

## Prevalence of Metabolic Syndrome and Its Association with Carotid Artery Intima-Media Thickness in Newly Diagnosed Hypertensive Patients

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### Özet

**Amaç:** Bu çalışmada yeni tespit edilmiş hipertansif hastalarda metabolik sendrom sıklığının ve karotis intima media kalınlığının araştırılması amaçlanmıştır.

**Gereç ve Yöntem:** Çalışmaya yeni tanı hipertansiyon ile dahiliye, nefroloji ve endokrinoloji polikliniklerine başvuran 98 hasta alındı. Metabolik Sendrom tanısı için NCEP / ATP III kriterleri kullanıldı. Tüm katılımcılara karotis intima media kalınlığını ölçmek için yüksek çözünürlüklü B-mod ultrasonografi yapıldı.

**Bulgular:** Çalışmaya toplam 98 hasta alındı. Hastaların yaş ortalaması  $47.5 \pm 8.7$  yıl idi ve % 57'si kadın olan grubumuzun % 62.2 'si NCEP / ATP III Metabolik Sendrom kriterlerinin en az 3' ünü karşılamaktaydı. (kadınlarda% 64.9 ve erkeklerde% 58.5). Abdominal obezite Metabolik Sendrom komponentlerinden en sık gözlenen idi (% 56,1). Metabolik Sendrom olan ve olmayan gruplarda karotis intima media kalınlığı arasında fark yoktu ( $p = 0,887$ ) ve karotis intima media kalınlığı metabolik sendrom bileşenlerinin sayısındaki artışla da değişmedi ( $p = 0.071$ ).

**Sonuç:** Çalışmamızda yeni tespit hipertansif hastalarda metabolik sendromu sıklığının oldukça fazla olduğunu ve Metabolik Sendrom varlığının karotis intima media kalınlığı artışına ilave risk katmadığını saptadık.

**Anahtar Kelimeler:** Yeni tespit hipertansiyon, metabolik sendrom, karotis intima media kalınlığı

### Abstract

**Objective :** The aim of this study was to investigate the prevalence of metabolic syndrome and carotid artery intima-media thickness in newly diagnosed hypertensive patients.

**Materials and Methods:** This study included 98 patients, aged 30-69 years who were consecutively admitted to our internal medicine, nephrology and endocrinology outpatient clinics because of newly diagnosed hypertension. We used the NCEP/ATP III criteria for the diagnosis of metabolic syndrome. All participants underwent high-resolution B-mode ultrasonography to measure carotid artery intima-media thickness.

**Results:** We enrolled a total of 98 patients in the current study. Their mean age was  $47.5 \pm 8.7$  years and 57% were female. 62.2% of the subjects (64.9% in females and 58.5% in males) met at least 3 criteria of ATP III and were diagnosed with metabolic syndrome. Abdominal obesity was the most frequent (56.1%) component of metabolic syndrome among the subjects. Carotid artery intima-media thickness was not different in the metabolic syndrome positive and negative groups ( $p=0.887$ ) and did not change with increasing numbers of metabolic syndrome components ( $p= 0.071$ ).

**Conclusion:** Our study highlights the importance of an increased burden of metabolic syndrome in newly diagnosed hypertensive patients and co-existence of metabolic syndrome in hypertensive patients does not add additional risk in the increase of carotid intima media thickness.

**Key words:** newly diagnosed hypertension, metabolic syndrome, and carotid intima- media thickness

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**Running title:**

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**Introduction:**

Hypertension (HT) is an important cardiovascular disease (CVD) risk factor worldwide and frequently coexists with many other risk factors such as obesity, dyslipidemia, impaired glucose tolerance, and hyperuricemia<sup>1,2</sup>. When hypertension and other metabolic risk factors are concomitantly present in an individual, the total cardiovascular risk may increase<sup>3</sup>.

