

Original Article / Orijinal Araştırma

Carotid intima-media thickness and Doppler ultrasonographic findings in patients with chronic obstructive pulmonary disease

Kronik obstrüktif akciğer hastalığı bulunan hastalarda karotis intima-media kalınlığı ve Doppler ultrasonografi bulguları

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Abstract

Aim. The effect of chronic obstructive pulmonary disease (COPD) on the selected arterial and venous ultrasonographic parameters including the intima-media thickness (IMT) of common carotid arteries (CCAs) and Doppler blood flow parameters of blood vessels were assessed. **Methods.** Ultrasonographic data of common carotid, right, and left internal carotid, vertebral, and femoral arteries in 80 asymptomatic COPD patients in stable phase with mild, moderate, severe, and very severe disease (20 patients in each group) were reviewed retrospectively. **Results.** Overall, the IMT of CCA increased with regard to the severity of COPD. Although increases were observed in the PSV, EDV, RI of left and right CCAs according to the severity of COPD, they were considerable equivocal. The PSV and EDV of internal carotid arteries (ICAs) and vertebral arteries did not changed according to the severity of COPD, although their RIs were increased in the severe and very severe cases. The Doppler parameters of femoral arteries of study groups revealed no meaningful change. **Conclusions.** COPD may increase the IMT of CCA; however, a meaningful change in the PSV, EDV, and RI of CCA, ICA, vertebral, and femoral arteries may not be observed. These findings suggest that in addition to the severity of COPD, the duration of COPD may be an important contributor to atherosclerosis.

Keywords: chronic obstructive pulmonary disease, intima-media thickness, blood-flow velocity, Doppler, ultrasonography

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Güner et al.: Carotid intima-media thickness and Doppler ultrasonographic findings in patients with chronic obstructive pulmonary disease

77

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Özet

Amaç. Kronik obstrüktif akciğer hastalığının (KOA) karotid arterlerinin intima media kalınlıkları ve kan damarlarının Doppler kan akım hızlarını içeren seçilmiş arteriyel ve venöz ultrasonografik parametreleri üzerine etkileri incelendi. **Yöntem.** Asemptomatik hafif, orta ve şiddetli ve çok şiddetli (her altgrupta 20 hasta olacak şekilde) kronik obstrüktif akciğer hastalığı olan 80 olgunun ana karotid, sağ ve sol karotid, vertebral ve femoral arterlerinin ultrasonografi raporları değerlendirildi. **Bulgular.** Genel olarak, ana karotid arterlerin intima media kalınlığı hastalığın şiddeti ölçüsünde artmış bulundu. Ana karotid arterlerin PSV, EDV ve RI değerleri büyük ölçüde artmış bulunmakla birlikte önemli tutarsızlıklarda gözlemlendi. Internal karotid ve vertebral arterlerin PSV ve EDV değerlerinde hastalığın şiddeti ile ilişkili değişiklikler gözlenmezken, RI değerlerinin şiddetli ve çok şiddetli olgularda arttığı gözlemlendi. Femoral damarların Doppler parametreleri hastalığın şiddeti ile anlamlı ilişki göstermedi. **Sonuçlar.** KOA ana karotid arterlerin intima media kalınlıklarını arttırabilir. Buna rağmen, incelenen damarlarda hastalığın durumu ile tutarlı bir değişiklik PSV, EDV ve RI parametreleri açısından önemli kabul edilebilecek bir değişiklik gözlenmedi. Bu durum hastalığın şiddeti kadar hastalığın süresinin de ateroskleroz gelişiminde önemli olduğunu desteklemektedir.

