

# The Effect of Clinical and Radiological Features on Prognosis in the Top of The Basilar Syndrome

Baziller Tepe Sendromunda Klinik ve Radyolojik Bulguların Prognoz Üzerine Etkisi

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## Öz

Objective	The 'top of the basilar syndrome' (TOBS) may occur when an embolus impacts in the distal basilar artery. We aimed to investigate the relationship between the clinical, radiological parameters of TOBS, its prognosis, and mortality rates, in Sakarya, Turkey.
Materials and Methods	Age, sex, presenting symptoms, National Institutes of Health Stroke Scores (NIHSS), infratentorial infarct volume (IIV), supratentorial infarct volume (SIV) length of stay (LOS) in neurology clinic and intensive care unit (ICU), the duration of mechanical ventilation (MV) and mortality were recorded.
Results	Thirty-one patients (18 female,13 male) with diagnosed TOBS were included. The frequency was 2.2% among 1379 patients within 2,5years. The mean age was 69.0±12.1years. According to NIHSS, 11 (35.5%) patients had mild stroke, 16 (51.6%) moderate, and 4 (12.9%) severe stroke. The mean IIV was 8.84±10.44mm <sup>3</sup> (0.17-33.88), SIV was 15.11±22.32mm <sup>3</sup> (0.11-87.91). The average LOS in neurology clinic was 6.0±3.6, in ICU was 40.8±40.3days. Twenty-one (67.7%) patients needed to be in an ICU. Patients admitted to the ICU had significantly higher decreased level of consciousness (DLC) and visual abnormalities, NIHSS, IIV. 13/21 (61.9%) patients admitted to the ICU required MV. The mean duration of MV was 33.8±45.3days. DLC, ataxia, visual abnormalities as an initial symptoms, NIHSS, IIV were higher among patients who required MV compared with who did not. The mortality rate was 32.3%. NIHSS, LOS in clinic and ICU, the duration of MV of patients who died were statistically higher.
Conclusion	: It is important to determine effective parameters in order to prognose TOBS which is a rare stroke syndrome.
Keywords	Basilar artery; Prognosis; Mortality

## Abstract

Amaç	Koronavirüs hastalığı 2019 (COVID-19), solunum ve gastrointestinal sistem bozukluklarına ek olarak nörolojik bozukluklara da neden olabilir. Bu çalışmada COVID-19 hastalarında nörolojik semptomların sıklığı ve klinik korelasyonlarının araştırılması amaçlandı.
Gereç ve Yöntem	Hastaların yaşı, cinsiyeti, başlangıç semptomları, National Institutes of Health Stroke skorları (NIHSS), infratentorial ve supratentorial enfarkt hacimleri, nöroloji klinik ve yoğun bakım ünitelerinde (YBÜ) kalış süreleri, mekanik ventilasyon (MV) süreleri, mortalite oranları kaydedildi.
Bulgular	BTS tanısı almış 31 hasta (18 kadın, 13 erkek) alındı. Hastalık 2,5 yıl içinde 1379 inme hastası içinde %2,2 oranında görüldü. Hastaların yaş ortalaması 69,0 ± 12,1 (42-97) idi. NIHSS'ye göre 11 hasta (%35,5) hafif, 16 hasta orta (%51,6), 4 hasta ağır (%12,9) inme tablosuna sahipti. İnftratentorial bölgenin ortalama enfarkt hacmi 8,84±10,44 mm <sup>3</sup> (0,17-33,88), supratentorial bölgeninki 15,11±22,32 mm <sup>3</sup> (0,11-87,91) idi. Nöroloji kliniğinde ortalama kalış süresi 6,0±3,6, YBÜ'de 40,8±40,3 gündü. Yirmibir (%67,7) hastanın YBÜ ihtiyacı gelişti. YBÜ'ye ihtiyacı olan hastaların bilinç değişikliği ve görme bozukluğu ile başvuru oranı, NIHSS, infratentorial enfarkt hacmi istatistiksel olarak anlamlı oranda yüksekti. YBÜ'ye giren hastaların 13/21'inde (%61,9) MV ihtiyacı gelişti. Ortalama MV'da kalış süresi 33,8±45,3 gündü. MV ihtiyacı olan hastalarda olmayanlara göre bilinç değişikliği, dengesizlik, görme bozukluğu ile başvuru, NIHSS, infratentorial enfarkt hacmi istatistiksel olarak anlamlı oranda yüksekti. Mortalite oranı %32,3'tü. Mortal seyreden olguların NIHSS, nöroloji kliniği ve YBÜ yatış süreleri, MV gün sayısı istatistiksel olarak anlamlı oranda yüksekti.
Sonuç	Nadir bir inme olan BTS'nin prognozu için etkin parametrelerinin belirlenmesi önemlidir.
Anahtar Kelimeler	Baziller arter; Prognoz; Ölüm Oranı

