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Araştırma Makalesi

The Coexistence of Obesity and Physical Inactivity in Obstructive Sleep Apnea Patients with Slow Coronary Flow: Lifestyle Change Requirement

Yavaş Koroner Akım Tanısı Alan Obstruktif Uyku Apnesi Hastalarında Fiziksel İnaktivite ve Obezite Birlikteliği: Yaşam Tarzı Değişikliği Gereksinimi

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ABSTRACT

Purpose: Life style characteristics including physical inactivity and unhealthy eating cause obesity. With rising obesity, the number of people suffering from obstructive sleep apnea (OSA) syndrome is also increasing. If untreated, OSA causes increased cardiovascular morbidity and mortality. This study examined coexistence of obesity and physical inactivity in the OSA patients which were diagnosed with slow coronary flow. **Material and Methods:** After coronary angiography of 4515 patients, 316 patients were diagnosed with slow coronary flow. These patients were examined by an ear nose throat specialist and 276 patients were diagnosed in terms of OSA by using Berlin questionnaire (BQ). Control group patients (n=40) had normal coronary artery, which means they did not have slow coronary flow. Two hundred seventy-six patients with OSA were investigated for obesity and physical inactivity. The diagnosis of obesity was based on the Body Mass Index (BMI) according to the rules of the World Health Organization. Physical activity levels of the patients were evaluated with the International Physical Activity Questionnaire-Short Form (IPAQ, the short form). **Results:** The study group consisted of 276 patients (188 males, 88 females). The mean ages of the study group were 48.48 ±7.61 years. Of 276 patients, 258 patients were obese (BMI >30 kg/m2) according to WHO criteria. Mean BMI in the study group patients was 33.02±2.18 kg/m2. According to IPAQ-short form, 74% patients were inactive, 17% patients had low level activity, and 9% patients were active. **Conclusion:** We determined that obesity and physical inactivity coexist in OSA patients with slow coronary flow. Therefore, we recommend lifestyle changes, including increasing physical activity and healthy dietary habits to prevent obesity.

Key Words: Slow coronary flow; Obesity; Obstructive sleep apnea; Lifestyle changes

ÖZ

Amaç: Fiziksel inaktivite ve sağlıksız beslenme alışkanlıkları içeren yaşam tarzı obeziteye neden olmaktadır. Obezite hastalarında artışla birlikte obstruktif uyku apnesi sendromu sıklığı da artmaktadır. Obstrüktif uyku apnesi tedavi edilmezse kardiovaskuler mortalite ve morbidite artışına sebep olmaktadır. Bu çalışmada yavaş koroner akım tanısı konulan obstrüktif uyku apnesi hastalarında obezite ve fiziksel inaktivite birlikteliği araştırılmıştır. **Gereç ve Yöntem:** 4515 hastanın koroner anjiyografisi sonrası, 316 hasta yavaş koroner akım tanısı almıştır. Bu hastalar, kulak burun boğaz hastalıkları uzmanı tarafından değerlendirilmiş ve Berlin anketi kullanılarak 276 hastaya obstrüktif uyku apnesi tanısı konulmuştur. Obstrüktif uyku apnesi tanısı olan 276 hasta obezite ve fiziksel inaktivite açısından araştırılmıştır. Obezite tanısı Dünya Sağlık Örgütü (DSÖ) kurallarına göre Vücut Kitle İndeksi (VKİ) esas alınarak konulmuştur. Hastaların fiziksel inaktivite düzeyi ise Uluslararası Fiziksel Aktivite anketi-Kısa Form (UFAA-KF) ile değerlendirilmiştir. **Sonuçlar:** Çalışma grubu 276 hastadan oluşturuldu (188 erkek, 88 kadın). Ortalama yaş 48.48 ±7.61 yıl idi. Bu hastaların VKİ ortalamaları 33.02±2.18 kg/m2 olarak belirlendi. 276 hastanın 258'inde DSÖ kriterlerine göre obezite (VKİ> 30 kg/m2) saptandı. UFAA-KF skoruna göre hastaların %74 ü inaktif, %17 düşük seviyede aktif, %9 u aktifti. **Tartışma:** Yavaş koroner akımlı obstrüktif uyku apne hastalarında obezite ve fiziksel inaktivite birlikteliği saptandı. Fiziksel aktivitenin ve sağlıklı beslenme alışkanlıklarının arttırılması şeklinde yaşam tarzı değişiklikleri öneriyoruz.

