

## Risk factors of early recurrence of ischaemic stroke

### *İskemik inmenin erken dönem tekrarında risk faktörleri*

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#### Abstract

**Purpose:** Despite acute and preventive treatments for ischemic stroke, it remains a cause of high mortality and morbidity due to recurrence of ischemic stroke. The generally accepted point of view is that the risk factors that caused the initial stroke are also important in the recurrence of ischemic stroke. Our study was conducted to determine the risk factors involved in early ischemic stroke recurrence.

**Material and method:** We selected ischemic stroke patients from our own stroke database, and among the patients included in this study, 521 patients who could be followed up for 3 months after the first stroke and had complete examinations were included in the analysis.

**Results:** Seventy-one patients (14%) had another stroke within 3 months of the first stroke. The mean time to early stroke recurrence is 21 days. Significant risk factors for early stroke were coronary artery disease (43%,  $p<0.016$ ) and congestive heart failure (38%,  $p<0.016$ ). Age, atrial fibrillation, hypertension, diabetes mellitus, hyperlipidaemia, smoking, and alcohol use were not found to be significant risk factors for stroke recurrence in the early period.

**Conclusion:** Despite appropriate treatments, coronary artery disease and congestive heart failure have emerged as important risk factors for stroke recurrence in the early period after stroke, indicating that more attention should be paid to this issue.

**Key words:** Ischemic stroke, risk factors, stroke recurrence.

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#### Öz

**Amaç:** İskemik inme gelişen akut ve koruyucu tedavilere rağmen, iskemik inmenin tekrarlaması nedeniyle de yüksek ölüm ve morbidite nedeni olarak kalmaya devam etmektedir. Genellikle kabul edilen görüş, ilk inmeye neden olan risk faktörlerinin, iskemik inme tekrarında da önemli olduğudur. Bizim çalışmamız erken dönem iskemik inme tekrarında yer alan risk faktörlerini belirlemek amacıyla yapılmıştır.

**Gereç ve yöntem:** İskemik inme hastalarını kendi inme veri tabanımızdan seçtik ve bu çalışmaya alınan hastalar içinde ilk inmeden sonraki dönemde 3 ay takip edilebilen ve incelemeleri eksiksiz olan 521 hasta analize dahil edilmişlerdir

**Bulgular:** Yetmiş bir hasta (%14) ilk inmeden sonraki 3 ay içerisinde tekrar inme geçirmişlerdir. Erken inme tekrarı için geçen ortalama süre 21 gündür. Erken inme için belirgin risk faktörleri koroner arter hastalığı (%43,  $p<0,016$ ) ve konjestif kalp yetmezliği (%38,  $p<0,016$ ) olarak saptanmıştır. Yaş, atriyal fibrilasyon, hipertansiyon, diabetes mellitus, hiperlipidemi, sigara, alkol kullanımı erken dönemde inme tekrarı için anlamlı risk faktörü olarak bulunmamıştır.

**Sonuç:** Uygun tedavilere rağmen, koroner arter hastalığı ve konjestif kalp yetmezliği inmeden sonraki erken dönemde inme tekrarı için önemli risk faktörleri olarak öne çıkmıştır ve bu konuya biraz daha fazla önem verilmesi gerektiğine işaret etmektedir.

**Anahtar kelimeler:** İskemik inme, risk faktörleri, inme tekrarı.

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## Introduction

Despite acute and preventive treatments for ischemic stroke, it remains a cause of high mortality and morbidity due to recurrence of ischemic stroke. The risk factors that cause ischemic stroke to recur have not been studied as thoroughly as the risk factors that cause ischemic stroke. In studies on this subject, it has been shown in hospital and population-based studies that stroke recurrence is higher in the very early and very late periods after ischemic stroke. The generally accepted point of view is that the risk factors that caused the initial stroke are also important in the recurrence of ischemic stroke. Among these, cardiovascular risk factors, hypertension, diabetes mellitus, dyslipidaemia and atrial fibrillation stand out as modifiable risk factors [1]. Our study was conducted to determine the risk factors involved in early ischemic stroke recurrence.

## Materials and methods

It was approved by Eskisehir Osmangazi University, Non-Interventional Clinical Research Ethics Committee with the decision numbered 80558721/G-191 on 13 June 2017. Study data were compiled in the Stroke Data Collection Form created by the Department of Cerebrovascular Diseases. The records of patients presenting with ischemic stroke from May 2017 to October 2007 were transferred to the database. Among these patients, 521 patients who could be followed up for 3 months after the first stroke and whose examinations were complete were included in the analysis. Ischemic stroke patients were defined by demonstrating lesions with CT or MRI. Doppler ultrasonography and transcranial Doppler sonography of the patients were performed in the Neurosonology unit of the department. Stroke subtypes were made according to the Trial of ORG10172 in Acute Stroke Treatment (TOAST) classification [2] and clinical stroke types according to the Oxfordshire Community Stroke Project (OCSP) classification [3]. All information about the demographic data and risk factors of the patients were transferred to the database. Statistical analyses were performed with SPSS-24 software and categorical data were evaluated with Chi-square analysis.

## Results

Seventy-one patients (14%) had another stroke within 3 months of the first stroke. The mean time to early stroke recurrence is 21 days. The mean age of patients with recurrent stroke was 73 years, while the mean age of patients without recurrent stroke was 70 years, and there was no significant difference between them.

When the clinical types of ischemic stroke were evaluated (Table 1), stroke recurrence was observed in 8 of 68 patients in the total anterior circulation infarcts (TACI) group, 49 of 316 patients in the partial anterior circulation infarcts (PACI) group, 3 of 36 patients in the lacunar infarct (LACI) group, and 11 of 99 patients in the posterior circulation infarcts (POCI) group within the first 3 months. However, no significant difference was found in stroke recurrences according to clinical classification.