## INTRODUCTION

Basilar artery occlusion comprises around 1-4 % of all ischemic cerebrovascular diseases. The 'top of the basilar syndrome' (TOBS) is a description of symptoms and signs that may occur when an embolus impacts in the distal basilar artery, resulting in bilateral ischemia of upper brainstem structures and of the posterior cerebral artery territories.<sup>1</sup> Alteration of consciousness, amnesic states, hallucinations, involuntary movements, visual abnormalities, altered pupillary responses, supranuclear paresis of vertical gaze, ptosis or eyelid retraction can be signs of TOBS.

TOBS are found at a lesser frequency than the other cerebrovascular occlusive artery disease. There is a limited literature about TOBS.<sup>2-4</sup> Most of the reports were posterior circulation and basilar artery.<sup>5-7</sup> No study has yet investigated the certain frequency of the disease. In this study, we aimed to investigate relationship between clinical and radiological parameters, prognosis of TOBS and mortality, which are known to be rare, in Sakarya city, Turkey.

## MATERIALS and METHODS

In this descriptive study, we retrospectively reviewed 1379 patients with stroke between February 1, 2015 and July 1, 2017 in our center. Thirty-one patients meeting the detailed inclusion criteria of the study, who were diagnosed with TOBS and admitted to the hospital, department of neurology for examination and treatment were included in the study. Age, sex, presenting symptoms, premorbid medical histories (hypertension (HT), diabetes mellitus (DM), coronary artery disease (CAD), congestive heart failure (CHF), cerebrovascular disease (CVD), atrial fibrillation (AF) were recorded. Also, we recorded National Institutes of Health Stroke Scores (NIHSS), length of stay (LOS) in neurology clinic and intensive care unit (ICU), the duration of mechanical ventilation (MV), mortality. The results of all tests and studies performed to determine stroke, which included CT and/or MRI.

Localization of infarct separated two groups: infratentorial and supratentorial areas. Infarct volumes were measured using the hyperintense lesion on diffusion MRI area and hypointense lesion on CT by radiologist. Brain CT was performed with Toshiba Aquilion 64 CT scanners. The acquired images were processed in the TeraRecon Aquarius Workstation (San Mateo, Calif) and the volume values were measured. MRI was performed on a 1,5T system (Signa, Voyager; GE Healthcare, WI, USA) using the body coil as a transmitter and a dedicated 16-channel phased-array receiver coil (Sentinelle Vanguard, Toronto, Canada). Diffusion weighted imaging (DWI) MRI examination was performed in the patients. Axial DWI MR imaging was performed using 2D, DW single-shot, dual spin echo-planar imaging (EPI) sequences (TR 6,000 ms; minimum TE; flip angle 90°; acquisition matrix: 128×128; reconstructed matrix: 256×256; FOV 25 x 25 cm; slice thickness: 5 mm; NEX 4; slice gap: 0-1 mm. DWI was acquired at b-values of 0 and 1000 s/mm<sup>2</sup>. Infarct volumes were calculated using the workstation (Volume Share 7.4.1) in the examinations.

Ethical committee approval was obtained from the Ethics Committee of Sakarya University Research and Training Hospital (approval number: 050.01.04/164, date: 02.10.2017).

