THE METABOLIC SYNDROME IN PATIENTS WITH OSTEOARTHRITIS

OSTEOARTRİT OLAN HASTALARDAKİ METABOLİK SENDROM

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ABSTRACT

Objective: The aim of our study was to examine the frequency of the metabolic syndrome in OA patients and investigate the relationship between the MS components and degree of degenerative knee OA.

Material and Methods: Patients with knee OA and 70 healthy control subjects were participated in this study. Demographic data including age, sex, body mass index, disease duration, cigarette and alcohol consumption, physical activity, comorbid diseases and medication of all subjects were recorded. Radiological assessments for the degree of OA were carried out in patients group.

Results: 54 female and 16 male OA patients, 50 female, 20 male healthy control subjects with a mean age of 66.2±9.0 and 61.6±9.1 years respectively, were included to the study. There was no difference between the demographic characteristics of the patients and control groups. Among patients with OA, the frequency of the MS were 66.7 % in female and 31.3 % in male subjects, while in the control group the frequency was 42.0 % and 35.0 % in female and male control subjects respectively. There was a significant correlation between the Kellgren-Lawrence scores and systolic and diastolic blood pressure levels in OA patients with the metabolic syndrome ($p<0.05$).

Conclusion: In conclusion female patients with OA have higher rates of MS compared with subjects without OA. Our findings highlight the importance of assessing the component of MS in patients with OA, which may offer the possibility to direct future efforts to reduce the morbidity of this condition.

Key words: metabolic syndrome, obesity, osteoarthritis, body mass index

ÖZET

Amaç: Çalışmamızın amacı, OA hastalarında metabolik sendrom sıklığını incelemek ve diz OA nin dejeneratif değişiklik derecesiyle MS komponentleri arasındaki ilişkiyi araştırmaktır.

Materyal Metod: Diz OA olan 70 hasta ve 70 sağlıklı kontrol bu çalışmaya dahil edildi. Tüm hastaların, yaş, cinsiyet, vücut kitle indeksini içeren demografik bilgileri, hastalık süresi, sigara ve alkol tüketimi, fiziksel aktivite, komorbid hastalıklar ve ilaç kullanımı öğrenilerek kaydedildi. Hasta grubunda, OA derecesini belirlemek için radyolojik değerlendirme gerçekleştirildi.

Bulgular: 54 kadın ve 16 erkek OA hastası, 50 kadın, 20 erkek sağlıklı kontrol, yaş ortalamaları sırasıyla 66.2±9.0 ve 61.6±9.1yıl olan şahıslar çalışmaya dahil edildi. Hasta ve kontrol grubu arasında demografik özellikler açısından fark yoktu. MS görülme sıklığı, OA'li kadın hastalarda %66.7 ve erkeklerde %31.3, kontrol grubunda ise kadınlarda %42.0, erkeklerde %35.0'dü. MS'lu OA hastalarında, sistolik ve diastolik kan basıncı düzeyi ile KellgrenLawrence skorları arasında önemli bir korelasyon mevcuttu ($p<0.05$).

Sonuç: Sonuç olarak, OA olan kadın hastalarda OA olmayanlarla kıyaslandığında MS görülme sıklığı daha yüksekti. Bizim bulgularımız göstermiştirki, OA'li hastalarda MS komponentlerini değerlendirmek, bu durumla ilgili morbiditeyi azaltmak için gerekli çabayı gösterme olasılığı sunar.

Anahtar kelimeler: metabolik sendrom, obezite, osteoartrit, vücut kitle indeksi, rehabilitasyon

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INTRODUCTION

The metabolic syndrome (MS) is one of the most common metabolic illnesses, comprised of a heterogeneous group of metabolic abnormalities (1,2). MS patients have been defined as having several findings like abdominal obesity, insuline resistance (elevated fasting glucose), hypertension and dyslipidemia (elevated triglyceride and decreased high-density lipoprotein (HDL) cholesterol levels) (3). The MS is associated with mortality and morbidity and the prevalence of MS is likely to grow even higher in coming years and it will likely be an increasingly important focus in disease prevention (4).

