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Assessing Mortality in Patients with Acute Ischemic Stroke: A Turkish Cohort

Omer Jaradat[1], Haci Mehmet Caliskan[2], Asuman Celikbilek[3]

[1]Kırşehir Training and Research Hospital, Clinic of Emergency Medicine, Kırşehir, Türkiye
[2]Kırşehir Ahi Evran University Faculty of Medicine, Department of Emergency Medicine, Kırşehir, Türkiye
[3]Kırşehir Ahi Evran University Faculty of Medicine, Department of Neurology, Kırşehir, Türkiye

Abstract

Aim: Acute ischemic stroke (AIS) has a high morbidity and mortality. We aimed to investigate the etiologic types, involved vascular territory, and mortality rates of patients with AIS in a Turkish cohort.

Materials and Methods: The archive records of a total of 403 patients with AIS were included retrospectively. Medical histories, neurological examinations, and death dates were collected through the hospital automation system. Based on the clinical data and imaging features, all patients were etiologically categorized according to the the Trial of Org 10172 in Acute Stroke Treatment classification.

Results: The mean age was 72.3±12.4 years, with a slight female predominance at 50.4%. According to the Acute Stroke Treatment classification, the etiologic types of AIS patients were as follows: large-artery atherosclerosis at 50.6%, cardioembolism at 28.3%, small-vessel occlusion at 12.4%, undetermined etiology at 7.2%, and other determined etiology at 1.5%. Compared to the other vascular territories, the middle cerebral artery (MCA) was the most frequently involved territory (45.7%) and also had the highest mortality rate in older patients with AIS ($p<0.001$). When compared to inferior divisions, superior divisional infarctions had higher mortality for both right and left MCA strokes ($p<0.001$). Compared to male patients, female patients had significantly higher mortality rates at 0-30 days for internal cerebral artery stroke ($p=0.048$) and at all time periods for right MCA stroke ($p=0.046$).

Conclusion: We found that advanced age, being female, having right-sided and having superior divisional MCA infarctions were highly related to mortality in patients with AIS.

Keywords: Acute ischemic stroke, female, middle cerebral artery, mortality, TOAST

Introduction

Stroke is the second leading cause of death worldwide and a major cause of disability (1,2). Notably, 63% of stroke cases occur in people under the age of 70, challenging the perception that stroke is primarily a disease of the elderly (3). While stroke rates vary by region, ischemic strokes account for the majority of cases (4).

In more than 20% of patients with acute ischemic stroke (AIS), the underlying etiology remains unknown (1). Because of its high mortality and associated costs, identifying and preventing AIS is critical (5). Prevention is possible because most risk factors can be controlled, even in older adults. Several classification systems have been developed, with the most widely used being the Trial of Org 10172 in Acute Stroke Treatment (TOAST) (6). In this study, we aimed to retrospectively investigate the etiologic types, involved vascular territory, and mortality of patients with AIS in Kırşehir region, known as Central Anatolia.

Materials and Methods

Study Population

In the present study, the archival records of a total of 403 patients, aged between 20 and 85 years, who were admitted to the emergency department and diagnosed with AIS at Kırşehir Training and Research Hospital, Kırşehir, Türkiye between January

Corresponding Author: Asuman Celikbilek MD. Kırşehir Ahi Evran University Faculty of Medicine, Department of Neurology, Kırşehir, Türkiye
E-mail: asunebioglu@yahoo.com **ORCID ID:** orcid.org/0000-0002-2367-1128
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2019 and December 2021 (during the COVID-19 pandemic) were retrospectively reviewed. The study was approved by Kırşehir Training and Research Hospital, Kırşehir Ahi Evran University Faculty of Medicine Local Research Ethics Committee (decision number: 2022-02/19, date: 25.01.2022). Patients with hemorrhagic stroke, patients with transient ischemic attack, and those with missing data were excluded from the study.

Data Collection

Due to the retrospective nature of the study, we did not obtain informed consent from the included patients; most of whom were conservatively managed with antiaggregant and/or anticoagulant therapy. Demographic data included age and sex. Medical history, neurological examination, and date of death were collected through the hospital's automated system.