## Statistical Analysis

In the descriptive statistics of the data, mean, standard deviation, median minimum and maximum, frequency, and ratio values were used. The distribution normality of variables was tested with the Kolmogorov-Smirnov test. The Mann-Whitney U-test was used to analyze quantitative independent data. The Chi-square test was used in the analysis of qualitative independent data and the Fischer test was used when the conditions of the chi-square test were not met.  $p < 0.05$  was considered statistically significant. The statistical analyzes were performed via the software of SPSS, version 27.0 (IBM Corp.; Armonk, NY, USA).

## RESULTS

This study involved a total of 31 (2.2%) patients with TOBS among 1379 patients with stroke for 2,5 years in Sakarya, Turkey. Eighteen (58.1%) were female and 13 (41.9%) were male. (Table 1) The mean age of the study population was 69.0±12.1 (42-97) years. Among the whole study population, 20 patients (64.5%) had HT, 14 (45.2%) had CAD, 13 (31.9%) DM, 11 (35.5%) CVD, 3 (9.7) had CHF, 2 (6.5%) had AF (Table 1).

	Number	Percentage
<b>Gender</b>		
Female	18	58.1%
Male	13	41.9%
<b>Premorbid Disease</b>		
HT	20	64.5%
DM	13	41.9%
CAD	14	45.2%
CHF	3	9.7%
CVD	11	35.5%
AF	2	6.5%
<b>Presenting Symptoms</b>		
Decreased level of consciousness	15	48.4%
Speech disorder	9	29.0%
Paresia and/or parestesia	9	29.0%
Ataxia	5	16.1%
Visual abnormalities	5	16.1%
Seizure	1	3.4%
<b>NIHSS</b>		
Mild	11	35.5%
Moderate	16	51.6%
Severe	4	12.9%
HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, CHF: congestive heart failure, CVD: cerebrovascular disease AF: atrial fibrillation, NIHSS: National Institutes of Health Stroke Scores		

The most common presenting symptom of TOBS was decreased level of consciousness (n=15, 48.4%). 9 patients (29.0%) had speech disorder, 9 patients (29.0%) had paresia and/or parestesia, 5 (16.1%) patients had ataxia, 5

patients (16.1%) had visual abnormalities. One patient (a 84-year-old-woman) (3.4%) had epileptic seizure as an initial symptom of TOBS (Table 1).

The patients were categorized into three groups according to NIHSS. (0-6=mild, 7-15=moderate, 16-42=severe) According to stroke severity, the groups were categorized as 11 (35.5%) patients with mild stroke, 16 (51.6%) patients with moderate stroke, and 4 (12.9%) patients with severe stroke (Table 1).

The mean infratentorial infarct volume was 8.84±10.44 mm<sup>3</sup> (0.17-33.88). Supratentorial infarct volume was 15.11±22.32 mm<sup>3</sup> (0.11-87.91).

Total of 31 patients of who 11 patients were admitted to neurology clinic, 5 patients were admitted to neurology clinic initially, when patients had worse clinically outcome they were admissions ICU from neurology clinic, 15 patients were direct admissions to ICU. (Table 2)

Department of Hospital	Total Number of Patients n (percentage)	Exitus n (percentage)	Alive n (percentage)
Neurology clinic	11 (35.5%)	0	11 (35.5%)
ICU	15 (48.4%)	8 (25.8%)	7 (22.6%)
ICU from Neurology clinic	5 (16.1%)	2 (6.5%)	3 (9.6%)
Total	31 (100%)	10 (32.3%)	21(67.7%)

The average LOS in neurology clinic was 6.0±3.6 days. Twenty-one (67.7%) patients needed to be in an ICU. The average LOS was in ICU was 40.8±40.3days. Patients admitted to the ICU had significantly higher the presence of DLC and visual abnormalities as an initial symptom, NIHSS, infratentorial infarct volume than patients admitted to the neurology clinic. (p=0.003, p=0.008, p=0.047) (Table 3) Thirteen patients (61.9%) admitted to the ICU required MV. The mean duration of MV was 33.8±45.3