Metabolic syndrome (MetS) is the clustering of multiple CVD risk factors. Actually, presence of HT is one of the components for diagnosis of MetS according to the National Cholesterol and Education Program Adult Treatment Panel III (NCEP ATP III) 4. Presence of three of the following five conditions is needed for diagnosing a patient as MetS: abdominal obesity (waist circumference >102 cm in men and >88 cm in women); hypertriglyceridemia: >150 mg/dl (1.695 mmol/l); low high-density lipoprotein cholesterol: <40 mg/dl (<1.036 mmol/l) in men and <50 mg/dl (<1.295 mmol/l) in women; high blood pressure: >130/85 mmHg; and high fasting glucose: >100 mg/dl (5.6 mmol/l). MetS has been associated with an increased tendency to develop type -2 diabetes mellitus and cardiovascular diseases<sup>5</sup>.

Carotid artery intima-media thickness (CIMT) is an intermediate phenotype for early atherosclerosis. High CIMT values have been associated with cardiovascular disease, coronary atherosclerosis, and related risk factors in cross-sectional studies<sup>6,7</sup>. Further, since CIMT can be measured relatively simply and noninvasively; it represents a useful diagnostic tool.

In the current study, our first aim was to investigate the prevalence of metabolic syndrome in newly diagnosed hypertensive patients. Secondly, we aimed to evaluate whether carotid artery intima-media thickness may differ in hypertensive patients according to the presence of metabolic syndrome.

**Patients and Methods**

This study included 98 patients, aged 30-69 years who were consecutively admitted to our internal medicine, nephrology and endocrinology outpatient clinics because of newly diagnosed hypertension. The patients who receive antihypertensive medication, antidiabetic drugs and antihyperlipidemic agents were excluded from the study and also patients with a

previous cardiovascular event were excluded. All the patients gave written informed consent.

Arterial blood pressure (BP) measurements were performed by the same calibrated sphygmomanometer after 5 minutes of rest in sitting position. Measurements were performed on both arms at 5 minutes interval. The average of the two measurements obtained in each arm was taken as the subject's blood pressure. Patients with blood pressure values greater than 140/90 mmHg were considered hypertensive<sup>3</sup>.

Patients' demographic characteristics were recorded. Height, weight and waist circumference values were obtained by the same measurement tools. The waist circumference (WC) was measured at the high point of the iliac crest at minimal respiration to the nearest 0.1 cm. The body mass index (BMI) was calculated by dividing the body weight in kilograms by the square of the height in meters. We used the NCEP/ATP III criteria for the diagnosis of metabolic syndrome<sup>4</sup>.

Blood samples were obtained from all subjects to test the levels of fasting glucose, total cholesterol, triglyceride (TG), high-density lipoprotein cholesterol (HDL-cholesterol) and low-density lipoprotein cholesterol (LDL-cholesterol). The hexokinase method was used to measure glucose levels, and photometric method (Abbott Architect c16000 auto analyzer) was used to measure the TG, total cholesterol, and HDL-cholesterol and LDL-cholesterol levels.

All participants underwent high-resolution B-mode ultrasonography (Aplio 500, Toshiba Medical Systems, Tokyo, Japan). All scans and image measurements were carried out by the same investigator, who was blinded to the risk factor status of the participants at the distal common carotid artery (CCA) (1 cm proximal to dilation of the carotid bulb) at the far wall. Manual measurements were taken from both the right and the left side. The final CIMT obtained was the maximum CIMT between both sides.

**Statistical analysis**

Data were analyzed using SPSS Software (Version 17, SPSS, Inc., Chicago, IL, USA). Results were expressed as mean ± standard deviation. The Mann-Whitney U test was used to

compare the continuous variables and the Chi-square test was used to compare categorical variables. Spearman's rank correlation test was used for calculation of associations between variables. A p value of less than 0.05 was considered to be statistically significant.

## Results

We enrolled a total of 98 patients in the current study. Their mean age was  $47.5 \pm 8.7$  years and 57% were female. 79.6% of the patients had first-degree relatives with a history of hypertension.

62.2% of the subjects (64.9% in females and 58.5% in males) met at least 3 criteria of ATP III and were diagnosed with MetS. It has been shown that 31.6% of the all patients met 3 criteria, 19.4% met 4 and 11.2% met 5 criteria. Abdominal obesity was the most frequent (56.1%) component of MetS among the subjects. The prevalence of components of MetS are shown in table 1.

