CLINICAL INVESTIGATION

Cerebrovascular Risk Factors and Stroke Subtypes in Different Age Groups: A Hospital-Based Study

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Abstract: We prospectively studied the characteristics of 401 patients with first-ever-in-a lifetime stroke who have been admitted consecutively into stroke care unit. During the evaluation of distribution according to age, patients were divided into 7 age groups with 10-year intervals. It was determined that ischemic stroke was mostly seen in the age group 71-80 (32.2%) and the age group 61-70(28.2%). The major risk factor of ischemic stroke was hypertension, followed by diabetes mellitus, ischemic heart disease, smoking and hypercholesterolemia. The three most frequent etiologic categories were small-vessel disease, atherosclerotic large vessel disease and cardioembolism. The anatomical distribution of ischemic stroke were made according to the Oxfordshire Community Stroke Project. The distribution of patients in term of vascular territories was most frequently seen in lacunar infarction. It was determined that lacunar infarcts were more significant in males whereas posterior circulation infarcts were more significant in females. When the distribution of vascular territories was evaluated in terms of risk factors, it was seen that hypertension and ischemic heart diseases were significant in total anterior circulation infarcts, and transient ischemic attack was significant in posterior circulation infarcts.

Key Words: Stroke, age groups, etiology, vascular territory

Introduction

Stroke is a significant healthcare problem in many countries with major morbidity and mortality rates. The most promising strategy to reduce the worldwide burden of stroke is effective stroke prevention. However, the success of this strategy depends on the recognition and control of all-important causal and modifiable risk factors (1).

The diagnosis of ischemic stroke subtype in the first few hours after hospital arrival has traditionally been performed through educated guesswork. Deductions regarding neuroanatomic localization involves vascular territory, and etiologic vascular mechanisms are reached on the basis of clues in the clinical history and the pattern of deficits on physical examination. This conventional approach has substantial accuracy limitations, even when stroke subtype classification criteria are used. Proper identification of causes of stroke is important for clinical practice and research studies. Many studies have been performed in order to determine the incidence, risk factors and proper classification of stroke subsets. However, it was observed that there were important variations among results of the published series during the classification of stroke. One of the reasons is the fact that some vary in terms of patient population and some vary in terms of diagnostic criteria, resulting in problems in specific etiology in the classification of strokes. Some studies have been performed based on hospital records and some on the general population (2-5).

The aim of this study was to analyze the underlying vascular risk factors and causes of ischemic cerebrovascular disease in a hospital-based study in İstanbul-Turkey.

Material and Methods

Study design and setting

We present the profile of risk factors, etiologic and clinical data of 401 consecutive patients with first-ever-in-a lifetime stroke (ischemic cerebrovascular disease), admitted to the Haydarpaşa Numune Educational and Research Hospital (HNERH) (İstanbul, Turkey) between January 1998 and September 2002. A prospective hospital-based registry using medical records for hospitalized subjects of data of all stroke patients has been used. Local ethical committee permission regarding this study was obtained.

Neuroradiological Analyses and laboratory

All patients were examined by a neurologist and they had brain Computerized Tomography(CT) and/or Magnetic Resonance Imaging (MRI) (when no lesion was seen in CT, we performed MRI including T1, T2 and proton weighted images, 10 mm thick slices, for confirming infarct areas), Electrocardiography (ECG), and transthoracic Echocardiography (ECO) and high resolution B-mode Doppler Ultrasonography (DUSG) investigations. A brain CT scan was obtained in all patients. MRI was performed in 156 patients (38.9%) and MR-Angiography (MRA) in 80 patients (19.9%). Some patients underwent both procedures. The first CT imagings were performed in the first 12-24 hours of stroke. Detection rate of the lesion during the first few hours was 49.8%. MRI and MRA investigations were performed during the first 72 hours of hospitalization.

Stroke was defined as a clinical syndrome characterized by rapidly developing clinical symptoms and/or signs of focal and, at times, global loss of brain function , with symptoms lasting >24 hours or leading to earlier death, and with no apparent cause other than that of vascular origin (6). Ischemic stroke was defined as a stroke with either a normal CT scan or evidence of a recent infarct in the clinically relevant area of the brain on a computed tomography or MRI performed within 72 hours of the event. Patients with cerebral hemorrhage or cerebral venous thrombosis were not included.

