

Research Article

# Acute Ischemic Stroke and Metabolic Syndrome Comorbidity

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## Abstract

### Aim

Cerebrovascular diseases (CVD) lead to serious disabilities and loss of labor in society in addition to mortality. Metabolic syndrome (MetS) is a group of known metabolic risk factors such as high blood pressure, dyslipidemia, glucose intolerance, or high blood sugar, due to insulin resistance.

The present study aimed to investigate MetS and its components in acute ischemic stroke patients and analyze these components as risk factors.

### Material-Method

The study was conducted with 80 patients, 46 males and 34 females, who were admitted to the Taksim Training and Research Hospital Neurology Clinic with acute ischemic stroke diagnosis between April and October 2007 within the first 48 hours of the disease onset. The presence of MetS was investigated in 80 patients, including large artery atherosclerosis (BAA), small artery occlusion (CAO), and cardioembolic disease (CE).

### Findings

MetS was determined in 48 patients out of 80. The MetS presence rate was 60%. The analysis of the MetS rates in disease groups revealed that the highest rate was in 30 of 39 BAA patients (76.90%). The mean MS criterion count was statistically significantly higher in the BAA group when compared to the CE and CAO groups. A statistically significant difference was determined between the abdominal obesity distributions in BAA, CE, KAO groups. A statistically significant difference was determined between the MS presence in the BAA, CE, CAO groups.

### Conclusion

Certain modifiable stroke risk factors are included in a cluster of risk factors called MetS. Efforts to reduce the MetS parameters could be effective in stroke prevention.

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**Keywords:** Cerebrovascular diseases (CVD), acute ischemic stroke, metabolic syndrome (MetS).

## Introduction

Cerebrovascular diseases (CVD) lead to serious disabilities and loss of labor in society in addition to mortality. Thus, the determination of CVD risk factors has been the foundation of the studies aimed to reduce CVD prevalence and incidence. Modifiable risk factors such as hypertension, DM, heart disease, dyslipidemia, and smoking definitely play a role in the etiology of CVD. Metabolic syndrome (MetS) is a group of known metabolic risk factors such as high blood pressure, dyslipidemia, glucose intolerance, or high blood sugar, due to insulin resistance. Although epidemiological studies reported variable rates based on the socio-cultural demographics, age, and gender, it is known that sedentary life and high-calorie diet increase the frequency and

severity of MetS. MetS was reported to be a risk factor in the development of diabetes, coronary artery, and other atherosclerotic cardiovascular diseases. European Heart Society (ESC) categorized Turkey among the countries with high vascular mortality risk. This is important for both the physicians and patients. It demonstrated the significance of MetS in Turkey. Recent studies investigated MetS and ischemic cerebrovascular disease comorbidity and reported an increase in prevalence. However, the studies conducted in Turkey are limited. The present study aimed to investigate MetS and its components in acute ischemic stroke patients and analyze these components as risk factors.

## Material and Method

The study was conducted with 80 patients, 46 males and 34 females, who were admitted to the Taksim Training and Research Hospital Neurology Clinic with acute ischemic stroke diagnosis between April and October 2007 within the first 48 hours of the disease onset. The patients with a history of surgery or trauma within the last month, a known hepatic or hematological disease, under parenteral nutrition, and history of a hemorrhagic stroke were excluded from the study. Stroke was diagnosed based on the WHO definition (Clinical findings that developed rapidly due to focal or global impairment of cerebral functions that lasted 24 hours or longer, or death.) Patient anamnesis was conducted to determine previous cerebrovascular incidents, systemic diseases (DM, HT, Heart disease), family history, smoking, alcohol consumption, and medications. Cranial CT scans were conducted on all patients within 24 hours. Then, systemic and neurological examinations were conducted. Blood pressure of patients was determined with a mercury manometer in an upright, sitting position, on the right arm, and after at least 5 minutes of rest. Waist circumference was measured with a tape measure between the lower rib edge and the iliac crest median. The hemograms, routine biochemistry results, hemostasis and lipid panels of the patients were examined. ECG and PA chest radiography were conducted on all patients. These were performed between the first day at the earliest and the third day at the latest. Blood samples were collected between 07:00 and 09:00 in the morning after fasting for at least 12 hours. Glucose, biochemistry, and lipid panels were studied in the central biochemistry laboratory. Transthoracic echocardiography, transesophageal echocardiography, carotid vertebral Doppler ultrasonography, cranial MRI, MR angiography, vasculitis tests, and coagulation tests were conducted when further examination was required for etiopathogenesis. Ischemic LVH was classified based on the TOAST for etiopathogenesis. The patients with an identified cause (vasculitis, dissection, blood diseases, etc.), those without an