**Table 1: Prevalence of components of MetS in hypertensive patients according to the NCEP-ATP III criteria**

Criteria	All subjects (n=98)
Elevated BP (%)	100%
Increased WC (%)	56.1%
Elevated FPG (%)	54.1%
Elevated TG (%)	40.8%
Low HDL-C (%)	46.9%

We compared the patients according to the presence of MetS (table 2). Weights, BMI, waist circumference, triglyceride levels were significantly higher and HDL-C levels were significantly lower in patients with MetS (table 2).

CIMT was not different in the MetS positive and negative groups (CIMT MetS(+)/MetS(-)= $0.7 \pm 0.1/0.69 \pm 0.2$ mm, and  $p=0.887$ ) and did not change with increasing numbers of metabolic syndrome components ( $p=0.071$ ). In a subgroup analysis according to the gender, CIMT values were significantly higher in male subjects with MetS ( $0.78 \pm 1.1$  mm vs  $0.68 \pm 1.1$  mm) than female subjects with MetS ( $p=0.018$ ). In addition, male subjects with MetS had higher TG levels ( $224.9 \pm 135$  mg/dl vs  $159.8 \pm 90.9$  mg/dl,  $p=0.028$ ), and lower

HDL-C levels ( $35.5 \pm 6.3$  mg/dl vs  $48.2 \pm 11.1$  mg/dl,  $p=0.0001$ ) compared to female patients with MetS. However, there was no difference in age, BMI, FPG, blood pressure and WC between male and female patients. A significant positive correlation was found between the CIMT and age, systolic blood pressure and LDL-C in the whole group (table 3).

**Table 2: The comparison of hypertensive patients according to the presence of metabolic syndrome**

Variable	Patients with MetS (n=61)	Patients without MetS(n=37)	p
Age (years)	$47.38 \pm 9$	$47.7 \pm 8.4$	0.826
Gender (% female)	60.6%	54%	0.333
Presence of smoking (%)	26.2%	21.6%	0.832
Systolic blood pressure (mmHg)	$160.3 \pm 16$	$157.8 \pm 13.5$	0.432
Diastolic blood pressure (mmHg)	$93.3 \pm 8.1$	$93.2 \pm 6.5$	0.969
Weight (kg)	$89.4 \pm 16.3$	$79.6 \pm 13$	0.002
BMI (kg/m <sup>2</sup> )	$32.9 \pm 5.4$	$29.4 \pm 4.7$	0.002
Waist circumference(cm)	$99 \pm 10.1$	$91.5 \pm 9.1$	0.0001
Fasting plasma glucose (mg/dl)	$108.5 \pm 21.7$	$101.8 \pm 26.9$	0.179
Triglyceride (mg/dl)	$185.4 \pm 113.9$	$112.7 \pm 45.5$	0.0001
HDL- C (mg/dl)	$43.28 \pm 11.3$	$55.2 \pm 11.8$	0.0001
Total- C (mg/dl)	$218.7 \pm 36.2$	$226.1 \pm 38.4$	0.343
LDL- C (mg/dl)	$138.5 \pm 30.7$	$147.1 \pm 32.6$	0.2
Uric acid	$4.6 \pm 1.8$	$4.8 \pm 1.5$	0.753
Carotid intima media thickness (mm)	$0.7 \pm 0.1$	$0.69 \pm 0.2$	0.887

*BMI* body mass index, *HDL-C* high density lipoprotein cholesterol, *Total- C* total cholesterol, *LDL-C* low density lipoprotein cholesterol