Anahtar sözcükler: kronik obstrüktif akciğer hastalığı, intima media kalınlığı, kan akım hızı, Doppler ultrasonografi

Introduction

Chronic obstructive pulmonary disease (COPD) is a term used to describe a number of chronic conditions presenting with many clinical and laboratory findings including fluctuating hypoxia-hypercapnia mainly due to the airway obstruction that is not fully reversible because of lung damage. These changes result in the clinical manifestations of COPD: dyspnea, cough, hypoxemia, and mucous production. Acute exacerbations and comorbidities add to the overall severity and complications of the disease. COPD is the fourth largest cause of death worldwide, in addition to many co-morbidities [1-3]. As a powerful, independent risk factor, COPD contributes to the development of cardiovascular diseases [4-6]. In COPD, patients have chronic systemic inflammation, hypercoagulable status, platelet activation and oxidative stress, as a whole, leading to atherosclerosis [7, 8]. However, according to current literature, the evidence of a causal relationship between COPD and vascular dysfunction is insufficient and more research are required to clarify their association with cofactors that are contributing clinical outcome. In radiological studies, the status of cardiovascular disease is under investigation. Carotid intima-media thickness (IMT) increases in COPD patients [9, 10]. Doppler ultrasonography is one of the important modalities to assess vascular disorder. There are studies investigating blood flow velocities in COPD patients [11-14].

According to our knowledge, there are not sufficient data to determine the effect of COPD on major vessels and their blood flows in a population asymptomatic for other systemic disorders. The aim of the present study was to assess the effect of COPD on the selected

Güner et al.: Carotid intima-media thickness and Doppler ultrasonographic findings in patients with chronic obstructive pulmonary disease

78

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arterial ultrasonographic and Doppler ultrasonographic parameters including the IMT, peak systolic velocity (PSV), and end diastolic velocity (EDV), resistive index (RI), blood flow velocity of common carotid arteries (CCAs), internal carotid arteries (ICAs), vertebral, and femoral arteries in an asymptomatic population.

Material and methods

In this study, Doppler ultrasonography examinations performed at our Radiology Service from September 2010 to February 2011 were reviewed retrospectively in 80 COPD patients in stable phase. These Doppler ultrasound examinations were requested by pneumologist for the differential diagnosis of comorbidities. For each case, a detailed review was conducted to confirm the absence of any vascular pathology. Patients with a history of any type of vascular abnormalities were excluded. Bilateral vascular ultrasonography and Doppler ultrasonography of common, right, and left internal carotid, vertebral, and femoral arteries were performed by using broadband 10 MHz linear transducers. Patients were examined while they were in a supine position. Heart rate and blood pressure were recorded prior to US examination. One radiologist performed all ultrasound examinations by an ultrasonography device (General Electric Logic 9; Waukesha, WI, USA) equipped with a 10 MHz linear probe. Intraobserver reliability was determined as Kappa coefficient ranged from 0.74-0.85.

Staging of COPD

During spirometry, the patient's age, sex, and height were recorded and entered into the spirometer. The time of last bronchodilator inhaler use were asked and patients were seated for the procedure. The most important values of spirometry were recorded as the forced expiratory volume in one second (FEV₁) and the forced vital capacity (FVC). The postbronchodilator ratio of FEV₁/FVC was accepted as the presence of airflow limitation; the postbronchodilator percent predicted value for FEV₁ were used to determine the severity of airflow limitation according to the Global Initiative of Chronic Obstructive Lung Disease (GOLD) criteria as shown in the Table 1 [3].

Table 1. Staging of COPD according to severity based on postbronchodilator FEV₁ [3].

Patients with FEV ₁ /FVC<0.7		
Stage I	Mild	FEV ₁ ≥80 percent predicted
Stage II	Moderate	50%≤FEV ₁ <80% predicted
Stage III	Severe	30%≤FEV ₁ <50% predicted
Stage IV	Very severe	FEV ₁ <30% predicted

FEV₁: forced expiratory volume in one second; FVC: forced vital capacity; respiratory failure: arterial partial pressure of oxygen (PaO₂) less than 60 mmHg (8 kPa) with or without arterial partial pressure of CO₂ (PaCO₂) greater than 50 mmHg (6.7 kPa) while breathing ambient air at sea level.