identified cause, and those where more than one cause was determined were excluded from the study. The presence of MetS was determined in 80 patients: 39 had large artery atherosclerosis (22 men, 17 women), 27 had small artery occlusion (16 men, 11 women), and 14 had cardioembolic disease (8 men, 6 women). Patients were analyzed based on the MetS diagnostic criteria specified in the NCEP ATP-III: 1- BCS E > 102 cm, K > 88 cm 2- TG ≥ 150 mg/dl 3- HDL – K E < 40 mg/dl, K < 50 mg/dl 4- Blood Pressure ≥ 130 /85 mmHg 5- FBG ≥ 110 mg/dl. Patients who met 3 or more of these 5 criteria were diagnosed with MetS.

### Statistical Analysis

Statistical analyzes were conducted on the NCCS 2007 software. In addition to descriptive statistical methods (mean, standard deviation), one-way analysis of variance was employed to compare inter-group data, subgroups were compared with Tukey's multiple comparison, and the chi-square test was used to compare qualitative data. Significance interval was determined as  $p < 0.05$ .

### Findings

80 patients who were admitted with acute ischemic stroke diagnosis at Taksim Training and Research Hospital Neurology Clinic between April and October 2007 were included in the study. Based on the TOAST classification, 39 patients (48.75%) were in the BAA group, 27 patients (33.75%) were in the CAO group, and 14 patients (17.50%) were in the CE group. Descriptive patient statistics are presented in Table 1. Patient groups and demographics based on the TOAST classification are presented in Table 2. The patient age, gender and disease groups are presented in Table 3. No statistically significant difference was determined between the mean patient age in the BAA, CE, KAO groups ( $p = 0.111$ ). No statistically significant difference was determined between the patient gender in the BAA, CE, KAO groups ( $p = 0.973$ ). The patients in various groups and related MetS criteria are presented in Table 2. The distribution of patients based on the MetS criteria count is presented in Table 5.

**Table 1: Descriptive Statistics (n= 80)**

	Minimum	Maximum	Mean	SD
Age	43	86	64,76	11,31
Height	147	185	163,72	8,18
Weight	57	104	76,15	8,78
Waist circumference	86	115	99,98	7,47
BMI	18,61	36,88	28,47	3,35
Systolic P.	100	230	146,50	29,47
DiastolicP.	60	130	88,75	15,21
AKS	58	310	113,33	48,54
T. Cholesterol	122	267	184,64	39,58
Triglyceride	52	518	151,39	85,22
LDL – K	34	193	114,96	34,25
VLDL – K	12	92	29,93	13,61

**Table – 2 TOAST categories and patient demographics**

		BAA Group n:39		CE Group n:14		CAO Group n:27		
<b>DM</b>	No	20	51,30%	14	100,00%	24	88,90%	$\chi^2:17,75$
	Yes	19	48,70%	0	0,00%	3	11,10%	<b>p=0,0001</b>
<b>HT</b>	No	8	20,50%	7	50,00%	12	44,40%	$\chi^2:6,09$
	Yes	31	79,50%	7	50,00%	15	55,60%	<b>p=0,048</b>
<b>AF</b>	No	37	94,90%	8	57,10%	26	96,30%	$\chi^2:17,01$
	Yes	2	5,10%	6	42,90%	1	3,70%	<b>p=0,0001</b>
<b>SVH (Ischemic)</b>	No	26	66,70%	11	78,60%	23	85,20%	$\chi^2:3,03$
	Yes	13	33,30%	3	21,40%	4	14,80%	p=0,219
<b>Smoking</b>	No	18	46,20%	5	35,70%	11	40,70%	$\chi^2:0,511$
	Yes	21	53,80%	9	64,30%	16	59,30%	p=0,775
<b>Alcohol</b>	No	28	71,80%	8	57,10%	22	81,50%	$\chi^2:2,75$
	Yes	11	28,20%	6	42,90%	5	18,50%	p=0,252
<b>Antihypertensive</b>	No	7	17,90%	6	42,90%	15	55,60%	$\chi^2:10,37$
	Yes	32	82,10%	8	57,10%	12	44,40%	<b>p=0,006</b>
	No	31	79,50%	14	100,00%	25	92,60%	$\chi^2:4,93$