Cardiac evaluation, including standard 12-lead electrocardiogram (ECG), and transthoracic echocardiography and, if indicated, 24-hour ECG monitoring, was performed to rule out a possible cardiac source of cerebral embolism. Duplex scanning of the carotid and vertebral arteries performed during hospitalization was used to document any stenosis or plaque suggestive of atherothrombotic etiology. Patients with vertebrobasilar stroke were evaluated with computed tomography (CT) angiography of the brain and neck. Admission brain CT and diffusion-weighted magnetic resonance imaging were used to determine the involved vascular territory.

Based on clinical data and imaging features, all patients were etiologically categorized according to the TOAST classification, which included large-artery atherosclerosis, small-vessel occlusion, cardioembolism, other determined etiology, and undetermined etiology (6).

Statistical Analysis

Histograms and q-q plots were examined, and the Kolmogorov-Smirnov test was performed to assess the normality of the data. Values are expressed as frequencies (n) and percentages (%), means and standard deviations, or medians (minimum-maximum). chi-squared analysis was used to determine associations between categorical variables. ANOVA was performed after assessing the normality of the quantitative data. Analyses were performed using SPSS 23.0 (SPSS; Chicago, IL; USA), with $p<0.05$ considered statistically significant.

Results

The demographic and clinical characteristics of the patients with AIS are summarized in Table 1. The mean age of the patients was 72.3±7.4 years and 50.4% were female. The median length of hospital stay was 6 days (2-106). 80.9% of patients had hypertension (HT); 43.7% had diabetes mellitus (DM); 32.3% had previous ischemic stroke; 32.3% had atrial fibrillation (AF); 31.5% had hyperlipidemia (HL); 31.3% were smokers; 30.0% had coronary artery disease; and 13.4% had congestive heart failure (Table 1). In terms of vascular territories, AIS was most common in the middle cerebral artery (MCA) territory with a rate of 45.7%. This was followed by the posterior cerebral artery with 11.4%, the basilar artery with 8.7%, the internal carotid artery (ICA) with 5.9%, the vertebral artery with 5.2%, and the anterior cerebral artery with 2.2%. In addition, 12.9% of patients had multisite infarcts and 8% had watershed infarcts. Mortality rates were 20.6% for 0-30 days, 6.4% for 31-90 days, and 10.4% for 91 days to 1 year (Table 1). According to the TOAST classification, the etiology types of AIS patients were as follows: large-artery atherosclerosis in 50.6%, cardioembolism in 28.3%, small-vessel occlusion in 12.4%, undetermined etiology in 7.2%, and other determined etiology in 1.5%.

Table 1. The demographic and clinical features of the patients with acute ischemic stroke (n=403)

Age	72.3±12.4
Female gender	203 (50.4%)
Length of hospitalization	6 (2-106)
Medical history	
Hypertension	326 (80.9%)
Diabetes mellitus	176 (43.7%)
Hyperlipidemia	127 (31.5%)
Coronary artery disease	121 (30.0%)
Congestive heart failure	54 (13.4%)
Atrial fibrillation	129 (32.0%)
Smoking	126 (31.3%)
Previous ischemic stroke	130 (32.3%)
Involved vascular territory	
Internal carotid artery	24 (5.9%)
Middle cerebral artery	184 (45.7 %)
Anterior cerebral artery	9 (2.2%)
Vertebral artery	21 (5.2%)
Basilar artery	35 (8.7%)
Posterior cerebral artery	46 (11.4%)
Multiple	52 (12.9%)
Watershed	32 (8%)
Mortality rates	
0-30 days	83 (20.6%)
31-90 days	26 (6.4%)
91 days -1 year	42 (10.4%)

Values are expressed as frequencies (n) and percentages (%), means and standard deviations (SD), or medians (minimum and maximum).
SD: Standard deviation

Mortality rates by vascular territory are shown in Table 2. Compared to the other vascular territories, MCA strokes were significantly higher in all mortality groups (p<0.001). Mortality rates in pure MCA strokes are shown in Table 3. Compared to inferior territory infarcts, superior territory infarcts had higher mortality for both right and left MCA strokes (p<0.001). However, mortality rates were similar between right and left MCA total infarctions (p>0.05). Regarding the mortality rates by sex in the different vascular territories, female patients had significantly higher mortality rates within 0 to 30 days for ICA stroke (p=0.048) and in all mortality groups for right MCA stroke (p=0.046) compared to male patients. However, there were no significant differences in other vascular territories (p>0.05).