## Discussion

In the present study, we found that 62.2% of newly diagnosed hypertensive had metabolic syndrome, especially abdominal obesity was the most frequent (56.1%) component of MetS among the subjects. These findings suggest that all the hypertensive patients must be evaluated for the presence of MetS at the time of diagnosis. Secondly, carotid intima media thickness, which is associated with subclinical atherosclerosis, was associated with age, systolic blood pressure and LDL-C, however there was not a correlation between CIMT and the other components of MetS. Our study suggests that co-

existence of MetS in hypertensive patients does not add additional risk in the increase of carotid intima media thickness. In 2006, a large population study showed that more than one-third (35.08 %) of the participants were obese and 27.38% of the individuals had MetS in Turkey<sup>8</sup>. Recently, a study TUR-DEP-2, that investigates the prevalence of pre-diabetes and diabetes in 26.499 adults, has demonstrated that prevalence of obesity is 36 % and hypertension is 31.4 % in Turkey<sup>9</sup>. While the rate of obesity increased by 40%, hypertension decreased by 11 % during the last 12 years in our country. Our study included newly diagnosed hypertensive patients, showed higher ratio of obesity and MetS than these studies.

**Table 3: The correlation between CIMT and clinical and metabolic parameters in patients with metabolic syndrome**

Age	0.628	0.0001*
Systolic blood pressure	0.264	0.047*
Diastolic blood pressure	0.195	0.155
Weight	0.148	0.271
BMI	0.007	0.957
WC	0.056	0.677
Fasting plasma glucose	0.144	0.287
Triglyceride	-0.039	0.772
HDL-C	-0.003	0.983
Total-C	0.205	0.133
LDL-C	0.267	0.049*
Uric acid	0.122	0.376

*BMI body mass index, WC waist circumference, HDL-C high density lipoprotein cholesterol, Total- C total cholesterol, LDL-C low density lipoprotein cholesterol*

The prevalence of MetS in hypertensive patients vary in different countries and is reported 34-65%. On the other hand, the prevalence of MetS in newly diagnosed hypertensive patients was evaluated in a few studies. In Italy the ratio was found 30.2% and in Nigeria 31.2% similarly. In the current study, we observed a higher prevalence compared to these studies and the most frequent component of MetS was abdominal obesity. The difference can be explained by the increasing trend rate of obesity in our country.

CIMT has been related to cardiovascular events, but the link between this finding and clinical parameters in specific populations are not clear yet. The association between CIMT and MetS were evaluated in numerous studies, however the results are conflicting. Most of the studies have reported an association between MetS and increased CIMT<sup>10-13</sup>. The Bogalusa Heart Study<sup>13</sup> reported that MetS, defined by either NCEP ATP III or WHO criteria, was associated with increased CIMT in young adults. However, Richart T. et al did not find such a correlation between CIMT and MetS<sup>14</sup>. A study by Della-Morte and colleagues also showed that MetS was not associated with CIMT<sup>15</sup>. In the present study, we did not find a difference between CIMT values of hypertensive subjects according to co-existence of MetS. This finding may be due to our study population, which comprises hypertensive patients. Hypertension is a well-known risk factor for cardiovascular diseases and association between CIMT and hypertension was demonstrated in the researches<sup>16,17</sup>. In our study, systolic blood pressure levels were also associated with carotid intima-media thickness in MetS positive group.

The identification of risk factors associated with hypertension and subclinical atherosclerosis is important to prevent cardiovascular events. Increasing age, obesity, dyslipidemia and diabetes are closely associated with CIMT<sup>18</sup>. Trindade M. et al demonstrated a significant correlation between CIMT and age, systolic blood pressure and LDL-C<sup>19</sup>. In agreement with these results, we also observed a correlation between CIMT and age, systolic blood pressure and LDL-C.

Several studies have examined the relationship between subclinical atherosclerosis and obesity indicated by elevated body mass index or waist circumference<sup>2-24</sup>. However, this association is still controversial. We found that BMI or waist circumference had no effect on CIMT in subjects with MetS. Age is an important determinant factor for CIMT value. In some studies, age was an independent predictor factor for increased CIMT<sup>25,26</sup>. In our study also CIMT was associated with increasing age.

### Conclusion

In conclusion, our study highlights the importance of an increased burden of metabolic syndrome in newly diagnosed

hypertensive patients. Our study shows that co-existence of MetS in hypertensive patients does not add additional risk in the increase of carotid intima media thickness.

**Conflict of Interest:**

Authors declare no competing interest.

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