Anahtar Kelimeler: Yavaş koroner akım; Obezite; Obstrüktif uyku apnesi; Yaşam tarzı değişikliği

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Atherosclerotic heart disease is a reason of significant morbidity and mortality. In 2010, the American Heart Association stated the cardiovascular health (CVH) score, including seven parameters (i.e., body mass index (BMI), healthy diet, physical activity, smoking status, blood pressure, blood glucose, and total cholesterol) (Lloyd-Jones, Hong, Labarthe et al, 2010). If untreated obstructive sleep apnea (OSA) is also related with cardiovascular morbidity and mortality (Punjabi, Caffo, Goodwin et al, 2009). Obesity is known to be one of the major risk factors of OSA (Stefan, Schick, and Haring 2017; Canoy, Boekholdt, Wareham et al, 2007). Unhealthy dietary habits are known to have highest risk for obesity and the second common risk is reported as physical inactivity (Stefan, Schick, and Haring 2017; Canoy, Boekholdt, Wareham et al, 2007).

Coronary slow-flow phenomenon (CSF) has been defined as distal opacification of the coronary artery is delayed on angiography in the absence of significant coronary artery disease (Tambe, Demany, Zimmerman et al, 1972). The pathogenesis of CSF involves multifactorial reasons, including functional and morphological abnormalities in the microvasculature, endothelial dysfunction, raised inflammatory markers, occult atherosclerosis and anatomical factors of epicardial arteries (Beltrame, 2012).

This study examined coexistence obesity and physical inactivity in OSA patients which diagnosed to have slow coronary flow (SCF).

MATERIAL AND METHODS

The prospective study included 4515 patients admitted angiography laboratory because of possible coronary artery disease in between April 2017 to June 2018. The study was approved by the ethics committee of Medicana International Ankara Hospital. The study was conducted in accordance with the principles of Declaration of Helsinki and written informed consent was obtained from each patients.

The 316 patients were diagnosed to have slow coronary flow (CSF). The demographic data, clinical histories, atherosclerosis risk factors, and laboratory and angiographic findings of all CSF were collected. CSF was diagnosed based on the corrected TIMI Frame count (CTFC) (Gibson, Cannon, Daley et al, 1996).

These 316 patients were examined by an ear nose throat specialist and were asked questions by using Berlin Questionnaire (BQ). 276 of 316 patients were diagnosed as OSA. Control group patients (n=40) had normal coronary artery, which was no slow coronary flow and non OSA patients.

Of 276 OSA patients, 258 patients were obese (BMI >30 kg/m2) according to World Health Organization criteria 2000.

The International Physical Activity Questionnaire – Short Form (IPAQ score, the short form) has been investigated in OSA patients (Craig, Marshall, Sjöström et al, 2003). The physical activity divided into three groups (inactivity group; <600 MET-minute/week, low level active group; 600-3000 MET-minute/week, active group >3000 MET-minute/week).

The exclusion criteria were anatomic nasal and oropharingeal obstruction, valvular heart disease (more than mild), ventricular dysfunction pulmonary arterial hypertension (pulmonary artery systolic pressure above 25 mm Hg in transthoracic echocardiography), CSF secondary to coronary ectasia or spasm, connective tissue disorders, presence of congenital heart anomalies, heart rhythm disorders other than sinus tachycardia, and acute coronary syndrome.

Coronary angiography; CSF

Standard left and right coronary angiography was performed in all cases and control patients via the femoral approach, using Judkins catheters (Bangalore, and Bhatt, 2011). The angiograms were assessed, and coronary flow quantification was performed using the CTFC described by Gibson et al. The assessment was performed by an expert interventional cardiologist who was blinded to the clinical details of the study population. The first frame was defined as the first frame in which dye completely filled the entrance of the artery with ante grade flow, and the last frame was defined as the frame in which dye entered the distal landmark branch. After then, the values CTFC method described by Gibson et al. was obtained (Gibson, et al, 1996). The frame counts in the left anterior descending artery (LAD) were divided by 1.7 to correct for the increased length. The diagnosis of SCF was defined as CTFC >27 frames (images acquired @ 30 frames/s) and the delayed distal vessel opacification is in at least one epicardial vessel.

