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The relationship between clinical and laboratory findings and duration of sleep where oxygen saturation remains below 90–95% in obstructive sleep apnea

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Abstract

Objective: The aim of the present study was to determine correlations between CT_{90} and CT_{95} values and physical examination parameters, chronic metabolic diseases, smoking, mean platelet volume, cerebral magnetic resonance imaging (MRI), presence and number of hyperintense foci in obstructive sleep apnea (OSA).

Methods: A total of 1154 patients who underwent polysomnography in our sleep laboratory between 2011 and 2014 were screened retrospectively. Among them, 72 cases who underwent ear, nose and throat examinations, cerebral MR, CBC and biochemical tests were included in the study. All patients underwent a detailed anamnesis together with (1) measurements of BMI (body mass index) (2) circumferences of neck and abdomen, (3) examination of oropharynx, (4) Müller maneuver with the aid of fiberoptic endoscope, (5) estimation of Epworth sleep scale scores, (6) and polysomnographic (PSG) tests.

Results: According to the severity of OSA, the patients had simple snoring (22.2%), mild (19.4%) and severe OSA (38.9%). In multivariate regression analysis, body mass index (BMI) (p=0.026) and apnea/hypopnea index (AHI) (p=0.013) were seen as independent variables affecting CT_{90} (R^2=49%). Multivariate linear regression analysis demonstrated that independent variables of smoking (p=0.001), AHI (p= 0.003) and number of hyperintense foci (p=0.013) affected CT_{95} (R^2=%47.9), while relationships between diabetes, BMI and CT_{95} were not statistically significant.

Conclusion: Since CT_{95} values are affected by smoking without any statistically significant correlation with retropalatal and retroglossal Müller stages, we think that consideration of CT_{90} value will be more appropriate in the evaluation of the severity of chronic intermittent hypoxia in patients with obstructive sleep apnea. However, the correlation between CT_{90} value and AHI is closer to the value indicated in the literature, but not stronger.

Keywords: Obstructive sleep apnea, duration of sleep, clinical, laboratory.

Özet: Obstrüktif uyku apnesinde oksijen satürasyonunun %90-95 altında kaldığı durumlarda uyku süresi ile klinik ve laboratuvar bulguları arasındaki ilişki

Amaç: Bu çalışmanın amacı obstrüktif uyku apnesinde (OUA); CT_{90} ve CT_{95} değerleri ile fizik muayene parametreleri, kronik metabolik hastalıklar, sigara içimi, ortalama trombosit hacmi, beyin manyetik rezonans görüntülemesinde (MRG) hiperintens odak varlığı ve sayısı arasındaki ilişkileri saptamaktı.

Yöntem: Hastanemiz uyku laboratuvarında 2011–2014 tarihleri arasında polisomnografi uygulanan 1154 olgu retrospektif olarak tarandı. Bu hastalardan kulak burun boğaz muayenesi yapılmış, beyin MRG, CBC ve biyokimya tetkikleri bulunan 72 olgu çalışmaya dahil edildi. Tüm hastalarda ayrıntılı anamnez ile birlikte (1) Vücut kitle indeksi (VKİ), (2) boyun ve karın çevresi ölçümü, (3) orofarenks muayenesi, (4) fiberoptik endoskop ile Müller manevrası uygulaması, (5) Epworth uyku skalası ve (6) polisomnografi (PSG) tetkikleri yapıldı.

Bulgular: Olguların OUA şiddetine göre dağılımı: %22.2 basit horlama, %19.4 hafif, %19.4 orta ve %38.9 ağır OUA idi. Çoklu doğrusal regresyon analizi yapıldığında apne-hipopne indeksi (AHİ) (p=0.026) ve vücut kitle indeksinin (VKİ) (p=0.013) CT_{90}'ı etkileyen bağımsız değişkenler olduğu (R^2=%49) görüldü. Çoklu doğrusal regresyon analizi yapıldığında sigara içimi (p=0.001), AHİ (p=0.003) ve hiperintens odak sayısının (p=0.013) CT_{95}'i etkileyen bağımsız değişkenler olduğu (R^2=%47.9), diyabet ve VKİ ile CT_{95} ilişkisinin istatistiksel olarak anlamlı olmadığı görüldü.

