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Nailfold capillaroscopic changes of sleep apnea patients

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ABSTRACT

Background: Obstructive Sleep Apnea Syndrome (OSAS) have frequent association with comorbidities and this makes it an independent risk factor for cardiovascular disease. Not only endothelial dysfunction, but also arterial stiffening, increased inflammatory mediators, oxidative stress after hypoxemia that develops due to OSAS, cause vascular pathologies in all diameters of vessels. Nail bed capillaroscopy is a simple, noninvasive, useful method to examine microcirculation and evaluate nail bed capillary abnormalities in diseases that cause vascular damage. The aim of this study is to examine microvascular changes in the nail bed of OSAS patients by capillaroscopy.

Methods: 59 OSAS patients and 60 healthy cases (totally 119) were included. One single attended polysomnography was applied with Embla N7000 series (RemLogic Eastmed, Natus); and apnea-hypopnea index (AHI), oxygen de-saturation index >4% (ODI4%), minimum oxygen saturation (SaO2 Min.), total duration of oxygen desaturation, comorbidities, body mass index (BMI), smoking habit, sleep questionnaire applications were analyzed. Nailfold capillaroscopy was performed using a digital dermoscope (Molemax II, X30) and all images were evaluated for capillary density, capillary loop enlargement, capillary tortuosity, branching vessels, micro hemorrhages, avascular areas and splinter hemorrhages.

Results: The prevalence rates of all capillaroscopy findings were significantly higher in the patient group ($p < 0.05$). There was an inverse and moderate relationship between AHI and mean saturation ($p < 0.05$). A statistically significant correlation was detected between the presence of hypertension (HT) and the severity of capillary tortuosity (CT) ($p = 0.002$), avascular area (AA) ($p = 0.004$), and periungual cyanosis (PUC) ($p = 0.042$); also between smoking habit and intensity of capillary dilatation, enlargement dilatation-enlarged giant capillaries (CELON) ($p = 0.004$), CT ($p = 0.018$) findings. Capillary distribution (CD), CELON, CT and AA findings were significantly higher in the group with low mean saturation ($p < 0.05$). DM was found to be significantly higher in individuals with high Epworth Sleep Scale (ESS) ($p = 0.035$).

Conclusion: In this study; 1) the nail bed capillaroscopy was used to examine vascular damage in OSAS, and 2) irregularities detected in the distal nail bed specific to a disease have been mentioned for the first time. It has been shown that endothelial damage is particularly related to the severity of hypoxia. HT and smoking history causes endothelial damage independent of the severity of the disease and hypoxia. Also, ESS may be more determinant in the screening of sleep disorders in diabetic patients.

1. Introduction

1.1. Background

Obstructive Sleep Apnea Syndrome (OSAS) is an increasing health problem and affects more than one billion people around the world. Its frequent association with conditions such as obesity, insulin resistance, hypertension, arrhythmia, coronary artery disease, and heart failure has made OSAS an independent risk factor for cardiovascular disease. When mechanisms by which these two diseases affect each other were analyzed, increasing cortisol levels and impaired glucose tolerance were first mentioned (Spiegel et al., 2005). Later on, it was argued that the

Abbreviations: OSAS, Obstructive Sleep Apnea Syndrome; AHI, apnea-hypopnea index; BMI, body mass index; CT, capillary tortuosity; AA, avascular area; CELON, capillary dilatation, enlargement dilatation-enlarged giant capillaries; CD, capillary distribution; BC, branching capillaries; MH, microhemorrhage; DNI, distal nailbed irregularities; PUS, periungual cyanosis; SBQ, STOP-BANG questionnaire; ESS, Epworth sleep scale.