Güner et al.: Carotid intima-media thickness and Doppler ultrasonographic findings in patients with chronic obstructive pulmonary disease

79

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Mild (n=20), moderate (n=20), severe (n=20), and very severe (n=20) COPD patients were included in this study. Ultrasonography and Doppler ultrasonography were performed after an accommodation period for at least 20 min rest in supine position.

Assessment of carotid IMT

Participants underwent B-mode ultrasonography of the carotid arteries. IMT of the CCA were assessed. IMT in the CCA was determined in the far wall according to the leading edge principle. CCA IMT was then determined off-line as the mean wall thickness 1 cm proximal to the bifurcation.

Participants were examined supine with the head rotated 45° towards the left or right side. Imaging was done in the plane parallel to the neck with the jugular vein lying immediately above the common carotid artery. Images of the right common carotid artery were centered 10 to 15 mm below (caudad to) the right common carotid artery bulb. End-diastolic images (smallest diameter of the artery) were captured. IMT measurements were made on the far-wall of the common carotid artery over a distance of approximately 10 mm starting at least 5 mm to 10 mm below (caudad to) the right common carotid artery bulb. Carotid artery plaque was excluded [6, 7].

Assessment of vascular ultrasound and Doppler ultrasound parameters

The participants underwent ultrasonography of the common, right, and left internal carotid, vertebral, and femoral arteries for the measurement of Doppler flow parameters including the peak systolic velocity (PSV) and end diastolic velocity (EDV) and resistive index (RI). In all patients, routine carotid US studies were performed, which included gray-scale, pulsed Doppler, and color Doppler flow US examinations of the left and right CCAs and ICAs. Doppler spectral waveforms were obtained at prescribed intervals in the CCA and ICA. All measurements were made by using angle correction. Sampling sites in the CCA were defined as proximal (as close to the aortic arch as possible). The ICA was sampled proximally just beyond the bulb widening and distally in the most distal segment of ICA visible. The measured angle of insonation was less than 60° for all measurements [15].

Statistical analysis

Data were expressed as mean ± SD. The age, gender, body mass index (BMI), FEV₁, FEV₁%, FVC, PaO₂, PaCO₂, and pH levels, ultrasonographic and Doppler ultrasonographic parameters were analyzed with ANOVA with post hoc Tukey test. Significance was determined at the p<0.05 level.

Results

Table 2 presents age, sex ratio, BMI, and FEV₁, FEV₁%, FVC, PaO₂, PaCO₂, and pH levels of the mild, moderate, severe, and very severe COPD groups. The FEV₁, FVC, and paO₂ levels of mild and moderate groups were significantly higher than those of the severe and very severe groups (p<0.05). The FEV₁ and FEV₁% levels of mild group were significantly higher than those of the moderate, severe and very severe groups. However the paCO₂

Güner et al.: Carotid intima-media thickness and Doppler ultrasonographic findings in patients with chronic obstructive pulmonary disease 80

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level of mild group were significantly lower than those of the moderate, severe and very severe groups. The age, BMI, and pH levels were found comparable among the study groups.

Table 2. Selected clinical and spirometer data of study groups.

	Mild (n=20)	Moderate (n=20)	Severe (n=20)	Very severe (n=20)
Age (y)	60.1±10.4	60.8±7.8	62.8±8.3	61.1±8.7
Sex ratio (F/M)	12/8	6/14	5/15	5/15
BMI (kg/m ²)	30.6±6.5	29.3±5.4	28.6±3.7	29.9±3.9
FEV ₁	2.2±0.6a	1.6±0.5b	1.0±0.2	0.7±0.2
FEV ₁ %	85.0±14.7c	61.8±8.3d	37.8±4.7e	23.8±4.3
FVC	3.3±0.9f	2.8±0.9f	1.9±0.5	1.6±0.7
PaO ₂	71.5±16.1g	59.5±17.7g	56.0±14.5	51.8±12.3
PaCO ₂	35.0±7.1h	41.0±10.6	44.0±13.0	41.5±8.2
pH	7.44±0.04	7.41±0.05	7.44±0.05	7.42±0.05
a,c,hP<0.05 vs. moderate, severe and very severe groups. b,d,f,gP<0.05 vs. severe and very severe groups. eP<0.05 vs. very severe group.				