Sonuç: CT_{95} değerinin sigara içiminden etkileniyor olması, ancak retropalatal ve retroglossal Müller evreleri ile istatistiksel anlamlı ilişkisi bulunmaması nedeniyle, obstrüktif uyku apnelilerde kronik entermitan hipoksi şiddetinin değerlendirilmesinde CT_{90} değerinin dikkate alınmasının daha uygun olduğu düşünülmüştür. Bununla birlikte CT_{90} değerinin AHİ ile korelasyonu ST_{90} için literatürde belirtilen değere yakın, ancak daha güçlü değildir.

Anahtar sözcükler: Obstrüktif uyku apnesi, uyku süresi, klinik, laboratuvar.

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Obstructive sleep apnea (OSA) is a prevalently seen syndrome characterized by recurrent collapses and intermittent hypoxia of upper respiratory tract. Impairment of gas exchange leads to oxygen desaturation, hypercapnia and fragmentation of sleep with resultant metabolic, neurocognitive and cardiovascular disorders.[1] Apnea/hypopnea index (AHI) is used in the determination of the severity of OSA; however, AHI does not provide information about the duration of apnea and its morphology.[2] Whereas, the longer the apneic episodes persist, the deeper is the hypoxia. Therefore, AHI does not fully reflect pathophysiologic characteristics of hypoxia.[3] Cases with similar AHI values may have different clinical symptoms and sign.[4,5] Chronic intermittent type is generally described as recurrent hypoxemic attacks followed by periodic reoxygenation.[6] Nowadays, a globally accepted quantitative clinical test which can be used in the measurement of the severity of hypoxia does not exist.[1]

In recent years, due to a direct correlation between ST_{90} value, severity and duration of hypoxia, OSA has attracted gradually increasing attention in investigations performed on OSA.[7–9] Bostanci et al. investigated the relationship between various polysomnographic parameters and ST_{90} and reported age, body mass index (BMI), male gender, AHI, mean oxygen saturation as independent variables affecting ST_{90}.[1] They indicated that AHI and ST_{90} values should be evaluated in combination as an appropriate approach to the determination of prognosis of the disease and selection of suitable treatment modality for the patient. 1 In this study, the ratio between total of sleep durations where oxygen saturations stayed below 90, and 95% and total duration of sleep was determined as CT_{90} and CT_{95} values, respectively. Since these values represent the ratio between the time passed at the hypoxic state and total duration of sleep, they are considered to be a better indicator than ST_{90} values.

The aim of the present study was to determine correlations between physical examination parameters, chronic metabolic diseases, smoking, mean platelet volume, cerebral magnetic resonance imaging (MRI), presence and number of hyperintense foci.

Materials and Methods

A total of 1154 patients who underwent polysomnography in our sleep laboratory between 2011 and 2014 were screened retrospectively. Among them, those who underwent ear, nose and throat examinations, cerebral MR, CBC and biochemical tests were included in the study.

All patients underwent a detailed anamnesis together with (1) measurements of BMI, (2) circumferences of neck and abdomen, (3) examination of oropharynx, (4) Müller maneuver with the aid of fiberoptic endoscope, (5) estimation of Epworth sleep scale scores, (6) and polysomnographic (PSG) tests. Hypertension, other cardiovascular diseases, diabetes, and smoking habits were questioned. Tonsil size was graded. The patients were requested to open their mouths with their tongues remaining in their mouths. Oral cavity was inspected, and the position of the palate and root of the tongue was evaluated and modified Malampati score was determined. All patients were subjected to Müller maneuvers while seated and degree of obstruction at the level of the soft palate and tongue root was assessed. For the assessment of an upper respiratory tract of a patient seated erect, a fiberoptic endoscope was inserted through nasal route complying with the Frankfurt line parallel to the ground. Fibroscope was advanced till epiglottis was visible. During Müller maneuver (forced inspiration with the closed mouth and nose) retropalatal and retroglossal regions were observed. Müller maneuvers were repeated three or more times in case of need till we were certain that the patient made a forceful inspiration. The degree of retropalatal and retroglossal collapse was staged (Table 1).

Patients with chronic renal, heart or liver failure, abnormal pulmonary functions or sleep disorders other than OSA and patients who experienced previously any surgical intervention or those using any respiratory device for their treatment were not included in the study.