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metabolic syndrome causing increased blood pressure gave rise to this condition (Bansil et al., 2011). However, recent studies mention low-level inflammation supporting the hypothesis associated with both metabolic syndrome and increased stress (Penev, 2011; Meier-Ewert et al., 2004; Vgontzas et al., 2004). This inflammation occurs mainly at the level of the vascular endothelium, which is responsible for the vasodilation balance (Hoyos et al., 2015). Endothelium cells ensure this balance by producing nitric oxide that prevents atherosclerosis by providing local vasodilation, and by preventing platelet aggregation, monocyte adhesion and vascular smooth muscle proliferation (Celermajer, 2008). During apnea episodes, a decrease in cardiac output and pulmonary blood flow and an increase in pulmonary artery pressure are observed (Floras, 2018). In patients with OSAS, not only endothelial dysfunction, but also arterial stiffening, increased inflammatory mediators and oxidative stress after hypoxemia that develops due to this cause vascular pathologies (Wang et al., 2015). These changes in the vascular bed affect vessels of all diameters. Epworth Sleep Scale (ESS) and STOP-BANG (**s**noring, **t**iredness, **o**bserved apnea, hyper**t**ension, **b**ody mass index, **a**ge, **n**eck diameter, **g**ender) questionnaires are utilized to determine the risk and severity of OSAS in patients admitted to the outpatient clinic, and often associated with the severity or the presence of the medical condition (Vicente-Herrero et al., 2018; Kahramfar and Rahimi, 2018; Pearson et al., 2019).

Nail bed capillaroscopy is a simple, noninvasive, useful method to examine microcirculation (Fonollosa et al., 2001). The widespread use of the dermoscope has become a standard procedure in clinical practice to evaluate nail bed capillary abnormalities in diseases that cause vascular damage. The density, dimension, morphology of capillaries and presence of hemorrhages can be evaluated in order to examine microvascular circulation (Smith et al., 2020). Morphological changes observed through the dermoscope are used; in Raynaud's phenomenon (RP), which can be the first manifestation of systemic sclerosis (SSc) or other connective tissue diseases (Gualtierotti et al., 2017; Pizzorni et al., 2017), in SSc patients to identify the proper pattern of microvascular damage (Ruaro et al., 2016) and patterns of microangiopathy (Ruaro et al., 2018), in the diagnosis of autoimmune connective tissue diseases and in evaluating the systemic effects of the disease (Aytekin et al., 2011). Not only dermatological and rheumatic diseases but also diabetes, hypertension (Junqueira et al., 2018), normotensive glaucoma, non-rheumatic conditions (like radiation exposure, being musician or athletes) have been studied with dermoscope (Aytekin et al., 2011; Sontheimer, 2004a; Sirufo et al., 2021). In systemic sclerosis giant capillary, loss of capillary density and angiogenesis were the most frequently observed characteristic findings (Castellví et al., 2015). Definitions such as avascular areas, splinter hemorrhage, microhemorrhage, capillary tortuosity, capillary distribution are also used in capillaroscopic evaluation (Smith et al., 2016).

The goal of this study was to examine microvascular changes in the nail bed of OSAS patients by capillaroscopy who underwent polysomnography after ESS and SBQ questionnaire applications, and to evaluate the relationship between the pathological changes observed by capillaroscopy with the survey results and demographic characteristics of the patients.

2. Material and method

This study is designed with 59 OSAS patients (46 male, 13 female), to whom one single attended polysomnography was applied after ESS and SBQ questionnaires, and 60 healthy cases (totally 119). Patients and healthy subjects were not matched according to their age and sex. Healthy subjects were chosen from patients whom were attending to the dermatology unit for cosmetic consultancy and have none of dermatologic or systemic disease, and smoking habit. Written consent was obtained from all the patients.

The exclusion criteria were any pulmonary disease progressing with hypoxia, having apnea hypopnea index (AHI) $\leq$20, any other dermatological disorders or signs of cutaneous involvement, presence of systemic diseases known to disturb capillary bed like systemic sclerosis. Because there is a potential dose-response relationship between the severity of OSAS and the risk of essential hypertension (Xia et al., 2018), and the OSAS patients were both moderate and severe, the hypertension patients were not excluded. A synergistic effect was observed between smoking and OSAS on metabolic disorder parameters, but cessation of cigarette smoking seems to have no significant benefit for smoking patients with OSAS (Zhu et al., 2017). So patients with smoking habits were not excluded too. Using quality and duration of sleep as a marker of cardiovascular disease is nor certainly recommended because of changes according to sex and age (Matthews et al., 2013; Kim et al., 2015). Also, because of the fact that hypoxia is not specific for CVD and diabetes mellitus, patients having these comorbidities were not excluded.