When we look at the etiological classification (Table 2), stroke recurrence developed in 21 of 126 patients with large artery disease, 4 of 39 patients with small artery disease, 24 of 166 patients with cardio embolism, and 21 of 170 patients with cryptogenic causes. In contrast, stroke recurrence was not seen in any of the 5 patients with haematological causes and none of the 9 patients who were considered for ESUS.

In the analysis of risk factors, gender, alcohol and smoking, hypertension, hyperlipidaemia, diabetes mellitus, obstructive sleep apnoea, patent foramen ovale, atrial fibrillation did not differ significantly in early stroke recurrence (Table 3). Conversely, early stroke recurrence was significantly higher in patients with coronary artery disease and congestive heart failure ( $p < 0.016$ ).

## Discussion

There has been no significant change in stroke recurrence in the last 20 years [4], and large artery disease and cardioembolic strokes have come to the fore in recurrent strokes [5]. However, there are differences between the recurrence times of stroke in studies. In our study, although the recurrence rate was higher in large vessel disease, cardioembolic strokes and cryptogenic strokes, no significant differences were found in early stroke recurrence. Similarly, although PACI showed a higher rate of recurrence among recurrent strokes, it did not make a significant difference.

**Table 1.** Stroke recurrence data by stroke clinical subtypes

	Recurrent stroke (n=71)	Non-recurring stroke (n=450)	p value
TACI (total anterior circulation infarcts)	8 (11.3%)	60 (13.3%)	0.63
PACI (partial anterior circulation infarcts)	49 (69.0%)	267 (59.3%)	0.12
LACI (lacunar infarct)	3 (5.6%)	33 (7.8%)	0.34
POCI (posterior circulation infarcts)	11 (15.5%)	88 (19.6%)	0.42

Pearson Chi-square

**Table 2.** Stroke subtypes by etiological classification

	Recurrent stroke (n=71)	Non-recurring stroke (n=450)	p value
Large artery disease	21 (29.6%)	105 (23.3%)	0.25
Small artery disease	4 (5.6%)	35 (7.8%)	0.52
Cardioembolism	24 (33.8%)	142 (31.6%)	0.71
Haematological	0 (0.0%)	5 (0.9%)	0.42
Cryptogenic	21 (29.6%)	149 (33.1%)	0.56
ESUS	0 (0.0%)	9 (2.0%)	0.23

Pearson Chi-square

**Table 3.** Distribution of risk factors

	Recurrent stroke (n=71)	Non-recurring stroke (n=450)	OR (95% CI)	p value
Gender (W/M)	33/38	203/247	0.95 (0.57-1.56)	0.83
Atrial Fibrillation	20 (28.2%)	118 (26.2%)	1.10 (0.63-1.93)	0.73
Patent Foramen Ovale	0 (0.0%)	5 (1.1%)	0.99 (0.98-1.00)	0.37
Congestive heart failure*	27 (38.0%)	110 (24.4%)	1.90 (1.12-3.20)	0.016
Coronary artery disease*	31 (43.7%)	132 (29.3%)	1.87 (1.12-3.11)	0.016
Diabetes Mellitus	27 (38.0%)	137 (30.4%)	1.40 (0.83-2.36)	0.20
Hypertension	53 (74.6%)	298 (66.2%)	1.50 (0.85-2.65)	0.16
Hyperlipidaemia	27 (38.0%)	188 (41.8%)	0.86 (0.51-1.43)	0.55
Obstructive sleep apnoea	0 (0.0%)	1 (0.2%)	0.99 (0.99-1.00)	0.69
Alcohol usage	2 (2.8%)	13 (2.9%)	0.97 (0.21-4.41)	0.97
Smoking	22 (31.0%)	154 (34.2%)	0.86 (0.50-1.48)	0.59

In the literature, especially hypertension and diabetes mellitus, atrial fibrillation, angina pectoris, ischemic heart disease, cardiomyopathy and smoking emerge as independent risk factors for recurrent strokes [5, 6]. As mentioned above, these risk factors become more prominent in long follow-up periods after stroke. The fact that the treatment and follow-up of modifiable risk factors in the early period is more intense may have led to this result. In particular, antiaggregant therapy plays an important role in the prevention of recurrence of ischemic stroke in the early period [7]. In our study, early stroke recurrence was found to be significantly higher in patients with congestive heart failure and coronary artery disease.

According to the Framingham study, among the risk factors for congestive heart failure are primarily hypertension and coronary heart diseases. In addition to these, rheumatic heart valve diseases, diabetes mellitus, hyperlipidemia and even atrial fibrillation are also included. In the presence of these diseases, congestive heart failure occurs as a result [8]. In addition, the rate of congestive heart failure in our patient group was found to be higher than expected. Therefore, our results are an expected result. Despite appropriate treatments, coronary artery disease and congestive heart failure can still lead to stroke recurrence, indicating that more attention should be paid to this issue.

The most important limitation of this study is that it is a retrospective evaluation. In this process, the loss of data of many patients caused a decrease in the number of patients included in the study. Apart from this, although our unit is the most comprehensive examination and treatment centre in the region, hospital data do not reflect the whole society. Nevertheless, large differences were not found between population-based studies and hospital-based studies [1]. Though, there is a need for well-ordered population-based studies.

**Conflict of interest:** No conflict of interest was declared by the authors.

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### Contributions of authors

G.T.U.; Organizing the study, projecting, evaluating the data, evaluating the statistical results, making it into a draft text  
Y.T.; Entering data, evaluating results, contributing to draft text  
N.U.; Organization of the study, Doppler analysis and evaluation of data, statistical analysis, evaluation of results, draft text writing, literature control, finalization of the manuscript.