All patients underwent all-night polysomnographic examination in the Sleep Laboratory of Chest Diseases, Alanya Hospital of Başkent University using 44-channel Compumedics brand E series (Abbotsford, Australia) computerized system under the surveillance of an experienced technician. Polysomnographic examinations included (EEG), 2-channel electro-oculography (EOG), single-channel submental muscle electromyography (EMG), 2-channel EMG whose electrodes were placed on both anterior tibial muscles, 1-channel nasal cannula for the measurement of oronasal airflow, 1-channel oronasal thermal sensor, 2-channel inductive plethysmography to display respiratory efforts of thorax, and abdomen, "body position" sensor to determine position of the body, pulse oximetry device with a single-channel finger probe to measure arterial oxyhemoglobin (SpO_2) concentration and simultaneous video recordings. Apnea was defined as cessation of respiration for ≥10 seconds. At least 50% drop in respiratory effort together with 4% drop in SaO_2 was considered as hypopnea. AHI is the number of apneas and hypopneas per hour (Table 1).

Statistical analysis

Data were analyzed using the IBM Statistical Package for Social Sciences v21 (SPSS Inc., Chicago, IL, USA). A normal distribution of the quantitative data was checked using Shapiro-Wilk test. Parametric tests (independent-samples t-test and posthoc Tukey test) were applied to data of normal distribution and non-parametric tests (Mann-Whiney U test and Kruskal-Wallis test) were applied to data of questionably normal distribution. To calculate correlation coefficients, Spearman correlation was used. Data are expressed as mean±SD or median (interquartile range), as appropriate. Statistical significance was considered as $p<0.05$.

Table 1. Staging system of polysomnographic and physical examination findings used in patients evaluated for OSA.

Parameter	Stage	Description
Apnea hipopnea index (AHI)	1 (primary snoring)	AHI ≤ 5
	2 (mild)	5 < AHI ≤ 15
	3 (moderate)	15 < AHI ≤ 30
	4 (severe)	>30
Body mass index (BMI) (kg/m²)	1	<25
	2	25 ≤ BMI ≤ 30
	3	30 < BMI ≤ 40
	4	>40
Size of the tonsils	0	Tonsillectomized
	1	Tonsils are in the tonsillar fossa, lateral to the plicas
	2	Occupies 25–50% of oropharynx
	3	Occupies 50–75% of oropharynx
	4	Occupies >75% of oropharynx; it nearly joins at midline
Modified Malampati	1	Soft palate, plicas and tonsils can be seen
	2	Uvula, plicas and upper poles of tonsils can be seen
	3	Soft palate can be partially seen
	4	Only hard palate is visible
Retropalatal Müller stage	1	Less than 25 collapse of pharyngeal walls during Müller maneuver
	2	25–50%
	3	50–75%
	4	>75%
Retroglossal Müller stage	1	Vallecula and vocal cords are completely visible
	2	Vallecula and vocal cords are partially visible
	3	Root of the tongue touches epiglottis, amd arythenoids are visible
	4	Root of the tongue pushes epiglottis and arythenoids cannot be seen.

Results

General characteristics of the patients are seen in Table 2. The mean age of the patients was 47.6±12.2 (range: 23 to 75) years. The study population consisted of 64 (88.9%) male and 8 (11.1%) female patients. According to severity of OSA, the patients had simple snoring (22.2%), mild (19.4%) and severe OSA (38.9%).

Based on Spearman correlation analysis CT_{90} was correlated with Epworth sleep score ($r=0.29$, $p=0.013$), AHI ($r=0.713$, $p<0.001$) and BMI ($r=0.549$, $p<0.001$). However, variables of diabetes mellitus ($p=0.040$), retropalatal Müller stage ($p=0.018$) and retroglossal Müller stage ($p=0.034$) affected CT_{90} (Table 3). However, in multivariate regression analysis only BMI ($p=0.026$) and AHI ($p=0.013$) were

Table 2. General characteristics of the patients (n=72).

		mean±SD	min–max
CT_{90}, %		7.16±14.68	0–75.6
CT_{95}, %		44.6±31.57	0–100
Epworth sleep score		9.13±5.18	0–24
Hemoglobin (g/dL)		14.43±1.29	10.2–17.1
Mean platelet volume (fl)		7.86±1.51	5–15.3
Apnea hypopnea index		28.15±24.84	0–93
Body mass index (kg/m²)		31.12±5.33	21.9–48
		n	%
Hyperintense foci	Absent	38	52.8
	Present	34	47.2
Number of hyperintense foci	Absent	34	47.2
	1–4	16	22.2
	≥5	22	30.6
Hypertension	Absent	40	55.6
	Present	32	44.4
Diabetes	Absent	58	80.6
	Present	14	19.4
Cardiovascular disease	Absent	59	81.9
	Present	13	18.1
Hyperlipidemia	Absent	54	75.0
	Present	18	25.0
Smoking	Absent	46	63.9
	Present	26	36.1

seen as independent variables affecting CT_{90} (R^2=49%) (Table 4). Spearman correlation analysis revealed correlation between CT_{95} and AHI (r=0.604, p<0.001) and BMI (r=0.473, p<0.001). However, variables of diabetes (p=0.005), smoking (p=0.017) and number of hyperintense foci (p=0.011) affected CT_{95} (Table 3). Multivariate linear regression analysis demonstrated that independent variables of only smoking (p=0.001), AHI (p=0.003) and number of hyperintense foci (p=0.013) affected CT_{95} (R^2=47.9%), while relationships between diabetes, BMI and CT_{95} were not statistically significant (Table 4).