Control group was composed of 60 healthy individuals who applied to the dermatology department with any symptoms of OSAS like snoring, daytime tiredness, witnessed to stop breathing, having none of hypertension, diabetes mellitus, coronary artery disease (CAD) or smoking habit.

2.1. Polysomnography

The polysomnographic examination was performed with Embla N7000 series (RemLogic Easmed, Natus, Germany). At least 5 h of records are considered valid. All polysomnographic records were interpreted always by the same trained specialist. Standard overnight PSG included continuous monitoring with central electroencephalograms, electrooculograms, submental and anterior tibial electromyograms, and electrocardiograms with conventional leads. Airflow was monitored by oral and nasal cannula, using pressure transducers and thermistors. Respiratory inductance polysomnography was performed to measure the degree of respiratory effort, with the transducers placed around the chest and abdomen. The oxyhemoglobin saturation was recorded continuously by pulse oximetry (Zhan et al., 2018; Karaman Koç et al., 2019) Variables considered in the PSG were apnea-hypopnea index (AHI), oxygen de-saturation index >4% (ODI4%), minimum oxygen saturation (SaO2 Min.), total duration of oxygen saturation with less than 90% (SpO2), the percentages of the sleep stages, as recommended by the American Academy of Sleep Medicine (AASM). OSAS was defined in events per hour as mild (AHI 5 to <15), moderate (AHI 15 to <30), or severe (AHI $\geq$30). Patients having polysomnography results of AHI $\geq$20 were included to study. Their body mass index (BMI), positional sleep apnea presence, smoking habit, systemic disorder creature (hypertension, diabetes mellitus, coronary artery disease), mean and lowest oxygen saturation values were analyzed.

2.2. Nail fold capillaroscopy

Capillaroscopy was performed before non-invasive mechanic ventilation therapy in order to investigate microvascular function by the same specialist and by using a digital dermatoscope (Molemax II, X30). The room temperature was kept approximately at 22–25 C^0 and patients were kept inside for at least 15–20 min to adapt their body temperature with the environment. The hands were placed at the same level of the heart in sitting position. The periungual zone of ten fingers were examined. Transparent gel was used between the probe and the periungual area in order to prevent artefacts and improve the quality of images. All capillaroscopy images were evaluated for capillary density, capillary loop enlargement, capillary tortuosity, branching vessels, micro hemorrhages, avascular areas and distal nailbed irregularities (Pancar and Kaynar, 2020).

1- *Capillary distribution (CD)*; disorganization of capillary loops as regular or irregular (Hasegawa, 2011).
2- *Capillary Dilatation, enlargement dilatation-enlarged giant capillaries (CELON)*; which display a width of four or more times the width of

normal neighboring loops, considered as abnormal angiogenic responses secondary to peripheral ischemia (Hasegawa, 2011).

3- *Capillary Tortuosity (CT)*; is the morphology of the capillaries defined as the capillary limbs bend but do not cross, that is found in hypovascular area advanced vascular damage as abnormal angiogenic response against hypoxic state. (Hasegawa, 2011; Rostey and Souto, 2015; Guido et al., 2018).
4- *Branching Capillaries (BC)*; elongated capillaries without bending or crossing of limbs, branch along each other are interpreted as abnormal shapes (Hasegawa, 2011; Rostey and Souto, 2015; Guido et al., 2018).
5- *Microhemorrhage (MH):* Hemorrhages are defined as extravasation of red blood cells into the perivascular tissue as extra-capillary brown aggregations of erythrocytes at least two punctate hemorrhages were accepted. The hemorrhages likely reflect the injury of capillaries by ischemic reperfusion (Hasegawa, 2011; Sontheimer, 2004b).
6- *Avascular Area (AA):* Loss of at least two consecutive capillaries were determined as avascular area (Hasegawa, 2011, Sontheimer, 2004b).
7- *Distal nail bed irregularities (DNI)*; changes in the shape, thickness and distribution of the veins that occur in the part of the nail bed close to the hyponychia.
8- *Periungual cyanoses (PUC)*; blue or purple discoloration of the nail bed and digits as a result of lower oxygen saturation causing accumulation of deoxyhemoglobin in the small blood vessels.