Previous reports have indicated that the MS may be linked to adverse health outcomes through an association with obesity (5). These findings suggested that obesity may precede the development of other metabolic syndrome components. The effects of excess weight on morbidity and mortality have been known for many years (6-8). Osteoarthritis (OA) is significantly increased in overweight individuals (9). The OA that develops in the knees may be directly related to the trauma that is associated with the degree of excess body weight (7). Obesity is one of the major risk factors both for the MS and OA and there is several data about the relationship between OA and the MS (10,11,12).

The aim of this study was to examine the frequency of the metabolic syndrome in OA patients and investigate the relationship between the metabolic syndrome components and degree of degenerative knee OA.

MATERIALS AND METHODS

Seventy patients with knee OA (54 female and 16 male), meeting the American College of Rheumatology criteria for classification of knee OA (13), and 70 healthy control subjects (50 female, 20 male) were enrolled from out-patient clinic of Physical Medicine and Rehabilitation. Demographic data including age, sex, body mass index, disease duration, comorbid diseases and medication of all subjects were recorded. We also assessed the alcohol consumption, smoking habits and exercise status. Subjects who exercised regularly were asked the number of hours they exercised per week. Physical inactivity was defined as no leisure-time physical activity in the past month. Smokers were questioned about the total number of packs of cigarettes per year. We counted participants who reported currently using antihypertensive or antidiabetic medication as participants with high blood pressure or diabetes, respectively.

Height and body weight were measured and body mass index (BMI) was calculated from height and weight measurements; with the formula weight (kg) / height (m^2). Waist circumference (cm) of the subjects was measured at the umbilical level, to the nearest 0.1 cm at the narrowest point between the lowest rib and the upper most lateral border of the right iliac crest. Obese patients were divided into 5 groups according to their BMI, based on the obesity classification of World Health Organization (WHO): Low-weighted ($\leq$18.5 kg/m^2), normal weighted (18.5-24.9 kg/m^2), grade 1 over-weighted (25-29.9 kg/m^2); grade 2 over-weighted (30-39.9 kg/m^2); grade 3 over-weighted (>40kg/m^2) (14). Blood pressure of the patients was measured with a sphygmomanometer (Riester Rİ-1002, desk model) after the subject has rested for 5 min in a sitting position. Three readings of systolic and diastolic blood pressure were recorded and the average of each measurement was used for the data analysis. The subjects refrained from smoking or ingesting caffeine for 30 min before the measurement. All participants were examined by the same physician. Blood samples were collected from the antecubital vein to measure serum concentrations of glucose, total cholesterol, triglycerides, HDL cholesterol, after 10-12 hours of starvation. The biochemical analyses were carried out within 2 hours of blood sampling and were measured by calorimetric method using a Cobas Mira Plus autoanalyzer (Roche diagnostics, Mannheim, Germany). Details of the laboratory procedures of all these tests were published elsewhere. The bilateral knee radiographs of the patients were performed at standart positions and assessed according to Kellgren-Lawrence scale in order to identify the degree of OA (15).

We used the 2001 definition of the metabolic syndrome suggested by the National Cholesterol Education Program Adult Treatment Panel III (16). The metabolic syndrome was defined as 3 or more of the following 5 risk factors: 1) Abdominal obesity (waist circumference >90 cm for men and >80 cm for women), 2) serum triglyceride level >150 mg/ dL, 3) serum HDL cholesterol <40 mg/ dL for men and <50 mg/dL for women, 4) systolic/diastolic blood pressure >130/85 mm Hg, and 5) fasting plasma glucose >110 mg/dL. We calculated the frequency of metabolic syndrome by sex and degree of obesity in the study groups. The relationship between the components of MS and degree of OA according to Kellgren-Lawrence scores were also investigated.