<b>Oral Antidiabetic</b>	Yes	8	20,50%	0	0,00%	2	7,40%	p=0,085
<b>Insulin</b>	No	32	82,10%	14	100,00%	27	100,00%	$\chi^2:8,06$
	Yes	7	17,90%	0	0,00%	0	0,00%	<b>p=0,018</b>
<b>Anti Agregant</b>	No	18	46,20%	12	85,70%	18	66,70%	$\chi^2:7,47$
	Yes	21	53,80%	2	14,30%	9	33,30%	<b>p=0,024</b>
<b>Anti Coagulant</b>	No	37	94,90%	9	64,30%	27	100,00%	$\chi^2:15,97$
	Yes	2	5,10%	5	35,70%	0	0,00%	<b>p=0,0001</b>

**Table – 3 Groups based on patient age, gender and TOAST categories**

		<b>BAA Group n:39</b>	<b>CE Group n:14</b>	<b>CAO Group n:27</b>		<b>p</b>
<b>Age</b>		67,21±11,6	64,71±10,34	61,26±10,82	F:2,28	0,11
<b>Gender</b>	Male	22 (%56,4)	8 (%57,1)	16 (%59,3)	$\chi^2:0,05$	0,973
	Female	17 (%43,6)	6 (%42,9)	11 (%40,7)		

**Table –4 :Comparison of the patients based on fasting blood glucose, triglyceride, VLDL and MetS criteria and Tukey multiple comparison test.**

<b>Tukey Multiple Comparison test</b>	<b>Fasting Blood Glycose</b>	<b>Triglyceride</b>	<b>VLDL</b>	<b>MS Criteria</b>
<b>BAA Group/CE Group</b>	<b>0,031</b>	<b>0,018</b>	<b>0,044</b>	<b>0,001</b>
<b>BAA Group/CAO Group</b>	<b>0,01</b>	<b>0,03</b>	<b>0,047</b>	<b>0,001</b>
<b>CE Group/CAO Group</b>	0,987	0,781	0,801	0,998

**Table – 5 : Patient Distribution Based on MetS Criteria(n=80)**

	<b>Normal</b>	<b>%</b>	<b>Pathologic</b>	<b>%</b>
<b>ABDOMINAL OBESITY</b>	24	30	56	70

<b>HIGH TRIGLYCERIDE</b>	52	65	28	35
<b>LOW HDL-K</b>	23	28,8	57	71,3
<b>HIGH BLOOD PRESSURE</b>	19	23,8	61	76,3
<b>HIGH AKS</b>	47	58,8	33	41,3

MetS was determined in 48 out of 80 patients and was not identified in 32 patients. The MetS rate was 60% in the present study. Based on gender, 22 of 46 male patients (47.82%) and 26 of 34 female patients (76.47%) exhibited MetS, demonstrating that the MetS rate was significantly higher among females when compared to males.

Comparison of the patient groups based on fasting blood glucose, triglyceride, VLDL and MetS criteria count is presented in Table based on Tukey multiple comparison test results. Mean triglyceride was statistically significantly higher in the BAA group when compared to the CE and CAO groups ( $p = 0.018$ ,  $p = 0, 03$ ), the mean VLDL was statistically significantly higher in the BAA group when compared to the CE and KAO groups ( $p=0.044$ ,  $p=0.047$ ), the mean MS criteria positivity was statistically significantly higher in the BAA group when compared to the CE and CAO groups ( $p=0.001$ ,  $p= 0.001$ ).

### Discussion

Stroke is an important disease that threatens public health and leads to premature death and functional failure. It is one of the leading health burdens (1). Stroke incidence could be reduced with the identification of risk factors and the employment of a multifactorial approach (2). MetS is a set of metabolic abnormalities and risk factors associated with high cardiovascular risks and Type 2 DM risk. Characteristics of this syndrome include atherogenic dyslipidemia, impaired glucose regulation and / or insulin resistance, endothelial dysfunction, proinflammatory and prothrombotic states, and elevated blood pressure.