3. Results

When the relationship between the demographic characteristics of 59 OSAS patients and the findings of capillaroscopy was examined, there was no significant relationship in terms of gender and BMI (Table 1). However, smoking was found to be associated with the increase in CELON ($p = 0.004$) and CT ($p = 0.018$) intensity of capillaroscopy findings.

While the presence of CAD and DM did not cause a statistically significant change in the nail bed, there was a statistically significant correlation between the presence of HT and the severity of CT ($p = 0.002$), AA ($p = 0.004$), and PUC ($p = 0.042$) findings ($p < 0.05$). According to the cross table rates, it was determined that individuals with HT are more likely to have CT and AA, and less likely to have PUC than those who do not have HT.

AHI level and presence of positional sleep apnea did not cause a significant change in capillaroscopy findings. However, according to the Pearson correlation coefficient ($r = -0.501$), there is an inverse and moderate relationship between AHI and mean saturation. According to this, the increase in AHI value may lead to a decrease in the average saturation value ($p < 0.05$) (Table 2).

While the relationship between ESS and SBQ questionnaire values and the presence and severity of capillaroscopy findings could not be determined, in terms of underlying systemic diseases, the rate of DM was found to be significantly higher in individuals with high ESS compared to the other groups ($p = 0.035$).

When the patient and control groups were examined, the prevalence rates of all capillaroscopy findings were significantly higher in the patient group compared to the control group ($p < 0.05$) (Table 3). In the patients group different from the control group; AA, CD and CD like appearances, which were observed in distal nailbed and have not been reported previously in the literature, were defined as DNI and presence of this was statistical significant (p<0,001).

When the average saturation value is determined as 91.1% and divided into 2 groups as above and below of this value, presence rates of CD, CELON, CT and AA capillaroscopy findings were significantly higher in the group with low mean saturation ($p < 0.05$) (Table 4) (Figs. 1 and 2).

No significant relationship was found between the patient groups with values above and below 76.3%, which is the average of the lowest saturation values, in terms of capillaroscopy findings.

When the data of patients with prominent distal nail bed irregularities were examined, it was observed that none of the patients except one patient had a history of smoking and all cases except the same patient had AHI $\geq$ 30. When the cases in which PUC is remarkably prominent are analyzed among themselves, all had BMI $\geq$ 30, AHI $\geq$ 30, the highest average saturation was 93% and HT was observed frequently. However, statistically significant results could not be obtained.

4. Discussion

In this study, the aim was to examine the changes caused by respiratory events with hypoxia developed during the night in patients with OSAS in the cardiovascular system and thus in the capillary bed. Nail capillaroscopy was used both for this purpose and to evaluate the predictive adequacy of OSAS severity. All capillaroscopy findings in the patient group were significantly different from the control group, it was determined that as the AHI increases mean saturation level decreases and the changes in the capillary bed were affected by the desaturation level, smoking and the presence of HT rather than the severity of sleep apnea.

Table 1
Demographic characteristics of study group.

