R, De Santis F, Ciancarelli I. et al. Stroke in young adults in the community-based L'aquila registry: Incidence and prognosis. Stroke 2001; 32: 52-56.
10. Williams LS, Garg BP, Cohen M, Fleck JD, Biller J. Subtypes of ischemic stroke in children and young adults. Neurology 1997; 49: 1541-1545.
11. Bogousslavsky J, Regli F. Ischemic stroke in adults younger than 30 years of age. Arch Neurol 1987; 44: 479-82.
12. Tzourio C, Tehindrazanarivelo A, Iglasias S, Alperovitch A, Chedru F, d' Anglejan-Chatillon J, Bousser M-G. Case-control study of migraine and risk of ischemic stroke in young women. BMJ 1995; 310: 830-833.
13. Martin PJ, Enevoldson TP, Humprey PRD. Causes of ischemic stroke in the young. Postgrad Med J 1997; 73: 8-16.
14. Kristensen B, Malm J, Carlberg B, Stegmayr B, Backman C, Fagerlund M, Olsson T. Epidemiology and etiology of ischemic stroke in young adults aged 18 to 44 years in Nothern Sweden. Stroke 1997; 28: 1702-1709.
15. Blecic S, Bogousslavsky J. Stroke in young adults. Ed. Barnett HJM, Mohr JP, Stein BM, Yatsu FM. Stroke pathophysiology, diagnosis, and management. Churchill Livingstone, third edition, Chapter 42: 1001-1013.