Statistical Analysis:

Demographic data were analysed by descriptive statistics. Statistical analyses were performed by student t test for comparison of means and chi square tests as appropriate. The difference between male and female subjects in patient and control groups were also assessed by student t test and chi square tests. Logistic regression models were used to examine the relationship between demographic variables and the MS. The frequency of MS was assessed by counting the subjects in patient and control groups. The subjects with metabolic syndrome were defined as percent of the participitans according to the groups. The difference between the characteristics of the patients with and without metabolic syndrome were also analyzed by Mann Whitney-U test and students t test as appropriate. Spearman correlation analysis was used to assess the relationship between the components of MS and Kellgren-Lawrence scores. SPSS 11.0 version was used for all the statistical analyses. p values less than 0.05 were considered as statistically significant.

RESULTS

Seventy OA patients and 70 healthy control subjects with a mean age of 66.2±9.0 and 61.6 ± 9.1 years respectively, were included in the study. The demographic characteristics of the two groups are presented in Table 1. There was no statistically significant difference between the groups according to sex, BMI, exercise status, smoking habits and alcohol consumption (p>0.05). The mean duration of OA was 7.0±2.2 years in this study group. The mean number of comorbid diseases (hypertension and diabetes mellitus) were 40 (57%) and 35 (50%) in patients and control groups respectively. 36 patients were on antihypertensives and antidiabetics medication and 25 control subjects were using antihypertensives and antidiabetics drugs. Patients with OA were more likely to use analgesics and NSAIDs.

Tablo-II

The prevalance of metabolic syndrome in study and control groups according to sex

	Study group n= 100	Control group n=72
Metabolic syndrome (+) (F/M)	36/5	21/7
Metabolic syndrome (-) (F/M)	18/11	29/13

F: female M: male

Twenty-five subjects in the patient group and 22 subjects in the control group were smokers. Four subjects in the patient group and two patients in the control group were taking alcohol regularly. There was only 10 patients and 6 controls that exercised regularly with a mean number of 3 hours/week. 90 % of the subjects were physically inactive.

Among patients with OA, the frequency of the MS was 66.7 % in female and 31.3 % in male subjects, while in the control group the frequency was 42.0 % and 35.0 % in female and male control subjects respectively (Table 2). The frequency of the MS did not differ in male patients and control subjects, but it has significantly differed among female patients and control participants.

Most of the patients had grade 2 degree of OA. Sixty four patients in the OA group and 60 patients in the control group were obese. The distribution of subjects in shown obesity classification of WHO were

Tablo-I

The demographic and metabolic characteristics for the study and control groups (mean±SD).

Variables	Study group n=100	Control group n=72	p
Age (year)	66.2±9.0	61.6±9.1	0.00
BMI (kg/m^2)	30.8±3.8	29.8±5.0	0.05
Sistolic blood pressure (mmHg)	157.3±30.2	151.7±28.7	0.32
Diastolic blood pressure (mmHg)	97.2±15.4	92.8±15.9	0.02
Fasting glucose level (mg/dl)	118.4±49.3	123.2±59.8	0.85
Hypertriglyceridemia (mg/dl)	137.8±98.3	123.2±59.8	0.70
Low HDL cholesterol (mg/dl)	45.7±7.1	45.5±8.0	0.83
Abdominal obesity (cm)	95.3±10.6	91.4±11.4	0.02
CRP (mgr/dlt)	1.1±0.7	0.6±0.1	0.95
ESR (mm/h)	25.5±19.7	23.4±18.2	0.73

MS: *Metabolic Syndrome* ***BMI****: Body mass index* ***CRP****:C-reactive protein* ***ESR****:Erythrocyte sedimentation rate*
±SD*: Standart Deviation*

Tablo-III
The comparison of obesity classification between the groups according to WHO

BMI	Study Group F/ M n=70	Control Group F/ M n=70
Low –weighted (≤18.5 kg/m^2)	-	-
Normal- weighted (18.5-24.9 kg/m^2)	4 / 2	6 / 5
Grade 1 over-weighted (25.0-29.9 kg/m^2)	15 / 8	22 / 9
Grade 2 over-weighted (30.0-39.9 kg/m^2)	35 / 6	20 / 5
Grade 3 over-weighted (≥40.0 kg/m^2)	0 / 0	3 / 0

BMI; Body Mass Index **WHO**; World Health Organization
F;female **M**;male

indicated in Table 3. When we compared the groups according to obesity classification, the frequency of the MS was 73.2 % (n=30) in patients with OA (≥grade 2, n=41) and the frequency of the MS was 63 % (n=17) in the control group (≥grade 2, n=27).