Discussion

The total duration of sleep where oxygen saturation remains below 90% and 95%, is an easily measurable objective parameter. In this study a statistically significant correlation was not detected between retropalatal Müller stage, retroglossal Müller stage and CT_{95} values, However, correlations between retropalatal Müller stage and retroglossal Müller stage CT_{90} values were seen (p=0.018 and p=0.034, respectively).

Li and Jin reported a strong correlation between AHI and total duration of apnea (r=0.770 and 0.776, respectively).[7] In our study, a strong correlation was found between CT_{90} value and AHI; however, it was not so strong as ST_{90} value indicated in the study by Li and Jin. (r=0.0713). A moderate degree of correlation was found between CT_{95} and AHI (r=0.604). Besides, a correlation between Epworth sleep score and CT_{90} (r=0.290) was found, whereas, a statistically significant correlation was not detected between CT_{95} and EUS.

Table 3. Factors affecting CT_{90} and CT_{95}.

		CT90		CT95	
		Median [min–max]	p value	Median [min–max]	p value
Hyperintense foci	Absent Present	0.40 [0–75.63] 1.11 [0–41.02]	0.364	31.7 [0.04–100] 48.6 [2.86–92.21]	0.146
Hypertension	Absent Present	0.61 [0–48.66] 0.78 [0–75.63]	0.692	36.4 [0.04–96.61] 44.1 [1.63–100]	0.362
Diabetes	Absent Present	0.40 [0–48.66] 4.46 [0–75.63]	0.040	30.0 [0.04–100] 74.3 [12.3–92.6]	0.005
Cardiovascular	Absent Present	0.64 [0–75.63] 0.32 [0–41.02]	0.482	42.3 [0.04–100] 43.4 [1.63–86.3]	0.703
Hyperlipidemia	Absent Present	0.61 [0–75.63] 1.04 [0–60.58]	0.696	41.4 [0.04–96.61] 51.5 [1.63–100]	0.830
Smoking	Absent Present	0.31 [0–60.58] 2.21 [0.01–75.63]	0.088	28.0 [0.04–89.2] 63.9 [1.12–100]	0.017
Gender	Male Female	0.71 [0–75.63] 0.27 [0–33.16]	0.405	44.9 [0.04–100] 22.2 [0.05–92.12]	0.333
Number of hyperintense foci	WML absent WML 1–4 WML >5	0.40 [0–75.63] 0.42 [0–33.16] 1.72 [0.05–41.02]	0.319	31.7 [0.04–100] 24.3 [0.13–91.85] 62.4 [12.91–92.21]	0.011
Mallampati stage	1 2 3-4	0.25 [0.01–33.16] 0.46 [0–41.02] 0.85 [0–75.63]	0.276	43.4 [0.05–92.12] 29.5 [0.13–100] 65.0 [0.04–92.63]	0.169
Tonsillar stage	1-2 3 4	0.30 [0–60.58] 0.91 [0–75.63] 7.34 [0.09–19.14]	0.128	30.9 [0.04–92.21] 46.4 [1.63–100] 53.6 [26.9–86.3]	0.213
Retropalatal Müller stage	1 2 3 4	0.17 [0–6.51] 0.27 [0–33.16] 1.80 [0.04–60.58] 6.11 [0–75.63]	0.018	20.3 [0.05–91.85] 26.1 [0.13–96.61] 54.8 [6.93–92.21] 60.2 [0.04–100]	0.063
Retroglossal Müller stage	1 2 3-4	0.62 [0–41.02] 0.32 [0–36.29] 17.1 [0.05–75.63]	0.034	35.6 [1.63–100] 32.8 [0.04–96.61] 79.5 [9.96–92.63]	0.072

Recent studies have demonstrated the close relationship between obesity and OSA, insulin resistance and metabolic syndrome.[10,11] The studies performed more recently have detected that metabolic dysfunction developed in OSA which is not only correlated with obesity but also related closely to the severity of OSA irrespective of the presence of obesity.[12,13] Punjabi et al. demonstrated that the insulin resistance developed in patients with OSA increases in parallel with the increase in the severity of the disease and pointed out to the severity of oxygen desaturation as one of the important factors which increase the insulin resistance.[14,15] In our study, CT_{90} and CT_{95} values were found to be correlated with the presence of diabetes (p=0.040 and p=0.005, respectively).