Variable	Group	Patient (n)	Control(n)
Gender	Male (%)	46 (78)	42 (70)
	Female (%)	13 (22)	18 (30)
Age (median ± SD)		53.07 ± 11.56	54.87 ± 12.16
CAD	No (%)	49 (83.1)	0 (0)
	Yes (%)	10 (16.9)	0 (0)
DM	No (%)	51 (86.4)	0 (0)
	Yes (%)	8 (13.6)	0 (0)
HT	No (%)	34 (57.6)	0 (0)
	Yes (%)	25 (42.4)	0 (0)
Smoking	No (%)	44(%74,5)	0 (0)
	Yes (%)	15(%25.5)	0 (0)
BMI (median ± SD)		35.15 ± 6.82	

CAD: coronary artery disease; DM: diabetes mellitus; HT: hypertension; SD: standard deviation; BMI: body mass index.

Table 2
Correlation analyses between AHI and mean saturation.

	AHI	Mean saturation
AHI	1	−0.501**
Mean saturation	−0.501**	1

** <0.01 AHI: apnea hypopnea index.

Table 3
Comparison results of capillaroscopy findings according to patient and control groups.

Variable	Group	Disease-Control		*p*-Value
		Patient (n = 59)	Control (n = 60)	
CD	No			<0.001
	Yes	50 (84.7%)	8 (13.3%)	
CELON	No	16 (27.1%)	54 (91.5%)	<0.001
	Yes	43 (72.9%)	5 (8.5%)	
CT	No	10 (9.1%)	54 (90%)	<0.001
	Yes	49 (90.9%)	6 (10%)	
BC	No	18 (30.5%)	54 (90%)	<0.001
	Yes	41 (69.5%)	6 (10%)	
MH	No	29 (49.2%)	52 (86.7%)	<0.001
	Yes	30 (50.8%)	8 (13.3%)	
AA	No	10 (9.1%)	54 (90%)	<0.001
	Yes	49 (90.9%)	6 (10%)	
DNI	No	3 (5.1%)	53 (88.3%)	<0.001
	Yes	56 (94.9%)	7 (11.7%)	
PUC	No	2 (3.4%)	60 (100%)	<0.001
	Yes	57 (96.6%)	0 (0%)	

Table 4
Comparison results of capillaroscopy findings according to mean saturation groups.

Variable	Group	Mean saturation		p-Value
		91.1 < (n = 29)	91.1≥ (n = 30)	
CD	No	1 (3.4%)	8 (26.7%)	0.015
	Yes	28 (96.6%)	22 (73.3%)	
CELON	No	4 (13.8%)	12 (40%)	0.023
	Yes	25 (86.2%)	18 (60%)	
CT	No	2 (6.9%)	9 (30%)	0.045
	Yes	27 (93.1%)	21 (70%)	
BC	No	6 (20.7%)	12 (40%)	0.092
	Yes	23 (79.3%)	18 (60%)	
MH	No	12 (41.4%)	17 (56.7%)	0.181
	Yes	17 (58.6%)	13 (43.3%)	
AA	No	1 (3.4%)	9 (30%)	0.007
	Yes	28 (96.6%)	21 (70%)	
DNI	No	0 (0%)	3 (10%)	0.125
	Yes	29 (100%)	27 (90%)	
PUC	No	0 (0%)	2 (6.7%)	0.254
	Yes	29 (100%)	28 (93.3%)	

With the intent of non-invasive evaluation of the capillary bed, fundus photography has reported that changes in the retinal vascular bed may be an early predictor of cardiovascular abnormalities (Wang et al., 2017). In the same group of patients, sublingual area was examined using 'Sidestream darkfield imaging' to evaluate microcirculation, and a decrease in vascular bed flow and an increase in flow heterogeneity were observed (Ruzek et al., 2017). Capillaroscopy was used to examine the endothelial tissue damage of patients with chronic viral hepatitis, significant differences were found in the nail beds of hepatitis B and C patients compared to the control group (Pancar and Kaynar, 2020). The use of nail capillaroscopy in lung diseases, until now, has often been for the purpose of examining the effects of hypoxia and pulmonary hypertension on peripheral circulation due to lung parenchymal damage of connective tissue diseases such as systemic sclerosis (SSc). Hasegawa et al. mentioned that nail bed capillary findings obtained by using dermoscope can be utilized for diagnosis and evaluation of microcirculation in SSc, diabetes, and rheumatic diseases. (Hasegawa, 2011). In a study in which they examined microvascular function in obese patients, Maranhão et al. (Maranhão et al., 2016) reported that the examination of the nail bed and dorsal finger with videocapilleroscopy was useful in determining and following the changes in the vascular bed. Soon Karaman Koc et al. had examined cutaneous microvascular reactivity in OSAS patients and suggested using nailfold capillaroscopy to evaluate systemic microvascular function (Karaman Koç et al., 2019). In our study we examined that; all of the pathological capillaroscopy findings were observed in the OSAS patients different from the control group. Also it was detected that; patients, who have especially the