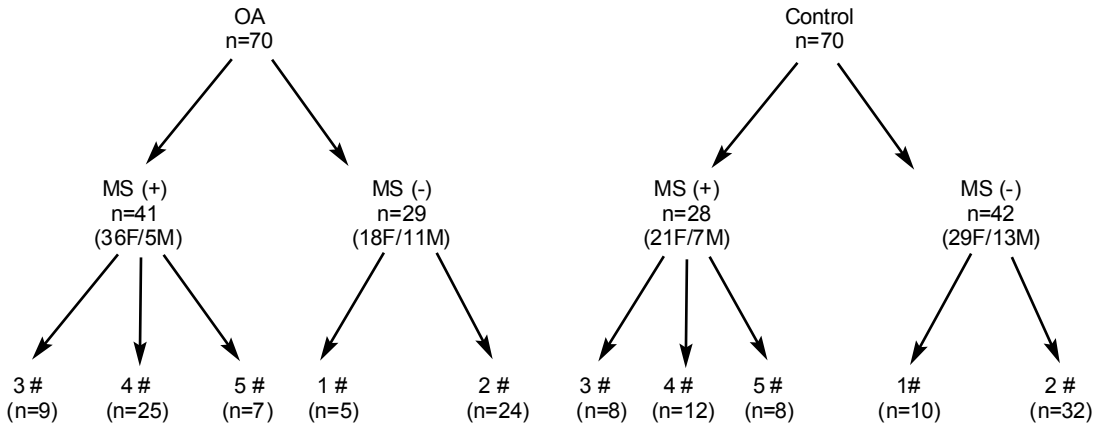
The distribution of patients and control subjects according to presence of MS and number of the MS components is shown in Figure 1. Most of the patients with the MS had three and four components of this syndrome, while patients without the MS syndrome were more likely to have two components of the MS.

When we compared the OA patients with and without the MS, there was no statistically significant difference between the groups according to comorbid disease, alcohol and cigarette consumption and exercise status (p>0.05). There was a significant correlation between the Kellgren-Lawrence scores and systolic and diastolic blood pressure levels in OA patients with the MS (Table 4). No other components of this syndrome was correlated with the degree of OA in the patients group (p>0.05). Also, there was a poor correlation between the K&L scores and SBP and DBP levels in female patients with OA (r=0.35 p=0.02, r=0.32 p=0.01, respectively). In patients with the MS, there was a significant correlation between each of the

Tablo-IV
The correlation of between the MS components and the K&L scores in OA patients with and without the MS.

OA Group (K&L scores)	SBP	DBP	Fasting glucose level	Hyper triglyceridemia	Low HDL cholesterol	Abdominal obesity
MS(+)	**0.35**	**0.32**	-0.10	0.05	-0.23	0.15
n=65	**0.02***	**0.01***	0.53	0.72	0.14	0.34
MS (-)	0.20	0.16	0.13	-0.19	0.05	-0.30
n=35	0.29	0.38	0.48	0.31	0.79	0.10

***OA:** Osteoarthritis **MS:** Metabolic syndrome **SBP**: Sistolic blood pressure (mmHg) **DBP**: Diastolic blood pressure (mmHg)*
**p value*



Şekil 1. The distrubition of patients and control subjects according to the presence of the MS and number of its components.

:Number of the components of the MS

components of the MS, as expected (spearman $p<0.05$).

DISCUSSION

The metabolic syndrome is a common population trait comprised of a heterogeneous group of disorders including abdominal obesity, hypertension, dyslipidemia and elevated fasting blood glucose (8,17). Importantly the MS predicts a high risk for the future development of type-2 diabetes and coronary artery disease (18). A recent cohort study found an increased risk of both cardiovascular disease morbidity and all cause mortality in patients with the MS (2,3). Although the mechanism underlying the development of the metabolic syndrome is not understood fully, it has been proposed that this syndrome appears as a result of the reciprocal action of several environmental factors, such as diet, smoking and physical activity, in individuals with a genetic predisposition that is not yet well known (19,20).