In obstructive sleep apnea, hyperintense foci (= alterations in white matter) on cerebral periventricular and subcortical areas at T2-weighted and FLAIR (fluid attenuated inversion recovery) sequences of magnetic resonance imaging in obstructive sleep apnea were found to be correlated with, dementia and mortality.[16–18] They are related to cognitive function and their preventable and treatable causes should be revealed.[19,20] Even though heterogeneous pathological relations exist, the presence of gliosis related to focal myelinosis, axonal loss and hyalinosis suggests a role of chronic hypoperfusion in the development of hyperintense foci.[21,22] Obstructive sleep apnea is related to the development of hypertension and hypertension was correlated with the development of hyperintense foci.[16,23,24] Therefore, the presence of a correlation between OSA and the presence of hyperintense foci is reasonable.[25] In this study, a correlation between CT_{90} value and the presence of hyperintense foci in the brain could not be found. However, a correlation was found between CT_{95} value and number of hyperintense foci in the brain (p=0.011).

Increased activation of platelets plays an important role in the development of cardiovascular complications.[26] Some authors have indicated an increase in platelet activation and aggregation.[27–30] Mean platelet volume is an indicator of thrombocytic activation and plays a role in the pathophysiology of cardiovascular diseases as hypertension, diabetes, hypercholesterolemia and acute myocardial infarction.[26,31] In this study, a statistically significant correlation was not detected between mean platelet volume, CT_{90} and CT_{95} values. Besides, statistically significant effect of smoking on CT_{95} (p=0.017) was seen; however, it did not affect CT_{90} values.

Polysomnographic, brain MR and blood values obtained at different time points because of retrospective design of the study and a scarce number of cases are major limitations of our study. Besides among cases who had undergone polysomnographic examinations, selection of only those who had cerebral MR and biochemical values might create a bias towards the cases who had health problems apart from OSA.

Based on the results of this study, correlations exist between CT_{90} value, AHI, BMI, Epworth sleep score,

Table 4. Factors affecting CT_{90} and CT_{95} (multivariate linear regression analysis).

		Regression coefficient (95% confidence interval)	p value	R^2
CT_{90}	Retroplatal Müller stage	0.419 (-2.58–3.419)	0.781	49%
	Retroglossal Müller stage	3.659 (-0.501–7.818)	0.084	
	Smoking	-0.049 (-5.719–5.621)	0.986	
	Diabetes	1.440 (-6.331–9.211)	0.712	
	Apnea hipopnea index	0.384 (-0.168–0.936)	0.169	
	Body mass index	0.173 (0.022–0.323)	0.026	
	Number of hyperintense foci	0.834 (0.180–1.488)	0.013	
CT_{95}	Retroplatal Müller stage	1.546 (-5.041–8.133)	0.641	47.9%
	Retroglossal Müller stage	-5.783 (-14.873–3.307)	0.208	
	Smoking	21.198 (8.906–33.490)	0.001	
	Diabetes	6.337 (-10.440–23.114)	0.453	
	Apnea hipopnea index	0.504 (0.178–0.830)	0.003	
	Body mass index	1.052 (-0.334–2.439)	0.134	
	Number of hyperintense foci	8.615 (1.855–15.376)	0.013	

retropalatal, retroglossal stage and presence of diabetes. On the other hand, CT_{95} value is correlated with AHI, BMI, diabetes, smoking and number of hyperintense foci detected on brain MR. In multivariate linear regression analysis, CT_{90} value was correlated with only AHI and BMI and CT_{95} value was correlated with AHI, smoking and a number of hyperintense foci in the brain. Since CT_{95} values are affected by smoking without any statistically significant correlation with retropalatal and retroglossal Müller stages, we think that consideration of CT_{90} value will be more appropriate in the evaluation of the severity of chronic intermittent hypoxia in patients with obstructive sleep apnea. However, the correlation between CT_{90} value and AHI is closer to the value indicated in the literature, but not stronger.

Conflict of Interest: No conflicts declared.

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