Figure 1 presents the IMTs of right and left common carotid arteries of the mild, moderate, severe, and very severe groups of COPD. The IMT of left common carotid artery of severe group was significantly higher than those of the mild, moderate and very severe groups ($p<0.05$). The IMT of right common carotid artery of mild group of COPD was significantly lower than those of moderate, severe, and very severe groups of COPD ($p<0.05$).

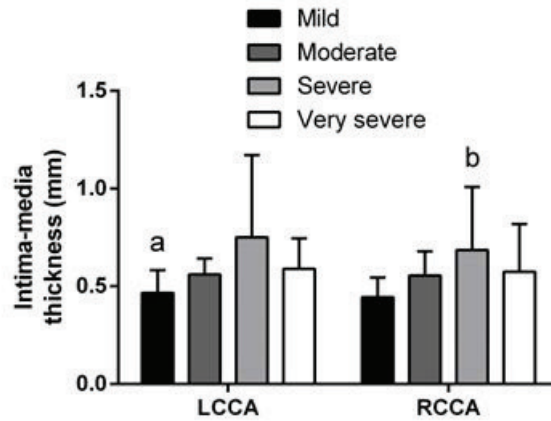


Figure 1. Intima-media thicknesses of right and left common carotid arteries of study groups. Data were expressed as mean±SD. LCCA, left common carotid artery; RCCA, right common carotid artery.
^aP<0.05 vs. moderate, severe and very severe groups.
^bP<0.05 vs. mild, moderate and very severe groups.

Figure 2 shows the peak systolic and end diastolic velocities, and resistive indices of left and right common carotid arteries of the mild, moderate, severe, and very severe groups of COPD. The PSV of right CCA of very severe group was significantly higher than those of the mild, moderate, and severe groups ($p<0.05$). The PSVs of left CCA of very severe and severe groups was significantly higher than those of the mild and moderate groups.

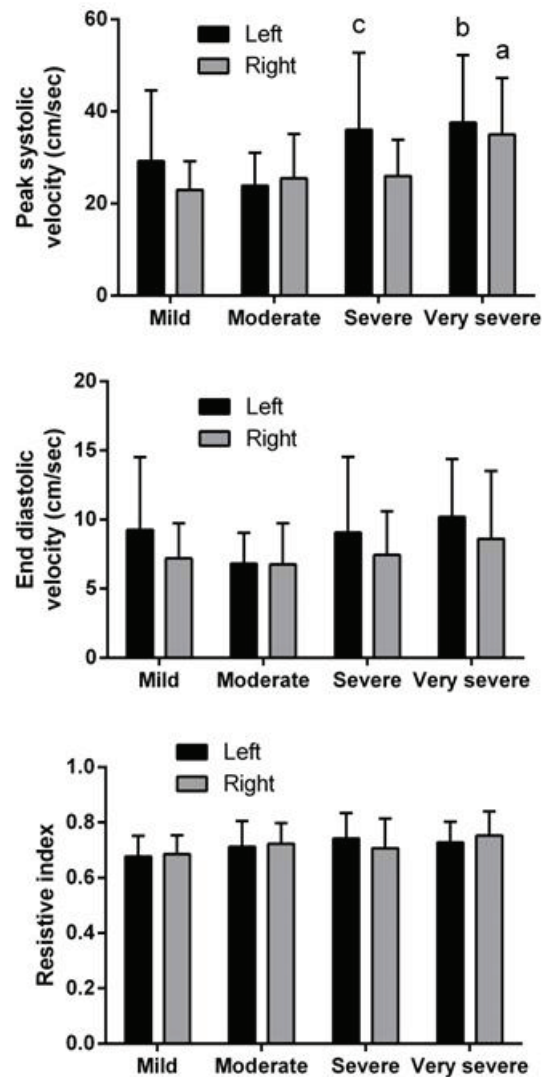


Figure 2. Peak systolic and end diastolic velocities, and resistive indices of left and right common carotid arteries of the mild, moderate, severe, and very severe groups of COPD. Data were expressed as mean±SD.