Definition of risk factors, etiology and localization

Clinical information included age, sex and risk factors. We used the following definitions for vascular risk factors. Patients were estimated as hypertensive if the average systolic blood pressure was ≥140mmHg and average diastolic BP was ≥90 mmHg or if they were taking antihypertensive medication. 61 (25.3%) of the patients were uncontrolled hypertensives and 180 (74.6%) of the patients were under anti-hypertensive treatment. Diabetes Mellitus (DM) was defined in two ways; (1) by history if the patient had this diagnosis and (2) if there were at least two fasting glucose concentrations of ≥140 mg/dl. Patients with diabetes mellitus either had dietary therapy or took oral antidiabetics (80.5%) or insulin medication (19.4%) at the time of admission. While 83% of the patients had been diagnosed as DM previonaly, 16% were newly diagnosed. Hypercholesterolemia (HC) was diagnosed if the patient had this diagnosis and was on treatment or if a fasting cholesterol level was >240 mg/ dl. Isolated hypertriglyceridemia was not included in the risk factor profile. Ischemic Heart Disease (IHD) was defined by a history of angina or myocardial infarction. A patient was defined as a smoker if he/she was a current smoker in the last 12 months. Transient ischemic attack(TIA) was defined as an acute loss of ocular or focal cerebral function lasting less than 24 hours that was presumed to be due to ischemic vascular disease. In addition, the patients were questioned about alcohol consumption and other similar risk factors (history of migraine, oral contraceptive usage, etc.).

Patients were divided into 7 age groups with 10-year intervals during the evaluation of distribution according to age groups.

On the basis of clinical evaluation and results of imaging studies, the neurologist classified all strokes into 6 major etiologic subtypes according to the following criteria (7, 8):

1. Large-artery disease(LAD): ischemic stroke with

    (a) evidence of extracranial or intracranial occlusive large-artery disease,

    (b) no cardioembolic source, and

    (c) clinical opinion that the most likely cause of brain infarction was atherothrombosis involving the aortic arch, carotid arteries or major branches, or vertebral, basilar, and posterior cerebral arteries;

2. Small-artery disease (SAD, lacuna): ischemic stroke with

    (a) consciousness and higher cerebral function maintained plus

(b) One of the classic lacunar syndromes or nonlacunar small-artery syndromes, and

(c) CT or MRI brain scan, performed within 3 weeks of symptom onset that is either normal or shows a small deep infarct in the basal ganglia, internal capsule, or brain stem;

3. Cardioembolic (CE) disease: ischemic stroke with

(a) a major cardioembolic source (atrial fibrillation, mitral stenosis, atrial mixoma, prosthetic valve, etc) plus

(b) no definite evidence of occlusive large-artery disease, and

(c) clinical opinion that the most likely cause of brain infarction was embolism from the heart;

4. Mixed causes (if together with the three steps listed above)

5. Unknown (stroke of undetermined etiology)

6. Vasculopathy

The anatomical distribution of ischemic stroke were classified according to the Oxfordshire Community Stroke Project. The Oxfordshire classification method contains 4 subtypes based on anatomic distribution of infarcts and corresponding clinical symptoms:(1) lacunar infarcts (LIs), (2) posterior circulation infarcts (PCIs), (3) partial anterior circulation infarcts (PACIs), and (4) total anterior circulation infarcts (TACIs) (9).

All of the data obtained were evaluated according to age, gender, risk factors, etiologic subgroups, and clinical subtypes of ischemic stroke.

Statistical Analysis

In this study, statistical analyses were made by a biostatistics specialist using the package program GraphPad Prisma V.3. X-square method was used in the evaluation of data, the comparison of descriptive statistical methods (average, standard deviation), and qualitative data. Significance was found to be P < 0.05, and confidence range 95%.

Results

The patients included in the study composed of 199 male (49.6%) and 202 female (50.4%) patients. The median age was determined as 64.23 ± 13.29 and the age group ranged between the ages 22-97. No significance was determined in terms of sex.

The percentages of 7 age groups classified according to 10 years   intervals are seen in Figure 1. It was determined that patients suffering from ischemic stroke were mostly seen in the age groups 71-80 and 61-70.