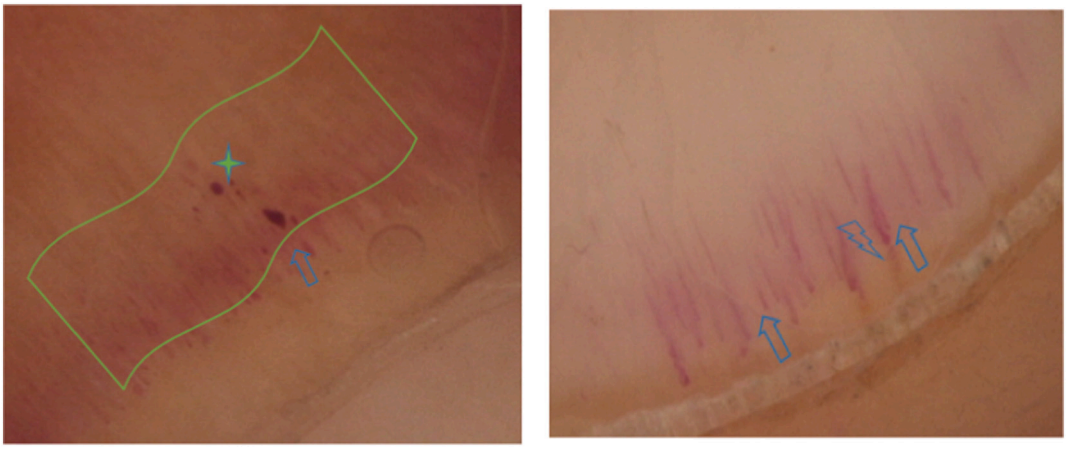

Fig. 1. Capillaroscopic changes in OSAS.
micro hemorrhage distal nail bed irregularities
avascular area capillary tortuosity.

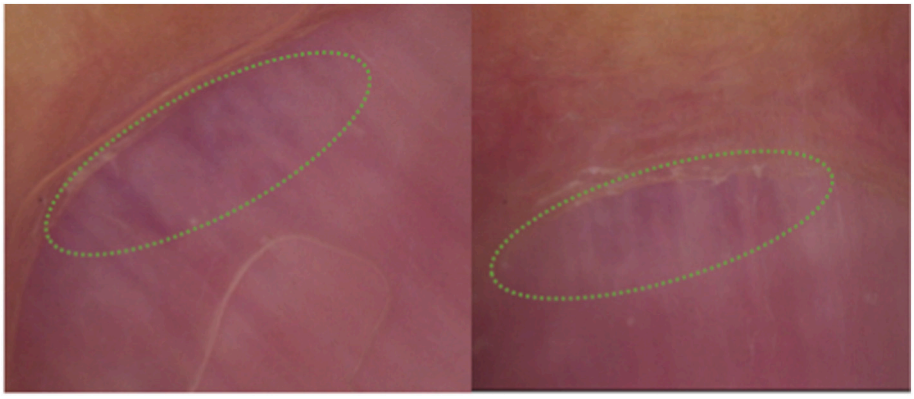

Fig. 2. Periungual cyanosis in OSAS.

remarkable splinter hemorrhage and periungual cyanosis, were observed to have an AHI of over 30.