^aP<0.05 vs. mild, moderate, and severe groups of right common carotid artery.

^{b,c}P<0.05 vs. mild and moderate groups of left common carotid artery.

Figure 3 shows the peak systolic and end diastolic velocities, and resistive indices of left and right internal carotid arteries of the mild, moderate, severe, and very severe groups of COPD. The resistive index of left and right ICA of very severe group was significantly higher than those of the mild, moderate, and severe groups (p<0.05).

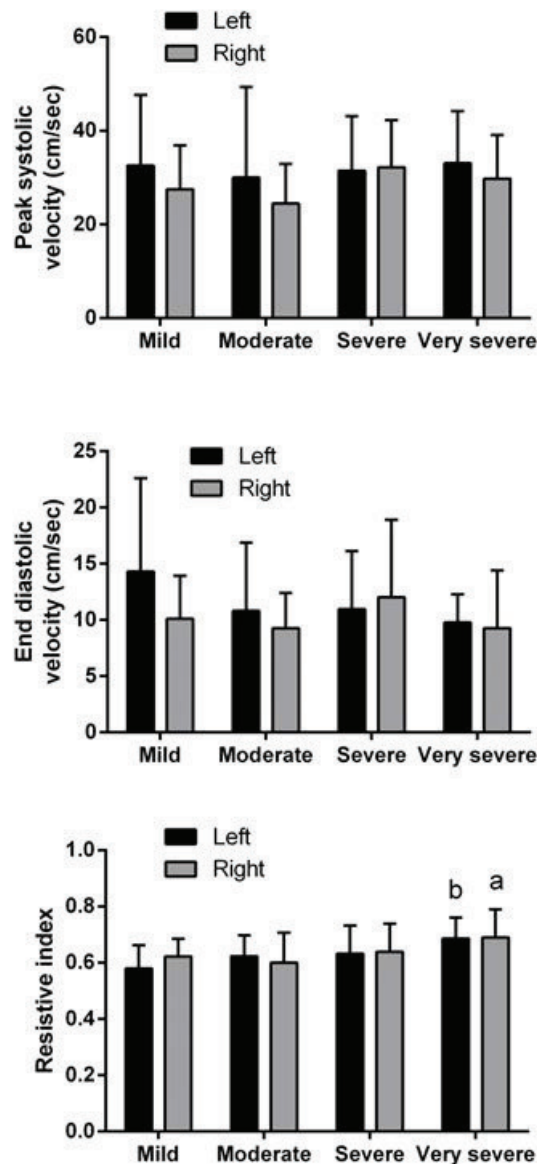


Figure 3. Peak systolic and end diastolic velocities, and resistive indices of left and right internal carotid arteries of the mild, moderate, severe, and very severe groups of COPD. Data were expressed as mean±SD.

^{a,b}P<0.05 vs. mild, moderate, and severe groups of left and right internal carotid artery.

Figure 4 shows the peak systolic and end diastolic velocities, and resistive indices of left and right vertebral arteries of the mild, moderate, severe, and very severe groups of

COPD. The resistive index of right vertebral artery of severe group was significantly higher than those of the mild, moderate, and very severe groups ($p < 0.05$).