The frequencies of the various risk factors of ischemic stroke among patients are demonstrated in Table 1. Stroke risk factors were hypertension in 60.1 % of the patients, ischemic heart disease in 40.1 %, hypercholesterolemia in 29.2%, current smoking in 31.4%, diabetes mellitus in 21.4%, TIA in 4.2%, alcohol consumption in 11% and other risk factors in 1% overall, respectively. Hypertension, ischemic heart disease, smoking, hypercholesterolemia, and DM were listed as the most significant risk factors. When risk factors were evaluated in terms of sex, it was determined that HT,
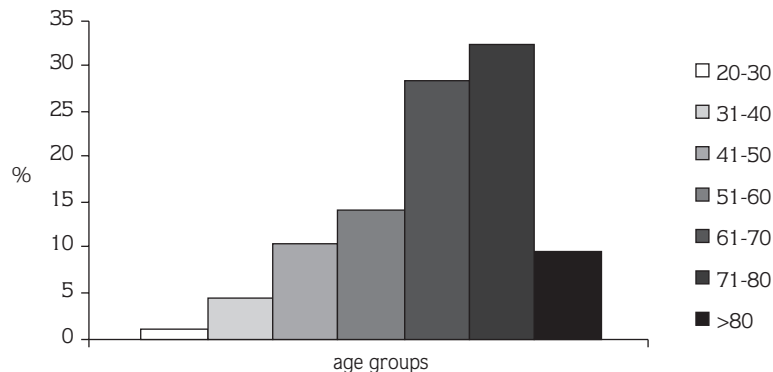

Figure 1. Distribution of patients according to age groups:
*Patients were most often between ages 61-70 and 71-80 according to age group.

Table 1. Distribution of risk factors according to sex.

	Total(%)	Female	Male	χ^2	P
Hypertension	60,1	105 (42.5%)	136 (55%)	χ^2 8.86	P < 0.001*
Diabetes mellitus	21,4	41 (47.6%)	45 (52.3%)	χ^2 0.16	P > 0.05
IHD	40,1	67 (41.6%)	94 (58.3%)	χ^2 0.50	P > 0.05
TIA history	4,2	7 (41.1%)	10 (58.8%)	χ^2 6.70	P < 0.01*
Hypercholesterolemio	29,2	57 (48.7%)	60 (51.2%)	χ^2 0.50	P > 0.05
Smoking	31,4	29 (23%)	97 (76%)	χ^2 54.57	P < 0.0001*
Alcohol	11	5 (11.3%)	39 (88.6%)	$\chi^2$30.29	P < 0.0001*

TIA, smoking and alcohol consumption were seen significantly more frequently in males than in females (Table 1).

The distribution of patients in terms of vascular territories was as follows; seven percent of patients had TACIs, 67.8% of patients had LIs, 19.7% of patients had PACIs, and 11.2% of patients had PCIs. In our group when evaluated according to the anatomical distribution, LI was the leading type, followed by PACI distribution enfarct. When infarct settlement was reviewed according to sex, it was determined that LIs were more significant in males (P < 0.05) while PCIs were more significant in females (P < 0.05). No statistically significant difference with sex was determined in other localizations (Table 2).

When distribution of vascular territories was evaluated in terms of risk factors, it was seen that hypertension (P < 0.05) and ischemic heart disease (P < 0.001) were significantly present in TACIs, and that TIA was significantly present in PCIs (P < 0.0001) (Table 3).

The patients were classified according to etiologic subgroups (Table 4). Large artery diseases (LAD) were diagnosed in 113 patients (28.2% of the cases), mostly in those aged over 50 years (52 cases). Small artery diseases (SAD) were found in 151 patients (37.7% of the cases), mostly in those aged between 41-60 years (104 cases). Cardioembolic (CE) stroke was diagnosed in 78 patients (19.5% of the cases), mostly in patients aged between 40-60 years (54 cases). Mixed etiology was found in 27 patients (6.7%) and unknown etiology was noted in 21 patients (5.2%) and vasculopathy was found 11 (2.7%) patients.