Discussion

Accumulating data showed that HT, DM, HL, AF, ischemic heart disease, smoking, and previous cerebrovascular events are primary risk factors for AIS (7). Among these, advanced age is the best-defined risk factor (8). In agreement with the literature, we found a mean age of 72.3±7.4 years, which is indicative of vascular aging leading to stenosis (8). In addition, 50.4% of the patients were female, which is consistent with the literature and may indicate the predisposing hormonal factors for thrombosis formation (5). Among the modifiable factors, HT was the most obvious, being present in 80.9% of the patients in our study. This prevalence was significantly higher in all types of stroke, except for the "other determined etiology" group according to the TOAST classification. These findings are similar to those of the Indonesian (83%) and Lebanese (77%) cohorts (9,10). The INTERSTROKE study, which included 32 countries, also highlighted HT as the most prevalent risk factor (11). Effective treatment of HT has been shown to reduce the risk of stroke by 22% (12). DM is another significant risk factor, as demonstrated in our study, with 43.7% of the cohort exhibiting this risk factor. This is consistent with the 48.5% prevalence of DM reported by Harris et al. (9), in their retrospective cross-sectional study. In addition, DM was shown to be an important risk factor for atherothrombotic stroke in the same study. Our study showed a significantly higher frequency of DM in both atherothrombotic and lacunar stroke, which is in agreement with the study by Malek et al. (10). This suggests that poor glycemic control may contribute significantly to the pathogenesis of both large and small vessel disease (13). Another risk factor, HL, was found in 31.5% of the patients, which is consistent with the literature (14). Consistent with the literature, AF is also high (32.3%) in our AIS patients (15). In contrast to the previous report, we found a high prevalence of smoking (50%) in the "other determined etiology" group (10). This finding may be due to the small number of patients in this subgroup.

Based on the TOAST classification, atherothrombotic stroke (50.6%) and cardioembolic stroke (28.3%) were more common than the other types of stroke (in line with the literature) (16). The oldest patients were found among those with cardioembolic stroke, a difference that was statistically significant. This may

Table 2. Mortality rates according to involved vascular territories in patients with acute ischemic stroke (n=403)

Mortality rates	Vascular territory								p value
	Internal carotid artery	Middle cerebral artery	Anterior cerebral artery	Vertebral artery	Basilar artery	Posterior cerebral artery	Multiple	Watershed	
Alive	15 (6.0%)	114 (45.8%)	8 (3.2%)	14 (5.6%)	21(8.4%)	30 (12.0%)	21 (8.4%)	26 (10.4%)	**<0.001**
0-30 days	6 (7.3%)	38 (46.3%)	0 (0.0%)	5 (6.1%)	10 (12.2%)	8 (9.8%)	12 (14.6%)	3 (3.7%)	**<0.001**
31-90 days	3 (11.5%)	12 (46.2%)	1 (3.8%)	1 (3.8%)	1 (3.8%)	2 (7.7%)	6 (23.1%)	0 (0.0%)	**<0.001**
91 days-1 year	0 (0.0%)	20 (54.1%)	0 (0.0%)	1 (2.7%)	3 (8.1%)	6 (16.2%)	4 (10.8%)	3 (8.1%)	**<0.001**

Values are expressed as frequencies (n) and percentages (%)

Table 3. Mortality rates in patients with acute ischemic stroke involving pure middle cerebral artery (n=127)

Middle cerebral artery territory	Mortality rates					p value
		Alive	0-30 days	31-90 days	91 days-1 year	
Left MCA	Superior division	17 (36.2%)	4 (40.0%)	2 (66.7%)	0 (0.0%)	**<0.001**
	Inferior division	30 (63.8%)	6 (60.0%)	1 (33.3%)	4 (100.0%)	**<0.001**
Right MCA	Superior division	21 (34.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	**<0.001**
	Inferior division	40 (65.6%)	0 (0.0%)	0 (0.0%)	2 (100.0%)	**<0.001**

Values are expressed as frequencies (n) and percentages (%). MCA: Middle cerebral artery

be related to the increasing prevalence of AF with age, as shown in a Norwegian (15). In addition, the young patients were predominantly of "other determined etiology," which is consistent with the literature (17). Moreover, the female gender was most common in the cardioembolic stroke group, but this difference was not statistically significant. Regarding survival times, patients with lacunar stroke had the highest survival rate, which is consistent with the study by Hauer et al. (13).