Studies conducted with NCEP ATP-III criteria reported MetS prevalence figures between 7.9% and 43.6% in males and between 7% and 56.7% in females (3). K. W. Paek et al. conducted a study with 5742 adult Koreans based on the NCEP ATP III criteria and reported that MetS prevalence was 25.5% in males and 28.7% in females. Its correlation with MetS was evident in young males and females with a family history of HT/Stroke or DM (4). In our study, we used the NCEP ATP-III criteria, most applicable in daily practice. In our analysis, we determined that 60% of the patients met at least 3 MetS criteria in the patient group of 80 individuals. S. Kurl, et al. reported that the relative risk of stroke adjusted for age and year of examination was 2 times higher in men with MetS [5]. R. Kowawoto, H. et al. conducted a study with 197 stroke patients and 356 controls, and after the findings were adjusted for age, gender, and smoking, they reported a significant correlation between MetS and atherothrombotic stroke risk (OR: 3.08, 95% confidence interval, 1.69 – 5.61) (5). HS Milionis, et al. conducted a study with 163 stroke and 166 controls and reported that the MetS prevalence was 46.0% in the patient group and 15.7% in the control group (6). The 3<sup>rd</sup> National Health and Nutrition study reported that MetS was significantly correlated with self-reported MI and stroke. A study conducted with hypertensive patients without CVD reported that MetS was an independent marker for both CVD and LVH. Another study reported that those who developed ischemic stroke during follow-up were older, less educated, had abdominal obesity, high blood pressure, high FBG, and had more baseline MetS components (7). Koren Morag et al. analyzed more than 14000 coronary heart patients

and reported a significant increase in ischemic stroke or TIA risk when MetS was present without DM. A 1.5-fold increase was reported in the risk in the presence of MetS alone and >2-fold in the presence of DM, demonstrating that the identification of MetS before DM would help the determination of high-risk patients for ischemic CVD. This risk is higher in women when compared to men (8.). A study conducted in 2003 analyzed MetS prevalence in CHD, LVH, peripheral artery disease or abdominal aortic aneurysm patients and reported that MetS prevalence was higher in women, and the waist circumference and HDL-C levels of the women who met the criteria were significantly different. The difference in MetS prevalence based on gender was attributed to differences in BCS and HDL-K criteria (9). To determine the MetS prevalence in Turkish population, TEKHARF (heart disease and risk factors in Turkish adults) database was reviewed for the year 2000 based on NCEP ATP – III guidelines, and it was observed that MetS was identified in 37% of the population over the age of 30. The MetS prevalence of 60% among our ischemic stroke patients was higher than the MetS prevalence in Turkish population (10). N. Cansaran, Ş. et al. conducted a study with 100 acute LVH patients and 100 controls to determine MetS prevalence. 76% of the patients was ischemic and 24% was hemorrhagic. The comparison of the age-adjusted patient and control groups revealed a significant difference in MetS prevalence. MetS was identified in 61.5% of the patients and 35.8% of the controls (11). The MetS prevalence reported in that study was consistent with our findings. In our study, pathologies were identified in the BCA analysis (87.2% in the BAA group, 64.3% in the CE group and 48.1% in the CAO group). Statistically significant differences were determined between the abdominal obesity rates in the BAA, CE and KAO groups ( $p = 0.003$ ). In the present study, low HDL - K was observed in 87.20% of the BAA group, 64.30% of the CE group, and 51.90% of the CAO group at pathological levels. 57 statistically significant differences were observed between the HDL-K levels in the BAA, CE, KAO groups ( $p=0.006$ ). N. Cansaran, et al. determined that 55.8% of the female patients and 27.2% of the male patients met the positive criteria in the analysis of HDL-C levels (11). In the present study, HDL - K level was  $38.68 \pm 6.17$  in the BAA group,  $41.46 \pm 7.7$

in the CE group, and  $41.21 \pm 7.15$  mg/dl in the CAO group. No statistically significant difference was determined between the mean HDL - K in the BAA, CE, KAO groups ( $p = 0.232$ ).

MetS was present in 76.90% of the BAA group, 42.90% of the CE group, and 44.40% of the CAO group, and statistically significant differences were determined between the groups ( $p = 0.011$ ).

In conclusion, Certain modifiable stroke risk factors are included in MetS factors. Stroke risk increases with the increase in both MetS and individual MetS components. Efforts to reduce the MetS components could be effective in stroke prevention.

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