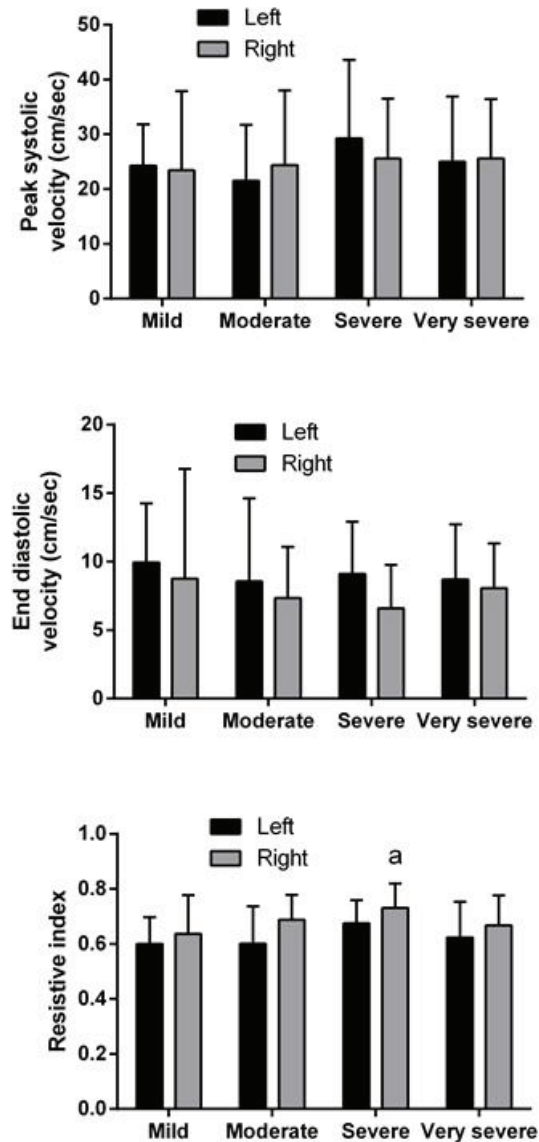


Figure 4. Peak systolic and end diastolic velocities, and resistive indices of left and right vertebral arteries of the mild, moderate, severe, and very severe groups of COPD. Data were expressed as mean±SD. ^a $P < 0.05$ vs. mild, moderate, and very severe groups of right vertebral artery.

Figure 5 shows the peak systolic and end diastolic velocities, and resistive indices of femoral arteries of the mild, moderate, severe, and very severe groups of COPD. There was no significant difference among the study groups with regard to the Doppler parameters ($p>0.05$).

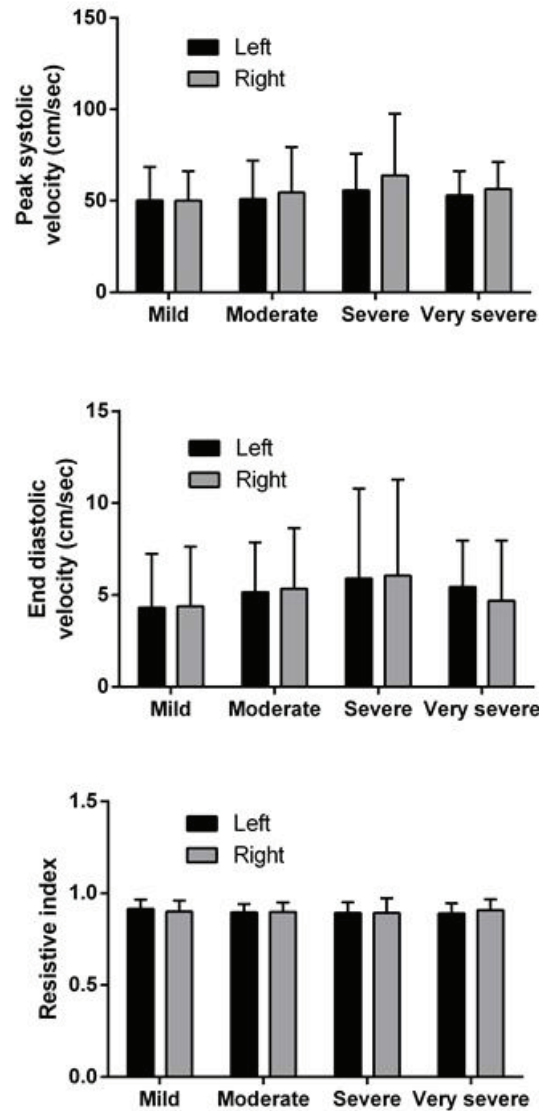


Figure 5. Peak systolic and end diastolic velocities, and resistive indices of femoral arteries of the mild, moderate, severe, and very severe groups of COPD. Data were expressed as mean±SD.