days. The presence of DLC, ataxia, visual abnormalities as an initial symptoms, NIHSS, infratentorial infarct volume were higher among patients who required MV compared with who did not. (p=0.007, p=0.038, p=0.038, p=0.005, p=0.005) The average timing of intubation was 16.1±24.9 days (1-90). The mean duration of MV in this cohort was 33.8±45.3 days (1-138). The mortality rate was 32.3 % (n=10). 8 of 15 patients who were direct admissions to ICU, were died. 2 of 5 patients who were admissions ICU from neurology clinic, were died. (Table 2) NIHSS, LOS in clinic and ICU, the duration of MV were statistically high-

er among patients who died from Top of the Basilar Syndrome in hospital compared with alive patients. (p<0.05) According to the evaluation of the stroke severity, the NIHSS score of patients who died was statistically higher than that of alive patients. (p=0.007) The mortality rate was found to be higher in patients who had prolonged LOS in neurology clinic and ICU. (p=0.015, p=0.008) It was determined that mortality rate was significantly increased in patients with prolonged duration of MV. (p<0.001) (Table 4)

Table 3. The comparison of clinical and radiological features of patients who were diagnosed with Top of the Basilar Syndrome, admitted to the ICU and not.

	No admission to the ICU n (percentage) Mean±SD	The patients admitted the ICU <sup>n</sup> n (percentage) Mean±SD	p
Age	67.5±16.3	69.8±9.9	0.635
Female	6 (60.0%)	12 (57.1%)	0.880
Male	4 (40.0%)	9 (42.9%)	
Premorbid Disease			
HT	7 (70.0%)	13 (61.9%)	0.660
DM	5 (50.0%)	8 (38.1%)	0.530
CAD	5 (50.0%)	9 (42.6%)	0.709
CHF	1 (10.0%)	2 (9.5%)	1.000
CVD	5 (50.0%)	6 (28.6%)	0.244
AF	1 (10.0%)	1 (4.7%)	1.000
Presenting Symptoms			
Decreased level of consciousness	1 (10.0%)	14 (66.7%)	<b>0.003</b>
Speech disorder	4 (40.0%)	5 (23.8%)	0.353
Paresia and/or parestesia	4 (40.0%)	5 (23.8%)	0.353
Ataxia	0	5(23.8%)	0.147
Visual abnormalities	4 (40.0%)	1 (4.7%)	<b>0.027</b>
Seizure	0	1 (4.7%)	0.123
NIHSS	6.2±3.3	10.8±5.0	<b>0.008</b>
Infratentorial infarct volume	5.2±9.7	10.6±10.6	<b>0.047</b>
Supratentorial infarct volume	7.7±9.2	18.6±25.9	0.933

HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, CHF: congestive heart failure, CVD: cerebrovascular disease AF: atrial fibrillation, NIHSS: National Institutes of Health Stroke Scores, ICU: intensive care unit.

Table 4. Clinical and radiological features of exitus and alive patients who were diagnosed with Top of the Basilar Syndrome.

	Exitus n (percentage) Mean±SD	Alive n (percentage) Mean±SD	p
Age	72.5±8.8	67.4±13.3	0.279
Female	4 (40.0%)	14 (66.7%)	0.160
Male	6 (60.0%)	7 (33.3%)	
Premorbid Disease			
HT	6 (60.0%)	14 (66.7%)	0.717
DM	5 (50.0%)	8 (38.1%)	0.530
CAD	4 (40.0%)	10 (47.6%)	0.690
CHF	1 (10.0%)	2 (9.5%)	1.000
CVD	5 (50.0%)	6 (28.6%)	0.244
AF	1 (10.0%)	1 (4.7%)	1.000
Presenting Symptoms			
Decreased level of consciousness	7 (70.0%)	8 (38.1%)	0.097
Speech disorder	3 (30.0%)	6 (28.6%)	<b>0.935</b>
Paresia and/or parestesia	2 (20.0%)	7 (33.%)	0.445
Ataxia	0	5 (23.8%)	0.147
Visual abnormalities	0	5 (23.8%)	0.147
Seizure	0	1 (4.7%)	<b>0.123</b>
NIHSS	13.5±5.6	7.3±3.2	<b>0.007</b>
Infratentorial infarct volume	11.8±10.0	7.5±10.6	<b>0.091</b>
Supratentorial infarct volume	21.1±26.1	12.3±20.3	<b>0.499</b>
LOS in neurology clinic	2 (20.0%)	14 (66.7%)	<b>0.015</b>
LOS in ICU	10 (100%)	11 (52.4%)	<b>0.008</b>
MV	9 (90.0%)	4 (19.0%)	<b>0.000</b>