Obesity is a multi-factorial, chronic disorder that has reached epidemic proportions in developed and developing countries and is threatening to become a global epidemic (2,7). Multiple environmental and genetic factors are thought to influence the manifestation of degenerative osteoarthritis (21). Obese patients are at higher risk for OA, commonly the knee OA. The presence of obesity is also associated with an increased risk for metabolic syndrome (1,22). In some countries obesity is the principal reason for the increased prevalence of the metabolic syndrome (1,5,22). In the present study we assessed metabolic syndrome profiles in patients with degenerative knee OA depending to the hypothesis that obesity which is very common in OA, is one of the major risk factors for the metabolic syndrome. Korochina and et al. were compared OA course in patients with MS and those not MS. Most of the patients were women (74%) (12). The results presented here demonstrate that, female patients with knee OA are more likely to have the MS compared with healthy subjects. As anticipated, women were more likely to have the components of the MS than men in both patient and control groups. The relationship between degree of OA and components of the MS was highest in systolic and diastolic blood pressure levels in female patients. The degree of OA was not associated with any individual components of MS in men. These findings suggest that there may be important gender differences in the role OA and obesity that play in the metabolic syndrome.

Previous studies indicated that prevalence of the metabolic syndrome has been increased during the past years according to the sedentary life style on rise and dietary factors in developed and developing countries (8, 17). A recent report suggested that the prevalence of the metabolic syndrome increases with age, affecting more than 40% of those older than 60 years (18). The metabolic syndrome is very common in westernized countries and varies with age, ethnicity and body mass index. Ford et al found a 24 % prevalence of MS in individuals with and without diabetes using USA national data (17). Alexander et al studied a subset of patients 50 years and older, and indicated a 43.5 % prevalence of the metabolic syndrome (23). Some epidemiological studies have shown that one in two individuals over 50 year of age may have the metabolic syndrome (17, 19, 21). The frequency of the MS among our healthy population was 27 % in men and 38.6 in women, which is relatively higher than in some developed countries. This may be due to the age, sedentary lifestyle and higher BMI of our study group. In the OA group, the frequency of the metabolic syndrome were found to be higher in female patients than in control subjects. In other words female patients with OA have higher rates of MS compared with those with no OA.

The prevalence of OA is rising in parallel with the increasing age of the population. Obese persons have a higher prevalence of elevated blood pressure than lean persons. Some reports suggest that the elevated blood pressure accompanying obesity is less likely to produce cardiovascular disease than when it occurs in lean persons (2, 24, 25, 26). We analyzed the relationship between degree of OA and each component of metabolic syndrome. The results of the present study suggest that only the blood pressure components of the MS are positively associated with the degree of OA. This relationship may be due to the effect of the NSAIDs on the blood pressure or the involvement of the autonomic nerve system in osteoarticular disease, which needs to be further studied (27, 28, 29).

A few studies were investigated the influence of MS on the clinical course of OA and showed that the presence of MS in patients with OA was accompanied by more severe cartilage lesions (10,11).

The cornerstones of metabolic syndrome treatment are the management of weight and ensuring appropriate levels of physical activity (8, 20, 30). The benefits of lifestyle modifications including loss of weight, increased physical activity and dietary modification are also well established in treatment guidelines of knee OA (31, 32). As the high prevalence of these conditions may have serious implications for health care costs, there is an urgent need to develop compre-

hensive efforts directed at controlling the obesity and improving physical activity levels (22, 30, 31).

Our findings here highlight the relationship between OA and MS and indicate the importance of better understanding the role of obesity, especially among women, in the MS. The identification of metabolic syndrome components can help target the high risk patients for this condition in patients with osteoarthritis. We suggest to focus on the high prevalence of the metabolic syndrome in female patients with OA and the link between obesity and MS. Given that obesity is common in patients with knee OA, health care professionals should take special care to assess the components of MS and develop treatments that take into account the associated metabolic conditions in patients with the MS. This approach may offer the greatest possibility to direct future efforts, aimed at reducing the frequency of the metabolic syndrome and morbidity of this condition.

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