Berlin questionnaire

The BQ includes questions about snoring, daytime somnolence, BMI, and hypertension, is a brief and validated screening tool that identifies patients who are at high risk for OSA. According to BQ, the patients were recorded as being at high-risk for OSA if they had a positive score on two or more categories (Netzer, Stoohs, Netzer et al, 1999). The Turkish version of BQ were used (Ulasli, Gunay, Koyuncu et al, 2014).

Statistical Analysis

Continuous variables were given as mean±S.D.; categorical variables were defined as percentage. Data were tested for normal distribution using the Kolmogorov-Smirnov test. The Student's t-test was used for the univariate analysis of the continuous variables and the x2-test for the categorical variables. All tests of significance were two-tailed. Statistical significance was defined as $p < 0.05$. The SPSS statistical software (SPSS 21 for windows, Inc., Chicago, IL, USA) was used for all statistical calculations.

RESULTS

Of 4515 patients, 316 (6.9 %) met the criteria for SCF. After BQ and exclusion criteria, 276 patients had high-risk for OSA. These 276 patients were evaluated. Of 276 patients had 188 male (68%), 88 female (%32). The mean ages were 48.48 ±7.61 years. Mean BMI of the 276 SCF patients were 33.02±2.18 kg/m2. Demographic data in 276 OSA subjects were presented in Table 1.

CTFC in SCF group were LAD 33.85±3.66, LCX (circumflex artery) 33.71±4.56, and RCA (right coronary artery) 34.31±4.04. CTFC values were compared with control group (non-OSA). In control group, CTFC values were LAD 23.83±1.80, LCX 20.83±2.51, RCA 21.75±2.86 ($p<0.05$). The comparison of the groups were showed in table 2.

Berlin Questionnaire

Of 276 high-risk OSA patients, 155 (56.1%) had a positive score in category 1 (snoring) of the BQ, 165 (59.7%) had a positive score in category 2 (day time somnolence), and 258 (93.4 %) had a positive score in category 3 (BMI > 30 kg/m2).

IPAQ score

This questionnaire was evaluated in the 276 patients in study group. Of the patients, 74% patients were inactive, 17% patients were low level active, and 9% patients were active.

Table 1. Baseline characteristics of OSA patients with slow coronary flow.

	X±SD	**%**
Age (years)	48.48 ± 7.61	
Men (gender) (n=)	188	68
Women (gender) (n=)	88	32
Hypertension (n=)	118	42.7
Diabetes Mellitus (n=)	27	7.5
BMI (kg/m2)	33.02 ± 2.18	
IPAQ total score	1.35 ± 0.65	

OSA: Obstructive Sleep Apnea, IPAQ: International Physical Activity Questionnaire-Short Form

Table 2. The comparison of Angiographic Corrected TIMI frame count features and Body Mass Indexes of study group (SCF (+), OSA (+)) with control group (SCF (-), OSA (-)).

	Study group (n=276)	Control group (n=40)	p
LAD ctfc	33.85 ± 3.66	23.83 ± 1.80	<0.001
LCX ctfc	33.71 ± 4.56	20.83 ± 2.51	<0.001
RCA ctfc	34.31 ± 4.04	21.75 ± 2.86	<0.001
BMI	33.02 ± 2.18	27.12 ± 2.16	<0.001

SCF: Slow Coronary Flow, OSA: Obstructive Sleep Apnea, LAD: Left Anterior Descending Artery, LCX: Left Circumflex Artery, RCA: Right Coronary Artery, CTFC: Corrected TIMI Frame Count, TIMI: Thrombolysis in Myocardial Infarction, BMI: Body Mass Index

DISCUSSION

OSA syndrome has short intermittent high-frequency hypoxemia. The cyclical changes of hypoxemia with re-oxygenation causes increased production of reactive oxygen species and oxidative stress (Dewan, Nieto, and Somers, 2015). Moreover, hypoxemia stimulates chemoreflex stimulation, which causes sympathetic activation and vasoconstriction (Somers, Mark, Zavala et al, 1989). The chemoreflex responses to hypoxemia are heightened in patients with OSA which increases risk of cardiovascular diseases. There are very high levels of sympathetic activation in the patients with OSA during normoxic daytime wakefulness.