HT: hypertension, DM: diabetes mellitus, CAD: coronary artery disease, CHF: congestive heart failure, CVD: cerebrovascular disease AF: atrial fibrillation, NIHSS: National Institutes of Health Stroke Scores, LOS: lenght of stay, ICU: intensive care unit, MV: mechanical ventilation.

There was no significant differences between age, sex, presenting symptoms, premorbid diseases, infratentorial, supratentorial infarct volume and mortality. (p >0.05)

### DISCUSSION

There are widespread lesions of the temporal and occipital lobes, thalamus, midbrain, pons and cerebellum in TOBS. The incidence of the disease is not certain. In a study of 100 patients with ischemic stroke, TOBS was detected in 4 patients.<sup>2</sup> In our study, patients with TOBS were detected in 31 of 1379 (2.2 %) all stroke patients within 2,5 years in Sakarya city. Voetsch et al. reported that 10 patients

(2.45 %) had distal basilar artery occlusive disease among 407 patients who had posterior circulation ischemia for 8 years.<sup>6</sup> A study showed that most patients were older age (average 75 years).<sup>2</sup> The mean age of patients with TOBS was 64.8±8.6 in an other study.<sup>3</sup> Similarly, the mean age of our study population was 69.0±12.1 years. It was also reported in the study that the mean age of the patients with TOBS was younger (61 years).<sup>4</sup> Voetsch et al. reported that men were more vulnerable to basilar artery occlusive disease than women.<sup>6</sup> Female dominance is noticable in TOBS for limited studies. A study reported that number of female patients were higher than male patients (16:9),

another study reported 16:14 female/male ratio.<sup>3,4</sup> In our study, 18 (58.1%) female patients were detected.

The disease's clinical course is usually characterized by visual, oculomotor disturbances, altered mental status, behavioral disorders, cerebellar disorders and hallucinations.<sup>8</sup> Kiroğlu et al. reported that most common presenting symptoms of TOBS were motor deficit (%53.3), loss of consciousness (46.6 %), visual/oculomotor symptoms (43.3%) cerebellar dysfunction (40.0%), behavioral disorder (26.6%) and speech disorder (16.6%).<sup>4</sup> A study with 25 patients with TOBS, the commonest clinical manifestations were: motor deficit (68%), abnormal eye movements (48%), cerebellar dysfunction (40%), alteration of the level of consciousness (32%), visual field defects (20%), pupil anomalies (16%).<sup>3</sup> Decreased level of consciousness (n=15, 48.4%) was the most common presenting symptom, in our study. Speech disorder, paresia and/or parestesia, ataxia, visual abnormalities, seizure were other initial symptoms, respectively. Seizure is a rare presenting symptom. In the literature, a 23-year-old patient who had seizure as an initial symptom of TOBS was reported.<sup>9</sup> In our study, a 84-year-old woman was diagnosed with TOBS whose presenting symptom was epileptic seizure.

There are conventional vascular risk factors for ischemic stroke. Basilar artery disease had a high co-morbidity of these risk factors.<sup>6</sup> HT is the most prevalent risk factor for stroke, has been reported in about 64% of patients with stroke.<sup>10,11</sup> Also HT was the most frequent (66.7%) risk factor in basilar artery occlusive disease.<sup>6</sup> DM is a recognized independent risk factor for stroke and is associated with higher morbidity and mortality.<sup>12</sup> Stroke and CAD are risk factors for one another.<sup>13</sup> AF is an important risk factor for ischemic stroke since it associates with a 5-fold higher risk of stroke compared with the general population.<sup>14</sup> In a study, HT (64%), CVD (28%), smoking (28%), DM (24%) and AF (20%) were most frequently associated with TOBS.<sup>3</sup> Similarly, HT (64.5%) was the most common disease in premorbid histories in our study. CAD (45.2%),

DM (41.9%), CVD (35.5%), CHF (9.7%), AF (6.5%) were other disease in premorbid medical histories. The patients with TOBS had no significant difference between premorbid diseases and mortality, in our study.