Recurrent apnea-hypopnea episodes during the night in OSAS patients give rise to cardiovascular diseases by causing hypoxia/hypercapnia, arousal, negative intra-thoracic pressure, oxidative stress, endothelial disfunction, systemic inflammation and activation in sympathetic nervous system (Bradley and Floras, 2009). Intermittent hypoxia is a condition associated with periods of hypoxia and re-oxygenation that produce effects similar to recurrent ischemia and reperfusion. This phenomenon increases the release of reactive oxygen radicals, activation of oxidative stress pathways and thus cardiovascular comorbidities connected to OSAS (Lavie, 2015). In OSAS patients, endothelial functions such as vasomotor tone, coagulation/hemostasis, endothelial pro-inflammatory/anti-inflammatory activity and endothelial repair capacity may be impaired.

The effect of OSAS on endothelin-1 is complex. According to the study of Gjørup et al. (Gjørup et al., 2007) when compared to the healthy control group nocturnal and diurnal endothelin-1 levels were higher in the hypertensive OSAS patient group, compared to the normotensive patient group. This result showed that the presence of cardiovascular disease (CVD) may affect the endothelin-1 level independent of OSAS. Similarly, in our study, we observed that CT and AA findings were milder in the hypertensive patient group, regardless of the severity of OSAS. observed that CT and AA findings were milder in the hypertensive patient group, regardless of the severity of OSAS. Except for endothelin-1 in OSAS patients with HT, different mechanisms such as prolonged oxidative stress reduce the enzymatic activity by blocking the phosphorylation of endothelial nitric oxide synthase in S1179 (Lavie and Lavie, 2009; Tanaka et al., 2005). In line with this mechanism, we determined that PUC, which occurs with the accumulation of deoxyhemoglobin in small vessels that causes oxidative stress in patients with HT in our study group, correlates with the severity of the disease. Oxidative stress associated with hypoxia/re-oxygenation also reduces the substrate required for nitric oxide synthesis (Laursen et al., 2001; Vasquez-Vivar et al., 1998). Epidemiological studies have shown that NO deficiency causing arterial stiffness, is associated with an increased risk of CVD. In our study, a relationship between OSAS patients with CVD and capillary findings could not be determined. We think that this result is because of the fact that; hypoxia is the major factor affecting the capillary bed, but is not a specific finding for CVD.

Damaged endothelial function is more apparent in cases which severe hypoxemia and associated oxidative stress is more pronounced. Seif et al. (Seif et al., 2013) found a correlation between the increasing desaturation index and endothelial function, and they suggested that some protective mechanisms from CVD were triggered in patients with mild-moderate OSAS, but endothelial dysfunction became involved in moderate-severe cases. In a meta-regression analysis made by (Wang et al., 2015) Wang et al., it has been established that the relationship between OSAS and endothelial dysfunction depends on the severity of OSAS. In our study; CD, CELON, CT and AA findings were associated with low mean oxygen saturation (mean saturation determined as 91.1%). Moreover, according to the correlation coefficient ($r = -0.501$), there is an inverse and moderate relationship between AHI and mean saturation. And we interpreted this result as an indicator that while the severity of OSAS and the related decline in mean oxygen saturation increases, endothelial damage becomes more pronounced.

In the nail bed, there are many longitudinal lines that facilitate the nail plate's adherence and blood vessels that follow these areas. The proximal nail bed determines the development and direction of the nail plate, and can provide information about the presence and prognosis of some chronic diseases. Hyponychium, covering the area where the nail bed separates from the nail plate, is the most distal part of the nail bed, and is often affected by diseases such as onychomycosis. In existing academic data, the presence of any pathology in the distal nail bed that causes irregularities and can be detected by capillaroscopy could not been found. In the patients involved in our study, the deterioration in the distal nail bed vascular structures and distribution was remarkable. These deteriorations can be sorted as increased capillary tortuosity, micro and splinter hemorrhages, impaired capillary distribution and avascular areas. While pathologies detected by capillaroscopy in diseases such as connective tissue diseases are mostly observed in the proximal bed and periungual area, we think that vascular irregularities evident in the distal nail bed (DNI) in OSAS patients can be used as a disease predictor ($p < 0{,}001$).