It is well known that more than half of AIS occurs in the MCA territory (18). Similarly, we observed a higher frequency of MCA strokes, especially on the left side, compared to the other territories. Previous data showed that the mortality rate of untreated patients with malignant MCA infarction can reach 80% (19). Consistent with this, we had a higher mortality rate for stroke than in other territories. Further analysis revealed that superior division infarcts were more lethal than inferior division infarcts in both right and left MCA strokes. Similarly, Seker et al. (20) found that upper division strokes had a worse outcome than lower division strokes despite similar recanalization and complication rates. However, the mortality rates were similar for total occlusion of either the right or left side, supporting a previous study by Mateo et al. (21) showing that the side of MCA infarction does not affect mortality during the initial hospitalization period for AIS. On the contrary, a long-term study (up to 10 years) by Aszalós et al. (22) showed a higher but not significant mortality rate in right MCA strokes compared to the control group. Naess et al. (23) and Hedna et al. (24) also showed that left cerebral hemisphere infarcts and left MCA strokes were more frequent and associated with higher mortality. female patients had a higher mortality rate than males for ICA and right MCA strokes. This may be because our female patients had a higher prevalence of comorbidities, which may have led to a higher risk of adverse outcomes (data not shown). Similarly, a very recent multicenter study by Wang et al. (25) showed that women with AIS in China tended to have a poor prognosis at 3 months compared with men. However, studies on sex-specific mortality in patients with AIS are controversial. For example, a German study showed that female patients had better functional outcomes at discharge, which may be related to differences in risk factors between populations (25,26). Overall, our mortality rates for all stroke subtypes were higher than those reported in the literature, which may be attributed to the underuse of definitive treatment options such as thrombolysis or thrombectomy, in acute cases complicated by the COVID-19 pandemic (25-27). Multiple studies have dominantly documented the overexpression of cytokines, hypercoagulable state, and thromboembolism as potential factors leading to stroke. However, the exact relationship between COVID-19 and ischemic stroke is unclear (28).

Study Limitations

This study has several limitations. First, it was retrospective, which may result in missing data that could potentially alter the results. Second, multiple pathologies were included in the "undetermined etiology" subgroup, which may affect the significance of other stroke subtypes. Third, this study was conducted during the COVID-19 pandemic, so the decrease and/or delay in hospital admissions, quarantine period, and high infection rates may have combined to affect our results.

Conclusion

The present study demonstrated that the majority of AIS occur in the MCA territory. The mortality rate for MCA strokes is higher than other vascular territories. Patients with occlusion of the upper branch of the MCA have a higher mortality rate compared to those with occlusion in the lower branch. Female patients with AIS in the ICA and right MCA territories were more likely to have a poor prognosis. This small cohort study needs to be further validated in a multicenter study population.

Ethics

Ethics Committee Approval: The study was approved by Kırşehir Training and Research Hospital Kırşehir Ahi Evran University Faculty of Medicine Local Research Ethics Committee (decision number: 2022-02/19, date: 25.01.2022).

Informed Consent: Due to the retrospective nature of the study, we did not obtain informed consent from the included patients; most of whom were conservatively managed with antiaggregant and/or anticoagulant therapy.

Footnotes

Authorship Contributions

Surgical and Medical Practices: O.J., Concept: O.J., Design: H.M.C., A.C., Data Collection or Processing: O.J., H.M.C., Analysis or Interpretation: O.J., H.M.C., A.C., Literature Search: O.J., A.C., Writing: O.J., A.C.

Conflict of Interest: The authors declare that they have no conflict of interest.

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