Stroke is the second leading cause of death. The mortality of ischemic stroke patients was found 52.7% in a study.<sup>15</sup> Many factors increase mortality of patients with ischemic stroke. Impaired consciousness is independent predictors of mortality for severe ischemic stroke during the acute stage.<sup>16</sup> But, according to presenting symptoms, there was no significant difference between decreased level of consciousness and mortality of TOBS which is a rare stroke, in our study. The NIHSS score of patients who died was statistically higher than that of other patients. ( $p < 0.005$ ). Fracalanza et al. reported that low NIHSS score of patients with basilar artery occlusion were associated with good clinical outcome.<sup>17</sup> The mortality rate of this study was 29.6%.<sup>17</sup> Mortality of patients with TOBS was 8% in a study.<sup>13</sup> In our study, high mortality rate was detected (32.3%). Similarly, 88 patients with basilar artery stenosis or occlusion had poor outcome in 54% cases as a severe disability or death.<sup>18</sup> Labauge et al. reported that the mortality rate was 86% in basilar artery occlusion.<sup>19</sup> Another study about basilar artery occlusive disease reported that involvement of the distal side of artery had an increased risk of death and disability.

LOS in hospital is a significant factor for prognosis of the disease. According to the evaluation of the ischemic stroke patients, LOS in ICU and the duration of MV of patients who died was statistically higher than alive.<sup>20</sup> The mean LOS in ICU was  $7 \pm 2$  days, length of MV was  $5 \pm 2$  days and mortality rate of stroke was 59.25% were reported in a study.<sup>21</sup>

The mortality of ischemic stroke patients admitted to ICU within 30 days of hospitalization in the study period was 21% and MV was associated with 5-fold higher mortality.<sup>20</sup> We have noted that our LOS in neurology clinic and

ICU were higher than the studies about ischemic stroke, and mortality was higher. But many factors lead LOS in hospital and mortality. Also, TOBS is a rare stroke syndrome. There are not large data base about prognosis and mortality of the disease. Therefore our datas were compared with literature of other stroke types and limited TOBS article.

### **Study Limitations**

The limitations of our study is absent of computed tomography angiography, magnetic resonance angiography, and digital subtraction angiography. Most of patients had no angiography, because of some patients had renal dysfunction, some patients had contrast allergy, some were died in a short-time. Neurovascular findings will add an important informations about prognosis of disease. There is a need for larger and more detailed studies to elucidate the factor that determine the prognosis of the disease.

Our study aimed to investigate relationship between clinical and radiological parameters and mortality of the disease. This study is significant because our cohort had an important series of TOBS. No study has yet investigated the relationship between clinical and radiological parameters and mortality in literature.

There is a critical importance of early diagnosis in emergency and quickly admission from the emergency department to ICU, because of high mortality of TOBS.

This study is significant because of its pioneering role in the investigation of prognosis in patients with TOBS for the first time in Sakarya city and Turkey. It is important to determine effective parameters in order to prognose TOBS which is a rare stroke syndrome. Initial symptoms, NIHSS, infratentorial infarct volume are important for ICU admission and MV, while NIHSS, LOS in clinic and ICU, the duration of MV are important parameters for mortality. The criterias related to mortality are important for more

effective approach to patients with TOBS.

### **Ethics Committee Approval**

**Ethical committee approval was obtained from the Ethics Committee of Sakarya University Research and Training Hospital (approval number: 050.01.04/164, date: 02.10.2017).**

### **Peer-review**

Externally peer-reviewed.

### **Informed Consent**

It was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

Author contributions ZÖA, DK, KA provided author's contributions concepts. DK, ZÖA, involved in design. ZÖA, DK, contributed materials. ZÖA, DK, KA collected the data. ZÖA, CT, KA performed literature search. ZÖA, DK, KA wrote the manuscript. ZÖA, DK, KA involved in critical reviews.

### **Conflict of Interest**

No conflict of interest was declared by the authors.

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