Smoking increases the risk of CVD by stimulating the procoagulant stage by causing platelet aggregation, increased fibrinogen concentration, decreased fibrinolysis, polycythemia and increased blood viscosity (Ambrose and Barua, 2004). Smoking also accelerates atherosclerosis and the inflammation increased by the damaged endothelium. It has been reported that the health effect of quitting smoking after ischemic stroke or trans ischemic attack became evident after 4.8 year (Epstein et al., 2017). Yuksel et al. (Yuksel et al., 2019) described that; nailfold capillaroscopic abnormalities were more common among asymptomatic chronic smokers than healthy nonsmokers, with the enlargement of nailfold capillaries being the most common abnormality. Smoking, in our study, was associated with the severity of CELON and CT findings occurring after abnormal angiogenesis due to possible hypoxia and the above-mentioned effects of smoking. OSAS is also associated with an increased risk of metabolic syndrome including CVDs such as dyslipidemia and insulin resistance, hypertension/coronary artery disease/arrhythmia/ischemic stroke/congestive heart failure (Gaines et al., 2018; Bonsignore et al., 2019; Dharia and Brown, 2017). When the effect of OSAS patients' comorbidities in our study on the capillary bed was examined, other than HT, the presence of DM or CVD did not make a statistically significant difference. We think, this is due to the fact that the presence of DM or CVD does not directly cause hypoxia, and that HT affects the capillary bed by the other mechanisms mentioned above.

Obesity has a relationship with OSAS, however, this relationship varies according to age and OSAS is not observed in each obese patient because of different anatomical, genetic and physiological mechanisms. Newman et al. have reported that (Newman et al., 2005) relationship of obesity and OSAS over the age of 70 is weak. In a study examining the effect of obesity on OSAS through anthropometric measurements according to age (Yu-Jin et al., 2017), it has been stated that middle-aged OSAS patients are more prone to obesity. Therefore, in a picture where OSAS and obesity do not show a full correlation with each other, it was not surprising that there was no relationship between BMI and capillaroscopy findings of the patients in our study.

OSAS is a heterogeneous clinical picture that differs from patient to patient. In practice, AHI is still the most important marker used for disease severity and treatment plan. Some questionnaires are used to estimate the presence and severity of the disease. However, by itself, AHI does not provide enough information about the patient's clinic. The desaturation severity and apnea duration of patients with the same AHI might differ. No significant relationship was found between the predictive values of the ESS and STOP-BANG questionnaires applied in this study and the findings of capillaroscopy. It has been a predictable result that, as AHI is insufficient to predict the clinical course, these questionnaires (which are indicative of AHI) are also insufficient in terms of providing information about capillary circulation. Zubair et al. (Zubair et al., 2018) found that in the study group, in which they applied the Pittsburg Sleep Quality Index and ESS to investigate the presence of sleep disorders in diabetic patients, ESS gave more significant results in people with diabetes Similarly, in our study group, the probability of having diabetes was found to be high in the patient group with high ESS values. Therefore, we think that instead of other questionnaires, ESS can be used for screening OSAS in the patient group with diabetes.

5. Conclusion

As far as we know, our study has been the first study in which severity of capillaroscopy images was rated to examine vascular damage

in OSAS, and again, for the first time, irregularities detected in the distal nail bed specific to a disease have been mentioned. It has been shown that endothelial damage in this disease group is particularly related to the severity of hypoxia, and the presence of HT and smoking history causes endothelial damage independent of the severity of the disease and hypoxia, moreover, ESS may be more determinant in the screening of sleep disorders in diabetic patients. We think that re-evaluation of these findings with capillaroscopy after positive airway pressure (PAP) applications used in the treatment of OSAS may be a guide in the adequacy of the treatment, however, more comprehensive studies need to be done in this regard.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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