Metabolic syndrome is a group of metabolic and cardiovascular abnormalities, including central obesity and is associated with an increase in cardiovascular morbidity and mortality (Alberti, Eckel, Grundy et al, 2009; Ford, 2005). OSA is increasingly recognized as a major health problem. Obesity is the most common risk factor in OSA and, the prevalence of OSA is undoubtedly rising given the epidemic of obesity. Recent data also suggest that OSA is highly associated with the metabolic syndrome, and contributes to cardiometabolic dysfunction, and vasculopathy. The potential mechanisms of OSA-obesity-metabolic syndrome interaction involve sympathetic activation, oxidative stress, inflammation and neurohumoral changes. However, the studies showed that, a healthy diet and appropriate lifestyle modifications towards better control of metabolic function are equally important as CPAP treatment in the holistic management of OSA (Somers, Dyken, Clary et al, 1995; Lam, Mak, and Ip, 2012). Present study demonstrated that 81.6 % of SCF patients were obese and 87.3 % of SCF patients had also OSA. Moreover, OSA patients had more coronary flow rate delaying than non-OSA patients (Table 2).

Future trends in obesity have significant consequences for public health policy and expenditures related to CVD (Murphy, Schlumpf, Wright et al, 2012). Olshansky et al. postulated a potential decline in US life expectancy during the 21st century due to obesity, in the absence of prevention of other cardiovascular risk factors (Olshansky, Passaro, Hershow et al, 2005). Improvements in life expectancy as decreased prevalence of cigarette smoking, hypertension and dietary fat intake may counterbalance the increasing prevalence of obesity (Arnett, McGovern, Jacobs et al, 2002).

Physical inactivity and sedentary lifestyle is a global problem which is related to many chronic health disorders (Salord, Gasa, Mayos et al, 2014). Of the many published questionnaires, the IPAQ has been investigated in several populations. The short form records four types of physical activity: vigorous activity such as aerobics; moderate-intensity activity such as leisure cycling; walking, and sitting. The short form has been preferred by many researchers because it has equivalent psychometric properties to the long form despite being one-third the length (Saglam, Arikan, Savci et al, 2010). In the present study, OSA patients were inactive (%74) and low level active (%17) according to IPAQ.

This study established that the patients with OSA and SCF have commonly increased BMI index and abnormal IPAQ score. To prevent these conditions, individuals must make lifestyle changes to fight with physical inactivity and obesity.

Conclusion

There is the coexistence of obesity and physical inactivity in OSA patients with slow coronary flow. Therefore, we recommend lifestyle changes, including increasing physical activity and healthy dietary habits to avoid OSA and coronary slow flow.

Kaynaklar

Alberti, K.G., Eckel. R,H., Grundy, S.M., Zimmet, P.Z., Cleeman, J.I., Donato, K.A.,& et al. (2009). Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American Heart Association; world Heart Federation; international atherosclerosis society; and international association for the study of obesity. *Circulation*, 120 (16), 1640-1645.

Arnett, D.K., McGovern, P.G., Jacobs, D.R. Jr,. Shahar, E., Duval, S., Blackburn, H., & et al. R.V.(2002). Fifteen-year trends in cardiovascular risk factors (1980–1982 through 1995–1997): the Minnesota Heart Survey. *Am J Epidemiol*, 156, 929– 935.

Bangalore, S., & Bhatt D.L. (2011). Images in cardiovascular medicine. Right heart catheterization, coronary angiography, and percutaneous coronary intervention. *Circulation*, 124(17), e428-33.

Beltrame, J.F. (2012). Defining the coronary slow flow phenomenon. *Circ J*, 76; 818-20.

Canoy, D., Boekholdt, S.M., Wareham, N., Luben, R., Welch, A., Bingham, S., & et al. (2007). Body fat distribution and risk of coronary heart disease in men and women in the European Prospective Investigation Into Cancer and Nutrition in Norfolk cohort: A population-based prospective study. *Circulation*, 116, 2933–2943.

Craig, C.L., Marshall, A.L., Sjöström, M., Bauman, A.E., Booth, M.L., Ainsworth, B.E., & et al. (2003). International physical activity questionnaire: 12-Country reliability and validity. *Med Sci Sports Exerc*, 35, 1381-1395.

Dewan, N.A., Nieto, F.J., & Somers, V.K. (2015). Intermittent hypoxemia and OSA: implications for comorbidities. *Chest,* 147(1), 266-274.

Flegal, K.M., Carroll, M.D., Kit, B.K., & Ogden, C.L. (2012). Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. *JAMA*, 307:491–497.