When vascular territories were evaluated in terms of etiologic subgroups, it was determined that infarct was seen more frequently TACIs (50%) and less frequently PCIs (8.8%) in cardioembolism; and more frequently LIs (37.5%) and less frequently TACIs (10.7%) in SVD. It was seen that the other etiologic subgroups did not vary in terms of vascular territories (Table 5).

Discussion

This hospital-based study was performed prospectively in İstanbul, Turkey. A hospital-based, systematical epidemiological study of the Turkish population profile had been previously done in our country, in which patients with cerebral infarction, cerebral hemorrhage and subarachnoid hemorrhage were chosen and clinical data were examined (10). Also in year 2000 a hospital-based multi-centric stroke trial (MST) with the participation of twenty-four medical faculties and sixteen government hospitals thoughout Turkey has been made in order to determine the distribution of cerebrovascular (ischemic and hemorrhagic) diseases and risk factors (11). On the other hand, we examined clinical features and etiological subgroups according to age groups and gender distribution of patients only with the diagnosis of ischemic cerebrovascular disease.

Patients were most often between ages 61-70 and 71-80 according to age group distribution, and there was no difference according to sex. This distribution is consistent with the studies that have been done up to present. Yearly incidences according to age groups were 1.7-3.6 /1000 people over the age of 55-64, 4.9-8.9/1000 people between ages of 65-74 and 13.5-17.9/1000 people over the age of 75 among the studies that have been reported before (12-14). In a multi-centric trial previously performed in our country,

Table 2. Distribution of patients according to vascular territories and sex.

	Total n(%)	Female	Male	χ^2	P
TACI	28 (7%)	11 (39.2%)	17 (60.7%)	χ^2 1.28	P > 0.05
LI	272 (67.8%)	124 (45.5%)	148 (54.4%)	χ^2 5.51	P < 0.05*
PACI	79 (19.7%)	46 (58.2%)	33 (41.7%)	χ^2 2.91	P > 0.05
PCI	45 (11.2%)	29 (64.4%)	16 (35.5%)	χ^2 4.43	P < 0.05*

Table 3. Risk factors related to vascular territories.

	TACI(%)	LI(%)	PACI(%)	PCI(%)	χ^2	P
HT	75	61	50.6	51.1	χ^2 6.86	P < 0.05*
DM	25	20.2	20.2	22.2	χ^2 0.42	P > 0.05
TIA History	10.7	4.04	2.5	24.4	χ^2 29.96	P < 0.0001*
IHD	50	42.2	31.6	6.6	χ^2 24	P < 0.001*
Hypercholesterol	28.5	30.1	24.05	26.6	χ^2 1.20	P > 0.05
Smoking	25	29.04	35.4	37.7	χ^2 2.65	P > 0.05
Alcohol	10.7	11.02	11	8.8	χ^2 0.19	P > 0.05

Table 4. Distribution of etiologic subgroups according to sex.

	Total %	Female	Male	χ^2	P
CE	19,5	32 (41%)	46 (58.9%)	χ^2 4.47	P < 0.05*
LAD	28,2	65 (57.5%)	48 (42.4%)	χ^2 3.92	P < 0.05*
SAD(lacuna)	37,7	78 (51.6%)	73 (48.3%)	χ^2 0.39	P > 0.05
Mixed	6,7	10 (37%)	17 (62.9%)	χ^2 1.83	P > 0.05
Unknown cause	5,2	10 (47.6%)	11 (52.3%)	χ^2 2.10	P > 0.05
Vasculopathy	2,7	2 (18.1%)	9 (81.8%)	χ^2 4.47	P < 0.05*

Table 5. Etiologic subgroups related to vascular territories.

	TACI(%)	LI(%)	PACI(%)	PCI(%)	χ^2	P
CE	50	19.4	12.6	8.8	χ^2 22.30	P < 0.0001*
LAD	32	26.1	24.1	26.6	χ^2 2.25	P > 0.05
SAD	10.7	37.5	29.4	22.3	χ^2 13.55	P < 0.01*
Mixt	0.3	7.7	5.06	2.2	χ^2 2.72	P > 0.05
Unknown cause	0	1.8	1.26	4.4	χ^2 2.29	P > 0.05
Vasculopathy	0.3	3.6	8.8	2.2	χ^2 4.57	P > 0.05

ischemic stroke rate was determined as 51.6% over 64 years of age, and 48.4% under 64 (11). Among our patients ischemic cerebrovascular disease has been especially observed between 50-80 years of age and its frequency significantly decreased below 50 and over 80 years of age.