Discussion

Of the 80 COPD patients classified as mild, moderate, severe, and very severe disease (20 patients in each group), ultrasonography and Doppler ultrasonography of selected vessels were performed. This is the first study in the pertinent literature evaluating the impact of COPD on the cranial and femoral blood flows according to severity of disease on stable phase. The study groups were comparable with regard to the age, BMI, and pH level. Overall, according to the severity of COPD, the IMT of CCA increased. Although an increase were observed in the PSV, EDV, RI of left and right CCAs according to the severity of COPD, the differences were assessed as considerable equivocal. The PSV and EDV of ICAs and vertebral arteries did not changed according to the severity of COPD, although their RIs were increased in the severe and very severe cases. The Doppler parameters of femoral arteries of study groups revealed no change according to the severity of COPD.

Cerebral blood flow increases according to the degree of hypoxemia and hypercapnia. Doppler ultrasonography of extracranial carotid and vertebral arteries is a well-known modality to assess cerebrovascular blood flow. It is used for the evaluation of impacts of various diseases or conditions on blood flow velocities [13]. Yildiz et al. [13] investigated the impact of COPD exacerbation on cerebral blood flow. In their study, ultrasonography and Doppler ultrasonography of ICAs and vertebral arteries were performed. They demonstrated that cerebral blood flow increased with an increase in cross-sectional areas of these vessels. They suggested that the role of vasogenic, metabolic and neurogenic cerebral autoregulatory mechanisms in controlling cerebral blood flow in the course of COPD needed to be clarified.

Albayrak et al. [14] conducted a study evaluating the impact of COPD on cerebral blood flow with Doppler ultrasonography of extracranial carotid and vertebral arteries. They examined the effects of normocapnia, chronic hypoxia and chronic hypercapnia–hypoxia in the COPD patients. They measured the time averaged flow velocity and cross-sectional areas of vessels. They found that COPD increased those parameters in patients especially with hypoxia alone and hypoxia with hypercapnia. They suggested that further studies taking into consideration the blood gases might be helpful to evaluate place of Doppler ultrasonography in the COPD patients.

Karakas et al. [10] evaluated the carotid IMT in the COPD patients. They found that carotid IMT was increase in accordance with FEV₁/FVC ratio and FEV₁ value. They suggested that carotid IMT can be used during laboratory work-up of COPD patients to determine cardiovascular disorders. In a study investigating the association of COPD and atherosclerosis [9], the carotid IMT was measured in participants with normal body mass index and metabolic parameters. In that study, the carotid IMT was found as an easily applicable method for evaluation of vascular effects of atherosclerosis. In our study, as a limitation, the blood gas alterations was not related to the findings of ultrasonography and Doppler ultrasonography. In our COPD patients, absence of a meaningful change in the findings of ultrasonography and Doppler ultrasonography of CCA, ICA, vertebral, and

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87

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femoral arteries may be related to this limitation. The lack of an age- and sex-matched control groups of non-COPD subjects was another limitation of this study.

In conclusion, according to our findings, COPD may have a potential to increase the IMT of CCA. In COPD, a meaningful change in the PSV, EDV, and RI of CCA, ICA, and vertebral and femoral arteries may not be observed. These findings suggest that in addition to the severity of COPD, the duration of COPD affecting cardiovascular system may be an important contributor to atherosclerosis altering blood vessels and their blood flows. In COPD patients with cardiovascular diseases as comorbidity, radiologists may keep in mind that small alterations in the ultrasonographic and Doppler ultrasonographic parameters may be encountered. Further studies for the assessment of blood vessels with ultrasonography and Doppler ultrasonography are needed in COPD patients taking into consideration the duration of disease and cardiovascular findings.