Flemons, W.W. (2002). Clinical practice. Obstructive sleep apnea. *N Engl J Med*, 347, 498–504.

Ford, E.S. (2005). Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. *Diabetes Care*, 28, 1769-78.

Gibson, C.M., Cannon, C.P., Daley, W.L., Dodge, J.T. Jr, Alexander, B. Jr, Marble, S.J, & et al. (1996). TIMI frame count: a quantitative method of assessing coronary artery flow. *Circulation*, 93, 879-88.

Jennum, P., & Riha, R.L. (2009). Epidemiology of sleep apnea/hypopnea syndrome and sleep-disordered breathing. *Eur Respir J,* 33, 907–14.

Lam, J.C., Mak, J,C, & Ip, M.S. (2012). Obesity, obstructive sleep apnea and metabolic syndrome. *Respirology,* 17, 223-36.

Lloyd-Jones, D.M., Hong, Y., Labarthe, D., Mozaffarian, D., Appel, L.J., Van Horn, L., & et al. (2010). American heart association strategic planning task force and statistics committee. Defining and setting national goals for cardiovascular health promotion and disease reduction: the American heart association's strategic impact goal through 2020 and beyond. *Circulation*, 121(4), 586-613.

Murphy, EL., Schlumpf, K., Wright, D.J., Cable, R., Roback, J., Sacher, R., & et al. (2012). NHLBI Retrovirus Epidemiology Donor Study II. BMI and obesity in US blood donors: a potential public health role for the blood centre. *Public Health Nutrition*, 6, 964-71.

Netzer, N.C., Stoohs, R.A., Netzer, C.M., Clark, K., & Strohl, K.P. (1999). Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Intern Med*, 131, 485–491.

Olshansky, S.J., Passaro, D.J., Hershow, R.C., Layden, J., Carnes, B.A., Brody, J., & et al. (2005). A potential decline in life expectancy in the United States in the 21st century. *N Engl J Med*, 352, 1138–1145.

Punjabi, N.M., Caffo, B.S., Goodwin, J.L., Gottlieb, D.J., Newman, A.B., O'Connor, G.T., & et al. (2009). Sleep-disordered breathing and mortality: a prospective cohort study. *PLOS Medicine*, 6(8), e1000132.

Saglam, M., Arikan, H., Savci, S., Inal-Ince, D., Bosnak-Guclu, M., Karabulut, E., & et al. (2010). International physical activity questionnaire: reliability and validity of the Turkish version. *Percept Mot Skills*, 111(1), 278-84.

Salord, N., Gasa, M., Mayos, M., Fortuna-Gutierrez, A.M., Montserrat, J.M., Sánchez-de-la-Torre, M., & et al. (2014). Impact of OSA on biological markers in morbid obesity and metabolic syndrome. *J Clin Sleep Med*, 10(3), 263-70.

Somers, V.K., Dyken, M.E., Clary, M.P., & Abboud, F.M. (1995). Sympathetic neural mechanisms in obstructive sleep apnea. *J Clin Invest*, 96 (4), 1897 – 1904.

Somers, V.K., Mark, A.L., Zavala, D.C., & Abboud, F.M. (1989). Influence of ventilation and hypocapnia on sympathetic nerve responses to hypoxia in normal humans. *J Appl Physiol*, 67 (5), 2095 – 2100.

Stefan, N., Schick, F., & Haring, H.U. (2017). Causes, characteristics, and consequences of metabolically unhealthy normal weight in humans. *Cell Metabolism*, 26, 292–300.

Tambe, A.A., Demany, M.A., Zimmerman, H.A., & Mascarenhas, E. (1972). Angina pectoris and slow flow velocity of dye in coronary arteries-a new angiographic finding. *Am Heart J*, 84 (1), 66-71.

Ulasli, SS., Gunay, E., Koyuncu, T., Akar, O., Halici, B., Ulu, S., et & al. (2014). Predictive value of Berlin Questionnaire and Epworth Sleepiness Scale for obstructive sleep apnea in a sleep clinic population. *Clin Respir J*, 8(3), 292-6.

WHO Consultation on Obesity (1999: Geneva, Switzerland) & World Health Organization. (2000). Obesity: Preventing and managing the global epidemic. Report of a WHO Consultation. WHO Technical Report Series, No 894. Geneva, *World Health Organization. 2019 http://www.who.int/iris/handle/10665/42330.*