Hypertension was the primary risk factor for all stroke types, which is known to be a risk factor with the rate of 75-89 %. It is particularly a risk factor in small vessel disease and lacunar infarction. In diabetes mellitus, stroke risk increases by 2-5 times compared to non-diabetics (15-17). Hypercholesterolemia is considered a risk factor for ischemic stroke in some populations, but not in other populations (18,19). In our study, hypertension was the most prominent risk factor in patients, being present in 60.1% of the patients. Hypertension, ischemic heart disease, smoking, hypercholesterolemia, and DM were listed as the most significant risk factors. This data is consistent with most of the recent studies (20-22). In the first epidemiological study in our country carried out by Kumral et al (10), 63% HT, 37% hypercholesterolemia, 35% diabetes mellitus, 23% ischemic heart disease and 17% cigarette smoking were detected. The MST group has similarly determined these rates for our country as 62.7% for hypertension, 23.1% for DM, 18.8% for AF, 41.5% for hyperlipidemia, and 17% for heart disease(11).

In the studies carried out according to TOAST criteria, it was determined that large vessel disease incidence was 15.3-16%, cardioembolism 29-30.2%, and lacuna 16-25.8%. It was determined that large artery diseases were 2-4 times more frequent in male patients (23,24). We obtained similar data with these studies. SAD, LAD and CE in this order have been most often detected in etiological subgroups. In small artery disease, LIs were the most common (37.5%) and TACIs were the least common site of infarct; while in cardioemboli TACIs showed the most and PCIs the least statistically significant results, and no difference was detected for the location of infarction among other groups. The syndrome provide the clinician with an indication of the most likely underlying vascular lesion. TACI/PACI are likely to be caused by occlusion of the large cerebral arteries, and clinicians should be thinking about cardiac sources of embolism, or carotid and aortic atherosclerosis (9, 25). In accordance with this determination, we detected that CE (50%) and LAD (32%) were etiologically effective in TACIs. Previous studies reported that 41-43% of patients with TACI had either ipsilateral ICA occlusion or, greater than 80% stenosis, and 33-37% had a major cardiac source of embolism (26,27).

Lindgren et al. (26) reported that 19% of patients with PACIs had either ipsilateral ICA occlusion or greater than 8%0 stenosis, and 46% had a major cardiac source of embolism. Heinzeus et al. (27) reported that 28% of patients had greater than 50% stenos is of the ipsilateral ICA, and 33% had a major cardiac embolism. Although it is not meaningful statistically in PACIs, we most frequently met with SVD, LVD and CE, in that order.

In our cases, LAD and SAD were the most frequently etiologies of PCIs. Our data, which expressed that PCIs were most frequently related with LAD, CE and SAD, is similar to those of a previous study by Caplan and Tettenbourn (28). Caplan et al. have evaluated vertebrobasilar artery infarcts by comparing with the carotic artery system. They have determined that there is not much different from the carotic, system, large vessel disease was effective in 43%, small vessel disease 18%, cardiac embolism 19%, intraarterial embolism 20% in the vertebrobasilar system.

Symptomatic lacunas are probably most often the results of vessel occlusion due to complex SAD or microatheroma (29). Although an embolic mechanism is possible (30) there is a low frequency of severe carotid stenosis or any cardiac source of CE (26,31). LIs were most frequently observed in SAD in our study, followed by LAD and CE less frequently.

In our study, small artery disease (37.7%), atherosclerotic large artery disease (28.2%) and cardioembolism (19.5%) have been determined as the most significant etiologic subgroups. Large artery disease was significantly high in females whereas vasculopathy and cardioembolism were significantly high in males. Lacunar infarctions were significantly in relation with female, PCI were in relation with the male gender. No significant difference was determined between the other etiologic groups and clinical syndromes in terms of sex.

In summary, the findings obtained from our study are compliant with general literature data. Hospital-based studies of subtype-specific ischemic stroke incidence rates and risk factors provide a means of obtaining more accurately information for each ischemic stroke mechanism.

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