Conflict of Interest

The authors declare that no scientific and/or financial conflicts of interest exists with other people or institutions.

References

1. Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. *Lancet*. 1997 May 17;349(9063):1436-42.
2. Gegick S, Coore HA, Bowling MR. Chronic obstructive pulmonary disease: epidemiology, management, and impact on North Carolina. *N C Med J*. 2013 Sep-Oct;74(5):411-4.
3. Global Strategy for the Diagnosis, Management and Prevention of COPD 2013, Global Initiative for Chronic Obstructive Lung Disease (GOLD), www.goldcopd.org.
4. Sin DD, Man SF. Chronic obstructive pulmonary disease as a risk factor for cardiovascular morbidity and mortality. *Proc Am Thorac Soc*. 2005;2(1):8-11.
5. Gürgün A, Gürgün C. [Chronic obstructive pulmonary disease and cardiovascular system]. *Tuberk Toraks*. 2008;56(4):464-71
6. Stone IS, Barnes NC, Petersen SE. Chronic obstructive pulmonary disease: a modifiable risk factor for cardiovascular disease? *Heart*. 2012 Jul;98(14):1055-62. doi: 10.1136/heartjnl-2012-301759.
7. Fimognari FL, Scarlata S, Conte ME, Incalzi RA. Mechanisms of atherothrombosis in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2008;3(1):89-96.
8. Maclay JD, MacNee W. Cardiovascular disease in COPD: mechanisms. *Chest*. 2013 Mar;143(3):798-807.
9. Beşir FH, Yılmaz Aydın L, Yazgan Ö, Dumlu T, Erkan ME, Önder E, Coşkun H. [Evaluation of carotis intima media thickness in chronic obstructive pulmonary disease patients]. [Article in Turkish] *Tuberk Toraks*. 2012;60(3):238-45.
10. Omer Karakas, Nesat Cullu, Ekrem Karakas, Zafer Hasan Ali Sak, Murat Yildizhan,

Güner et al.: Carotid intima-media thickness and Doppler ultrasonographic findings in patients with chronic obstructive pulmonary disease 88

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- Erdem Daglioglu, Osman Konukoglu, Ferit Dogan. Evaluation of carotid intima-media thickness in the patients with chronic obstructive pulmonary disease. *Acta Medica Mediterranea*, 2013, 29: 265-7.
11. Ives SJ, Harris RA, Witman MA, Fjeldstad AS, Garten RS, McDaniel J, Wray DW, Richardson RS. Vascular Dysfunction and Chronic Obstructive Pulmonary Disease: The Role of Redox Balance. *Hypertension*. 2013 Dec 9. [Epub ahead of print]
 12. Chen CY, Hsu TW, Mao SJ, Chang SC, Yang PC, Lee YC, Yang KY. Abnormal renal resistive index in patients with mild-to-moderate chronic obstructive pulmonary disease. *COPD*. 2013 Apr;10(2):216-25.
 13. Yildiz S, Kaya I, Cece H, Gencer M, Ziyilan Z, Yalcin F, Turksoy O. Impact of COPD exacerbation on cerebral blood flow. *Clin Imaging*. 2012 May-Jun;36(3):185-90.
 14. Albayrak R, Fidan F, Unlu M, Sezer M, Degirmenci B, Acar M, Haktanir A, Yaman M. Extracranial carotid Doppler ultrasound evaluation of cerebral blood flow volume in COPD patients. *Respir Med*. 2006 Oct;100(10):1826-33.
 15. Lee VS, Hertzberg BS, Workman MJ, Smith TP, Kliewer MA, DeLong DM, Carroll BA. Variability of Doppler US measurements along the common carotid artery: effects on estimates of internal carotid arterial stenosis in patients with angiographically proved disease. *Radiology*. 2000 Feb;214(2):387-92.